JML

Journal Médical Libanais

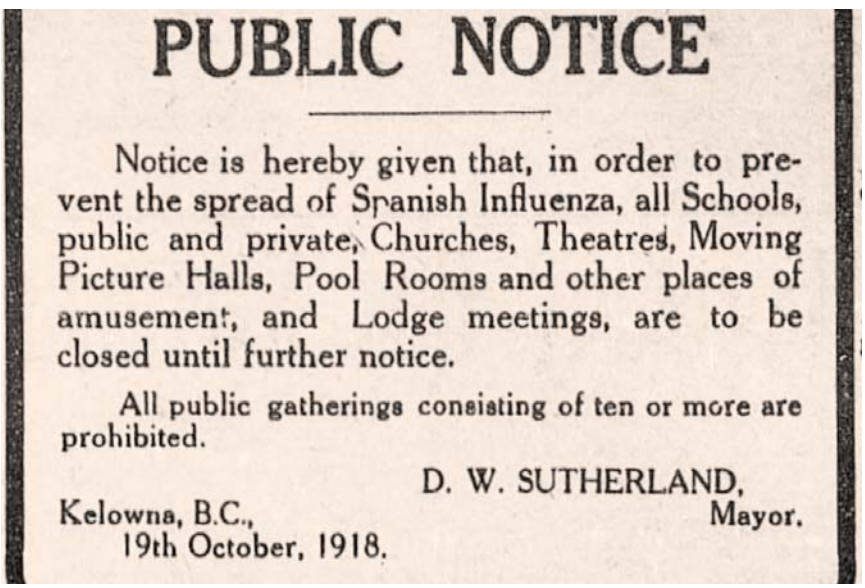
COVID-19 Special Issue

VOLUME 68 (1-2)

Janvier-Juin
January-June 2020

LMJ

Lebanese Medical Journal



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Notice is hereby given that, in order to prevent the spread of Spanish Influenza, all Schools, public and private, Churches, Theatres, Moving Picture Halls, Pool Rooms and other places of amusement, and Lodge meetings, are to be closed until further notice.

All public gatherings consisting of ten or more are prohibited.

D. W. SUTHERLAND,
Mayor.

Kelowna, B.C.,
19th October, 1918.

المجلة الطبية اللبنانية

Publication du Comité Scientifique de l'Ordre des Médecins du Liban
Publication of the Scientific Committee of the Lebanese Order of Physicians

ISSN 0023-9852 Indexed by • Index Medicus • Embase (Excerpta Medica)
Cab Abstracts and Global Health - CABI Publishing • Index Medicus (IMEMR)

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FRONT COVER

A public notice from Oct. 1918 advising that many public places were being shut down to combat the spread of the influenza virus. (Photo credit: Public domain)

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the Scientific Committee
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Adresser
toute correspondance au

Rédacteur en Chef
Journal Médical Libanais
Ordre des Médecins du Liban
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ISSN 0023-9852
Indexed by • **Index Medicus** • **Embase (Excerpta Medica)**
• Cab Abstracts and Global Health - CABI Publishing
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This exceptional issue was written by doctors who were applauded during the peak of the COVID pandemic. It is dedicated to Lebanese doctors living in exceptional circumstances that will only happen once in a lifetime, hoping that this will never happen again.

For the first time, the Lebanese Medical Journal is publishing a double issue, which will serve as a benchmark and reference to all Lebanese doctors. This was done with limited means knowing that finances are not at their best. I would like to hail the editorial board and those who reviewed the papers.

At last, my thoughts go to Michèle Valligny and Elie Ammar who are the backbone of the edition.

I wish you a good reading.

David Atallah MD, M.Sc
Editor In Chief

COVID-19 PANDEMIC

EDITORIAL

Lebanon COVID-19 Pandemic: A Game Changer

http://www.lebanesemedicaljournal.org/articles/68(1-2)/editorial.pdf

By the time this issue of the LMJ is released, and after less than five months from the first detected case of COVID-19 infection, the worldwide number of infected individuals with COVID-19 would have probably reached more than 10 million with around 500 000-750 000 deaths. This pandemic has exerted significant stress on most governments around the world and revealed the precarious state of many of them, from the most developed to the poorest ones, including Lebanon. It showed how unprepared we all are to meet the challenges this pandemic has created. While we have been able to create the most advanced weapons to kill one another and spent our wealth developing destructive weapons, we stand helpless in the face of an infection with an invisible microscopic enemy. Though countries stand equal in the face of this dismal viral infection, yet they remain divided in how to fight it.

Over a very short period of time, health systems, all over the world, have crumbled under the stress created by the high volume of infected individuals, and the large number of the very sick ones who swamped hospitals and medical care centers. The acute shortage of personal protective medical equipment, hospital beds, intensive care unit (ICU) beds, ventilators, specific diagnostic tests and many others, have only been compounded to the lack of knowledge on the course of the disease, its pathophysiology and more importantly effective medical treatment and vaccination. This has led many countries and health systems to compete for scarce medical resources. This pandemic has also challenged some physicians, such as in Italy and Spain, to make ethically difficult life and death decisions regarding whom to intubate and whom to admit to the ICU. The large number of deaths exceeded the capacity of many cemeteries and created significant emotional stress, especially with the strictly enforced social distancing. This was heightened by the fear of the medical treating teams from the exposure to this infection that might threaten their lives and the lives of their colleagues, families and loved ones.

The lack of published evidence-based medical treatment has led to the use of unproven medications and to bypass what most respected medical institutions have considered the cornerstone of any treatment. From Level A recommendations to the dubious Level D expert opinion and the use of "what make sense" led to practices that reminded us the turn of the century medicine. The pressure on the government in the USA led the FDA and CDC to expedite the approval of the use of medications to a mere few days, which under normal times takes from months to years. Also, clinical trials, that usually take months to approve, started within few days of their submission. High-ranking officials of the most powerful country in the world stood helpless in front of fellow citizens and the whole world. High impact journals such as the *New England Journal of Medicine* have raced to accept and publish whatever came as "expert opinion", case reports, small case series, guidelines, recommendations, in a record time of few days. This led to a "deluge" of reports bombarding us on a daily basis. Moreover, major medical societies, all over the world, have all competed to publish their "consensus" recommendations which they modified from one week to the next.

Moreover, the overtaxing of the health systems has significantly affected the care of the non-COVID-19 patients, whether because of the lack of hospital beds and medical personnel or the fear of virus transmission to personnel or patients. This has led to the cancellation of "non-emer-

gency medical and surgical procedures" and to significant delays in the care of acutely sick patients such as those with acute cardiac events, neurologic events, patients with cancer and pregnant patients to only mention a few. In addition, medical committees in most medical centers have struggled to come up with and implement recommendations and to set up draconian rules on "do's and don'ts" based on limited clinical data, only to change and modify them shortly after their release.

The economic repercussions of this pandemic are beyond the grasp of most of us. They have caused the wealthiest countries to suspend most of their industrial and economic activities and have hindered the transportation of persons and goods across the world. The pandemic has literally brought bustling cities to a halt. Once overcrowded cities now look more like ghost towns. The effect on the low-middle and low-income countries, such as Lebanon, is not only already visible but remains to be fully comprehended.

Notable, among the many deleterious impacts of this viral episode, is the social distancing. This has led to the modification or cessation of all face-to-face medical teaching, meetings, rounds, boards and clinical training. Teaching medical students and training residents and fellows have been significantly curtailed and only partially replaced by virtual meetings, leaving many medical schools and training centers struggling to figure how to compensate and make up for the lost time and practical experience in patient's assessment and management.

The situation in Lebanon was compounded by the continuing struggle with our economic and political turmoil. Despite this difficult situation, Lebanon has risen to this challenge on a social, medical and political level and fared much better than many more "advanced" countries of the world.

In the context of all the above, the editorial board members of the Lebanese Medical Journal decided that it was important to reflect on the current COVID-19 pandemic in Lebanon by producing this special issue. It will address the gained experience on how Lebanon confronted the pandemic not only on the purely medical and scientific levels but also on the political, ethical, social, and medical education and clinical training levels.

On behalf of the editorial board,

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COVID-19 PANDEMIC

COVID-19 PANDEMIC IN THE MIDST OF LEBANON'S WORST FINANCIAL CRISIS
Capital Control or Captain Control ?

http://www.lebanesemedicaljournal.org/articles/68(1-2)/pandemic1.pdf

Riad SARKIS[1], Hamad HASSAN[2], Anthony LICHAA[1], Ray HACHEM[3]

Sarkis R, Hassan H, Lichaa A, Hachem R. COVID-19 pandemic in the midst of Lebanon's worst financial crisis: Capital control or captain control? J Med Liban 2020; 68 (1-2) : 4-8.

INTRODUCTION

COVID-19, caused by the coronavirus-2 (SARS-COV-2) pathogen, started as an epidemic in China. It later spread throughout the Eastern Hemisphere and the rest of the world, ultimately becoming a global pandemic as confirmed by the World Health Organization (WHO) [1].

There are approximately 3,500,000 cases around the world of COVID-19, 250,000 dead, 185 world regions affected, it's a pandemic (global epidemic). Concurrently, the Lebanese economic crisis had worsened in November 2019, which ultimately led to a state of total national economic blockage by December 2019. A reduction of national and foreign currencies in the banks resulted in an inability to transfer foreign currency, which resulted in an almost complete cessation of tourism in Lebanon, one of Lebanon's top economic resources [2]. The direct consequence was an 80% reduction in Lebanese foreign travel for the holiday season at the end of the year, and the cancellation of 90% of visitor reservations who planned to come and spend the holidays in Lebanon. Hotel occupancy fell dramatically from 75% to less than 5% after October 17th.

Further, impacting the Lebanese tourism industry and economy has been the inability for existing investors to buy into Chinese and Far East business, as well as travel bans set in place to mitigate COVID-19 transmission [3]. These two factors have left Lebanon in a precarious situation to deal with its existing economic instability and unstable public health and environmental programs, while trying to simultaneously create and implement COVID-19 public health policies. Unfortunately, managing Lebanon's economic crisis and its COVID-19 response are directly impacting one another, and must go hand in hand in order to protect the citizens of Lebanon and improve the country's overall economic status.

The purpose of this paper is to summarize the decisions that influenced Lebanon's response to the COVID-19 pandemic and outline the current governing public health policies and procedures that have been adopted to manage COVID-19 in Lebanon.

IMMEDIATE RESPONSE

During the early outbreak of COVID-19 around the world, Lebanon was confronted to its worst public health challenge for decades along with its worst financial breakdown. At first, Lebanon continued to receive flights from countries where there were high rates of COVID-19 cases, in particular from Italy and Iran, which unfortunately served as the original source of the virus in Lebanon. These countries were not locked down at that time allowing infected persons to fly off and spread disease abroad.

After seeing what was happening in the news around the world, the Lebanese citizens reacted out of fear and tried to withdraw their bank deposits, stock up on chronic treatment drugs, and reserve major food supplies in order to stay home and isolate themselves from others. Although this caused food reserves to decrease, these actions taken by the people were critical in the early response to decreasing the transmission of COVID-19 by reducing human contact.

The health crisis hit the country when Lebanon was already confronting an unprecedented economic and financial collapse, only to exacerbate it. Collective and coordinated effort is thus necessary to reduce the strain of the different crises shaking the country, on all those who are most severely affected, especially the poor.

Public institutions have received help from UN agencies, nongovernmental organizations (NGOs) and civil society organizations, with the aim of preventing the spread of the virus, avoiding to overload the national health system and simultaneously prevent the exacerbation of the socio-economic meltdown.

To face the COVID-19 health emergency, the Lebanese Government had to adopt strict public health measures in an attempt to limit the pandemic locally [4-5]. The Lebanon's Ministry of Public Health, and its various partners have worked, under the guidance of the Lebanese Prime Minister, to coordinate a national response

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which incorporates detection, diagnosis, treatment and isolation of cases and tracing and follow-up of contacts [6].

Material support has been provided to Rafik Hariri University Hospital (RHUH), which is the governmental referral hospital for COVID-19, hence increasing the number of available testing kits of RT-PCR (reverse transcriptase-polymerase chain reaction) and reagents [7]. The hospital has been initially conducting around 200 tests daily and its ability has increased to reach up to 450 tests per day. Additional kits have been made available to perform screening tests in different Lebanese regions. RHUH has also been provided with personal protective equipment (PPE) sets enough to cover two months. The UN also granted ventilators, hence expanding the Intensive Care Unit capacity of the hospital.

The Lebanese Order of Nurses has also organized training sessions for nurses working at primary healthcare facilities and hospitals. The sessions included topics such as infection prevention and control and clinical care for severe acute respiratory infection.

Additional measures are also being taken to raise awareness about the pandemic, inform about standard precautions, communicate risk, screen at Rafik Hariri International Airport and borders, hence managing importation risk and perform epidemiological surveillance [8].

LEBANESE GOVERNMENT MEASURES IN COVID-19 RESPONSE

A cause of economic bankruptcy, requests to import products have increased concomitantly with the regulation of foreign currency transfers from the Central Bank of Lebanon (Banque du Liban or BDL) to reduce capital flight of foreign currencies. In this regard, a commission was set up at the request of the governor of the BDL to monitor the requests and the estimate of integration and remove fraudulent invoices. The number of COVID cases has increased the need for general and specific medical equipment for COVID-19 and PPE; the commission facilitated a new procedure for medical equipment and devices through a collaboration between importers and their union, the very dynamic Ministry of Health, the banking sector, the suppliers in the country of origin of the material, with rapid and express interaction from the Bank of Lebanon, verifying the needs of hospitals so as not to miss products, with the steadfast support of the Lebanese Prime Minister, the Minister of the Economy and embassies of several countries to note in particular.

The government hospital RHUH was the first to welcome patients with COVID-19, with high-quality equipment and the introduction of RT-PCR for viral screening. Soon after, Hôtel-Dieu de France dedicated a service to welcome patients with the development of a flu center and laboratory equipment allowing diagnosis by PCR, and then several hospitals followed. The spread of the disease forced the Ministry of Health, under the guidance of the Prime Minister, in collaboration with medical experts, to propose a total lockdown to reduce the risks of contagiousness.

This containment evolved in curfew to prevent people from going out and reactivate the viral cycle.

A controlled medical repatriation of citizens detained abroad was possible with a screening on arrival in Lebanon, confinement in a hotel, then self-isolation for 14 days at home.

At the end of four weeks, the number of screened cases fell with a flattened curve of new cases. At this stage a widespread screening on the Lebanese ground of the order of 1000 PCR per day was made. Then followed the importation of rapid tests for total screening with containment management – namely the rapid nasal test for viral antigens, and rapid serological tests to check the IgM immunoglobulins during recent infections with possible contagiousness and the IgGs immunoglobulins which testify to an elevation of chronic viral antibodies that could be protective.

CLINICAL PROFILE & APPROPRIATE MEDICAL RESPONSE GUIDELINES OF COVID-19

COVID-19 is clinically characterized on a spectrum, ranging from asymptomatic, to mild, to severe and critical cases [9-11]. Older age and comorbidities such as diabetes, cardiovascular disease, hypertension, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD) and cancer have been associated with severe COVID-19 illness and increased the rate of mortality [11-15].

The frequent symptoms at presentation are cough, fever, myalgia with fatigue [16,17]. Patients may present with other symptoms including sore throat, nausea, vomiting, diarrhea, headache and rhinorrhea [11,12,16].

I. Staging Clinical Presentation of COVID-19 [18,19]

1. Mortality of the patient.
2. The patient is hospitalized:
   a. Intensive care unit with ventilator or Extracorporeal Membrane Oxygenation (ECMO);
   b. Equipment for a high flow oxygen without intubation;
   c. The patient requires low flow of oxygen;
   d. The patient needs medical care only without oxygen;
   e. Specific treatment with OH-Chloroquine and Azithromycin, or Remdesivir administration.
3. The patient is not hospitalized.

II. How to confirm the diagnosis of COVID-19 [19,20]
The presence of the RNA of COVID-19 on the nasal swab is the key of diagnosis. The amplification of the genome's components by RT-PCR is considered the most accurate technique for viral detection.

The shedding of the virus may vary with a median duration of 20 days [12]. Studies on viral dynamics in COVID-19 RT-PCR confirmed cases showed that patients with severe diseases had a higher viral load and a prolonged period of virus shedding (beyond 10 days) compared to those with mild diseases [21]. Viral load could serve as a biomarker of disease severity and may have a diagnostic and prognostic role in patients with COVID-19. Virus clearance has been defined as two consecutive negative swab test results obtained at 24 hours apart. [12,22]

III. Management of COVID-19
Continuous vigorous effort is ongoing to try to evaluate the best management approach, identify drugs and strategies for the treatment, to develop vaccine and prevent this infection.

Several therapeutic agents with different mechanisms of action showed promising activity against COVID-19 but with limited data. Among these therapeutic agents, hydroxychloroquine used alone or in combination with azithromycin are currently recommended for the treatment of hospitalized patients [23].

Limited clinical studies suggested that remdesivir, an inhibitor of RNA polymerase, could be a therapeutic option [24,25]. Moreover, other therapeutic agents are in clinical trial such as favipiravir and lopinavir/ritonavir [26-28]. Cytokine release syndrome with elevated interleukin 6 (IL-6) have been reported in severe cases which triggered the use of IL-6 receptor inhibitor tocilizumab or siltuximab that are currently under investigation.

In addition monoclonal antibody therapies are being considered during this pandemic situation [29]. Convalescent plasma from recovered donors has been used anecdotally in five severe cases with promising results [30]. Corticosteroids are not recommended unless they are used for other indications [31].

IV. COVID and science [18]
This RNA virus (diameter = 1/107 meter, volume = 1/1018 liter, weight = 1/1015 g) needs two minutes to enter a cell, ten hours to release 1000 virions per cell. The concentration of the RNA virus is variable depending on the sampling site: nasopharynx = 1015, throat = 104, stool = 108/g, sputum = 1011/ml.

V. Use of masks with COVID-19
We had doubts about the surgical mask, but the study of sputters released into the air by a laser visualization when a person speaks, with a diameter between 30 and 500 micrometers, their number increases with the intensity of the voice. Wearing a mask considerably reduces the number of sputters in the air. [32].

VI. COVID-19 vaccine possibilities
An effective MERS-CoV vaccine has been tested with promising results for the development of the coronavirus vaccine. [33,34]

VII. COVID-19 transmission and outbreak
The transmission from a patient infected with SARS-CoV-2 varies according to the duration and type of exposure, the amount of virus in the sputters, the viral load, the severity of the infection and the comorbidities.

Transmission occurs primarily between family members, in assembly or health care settings when personal protective equipment is not in use (including hospitals and long-term care facilities, and in closed places (e.g. cruise ships). However, groups of cases were reported after professional or social gatherings. The risk of transmission by close contact is also known. Asymptomatic people carrying the virus are contagious 1 to 3 days before the onset of symptoms, the transmission of the virus decreases from the onset of symptoms, continues to decrease over time, but it is difficult to select all the carriers and to isolate them during the asymptomatic incubation phase. [35-37]

RESULTS TO RESPONSE PROTOCOLS AND THE FUTURE OF SARS-COV-2 RESPONSE

Following the outbreak of the pandemic with the progression of cases detected by RT-PCR, the Ministry of Health (MOPH) opened its offices for all commissions representing the various orders of health: the orders of doctors, hospitals, pharmacists, medical devices, and importers of PPE and all those able to help in the process of screening affected cases, and promoting total containment to reduce the spread. A comprehensive national education in behavior supported by the MOPH and all media to limit dissemination during the confinement period was set in motion. A special commission has been appointed to monitor the progress of the pandemic in Lebanon. Recently, several NGOs and institutions participated on a humanitarian basis with decentralized screening and forming a mobile clinic visiting villages in search of asymptomatic cases; moreover the MOPH opened regional screening centers to reach a total number that exceeds 1300 tests per day. In this period (end of April 2020) the number of positive tests exceeded 700 while the number of tests carried out was around 15000.

The MOPH's strategies were objective and reason-

able with good results which limited the outbreak. Due to the economic isolation of the country, an express procedure of the Bank of Lebanon allowed transfers of foreign currency to subsidize raw materials, flour, fuel and especially all medical devices and drugs in particular for the importation of all COVID-19 orders to fight the pandemic.

With the situation under control, the discussion on rapid tests was concluded in the interest of importing the nasal test by mucous swab and screening by the rapid antigen test which only requires ten minutes, in order to prepare for the phase of gradual return in five phases from the complete lockdown.

Therefore, four measures should be taken into consideration in order to safely reopen the country:

a. Hospitals must be able to treat inpatients without being overwhelmed.
b. All symptomatic patients should be tested.
c. Monitoring of positive cases and confinement. Daily contact with patients in confinement is mandatory to prevent a recurrence of an epidemic.
d. Controlled confinement will lead to a considerable reduction in the number of patients in fourteen days.

CONCLUSION

MOPH strategies were objective and reasonable with good results which blocked the outbreak. Unfortunately, managing Lebanon's economic crisis and its COVID-19 response are directly impacting one another, and must go hand in hand in order to protect the citizens of Lebanon and improve the country's overall economic status.

This paper summarized the decisions that influenced the good preventive results in Lebanon and outlined the current governing public health policies and procedures that have been adopted to manage COVID-19 in Lebanon.

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COVID-19 PANDEMIC

THE VIROLOGY OF SARS-CoV-2

http://www.lebanesemedicaljournal.org/articles/68(1-2)/pandemic2.pdf

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Bizri AR, Moghnieh R. The virology of SARS-CoV-2. J Med Liban 2020; 68 (1-2) : 9-15.

INTRODUCTION TO CORONAVIRUSES

Coronaviruses are positive sense RNA viruses that belong to the Nidovirales order and Coronaviridae family. The name is derived from their appearance as a crown under electron microscopy [1]. Small, with diameter ranging between 65-125 nm, they are enveloped with a positive sense single-strand RNA genome that varies from 26 to 32 kbs in length [2,3]. In the Coronaviridae family, some members are known to produce disease among a wide range of humans and vertebrates. Their disease spectrum includes respiratory, gastrointestinal and central nervous system infections. They have varying manifestations from symptoms associated with upper and lower respiratory symptoms, affecting several organ systems including renal disease [1,2].

Prior to the severe acute respiratory syndrome (SARS-CoV) outbreak in 2002 in Guangdong Province of China, it was believed that coronaviruses produced enzootic infections and were not highly pathogenic to humans, causing mild infections in immuno-compromised hosts. This belief was debunked with the subsequent discovery of the Middle East Respiratory Syndrome virus (MERS-CoV), which plagued mainly the Arabian Peninsula ten years later [4]. Coronaviruses have bypassed the human-animal barrier and have become zoonotic diseases [5].

In December 2019, a novel coronavirus dubbed SARS-CoV-2 caused an outbreak, COVID-19, in the city of Wuhan, China, leading to the death of one thousand eight hundred individuals and affecting around seventy thousand individuals within the first fifty days [3]. As of March 2020, more than two million individuals have been infected with a death toll of around one hundred and forty thousand individuals. COVID-19 has truly taken the world by storm becoming one of the worst pandemics in modern times.

The Coronaviridae family is divided into four main genera, classified based on their genomic characteristics: Alphacoronavirus (α-CoV), Betacoronavirus (ß-CoV), deltacoronavirus (∂-CoV) and gammacoronavirus (γ-CoV) [4].

The genus Beta coronavirus is subdivided further into 4 lineages: A, B, C and D [1]. The first two genera infect only mammals. They can also cause severe infection to livestock. The latter two genera mainly target birds and certain mammalian species [4]. Both intra- and inter-species transmission of the virus as well as genetic recombinant events contribute to the appearance of new coronavirus strains (Table I).

As a result of two large overlapping reading frames (ORFs), coronaviruses have many similarities, particularly in their genome organization and expression. At the 5' end terminus, is ORF1a/b which encodes 16 non-structural proteins (Nsp1 to Nsp16), followed by the ORFs at the 3' end which encode for the 4 main structural proteins: spike (S), envelope (E), membrane (M) and nucleocapsid (N) [1].

Some coronaviruses do not require all the structural proteins to produce an infectious virion. This suggests that the virus might not require all the structural proteins, or it encodes additional proteins that have overlapping compensatory functions [6]. The S protein is required for fusion of the virus to membrane cells of the host by attaching to surface receptors on the host cell, enabling

TABLE I

CORONAVIRUSES AND THEIR GENERA DISTRIBUTION

Order	Nidovirales
Family	Coronaviridae
Sub-Family	Coronavirinae
Genera (according to genome characteristics)	Alpha coronavirus Beta coronavirus Delta coronavirus Gamma coronavirus #Several subgenera, lineages & species

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infection. It was also revealed that the S protein has a role in cell-cell fusion forming large syncytia, which is another proposed mechanism of intercellular spread.

The N protein is primarily engaged in binding the RNA genome. M protein is a major protein found in and defines the envelope. It requires interaction with all other structural proteins; homotypic interactions are the driving force for envelope development but alone it is not enough for virion formation.

The E protein is the smallest among the structural proteins, yet it has an important role in viral assembly and release of the virions [5].

HUMAN CORONAVIRUSES

There are currently seven different human coronavirus (HCoVs) belonging to the alpha and beta genera. The HCoV-229E (229E) and HCoV-NL63 (NL63) belong to the genus Alphacoronaviruses. Meanwhile HCoV-OC43 (OC43), HCoV-HKU1 (HKU1), SARS-CoV, MERS-CoV and SARS-CoV-2 belong to the genus Betacoronaviruses [7] (Table II).

229E is the prototypical virus that has a global distribution and exhibits peaks in transmission during the winter period in temperate climates. It was discovered in 1966 by a group of researchers trying to characterize agents leading to the common cold. Presenting symptoms include malaise, nasal discharge, sore throat, headache and sneezing. In around 10 to 20% of cases the patient will exhibit fever and a cough. 229E has an incubation period of 2 to 5 days preceding an illness of approximately 2 to18 days in duration [1,8].

The second HCoV is NL63 which is associated with mild respiratory illnesses in the immunocompromised as well as young children and elderly individuals [9]. It has a global distribution, an incubation period of 2-4 days and phylogenetically it is similar to HKU1. Presenting symptoms include cough, rhinorrhea, hypoxia, fever, tachypnea and croup (obstructive laryngitis) [1,10].

The Betacoronavirus genera is further subdivided into lineages, each with its own HCoV: OC43 and HKU1 (lineage A, subgenus Embecovirus), SARS-CoV (lineage B, subgenous Sarbevirus) and MERS-CoV (lineage C, subgenous Merbecovirus).

OC43 is the prototype virus for this genus. It was isolated in 1967 from a patient with the common cold. It has a global distribution and an incubation period of 2-5 days. Clinical symptoms are very similar to those of 229E, with no serological cross-reactivity. HKU1 has global distribution with a short incubation period ranging between 2-4 days. Symptoms depend on the location of the infection. In the upper respiratory tract, patients have fever, runny nose, and cough. Whereas, in the lower respiratory tract they complain of fever, dyspnea and productive cough. There is also a high association for the development of seizures and meningitis. [1,11]

SARS-CoV was first detected in the Guangdong province of China, spreading to surrounding Asian countries and several other regions, affecting a total of thirty-seven countries worldwide. Originally found in bats, it then spread to civets before eventually reaching humans. The incubation period ranges between 2 to 11 days with a fatality rate of 9.7%, reaching up to 50% in elderly patients. Initial presenting symptoms include fever and chills, headache, myalgia, and malaise to be followed by respiratory distress, cough, and dyspnea. Pathological changes in the lungs of affected individuals include epithelial proliferation, diffuse alveolar damage and increase in macrophages. The infection may involve the gastrointestinal, liver, kidney, brain and spleen causing white pulp atrophy (similar to H5N1 infection) [1,12].

MERS-CoV was initially recognized in Saudi Arabia in 2012. Transmitted from camels to humans, the infection spread throughout the Arabian Peninsula and to twenty-six countries worldwide. The virus has an incubation period ranging between 2 to13 days and a mortality rate of 37%, making it one of the deadliest viruses in modern times [13]. The severity of the disease ranges from

TABLE II

HUMAN CORONAVIRUSES AND THEIR RESPECTIVE DISEASES

Genus	Virus	Disease	Severity	Mortality	Year
Alpha	CoV-NI-63	Respiratory tract infection	Mild	Rare	1965
Alpha	CoV-229E	Respiratory tract infection	Mild	Rare	1967
Beta	CoV-HKU-1	Respiratory tract infection Pneumonia	Mild Moderate	Rare Unusual	2005
Beta	CoV-OC43	Respiratory tract infection	Mild	Rare	2004
Beta	SARS-CoV	Acute respiratory syndrome	Severe	10 %	2002
Beta	MERS-CoV	Acute respiratory syndrome	Severe	37 %	2012
Beta	SARS-CoV-2	Acute respiratory infection	Severe	~2 %	2019

*Modified from Loeffelholza, M.J.; Tang, Y.W. Emerging Microbes & Infections. 17 March 2020, VOL.9 [39]

asymptomatic or mild infection to difficulty in breathing and respiratory distress, severe pneumonia, septic shock and renal impairment and even death. The illness usually starts with cough, sore throat, fever, myalgias and arthralgias. It then rapidly develops to dyspnea and pneumonia. Gastrointestinal involvement is seen in around one third of patients manifesting with vomiting and diarrhea [1,14].

SARS-CoV-2 BEGINNINGS

Unexplained number of patients with pneumonia appeared in Wuhan, Hubei Province, China, in December 2015 [15]. Applying sequence analysis technique, the causative agent for these pneumonias turned out to be a new coronavirus (CoV) named then 2019-nCoV [16]. Later by February 11, the World Health Organization (WHO) named this novel viral entity "Coronavirus Disease-2019 (COVID-19)" [17]. Meanwhile, the International Committee on Taxonomy of Viruses named it SARS-CoV-2 [18]. Both nomenclatures avoided linking this virus to any specific geographic location, city, country or ethnic group, avoiding any unnecessary stigma or future discrimination. The source of the novel virus remains unclear. A recent phylo-epidemiological analysis hints that the virus, that circulated at Huanan Seafood Market, might have been introduced from other places [19]. The possibility that at least two different strains of SARS-CoV-2 had occurred before the official recognition of COVID-19 adds further to the confusion about its origin [20].

SARS-CoV-2 IDENTIFICATION, CLASSIFICATION & GENOME ORGANIZATION

The first recognition of the SARS-CoV-2 virus was from an infected individual in Wuhan Province on December 30, 2019. The virus was identified from bronchoalveolar lavage (BAL) of the patient [16]. It was classified as a member of the ß-CoVs through sequencing and evolutionary tree analysis [16,21]. Both MERS-CoV and SARS-CoV are also members of ß-CoVs [22].

The SARS-CoV-2 has a genome sequence identity of 79.5% and 50% with both SARS-CoV and MERS-CoV, respectively [16,21,23]. Based on the similarities in sequence identity between the SARS-CoV-2 and the SARS-CoV (94.6%) and with that of other betacoronaviruses (less than 90%), experts suggested that SARS-CoV-2 can be placed in the lineage B of CoVs [16,24]. (Figure-1)

The genome of SARS-CoV-2 is 29.9 kb in size, similar to other betacoronavirus [25]. Like all coronaviruses it has a nucleocapsid made of genomic RNA and N protein. The N protein is hidden within phospholipid layers and concealed by two different classes of spike proteins. The first is the S protein, a glycoprotein trimmer unanimously present in CoVs. The second is the hemagglutinin-esterase (HE) which forms a discrete inner border of short peplomers only found in certain group II CoVs (OC43, bovine CoV). Both the M protein and the E protein are situated amid the S proteins in the viral envelope. The gene order of SARS-CoV-2 is as follows: (5') replicase ORF1ab – S – E – M – N (3'). SARS-CoV-2,

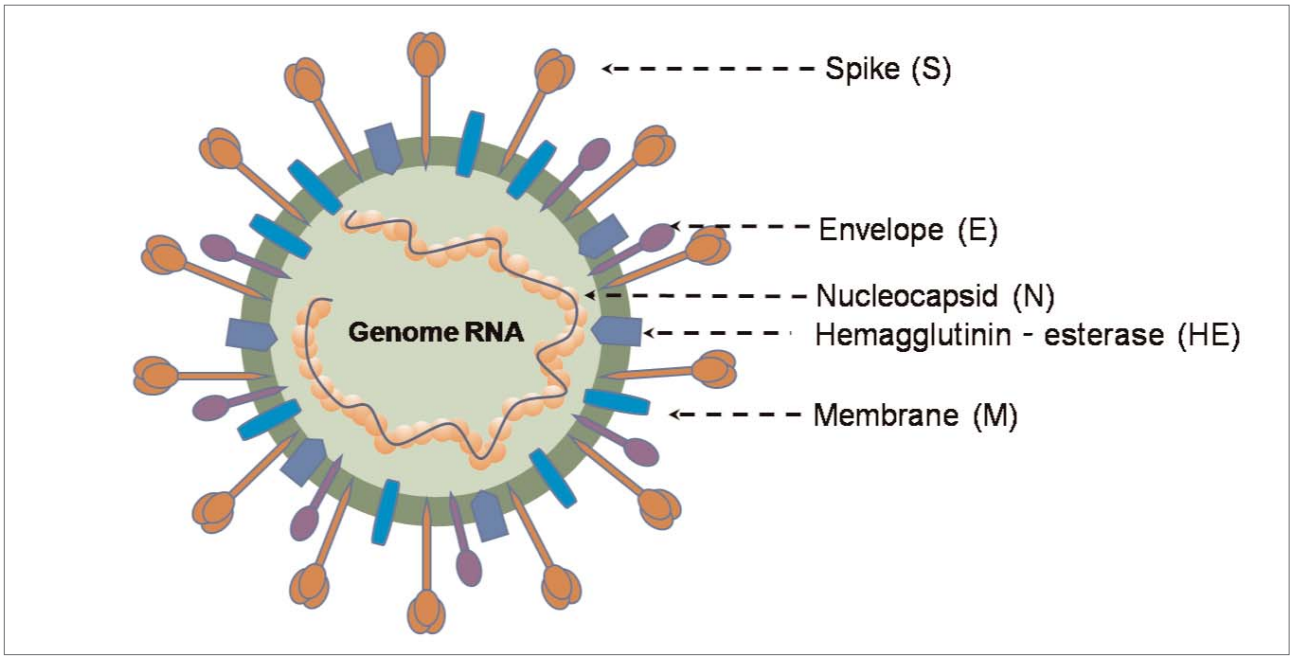

Figure 1. SARS-CoV-2 virion
*From Jin Y, Yang H, Ji W et al. Virology, epidemiology, pathogenesis, and control of COVID-19. Viruses 2020; 12 (4): 372. [40].

encodes for an ORF8 gene situated between the M and N ORF genes, a characteristic similar to SARS-CoV [24]. (Figure-2)

SARS-COV-2 PHYSICAL & CHEMICAL PROPERTIES

The viral particle appears as round or oval and has a dameter of 60-100 nm. It can be deactivated by heating for 30 min at 56 °C or by ultraviolet light. It is susceptible to most disinfectants including 75% ethanol, diethyl ether, peracetic acid, chlorine, and chloroform [26]. Viral stability depends on the nature of surfaces, where it is believed to be more stable on stainless steel and plastic than on cardboard and copper where viable viruses were detected up to 3 days. SARS-CoV has a shorter half-life than SARS-CoV-2 on cardboard. However, both viruses had long viability on plastic and stainless steel [27].

SARS-COV-2 LIFECYCLE

The virus gains entry to human cells via angiotensin-converting enzyme 2 (ACE2) receptors. These type I membrane proteins are mainly associated with cardiovascular diseases and also present in lung, intestine, kidney, liver and brain tissues [21,28]. ACE2 offers a binding site for the S proteins leading to cleavage of angiotensin (Ang) I to yield Ang-(1-9) [29]. The S proteins go through significant structural reorganization to be able to fuse the virus with human host cell membrane. The S1 subunit binds with a host-cell receptor initiating fusion through destabilizing the prefusion trimer. This process results in the shedding of the S1 subunit and transition of the S2 subunit to an extremely stable postfusion adaptable conformation [30]. To be capable of engaging receptors on host-cells, S1 receptor-binding domain (RBD) undertakes hinge-like adaptive conformational movements that momentarily expose or hide receptor binding determinants [31]. Analyzing the RBD domain of the S protein in SARS-CoV-2 revealed through structural, physical and biological evidence that SARS-CoV-2 S protein probably binds to human ACE2 with 10-20 times higher affinity than SARS-CoV [32]. (Figure 3)

SARS-COV-2 EVOLUTION & ECOLOGY

All human CoVs are possibly zoonotic in origin and their most likely hosts in nature are bats [33]. During the SARS pandemic early signs suggesting a zoonotic source were civets being pointed out as the natural reservoirs for human infection [34]. The discovery of SARS-like CoVs isolated from various bat species in China indicated that the Chinese horseshoe bats can be the natural host of the SARS-CoV [35,36]. In the case of SARS-CoV-2, the high sequence identity to certain bat CoVs such as Bat-CoV RaTG13 (96.2% nt identity to SARS-CoV-2), pinpoints towards a potential bat origin [24,35]. Since bats habitats are ordinarily found in distant places far from human habitats, any CoV virus must have another intermediary animal host in order to infect humans. The bat SARS like-CoVs cannot directly affect humans without undergoing certain mutations or recombination in another animal host [34]. It is well known that the animal host for MERS-CoV is the camel, while civet cats are the natural hosts of SARS-CoV prior to being transmitted to humans. The intermediate animal host for the SARS-CoV-2 is not fully identified. However, SARS-CoV-2 and pangolin origin CoVs share 99% sequence identity suggesting that the former may have a pangolin origin [37]. (Figure 4)

SARS-CoV-2 GENOMIC VARIATION

Evaluating early COVID-19 patients, the ten genomic sequences obtained revealed extreme similarities reaching up to 99.8%. This implies that little or no variation has taken place [21,23]. However, since the virus uses RNA polymerase for replication, several copies are expected to be produced. This was supported by a study showing that around 120 substitution sites were uniformly spread over eight coding regions, without any obvious recombination episodes [19].

Meanwhile, Tang et al. in their report revealed that SARS-CoV-2 evolved into two major types. After evaluating and analyzing 103 genomes they concluded that as a result of selective pressure two main types L and S, that differ in their ability to spread and severity of illness, can be identified. L type can be more aggressive and spread faster than the S type [38].

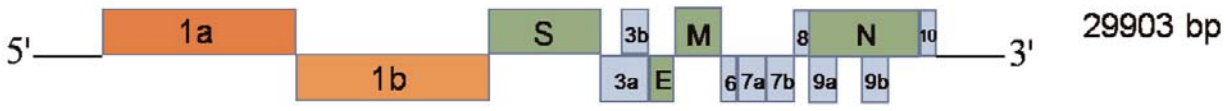

Figure 2. ß-coronavirus genome

*From Jin Y, Yang H, Ji W et al. Virology, epidemiology, pathogenesis, and control of COVID-19. Viruses 2020; 12 (4): 372. [40].

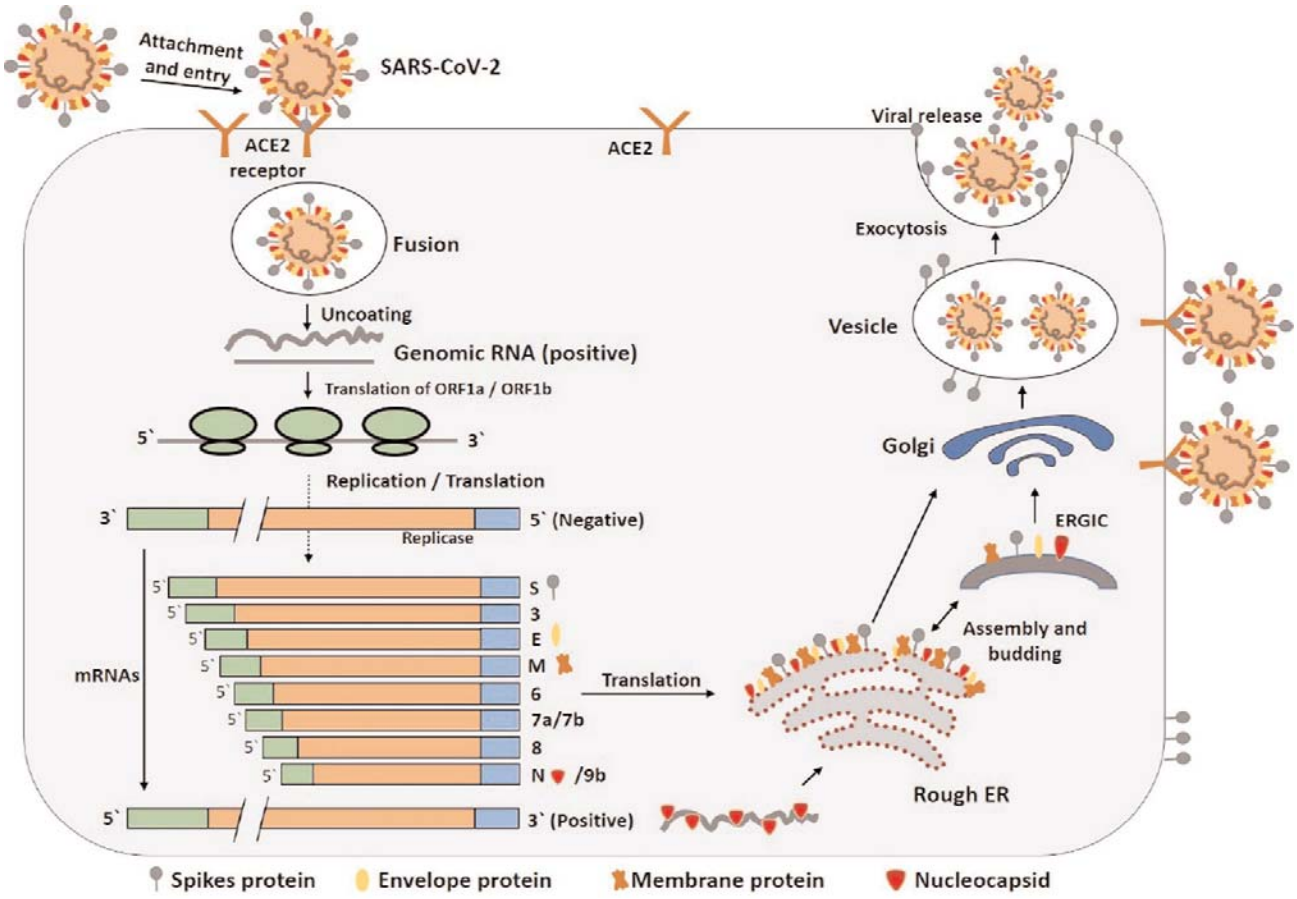

Figure 3. Life cycle of SARS-CoV-2
*Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. J Adv Res. 2020 Mar 16; 24: 91-98. [3]

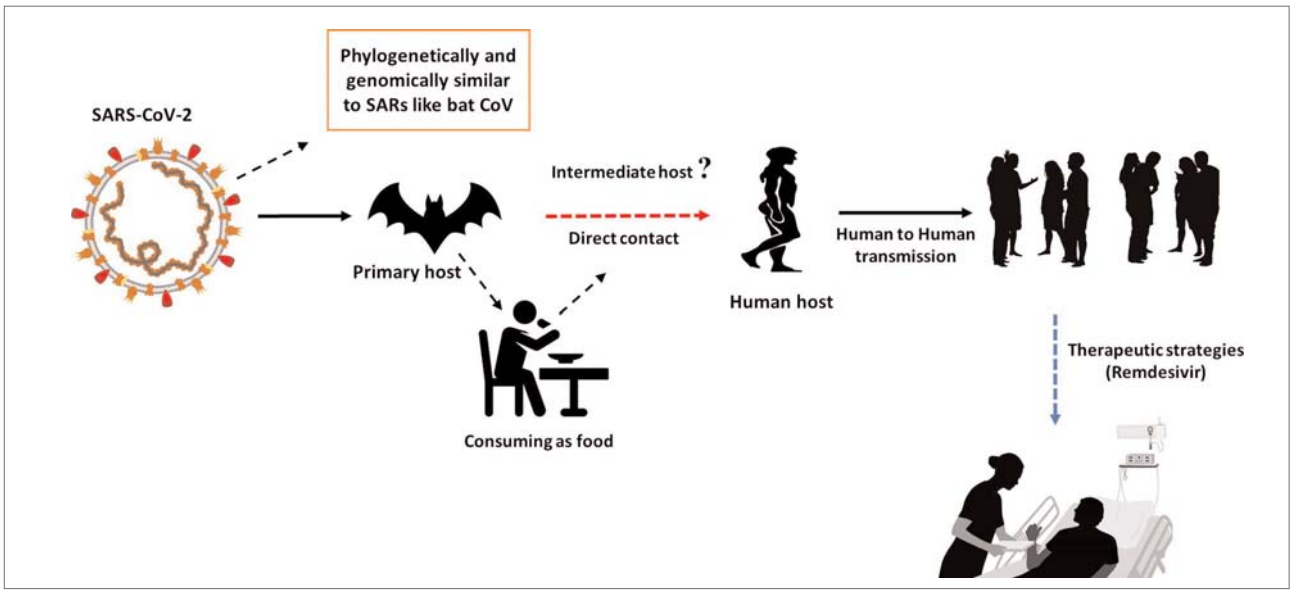

Figure 4. Reservoir and mode of transmission of SARS-CoV-2
*From Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. J Adv Res. 2020 Mar 16; 24: 91-98. [3]

CLINICAL & PUBLIC HEALTH SIGNIFICANCE OF HCoVs

Endemic HCoVs

In regions with temperate climates, endemic HCoVs demonstrate a winter seasonality.

Only HCoV-229E has been reported to cause sporadic disease all through the year. Endemic HCoVs are maintained in the human population and have a global distribution [39]. (Table III)

TABLE III

ENDEMIC AND EPIDEMIC HCoVs

Endemic HCoVs	Epidemic HCoVs
HCoV-229E	SARS-CoV
HCoV-NL63	MERS-CoV
HCoV-OC43	SARS-CoV-2
HCoV-HKU1	

Epidemic HCoVs

The SARS-CoV and MERS-CoV epidemics were caused in part by super-spreading events, where some humans have directly affected a disproportionately big number of individuals. On the other hand, the COVID-19 (SARS-CoV-2) outbreak started in a crowded fish market that sells exotic animals as well.

The SARS-CoV epidemic ended in 2003, less than one year from the date when the first case was reported. Meanwhile the MERS-CoV epidemic continued to be reported for more than seven years following the detection of the first case in Saudi Arabia. The natural reservoirs that maintain SARS-CoV and MERS-CoV are zoonotic. It is believed that SARS-CoV-2 has an animal reservoir but its distribution among various mammalian species is unknown. The role of pets and farm animals in the epidemiologic cycle of SARS-CoV-2 is not fully clear. Their ACE2 receptors share similarity with ACE2 human receptors [39]. On April 22 of this year, the Center for Disease Control and Surveillance declared that the National Veterinary Services Laboratories reported SARS-CoV-2 infection in two domestic cats. However, there is no clear evidence confirming cat to human transmission. (Table-III)

CONCLUSION

SARS-CoV-2 is the viral agent of the current COVID-19 pandemic. It is the 7th identified HCoV associated with respiratory infectious diseases and the 3rd HCoV associated with epidemics following SARS-CoV and MERS-CoV. Believed to have originated from BatCoV due to 96.2% genomic resemblance, intermediate host of SARS-CoV-2 is not clearly identified yet. It replicates efficiently in human cells gaining entry through ACE2 receptors virtually found in all organ systems. Its linear genome structure shares more similarities with SARS-CoV than MERS-CoV. Individuals with asymptomatic infection can spread the viral illness. It has affected more individuals than SARS-CoV or MERS-CoV but seems to be associated with less case fatality rate.

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COVID-19 PANDEMIC

TESTING FOR COVID-19: WHEN, WHO, AND WHAT TEST?

http://www.lebanesemedicaljournal.org/articles/68(1-2)/pandemic3.pdf

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Araj GF, Beaini M, Bizri NA, Ghizzawi L. Testing for COVID-19: when, who, and what test? J Med Liban 2020; 68 (1-2) : 16-26.

ABSTRACT • The laboratory diagnosis of COVID-19 is essentially based on three modalities. The reference method in lieu of viral culture is the molecular amplification assays, mostly by using the real-time reverse-transcriptase polymerase chain reaction (RT-PCR). However, due to its complexity, needed equipment and expertise as well as the high expense, other assay modalities have been introduced. These include antigen-based and antibody-based detection assays. This article provides a consolidated approach that will shed light on the different formats and utilities that these assays are intended for at this stage in time, addressing when, who, and what in the testing of COVID-19. It is worth noting that a combination of different assays is advisable to settle interpretation of test results to reflect the true scope of the patient's condition.

Keywords : COVID-19; lab diagnosis; rapid testing

INTRODUCTION

The laboratory diagnosis of COVID-19 has been rapidly and dynamically evolving [1-6]. Three types of laboratory diagnostic assays have been used in the diagnosis and evaluation of exposure to COVID-19, namely molecular, antibody and antigen detection tests. The RT-PCR, performed on respiratory specimens, is the reference standard for COVID-19 diagnostics [4-6].

Currently, very few tests for COVID-19 investigation have been approved by the US Food and Drug Administration (FDA). This is done in order to facilitate their use by the clinical laboratories aiming at expanding the testing towards assisting in controlling virus spread. Many molecular and serologic immunoassay technologies have received Emergency Use Authorization (EUA) from the FDA for both hospital laboratory-developed assays and for several commercial kits [4-6].

Developed and employed tests/assays should be validated before use. Despite the variation in sensitivity, specificity and objective of utilization, the developed tests have been anticipated to provide reliable and rapid turnaround time (TAT) results in identifying infected or exposed cases. These assays are essential to control the viral spread and transmission, to initiate appropriate protective measures, and to start treatment when applicable. In addition, these assays can be used in epidemiologic surveillance and forecasting exposure to the community, helping the health policy makers initiate appropriate control measures and actions.

Overall, a successful laboratory diagnosis necessitates keeping in mind two important key factors: the correlation of test results with clinical picture/history and the need to use a combination of two testing modalities. This is necessary for appropriate interpretation of COVID-19 case definition/status as being proven, suspected, or asymptomatic/exposed, as well as any other relevant decision a test result will help to inform [4-6].

The text that follows addresses the three main laboratory diagnostic modalities for COVID-19 case diagnosis or exposure:

- Molecular tests, also known as Nucleic Acid Amplification Tests (NAAT) that target detection of specific nucleic acid sequences of the virus;
- Antigen detection tests: detection of viral antigenic epitopes;
- Antibodies detection tests: detect the humoral immune response (e.g. IgM, IgG) following an infection.

MOLECULAR LABORATORY DIAGNOSIS OF COVID-19

Introduction

Molecular assays are considered the cornerstone and reference method for the lab diagnosis of the COVID-19 infection [4-6]. The discussion that follows will address the viral aspects as it relates to the molecular diagnostic methods, emphasizing the RT-PCR and its utilization in the diagnosis of viral diseases.

Description and classification of the molecular lineages of human coronaviruses were first identified in the mid-1960s. This warranted the understanding of current

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molecular tests used for the diagnosis of this virus. Four main sub-groupings of coronaviruses were revealed as: alpha, beta, gamma, and delta [7; Refer to the virology article in this special issue by Bizri AR].

Few are known to cause infection among humans, a couple belong to the alpha coronaviruses (229E, NL63), while the rest are Beta-CoVs. The greatest clinical importance concerning humans of the Beta-CoVs are OC43 (which can cause the common cold) and HKU1 of the A lineage, SARS-CoV and SARS-CoV-2 (which causes the disease COVID-19) of the B lineage and MERS-CoV of the C lineage [8].

As the clinical description of COVID-19 continues to evolve and transmission of the disease by asymptomatic individuals progresses, widespread testing has become a necessity, warranting the probing in molecular testing [9-10].

Viral genome sequence events of COVID-19

On January 4th, 2020, the Food and Drug Administration (FDA) issued emergency use authorization (EUA) to enable Centers for Disease Control and Prevention (CDC) to offer molecular diagnostic tests for COVID-19. The complete viral genome sequence was released for immediate public health support via the community online resource virological.org on January 10th, 2020, (Wuhan-Hu-1, GenBank accession number MN908947), followed by four other genomes deposited on 12th January in the viral sequence database curated by the Global Initiative on Sharing All Influenza Data (GISAID). On January 17th CDC developed and validated the first molecular test for COVID-19 detection and on January 24th, CDC publicly posted the assay protocol for this test. All along, close cooperation and continuous monitoring to evolve such diagnostic tools have been ongoing among CDC, FDA, World Health Organization (WHO) and advisories from other reference labs worldwide for updates.

Type/methods of molecular assays

Rapid evolution in molecular assays has been ongoing. For example, the earlier hybridization methods, which were used for identification of pathogens were not sensitive enough for their detection. They were superseded by NAAT, which makes millions of copies of a specific section of the pathogen genome, amplifying small amounts to detectable levels.

Several amplification methods have been developed for the identification of COVID-19 including RT-PCR, nucleic acid sequence based amplification (NASBA), transcription mediated amplification (TMA), strand displacement amplification (SDA) and loop mediated isothermal amplification (LAMP) [11].

RT-PCR-reference method for COVID-19 laboratory diagnosis

In COVID-19 exposure or infection, RT-PCR is globally known as the mainstay and reference method for its laboratory diagnosis. It is highly sensitive and specific in its ability to detect the virus in people suspected of being exposed (asymptomatic) or to confirm its diagnosis in symptomatic patients. [12].

Gene targets for RT-PCR and other NAAT molecular diagnosis

WHO and the European Center for Disease Prevention and Control (ECDC) via GISAID have published the different SARS-CoV-2 specific target genes (*E*-gene, *ORF1* and *N*-gene), genome positions, amplicon length, institutes along with the corresponding available protocols. Details of these are noted in the link together with the rate of mutation in the listed primers and probes. [https://www.who.int/who-documents-detail/molecular-assays-to-diagnose-covid-19-summary-table-of-available-protocols] [https://primerscan.ecdc.europa.eu/?assay=Overview, 4/28/2020, www.eurosurveillance.org].

These protocols are shown in the Table and they are under continuous revision and update by Foundation for Innovative New Diagnostics (FIND) and WHO. [https://www.finddx.org/covid-19/]; [file:///G:/COVID-19/FIND COVID-19-GUIDE_24.03.2020.pdf. https://www.finddx.org/covid-19/pipeline/ For an overview of COVID-19 diagnostics that are currently available or in development. https://www.360dx.com/coronavirus-test-tracker-launched-covid-19-tests: Coronavirus Test Tracker: Commercially Available COVID-19 Diagnostic Tests].

TABLE

SUMMARY TABLE OF AVAILABLE PROTOCOLS IN THIS DOCUMENT

Institute Gene	Targets
China CDC, China	*ORF*1ab and *N*
Institut Pasteur, Paris, France	Two targets in *RdRP*
US CDC, USA	Three targets in *N* gene
National Institute of Infectious	Pancorona & multiple targets
Diseases, Japan	Spike protein
Charité, Germany	*RdRP, E, N*
HKU, Hong Kong SAR	*ORF*1b-*nsp*14, *N*
National Institute of Health, Thailand	*N*

Commercial molecular platforms

Currently, the performance characteristics of COVID-19 PCR testing available in the market are not well established as clinical trials were not performed prior to the reagents being released under a EUA status by the FDA. These were originally released under Research Use Only (RUO) while waiting for EUA approval. The slow im-

plementation of testing and a lack of testing capacity are due to a lack of: positive control materials, personnel/time, primers/probes, specificity panel, funds, quality control system, commercial tests, procurement procedures, training and equipment. However, every laboratory should perform test validation on each EUA granted test kit before use through implementation of quality control (QC) and in accuracy and precision studies [13]. Examples of available RT-PCR and other molecular platforms include: Applied Biosystems® 7500, BioRad CFX96TM, Cepheid SmartCycler®, Cobas® Z480, LightCycler® 2.0, Rotor-Gene® 6000, Abbott Molecular, Becton Dickinson BD MAX™ System, SeeGene. These have TAT that vary from around more than one hour up to 150 minutes.

However, rapid TAT and performance as point of care, as an estimate of less than one hour, were reported for Roche ID NOW COVID-19 (5 minutes), Qiagen QiaStat-Dx (43 minutes) and Cepheid Xpert® Xpress SARS-CoV-2 (45 minutes).

Diagnostic kits

Updates on FDA/WHO approved *in-vitro* diagnostic kits having EUAs/CE/RUO for COVID-19 testing on the various platforms based on the different target genes available globally, including Lebanon, are (alphabetically):

- Abbott RealTime SARS-CoV-2 Assay, (RdRp and N genes), (Abbott Molecular);
- AccuPower® COVID-19 Real-Time RT-PCR Kit, (E gene and RdRp gene), Bioneer;
- Allplex™ 2019-nCoV Assay, (E gene, RdRP gene, N gene), (SeeGene);
- BioGX SARS-CoV-2 Reagents, (N1, N2 and RP gene), (Becton Dickinson);
- CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel, (N1, N2 and RP gene), (CDC);
- Cepheid Xpert Xpress SARS-CoV-2 assay, (N2/E gene), GeneXpert Infinity Systems;
- Cobas SARS-CoV-2, (ORF-1a/b and pan E-gene), (Roche Molecular Systems, Inc.);
- ID NOW COVID-19 assays, (RdRP), (Abbott Molecular);
- Panther Fusion SARS-CoV-2, (ORF 1ab (ORF1a/ORF1b gene), (Hologic, Inc);
- PerfeCTa SYBR Green FastMix, (open system), Quantabio;
- QIAstat-Dx Respiratory SARS-Cov-2 assay, (Orf1b poly gene (Rdrp gene) and E genes), (Thermo Fisher Scientific, Inc);
- RealStar® SARS-CoV-2 RT-PCR Kit RUO, (E and S gene), Altona;
- SARS-COV-2 R-GENE, (N, RdRp andE gene), (bioMérieux SA);
- Script® One-Step qRT-PCR Kit, (open system), Invitrogen;
- TaqPath COVID-19 Combo Kit, (ORF1ab, N Protein and S Protein gene), (Thermo Fisher Scientific, Inc.).

These kits have high sensitivity and specificity, and their TAT for test performance varies from around 5 to 150 min. [www.fda.gov › media] [https://www.fda.gov/medical-devices/emergency-situations medical-devices/emergency-use-authorizations.]; [file:///G:/COVID-19/FIND_COVID-19-GUIDE_24.03.2020.pdf. https://www.finddx.org/covid-19/pipeline/ For an overview of COVID-19 diagnostics that are currently available or in development.]

Specimen collection and management

The specimens, mainly respiratory, are obtained from patients who fulfill a case definition of COVID-19, while using appropriate personal protective equipment (PPE) and testing under biological safety laboratory level-2 (BSL2) [14]. Failure to abide by good laboratory practices will lead to lab contamination, risk of infection and invalid test results. The collected specimens are placed into virus transport medium (VTM) and forwarded immediately to the lab for molecular testing. In case of delay in testing, specimens need to be appropriately stored, while maintaining stable cyclic threshold (Ct) values, as follows: –4°C for up to 72 hrs, and –70°C for a longer period. The extracted RNA can be stored at –70°C or lower for long periods. In the shortage of VTM swabs, regular flocked/polyester swabs in a normal saline/phosphate buffer solution/tissue culture solution are all acceptable. [https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html].

Heat inactivation of samples (56°C for 30 minutes) after collection from patients and before performing PCR are necessary, in order to avoid infection and health hazards during transport and in the preanalytical and analytical phases [15].

The quality of results depends significantly on the quality of sample collection, the length of time the patient has been symptomatic, and the viral burden at the time of testing. The sensitivity of PCR-based testing is generally very high, when a good sample is obtained.

Specimen types and PCR detection rates

The respiratory specimens are the main test for detecting or confirming COVID-19 infection, though other specimen types were also investigated. For example, a study conducted by Wang et al., revealed the detection rates in different specimens to be: 93% in bronchoalveolar lavage (BAL), 72% in sputum, 63% in nasal swab, 46% in fibrobronchoscope brush, 32% in pharyngeal swab, 29% in feces, 1% in blood and 0% in urine [16]. Lately, saliva

samples (a noninvasive alternative) revealed importance as a source of molecular virus recovery and IgA detection. This is attributed to the fact that saliva has the highest viral load near presentation, and can account for the fast-spreading nature of this epidemic [17]. However, simultaneous collection from multiple respiratory sites (combined in one vial) for testing is advisable in order to improve the sensitivity and reduce false-negative PCR test results.

Duration of viral detectability

Studies attempted to answer the question on when can the virus be detected before symptoms onset and for how long thereafter.

Arons et al., using cell culture, reported that viable virus was recovered 6 days before to 9 days after the first evidence of symptoms [18]. Wolfel et al. 2020, reported that the virus was isolated during the first week of symptoms from 16.66% in throat swabs, and 83.33% in sputum samples. No isolates were recovered from samples taken after day 8. The virus isolation success depended on viral load: samples containing < 100,000 copies/mL (or copies per sample) never yielded an isolate. They also suggested that such a load was unlikely to be infectious [19]. Gautret et al. reported in an observational study of 80 inpatients treated for 3 days that the PCR test of nasopharyngeal viral load rapid fall: 83% negative at Day 7, and 93% at Day 8 [20]. Zou et al. also indicated that COVID-19 viral load from nasal and throat swabs decreased close to detection limits 12 days after onset of symptoms, and from saliva in 11 days [21].

Details for timings of the specimen's collection from symptomatic patients and contacts and for each transmission scenario are clearly stated in both WHO guideline interims. Patients' viral loads in the nasopharynx is highest around the time of symptom onset. [22]. Kim et al. conducted a follow-up study on the kinetics of viral load in quarantined patients infected with COVID-19 during the first 14 days of exposure. The asymptomatic patients showed Ct values > 35 while the presymptomatic (had highest viral load) showed Ct values < 20. Live virus couldn't be recovered from culture in PCR of Ct > 35 [23].

Persistence of positive PCR after resolution of infection

The aforementioned studies and others indicate that detection of active virus by PCR post 14 days of infection (post onset of clinical signs) in an individual who is symptom free and no longer infectious is unlikely [18-21]. However, the persistence of molecular (PCR) positive test results lingering for several weeks (up to 8 weeks if not more) despite patients/individuals being recovered and becoming asymptomatic has been encountered [24].

This can constitute a challenging global dilemma for physicians, laboratory directors, and for health authorities, especially in the lack of access to COVID-19 cell culture that can determine for these unique patients if they do have functioning infectious viral particles or just residual RNA. Again, and based on the aforementioned studies, one can most likely interpret that the PCR in this situation is picking up specific segments of the nucleic acid/residual nucleic acid of an inactive virus and cannot be equated to an infectious organism. In this situation, resorting to other tests such as the rapid antibodies and/or antigen detection tests would be warranted in helping resolve this problem taking into consideration the overall clinical history and current situation of the individual.

Testing approach and algorithm

Testing for COVID-19 virus is a two-step process, involving first a screening assay for sarbecovirus Subgenus (both SARS virus and COVID-19 virus), and if positive followed by a confirmatory assay for COVID-19 virus only.

The best time to test a COVID patient using a molecular assay is early in the course of disease. In symptomatic COVID patients, SARS-CoV-2 viral RNA can be detected about 1 day prior to symptom onset and remains detectable at high levels for about 6-7 days. Then it substantially decreases to negligible levels after 10 days post symptom onset, and typically does not represent infectious virus, though PCR can remain positive for sometime due to its high sensitivity in detection of nonviable genetic particles of a dead virus. Retesting is advised for initially negative PCR patients with a deteriorating respiratory clinical course consistent with COVID-19 infection and have had exposure to a COVID-19 positive individual [22]. Suspected patients with repeated negative PCR testing, up to 3 times at least 24hrs apart in an upper respiratory specimen, should be tested with an alternative specimen type. Differences on viral loads between specimen sources and the sensitivity of the assays were detected in multiple studies [16,21].

Interpretation of results

The differences in the performance of the molecular test protocols are affected greatly by the mismatches that are likely to arise from primer design rather than by virus mutation and these are mainly Charite Germany *RdRP* and Japan NIID *N*-gene [https://primerscan.ecdc.europa.eu/?assay=Overview,4/28/2020, www.eurosurveillance.org].

Combination of PCR results in both screening and confirmatory genes in different protocols have led to increased detection and specificity [25-27].

A load result between 0 and 40 can be obtained, and this is called the Ct value or threshold cycle. If a sample

has Ct of over 35, the viral load is low. The level of Ct correlates to disease severity. According to the WHO accepted protocols there is no clear standardized Ct threshold used and there should be two positive genes in order to report samples as COVID-19 positive. In one study, Leiberman et al. assessed the performance characteristics of five separate molecular assays for the detection of SARS-CoV-2. They showed 100% sensitivity and specificity for all samples with high viral load (Ct < 35). Inconclusive/discordant specimens had low viral titers (Ct > 37). A combination of the two genes resulted in better detection of the positive samples especially of high Ct [12].

A recent multicenter study that compared the Ct values in relation to different target genes, showed that E target had lower Ct values than the *N2* and *RdRp* targets, while the *RdRp* target was consistently the least sensitive with NPA of 74%. The combination of *E* and *N2* targets provided the highest sensitivity across the range of specimen types tested, and therefore the *RdRp* target was excluded in the EUA version of the test [28].

Testing at Rafik Hariri University Hospital (RHUH)
At RHUH, the main governmental CoVID-19 designated center in Lebanon, COVID-19 testing is performed using primers sequences and probes separately of the COVID-19 virus. These sequences are directly purchased from TIBMol BIOL or through commercial companies such as Roche (LightMix® - Roche Diagnostics) adapted for the Charité Germany protocol. [https://www.who.int/who-documents-detail/molecular-assays-to-diagnose-covid-19-summary-table-of-available-protocols ; ref-005-procurement-lab-request-list.pdf, www.who.int › ref-005-procurement-lab-request-list].

Around 20,000 tests were performed as of 27-5-2020. False negative and false positive results, in this test and others, can be expected during high or low viral prevalence, respectively. However, to ensure reliability of testing, the WHO recommendation in random confirmation of 30% among positive specimens is followed. Also, all positives for *E*- gene are repeated twice with a confirmatory test using the German protocol that targets *RdRP* gene. Positive results are reported based on the WHO recommendations if both the *E* and *RdRP* genes reveal positive results. E-gene results of Ct > 35 rarely displayed positive results for the *RdRP* confirmatory gene. Concerning clinical classification of cases based on Ct values, this aspect remains pending.

In conclusion on molecular testing
Molecular assays, to-date, are the standard reference tools in use to diagnose and confirm COVID-19 infection in symptomatic or asymptomatic individuals. However, their limitations include: requirement of sophisticated equipment, need of special training, complicated assay procedures and use of dedicated reagents. Such complex requirements prompted the search for other diagnostic modalities such as antigen-based and antibody-based detection

ANTIGEN DETECTION-BASED DIAGNOSIS

Background-relevance
Antigen detection-based diagnosis of infectious etiologies utilizes different assays to detect and identify the etiologic agent. Like molecular assays which target detection of specific nucleic acid sequences compatible with the virus in the respiratory specimens, antigen detection assays are another approach used to detect parts (antigenic epitopes) of the novel COVID-19 virus as an indicator/marker of the viral infection in the same type of specimens. They are similar to PCR in utilization purposes of detecting new cases. However, compared to molecular assays, antigen detection assays don't need expensive machines, faster in TAT (provide yes-or-no-results on the spot), cheaper and easier to perform, but their sensitivity and specificity still need fine tuning to match that of the PCR [4-6,29].

Antigen-based detection tests and formats
To date, a couple of in-vitro diagnostic kits for COVID-19 antigen detection were developed and commercially introduced in the market based on different formats of testing, with or without EUA from FDA. The antigen detection assays are mainly based on either lateral flow (LF) immune-chromatography or enzyme-linked immunosorbent assays (ELISA) regarding COVID-19 testing, primarily testing the antigen in respiratory specimens.

Lateral flow (LF) rapid diagnostic test (RDT)
The LF RDT is based on Antigen (Ag)-Antibody (Ab) binding. The test device includes a well for sample dispensing, and a paper-like nitrocellulose membrane composed of two lines: a control line that is coated with gold nano-particle-polyclonal anti-human globulins conjugates (assure test validity), and a test line that is coated with specific capture Abs [30]. The TAT of these tests ranges between 10-30 minutes.

Commercial LF kits (qualitative) are being marketed. Examples of these include: "COVID-19 Ag GICA Rapid" kit (manufactured by PCL, Korea) and claiming an accuracy of 85%. Another Korean kit is the CE (certification by European Union and Economic Area) – marked "Biocredit COVID-19 Ag" (manufactured in Korea by RapiGEN, Inc.) claiming a sensitivity of 92% and a specificity of 98%, and a CE-marked kit "BioEasy Diagnostic kit

for 2019-Novel Coronavirus (2019-nCoV)" (manufactured by Shenzhen BioEasy Biotechnology Co., China), claims to have a sensitivity and a specificity of 91.72% and 100%, respectively. Another model for LF is the CE-marked Belgian kit "COVID-19 Ag Respi Strip" (manufactured by CORIS BioConcept - Belgium) utilizes LF in dipstick. It is reported to have a viral detectability of 5x10exp3 pfu/mL and recombinant protein detectability of 0.25ng/mL. Moreover, the kit was validated in comparison with RT-PCR on two different populations revealing a sensitivity of 85.7%, a specificity of 100%, PPV of 100%, and NPV of 85.2%. Very Recently (May 11, 2020), the first FDA approval of rapid COVID-19 Ag detection test was granted to Quidel Corporation (San Diego, USA) "Sofia 2 SARS Antigen FIA". The test is based on LF immunofluorescent sandwich assay for the qualitative detection of nucleoprotein (NP) Ag utilizing dedicated Sofia 2 instrument. The claimed sensitivity and specificity were 80% and 100%, respectively, showing no cross reactivity with the common respiratory coronaviruses [https://www.fda.gov/media/137885/download]

ELISA based tests

ELISA is the other format of COVID-19 Ag detection assays which can be qualitative or quantitative. Most available kits are based on "Sandwich ELISA", where Micro-wells are coated with specific monoclonal Ab against viral Ag protein. The sample is added into the wells. If it contains Ag, it will react with the corresponding specific Ab, forming Ag-Ab complex. An enzyme (e.g. alkaline phosphatase, horseradish peroxidase) conjugated with a second Ab specific for the COVID-19 Ag will attach to the complex and the reaction is revealed by a color enzyme substrate. The color absorbance is measured and can be correlated with presence/absence of Ag in qualitative ELISA. Generally, the TAT for this type of assay takes 2-5 hours [5].

Few commercial ELISA kits for COVID-19 Ag detection are released to the market without US-FDA approval. For example, "SARS-CoV-2 Antigen ELISA Kit (DEIA 2020)" (manufactured by Creative Diagnostics-USA), is an example for quantitative ELISA tests that detect COVID-19 Nucleoprotein (NP) Ag. The sample could be human serum or plasma, and the claimed sensitivity of this test is 6.25ng/mL. Another example is the "COVID-19 Antigen ELISA Kit" (manufactured in China by Beijing Kewei Clinical Diagnostic Reagent Inc). It detects the viral Ag of COVID-19 qualitatively in nasal swabs, throat swabs, serum, or plasma samples, claiming a sensitivity of 98.7% and a specificity of 97.1%. Concerning cross reactions among these 7 antigen detection kits, only the CORIS BioConcept and the Biocredit kits noted weak cross reactions with some other coronaviruses.

In conclusion on rapid antigen-based testing

Rapid antigen-based diagnostic assays were introduced in anticipation to be similar in utility to the reference molecular tests, while alleviating their sophisticated and complex limitations. Though the test sensitivity and specificity remain to be refined to avoid false negative results, the rapid antigen testing is of value in helping control viral spread, in decision for returning to work, normalizing life and minimizing the apprehensiveness of individuals, as well as in unlocking mass testing capabilities. However, reliability of their performance remains in need of further validation in correlation with the clinical history.

RAPID IgG/ IgM SEROLOGIC TESTS FOR COVID-19

Introduction

Appropriate and accurate elucidation of the serodiagnostic features and immune responses of COVID-19 remain a priority for researchers as a possible strategy for detection. Mystery surrounding the pathogenesis, clinical and diagnostic features of the virus are attributed to its morbidity and sequelae. Very few guiding reports about the testing strategy are available regarding the laboratory diagnosis of this virus [4-6].

One would assume that infection with COVID-19, like any other infectious etiology, would stimulate the immune response by triggering mobilization of the T and B cells of the immune system, initiating an immune response from both cell-mediated immunity (CMI) and antibodies-mediated immunity respectively. The latter entails the production of specific immunoglobulins (Ig) of the IgM, IgG and IgA classes of antibodies. In the immune response to COVID-19 exposure, the evolution and role of CMI as a diagnostic or determinant of exposure remain unclear. The specific immunoglobulins, however, were reported mainly to be used as immune response indicators of exposure to the virus, and in certain situations can have diagnostic value [31].

Infectious viral dose and antibody response

The exact infectious viral dose (number of viruses) that can cause infection in humans and subsequently lead to the symptomatic or asymptomatic status remains to be determined. The justified rational of using face masks is to prevent or to minimize the infectious dose of the virus, thus allowing the immune response to handle without consequences.

Studies on the timing of antibody production due to infection indicated that it takes days to weeks to be reliably detectable. For example, Zhao et al. reported that in patients with post viral exposure, it took between 8 to 11 days for both specific IgM and IgG to be detected. Moreover, after the onset of symptoms, the positive rates of

detecting specific COVID-19 immunoglobulins (IgM, IgG, IgA) were revealed to range between 77.9% and 92.7% [32].

On the other hand, Guo et al. reported longer time (17-19 days) for the appearance of specific IgG and IgM among patients with acute COVID-19 infection (n = 285) [31]. In addition, they observed three types of seroconversion: simultaneous appearance of IgG and IgM (34%), IgM appearance earlier than IgG (27%), and IgG appearance earlier than IgM (39%). Moreover, they reported that in few cases of asymptomatic infection (n = 7), positive IgG and IgM were detected while the PCR was negative [31]. These thought-provoking findings require further verification since these observations were elicited from a small sample size.

Antigens used in serodiagnostic assays

The basis for most COVID-19 serological assays are on antibody detection against different viral antigens such as: immunogenic spike protein [especially the receptor binding domain (RBD) and/or NP], viral nucleocapsid proteins and developed recombinant antigens. Some of these share homology among other human coronaviruses. So, one has to be familiar with the antigen being used in the assay since difference in seroconversion is noted among these antigens. This is so because the onset of seropositivity was earlier for anti-RBD vs. anti-NP, for both IgG and IgM. In general, earlier seroconversion was seen for IgG vs. IgM for both anti-RBD and anti-NP [31].

Rapid diagnostic tests (RDTs) for antibody detection

To assess the generated humoral immune response, numerous commercial and laboratory-developed RDTs (mostly qualitative) have been introduced. Few products, however, have received FDA's EUA, while others are performing internal validation or lack appropriate ones.

Detailed information can be found through the following links: [FAQs on Diagnostic Testing for SARS-CoV-2.https://www.fda.gov/medical-devices/emergency-situations-medical-devices/faqs-diagnostic302testing-sars-cov-2; and the Emergency Use Authorizations. https://www.fda.gov/medical304devices/emergency-situations-medical-devices/emergency-use-authorizations#covid19ivd305]. Updating the list of FDA approved or pulled out kits is an ongoing process.

These tests are designed to detect and identify different antibody classes (IgG, IgM, IgA or total antibodies) in individuals infected or exposed to COVID-19. Most tests use blood specimens (serum, plasma or whole blood) while few are geared to detect secretory IgA antibodies from saliva [32,33]. Examples of these commercial tests were cited by John Hopkins Center for Health security (found in the link below). It describes and categorizes tests as those approved for diagnostic use in the USA (n = 7), for diagnostic use in other countries (n = 9), for research or surveillance purposes only (n = 34), and tests that are still in development (n = 15).
[http://www.centerforhealthsecurity.org/resources/COVID-19/Serology-based-tests-for-COVID-19.html]

In the USA, the FDA granted EUA to tests, enabling their use in diagnostic laboratories. So far, only one test was granted approval by the USA FDA, namely the Cellex rapid, a lateral flow IgG and IgM test, where results are available in 15-20 minutes, once the blood is processed.

The main testing formats of these serodiagnostic tests are based on immunochromatographic LF immunoassay (also used as point of care test), ELISA, and chemiluminescent immunoassays (CLIA). These have rapid turnaround time (TAT), being cheaper and less complex to perform than the molecular tests, but not in lieu of the molecular tests [31,34].

ELISA antibody detection immunoassay

The ELISA test is similar in its procedure to that described in the antigen detection section above. It differs in that the micro-wells would be coated with specific Ag, and the enzyme is conjugated with a secondary Ab against the specific antibody being tested for in the patient's serum [5].

According to Roche, their antigen is the NP because it "provided the best specificity with a collection of pre-pandemic specimens." They say their upcoming package insert will state sensitivity of > 95% and specificity of 99.8%. It is an automated, 18 minute assay and is sold in packs of 200 tests. [https://www.roche.com/media/releases/med-cor-2020-05-03.htm].

Lateral flow format for antibodies detection

The rapid (10-15 minutes) LF test is similar in its procedure as that described under the antigen detection section above. However, instead of COVID-19 Abs being used, specific COVID-19 viral Ag proteins are coated so that the antibody in the patient sample (serum, plasma or whole blood), if present, would bind/react with the antigen forming Ag-Ab colored complex at the IgG, or IgM, or both lines and the control line [5].

Examples of EUA FDA approved automated assays include:

The Abbott SARS-CoV-2 IgG test detects COVID-19 IgG, qualitatively, in serum and plasma specimens based on using the Architect instruments based on chemiluminescence microparticle immune-assay, using microparticles precoated with COVID-19 NP Ag. The sample is incubated with microparticles precoated with specific

COVID-19 NP Ag. A conjugate anti-human IgG labeled with acridinium is added. Substrates (pre-trigger & trigger) are then added to yield chemiluminescence which reflects presence/absence of IgG. The claimed sensitivity for this kit is 100% at day 17 after symptom onset and day 13 after PCR positivity, and the specificity is 99.90%. It is CE-marked and has received FDA-EUA and has a TAT of about 29 minutes [35].
[https://www.fda.gov/medical-devices/emergency-situations-medical-devices/eua-authorized-serology-test-performance]

The Roche Elecsys Anti-SARS-CoV-2 assay uses Cobas instrument based on sandwich electrochemiluminescence for the qualitative detection of COVID-19 Ab in serum and plasma against NP Ag. The sample is mixed with two biotinylated specific recombinant Ags, one is labelled with ruthenium element and the other is unlabeled to form a complex. Subsequently, streptavidin-coated magnetic microparticles are added so that the complex becomes bound to solid phase via interaction between biotin and streptavidin. If positive for Ab, chemiluminescent emission is detected. The claimed sensitivity for this kit depending on days of onset of symptoms is 65.5% (0-6 days), 88.1% (7-13 days) and 100% (≥ 14 days), whereas the claimed specificity is 99.8%. It received FDA-EUA and has a TAT of about 18 minutes. [https://www.roche.com/media/releases/med-cor-2020-05-03.htm].

Cross reactivity

False positive COVID-19 testing was estimated to be around 2%, generated by antibodies present due to past or present infection with other human coronaviruses strains such as coronavirus HKU1, NL63, OC43, or 229E [36].

Sensitivity and specificity

A wide variation in the accuracy of sensitivity and specificity rates were reported among the marketed serodiagnosis RDT kits. For example, among 14 commercial kits manufactured in China, Korea and other countries that were proposed from vendors to AUBMC in Lebanon, the claimed sensitivity and specificity for IgG were 95%-100% and 85%-100%, respectively, and for IgM 88%-98% and 85%-100%, respectively. In the document from Johns Hopkins, it was noted that serology tests in development have a range of sensitivity (87% to 93%) and specificity (95% to 100%) [5]. However, in an interview with Embed, Dr. Gary Procop at Cleveland Clinic reported lower sensitivity (85.2%) for the ID Now kit based on testing 239 specimens known to contain the coronavirus. This is unacceptable as 14.8% of the tested patients would be called negative. More comforting for use, especially for accredited laboratories by the College of American Pathologists, is the first FDA approved RDT by Cellex which has a sensitivity of 93.8% and a specificity of 95.6%. [https://www.centerforhealthsecurity.org/our-work/publications/developing-a-national-strategy-for-serology-antibody-testing-in-the-US].

In the link below, FDA has summarized the expected performance characteristics of 11 serologic assays granted an EUA, assuming a prevalence of 5% for PPV and NPV calculations.
[https://www.fda.gov/medical-devices/emergency-situations-medical-devices/eua-authorized-serology-test-performance]

However, FDA is keeping an ongoing dynamic revision and update about commercial manufacturers of antobody tests: list of antibody tests.

Utility and potential use of RDTs

The utilities of the RDTs are essentially defined by the evolution and profile of the immune response post infection with COVID-19. Scattered information about the utility of RDTs were cited by different individuals, universities and societies [4-6].

One should keep in mind that these RDTs should be supported by the molecular PCR in many situations to achieve proper interpretation of results. Clarification of the different aspects, potential utility and facilitation of RDTs include:

- Assessment of community seroprevalence, contact tracing, surveillance and tracking spread of the virus nationwide. This is essential for epidemiologic studies and in defining the size and nature of the epidemic, guiding lockdown, reopening and integrating society decisions.
- Serologic assays are relevant to use when RT-PCR may be falsely negative such as in case of patients presenting to medical care with late complications of disease (viral shedding drops over time) [33]. The suggestion to use both methods concurrently was also noted in retrospective studies from China indicating that some COVID-19 infected patients were PCR negative, yet serology positive [31].
- At a hospital or medical center level, RDTs would be useful to test asymptomatic or pre-symptomatic staff: attending physicians, residents, nursing, as they might play an important role in transmission of infection to the high-risk population. This mass testing ability in a rapid TAT would guide and expedite the consideration of additional prevention measures, cohorting strategies and the decision to remove a suspect COVID-19 patient from isolation [37].
- RDTs would assess healthcare workers (HCWs) for post-infection. Test results can be helpful in decisions pertaining to return-to-work deploy-

ment, assuming there is a protective immunity by potent neutralizing antibodies.

- Identification of immune recovered patients to serve as convalescent plasma donors (based on quantitative antibody assays) for the potential of treating acutely ill patients or to provide passive immunity to non-immune health care workers on the front lines.

Having noted the above utilities of the RDTs, and though they are easy to perform, they require very cautious interpretation of results in correlation with the clinical condition and exposure history. Moreover, and prior to use, the performance characteristics of the test kit need to be properly validated according to established international guidelines.

Immunity - antibody neutralizing activity and dilemma

The serologic RDTs, though introduced to detect and determine IgG and IgM antibodies post infection, information about the ability of these antibodies to impart an "immunity" or protective status is evolving in this favor. Moreover, studies are still needed to learn about the antibody cut-off value, titer, or units associated with protective immunity or how long protective immunity may last.

Recent evidence from in-vivo experimental COVID-19 infected Rhesus Macaque primate (close to humans in their immune system), indicated that the immune response was protective against subsequent re-infection after resolution of a primary infection [38]. Such immune activity can also be reinforced by the in vitro study revealing neutralizing antibodies in sera of patients infected with COVID-19 [39]. Further supporting evidence can be elicited from earlier studies among high percentage (89%) of patients with SARS infection whose sera showed neutralizing antibodies for long duration (2 years) [40]. No doubt, all of these immune protective evidences empower the practical drive to the value of using plasma from recovered patients in the management of COVID-19 infection [41].

Based on the aforementioned evidence, one would wonder about those who question and doubt that these antibodies (recently labelled as "immunity passports") act as a signal of protective immunity against the COVID-19. Does it mean that this virus has a potent and rapid mutational capability to escape these antibodies? Are there different viral strains circulating globally, or is there a rapid deterioration and fading of these antibodies, defying their active persistence to defend against the re-exposure? In addition, one would wonder how would "herd immunity" be defined and achieved. Hopefully, the ongoing studies and research will find rapid answers to settle such difficult and valid questions.

Interpretation and meaning of serologic RDTs results

Testing and interpretation of the sero-RDTs should be done in coordination with the clinical history for proper assessment. This is necessary especially in case needed to advise about self-isolation, quarantine or hospital admission.

- Since these RDTs turn positive for specific COVID-19 IgM/IgG in around 8 to 11 days or more post viral exposure, they can show false negative results prior to this time in patients with symptomatic or early asymptomatic presentation [31]. Thus, this post viral exposure gap/delay in antibody production makes these RDTs not rule out infection during this period. In this situation, follow-up with a molecular diagnostic test should be considered to rule out infection in these individuals [21].
- A reactive/positive anti-COVID IgM antibody indicates recent acute infection or exposure. This warrants PCR testing for confirmation, and if positive can reflect the ability of transmission of the virus. If no symptoms, individuals would require self-isolation with symptoms monitoring. A quarantine or hospitalization would be required, if symptoms start appearing.
- A reactive/positive anti-COVID IgG antibody, indicates history of viral exposure (unknown time of recent or past), and needs to consider self-isolation for 14 days with symptoms monitoring. Referring to PCR if they become symptomatic. Some physicians may advise to determine if this is past (asymptomatic) or recent exposure by performing PCR to confirm. If PCR turns positive it indicates that the person can still shed and transmit the virus. If PCR is negative, it can reflect "immunity" against the virus, indicating asymptomatic or resolution of infection.
- Both IgG and IgM could show reactive/positive results simultaneously, and PCR would be considered especially if a patient needs admission to hospital.
- A nonreactive/negative anti-COVID IgM and IgG indicates either no exposure and no need for PCR, or an early exposure (asymptomatic) if contact is anticipated in a duration of less than 12 days where period during which a delay in antibody formation is expected, thus warranting PCR test to exclude early asymptomatic infection. If the latter turns out negative then no exposure to the virus is determined, while if it turns out positive then this would indicate recent exposure and possibility of trans-

mission of the virus. Bear in mind the possible negative findings due to immunosuppressed patients.

In conclusion on rapid antibody-based testing

Antibody-based testing is essentially targeted to determine the person's exposure to COVID-19 infection and its extent in the community. These rapid assays are also well suited in their diversified utility to help control viral infection and minimize apprehensiveness of individuals. It is of essential essence to take into consideration the need for appropriate interpretation of their results in conjunction with the clinical picture, risk factors of exposure and resorting to molecular assays when warranted.

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COVID-19 PANDEMIC

ESCALATION OF STANDARD PRECAUTIONS DURING COVID-19 PANDEMIC
Review of Electronic Literature and Position Paper

http://www.lebanesemedicaljournal.org/articles/68(1-2)/pandemic4.pdf

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.Moghnieh R, Bizri AR. Escalation of standard precautions during COVID-19 pandemic: Review of electronic literature and position Paper. J Med Liban 2020; 68 (1-2) : 27-42.

ABSTRACT • Introduction : It has been proven that COVID-19 asymptomatic carriers and presymptomatic patients do transmit the virus and potentially infect their contacts and caregivers. International medical and scientific societies, as well as governmental and public health bodies, from all over the globe, have issued recommendations about infection prevention and control measures that should be taken, in addition to the general standard precautions measures, while dealing with hospital patients during this pandemic. In this article, we did an electronic review of the published and posted recommendations in different medical scenarios. Accordingly, we put a position set of recommendations about the precautions that are needed to be taken with all patients when the virus is still circulating in the community from an Infectious Disease specialist perspective. **Methods :** This is a narrative electronic review of the available and latest interim guidelines recommendations, position statements, expert commentaries and opinions issued by international scientific societies, international organizations, governmental bodies and public health authorities from different medical specialties in the United States of America, Canada, United Kingdom, Europe, France, Italy, China, Australia, and Asia Pacific region. We searched PubMed and Google Scholar for articles and written material published in English and French between January 1, 2020, and April 25, 2020. **Results :** Recommendations were retrieved from around 50 documents. We endorse the general recommendations that appear in all reviewed specialties. From an infectious disease specialist perspective, the following should be applied to all patients in healthcare settings: • Triage based on a checklist with the timely updated case definition at the entrance and admission to any health facility ward or service. • Aerosol generating procedures to all patients like tracheal intubation for medical reasons or anesthesia, gastrointestinal endoscopy is preferably done under airborne/contact precautions. • Areas of the hospital where patients potentially would undergo aerosol generating procedures should be adequately ventilated and with negative pressure. • All staff should be trained for donning and doffing personal protective equipment, and well trained regarding infection prevention measures in their respective departments. • Face-to-face consultations especially in the vulnerable at risk population, like immunocompromised patients and pregnant women, should be reasonably minimized along with prioritization and deferral of care as much as possible. • Workforce and personal protective equipment management should become a priority in the planning of care. **Conclusion :** The COVID pandemic has become a turning point in the standard of care in healthcare settings. At least, until the availability of universal vaccination or mortality-reducing therapies, healthcare settings will have to apply additional measures to the classical standard precautions, not only to those infected, but to asymptomatic patients, healthcare personnel and visitors.

Keywords : COVID-19; infection prevention and control; standard precautions

INTRODUCTION

The novel coronavirus and its corresponding infection, COVID-19, has become a global threat to human life and well-being, as well as to the global economy. It is suspected that the outbreak originated in the Huanan sea-food market in Wuhan City, China [1].

Since the beginning of the outbreak in December 2019 which transformed into a pandemic, as declared by the WHO in March 2020, more than 3 million people were infected worldwide, with 185 countries affected in five continents by end of April 2020 [2]. A toll death of 227,000 patients was reported by end of April 2020 [2]. Mortality rate has reached 3% with an infectivity index (R0) of 2.3 [2,3]. Two major factors contributed to the snowball effect of the COVID-19 pandemic: the movement of people in the era of globalization, and the human immune system that is completely naïve to the novel coronavirus.

Due to the unavailability of a vaccine and/or definite therapy, the infection prevention strategies in the community and healthcare facilities were the only ways of mitigation against the pandemic. Accordingly, most of the world became under confinement with people staying at home leading to detrimental consequences globally and to individual countries economies [4]. Ultimately, societies will be forced to apply a deconfinement plan, and people will go back to their normal lives, but, until a vaccine is discovered, approved and used universally, COVID-19 will still be smoldering in the communities and finding its way to hospitals [5]. If firm and optimal precautions were not taken properly, there is a big probability of new waves of the pandemic [6].

One of the most important features of COVID-19, in terms of public health and spread of the disease, is the infectivity of asymptomatic and presymptomatic infected individuals [7-9]. The implications of this fact are tremendous. In order to prevent another wave of the pandemic, major changes in our lifestyles and the community are needed and an escalation of the concept of standard precautions in hospitals is crucial.

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In hospitals, an asymptomatic healthcare worker (HCW) or an asymptomatic infected patient would trigger a superspreading event, spreading the infection to other HCWs and to other patients, when the virus is circulating in the communities, theoretically any admitted patient should be considered as a potential carrier of COVID 19 [7]. In order to prevent these superspreading events in hospitals, respiratory precautions from COVID-19 infections in hospitals should become part of standard precautions [10]. The latter encompass the basic principles of infection prevention and control, which aim at preventing infection transmission via healthcare workers, as well as protecting the healthcare workers themselves from contracting any possible infection [11].

The aim of this article is to review the recommendations of the different medical societies in different specialties, about the additional measures that should be applied empirically in hospitals in the context of the 2020 pandemic. These measures are to complement the basic classical set of standard precautions. It is worth noting that infection prevention and control considerations when dealing with suspect and confirmed cases are outside the scope of this article. Thus, this review deals with the empirical precautions to be taken for all patients during the pandemic, in communities where the virus is still circulating.

Based on this review, we will put a position opinion on the additional precautions that have to complement the standard practice in the different specialties in Lebanese hospitals. That being said, we should all take into consideration the epidemiology of the pandemic in Lebanon, as well as the nature of the health system in Lebanon, and the availability of tests and personal protective equipment (PPE).

METHODS

This is a narrative electronic review of the available and latest interim guidelines recommendations, position statements, expert commentaries and opinions issued by international scientific societies, international organizations, governmental bodies and public health authorities from different medical specialties in the United States of America (USA), Canada, United Kingdom (UK), Europe, France, Italy, China, Australia, and Asia Pacific region. We searched PubMed (MEDLINE) and Google Scholar for articles and written material published in English and French between January 1, 2020, and April 25, 2020.

The included papers and documents were either published in peer-reviewed journals or on the official websites of the organizations or scientific societies in question. Medical specialties involved were emergency medicine, critical care medicine, anesthesia, endoscopy, dialysis, radiology, oncology, hematopoietic cell transplantation, obstetrics, blood transfusion, and medical laboratory biosafety practices.

Keywords for the search included: COVID-19, SARS-CoV-2, pandemic, triage, screening, personal protective equipment, social distancing, infection prevention and control, hand hygiene, environmental disinfection, negative pressure systems, airborne/droplet/contact precautions, surgical masks, N95 of FFP2/3 respirators, preparedness, organization, contingency plans, management of workforce, etc. Inclusion criteria for the paper or document were the presence of empiric use of infection prevention measures or facility preparedness irrespective of the COVID-19 status of the patients.

All papers detailing infection prevention interventions among COVID-19 suspect or confirmed cases were excluded. The number of selected papers per specialty is illustrated in Figure 1.

RESULTS

One hundred forty-four documents were retrieved from the electronic search that fulfilled the defined criteria. They dealt with infection control precautions in the Era of COVID-19 Pandemic. They belonged to general international societies and to 10 specialty societies or scientific bodies (Figure 1).

Ninety-three documents were excluded according to the exclusion criteria.

Fifty-one documents were included in the review distributed among the different specialties. Below are the recommendations in general and in different specialties (Tables I and II).

Non-speciality organizations or bodies recommendations

Infection prevention and control precautions for suspected or confirmed COVID-19 cases are well known so far [12-14]. However, in view of the possibility of viral transmission from presymptomatic/asymptomatic patients [7-9] and the potential virus persistence in the community, clinicians, healthcare personnel and policymakers, are concerned with the empiric or additional precautions to be applied to all patients regardless their COVID-19 infection status in multiple inpatient care settings. Several international organizations and governmental services including the World Health Organization (WHO) [12, 13], the US Center for Disease Control and Prevention (CDC) [14], the European Center for Disease Control and Prevention (ECDC) [15], and the United Kingdom National and Public Health Services (Public Health England) (PHE) [16] have published general recommendations regarding these additional precautions. All these

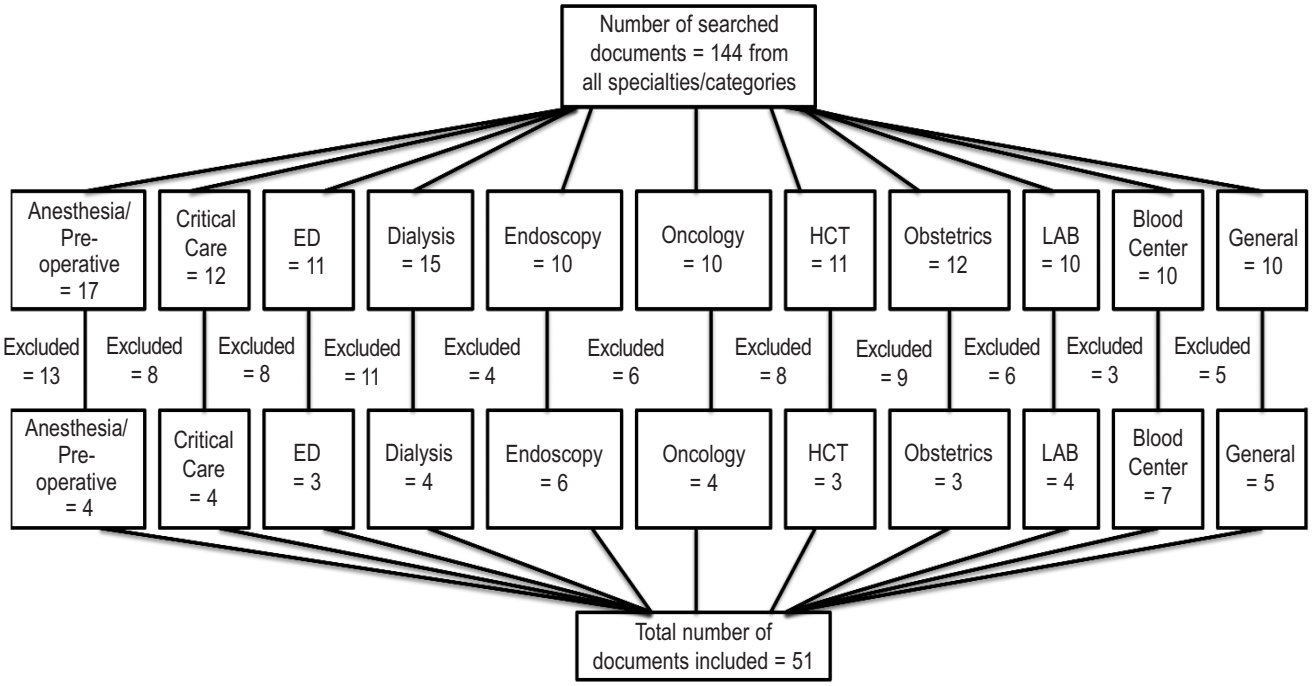

Figure 1. Search results

international organizations have generally agreed on the necessity of applying the following measures to all patients [12-16] (Table I):

1. Triage and assessment of patients presenting to acute care facilities at multiple times and checkpoints (prior to admission, upon admission, during admission, etc.) for fever, upper respiratory tract infection signs and symptoms, as well as contact with COVID-19 suspect/confirmed cases according to predefined checklists.
2. Implementing standard precautions, the minimum infection prevention practices that are designed to both protect the healthcare personnel and prevent them from spreading the infection [11]. These include hand hygiene, use of personal protective equipment according to risk assessment, respiratory hygiene, sharps safety and safe injection practices, proper use of sterile equipment, environmental surfaces cleaning and disinfection, safe handling and cleaning of soiled linen and waste management [11].
3. Social distancing considerations and design modifications inside the facility including distancing 1 to 2 meters between patients in waiting rooms and common treatment areas, separate units for care and separate equipment for COVID-19 patients, organization and proper labeling of entrances, check-in points/patient desks, waiting areas, hallways, patient transport routes, as well as posting infection prevention alerts where necessary.
4. Education and systemic training on in-hospital infection control measures for all healthcare personnel (donning and doffing PPE, hand hygiene, safe use and decontamination of medical equipment, environment cleaning and disinfection).
5. Implementing daily staff screening for COVID-19 for symptoms and/or temperature checks and establishing clear stay-at-home/sick leave policies and return-to-work guidelines.
6. Rigorous patients' visitors and companions policy restricting unnecessary access to the facility to the minimum necessary levels.
7. Crisis planning and management of the workforce (including privileging virtual meetings/continuous education/e-learning/telecommunication between personnel, organization of work schedules, etc.)
8. Judicious management of the resources (mainly for PPE) (prioritization of use, stock management, prolonged use and recycling).

Other special measures were recommended individually by the formely mentioned organizations to include the following (Table II):

1. Prioritization of care and deferral in case of non-urgent procedures as per the WHO [12] and CDC [14] guidelines.
2 Following contact and droplet precautions for all non-aerosols generating (non-AGP) procedures in patient care using proper PPE (disposable head covers, gloves, fluid-resistant long-sleeved gowns, shoe covers, goggles, full-face shields and surgical masks) as per the ECDC [15] and PHE [16] guidance.

TABLE I GENERAL INFECTION PREVENTION AND CONTROL PRECAUTIONS IN ACUTE CARE FACILITIES DURING THE COVID-19 PANDEMIC AS RECOMMENDED BY INTERNATIONAL ORGANIZATIONS AND SOCIETIES FROM DIFFERENT MEDICAL SPECIALTIES

Measures	General/ Specialty nonspecific	Anesthesia, Preoperative unit	Intensive Care Unit	Emergency Department	Dialysis	Endoscopy	Oncology	Hematopoietic cell transplantation	Obstetrics/ Delivery	Radiology/ Imaging	Clinical Diagnostics/ Laboratory Biosafety (specimen handling/ processing)	Blood Centers/ Banks
Patient triage/screening at different checkpoints/times based on checklists for fever, respiratory signs and symptoms, other physical examination, and contact with COVID-19 suspect/confirmed cases	- PHE [16] - WHO [12,13] - CDC [14] - ECDC [15]	- Greenland J. et al. [21] - CSA/CAA [22]	- - ANZICS [20] - WHO [12] - CDC [14]	- ACEP [17] - EUSEM [19]	- CDC [33] - ASN [34] - ERA/EDTA [35] - NICE (NG160) [36] - ISN [37]	- APSDE [25] - CAGEF [26] - ESGE/ ESGENA [27] - BSG [28] - AGA, ASGE [29,30] - WEO [31] - Repici A. et al. [32]	- ASCO [40] - ESMO [41] - NCCN [43] - NICE (NG161) [42]	- BSBMTCT [44] - NICE (NG164) [45] - EBMT [46]	- CDC [14] - ACOG/ SMFM [38] - RCOG [39]	- *Radiology* SEP [47] - BSTI [48] - SFR/SF2H [49]	Not applicable	- CDC [50] - FDA [51] - CSBT [52] - WHO [53] - APBN [54] - NHS [55]
Standard precautions including the use of standard appropriate personal protective equipment (PPE), hand hygiene, respiratory hygiene, equipment use/ decontamination & surface cleaning/disinfection between cases	- PHE [16] - WHO [12,13] - CDC [14] - ECDC [15]	- Greenland J. et al. [21] - CSA/CAA [22] - ASA/APSF [23] - AAGBI [24]	- - ANZICS [20] - WHO [12] - CDC [14]	- ACEP [17] - IFEM [18] - EUSEM [19]	- CDC [33] - ASN [34] - - ERA/EDTA [35] - NICE (NG160) [36] - ISN [37]	- APSDE [25] - CAGEF [26] - ESGE/ ESGENA [27] - BSG [28] - AGA, ASGE [29,30] - WEO [31] - Repici A. et al. [32]	- ASCO [40] - ESMO [41] - NCCN [43] - NICE (NG161) [42]	- BSBMTCT [44] - NICE (NG164) [45] - EBMT [46]	- CDC [14] - ACOG/ SMFM [38] - RCOG [39]	- *Radiology* SEP [47] - BSTI [48] - SFR/SF2H [49]	- WHO [56] - CDC [14] - PHE [16] - ABSA [57]	- CDC [50] - FDA [51] - CSBT [52] - WHO [53] - APBN [54] - NHS [55]
Social distancing considerations and design modification inside the facility (including separate units for care & equipment, entrances, check-in points, waiting areas organization, hallways, patient transport routes, posted infection prevention visual alerts)	- PHE [16] - WHO [12,13] - CDC [14] - ECDC [15]	- Greenland J. et al. [21] - CSA/CAA [22] - ASA/APSF [23] - AAGBI [24]	- - ANZICS [20] - WHO [12] - CDC [14]	- ACEP [17] - IFEM [18] - EUSEM [19]	- CDC [33] - ASN [34] - - ERA/EDTA [35] - NICE (NG160) [36] - ISN [37]	- APSDE [25] - CAGEF [26] - ESGE/ ESGENA [27] - BSG [28] - AGA, ASGE [29,30] - WEO [31] - Repici A. et al. [32]	- ASCO [40] - NICE (NG161) [42]	- BSBMTCT [44] - NICE (NG164) [45] - EBMT [46]	- CDC [14] - ACOG/ SMFM [38] - RCOG [39]	- *Radiology* SEP [47] - BSTI [48] - SFR/SF2H [49]	- WHO [56] - CDC [14] - PHE [16] - ABSA [57]	- CDC [50] - FDA [51] - CSBT [52] - WHO [53] - APBN [54] - NHS [55]
Patient visitors/companions policy	- PHE [16] - WHO [12,13] - CDC [14]	Not mentioned in reviewed documents	- WHO [12] - CDC [14]	- ACEP [17]	Not mentioned in reviewed documents	- ESGE/ ESGENA [27] - Repici A. et al. [32]	- ASCO [40]	- EBMT [46]	- CDC [14] - RCOG [39]	- SFR/SF2H [49]	Not applicable	- CSBT [52]
Staff education/training regarding infection prevention measures during COVID-19 pandemic (hand hygiene, use of PPE, equipment use/ decontamination, surface cleaning/disinfection)	- PHE [16] - WHO [12,13] - CDC [14] - ECDC [15]	- Greenland J. et al. [21] - CSA/CAA [22] - ASA/APSF [23] - AAGBI [24]	- - ANZICS [20] - WHO [12] - CDC [14]	- ACEP [17] - IFEM [18] - EUSEM [19]	- CDC [33] - ASN [34] - - ERA/EDTA [35] - NICE (NG160) [36] - ISN [37]	- APSDE [25] - CAGEF [26] - ESGE/ ESGENA [27] - BSG [28] - AGA, ASGE [29,30] - WEO [31] - Repici A. et al. [32]	- ASCO [40] - ESMO [41]	- BSBMTCT [44] - NICE (NG164) [45] - EBMT [46]	- CDC [14] - ACOG/ SMFM [38] - RCOG [39]	- *Radiology* SEP [47] - BSTI [48] - SFR/SF2H [49]	- WHO [56] - CDC [14] - PHE [16] - ABSA [57]	- CDC [50] - FDA [51] - CSBT [52] - WHO [53] - APBN [54] - NHS [55]

Daily staff screening for COVID-19 for signs/ symptoms including fever and contact with COVID-19 suspect/confirmed cases according to checklist	- PHE [16] - CDC [14]	Not mentioned in reviewed documents	CDC [14]	- ACEP [17]	Not mentioned in reviewed documents	- ESGE/ ESGENA [27]	- ASCO [40] - ESMO [41] - NCCN [43] - NICE (NG161) [42]	- BSBMTCT [44] - NICE (NG164) [45] - EBMT [46]	CDC [14]	Not mentioned in reviewed documents	Not mentioned in reviewed documents	- CDC [50] - FDA [51] - CSBT [52] - WHO [53] - APBN [54] - NHS [55]
Crisis Planning & Management of the workforce (including virtual meetings/continuous education/e-learning/ telecommunication between personnel, organization of work schedules, etc.)	- PHE [16] - WHO [12,13] - CDC [14] - ECDC [15]	- Greenland J. et al. [21] - CSA/CAA [22] - ASA/APSF [23] - AAGBI [24]	- - ANZICS [20] - WHO [12] - CDC [14]	- ACEP [17] - IFEM [18] - EUSEM [19]	- CDC [33] - ASN [34]	- APSDE [25] - CAGEF [26] - ESGE/ ESGENA [27] - BSG [28] - AGA, ASGE [29,30] - WEO [31] - Repici A. et al. [32]	- ASCO [40] - ESMO [41] - NCCN [43]	- BSBMTCT [44] - NICE (NG164) [45] - EBMT [46]	CDC [14]	- *Radiology* SEP [47] - SFR/SF2H [49]	Not mentioned in reviewed documents	- CDC [50] - CSBT [52] - WHO [53] - APBN [54] - NHS [55]
Management of the resources (mainly PPE) (prioritization of use, stock management, prolonged use and recycling of PPE)	- PHE [16] - WHO [12,13] - CDC [14]	- ASA/APSF [23]	- - ANZICS [20] - WHO [12] - CDC [14]	- ACEP [17] - IFEM [18] - EUSEM [19]	- CDC [33] - ASN [34]	- ESGE/ ESGENA [27] - AGA, ASGE [29,30] - WEO [31] - Repici A. et al. [32]	- ASCO [40] - ESMO [41] - NCCN [43]	Not mentioned in reviewed documents	CDC [14]	- *Radiology* SEP [47] - SFR/SF2H [49]	Not mentioned in reviewed documents	Not mentioned in reviewed documents

Abbreviations per each category/specialty:

- *General/Speciality non-specific*
  - **CDC**: Center for Disease Control and Prevention **ECDC**: European Center for Disease Prevention and Control **PHE**: Public Health England **WHO**: World Health Organization
- *Anesthesia and Preoperative Unit*
  - **AAGBI**: Association of Anaesthetists of Great Britain & Ireland **ASA**: American Society of Anesthesiologists **APSF**: Anesthesia Patient Safety Foundation **CAA**: Chinese Association of Anesthesiologists **CSA**: Chinese Society of Anesthesiology
- *Intensive Care Unit*
  - **ANZICS**: Australian and New Zealand Intensive Care Society **CDC**: Center for Disease Control and Prevention **WHO**: World Health Organization
- *Emergency Department*
  - **ACEP**: American College of Emergency Physicians **EUSEM**: European Society for Emergency Medicine **IFEM**: International Federation for Emergency Medicine.
- *Dialysis*
  - **ASN**: American Society of Nephrology **CDC**: Center for Disease Control and Prevention **EDTA**: European Dialysis and Transplant Association **ERA**: European Renal Association **ISN**: Italian Society of Nephrology **NICE (NG160)**: National Institute for Health and Care Excellence guideline
- *Endoscopy*
  - **AGA**: American Gastroenterological Association **APSDE**: Asian Pacific Society for Digestive Endoscopy **ASGE**: American Society of Gastrointestinal Endoscopy **BSG**: British Society of Gastroenterology **CAGEF**: Canadian Association of Gastroenterology for Endoscopy Facilities **ESGE**: European Society of Gastrointestinal Endoscopy **ESGENA**: European Society of Gastroenterology and Endoscopy Nurses and Associates **WEO**: World Endoscopy Organization.
- *Oncology*
  - **ASCO**: American Society of Clinical Oncology **ESMO**: European Society for Medical Oncology **NCCN**: National Comprehensive Cancer Network **NICE (NG 161)**: National Institute for Health and Care Excellence guideline.
- *Hematopoietic cell transplantation*
  - **BSBMTCT**: British Society of Blood & Marrow Transplantation **EBMT**: European Society for Blood and Marrow Transplantation **NICE (NG164)**: National Institute for Health and Care Excellence guideline.
- *Obstetrics/Delivery*
  - **ACOG**: American College of Obstetricians and Gynecologists **CDC**: Center for Disease Control and Prevention **RCOG**: Royal College of Obstetricians and Gynaecologists **SMFM**: Society for Maternal Fetal Medicine.
- *Radiology/Imaging*
  - **BSTI**: British Society of Thoracic Imaging **SEP:** Scientific Expert Panel **SF2H**: Société Française d'Hygiène Hospitalière **SFR**: Société Française de Radiologie
- *Clinical Diagnostics/Laboratory Biosafety (specimen handling/processing)*
  - **ABSA**: American Biological Safety Association **CDC**: Center for Disease Control and Prevention **PHE**: Public Health England **WHO**: World Health Organization
- *Blood Centers/Banks*
  - **APBN**: Asia Pacific Blood Network **CDC**: Center for Disease Control and Prevention **CSBT**: Chinese Society of Blood Transfusion **FDA**: US Food and Drug Administration **NHS**: United Kingdom National Health Service **WHO**: World Health Organization

3. For aerosol generating procedures (AGP), the application of airborne, droplet, and contact precautions becomes necessary with suitable PPE [disposable head covers, beard covers, gloves, fluid-resistant long-sleeved gowns, waterproof aprons, shoe covers, goggles, full-face shields, and N95 or filtering face piece (FFP2/FFP3) respirators or powered air-purifying respirator (PAPR)], in addition to the use of special areas of care with negative pressure systems and specific ventilation requirements (anesthesia and operating rooms) as per PHE recommendations [16].

Recommendations that are specific to individual departments or services (Table II)

Emergency department

Healthcare teams in emergency departments (ED) are in the front-line in this pandemic, in terms of identification and early management of potential COVID-19 cases. Early identification and immediate isolation of cases are cornerstones for preventing spread of the infection in the hospital, and this is based on active triage according to a checklist based on the latest local case definition of COVID-19 infection [17-19].

Several international societies of emergency physicians from all over the world including the US and Europe recommended applying the general measures outlined in the previous section of this paper, in order to minimize the impact of this virus, in line with the CDC, ECDC, and WHO (Table I) [12,14,15]. These societies also recognize that emergency care systems in different regions and countries around the world will vary in their capacity to respond to a surge of cases.

There is also a specific set of measures to be considered precisely in ED. It is worth relisting triage because it is the most important measure in ED. PPE procurement management and avoiding PPE supply shortage, organization of workflow through managing staff shortage and absenteeism should both be among the pillars of the ED management plan [17-19]. Adequate PPE include N95 respirators, surgical masks, eye and face protection, gowns, and gloves.

ED clinicians and healthcare personnel should be empirically wearing surgical masks and applying droplet and contact precautions at all times irrespective of the patient's COVID-19 status [17]. Airborne precautions are empirically applied only when performing aerosol-generating procedures irrespectively, whether the patient is known or suspected for COVID-19 infection [17].

All patients should be wearing facemasks or facecloths when presenting to emergency departments; if not, they should be provided with facemasks at triage to put on during their stay in ED [17].

Other measures to protect the staff and preserve hospital capacity are through implementing telemedicine where possible and prioritization of care such as transferring patients not requiring hospitalization to outpatient care [18].

A functional redesign of the emergency department to provide adequate ventilation in all the areas to receive any patient irrespective of COVID-19 screening status is recommended by EUSEM [19].

Critical care medicine

During the pandemic, critical care teams should have a low threshold for COVID-19 suspicion. Position statements and interim guidance of international societies of critical care medicine have emphasized the importance of applying the aforementioned general precautions related to facility preparedness, logistics/surge capacity, triage, communication and protection of the workforce (Table I) [14,16,20].

Irrespective of the COVID-19 screening status in critically ill patients, supplementary measures include the necessity of adequate ventilation where separate room ventilation is recommended as well as negative pressure systems in the dedicated areas of care, where potential airborne generating procedures are performed. Droplet/contact precautions are used for all patients if their COVID status is not known [14,16,20]. In case of AGP, airborne precautions are employed (Table II) [14,16,20].

Preoperative and anesthesia units

International societies of anesthesiologists from the United States, United Kingdom and China have unanimously recommended applying the same measures mentioned in the general section for all patients entering the preoperative units or requiring urgent surgeries [21-24]. They included patient triage and risk assessment with deferral of surgeries if possible in case the patient has COVID-19 symptoms, the use of standard precautions, staff education and training, crisis management simulation and emergency planning, the organization of workflow, facility unit redesign to cope with the current situation and minimize traffic in and out areas of dedicated care, in addition to proper use of resources, especially in case of shortage of PPE supply (Table I) [21-24].

There are additional recommendations specific to patients undergoing general anesthesia with endotracheal intubation (Table II). Each patient should be considered a potential carrier of SARS-CoV-2 and dealt with accordingly. Subsequently, an escalation of standards of practice during airway management is necessitated in all patients to reduce exposure to secretions [21-24].

Healthcare workers should empirically use PPE that is appropriate for aerosol-generating procedures when

working near the airway with all patients, including disposable head covers, beard covers, gloves, fluid-resistant long-sleeved gowns, waterproof aprons, shoe covers, goggles, full-face shields and N95 or FFP2/FFP3 respirators or PAPR) [21-24].

Videolaryngoscopy is to be used for intubation to distance oneself from the airway [24]. Oral or tracheal suction should be performed with a closed suction system after intubation [21-24].

Endoscopy services

Several scientific societies of gastroenterology and gastrointestinal endoscopy from the US, Canada, UK, Europe, Asia-Pacific region and others have issued their own interim guidelines, joint statements, and expert commentaries regarding the management of endoscopic procedures during the COVID-19 pandemic [25-32]. In addition to the general recommendations (Table I), which are in line with those of the other specialties, further mandatory precautions should be empirically implemented, irrespective of the COVID-19 screening status (Table II) [25-32].

During rapid and high viral transmission in the community, most societies recommend postponing elective and non-urgent endoscopies, whereas urgent endoscopies are performed by a cohort trained team of staff to minimize concomitant exposure [25-32].

Whenever possible, all patients entering the gastrointestinal (GI) endoscopy unit should wear respiratory protective equipment (surgical mask) [27,32].

The European Society of Gastrointestinal Endoscopy recommends using telemedicine for follow-up after care, and contacting patients at 7 and 14 days after endoscopy to inquire about any new COVID-19 diagnosis, or development of COVID-19 symptoms [27].

Regarding the use of appropriate type of PPE during endoscopy procedures, it depends on the risk of generating aerosols.

All societies recommend using airborne/droplet/contact precautions empirically in upper GI endoscopy and bronchoscopy [25-32].

As for lower GI endoscopy, all societies recommend droplet/contact precautions in lower GIE, regardless of the COVID-19 status [25-28,31,32] except the American Gastroenterological Association (AGA) and American Society of Gastrointestinal Endoscopy (ASGE) that consider it as high risk, thus strictly necessitating airborne precautions [29,30].

All societies warrant using negative pressure systems for high risk and aerosol generating procedures in patients with respiratory symptoms and those who are suspect or confirmed cases [25-32]. For any patient undergoing a GIE regardless of the COVID-19, the empiric use of negative pressure systems has not yet been recommended by any scientific society.

Dialysis

Nephrology societies and scientific experts from the US, UK, Italy and Europe similarly shared the aforementioned general recommendations of societies from other medical specialties for mitigating the risk of COVID-19 [33-37].

Among these recommendations, it is worth emphasizing the importance of screening patients upon presenting to the dialysis unit for respiratory symptoms and fever, not to mention similar daily screening of healthcare workers in the unit [33-37].

In addition, nursing and medical staff working in dialysis rooms should follow droplet and contact precautions through wearing surgical masks, protective glasses, and disposable gloves with all patients [33-37]. Surgical masks should be changed every 4 to 6 hours, according to type and producer's instructions [37].

In areas of high COVID-19 prevalence, further testing with COVID-19 polymerase chain reaction is advised in dialysis patients [35]. In these settings as well, dialysis patients should be instructed to self-quarantine on non-dialysis days, to minimize any possible contact with potential carriers.

Generally speaking, waiting areas in dialysis treatment areas should be well aerated or have adequate ventilation, in order to clear droplets containing viruses from the air [35].

Obstetrics

Regarding obstetric and delivery services, scientific societies from the US and UK share the general recommendations we previously discussed (Table I) [14,38, 39].

In particular, pregnant women and their birth partners are instructed about hand and respiratoty hygiene [14, 39]. They are advised to wear face masks when coming to the delivery suite [14,39].

In high prevalence areas only, the American College of Obstetricians and Gynecologists recommends additional testing strategies because of the potential for asymptomatic patients presenting to labor and delivery units [38].

As per the *Royal College of Obstetricians and Gynaecologists*, maternity services should offer a combination of telemedicine and face-to-face consultations for antenatal and postnatal care (Table II) [39].

Visitors/birth partners are screened for symptoms and are instructed to only visit the patient room and should not go to other locations within the facility, including any newborn nursery [14,39].

TABLE II SPECIFIC INFECTION PREVENTION AND CONTROL PRECAUTIONS IN ACUTE CARE FACILITIES DURING THE COVID-19 PANDEMIC AS RECOMMENDED BY INTERNATIONAL ORGANIZATIONS AND SOCIETIES FROM DIFFERENT MEDICAL SPECIALTIES

Measures	Anesthesia Preoperative unit	Intensive Care Unit	Emergency Department	Dialysis	Endoscopy	Oncology	Hematopoietic cell transplantation	Obstetrics/ Delivery	Radiology/ Imaging	Clinical Diagnostics/ Laboratoty Biosafety (specimen handling/ processing)	Blood Centers/ Banks
Empiric COVID-19 polymerase chain reaction testing/repeat screening considerations irrespective of triage results	-	-	-	-	-	-	- BSBMTCT [44] - NICE (NG164) [45] - EBMT [46]	-	-	-	-
Pre-care quarantine and/or contacting patients after care to inquire about their health status especially any new COVID-19 diagnosis or development of symptoms	-	-	-	- CDC [33] - ASN [34] - ERA/EDTA [35] - ISN [37]	- ESGE/ ESGENA [27] - Repici A. et al. [32]	-	- BSBMTCT [44] - NICE (NG164) [45] - EBMT [46]	-	-	-	- FDA [51] - CSBT [52] - WHO [53] - APBN [54] - NHS [55]
Specfic ventilation and/or negative pressure systems for patient care areas irrespective of COVID-19 screening status	- CSA/CAA [22] - PHE [16]	- ANZICS [20] - PHE [16]	- EUSEM [19] (Adequate ventilation system)	-	-	-	- BSBMTCT [44] - NICE (NG164) [45] - EBMT [46] (Specific ventilation systems/positive pressure system)	-	-	- WHO [56] - CDC [14] - PHE [16] - ABSA [57]	- CSBT [52] (Adequate ventilation not negative pressure system)
Empiric use of Airbome/ Droplet/Contact precautions in aerosol generating procedures irrespective of COVID-19 screening status [Personal protective equipment (PPE): Disposable head cover, hair caps, beard covers, gloves, fluid-resistant long-sleeved gowns, waterproof aprons,shoe covers, goggles, full-face shields and N95 or filtering face piece (FFP2/FFP3) respirators or powered air-purifying respirator (PAPR)]	- Greenland J. et al. [21] - CSA/CAA [22] - - ASA/APSF [23] - AAGBI [24]	- ANZICS [20] - WHO [12] - CDC [14]	- ACEP [17] - IFEM [18]	- ERA/EDTA [35] For nasopharynx swabs for COVID-19 PCR	*Upper GIE* - BSG [28] - CAGEF [26] - AGA/ASGE [29,30] - Repici A. et al. [32] - WEO [31] - APSDE [25] *Lower GIE* - AGA/ASGE [29,30] *Bronchoscopy* - BSG [28] - CAGEF [26] - AGA/ASGE [29,30] Repici A. et al. [32] - WEO [31] - APSDE [25]	-	-	-	- WHO [56] - CDC [14] - ABSA [57] (In viral isolation procedures)	-
Empiric use of Droplet/Contact precautions in non-aerosol generating procedures irrespective of COVID-19 screening status (PPE: Disposable headcover, hair caps, beard covers, gloves, fluid-resistant long-sleeved gowns, waterproof aprons,shoe covers, goggles, full-face shields and surgical masks)	-	-	- ACEP [17] - IFEM [18] - EUSEM [19]	- CDC [33] - ASN [34] - ERA/EDTA [35] - ISN [37] (Italian recommendation: Surgical masks to be changed every 4-6 h, according to type and producer's instructions)	*Lower GIE* - CAGEF [26] - Repici A. et al. [32] - WEO [31] - APSDE [25]	Type of PPE depends on disease status	- BSBMTCT [44] - NICE (NG164) [45] - EBMT [46]	-	- *Radiology* SEP [47] - BSTI [48] - - SFR/SF2H [49]	- WHO [56] - CDC [14] - PHE [16] - ABSA [57] (In non-viral isolation procedures, use standard laboratory measures)	- WHO [53] - APBN [54] - FDA [51]
Education to patients/ relatives/caregivers	Not applicable	Not applicable	ACEP [17]	- CDC [33] - ASN [34] - ERA/EDTA [35] - NICE (NG160) [36] - ISN [37]	-	- ASCO [40] - ESMO [41] - NCCN [43] - NICE (NG161) [42]	- BSBMTCT [44] - NICE (NG164) [45] - EBMT [46]	- CDC [14] - RCOG [39]	-	Not applicable	- FDA [51] - CSBT [52] - WHO [53] - APBN [54] - NHS [55]

Empiric use of PPE by patients (face masks) or facecloths irrespective of the COVID-19 status	-	-	ACEP [17]	- CDC [33] - ASN [34]	- ESGE/ ESGENA [27] - Repici A. et al. [32]	- ASCO [40] - ESMO [41] - NCCN [43] - NICE (NG161) [42]	- BSBMTCT [44] - NICE (NG164) [45] - EBMT [46]	- RCOG [39]	- *Radiology* SEP [47] - - SFR/SF2H [49]	Not applicable	- CSBT [ ]
Prioritization of care/deferral of procedures in case of non-urgency thus preserving hospital capacity	-	-	- IFEM [18] (e.g. transferring patients not requiring hospitalization to outpatient care)	-	- APSDE [25] - CAGEF [26] - ESGE/ ESGENA [27] - BSG [28] - AGA, ASGE [29,30] - WEO [31] - Repici A. et al. [32]	- ASCO [40] - ESMO [41] - NCCN [43] - NICE (NG161) [42]	- BSBMTCT [44] - NICE (NG164) [45] - EBMT [46]	-	-	-	-
Telemedicine for consultations/ follow-up on patient health status (Minimizing face-to-face consultations)	-	-	- IFEM [18]	-	ESGE/ESGENA [27]	- ASCO [40] - ESMO [41] - NCCN [43] - NICE (NG161) [42]	- BSBMTCT [44] - NICE (NG164) [45] - EBMT [46]	- RCOG [39]	-	-	-

Abbreviations per each category/specialty:

- *Anesthesia and Pre-operative unit*
  - **AAGBI**: Association of Anaesthetists of Great Britain & Ireland **ASA**: American Society of Anesthesiologists **APSF**: Anesthesia Patient Safety Foundation **CAA**: Chinese Association of Anesthesiologists **CSA**: Chinese Society of Anesthesiology.
- *Intensive Care Unit*
  - **ANZICS**: Australian and New Zealand Intensive Care Society **CDC**: Center for Disease Control and Prevention **WHO**: World Health Organization.
- *Emergency Department*
  - **ACEP**: American College of Emergency Physicians **EUSEM**: European Society for Emergency Medicine **IFEM**: International Federation for Emergency Medicine.
- Dialysis
  - **ASN**: American Society of Nephrology **CDC**: Center for Disease Control and Prevention **EDTA**: European Dialysis and Transplant Association **ERA**: European Renal Association **ISN**: ItalianSociety of Nephrology **NICE (NG160)**: National Institute for Health and Care Excellence guideline.
- *Endoscopy*
  - **AGA**: American Gastroenterological Association **APSDE**: Asian Pacific Society for Digestive Endoscopy **ASGE**: American Society of Gastrointestinal Endoscopy **BSG**: British Society of Gastroenterology **CAGEF**: Canadian Association of Gastroenterology for Endoscopy Facilities **ESGE**: European Society of Gastrointestinal Endoscopy **ESGENA**: European Society of Gastroenterology and Endoscopy Nurses and Associates **WEO**: World Endoscopy Organization.
- *Oncology*
  - **ASCO**: American Society of Clinical Oncology **ESMO**: European Society for Medical Oncology **NCCN**: National Comprehensive Cancer Network **NICE (NG 161)**: National Institute for Health and Care Excellence guideline.
- *Hematopoietic* cell transplantation
  - **BSBMTCT**: British Society of Blood & Marrow Transplantation **EBMT**: European Society for Blood and Marrow Transplantation **NICE (NG164)**: National Institute for Health and Care Excellence guideline.
- *Obstetrics/Delivery*
  - **CDC**: Center for Disease Control and Prevention **RCOG**: Royal College of Obstetricians and Gynaecologists.
- *Radiology/Imaging*
  - **BTSI**: British society of Thoracic Imaging **SEP**: Scientific Expert Panel, **SF2H**: Société Française d'Hygiène Hospitalière **SFR**: Société Française de Radiologie
- *Clinical Diagnostics/Laboratory Biosafety (specimen handling/ processing)*
  - **ABSA**: Amercican Biological Safety Association **CDC**: Center for Disease Control and Prevention, **PHE**: Public Health England **WHO**: World Health Organization
- *Blood Centers/Banks*
  - **APBN**: Asia Pacific Blood Network **CDC**: Center for Disease Control and Prevention **CSBT**: Chinese Society of Blood Transfusion **FDA**: US Food and Drug Administration, **NHS**: United Kingdom National Health Service **WHO**: World Health Organizations

Clinical oncology

The COVID-19 pandemic has complicated management of oncology patients, the patients themselves, their caregivers, family members and their unit health. All workers involved in patient care should take extra measures to prevent getting infected and spreading the infection to their vulnerable patient. Several international clinical oncology societies from the US, UK, and Europe have issued the same general interim recommendations mentioned earlier aiming at reducing the impact of the pandemic, where protection of this patient population is the ultimate aim of these approaches [40-43] (Table I).

Besides these common measures, other issues merit mention (Table II). All societies consider the importance of the "risk to benefit ratio" in the choice of management approach with a careful evaluation of the ultimate goal of anticancer therapy and its urgency, based on severity of illness and expected response to therapy [40-43].

Experts recommended privileging the use of virtual consultation and the use of web-based technology for transmitting important information to patients and their caregivers as in instructing them to self-quarantine before and after care, in addition to basics in hand and respiratory hygiene, and the strict use of facemasks when entering the facility regardless their COVID-19 status [40-43].

Another strategy is adapting the therapeutic approaches to reduce face-to-face contact with the immunosuppressed patient whenever appropriate and safe, i.e. when this approach does not compromise patient outcome and prognosis. This can be realized by postponing chemo/radiotherapy if safe, using shorter or fractionated treatment regimens if possible, shift intravenous to temporary oral or subcutaneous anticancer therapy if possible to improve disease control [40-43].

The type of PPE to be used by staff caring for cancer patients should follow standard operating procedures, based on the patients' severity of disease and immunosuppression [40-43].

Hematopoietic cell transplantation (HCT)

As in medical oncology, the essence of management in hematopoietic cell transplantation during this pandemic is protection, focused on patients, their caregivers and families and clinical staff.

Scientific societies from the Europe and UK have issued special recommendations for HCT practice, besides the general precaution measures, outlined at the beginning by all other medical specialties (Tables I and II) [44-46]. Cell transplantation societies recognize that transplant units are aware of the measures needed to prevent acquisition and transmission of respiratory viruses in their units [44-46]. It is crucial that they continue applying them during the COVID-19 outbreak, along with local hospitals along with institutional and national public health recommendations [44-46].

Any planned transplantation, whether autologous or allogeneic, should be reviewed and deferred if possible and non-urgent according to the patient's type of malignancy and status before transplantation [44-46].

Empiric testing for COVID-19 polymerase chain reaction by nasal and throat swabs is required at least 72 hours before starting conditioning irrespective of triage, taking into consideration the carriage of the virus and its potential transmission during the asymptomatic and presymptomatic phases. Testing may vary between different institutions [44-46].

Pre-transplant self-quarantine is necessary for patients and ensuring good hygiene practices for at least two weeks prior to conditioning [44-46]. Instructions regarding preventive measures are given to patients and caregivers and should be supported with written information [44-46].

Allogeneic donors are advised as well to self-quarantine and to practice good hygiene at least 4 weeks prior to donation [44-46]. Donors are screened twice prior to starting conditioning and on the day of donation [44-46]. Donors are contacted 2 weeks post-harvest to determine if they were diagnosed with COVID1-9 or experienced any symptoms suggestive of it [44-46].

After transplantation, patients and their caregivers, if possible, should be managed in strict reverse isolation, in addition to providing them with the proper instructions on how to avoid any contact risk after discharge [44-46]. Healthcare providers should take measures to reduce face-to-face visits through privileging telemedicine for consultation and follow-up [44-46].

Radiology, imaging and diagnostic services

Similar to other specialties, radiology and imaging scientific societies from France, UK and the US recommend the general precautions in their interim guidelines (Table I) [47-49]. Standard operating procedures for this department should be followed. To reduce patient movement between the floors, portable-imaging units should be used wherever possible [47-49].

Where CT is performed, departments may consider dedicated time slots [47-49]. This ensures delivering optimal imaging and treatment while reducing unnecessary movement and congregation of patients within the hospital environment. For this service specifically, the recommended respiratory precautions are the droplet and contact precautions [47-49]. Patients are advised to wear facemasks or facecloths [47-49] (Table II).

Blood donation

Several international societies and organizations including the WHO, CDC, US Food and Drug Administration (FDA) and UK National Health Service (NHS), in addition to specialty blood societies like Asia Pacific Blood Network (APBN) and the Chinese Society of Blood Transfusion (CSBT) issued recommendations to mitigate the potential risk of transmission through the transfusion of blood and blood components [50-55].

Any actions taken to mitigate this risk are considered precautionary, since transmission of respiratory viruses through blood or blood components has never been reported [50-55]. Besides recommendations considered as "general" which are in line with other specialties (Table I), other specific measures are waranted in blood donation (Table II).

Donors should be educated to postpone or refrain from blood donation if they were experiencing COVID-19 symptoms, or were diagnosed as carriers or being infected or had any contact with a confirmed case [50-55]. They must be wearing masks and have hand sanitizers during their visit to the blood donation unit or facility [52].

After donation, facilities should contact the donors to report a subsequent diagnosis of COVID-19 [50-55]. Accordingly, they may wish to consider to quarantine the blood products in such cases [50-55].

The CSBT recommends good air ventilation in donation rooms, through minimizing the use of central air conditioning and disinfecting air outlets at densely populated places after each shift [52].

Regarding infection prevention and control (IPC) precautions among staff, empiric droplet and contact precautions and the usual bloodborne pathogens precautions are requested [51,53,54]. Enhanced infection control measures through using additional PPE such as N95 respirators and double gloving for collection of blood are not currently considered necessary [54].

Medical laboratory biosafety practices for handling and processing specimens

Irrespective of the COVID-19 pandemic, good microbiological practices and standard operating procedures for handling and processing clinical specimens should be followed in all medical laboratories [12,14,56,57]. Individual site- and activity-specific risk assessments should be conducted in each facility to ensure its competence in safely performing the intended tests with suitable risk control measures in place [12,14,56,57].

The WHO, CDC, PHE, and the American Biological Safety Association (ABSA) international recommended some of the general measures mentioned before to minimize the risk of the pandemic (Table I) [12,14,56,57].

These include application of standard precautions as hand hygiene, PPE including laboratory coats or gowns, gloves, and eye protection, as well as universal precautions to be applied by all personnel. The type of PPE should be planned according to detailed risk assessment of each laboratory activity [12,14,56,57].

Safe use, cleaning and decontaminating laboratory equipment, as well as surface cleaning and disinfection should be followed according to standard guidelines [12, 14,56,57].

Redesigning the area of laboratory work should be done if necessary, not to mention posting infection prevention visual alerts and reminders to laboratory personnel [12,14,56,57].

Staff education and training on different IPC measures during COVID-19 pandemic is a must to all medical laboratory workers [12,14,56,57].

Laboratory activities involving handling patient samples (respiratory, blood, and urine), in addition to work involving full-length genomic ribonucleic acid (RNA) should be carried using standard precautions at Biosafety level (BSL) two (BSL-2) [12,14,56,57]. Primary and secondary barriers in BSL2 environment include the following. First, biosafety cabinets should be certified and maintained according to manufacturers' recommendations [57]. The laboratory should also have an adequate ventilation system that provides an inward flow of air and prevents recirculation of air in the same area. Policies and procedures for managing and disposal of infectious waste should be present [57]. The PPE used in BSL2 laboratories include surgical mask, single gloves, gown/lab coat, and eye protection [57].

Procedures involving viral propagation and isolation (high concentrations of live virus) or manipulating large volumes of infectious specimens should be basically performed at BSL-3 [12,14,56,57]. In a BSL3 environment, all infectious material should be manipulated within a specific biosafety cabinet, or other containment devices. Airborne protection PPE is recommended (N95 or PAPR respirators). Waste should be autoclaved before disposal, and the exhaust system must have high efficiency particulate air (HEPA) filtration [57].

Aerosol and/or droplet generating laboratory work should be carried out in Class II biosafety cabinets with additional precautions including droplet precaution PPE like a surgical mask or a splash field, a sealed centrifuge or other physical barriers [12,14,56,57]. N95 of FFP2/3 respirators are not a proper substitute for processing samples in these cabinets when a risk of aerosols/droplet production is present [12,14,56,57]. For decentralized and point of care testing, standard precautions are to be used in the presence of a shield between the patient and the healthcare worker [12,57].

DISCUSSION AND POSITION STATEMENT ABOUT APPLICATION OF EMPIRIC ADDITIONAL IPC MEASURES

Historically, universal precautions were introduced by the CDC in the wake of the Human Immunodeficiency Virus epidemic (HIV) between 1985 and 1988 [58-59]. The aim of these precautions was to prevent transmission of bloodborne pathogens in the hospital setting, since infected patients can carry and transmit HIV, while being asymptomatic. Clinicians are then expected to treat body fluids with precautions. In the turn of the 20th century, the concept of universal precautions was replaced by standard precautions whereby the latter are meant to prevent transmission of bloodborne pathogens and other infectious agents from all sources [11].

In 2020, with the COVID-19 pandemic, an escalation of the concept of standard precautions might be needed. Asymptomatic and presymptomatic individuals can harbor the novel coronavirus in their upper respiratorty tract and can potentially transmit it to others without showing signs of infection [7-9]. Although standard precautions include PPE, specification of which ones to use in which conditions has become a necessity for healthcare personnel during patient care, as long as the novel coronavirus is circulating in the community. Besides these precautions, other preventive measures have to be also considered during the pandemic.

These additional precautions converge all to the basic general principles that were recommended by the CDC, WHO, ECDC, in addition to specific recommendations for certain medical specialties that consider factors like the potential of aerosol production during patient care or the patient immune status.

Based on this review, we recommend additional measures to be taken in hospitals at least until the COVID-19 vaccine is available for widespread use in the country [60]. Before putting any recommendations, we need to consider the local epidemiology of the novel coronavirus, the availability of PPE and viral PCR testing, as well as hospital medical engineering aspects.

RECOMMENDATIONS

Checking for fever

- Every person entering the hospital premises including employees, patients or visitors should be checked for fever, at a distance. Visitors with body temperature above 37.5°C should not be allowed to enter the hospital and are advised to go to ER triage or consult their physicians [14,16].

Patient triage

- All patients admitted to the hospital, as regular cold admission or through ED, should undergo triage based on a predefined checklist to screen for symptoms or signs of COVID-19, or contact with confirmed case or sick respiratory or febrile patients [17-19].
- All patients coming for one-day surgical or medical treatment should be seen in triage to be checked for symptoms, signs or contact history of COVID-19 [14,16,33,29,30,47].
- Suspect cases as per the triage checklist when admitted to the hospital follow the known procedure of admitting such cases [17-19].

Physical distancing [12,14,16,17,29,46,47,54]

- Physical distancing among patients, medical staff, and visitors of at least 1 m should be respected in all waiting areas, whether in clinics, radiology, endoscopy, laboratory waiting areas, as well as and in the "one day" treatment pavilions.
- In waiting areas, suspect or confirmed COVID-19 cases should be isolated in specific, designated, and properly labeled spaces, while wearing surgical masks.

PPE [12-14,16-17,20,29,46-47,54]

- All medical personnel involved in patient care should be trained for proper donning and doffing techniques of PPE.
- All hospitals should have PPE procurement and management plans to avoid shortage of PPE supply.

Facemasks

- *Surgical/medical masks*
  - Healthcare workers should be wearing surgical/medical masks while caring for all patients and specifically those are under droplet/contact precautions with the proper donning and doffing techniques [11-14].
  - All healthcare workers in the ED, and in face-to-face triage rooms should be wearing a surgical/medical mask and a face shield [17-19].
  - Suspect or confirmed COVID-19 cases should wear surgical/medical masks as much as they can tolerate during their hospital stay [17-19].
- *N95 or FFP2/3 respirators*
  - The empiric application of aerosol/contact precautions should be considered while caring for patients in the following situations:
    - Anesthesia requiring intubation [21-24].
    - Upper and lower GI endoscopy [25-30].
    - Bronchoscopy [25-30].
    - Caring for patients on mechanical ventilation.

        - Nasopharyngeal or nasal specimen taking for nucleic acid amplification testing (NAAT) for COVID-19 [35, 57].
    - N95 or FFP2/3 respirator use can be extended to a shift of 6 hours [61]. They should be properly donned and doffed [12-16].
- *Cloth face masks*
    - Cloth facemasks are not PPE [33,34]. Yet their use potentially prevents the spread of the novel coronavirus from asymptomatic carriers to others. They should be worn by [33-34,39,40-42]:
        - Visitors.
        - Hospital employees in case of shortage of surgical masks, when they are in the hospital premises, but not while performing patient care.
    - Cloth facemasks should be donned and doffed according to the standard donning and doffing techniques of medical or surgical masks [12-16].

Hospital staff screening and management of absenteeism [14,16,27,29,30,33,43,53]

- Facilities should implement daily screening tools and/or temperature checks for their staff.
- They should establish clear stay-at-home/sick leave policies and return-to-work guidelines.

Management of the workforce and healthcare workers safety [14,16,27,29,30,33,43,53]

- This should be adequately planned and documented in the hospital policies for an efficient use of workforce.
- It is equally important for preventing exposure through minimizing the number of personnel entering the dedicated areas of patient care.

Environmental cleaning and disinfection [12,14,16,33]

- Thorough environmental cleaning and disinfection should occur between cases using hospital-approved disinfectants.
- It should be applied as per hospital schedules and protocols.

Specific engineering considerations

- Empiric negative pressure and specific air circulation frequency are recommended in the following conditions (other than in designated areas COVID-19 patient care):
    - Areas for endotracheal intubation in ED.
    - Areas for nasopharyngeal specimen collection for COVID-19 testing.
    - Laboratory area for nucleic acid amplification or virus culture.
    - Rooms of patients with COVID-19 that have a high potential of aerosol production.

NAATs

- Besides COVID-19 suspect cases, NAAT (PCR) is empirically recommended for asymptomatic patients in the following situations [44-46]:
    - Blood donors in case they report symptoms within 14 days after donation.
    - Patients planned to undergo HCT at least 72 h prior to conditioning.
    - Allogeneic donors at the medical and repeat at harvest.
    - Cryopreservation donation at the assessment and again at harvest of stem cells or donor lymphocytes.

Patient self-quarantine

- It is recommended in the following situations [44-46]:
    - HCT patients: 2 weeks prior to transplant.
    - Allogeneic donors: 4 weeks prior to transplant.

Telemedicine and prioritization of care [18, 25-32, 39-46]

- It is recommended to minimize face-to-face consultations of immunocompromised patients like cancer patients or pregnant women.
- Organizing the rules of telemedicine, recognizing its limitations and responsibilities, as well as physicians' rights.
- Prioritizing care according to a scale taking into consideration the risk of complications with COVID-19, severity and prognosis of underlying illness especially in patients with neoplastic disorders on chemotherapy or those with rheumatologic diseases on immunosuppresive treatment regimens.

Management of suspect cases

- All suspect patients for COVID-19 should be managed according to specific guidelines, yet this is outside the scope of this paper.

STRENGTHS AND LIMITATIONS

Despite that most of the reviewed documents were issued by international scientific societies and official governmental bodies, they were not all retrieved from peer-reviewed journals. These recommendations were not based on solid evidence-based medicine, rather than on expert opinions. This is inevitable in this early stage of the COVID-19 pandemic, even when the most prestigious journals had expedited publications to spread information about the pandemic. Nevertheless, this is the time where recommendations are most needed in order

to flatten the curve and to prevent the emergence of subsequent epidemic waves.

On the other hand, these infection prevention recommendations are provisional and might be subject to change with time according to the dynamics of the epidemic.

This review would help hospitals in Lebanon update their infection control policies in the pandemic era based on current international recommendations. It would also guide them to prioritize PCR testing, to decide which PPE to use in which situation, to effectively manage workforce, and to apply engineering changes where needed.

CONCLUSION

The novel coronavirus pandemic has stretched our understanding of standard precautions to include additional practices that should be simultaneously applied to all patients, as long as the virus is circulating in the community. Droplet/contact precautions have become part of daily care, and what once was a routine healthcare visit has become a daily exercise of triage and prioritization.

Acknowledgement: None
Funding: None
Conflict of interest: None

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COVID-19 PANDEMIC

STRATEGIES OF A PRIVATE UNIVERSITY HOSPITAL FACING COVID-19 IN LEBANON
Hôtel-Dieu de France Readiness: How Did We Do It?

http://www.lebanesemedicaljournal.org/articles/68(1-2)/pandemic5.pdf

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INTRODUCTION

Since the initial report of the SARS-CoV-2 virus outbreak in the Hubei province of China in late December 2019, the virus has spread across the world leading to over 1 765 000 cases of COVID-19 reported worldwide complicated by 108 000 deaths up to April 11, 2020 [1].

Lebanon has declared its first COVID-19 case on February 21, 2020, and since then the total number of positive cases has risen to reach 619 cases and 20 deaths (as of April 11, 2020) [2].

The speed of spread of the virus in 210 countries with no pre-existing scientific data coupled with media coverage [3] drove Hôtel-Dieu de France Medical Center (HDFMC) of the Saint-Joseph University (USJ) to hasten its organizational procedures and move to the frontlines to face the COVID-19.

HDF, is one of the leader university hospitals of Lebanon, with 430-bed tertiary care and 1600 working personnel. It was the first private hospital to manage COVID-19 patients in Lebanon, the first one being diagnosed on March 8, 2020. The hospital has taken on 78 cases since.

During the course of the COVID-19 pandemic, the key point in the HDF strategy has been to continuously try to anticipate the evolution of the pandemic and determine the optimal plan of action accordingly. The policies of the hospital being:

a. Provide prompt and timely medical management for the infected patients and fatalities reduction.
b. Prevent disease dissemination to hospital employees, patients and the general community.
c. Secure a healthcare pathway for the non-infected patients requiring the services of a general hospital.

Lebanon healthcare system depends on the private system in 80% of the hospitalized cases. Hereafter we describe the response to the COVID-19 challenge at our center. Hôtel-Dieu de France hospital is a private university hospital affiliated to Saint-Joseph University, its volunteer engagement in the war against SARS-CoV2 gives insights on the resilience of the Lebanese medical system against the pandemic.

ADMINISTRATIVE MANAGEMENT CLINICAL PATHWAYS IDENTIFICATIONS & ORGANIZATION

We determined four clinical pathways: emergency room, flu clinic, isolation and respiratory infection ward, and critical care.

Emergency departments

- Triage: Secured nurses with PPE (personnel protection equipment) triaged patients looking for upper respiratory infection (URI) symptoms and fever. A form was filled identifying symptoms and suspicious contacts. Patients fulfilling URI criteria were oriented to a separate zone in the emergency ward where diagnostic procedure were pursued.
- A negative pressure isolation room allowing nasopharyngeal sampling was organized.
- All walk-ins were oriented to the flu center during opening hours 8:00 am to 5:00 pm. Otherwise they were given an appointment for the next day.

Flu clinic

An outpatient area separated from the outpatient clinics was identified. Engineering work transformed this zone in a space under negative pressure. It was conceived as a one-stop shop for the patient including administrative and secretarial office, waiting and exam rooms. Samplings were done for all patients consulting for URI and fever. It was also used for patients follow-up and nasal sampling. All personnel were protected with adequate equipment as recommended by WHO and all patients

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wore masks. Flu clinic was attended only by pulmonary, infectious disease and internal medicine specialists. Medical residents were not allowed in.

A call center attended by volunteer students from Saint-Joseph University was put together. Its purpose was to triage patients, refer and schedule susceptible patients to the flu clinic and answer patient queries.

Pulmonary isolation unit (PIU)

Initially a 16-room unit with single beds was prepared and started admitting patients on March 10.

Nursing staff and aids worked together with one doctor of the following specialties: pulmonary, infectious disease, or internal medicine. This was a closed unit where visits were not allowed and one doctor attended all patients, avoiding back and forth movements in the unit and spare changing PPE. When the occupancy reached 70% another unit was adapted to reach a total of 32 isolation non-intensive care unit (ICU) beds.

A subunit of the PIU was identified as a quarantine unit for COVID-19 positive personnel unable to isolate themselves at home.

Medical intensive care unit (MICU)

Nine beds of the MICU were put on negative pressure in addition to 5 beds in the coronary care unit (CCU) and 8 beds in the surgical ICU; a total of 22 intensive care beds were ready to accommodate COVID-19 patients in case a surge was to happen.

Those units were separated by a lockup. A three-step plan of action was developed, thus (a) transforming the MICU to a COVID-19 ICU, (b) extending the COVID-19 ICU to the CCU and (c) admitting COVID-19 patients in the surgical ICU.

A secured elevator dedicated for COVID-19 patients was identified for patient transfer between the ER and the different inpatient wards.

Laboratories and radiology departments

Our hospital has a joint venture with Rodolphe Mérieux laboratory at the school of pharmacy where reverse transcriptase polymerase chain reaction (RT-PCR) laboratory screenings were done from the start of the Lebanese epidemic after accreditation by the Ministry of Health.

Later during the epidemic, ELISA quantitative serological tracing SARS-CoV-2 IgG and IgM antibodies were put in place at Hôtel-Dieu according to a specific medical protocol.

Imaging: a high-resolution CT scanner was reserved for suspected or confirmed COVID-19 patients with regular cleaning protocol enforced. Eventually a dedicated CT scan for the suspected patients with an isolated path was installed.

Pharmacy

The necessary drugs as per the Medical Task Force protocol (Addendum) were obtained by the pharmacy.

The hospital also developed a laboratory to manufacture hydro-alcoholic solutions which helped us to be autosufficient in this high demand time.

HUMAN RESOURCES MANAGEMENT

Different teams were put in place, including doctors from different specialties. They volunteered to address different issues besides their clinical duties. During a pandemic, a trans-professional cross-functional management is of paramount importance.

- *Epidemiological team*: infectious disease (ID) specialists joined the infection prevention and control (IPC) specialists with the pivotal role of tracking the origin of infection in every positive patient and healthcare worker. Their task was to recommend confinement and testing for whoever was suspected. They played a major role in keeping our staff safe and recommended time of confinement.
- *The Medical Task Force* was formed of physicians specialized in pulmonary and critical care (PCC), infectious disease (ID), internal medicine-clinical immunology (CI) and anesthesiologists (A) with an invited list of experts in the fields of pharmacy, anesthesia, hematology, cardiology and laboratory medicine. A weekly meeting reviewing scientific evidence, updates and medical needs led to recommendations embraced by the whole group. A medical treatment and testing protocol was put together and updated regularly according to the last evidence and the consensus of the board.
- The "crisis unit" was formed by the hospital administration and grouped all stakeholders: medical directors, Medical Task Force representatives, nursing directors, quality directors, human resources, pharmacy and laboratory directors. This unit steered all the administrative decisions mentioned under that section. Logistics, PPE, pharmacy and laboratory needs were all addressed. At some point meetings were held every other day.
- *Caring for the mental health of the medical professionals*: A specialized team headed by the Psychiatry department rounded on the different COVID-19 wards providing counseling and guidance for the healthcare workers on issues like coping with COVID-19 isolated patients in this stressful environment.

CLINICAL MANAGEMENT (Table I)

The Medical Task Force first met on multiple occasions to elaborate on March 11, 2020, the first version of the

TABLE I PATIENT STRATIFICATION AND MEDICAL OF COVID-19 PATIENTS PROTOCOL

Levels	Clinical presentation	Place	Treatment	Considerations
A	Asymptomatic	Home quarantine	Symptomatic	Close monitoring in case of deterioration
B	Mild cough w/o dyspnea No risk factors*	Home quarantine	Symptomatic	Close monitoring in case of deterioration
C	Mild cough w/o dyspnea/ No radiological infiltrates **with** risk factors	Home quarantine	1/ Hydroxycholoroquine 400 mg po q12 (D1) then 200 mg q8 for 7 days **+** 2/ Azithromycin 500 mg PO (D1) then 250 mg PO qd for 4 days **+** 3/ Pitavastatin (Livazo) 2 mg po qd (if patient not on statins) **+** 4/ Zinc (Amplified Zinc ou Immunofort) 2 tabs po qd for 7 days	1) Start treatment empirically before results 2) ECG. If prolonged QTc, no Azithromycin and monitor QTc q 72hrs 3) No steroids or NSAIDs 4) Inform of side effects 5) If on ACE inhibitors or ARB continue and consult cardiologist 6) Cs gynecologist if pregnant
D1	Moderate cough with dyspnea with radiological infiltrates of ground glasses (Rx or CT) **w/o** risk factors (*) : PSI < 71 CURB-65 < 2	Home quarantine (evaluated in 48 h)/ PIU (Pulmonary Isolation Unit)	**Same as C**	1 ➔ 6
D2	Moderate-cough with dyspnea with radiological infiltrates of ground glasses (Rx or CT) **w/o** risk factors (*) PSI > 71 CURB-65 > 2 NB : **SpO2 > 92% and RR < 24/minute**	PIU	**Same as C** **+** 5/Lopinavir 400 mg/ ritonavir 100 mg q12 for 10 days	1 ➔ 6 7/ Liver function tests q 72 hrs 8/ If diarrhea Racecadotril (Hidrasec) 1 tab q 8 hrs Alternative : Smectalia q 8 hrs
E	Moderate cough with dyspnea with radiological infiltrates **with** risk factors (*) PSI > 71 CURB-65 > 2 NB : **SpO2 > 92% and RR < 24/minute**	PIU	**Same as D**	**Same as D**
F	Severe: a. Respiratory: SpO2 < 92% and RR > 24/minutes on room air or O2 > 6l/min for SpO2 > 94% b. Organ failure	MICU	**Same as D** **+** Tocilizumab (Actemra) 8 mg/kg IV 1 dose (max 800 mg) If cytokine release syndrome upon H-score or IL6 > 30 pg/ml	**Same as D** 9/ Monitoring inflammation with ESR not CRP
G	**Same as F** **+** Intubation and mechanical ventilation	MICU	**Same as F** **+** Consider Remdesivir 200 mg D1 then 100 mg daily (compassionate use from Gilead) Or Convalescent plasma transfusion	**Same as F** 10/ Daily liver function tests

D: day NSAIDs: non-steroidal anti-inflammatory drugs ACE: angiotensin converting enzyme ARB: angiotensin II receptor blockers PSI: Pneumonia severity score RR: respiratory rate PIU: Pulmonary Isolation Unit MICU: Medical Intensive Care Unit

* Risk factors: Age > 70 years old Chronic kidney disease (Creatinine clearance < 30 ml/min) or dialysis Heart failure NYHA III or IV Advanced chronic respiratory failure (GOLD > B, GINA > 3, on oxygen, on non-invasive ventilation) Cirrhosis > stage B Diabetes mellitus type 1 Immunosuppression Cancer

medical protocol on the management of COVID-19 patients at Hôtel-Dieu de France. A weekly meeting was organized afterwards to adapt the appropriate management according to the scientific evidence, local possibilities, and board consensus. The meetings also aimed at homogenizing physicians practices, considering the different medical specialties involved and working together to fight the pandemic effects.

The clinical management protocol – at date of submission – addressed the following:

1. Admission criteria to the PIU based on the suspicion of a COVID-19 pneumonia and its severity (Pneumonia severity score > 71 or CURB-65 > 2).
2. Admission/transfer criteria to the ICU.
3. Stratification of the disease severity (from A to G). Treatment customization for each category and gradual increases according to severity went from a mere surveillance to multiple pharmacological treatments and reaching organ support (Cf. Table).
4. Prophylactic anticoagulation: COVID-19 patients have a marked inflammatory syndrome and hypercoagulability. The rate of thrombosis observed is very high. Prophylactic anticoagulation is recommended according to the level of risk:
   - Intermediate risk (BMI < 30): anticoagulation with usual prophylactic dose.
   - High risk (mechanical ventilation/high flow oxygen or BMI > 30): anticoagulation with reinforced prophylactic dose.
   - Very high risk (mechanical ventilation/high flow oxygen with BMI > 30; ECMO; marked inflammatory syndrome; hypercoagulability (fibrinogen > 8 g/L or D-Dimers > 3 μg/ml)): anticoagulation with therapeutic goal.
5. Nutrition: COVID-19 patients should be considered at risk of undernutrition beyond 2 to 3 days, particularly if they are ventilated, infected or have chronic illness. Oral/enteral nutrition should be preferred. It must be started as early as 24-36 hours after admission to PIU or 12 hours after intubation and mechanical ventilation in the MICU. The prone position does not contraindicate enteral nutrition.
   The energy target is 25-27 Kcal/kg/d and 30 Kcal/Kg/d in the malnourished. The carbohydrate-fat ratio should aim 50:50 ratio in ventilated patients with a protein intake of 1.3 g/kg/d.
6. Convalescent plasma: Plasma treatment is reserved for severe and early cases. It is prescribed to the patients with hyperacute (beginning) and biphasic (5-7 days) patterns. Donors must be confirmed diagnoses COVID-19, asymptomatic for at least 10 days, have a neutralizing antibodies titers > 40 with negative tests for: HIV, Hepatitis B and C, syphilis. The critical patient receives 2 consecutive transfusions of 200 mL of ABO compatible convalescent plasma (400 mL in total) on the same day as the donor sample.
7. Specific mechanical ventilation is applied to the acute respiratory failure of COVID-19 patients. Other supportive care including prone position, usage of Cytosob and ECMO (extracorporeal membrane oxygenation) are indicated upon specific protocols in MICU.

CONCLUSION

The support of the hospital management and its leadership, the participation of the different medical teams and nursing involvement are of upmost importance to succeed in our endeavor. Smooth and transparent communication with the different stakeholders helped us put together a fantastic team still working in synchrony after many weeks of epidemics.

Many health structures will be exposed to a rising number of patients with COVID-19 and will therefore have to anticipate and prepare.

Acknowledgement

This work would not have been possible without the unwavering support of our visionary and humanistic administration, namely the Society of Jesus, our president P. Salim Daccache S.J., our director Ms. Martine Orio and all the medical and nursing staffs.

This policy was at the service of humans and for humans in the image of our noblest principles.

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COVID-19 CORONAVIRUS

RAFIC HARIRI UNIVERSITY HOSPITAL PREPAREDNESS
Sharing Initial Experience on COVID-19

http://www.lebanesemedicaljournal.org/articles/68(1-2)/pandemic6.pdf

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Hassoun M, Abyad F, Feghali R, Olaywan L, Jaafouri H, Ghalayini W, Saliba M, Abi Hanna P. Rafic Hariri University Hospital preparedness: Sharing initial experience on COVID-19. J Med Liban 2020; 68 (1-2) : 47-51.

ABSTRACT • Background : The first cases of novel coronavirus (2019-ncov) infected patients occurred in Lebanon in February 2020 and March 2020. Rafic Hariri University Hospital was the first hospital in Lebanon that rapidly responded to this crisis through the effective use of scarce resources and the swift arrangement of departments as part of the contingency plan. It was able to mitigate the impact of the first COVID-19 wave in Lebanon through active management and proper preparedness. We analyzed data on the first 63 confirmed cases of COVID-19 to determine their epidemiological and clinical characteristics. **Methods :** We collected information on demographic characteristics, exposure history, the severity of clinical presentation and clinical outcomes of cases. **Results :** Among the first 63 patients with confirmed COVID-19, the median age was 37 years, where 55% were males. On average, the time to virologic cure was estimated at 17.5 days, while the length of stay was estimated at 16 days. The pattern showed a limited community transmission, with most cases either with a positive travel history to endemic areas or from close contact with index cases. Most of the cases were mild (65.1%), and few patients had comorbidities. Four patients presented with acute respiratory distress syndrome (ARDS), and two of them died. The fatality rate was 3.2%. **Conclusion :** This study describes the first cases of COVID-19 over one month after diagnosing the first case in Lebanon. Most of the cases were mild to moderate, but isolated in the hospital to limit community spread. This strategy has probably helped the country in containing the disease so far. Describing the clinical presentation over a more extended period might provide a better assessment of the clinical patterns. Meanwhile, the most effective measure is to prevent the spread of disease by a combination of proper infection prevention and control measures, early detection and isolation of cases, active contact tracing, and the quarantine of contacts.

Keywords : COVID-19; RHUH; Lebanon; épidémiologie

Hassoun M, Abyad F, Feghali R, Olaywan L, Jaafouri H, Ghalayini W, Saliba M, Abi Hanna P. Préparatifs à Rafik Hariri University Hospital: l'expérience initiale de COVID-19. J Med Liban 2020; 68 (1-2) : 47-51.

RÉSUMÉ • Contexte : Les premiers cas de nouveaux patients infectés par un coronavirus (2019-ncov) se sont produits au Liban en février et mars 2020. L'hôpital universitaire Rafic Hariri a été le premier hôpital au Liban à répondre rapidement à cette crise grâce à l'utilisation efficace de ressources limitées et l'organisation rapide de départements dans le cadre du plan d'urgence. Il a pu atténuer l'impact de la première vague COVID-19 au Liban grâce à une gestion efficace et une bonne préparation. Nous avons analysé les données des 63 premiers cas confirmés de COVID-19 pour déterminer leurs caractéristiques épidémiologiques et cliniques. **Méthodes :** Nous avons collecté des informations sur les caractéristiques démographiques, les antécédents d'exposition, la gravité de la présentation clinique et les résultats cliniques des cas. **Résultats :** Parmi les 63 premiers patients avec COVID-19 confirmé, l'âge médian était de 37 ans dont 55% d'hommes. En moyenne, le délai de guérison virologique était estimé à 17,5 jours, et la durée du séjour à 16 jours. La transmission communautaire s'est révélée limitée avec dans la plupart des cas soit des antécédents de voyages dans des zones endémiques, soit un contact étroit avec les cas index. La plupart des cas étaient bénins (65,1%) et peu de patients présentaient des comorbidités. Quatre patients ont présenté un syndrome de détresse respiratoire aiguë (SDRA) et deux sont décédés. Le taux de mortalité était de 3,2%. **Conclusion :** Cette étude décrit les premiers cas de COVID-19 sur une période d'environ un mois après le diagnostic du premier cas au Liban. La plupart des cas étaient légers à modérés, mais isolés à l'hôpital pour limiter la propagation dans la communauté. Cette stratégie a probablement aidé le pays à contenir la maladie jusqu'à présent. Décrire la présentation clinique sur une période plus longue pourrait fournir une meilleure évaluation des modèles cliniques. En attendant, la mesure la plus efficace consiste à prévenir la propagation de la maladie en combinant de bonnes mesures de prévention et de contrôle des infections, la détection précoce et l'isolement des cas, la recherche active des contacts et leur mise en quarantaine.

Mots-clés : COVID-19; RHUH; Liban; épidémiologie

INTRODUCTION

At the end of December 2019, and as a part of a surveillance system following the severe acute respiratory syndrome (SARS) outbreak in 2003, at the hospital of Hunan China, four cases which fulfilled the case definition of pneumonia of unknown etiology were detected [1].

The criteria included: fever, lung infiltrates on imaging studies, low or average white cell count or low lymphocyte count, and no improvement after three to five days of recommended intravenous antibiotic treatment. Polymerase chain reaction (PCR) for influenza and other respiratory pathogens was adverse.

All cases were linked to the Hunan seafood wholesale

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market, which is known for selling live and exotic animals.

On 31/12/2019, the Chinese government formally announced the outbreak, and the virus was rapidly isolated and sequenced. Its genome sequence was shared with the international community. It was found to be a new type of Coronavirus with some similarities to SARS.

On 30/01/2020, and after the spread to other countries, the World Health Organization (WHO) declared it a Public Health Event of International Concern (PHEIC).

On February 5, 2020, Rafik Hariri University Hospital (RHUH) admitted a few travelers returning from China for quarantine. Office testing using Reverse transcription (RT)-PCR for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the name of the newly discovered Coronavirus, was initiated with the support from the Lebanese Ministry of Public Health (MOPH) and WHO.

On 21/02/2020, the country declared its first case of Coronavirus Disease 2019 (COVID-19), a returning traveler from Iran. The case was mild but hospitalized. Subsequently, we had five cases from the same trip.

A contingency plan was enacted, and the hospital was physically divided into two parts – a part allocated for COVID-19 patients, and a separate part earmarked for the other patients. Four ICU beds equipped with negative pressure were also wholly separated from the other floors. An Emergency Room (ER) was added for patients with respiratory infections suspected with COVID-19. The hospital's third floor was evacuated in preparation, in addition to 64 naturally ventilated rooms for isolated patients.

Subsequently, another 24 rooms and two additional Intensive Care Units (ICUs) with 8 and 12 beds respectively were added. All the newly allocated premises had separate access from other parts of the hospital. The working staff was also assigned roles separately. Those working in COVID-19 units were required to don full personal protective equipment (PPE) precautions at the start of the shift, limit movement within the unit, and take a shower at the end of the shift before putting their clothes on.

Isolation rooms were naturally ventilated. The ventilation system at the Coronavirus allocated ER and ICU was transformed into negative pressure ventilation with high-efficiency particulate air (HEPA) filters.

Training for the working staff at RHUH was immediately started. It included training on donning and removing PPE in a way that avoids self-contamination. The essential PPE used included the following:

- _ Face masks or N95 respirator for aerosol generating procedures
- _ Eye goggles or face shields
- _ Impermeable gowns
- _ Gloves
- _ Hair cover and shoe cover in certain situations.

In this small descriptive study, we discuss the presentation of the first 63 cases diagnosed with COVID-19 at RHUH.

METHODOLOGY

This is a descriptive study of the first hospitalized cases with COVID-19 at RHUH over 25 days. Data were collected prospectively by two specialist medical doctors. The hospital's Institutional Review Board (IRB) approved this study. Patients' names were concealed to protect confidentiality.

Clinical severity was stratified as follows:

- Asymptomatic: no symptoms
- Mild: upper respiratory symptoms with no imaging abnormalities
- Moderate: moderate symptoms with imaging abnormalities
- Severe/critical:
  - o O_2 saturation ≤ 93%
  - o Respiratory rate ≥ 30 breaths per minute (BPM)
  - o PaO_2/FiO_2 ≤ 300 mmHg.

RESULTS

Epidemiology

During the first 25 days of the outbreak in Lebanon, 63 patients diagnosed with COVID-19 were hospitalized at RHUH. At that time, only symptomatic contacts or travelers from high-risk areas were screened and tested. All patients with a definite diagnosis based on RT-PCR were isolated at the hospital irrespective of the clinical severity at the time of presentation.

MOPH investigated the index cases. Asymptomatic contacts of patients were placed in quarantine for 14 days, and symptomatic contacts were tested and isolated.

The epidemic curve of the first 25 days is shown in Figure 1.

The first positive case, diagnosed on 21/02/2020, was a passenger on a returning flight from Iran presenting with mild symptoms. The second case followed on 24/02/2020 and the next three cases on 28/02/2020, with a marked increase in cases during March.

Table I shows the epidemiological characteristics. Table II lists the clinical features. The proportion of males was higher, at around 55% compared to 45% females. Most patients were young to middle-aged. The pattern showed a limited community transmission, with most cases either with a positive travel history to endemic areas or from close contact with index cases. Only one example during that period had an unknown route of exposure. Subsequently, it was determined that this patient was exposed to a traveler from an endemic area.

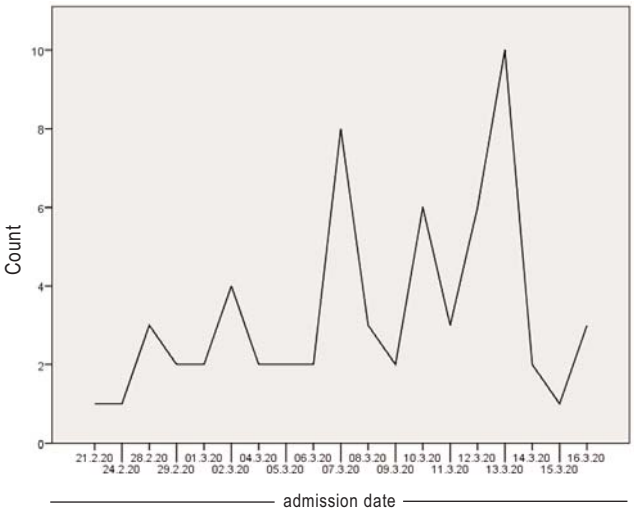

Figure 1
Epidemic curve during the first month of the outbreak

Most of the travel-related cases were from Iran and Europe. One case had a travel history to Egypt and two cases to UAE. The three diagnosed healthcare workers worked at other hospitals and were exposed to patients or visitors that were not initially suspected for COVID-19.

Clinical features (Tables II and III)
Most of the cases were mild (65.1%), and few patients had comorbidities.

Around 5% had prior cardiac problems, 5% had diabetes mellitus, and around 12% were active smokers. Four patients presented with acute respiratory distress syndrome (ARDS). Three were placed on mechanical ventilation, and one on noninvasive ventilation. Those four patients with ARDS presentation received a Lopinavir and Ritonavir combination. The other patients only received symptomatic treatments. Two patients died with a fatality rate of 3.2%.

Among the patients who had a chest computed tomography (CT) scan done, 44.4% had a ground-glass appearance. Sixty out of the 63 patients recovered completely. The median number of days for a virologic cure was 17.5 days, and the median length of stay 16 days.

The most common symptoms were fever and cough, although only present in 49% and 43% of the cases, respectively. Sore throat, runny nose, and fatigue were also common presentations, whereas diarrhea was present in only three patients (4.8%).

TABLE I
EPIDEMIOLOGICAL FEATURES OF COVID-19 CASES

	Patients (N = 63)
Sex	
Male	35 (55.5%)
Female	28 (44.5%)
Age (years)	
Median (IQR)	37 (5-81)
Exposure	
Travel	30 (48.4%)
Contact to Index case	31 (50%)
Unknown	1 (1.58%)
Missing	1
Countries	
Iran	13 (20.6%)
United Kingdom (UK)	5 (7.9%)
France	4 (6.34%)
United Arab Emirates (UAE)	2 (3.17%)
Italy	1 (1.58%)
Egypt	1 (1.58%)
Austria	1 (1.58%)
Regions	
Beirut	14 (22.2%)
Baabda	12 (19%)
Maten	11 (17.5%)
Jbeil	6 (9.5%)
Keserwan	5 (7.9%)
Other	15 (24%)
Healt Care Workers (HCW)	3 (5%)

DISCUSSION

This is a descriptive study of the cases during the first month after the emergence of COVID-19 in Lebanon. The Lebanese government and MOPH were active in screening travelers from high-risk endemic regions and investigating the contacts of index cases. RT-PCR tested symptomatic cases, and if positive, were isolated at the hospital. Asymptomatic travelers and contacts were quarantined at home for two weeks. This approach contributed to limiting the spread of this novel virus in the community. Afterward, when the numbers increased, the national lockdown slowed down the spread of the virus markedly.

Of notice is that no cases were reported from China. The first cases came from Iran, and the plane that carried the first case was screened at the airport before the outbreak was declared in Iran. This attests to the vigilance of MOPH officers. The first cases in Lebanon came from a few clusters. The first cluster from Iran was contained. The second cluster in Byblos went from a patient with a travel history to Egypt, at a time when no cases were reported from Egypt. During that time, a series of French travelers returning to their country tested positive [2]. A third cluster emerged in Keserwan, with the index case

presumed of not having a route of exposure. Subsequently, the MOPH investigation revealed that the index case was exposed to a traveler from Europe. A fourth cluster developed from a patient with a travel history to France.

In this series, only three patients were healthcare workers, and they did not work at our hospital. All three were exposed without donning PPE, or any protective precautions, to patients or visitors not suspected of having COVID-19. No cases were reported in RHUH staff working in the COVID-19 wards. Infection control practices are effective in protecting healthcare workers from contracting the virus.

Most of the cases were young or middle-aged, with few comorbidities, and a small percentage of smokers. This might explain why most cases were mild or moderate. In these series, patients who presented with mild or moderate symptoms recovered completely. The four cases with ARDS were transferred from other medical institutions in critical conditions. They were all aged above fifty with some comorbidities. Three required mechanical ventilation, and one required noninvasive ventilation. Two of those patients died. Also, one patient in his eighties, having multiple comorbidities and active cancer, required oxygen therapy and admission to the ICU; however, he recovered completely.

During February and March, there was no recommended specific treatment for COVID-19. We opted for symptomatic treatment for mild and moderate cases.

For the four critical cases, we opted for a Lopinavir/Ritonavir combination, which was after that shown ineffective in one small randomized study of severe cases. [3]

All mild and moderate cases recovered without specific treatment. Most of the cases were hospitalized at the start of their symptoms due to active follow-ups. RT-PCR remained positive long after recovery. The median duration for a virologic cure was 17.5 days. This is consistent with the experience published in the literature. [4-6] This can possibly be explained by the presence of non-infectious portions of the virus that persist for a long time. [7]

Nevertheless, we followed the international and national guidelines for defining a cure, which requires the cessation of symptoms and two consecutive negative RT-PCR tests of nasopharyngeal, oropharyngeal or sputum specimens.

Imaging studies, mainly chest CT scans, were found helpful in the diagnosis of COVID-19. [8] At the beginning of March, we started performing a chest CT scan for most of our hospitalized patients. The most common finding was bilateral ground-glass appearance. Mild cases with upper respiratory symptoms mostly had a normal chest CT scan. Another category with mild to moderate symptoms had an abnormal chest CT scan, but showed a favorable course. The third category of patients with severe symptoms sometimes ended up with ARDS and respiratory failure, and sometimes with death.

Fever and cough were present in about only half the cases, which is lower than the numbers in published literature. This reflects that many of our hospitalized patients had a mild presentation. Other common symptoms upon presentation included fatigue, sore throat, and runny nose.

TABLE II
CLINICAL CHARACTERISTICS AND SEVERITY OF COVID-19 CASES

	Patients (N = 63)
Comorbidities	
Chronic cardiac disease	3 (4.8%)
DM	3 (4.8%)
Smoking status	
Never	46 (73%)
Current	7 (11.1%)
Former	6 (9.5%)
Missing	4 (6.3%)
Severity	
Mild	41 (65.1%)
Moderate	18 (28.6%)
Severe/critical	4 (6.3%)
Intensive Care Unit (ICU)	5 (8.1%)
Mechanical Ventilation	3 (4.8%)
Noninvasive ventilation	1 (1.58%)
ARDS	4 (6.3%)
Mortality	2 (3.17%)
CT scan (ground glass appearance)	20/45 (44.4%)
Days to virologic cure	
Median (IQR)	17.5 (7-29)
Length of stay	
Median (IQR)	16 (4-32)

TABLE III
CLINICAL PRESENTATION OF THE CASES

Symptoms	Patients (N = 63)
Fever	31 (49.2%)
Cough	27 (42.9%)
Sore throat	12 (19.4%)
Runny nose	14 (22.6%)
Muscle aches	7 (11.3%)
Joint pain	1 (1.6%)
Fatigue/malaise	12 (19.4%)
Shortness of breath (SOB)	6 (9.7%)
Headache	4 (6.5%)
Diarrhea	3 (4.8%)

CONCLUSION

This study describes the first cases of COVID-19 over one month after diagnosing the first case in Lebanon. One of the strengths of this study is that the claims were documented prospectively. Most of the cases were mild to moderate, but isolated in the hospital to limit community spread. This strategy has probably helped the country in containing the disease so far.

This study is limited to the first 63 patients during the early 25 days of COVID-19 in Lebanon. Subsequently, mild cases were isolated at home, and only moderate and severe cases were hospitalized. Describing the clinical presentation over a more extended period might provide a better assessment of the clinical patterns.

Finally, our experience suggests four major patterns of this disease:

1. Asymptomatic patients that can spread the disease.
2. Patients with mainly mild upper respiratory symptoms.
3. Patients with moderate symptoms and abnormal imaging findings.
4. Patients with severe symptoms that might lead to ARDS.

It is essential to predict which patient might progress to the severe or critical form of the disease and whether any treatment might prevent this deterioration.

Meanwhile, the most effective measure is to prevent the spread of disease by a combination of proper infection prevention and control measures, early detection and isolation of cases, active contact tracing, and the quarantine of contacts.

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COVID-19 PANDEMIC

ANESTHETIC MANAGEMENT OF SUSPECTED OR CONFIRMED COVID-19 PATIENTS
A Narrative Review

http://www.lebanesemedicaljournal.org/articles/68(1-2)/pandemic7.pdf

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Gergess A, Dagher C, Jabbour K, Madi-Jebara S. Anesthetic management of suspected or confirmed COVID-19 patients - A narrative review. J Med Liban 2020; 68 (1-2) : 52-59.

ABSTRACT • COVID-19 is a new pandemic crisis with potentially severe complications. This paper aims to define available data concerning optimal anesthesia management for patients with COVID-19 and to provide safety recommendations for healthcare professionals.

Keywords : COVID-19; airway management; pediatric anesthesia; obstetrics; cardiac surgery

Gergess A, Dagher C, Jabbour K, Madi-Jebara S. Prise en charge anesthésique d'un patient COVID-19 suspect ou confirmé. J Med Liban 2020; 68 (1-2) : 52-59.

RÉSUMÉ • La pandémie COVID-19 est une pandémie virale qui est potentiellement grave. À ce jour, les données sur la physiopathologie et le management de cette maladie sont limitées. Cet article vise à décrire la prise en charge anesthésique optimale des patients atteints de cette maladie et à donner des recommandations pour assurer la sécurité du personnel soignant.

Mots-clés : COVID-19; intubation; anesthésie pédiatrique; obstétrique; chirurgie cardiaque

INTRODUCTION

In December 2019, a novel coronavirus now known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was identified in patients in Wuhan, China. Infection with SARS-CoV-2 led to Coronavirus Disease 2019 (COVID-19). Rapid international spread of this potentially lethal virus has caused global concern, with millions of cases and thousands of deaths [1].

The SARS-CoV-2 virus has also reached Lebanon, affecting more than 1500 cases to date. Healthcare workers are exposed to a high risk of infection as they provide direct care to infected patients. Anesthesiologists are at an even higher risk than healthcare workers of other subspecialties; several anesthesiologists have been infected after providing tracheal intubation for confirmed COVID-19 patients [2] or even after spinal anesthesia for cesarean section [3]. Therefore, urgent development of safe medical practices and infection prevention protocols for the perioperative management of patients with COVID-19 is needed. To provide better care for COVID-19 patients and to plan practical and precautionary measures, this review describes anesthesia-related characteristics of patients with confirmed or suspected COVID-19 presenting for surgery.

ANESTHESIA PREOPERATIVE EVALUATION

Non-urgent surgical procedures should be canceled or postponed. In cases of urgent procedure, the preoperative assessment should aim to identify high-risk patients and procedures, as well as to optimize patient's condition mainly focusing on reinforcing the patient's respiratory status.

- Assess airway carefully, allowing a management plan to be developed ahead.
- Evaluate the severity of respiratory compromise based on arterial blood gas, oxygen requirements, and chest X-ray changes or CT scan.
- Evaluate major organ systems such as cardiac, liver, and renal. Look for signs of shock and organ failure.
- Review current antivirals to avoid drug interactions with anesthetic medications [4].
- Determine postoperative need of the patient for intensive care support.
- Oral Midazolam should be avoided as a premedication agent in patients receiving antiviral drugs [4].

PERSONAL PROTECTIVE EQUIPMENT FOR HEALTHCARE PROFESSIONALS

It is of utmost importance to protect healthcare workers from infection. All healthcare professionals must be provided with personal protective equipment (PPE) to prevent droplet, contact, and airborne infections. PPE items consist of: long-sleeved fluid-repellent gown; fit tested and fit checked high filtration mask such as FFP2 (N95) mask; goggles or visor; disposable gloves (consider double gloves for the anesthesiologist performing the intubation); disposable hat and shoe covers [5-9].

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Institutions and medical staff should establish procedural protocols for donning and doffing PPE to avoid self-contamination, and training in the use of PPE is required for all staff involved in suspected or confirmed COVID-19 cases. Furthermore, hand hygiene should be performed in every step of PPE removal according to the hospital guidelines.

Ahead of the procedure, the anesthesia team should be given enough time for donning and full respect of safety measures need to be implied [2]. A complete check should be done including a self-check and, more importantly, a check by another colleague [10].

PATIENT TRANSPORT TO THE OPERATING ROOM

- The transfer of a confirmed or suspected COVID-19 patient to any intervention and return to an isolation room should be planned due to the risk of aerosolization.
- COVID-19 patient transportation, in the pre- and postoperative setting, should be done through a dedicated pathway. Disinfection needs to be regularly done [11].
- Corridors and elevators should be kept free.
- Take only the elevator dedicated to COVID-19 patients.
- Patients who do not require intubation before transport to the OR must wear a surgical mask.
- If the patient is intubated, it is recommended to use a ventilator during transfer with a high-efficiency particulate air (HEPA) filter inserted between the bag-valve-mask breathing device and the patient [12]. Moreover, it is preferable to cover the patient during the transport process with a transparent disposable plastic sheet [13].
- Healthcare professionals responsible for the transfer process should wear PPE.
- Hand disinfection should be done with hydroalcoholic solution before and after each contact with the patient [14].
- The surfaces of passageways and the elevator should be disinfected once the transport is done [11].

ANESTHESIA MANAGEMENT FOR ADULT PATIENTS

General considerations

- The dedicated operating room (OR) and anteroom should be equipped with a negative pressure system, and an appropriate level of negative pressure must be ensured [15]. In a hospital where negative pressure operating rooms are unavailable, the positive pressure system and air conditioning must be turned off [2].
- Warning signs for COVID-19 infection should be displayed on the door of the OR to minimize staff exposure.
- Only personnel involved in direct care are allowed to enter the allocated OR.
- An anesthesia machine is dedicated to the designated OR.
- A breathing circuit filter (HEPA filter) must be installed between the proximal end of the endotracheal tube (ETT) and the distal end of the circuit. An additional filter (HEPA) must be applied between the breathing circuit and the expiratory valve [12,13,15]. It is recommended to replace the filters after every COVID-19 positive patient and after every 3 to 4 hours of anesthesia use [2].
- A closed-loop aspiration system is highly recommended to avoid disconnection while suctioning the patient via the ETT [11].
- Before initiating any airway management, the airway strategy (primary plan and rescue plans, and when they are progressed to) should be set up and the airway team briefed. Use a cognitive aid if difficulty arises.
- All necessary equipment for airway management should be prepared and readily available before starting anesthetics. This preparation reduces the need for clinicians to reach into the anesthesia workstation drawers and bins once the patient has entered the procedure room. Use a tracheal intubation checklist [16].
- Aerosol box, if available, can provide additional protection during intubation and extubation [17,18].
- Trash cans and sharps containers should be readily available and open to avoid dropping equipment on the floor, which increases viral dispersion [16].
- For anesthesia drug dispensing workstations that require touching the screen, a plastic shield should be placed over the screen to minimize contamination [19].
- Clinicians should leave badges, keys, cell phones, pagers and pens outside the OR. Emergency phones may be kept in sealed bags to facilitate communication with other clinicians.
- Limit the number of health care providers while intubation is taking place. Three individuals are likely required to be present inside the OR to directly manage the patient: an intubator, an assistant, and a third person to administer drugs and watch monitors. A runner should be available outside the OR serving as a backup.
- In-situ simulation is vividly recommended to enable staff to familiarize themselves with PPE use and the management of resuscitation of COVID-19 patients [20]. In Lebanon, many videos were uploaded concerning anesthesia management for COVID-19 patients.
  https://www.youtube.com/watch?v=PH6RiVmBSn0
  https://www.youtube.com/watch?v=CLJGHsDs3Jg&feature=youtu.be

Types of anesthesia

Different types of anesthesia can be selected dependent on the type of surgery and individual patient's need.

General anesthesia (GA) with airway instrumentation in COVID-19 patients creates a risk to physiologically compromised patients and to attending healthcare providers, both during intubation and extubation. Healthcare professionals are 6.6 times more exposed to respiratory secretions during tracheal intubation compared to those kept away [21]. It is important to perceive that the use of tracheal intubation is preferable to the laryngeal mask. Furthermore, regional anesthesia (RA) has fewer effects on respiratory function and dynamics compared with GA. This could reduce postoperative pulmonary complications in COVID-19 patients who may already have decreased respiratory function from COVID-19-associated pneumonia or acute respiratory distress syndrome.

Subsequently, RA should be preferred over GA in managing these patients whenever possible [22-24].

General anesthesia for COVID-19 patients

Induction

- Induction must be initiated after a complete satisfactory check of PPE for every person in the OR.
- Standard monitoring, intravenous (IV) access, instruments, drugs, ventilator, and suction should be prechecked.
- Airway management must be carried out by the most experienced senior to maximize first-pass success [2,12-13].
- It is recommended that rapid sequence induction (RSI) should be used, and appropriate preparation for RSI should be similar to that of an ordinary patient.
- Aerosol-generating procedures should be avoided. This includes high-flow nasal oxygen, bag masking, noninvasive ventilation, and awake fiberoptic intubation [25,26].
- Meticulous preoxygenation for 3 to 5 minutes, with 100% oxygen, should be performed with a well-fitting mask. A closed-circuit is optimal and is preferable to a bag-mask. The anesthesia mask should be adjusted with both hands to minimize leakage [2,11-13].
- If RSI is impossible or undesirable, provide mechanical ventilation using either pressure or volume-controlled ventilation mode; PCV or VCV mode respectively, with small tidal volumes, positive end-expiratory pressure (PEEP) at 5cmH_2O with 100% oxygen [11-13,20].
- At all times, gas flow rates should be kept low < 6 ml/min while maintaining oxygenation [20].

General anesthesia drugs

It has been demonstrated that drug interactions between antiviral drugs (particularly Kaletra®-Lopinavir/Ritonavir) and anesthetic agents are common. However, it is noteworthy that no clear contraindications have been recommended for the use of any IV anesthetic or analgesic drug [4].

Intubation

- After induction, ventilation is stopped before removing the mask.
- The most experienced anesthesiologist available should perform the intubation. Using a videolaryngoscope with a separate screen allows the intubator to stay distant from the airway. Sufficient muscle relaxation should be obtained to prevent coughing during intubation [2,11-13,27).
- Remove the outer gloves immediately after completion of intubation.
- The endotracheal tube cuff should be inflated with air to a measured pressure of 20-30 cmH_2O before initiating mechanical ventilation.
- A regulation system balloon's pressure is to be put in place to avoid leaks.
- A closed airway suction system, if available, is recommended to reduce viral aerosol production [25,28].
- Vigorous intubation using the fiberscope should be avoided unless specifically indicated due to the risk of cough when spraying the local anesthetic, which promotes the dispersion of aerosols [21].
- If disconnection is necessary: stop the ventilator before disconnecting, then clamp the ETT.

Recovery from anesthesia

- Once the patient meets the criteria for extubation, he or she should be extubated in the OR. Patient coughing should be minimized, thus reducing the risk of exposure to droplets and aerosols at this time.
- Since SARS-CoV-2 virus can be spread through nausea and vomiting, prophylactic antiemetics such as 5-hydroxytryptamine receptor antagonist (Ondansetron®) can be given postoperatively [29]. However, the administration of Dexamethasone and NSAIDs remains controversial [30,31].
- The staff present is placed behind the patient's head.
- The weaning of the respirator will be carried out in PSV-Pro (Pressure Support Ventilation-Protect) or spontaneous manual mode.
- All necessary equipment for oxygen delivery via mask or low flow (< 5 l/min) nasal cannula should be prepared before extubation [32].
- Undertake appropriate tracheal and oral suction with a closed suction system before extubation [28]. The balloon is then deflated.

- After extubation, place immediately a surgical face mask on the patient above his/her oxygen mask or nasal cannula.
- After the procedure, all material used for ventilation and intubation is discarded or disinfected promptly with a standard disinfectant detergent. After disinfection, the anesthesia machine can be used for other non-COVID-19 patients; and no cross-infection has been reported so far. The carbon dioxide absorber is recommended to be replaced between cases [2].

Regional anesthesia (RA) for Covid-19 patients

- RA should be preferred over GA for delivering anesthesia care whenever possible. It should be performed by the most experienced anesthesiologist [33].
- Thrombocytopenia needs to be ruled out before neuraxial procedures [34] as well as abnormality in INR and PTT values.
- Nerve blocks that have minimum impact on respiratory function are privileged such as axillary or infraclavicular brachial plexus block and risk-benefit should be considered for perineural adjuvants and continuous perineural catheters. Currently, no dose adjustment for RA is recommended [22,33].
- Patients should keep the surgical mask [35].
- The sedation dose needs to be decreased; hence respiratory compromise requiring supplemental oxygen is avoided. To reduce the risk of aerosolization, the oxygen mask or nasal cannula should be applied under the surgical mask and the oxygen flow needs to be minimized while maintaining adequate oxygen saturation.
- Ultrasound guidance is required for peripheral nerve blocks and plastic covers should be used to protect ultrasound equipment [22].
- Before starting the surgery, RA should be thoroughly tested to avoid unplanned conversion to GA.

It is recommended that patients should be sent to an isolation room or ICU after surgery, bypassing the Postanesthesia Care Unit (PACU)**.** [33]

ANESTHESIA MANAGEMENT FOR PEDIATRIC PATIENTS

According to different cohorts of COVID-19 patients, children seem to be less affected by this virus. In Lebanon, the Ministry of Health reported to date that, in this pathology, 1.34% of patients are less than 10 years old and 6.99% are between 10 and 19 years old [36].

More than one fourth (27%) of laboratory-confirmed COVID-19 positive children are asymptomatic and relatively few of them are hospitalized [37-39].

Critical cases are rare in this population, but infants seem to be vulnerable since death was reported in infants [37].

Though in general, children seem to be relatively protected from the severe pulmonary complications due to this infection, they are one of its main vectors and during this pandemic season, special care should be taken by anesthesia teams in this regard.

The OR workflow will be the same as for adult patients. Children, except neonates, should wear a surgical face mask on their way to the OR.

In order to avoid vigorous crying and the need for physical restraints, the routine use of preprocedural sedatives to reduce anxiety is highly recommended. This will help increase compliance when an IV line is placed while awake [16].

Parents in the OR are not welcomed under these circumstances.

It is advisable to avoid non-rebreathing circuits [25].

It is highly recommended to perform an IV anesthesia with a RSI. Otherwise, a modified rapid sequence is preferred; effort should be made to rapidly put an IV line and to control the airway. The most experienced anesthesia professionals available should be behind the patient. Manual, pressure support or controlled ventilation could be considered with small tidal volumes (just enough to rise the child's chest wall) before intubation, but fresh gas flow should not exceed 6 L/min and 3 L/min for children whose weight is < 10kg [16].

Intubation should be made using videolaryngoscopy. Supraglottic devices are contraindicated [40].

The aim is to perform intubation and extubation as safely as usual and to avoid any coughing, agitation, or dispersion of secretions in the atmosphere. Therefore, the usage of a muscle relaxant could be considered or intraoperative clonidine or dexmedetomidine and antiemetics.

Extubation is a very delicate step: careful suction of the oropharyngeal cavity should precede either deep or awake extubation, trying to avoid cough and vomiting. Some teams consider extubating under a transparent plastic drape acting as a physical barrier against aerosolization of the patient's secretions [41]. An oxygen mask should be placed on the patient face and a surgical mask added over it after extubation.

Once the child is fully awaked, he will be directly transferred to the inpatient ward or the ICU bypassing the PACU [16, 42].

NON-OPERATING ROOM ANESTHESIA

All elective procedures during the COVID-19 outbreak should be deferred, especially endoscopic procedures. Because the infection is transmitted through inhalation of airborne droplets, conjunctival contact, and touch and feces contamination, optimal precautions must be used

to prevent the infection of healthcare providers in endoscopy units [43-47].

- Patients need to be assessed and COVID-19 risk stratification has to be performed one day before scheduled endoscopy (preferably by phone) and on the day of the procedure [44, 48].
- Family members and accompanying persons should not enter the endoscopy unit [49].
- All patients undergoing endoscopic procedures should wear a facial mask whenever possible [49].
- Procedures would be better performed in a negative pressure room – inside the OR – and all general precautions mentioned above should be used [50].
- ICU patients should not be transferred for gastrointestinal (GI) endoscopy. Thus, a bedside GI endoscopy should be performed.
- Urgent or semi-urgent procedures should be performed by an experienced medical team. The number of staff should be kept to a minimum and wear the appropriate PPE.
- To prevent airway manipulation, RA should be performed wherever possible [47,49].
- Prefer GA with intubation to secure the airways and prevent aerosolization [51].

ANESTHESIA FOR OBSTETRIC PATIENTS WITH SUSPECTED OR CONFIRMED COVID-19

Anesthesiologists could take care of these parturients either in the delivery room or in the OR; some may be asymptomatic and others may be in a very critical state.

General precautions to be adopted in the delivery room

- A negative pressure room – if possible – should be designed for labor and delivery and the number of medical and other attending staff minimized in the dedicated room.
- The caring medical team should wear the appropriate PPE while the patient wears a surgical face mask during labor and delivery.
- Clinical surveillance of the parturient is necessary to monitor any aggravation of the clinical state (hyperthermia, dyspnea, etc.) that might necessitate intervention or change of delivery mode. Routine monitoring should include frequent vital signs with the addition of continuous pulse oximetry and strict input and output measurements to assure fluid restriction. Pulse oximetry goal should be an oxygen saturation ≥ 95%.
- Dedicated trays (or carts) containing the most commonly used supplies and drugs for neuraxial labor analgesia should be available, to minimize traffic and contamination of anesthesia workstations and other anesthesia equipment [52].

Hemostasis assessment

- Make a hemostasis assessment upon arrival at the hospital: CBC, INR, PTT, fibrinogen, and D-dimers. In case an anomaly is detected, complete with the usual explorations [53].
- It should always be associated with the search for a hemorrhagic diathesis suggestive of a hemostasis disorder (HEMSTOP Score) [53].
- If the patient is taking low-molecular-weight heparin (LMWH) for thromboprophylaxis, dose and timing should be noted to manage any neuraxial analgesia or anesthesia.
- If maternal COVID-19 infection is severe with high values of fibrinogen and D-dimers (fibrinogen > 8 g/l; D-dimers > 3 g/ml) management should be discussed with the patient's gynecologist. The concentration of D-dimers can be greatly increased in pregnant women infected with COVID-19 without diagnostic or prognostic value for pulmonary embolism. If in doubt, other diagnostic methods such as an injected computed tomographic scan (CT scan) should be considered [52].

Analgesia for labor and delivery

COVID patient without signs of seriousness

Early epidural placement is desirable to avoid exacerbation of respiratory symptoms with labor pain, and to reduce the likelihood of GA if cesarean delivery becomes needed [52].

The risks of performing neuraxial analgesia are minimal, even absent since COVID-19 virus gives little or no viremia and no neurological damage has been observed with this virus. To this date, no particular problem has been reported with epidural analgesia such as hyperthermia cases which may be associated or promoted by the use of epidural analgesics [54-59].

The risk of COVID-19 exposure for the anesthesiologist during neuraxial labor analgesia placement is presumably low since this is not an aerosol-generating procedure; nevertheless, Zhong et al. [3] reported transmission of COVID-19 – confirmed by PCR – from patients having spinal anesthesia for cesarean section to 57.1% of anesthesiologists who were wearing category 1 PPE's limited to surgical mask, hat, gloves, and gowns. So for the time being, the proposal is not to modify the indications and analgesia practices in patients with little or no symptoms.

The decision of the management technique is the sole responsibility of the anesthesiologist. We suggest performing an epidural analgesia in the early stage of labor; either epidural or combined spinal-epidural analgesia in case of cervical dilatation > 6 cm; and spinal analgesia in case of a complete cervical dilatation or planned baby extraction in less than 60 minutes.

In case of failure of epidural analgesia or in case of insufficient epidural avoid N_2O and prefer RA.

In case of a patient with signs of severity

If the patient's status worsens during labor with signs of increasing severity (fever, respiratory distress, etc.), management will be discussed on a case-by-case basis between the anesthesiologist and the gynecologist. At the same time, obstetric care and resuscitation will be carried out [60-62].

In case an intubation is urgently required, a cesarean section will be made after intubation unless the fetus can be extracted within minutes.

In the event of a dural breach, similar to usual care, conservative measures should be initially provided. Postponing the epidural blood patch is recommended in women who are actively ill. Individual assessment of the benefits and risks should be assessed and shared decision-making should be engaged with the patient prior to proceeding [55].

Cesarean delivery per se

The cesarean delivery has to be performed in a negative pressure OR designed to accommodate COVID-19 patients. The presence of the spouse is prohibited in the OR.

GA has to be avoided unless neuraxial anesthesia is contraindicated. A publication from Wuhan, China, describing outcomes in 17 cesarean deliveries concluded that "excessive hypotension" occurred in 12 of 14 cases within comparison with three women who received GA; however, information about the blood pressure trends and description of the use of vasopressors were not reported. Another study suggested that SARS-CoV-2 can bind with the angiotensin-converting enzyme II (ACE2) receptor, which could explain partly the significant hypotension observed with COVID-19 positive women treated via neuraxial anesthesia.

The key to SARS-CoV-2 infection is its S protein binding with ACE2 receptor [59].

Spinal anesthesia administered in 49 patients (45 cesarean deliveries and 4 orthopedic procedures) was well-tolerated with stable blood pressure [3]; but the authors did not give any details about intraoperative blood pressure or vasopressors needed. Anesthesiologists should be aware of this risk and be ready to treat it.

Antiemetic medication should be administered to lower the risk of vomiting and viral spread. Although NSAIDs and dexamethasone seem to play a potential role in the treatment of COVID-19 patients, their use remains controversial [30].

Postpartum thromboprophylaxis

Given the absence of solid data and the significant thrombotic risk of this disease, postpartum thromboprophylaxis should be discussed on a case-by-case basis. It is however, strongly advised to put prophylaxis to all parturients whatever the delivery route and the personal risk factors [60-62].

ANESTHETIC MANAGEMENT OF CARDIAC SURGICAL PATIENTS

Clinical management of patients undergoing cardiac surgery is complex, and the cardiac anesthesiologist is faced with many challenges as these patients present with multiple comorbidities. Furthermore, perioperative hemodynamic management usually requires invasive monitoring. In patients with COVID-19 this might be associated with even greater challenges for the cardiac surgery team. Therefore, non-urgent cardiac surgeries should be delayed until COVID-19 virus screening tests are negative.

General considerations

- All necessary equipment including anesthesia machines, monitors, ultrasound machines, activated-clotting time (ACT) machines, blood gas, and transesophageal echocardiography (TEE) probes should be prepared and checked in advance in the OR.
- Ultrasound guidance for central venous and arterial catheterizations is highly recommended since it reduces procedure time and improves the success rate.
- Monitoring and optimization of cardiac output (CO) are central components of perioperative hemodynamic management in these patients. PiCCO, TEE, Swan-Ganz catheters, and other advanced monitoring are recommended to assess the need for inotropic or vasoactive drugs and guide fluid management. In addition, patients with acute myocardial injury should be considered for early intra-aortic balloon pump, ventricular assist device, or ECMO mechanical circulatory support [63].
- COVID-19 patients may have abnormal coagulation function. Therefore, platelet counts, prothrombin time (PT), international normalized ratio (INR), and partial thromboplastin time (PTT) should be regularly evaluated. Multiple blood conservation strategies such as preoperative hemodilution, antifibrinolytic medications, intraoperative blood salvage, mild hypothermia or normothermia during cardiopulmonary bypass, and autologous platelet-rich plasma technology are required to reduce blood transfusion and decrease transfusion-related lung injury.
- At the end of the procedure, the patient is left intubated. He is then transferred to an airborne isolation ICU room through a designated pathway. A HEPA-equipped portable ventilator should be used during the transfer.

CONCLUSION

Although to date many questions remain to be answered concerning the exact pathophysiology and therapeutic approach for the COVID-19 pandemic, this manuscript provides available data for both anesthetic management as well as healthcare professionals' security in this setting.

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COVID-19 PANDEMIC

COVID-19 AND PREGNANCY: LEBANON PREPAREDNESS WITHIN GLOBAL RESPONSE

http://www.lebanesemedicaljournal.org/articles/68(1-2)/pandemic8.pdf

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El Kak F. COVID-19 and pregnancy: Lebanon preparedness within global response. J Med Liban 2020; 68 (1-2) : 60-62.

Towards the end of 2019, in December, a new strain of coronavirus was identified in Wuhan, China, and found to cause severe acute respiratory syndrome (ARDS). The virus, known as novel coronavirus, was later named SARS-CoV-2, being one of seven coronaviruses, mostly close to SARS and MERS coronaviruses.

The WHO announced a name for the new coronavirus disease: COVID-19, and declared it as Public Health Emergency of International Concern. At the time of writing this manuscript, there are 4 589 526 confirmed SARS-CoV-2 positive cases and close to 310 391 death in 216 countries and territories [1]. Globally, countries went into staged precautionary measures to prevent spread of the outbreak [2]. In February 21, 2020, Lebanon identified its first case and immediately Ministries, Government bodies, and several agencies began a COVID-19 public health and awareness campaign along with escalated measures towards a state of medical emergency (banning travel from epidemic countries, closing schools/shops/malls/others up to a state of curfew) [3].

National efforts focused on flattening the curve of outbreak spread to avoid health system collapse in view of the limited number of beds, including intensive care beds, and the specificity of Lebanon demographics in relation to Syrian and Palestinian refugee camps and crowding, as well as the clinical course of COVID-19.

In a report from China on more than seventy thousand cases with COVID-19 disease [4], 19% of the cases had a disease spectrum from severe to critical with pneumonia being a major cause of maternal morbidity and mortality. WHO reports showed a mortality rate of 3%-4% [5], but with higher rate of patients requiring admission to the intensive care unit (ICU) [6]. The overwhelming and vast global spread of COVID-19 has raised concerns about its impact on pregnancy and childbirth, including neonatal health. Lebanon has an estimated population of pregnant women of around 125.000 Lebanese and non-Lebanese [7] that demands special attention, information, and guidance form health care providers, namely the obstetricians and gynecologists (OBGYN). Although international guidance consensus indicates that pregnancy is not a particular high risk event to COVID-19 [8], the physiologic changes during pregnancy are known to predispose pregnant women to worst outcomes with viral pneumonia, including higher rates of hospitalization [9], with consequent higher maternal and neonatal morbidity and mortality [10-11]. To our knowledge, data looking at the effect of COVID-19 disease on pregnancy remains limited which makes both counseling and management of these patients cautious and conservative. In this respect, comparisons were made with two other global outbreaks of highly-pathogenic coronaviruses: severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). Although SARS-CoV-2 is not identical to SARS and MERS, it shares some genetic structures and clinical manifestations in relation to pregnancy course and outcome. Data from the limited literature on SARS and MERS in pregnancy revealed cases of severe disease requiring need for intensive care admission [12-17]. Maternal mortality cases associated with SARS and MERS infection were reported. Comparing pregnant to non-pregnant outcomes with SARS infection in one case-control study showed that pregnant women with SARS disease had worst outcomes [18].

Globally, the community of OBGYN has been made responsive by the proactive response of the International Federation of Obstetrics and Gynecology (FIGO) in compiling resources, launching training webinars, and issuing statements related to COVID-19 outbreak in pregnancy, gynecologic oncology, essential sexual reproductive health services, and elective surgeries [19]. In specific, FIGO issued one of the earliest statement on COVID-19 and pregnancy that was contributed to by its vice president, the chair of the safe motherhood committee, and other experts from FIGO federations, highlighting priorities in dealing with pregnancy and maternal health care during the outbreak and in building the skills of OBGYNs to respond to it. FIGO aimed to reach its 132 national member societies which might have varied response and preparedness to COVID-19 pandemic depending on their resources and logistical preparations, more so in low and

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middle income countries (LMIC). Moreover, FIGO like other global agencies is adamant on ensuring interruption or delay to essential services that are mainly related to family planning and contraceptive methods, abortion (when legally allowed), post-abortion care, and identification and management of survivors of violence. There is an ongoing collaboration between FIGO and WHO to implement self-care guidelines whenever possible around services like contraception, cervical cancer screening self-test, dysmenorrhea, menopausal therapy, and counseling survivors of violence.

Lebanon was not also any different for early responders to COVID-19 and pregnancy. Considering potential risk of SARS-COV-2 on pregnancy, and aiming to protect pregnant women from the pandemic, the Ministry of Public Health in Lebanon (MOPH) formed a National Technical Committee on Corona and Pregnancy, the only specialized committee in the region, with the main aim to prevent COVID-19 outbreak among pregnant women and to raise professional and public awareness on COVID-19 and pregnancy. This aim presents a challenging priority to Lebanon in the presence of close to 50 thousands or more pregnant non-Lebanese women [20] spread across urban and camps settlements, with different patterns of antenatal care and suboptimal compliance with visits and supplement intake [21]. The Committee, chaired by Dr Faysal El Kak, included chairpersons (or their representatives) of the six main academic universities with teaching medical centers, the president of the Lebanese Society of OBGYN (LSOG), Director of the National Program on Mental Health, President of the Lebanese Order of Midwives, UNFPA, and representatives from the MOPH. The Committee was mandated to prepare response of health care providers (HCPs) to COVID-19 and pregnancy.

Over 10-12 weeks, the Committee achieved several tasks that included: Developing awareness and advocacy material on various aspects of COVID-19 and pregnancy (Pregnancy risk, breast-feeding, vertical transmission, protection measures, birth spacing, etc.) which were posted on social platforms and distributed to around 250 hospitals and primary health care centers all over Lebanon. The Committee members also developed clinical protocols and algorithms related to outpatient and inpatient management of pregnancy care and childbirth which was based on diverse global guidelines and adapted to the Lebanese context, and made available in Arabic, English, and French to OBGYNS and HCPs, as well as posted on the MOPH website, and on the International Federation of Gynecology and Obstetrics (FIGO) website (the Arabic version). Following that, a series of 12 training webinars were delivered in collaboration with the CME office at the American University of Beirut Medical Center (AUB-MC) that provided CME credits and certificate of attendance. The webinars were expected to reach close to one thousand participants in Lebanon and the region, and were instructed also in Arabic, English, and French. The webinars aimed to build the knowledge and skills capacity of service providers.

Looking at cases of COVID-19 in pregnancy revealed a report of only one case that presented to a hospital in the North of Lebanon. On presentation she had a low grade fever and her accompanying husband had suspicious symptoms. She was transferred to another hospital in the same area, and was considered a person under investigation (PUI), and was tested for SARS-COV-2 before delivery by cesarean section under precautionary measures with the medical team donning personal protective equipment (PPE). The newborn was healthy with good Apgar scores, and was separated temporarily from the mother, transferred to regular nursery and tested for SARS-COV-2. One day postpartum, the coronavirus test of the mother came positive, and that of the newborn came out negative. On the second day postpartum, the mother and newborn were discharged home with full isolation precaution instructions.

The fact that there is one documented case of COVID-19 in pregnancy might be related to the early precautionary actions taken by the Government, the intense health promotion addressing pregnant women urging them for self-isolation and lockdown, as well as the OBGYN community response to modifying antenatal care using telehealth. However, there is a strong global argument on universal screening of all pregnant women as they are a category more susceptible to respiratory illness complications [22]. In another study looking at 43 COVID-19-positive pregnant women over a period of 2 weeks, 33% infected women were often asymptomatic, supporting a role for universal testing upon admission to labor and delivery [23]. In a letter to the editor of the *New England Journal of Medicine* on universal screening, it was reported that out of 33 SARS-CoV-2 positive pregnancies on admission, 29 of them (87.9%) had no symptoms [24]. Universal screening of pregnant women depends on the degree of the pandemic spread and on the available funds and resources in a given setting. In Lebanon, universal screening is not affordable, especially that the current reporting of cases indicates successful containment of the outbreak. Nevertheless, precautionary measures of testing, isolating, and tracking should continue to avoid the second wave of the pandemic, and this of course includes pregnant women.

COVID-19 pandemic represents a global crisis that goes beyond health and health systems. Health care providers have been challenged and threatened as front-liners and one-liners at times, and OBGYNs managing

pregnancy and childbirth have to learn a lot about protecting themselves and the pregnant women. The Lebanese OBGYN community and other health care professionals (HCPs) are expected to continue seeking available resources of the National Committee on Corona and Pregnancy regarding modifications of antenatal care, special considerations in intrapartum and postpartum care, breastfeeding, and provision of long acting reversible contraceptives, as well as PPE for the protection of the much needed health personnel.

Disclosure

No conflict of interest.

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COVID-19 PANDEMIC

WHAT TO DO AS A GYNECOLOGIC ONCOLOGIST DURING THE COVID-19 PANDEMIC? MEMAGO Statement

http://www.lebanesemedicaljournal.org/articles/pandemic9.pdf

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Atallah D, Abdel Khalek Y, Mutlu Meydanli M, El Kassis N, Abdallah R, Ayhan A, Khoury C, Chahine G, Taskiran C, Kose F, Seoud M. What to do as a gynecologic oncologist during the COVID-19 pandemic? MEMAGO Statement. J Med Liban 2020; 68 (1-2) : 63-71.

ABSTRACT • The SARS-Cov-2 virus pandemic causes an acute public health emergency with millions of infected patients and thousands of deaths. The infection makes adults prone to severe and fatal consequences, especially when they suffer several comorbidities. Our oncologic patients are the most susceptible to its severe repercussions because of their initial diagnosis and the immunosuppressive adjuvant and neoadjuvant treatments they receive. The Chinese CDC reported a 5.6% risk of mortality among cancer patients compared to 0.9% in the general population; likewise, other studies showed a twofold higher risk of death in this patients' subgroup. In order to maintain the best quality of medical services during this crisis, along with the safety of healthcare providers, accurate triage of our oncologic patients must be done before any medical or surgical intervention to decide whether or not postponing treatments may be considered, without risking the disease progression and patients' worsening outcomes, otherwise inpatient and outpatient special precautions must be followed whenever interventions are currently scheduled, according to each gynecologic cancer type. The disease is worldwide but local and regional circumstances vary, thus practice guidelines must be individualized according to each country virus prevalence and available medical resources, in order to limit the burden of the COVID-19 infection on the health system during the crisis and the upcoming months after its resolution.

Keywords : COVID, gynecologic oncology management

INTRODUCTION

In December 2019, an outbreak of a novel beta coronavirus occurred in Wuhan, China. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; COVID-19) spreads rapidly causing severe symptoms, multiple organ failure and thousands of deaths worldwide. Two months later, the WHO declared the COVID-19 pandemic and a public health emergency of international concern; most countries were on lockdown in an effort to stop the spread of the disease and its fatal consequences.

All medical and paramedical staffs were requisitioned to work with patients infected by the COVID-19, meanwhile gynecological cancers and emergencies continued to occur requiring a management strategy to provide affected women with the highest quality of medical care and, at the same time, safety for the patients, their families and the working medical teams.

SURGERY IN GYNECOLOGY – THE TRIAGE

Surgical procedures in gynecology can be divided according to a priority level. Some need urgent interventions while others may be postponed for months after the resolution of the crisis, without compromising the patient's safety and quality of life. Therefore, multiple societies classified the indications of gynecological procedures according to the degree of urgency.

The Society of Gynecologic Oncology used the Elective Surgery Acuity Scale (ESAS), modified for gynecologic oncology procedures, to classify indications for surgery into elective/non-urgent, semi-urgent, and urgent/emergent [1]. According to their scale, gynecologic oncology procedures fall into high acuity surgery for healthy/unhealthy patient (Tier 3a/b) category, which means semi-urgent surgeries that cannot be postponed (Table I).

Similarly, the American College of Surgeons considered gynecologic cancers or suspected cancer cases (ovarian, tubal, peritoneal, endometrial, cervical, vulvar, vaginal, gestational trophoblastic neoplasm) as non-urgent surgeries but needing interventions with no delay to prevent significant harm [2].

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TABLE I

MODIFIED ELECTIVE SURGERY ACUITY SCALE [1] FOR PATIENTS WITH CANCER IN THE ERA OF COVID-19 [1]

Tiers/ Description	Definition	Locations	Examples	Action
1a	Low acuity surgery/healthy patient Outpatient surgery Not life threatening illness	ASC Hospital with low/no COVID-19 census	Surgery for benign-appearing ovarian cysts Hysterectomy for menorrhagia without anemia	Postpone surgery or perform at ASC
1b	Low acuity surgery/ unhealthy patient	ASC Hospital with low/ no COVID-19 census		Postpone surgery or perform at ASC
2a	Intermediate acuity surgery/healthy patient Not life threatening but potential for future morbidity and mortality May require in-hospital stay	ASC in select cases Hospital with low/ no COVID-19 census	Hysterectomy for precancerous conditions or low risk endometrial cancer	Postpone surgery or consider ASC
2b	Intermediate acuity surgery/ unhealthy patient	ASC Hospital with low/ no COVID-19 census		Postpone surgery if possible or consider ASC
3a	High acuity surgery/healthy patient Potentially life threating or patient is highly symptomatic Requires in-hospital stay	Hospital	Surgery for most cancers Resection of masses resulting in significant end-organ damage or quality of life impairment	Do not postpone
3b	High acuity surgery/ unhealthy patient	Hospital		Do not postpone

ASC: Ambulatory surgical center

SURGERY, ADJUVANT TREATMENT & MORTALITY IN COVID-19 INFECTED PATIENTS

In Wuhan, China, a multicenter retrospective study showed that all patients operated during the incubation period of the COVID-19 infection developed pneumonia shortly after surgery, and that 44.1% of them required ICU admission and 20.5% of them died [3].

The gynecologic oncology team must ensure that their patients are neither carriers nor infected with COVID-19, even if asymptomatic, prior to any surgery. Screening for COVID-19, if available, must be performed before any intervention, depending on local resources and priorities [4]. If the patient tests positive, surgery should be postponed, if possible, until recovery [4].

Furthermore, oncologic surgeries and any additional medical or radiotherapy treatments may result in immunosuppression and increase the patients' risk for infections. Studies show that, compared to the healthy population, patients are at a greater risk of acquiring the COVID-19 infection and developing severe complications. Until January 31, 1% of all the cases of COVID-19 in China had cancer, which is higher than the incidence of cancer in the general population (0.29%). These cancer patients were at higher risk of severe complications (39% vs. 8%, *p*-value = 0.0003), especially those who received chemotherapy or underwent surgery in the prior month (75% vs. 43%) (Figure 1) [5]. Similarly, He et al. showed a statistically significant increased risk of severe complications in the COVID-19 infected patients with cancer, with a hazard ratio of 3.56 (Figure 2) [6].

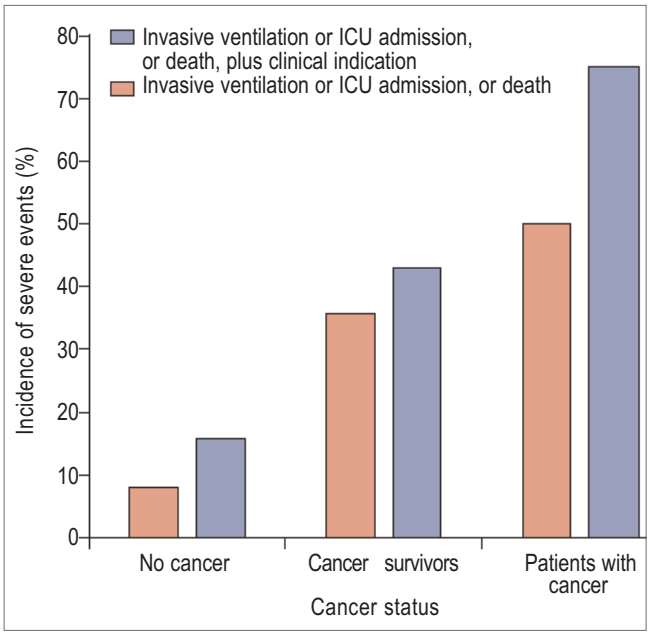

Figure 1

Severe events in patients without cancer, cancer survivors, and patients with cancer during the COVID-19 pandemic [5].

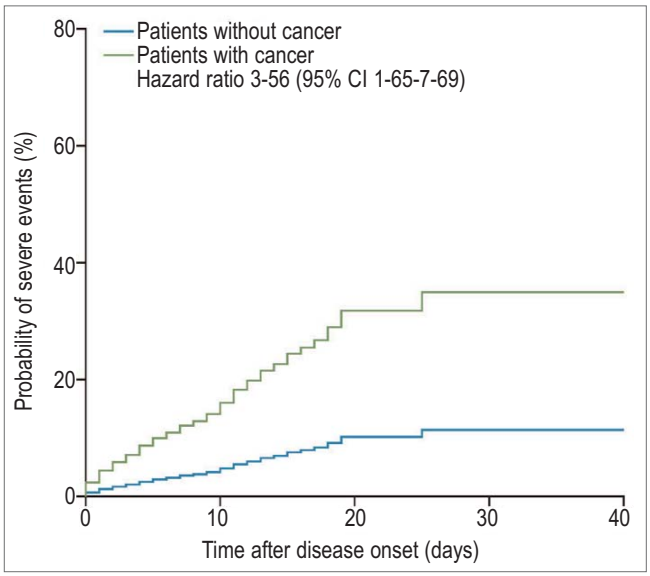

Figure 2
Probability of developing severe events for patients with and without cancer during the COVID-19 pandemic [5].

Another nationwide analysis in China showed an increased risk of intubation and death in patients with cancer who were infected with COVID-19 [7]. The Chinese Center for Disease Control reported a mortality rate of 5.6% among cancer patients compared with 0.9% in the rest of the population (Table II).

The problem is that the majority of these studies included a small number of patients. In an effort to precisely estimate the risk of death in cancer patients undergoing treatment and infected with COVID-19, data from the Chinese Center for Disease Control, the Italian public health authorities and the Diamond Princess cruise ship were combined, analyzed and compared to previous viral respiratory pandemics [7-8]. COVID-19 infection was associated with a twofold higher risk of death. However, it was not clear whether this higher risk was due to the cancer itself or increased with chemotherapy. Further, the risk of death in these patients was > 5% (Table II), which may be higher than the most benefits of adjuvant treatment [7]. Therefore, any benefit from gynecological, surgical or medical treatment during this pandemic, must be appropriately balanced against any increase in the risk of complications and death.

TABLE II
DEATH RATE OF PATIENTS WITH COVID-19 INFECTION ACCORDING TO PRE-EXISTING CONDITIONS. DATA FROM THE CHINESE CENTER FOR DISEASE CONTROL AND PREVENTION 2020

Pre-existing Condition	Death Rate	
	Confirmed cases	All cases
Cardiovascular disease	13.2%	10.5%
Diabetes	9.2%	7.3%
Chronic respiratory disease	8.0%	6.3%
Hypertension	8.4%	6.0%
Cancer	7.6%	5.6%
No pre-existing conditions	_	0.9%

In the oncology patients the risk factors of greater vulnerability include [9]:

- _ Age ≥ 65 years old.
- _ Significant comorbidity (cardiovascular disease, pulmonary disease, diabetes mellitus).
- – Eastern Cooperative Oncology Group (ECOG) performance status ≥ 2.
- – Cytotoxic chemotherapy.

OUTPATIENT VISITS

The following precautions are recommended in relation to outpatients visits of gynecologic cancer patients.

i. Screen patients for symptoms of COVID-19 by phone one day prior to the visit. Repeat at check-in (symptoms ± temperature) [9].
ii. Restrict visits to new diagnosed cancer patients, or those presenting acute symptoms and recurrent/active disease [9,10].
iii. Restrict accompanying visitors (one visitor can be allowed if necessary, for physical /psychological patients limitations, providing that this person is not suspected of being infected) [9,10].
iv. Limit the number of healthcare providers in the room to minimize the risk of exposure (physician, resident, nurse) [10].
v. Schedule the appointments to minimize the number of patients in the waiting area, to encourage physical distancing [9].
vi. Postpone routine visits, and schedule telemedicine appointments for postoperative visits, if feasible [9,10].
vii. Educate patients on symproms of COVID-19 infection and on the best practices to limit its transmission (hand washing, social distancing).

INPATIENT MANAGEMENT

When indicated, perform cancer surgeries only in centers free of COVID-19, if feasible, to limit the risk of complications for both patients and medical staff.

During inpatient interventions, for safety reasons, some practices must be encouraged:

i. Avoid surgeries with prolonged operative time, associated with major intraoperative and postoperative complications, risks of blood loss

and admission to intensive care units.

ii. Reduce hospital stay.

iii. Minimize the number of healthcare providers working with each patient [9].

iv. Opt for minimally invasive techniques. However, laparoscopic surgery may put medical staff at risk of aerosol exposure. Till now, no data confirmed the presence of COVID-19 in the surgical smoke, but like HPV and HIV, the novel coronavirus particles may be present in the body cavity thus disseminated through CO_2 release during laparoscopy [4]. Open surgeries should be promoted, otherwise use laparoscopy with caution to minimize gas dispersal during interventions (insertion and removal of ports, instruments, specimen, abdominal deflation) [4].

v. Avoid inpatient chemotherapy [9].

These guidelines may be followed, according to each hospital local resources and the presence of COVID-19 specialized centers.

In hospitals, as well as the lack of masks, gloves, hand sanitizers, ventilators and available beds, the healthcare staff is facing during this pandemic a shortage of blood supplies. Many blood donation centers are closed, donors are either sick or following social distancing measures, and most blood components have short expiration time, thus obtaining blood supply for transfusions during this crisis has become a real challenge [11]. One example is from New York City, where blood centers reported a 75% decrease in the number of donors [12].

Currently, the postponement of elective surgical interventions may reduce the need of blood products, but the possible progression of untreated cases may result in additional needs for transfusions during the upcoming period [11].

Although it is confirmed that the COVID-19 transmission occurs via respiratory droplets, more studies are needed to rule out its possible transmission via blood components [11].

Therefore, other strategies are crucial to optimize our patients' own blood supply. They can be classified into preoperative, intraoperative and postoperative practices:

[a.] Preoperative practices

On March 2020, both the WHO and the European Center for Disease Prevention and Control strongly recommended the implementation of "Patient Blood Management" measures to guaranty an effective treatment of all patients [11]. Meanwhile, for patients scheduled for delayed interventions, practices that must be undertaken are:

i. Early diagnosis and treatment of anemia:

Anemia is a contraindication for elective surgery [13], especially during the current crisis. A large meta-analysis by Fowler et al. including almost one million patients showed that preoperative anemia is associated with higher probability of mortality (OR = 2.9, $p < 0.001$) [14], infections (OR = 1.93, $p = 0.01$) [14], kidney injuries (OR = 3.75, $p < 0.001$) [14], needs for transfusion (OR = 5.04, $p < 0.001$) [14], and 22% of longer hospital stays (11 vs. 9 days, $p = 0.0001$) [15]. Iron deficiency is the major cause of anemia, thus oral or intravenous supplementation is essential while waiting for the planned delayed surgery. Other anemia related deficiencies must also be addressed via folate or vitamin B12 supplementation while chemotherapy induced bone marrow suppression can be treated via erythropoiesis stimulating agents administration [11,13].

ii. Early diagnosis and management of coagulopathy: When available, perform coagulation and platelet function testing to adequately diagnose coagulation disorders, and treat via administration of clotting factors and antifibrinolytic agents that may prevent the need of plasma and platelets transfusion [11,13].

[b.] Intraoperative practices

i. Meticulous surgical techniques and hemostasis [13].

ii. Cell salvage techniques [11,13].

iii. Antifibrinolytic agents [11,13].

iv. Topical hemostatic agents [11,13].

v. Local vasoconstrictive agents [11,13].

vi. Acute normovolemic hemodilution [11,13].

[c.] Postoperative practices

i. Rapid surgical intervention or embolization when interventional radiology is available to address postoperative bleedings [11].

ii. Prophylaxis of upper GI hemorrhage [13].

The accurate management of anemia leads to lower transfusion rates, fewer hospital acquired infections, reduced hospital stays thus better clinical outcomes [11].

Below, we list the management of each gynecological cancer separately.

Specific types of gynecological cancers

a. Pre-invasive cervical neoplasia:

The American Society of Colposcopy and Cervical Pathology (ASCCP) divided pre-invasive disease into low grade and high grade according to screening tests. The diagnostic evaluations of low-grade disease

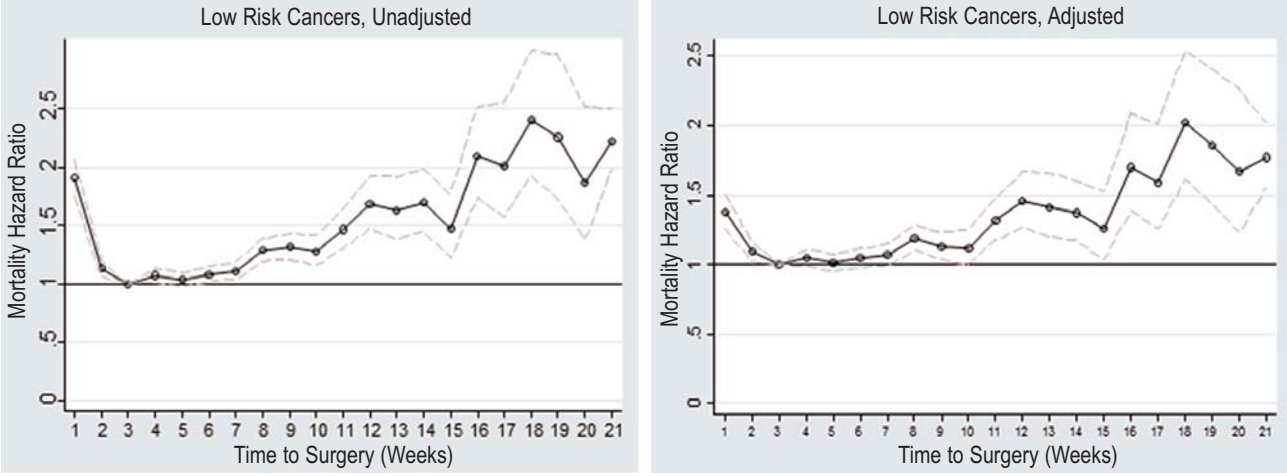

Figure 3. Hazard ratios for mortality of low grade endometrial cancer.
Dashed lines indicated 95% confidence interval. (Unadjusted/adjusted for patient's age, race, insurance status, stage, ...) [17].

can be postponed for 6-12 months, while it should be scheduled within 3 months for high grade lesions [9,10]. Patients with AIS should be individualized.

b. Early-stage cervical cancer:
Surgical intervention is recommended whenever feasible. In hospitals where oncologic surgeries are suspended, consider postponing localized disease for 6-8 weeks. Low risk/microscopic disease (< 2 cm, low grade) can benefit from conization or simple trachelectomy ± sentinel lymph nodes, while prolonged procedures associated with intra- and postoperative complications should be postponed [10]. Consider neoadjuvant treatment for gross visible tumors.

c. Locally advanced cervical cancer:
According to the American Brachytherapy Society, treatment should be offered with no delay for asymptomatic patients (COVID-19 negative).
   i. Patients with stages IB3, IIB-IVA should receive the standard treatment with concurrent chemotherapy and radiotherapy [16].
   ii. Patients with stage IVB: For the first line and/or for the first recurrence after more than one year from primary treatment, use cisplatin/paclitaxel + bevacizumab (if there is a contraindication for the use of cisplatin, it can be replaced with carboplatin or use GOG 240 protocol of paclitaxel, topotecan and bevacizumab) [16].
   iii. Consider hypofractionation of the radiotherapy sessions (increase dose, reduce number of fractions) and weekly telemedicine appointments to minimize the patient's visits to the hospital [10].
   iv. Radiotherapy for symptomatic localized recurrence or inoperable asymptomatic recurrence [16].

Endometrial cancer

a. Low-risk endometrial cancer:
   i. Low grade cancers are usually cured by surgery. This subtype of endometrial cancer is the most sensitive to delay [17]. One large study on the relation between surgical timing and survival outcomes was published in 2017. Low grade and high grade endometrial cancers cases from 2003 to 2012 recorded in the American National Cancer Database were collected.
   The results showed that 5-years survival rates are higher when surgery for low grade endometrial cancer is performed between week 3 and week 8 after the diagnosis, after that mortality rates are significantly higher (Figure 3) [17]. Thus, surgery must be the first line therapy for low grade endometrial cancers, whenever possible, according to local resources and the virus prevalence.
   ii. Consider conservative management (systemic/intrauterine hormonal therapy) in patient with atypical hyperplasia or grade 1 endometrial disease [8-10], when surgery is not feasible.

b. High-risk endometrial cancer:
Consider simple hysterectomy + bilateral salpingo-oophorectomy ± sentinel lymph nodes if feasible in grade 2/3 or high risk histology disease [10].
Consider brachytherapy in intermediate-high risk disease [18].

c. Advanced endometrial cancer:
Consider systemic treatment after tissue biopsy [10].
Consider radiotherapy for isolated vaginal relapse (curative) or asymptomatic pelvic recurrence [18].

Ovarian cancer

a. Suspected early ovarian cancer:
   Consider risk factors (age, family history, genetic predisposition), physical examination and radiological and biological tests to determine the risk of malignancy and the benefits of direct intervention [10].
   In early stage disease, in women with low or moderate risk factors (premenopause), it is safer to postpone the surgery [8].
b. Advanced ovarian cancer:
   i. Consider neoadjuvant treatment after obtaining tissue biopsy [10].
   ii. Use carboplatin/paclitaxel every 3-4 weeks for 4-6 cycles (4-5 cycles if response before adding PARP inhibitor ± early discontinuation of paclitaxel if toxicity) [19]. Consider adding bevacizumab if there is significant ascites and or no response to treatment.
   iii. Consider GCS to prevent leucopenia and limit dexamethasone to prevent immunosuppression [19].
c. Patients undergoing neoadjuvant chemotherapy:
   i. If feasible, consider administration of four to six cycles of chemotherapy, rather than three, before proceeding to cytoreductive surgery [8,10].
   ii. Consider chemotherapy agents and doses that have minimal complications (lymphopenia/neutropenia) in order to limit the need of hospitalization [9]
d. Patients who have completed up-front platinum-based chemotherapy:
   Consider stopping treatment; however, continue monitoring toxicity via telemedicine if available [10].
e. Patients who progress on current treatment:
   Consider additional chemotherapy if potential benefits are expected [10].

Vulvar cancer

The main symptom of vulvar cancers is pain. Perform resection, if possible, because it is the most successful method to relief the pain. Consider surgery under local anesthesia if feasible. Remove sentinel lymph nodes but postpone groin lymphadenectomy until the end of the crisis [8].

PSYCHOLOGICAL IMPACT OF TREATMENT DELAY

Any delay in the treatment of a patient with cancer can result in significant anxiety and depression. Both the patient and her physician may be concerned about disease progression resulting in a worse prognosis. However, data show that, in most cancers, a 3 to 8 weeks delay is acceptable [1].

If a delay in the treatment is chosen, consider reevaluation every 2 to 4 weeks to avoid disease progression and a worse outcome [1].

FOLLOW-UP

Complications are common following cancer surgery and treatment, and these may require urgent attention (such as examination, blood tests, imaging) and urgent interventions [16,18,19]. These complications include, but are not limited to:

- Bowel perforation, peritonitis
- Fistulization
- Anastomotic leak
- Intestinal or urinary obstruction
- Pelvic bleeding
- Pulmonary embolism
- Abscess.

INFORMED CONSENT

Even in this critical situation, the clinician should discuss with the patient all the available treatment modalities (surgery/medical treatment – immediate/delayed procedure) and the resulting risks and benefits of each intervention or the delay of such intervention. A shared decision should be taken based on different factors: the local resources, the local prevalence of COVID-19, the patient's performance status and comorbidities, the cancer characteristics and stage and the possible adverse outcomes that may result from any delay in the treatment [1]. As usual, a detailed informed consent should be signed before any intervention, with particular reference to the status of the COVID-19 infection in the community.

ACADEMIC ACTIVITIES AND STUDIES

In order to maintain the best quality of medical services, transparent communication should be encouraged to benefit from other institutions experiences in this outbreak. Academic activities must be maintained, such as morning meetings, journal clubs, tumor boards and multidisciplinary conferences, via web-based systems [6,10].

As for clinical trials, only those with curative intents or life prolonging opportunities must remain active [10]. All other trials may expose patients and health care providers to unnecessary risks, thus must be closed until the end of the crisis. If toxicity evaluation visits are needed, consider doing them via telemedicine. However, patients who test positive for COVID-19 must be removed from the study and referred for appropriate treatment by their physicians [10].

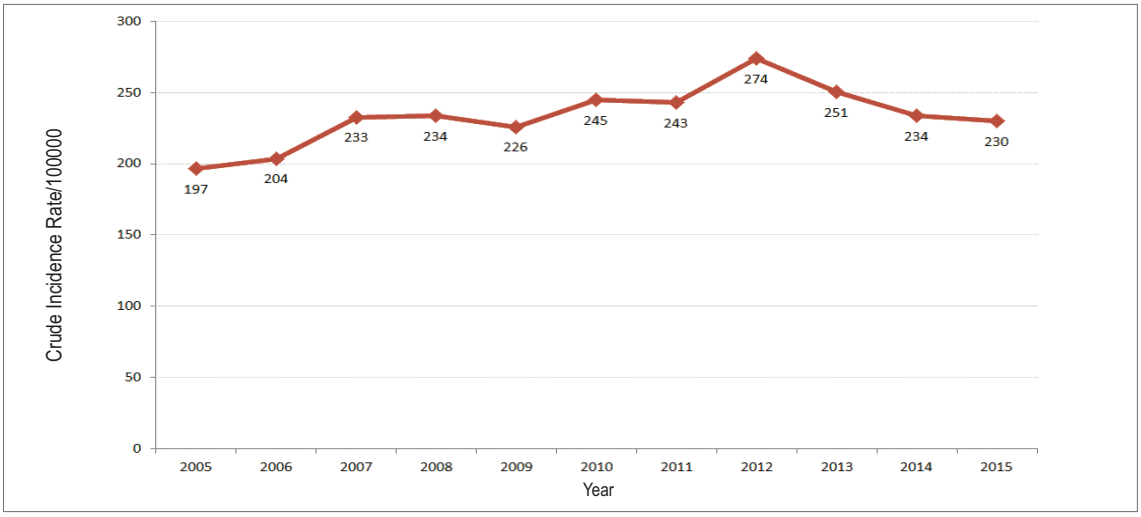

Figure 4. All cancers, crude incidence rates/100000, females, Lebanon, 2005-2015 [21]

COVID-19 BURDEN ON HEALTH CARE SYSTEMS

COVID-19 infection has caused a heavy burden on health systems all over the world, and it is expected that these repercussions will continue months after the resolution of the immediate crisis.

Due to the limited resources and the high risks of contamination, health care providers are mainly focusing on COVID-19 patients, postponing all other clinical practices.

Delaying proper management, especially of cancer patients may lead to disease progression and possible worse survival outcomes [6].

Moreover, stopping screening activities such as mammography, pap smear, colonoscopies, etc., may lead to increase morbidity and mortality. That is why scheduled appointments should be maintained whenever feasible and safe for both patients and health practitioners, otherwise they should be timely rescheduled after the resolution of the immediate crisis [6].

However, diverting all follow-up and screening visits until the end of the pandemic will lead to excessive accumulation of visits, which will result in a greater burden on an already overstretched health care system [6].

This is the distraction effect of COVID-19 and we should fear its menaces for the coming months [6].

LOCAL PREVALENCE AND RESOURCES

On the 8th of December 2019, the first case of COVID-19 infection was identified in Wuhan, China. Rapidly the virus spread worldwide with 9,551,507 cases and 485,423 deaths on June 25 [20].

In Lebanon, until April 20, we registered 677 cases of COVID-19 infected patients and 21 deaths, an incidence considered excessively low compared to other countries [20].

Furthermore, the local prevalence of cancer is particular to each population.

According to the NCR data 2015, the incidence rate of cancers among Lebanese females is 0.23% [21], and over a period of 10 years, the graph showed an increase in the incidence (Figure 4).

In 2015 and among 100000 cancer patients, the distribution varied according to cancer types.

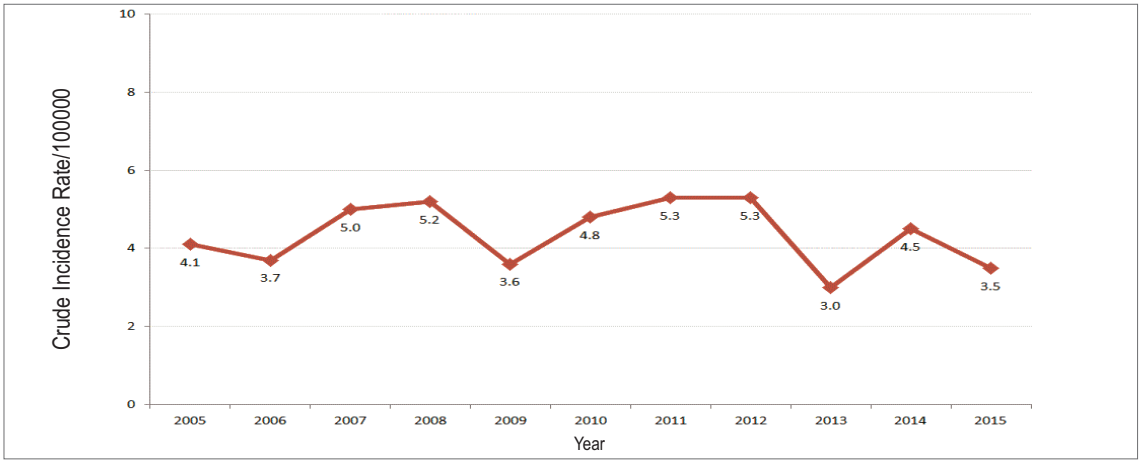

Figure 5. Cervical cancer, crude incidence rates/100000, Lebanon, 2005-2015 [21]

Cervical cancer

Below we list the numbers between some gynecologic cancers:

– Cervix: 3.5 (Figure 5)
– Ovaries: 7.6 (Figure 6)
– Endometrium: 7.9 (Figure 7)
– Breast: 84 (Figure 8)

Over a period of elven years, a recent Lebanese epidemiologic analysis showed that breast cancer account nowadays for 20% of all cancer types, an

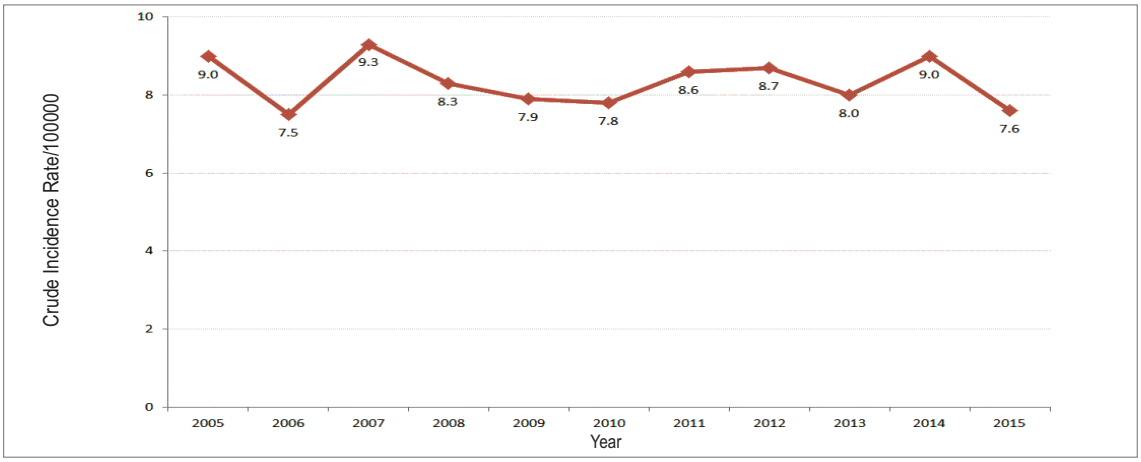

Figure 6. Ovarian cancer, crude incidence rates/100000, Lebanon, 2005-2015 [21]

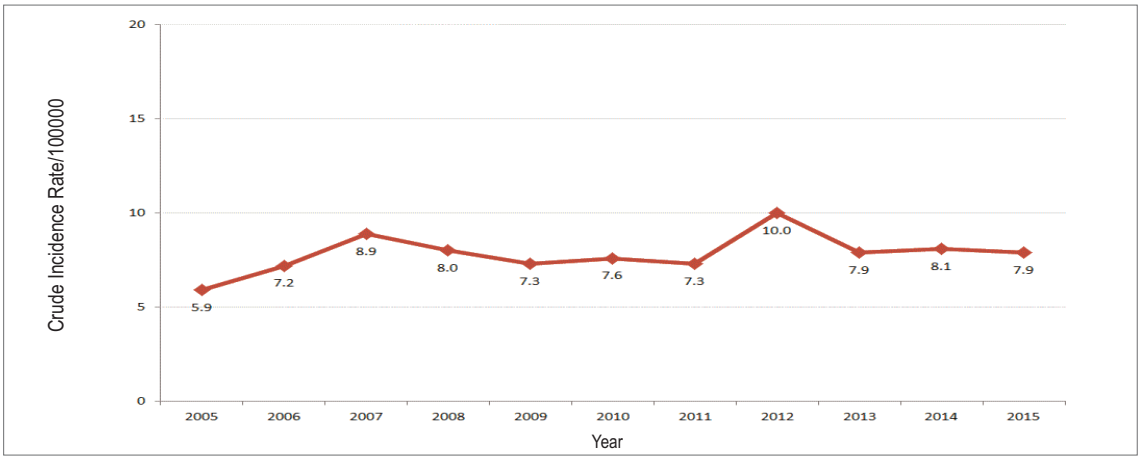

Figure 7. Endometrial cancer, crude incidence rates/100000, Lebanon, 2005-2015 [21]

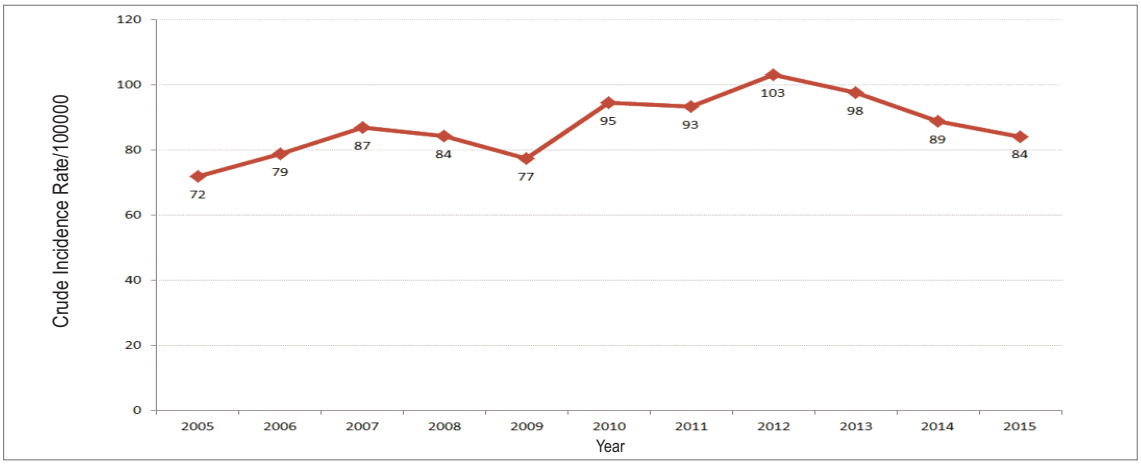

Figure 8. Breast cancer, crude incidence rates/100000, Lebanon, 2005-2015 [21]

incidence among the highest in the world [22].

Therefore, in Lebanon, the COVID-19 prevalence is low and gynecologic cancers are frequent. For social and political reasons, our health care system is already vulnerable and overstretched, thus we should manage our resources wisely in order to limit the burden of the crisis.

CONCLUSION

The COVID-19 infection is a serious disease that causes severe morbidity and mortality especially when it occurs in patients with cancer. In order to maintain the best quality of medical services for gynecologic cancer patients, accurate triage of cases according to the level of urgency is needed to prevent delay in the treatment and worsening of the prognosis and to safeguard the health care providers safety. The disease is worldwide but locoregional circumstances vary, thus practice guidelines must be individualized according to the prevalence of COVID-19 infection, the prevalence of various cancers and the available medical resources.

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COVID-19 PANDEMIC

THE LEBANESE SOCIETY OF MEDICAL ONCOLOGY (LSMO) RECOMMENDATIONS AND PERSPECTIVES ON ONCOLOGY CARE DURING COVID-19 PANDEMIC

http://www.lebanesemedicaljournal.org/articles/68(1-2)/pandemic10.pdf

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Nagi S. El SAGHIR[3], Hamad HASSAN[4]

Bitar N, Kattan J, Kourie HR, Mukherji D, El Saghir NS, Hassan H. The Lebanese Society of Medical Oncology (LSMO) recommendations and perspectives on oncology care during COVID-19 pandemic. J Med Liban 2020; 68 (1-2) : 72-75.

INTRODUCTION

COVID-19 is a viral disease caused by SARS-CoV-2 of the coronavirus family. It is very contagious and highly transmissible via coughing and sneezing droplets, contaminated surfaces and aerosols. Although airborne transmission is debatable, the Centers for Disease Control and World Health Organization in all countries recommend wearing face masks, in addition to physical distancing in order to reduce the spread of SARS-CoV2 coronavirus.

Cancer patients are known to be more susceptible and vulnerable to infections including viruses. Compared to the general population, the risk of mortality is 10 times higher, and the risk of hospitalization is 4 times higher in cancer patients. This is mainly in patients that have hematologic malignancy, or receiving numerous lines of chemotherapy, or patients that are presenting neutropenia and lymphopenia (Bitterman et al, Cochrane Database Syst Rev, 2018).

As stated in recent Chinese data, cancer patients had higher risks of COVID-19 infection, in addition to a higher incidence of severe events due to increased hospitalization risks for cancer patients with respect to the general population (1% vs. 0.29%). Furthermore, in cancer patients infected with COVID-19, the risk of developing respiratory complications that require intensive care was higher with respect to non-cancer patients (39% vs. 8%, p = 0.003). It was also reported that among cancer patients, age was the most important prognostic factor; but the study involved observation of only 18 patients out of a total of 1580 patients (Liang et al., Lancet, 2020).

In another Chinese study, 53% developed adverse events and 28.6% died among a 28 cancer patients cohort. An increased risk of severe events was reported in patients who had their last anti-neoplastic treatment within 14 days prior to COVID-19 diagnosis. Another Chinese study reported a higher rate of adverse events (53.6 %) and mortality (28.6%) among a 28 cancer patients cohort, with a higher risk of severe events in patients who had their last anti-tumor treatment within 14 days prior to diagnosis of COVID-19 (Zhang et al., Annals of Oncology, 2020).

A more recent study from New York reported that out of 5700 COVID-19 patients, the three most frequent comorbidities with COVID-19 were hypertension (56%), obesity (41%) and diabetes (33%). Only 6% (320 patients) had cancer. Authors did not report on prognostic related issues, except for age which was an indicator of more invasive mechanical ventilation for patients < 65 vs. patients > 65 years of age (Richardson et al, JAMA, 2020). Obesity was also reported in 35.8% of patients in another study from New York and may represent a risk factor for increased use of invasive mechanical ventilation (Goyal et al, NEJM, 2020).

COVID-19 IN LEBANON

By the 10th of June 2020, more than seven million of confirmed cases of COVID-19 were diagnosed worldwide with more than 400,000 deaths. In Lebanon, 1400 confirmed cases of COVID-19 were diagnosed with 31 deaths.

Huge efforts were implemented by the Lebanese Ministry of Public Health (MOH), from day one of the diagnosis of the first case of COVID-19 (21st of February 2020) to limit the spread of the virus in Lebanon:

1. Media campaigns for spreading awareness on the precautions to limit transmission of COVID-19, especially physical distancing, social distancing, hand washing, wearing facemasks, and school and university closures.
2. A national state of emergency called progressive national lockdown, in line with governmental measures and coordination with other ministries.
3. Immediate establishment of an operational and sep-

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arate well equipped coronavirus section at Rafik Hariri University Hospital (RHUH) for screening, testing, isolation, regular hospitalization and intensive care of COVID-19 patients.
4. Support for the establishment of Coronavirus centers at various University Hospitals in Beirut and other parts of the country.
5. Enhancement of the capacity of Lebanese governmental hospitals in distant cities in the country.
6. Increase in the number of PCR testing per day.
7. Providing safety precautionary measures, testing, and quarantine for Lebanese students and expatriates who wished to return home, isolating those who test positive for SARS-CoV2, and confining those who test negative for 14 days.

COVID-19 PANDEMIC AND ITS EFFECTS ON THE CARE OF CANCER PATIENTS IN LEBANON

A single institution experience was published from Hôtel-Dieu de France (HDF), Beirut, evaluating the impact of COVID-19 pandemic on the flow of cancer patients' treatment at the one-day clinic. The results showed that the number of patients at the one-day clinic for the month of March was almost equivalent to the number of February and that of January.

As a matter of fact, data collected from HDF records showed the admission of 743 patients during the month of January 2020, 696 patients during the month of February 2020 and 710 patients during the pandemic month of March 2020. Many patients seemed resistant to abide by these precautious directions as seen by the one-day hospital records of admissions (C. Kattan et al, 2020, Future Oncology). However, the number of patients visiting the oncologist' clinics for consultations was tremendously decreased during the COVID-19 pandemic.

From the beginning of the pandemic in Lebanon, the Naef K. Basile Cancer Institute at the American University of Beirut Medical Center (AUBMC) in coordination with the AUBMC Infection Control Committee and the newly established COVID-19 Task Force, started a comprehensive set of recommendations that included an initial triage of patients by the secretaries and nurses for symptoms, travel history and contacts, application of protective and distancing measures in clinics and chemotherapy units, postponement of elective appointments and routine screening.

The number of clinic visits dropped significantly in the initial phases. AUBMC instituted telemedicine to offer patients virtual clinic appointments. This was rapidly implemented using the videoconferencing facility linking the hospital electronic medical record system (Epic) and its built-in "MyChart" application accessible to patients. This has been welcomed by patients and staff, particularly for routine follow-up visits for patients, many of whom preferred it out of concerned about coming out of home confinement and travelling to the hospital facility. Hospital admissions and numbers of new patients on ambulatory chemotherapy infusion dropped initially...

In general, due to stringent protective measures, cancer-related services for patients were maintained while minimizing risk of exposure and transmission within this vulnerable patient population and health care workers. Multidisciplinary Tumor Boards were continued either in-person with a smaller number of essential attendees, or virtually via WebEx.

The experiences in other oncology departments in Lebanon are concordant with those seen reported at HDF and AUBMC. Many oncologists and hospital departments adopted the national guidelines related to the management of cancer patients during the COVID-19 pandemic.

It is expected that the incidence of new cases of cancer in Lebanon will probably drop during April and May 2020 because of the decreased number of routine clinic visits, imaging, biopsies, screening tests and elective surgeries, with a concern that advanced stage cases may resurface. This is expected to have a transient impact and decrease of the activity in oncology departments over the next few months.

The current maintained activity in these departments is mainly based on patients diagnosed before COVID-19 pandemic who are receiving adjuvant treatment or chronic metastatic patients on various palliative treatments.

THE LSMO GUIDELINES

In view of the spread of COVID-19 in the country and the National Lockdown (Called State of Mobilization in Lebanon) imposed by Health Authorities and Government, and based on worldwide experience, LSMO issued its first guidelines to help oncologists, oncology staff, patients and their relatives to cope and deliver the most optimal care while reducing the chances of contracting, and propagating the SARS-CoV-2 during the present outbreak.

With the rapid evolution of this pandemic and the tsunami of international recommendations, it was necessary to update this statement of LSMO on the care of patients with cancer during the COVID-19 pandemic. The LSMO team has disseminated guidelines via their website, as a rapidly published editorial and during regular online webinar meetings.

THE FIVE RECOMMENDATIONS FOR DAILY PRACTICE
(Bitar et al., Future Oncology, 2020)

1. Prevention of contamination: Screening of patients and visitors for travel history and symptoms. COVID-19 positive patients and suspected cases should not be admitted to oncology outpatient departments or oncology hospital floors. Suspected and infected cases should be referred to COVID-19 specialized departments and services for management.
2. Prioritization of patients by favoring curative therapies versus palliative, application of therapy pause when justified, and withholding chemotherapy and immunotherapy for patients with poor prognosis.
3. Avoid overcrowding of clinics by deferring regular routine follow-up with over-the-phone consultations, and of chemotherapy units by decreasing the number of patients receiving weekly chemotherapy versus more spaced regimens, consider switch to oral chemotherapy when possible versus intravenous treatment.
4. "Sanctuarization" of oncology department: Withhold any immunosuppressive treatment of patients diagnosed to have COVID-19 until full recovery. Admission of COVID-19 positive should be done in specialized departments.
5. Manage patients in need of supportive care and palliation by phone calls and [by] keeping them safe at home.

PREVENTION ADVICE FOR PATIENTS

- Avoid crowded places.
- Wash hands thoroughly according to WHO guidelines.
- Wear masks properly, use sanitizers and gloves when necessary and when going to a clinic/hospital.
- Do not have contact with family/friends with COVID-19 symptoms/possible exposure.
- Practice physical distancing and social distancing with all people to protect yourself and others.
- Keep in contact with medical team and report new symptoms by telephone first (particularly fever/cough/shortness of breath).

PRECAUTIONS FOR ONCOLOGY STAFF

- Wash hands and use sanitizers between examinations of patients.
- Maintain physical distancing of 1 meter (6 to 8 feet) apart even in waiting and examination rooms.
- Use masks, and gloves when examining patients.
- Disinfect commonly touched items.
- Reduce the number of daily clinic appointments and space them out.
- Reduce patient waiting time to a minimum.
- Limit the number of accompanying persons or visitors.
- Use online meeting tools for tumor boards, grand rounds and classes for medical students.
- Suspend travel for oncology staff during the pandemic.

MANAGEMENT OF PATIENTS IN OUTPATIENT SETTING

- Screening questions before admission to unit (Fever/cough/chest pain/travel history/contact travel history/exposure to patient with COVID-19 infection).
- For patients with symptoms: make sure surgical mask is worn by patient and companions; staff wearing masks and gloves direct patient to the nearest screening center if stable, escort to emergency department (ED) if unstable, informing ED team prior to arrival.
- Patients with travel/contact history and asymptomatic: request to self-quarantine for 14 days and reschedule appointment if possible. If not possible, patient to be isolated, patient and medical team to wear facemask, gloves. Full PPE (personal protectice equipment) including apron and arm covers are reserved for health care workers (HCW) caring for COVID-19 patients.

SUGGESTED STRATEGY IN DIFFERENT SETTINGS FOR CANCER PATIENTS
(Bitar et al., Future Oncology, 2020)

Patients on follow-up or endocrine/oral targeted therapies

- Prevention.
- Delay visits and follow-up appointments in absence of active disease/new symptoms requiring review.
- Delay routine restaging imaging if no new symptoms.
- Lab tests can be performed locally if required and reviewed by telephone/sending picture of results.
- Telephone contact/telemedicine in place of clinic visits.

Patients with early-stage cancer/curative setting:

- Prevention.
- Close monitoring for potential toxicity and for COVID-19 clinical symptoms.
- Consider increased use of GCSF to limit neutropenia.
- Discussion of risks vs. benefits of adjuvant ther-

apies with patients.

- Consider limiting duration of adjuvant therapy where appropriate (3 vs. 6 months adjuvant chemotherapy for "good risk" stage 3 colon cancer for example).
- Choose three weekly regimens instead of weekly regimen.

Patients with metastatic disease

- Prevention.
- Close monitoring for potential toxicity and for COVID-19 clinical symptoms.
- Consider delay in treatment or therapeutic break if not compromising disease control.
- Consider oral therapy options and telemedicine for toxicity management.
- Discuss risks vs benefits with patients.

EXPECTED CHALLENGES IN ONCOLOGY AFTER COVID-19 PANDEMIC

This pandemic will represent a continuous challenge for the medical community before a SARS-CoV-2 vaccine and curative treatment are available. As additional waves of new cases are expected in Lebanon and across the world, continuous adoption of preventive measures during the care of cancer patients in clinics, in chemotherapy units and during hospitalization seems mandatory.

Oncology departments should maintain the same vigilance regarding the implemented surveillance and protective measures for both patients and medical and hospital staff, as long as required to limit coronavirus spread. Increased testing capabilities, tracing contacts, as well as confinement and isolation as needed, adequate protective equipment, and hospital/intensive care readiness are in progress in Lebanon for facing any upcoming wave of the COVID-19 in Lebanon.

Reopening of oncology and hematology care, as well as general medical and surgical care after lockdown will have to be carefully planned and implemented, along with increasing capacity for diagnostic PCR testing of suspected cases, and immunity rapid antibody testing, particularly for medical staff, nurses and hospital staff, as well as essential services workers in the country.

CONCLUSION

COVID-19 pandemic presents a historical cancer care challenge for the Lebanese oncology community, as it is for the medical community worldwide. LSMO published its first recommendations at the beginning of the COVID-19 pandemic in the country and adopted a strategy of periodically communicating new data to ensure the best possible care for cancer patients.. Many webinars are being organized with the oncologists nationwide to increase awareness about these guidelines and to apply them in the various oncology clinics, departments and centers. Preventive measures by the oncology staff, clinics, departments and patients themselves were rapidly adopted based on our national recommendations.

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COVID-19 PANDEMIC

THE IMPACT OF COVID-19 ON UNDERGRADUATE MEDICAL EDUCATION

http://www.lebanesemedicaljournal.org/articles/68(1-2)/pandemic11.pdf

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Ayoub E, Bahous S, Chamsy D, ChouKair M, Yared N, Ghorayeb Z, Houry M, Nemr E. The impact of COVID-19 on undergraduate medical education. J Med Liban 2020; 68 (1-2) : 76-79.

ABSTRACT • Coronavirus disease COVID-19 upended the whole world with everyone needing to practice social distancing, and quarantine. These measures affected education in general, and medical education in particular. Educators were faced with the dilemma of protecting the students versus fulfilling the mission of preparing qualified future healthcare providers. In Lebanon, the seven medical schools had to act quickly to set up distance education in response to the requested closure of universities and social distancing measures, in a way that preserves student education despite the challenging times. This paper will focus on the changes introduced to the curricula of the undergraduate medical education programs in Lebanon, involving both the teaching and learning facets and the assessment component at the preclinical and clinical phases.

Keywords : medical education; distance learning; COVID-19; Lebanon

INTRODUCTION

During the 20th century, the modern world witnessed three influenza pandemics: the Spanish flu (1918-1919) caused by the influenza A virus H1N1 subtype, the Asian flu (1957-1958) linked to the H2N2 subtype, and the Honk Kong flu (1968-1969) caused by the H3N2 subtype. In the current century, a new H1N1 pandemic resurged in 2009, followed by the ravaging COVID-19 outbreak that the whole world is currently witnessing, affecting more than 8 million subjects worldwide and causing the death of more than 400 000 to date.

On 21 February 2020, Lebanon confirmed the first case of COVID-19 infection when a 45-year-old woman traveling from Iran tested positive for SARS-CoV-2. One week later, in a preemptive step to impede a coronavirus spread among students, Lebanon's Education Ministry issued a circular on the 28th of February mandating a nationwide week-long closure of all academic institutions as the cumulative number of patients who had tested positive was four. In a media statement issued by the Ministry, Dr Al Majzoub said: "In the interest of the health of students and their families, all educational institutions including kindergartens, schools, high schools, vocational institutions and universities are requested to shut down for a week, between March 1 and March 8 as a precaution against the spread of the disease." A governmental committee dedicated to follow up on the preventive measures against the Coronavirus was formed and extended, on the 6th of March, the closure of schools, universities and nurseries till March 14 over Coronavirus concerns. The committee also ordered the closure of gyms, cinemas, theatres and nightclubs.

On 15 March 2020, Prime Minister Hassan Diab, declared after an extraordinary cabinet session, a state of general mobilization until March 31st, 2020.

He announced a set of additional measures and decisions taken by the government to deal with the emerging Coronavirus COVID-19 outbreak, with the aim of protecting Lebanon and its citizens. All educational institutions would remain closed during this phase. Afterwards, the Lebanese government continued to extend the general mobilization depending on daily numbers of positive tests until May 7, stressing on social separation and preventing gatherings in different public and private places.

The internal security forces and army assisted in ensuring compliance with these measures. Despite the progressive ease of lockdown that was announced starting May 8, schools and universities would remain closed until the 25th of May, until further notice.

COVID-19 AND MEDICAL EDUCATION IN THE WORLD AND LEBANON

Coronavirus disease COVID-19 upended the whole world who turned to the healthcare frontlines, shedding the spotlights on the medical and paramedical professionals, the real soldiers of this "war" against an invisible and highly contagious enemy.

The pandemic forced the earthlings to adopt the same measures irrespective of their residence, gender, nationality, ethnicity, economic standing and educational level. It was everyone's call to practice social distancing, and

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quarantine when prescribed, as only effective weapons [1].

These measures affected education in general, and medical education in particular. Educators and administrators were faced with the dilemma of protecting the students versus fulfilling the mission of preparing qualified future healthcare providers. Most programs, if not all, felt the obligation to replace the "in-person" classes with online equivalents using various websites and platforms. Likewise, the clerkships, crucial for the acquisition of various skills and professional attitudes, were challenged by many factors forcing schools around the world to remove students from the clerkship environment. In March 2020, the Association of American Medical Colleges (AAMC) provided guidelines suggesting that medical schools support pausing clinical rotations for medical students [2].

In Lebanon, the seven medical schools had to act quickly by moving to distance education in response to the requested university closure and the social distancing measures, in a way that preserves student education despite the challenging times.

This paper will focus on the changes introduced to the curricula of the undergraduate medical education programs in Lebanon, involving both the teaching and learning facet and the assessment component at the preclinical and clinical phases.

I. Teaching and Learning

A. Large and small group teaching

In compliance with physical distancing safety measures, all medical schools initiated remote teaching to deliver the knowledge that students should normally acquire in preclinical and clinical phases.

To that end, multiple platforms for web teaching were available, namely Zoom, Webex, Microsoft TEAMS and Moodle.

Each medical school used one or more of those platforms to allow a fruitful interaction between the teacher and the students. Through the Web, information efficiently reached large groups of learners; whereas most of the small group events were either deferred or replaced by large group online activities.

Only rarely, small group case discussions occurred on social media tools like WhatsApp.

Frequently, power point presentations were provided with audio or video support; occasionally they were sent by email to students for convenience.

The advantage of online platforms compared to power point presentations and Moodle, is the fact that they allow a live interaction between lecturers and students and provide room for questions and feedback.

B. Clerkships

Clinical clerkships are essential for students to develop the ability to obtain a pertinent history from a patient, perform a proper physical examination, formulate a differential diagnosis and develop a diagnostic and therapeutic plan, develop communication skills when dealing with patients and their families and cultivate a professional relationship with patients, peers and healthcare professionals.

However, the clerkships were challenged by several factors [3]:

- diminished educational value with the cancelation of routine admissions, surgical procedures and outpatient appointments,
- risk that the students contract the disease or transmit it unknowingly to their patients and families,
- lack of universal COVID-19 testing at the start of the pandemic,
- shortage in adequate Personal Protective Equipment (PPE) for the protection of healthcare personnel.

All university hospitals developed COVID-19 units to welcome and care for affected patients. Two hospitals attended more than 50 COVID-19 patients, two hospitals provided care for 10 to 50 patients, and one hospital managed less than 10 patients. Hospital occupancy significantly decreased; 30 to 65% beds were vacant in all university hospitals and medical centers. All hospitals, except one, halted elective surgical procedures and close to 50% of hospitals decreased elective medical admissions.

Consequently, the number of students rotating in various hospital departments was significantly reduced by 40 to 100%. Night-shift duties were cancelled for medical students in most clinical rotations.

To compensate for the lack of clinical encounters, certain medical schools provided students with various online resources that offer supporting teaching material, video resources and virtual sample cases in various disciplines. Examples of such resources include OnlineMedEd and Aquifer.

In most university hospitals, students were kept out of the COVID-19 units and therefore, did not participate in the clinical care of any affected patient. This measure was implemented to protect the wellbeing of medical students and avoid putting them at the forefront of this highly infectious disease.

Many students assisted in specialized COVID-19 call centers to guide men and women with any questions and concerns.

Many students also volunteered in awareness campaigns via posters and social media.

II. Assessment

A. Overview

Though online teaching rapidly evolved to provide maximum education to students under coronavirus lockdown, yet the online approach for assessment, particularly for summative assessment, raises some challenges on different fronts: psychological, legal, logistical and ethical.

- *Psychological challenges* mainly related to the mindset of students, faculty and officials living in an unprecedented health and economic crisis; the vast majority were preoccupied by the unknowns of such crisis and felt unprepared for assessment.
- *Legal challenges* related to Lebanese laws regarding distance education or what is defined by the Ministry as "Internet education". Thus, the law regulating "the higher education" n° 2014/258 has no mention of distance education. In addition, the "Committee for the Recognition and Equivalence of Diplomas" can recognize so-called online certificates or programs only under "very specific" conditions, linked above all to "the proportion of courses authorized to be taught in an online mode" and which should not exceed "a percentage of the total of the courses included in the programs of universities and higher institutes le-gally recognized". In addition, the official website of the Ministry of Education and Higher Education states that diplomas issued for completion of programs using "Internet studies" are not eligible for recognition or equivalence.
- *Logistical challenges* linked to several factors such as:
  - The number of faculty and administrative staff needed to complete online assessment, especially tests necessitating one-to-one interaction, and the time necessary to conduct these assessments would be exhaustive and very resource demanding.
  - Performance assessments, testing for clinical performance in the workplace, poses significant challenges for the online approach.
  - The testing site has moved from the university or the workplace to the examinee's home. This has been associated with many concerns related to proper proctoring (exam security and fairness) and the challenge of stable connection with a proper traffic quota and bandwidth to support videoconferencing. On the other hand, conducting exams on the university premises was limited by the need to rearrange the physical facilities to accommodate students with proper physical distancing.
  - The exam dates had to be [done] within a reasonable time frame as not to affect the cycle of graduation-internship-residency, which in turn would affect the workflow at the hospitals.
- *Ethical challenges* stemmed from the need to maintain fairness, validity and transparency of the assessment in order to make just inferences and preserve patient safety. Such important characteristics of assessment are easily challenged by the online format and the risk of cheating in the absence of sufficient institutional oversight.

Given the complexity of the situation, decisions specific to each school were issued as detailed below.

B. Preclinical phase

Six medical schools practiced online *formative* assessment of student learning using a multitude of online tools (posting of clinical vignettes, feedbacks and others).

Summative exams were delayed at all seven medical schools. Afterwards, two medical schools decided to postpone all summative exams to a later date corresponding to a possible reopening of universities; two other schools made the decision to use online tests; one medical school used online assessment for low-stakes exams and administered high-stakes, onsite tests from various locations involving more than one university campus to respect physical distancing; one medical school adopted the online format for continuous assessment and deferred high-stakes exams to a later date, and one medical school opted initially for partial online assessment and deferral of final exams, to readopt, at a later stage, the full online assessment approach after positive experiences were published.

Regarding the types of assessments and monitoring systems used, some medical schools administered quizzes and multiple-choice questions controlled by an "automated proctoring tool", others gave homework assignments and projects, and one school adopted "open book tests" without any control program. The first feedback obtained from students was quite positive while waiting for the end of the academic year to further capture and analyze all opinions from students and faculty.

C. Clinical phase

Most medical schools initially opted for postponing scheduled final written exams. After few weeks had elapsed, three medical schools readjusted to perform the exams online using all the available technology to ensure maximal monitoring and security, and one medical school

resumed on-site administration of exams using various locations as stated above for the preclinical phase. The remaining three schools elected to move written exams to later dates when they could administer on-site examinations respecting physical distancing.

Given the difficulty of ensuring safe logistics to perform Objective Structured Clinical Examinations (OSCE) and other forms of in person standardized clinical exams, most medical schools postponed these tests to a proposed date when it would be safe to conduct them on premises. One medical school cancelled these exams, one school postponed them and conducted them in May, and one medical school conducted for the first time an online virtual OSCE for the graduating class while respecting all requirements for distancing.

The clinical evaluation of students' performance in the workplace was completely fulfilled after direct observation using online platforms in five medical schools with a switch to the Pass/Fail grading, while it was postponed till the students resume fully their rotations at two medical schools.

In three medical schools where a thesis is a graduation requirement, students submitted their theses online and assessment was fulfilled using this approach.

CONCLUSION

The impact of COVID-19 was unexpected, quick, and harsh, disrupting all sectors including medical education. Medical educators were faced worldwide, including here in Lebanon, with a disrupted system but not much past experience in tackling such challenging issues. However, with their collaborative efforts, educators have led the rapid creative development and implementation of new methods bypassing problems in curriculum content delivery, clinical placement, adjusting assessment methods, and making up for lost time.

Our seven medical schools were faced with similar problems; however, our advantage as a smaller country is that we were all affected similarly since there was no regional variations in the spread of COVID-19. While students were quarantined at home, the different medical schools had to find alternative ways to accomplish competency goals and use the remaining academic time wisely upon their return.

Clinical placement for clerkships was particularly challenging since that could not be resolved entirely by an online experience. Many factors came into play such as students' safety, their health care insurance coverage, availability of PPEs, faculty supervision, and availability of PCR testing. All of that was taken into account while trying to keep the students' experiences somewhat uniform and comparable while fulfilling the clinical objectives of each rotation.

Ethical issues came up in terms of exposing students to COVID-19. Definitely, student safety is primordial; however, they need to realize that they are eventually joining a profession where providing care to patients does sometimes require placing oneself at risk. This is a phase where transparency and communication between administrators and students are very important. Both parties should acknowledge stressors and work together in order to find solutions that are suitable for both. COVID-19 remains unpredictable with the possibility of a second wave affecting us later on in the year. Our medical schools will continue to evaluate the situation on a regular basis to make appropriate decisions regarding students in order to continue meeting their educational objectives and proficiencies without compromising their health and safety.

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COVID-19 PANDEMIC

RESIDENCY AND FELLOWSHIP TRAINING DURING THE LEBANESE FINANCIAL CRISIS AND THE COVID-19 PANDEMIC: NAVIGATING UNPRECEDENTED CHALLENGES

http://www.lebanesemedicaljournal.org/articles/68(1-2)/pandemic12.pdf

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Mirza FG, Ayoub E, Hubayter ZR, Malas S. Residency and fellowship training during the Lebanese financial crisis and the COVID-19 pandemic: Navigating unprecedented challenges. J Med Liban 2020; 68 (1-2) : 80-82.

INTRODUCTION

Lebanon has been witnessing extraordinary challenges that commenced at the end of the summer of 2019. The country had been going through a major financial crisis that further worsened with a nationwide uprising that started in October of that year. As anticipated, the fear of unforeseen protests and road disruptions, along with a sharp decline in the purchasing power of the Lebanese population, severely affected the approach and access of patients to medical care. This subsequently led to a sharp decline in the number of outpatient visits and inpatient admissions at almost all medical centers. Lebanon was not aware that an even more ferocious challenge awaited its healthcare sector.

The coronavirus disease 2019 (COVID-19) pandemic emerged and its burden on Lebanon was heavily felt only few months into its progressively worsening financial crisis. The combined effect of the local economic situation and worldwide COVID-19 pandemic had an unprecedented impact on the Lebanese population in general and the healthcare sector in particular. As such, the personal and professional lives of residents, fellows, and their families across the country were significantly impacted.

Graduate medical education in most countries, including Lebanon, was severely disrupted by the COVID-19 pandemic. The hands-on experience required during residency and fellowship training is highly dependent on the training site's patient load. During the pandemic, the number of outpatient visits dropped significantly, and the surgical volume at hospitals was restricted to emergencies. As such, the hands-on aspect of training was profoundly affected for specialties that are not heavily involved with the preparedness and management of COVID-19 patients. Additionally, the traditional educational activities, including didactic lectures, case discussions, morbidity and mortality conferences, and grand rounds, were suspended in many institutions in order to adhere to physical distancing practices. Thus, almost all aspects of graduate medical education were negatively impacted by the COVID-19 pandemic in the setting of a major ongoing financial crisis the country had been struggling with for months before the burden of the pandemic was fully appreciated.

PROFESSIONAL SOCIETIES

Professional societies around the world have issued valuable guidance in response to the COVID-19 pandemic. First and foremost, their recommendations focused on the safety of trainees and on coping with potential absences due to illness or the need for quarantine. Secondly, their guidelines strived to safeguard the quality of training in the context of the pandemic and the restrictions it has posed. Thirdly, they worked on modifying the certification process for the graduating trainees under these extremely unusual circumstances. Finally, some professional societies have called upon various training programs to modify the application process for the upcoming academic year. Lebanese institutions have relied on local guidance as well as that of the major professional societies of the United States and Europe.

SAFETY OF TRAINEES

To ensure the safety of their trainees, many institutions, often guided by directives from local health authorities as well international professional societies, have made major modifications to their clinical rotations. The American College of Obstetricians and Gynecologists (ACOG) have urged program directors to restructure resident, fellow, and medical personnel clinical schedules to limit exposure and preserve the workforce. [1] Many programs have transitioned to a call schedule with a lean team

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structure that features staffing with the fewest residents/fellows that are needed to provide adequate and safe patient care. In Lebanon, many academic medical centers have pursued a similar approach with minimizing the number of residents who are physically present on the premises, particularly with the cessation of all elective surgical procedures, in compliance with the directives of the Lebanese Ministry of Public Health and the Centers for Disease Control and Prevention (CDC).[2] It is noteworthy that many professional societies have stressed on the importance of protecting residents, fellows, and medical personnel with unique circumstances, such as those with significant health concerns or comorbidities that put them at risk as well as residents and fellows who live with children, spouses, or significant others that are immunocompromised.[1]

In one institution, the residents were divided into teams with alternating weeks in order to mitigate risks of exposure and to have a team on standby in case of unexpected exposure. Residents contacted their respective infectious control units before switching site and often needed to complete a 2-week quarantine. This is particularly important as several residents from the different schools rotate at the main referral center for COVID-19 in the nation. Some institutions have implemented protocols to test for pregnant patients at term in order to reduce the risk of exposure to the residents and other healthcare staff, often utilizing an internationally published algorithm.

All residents were instructed to use appropriate personal protective equipment (PPE), with N95 respirator masks whenever a patient is potentially – or confirmed – COVID-19 positive. Residents, like all other medical staff, were trained on the proper use of the PPE. In one center, the laboring patient, if not tested, is encouraged to wear a mask herself. Residents allowed to enter to a patient room were restricted to one resident. When a pregnant patient admitted for delivery is possibly COVID-19 positive, then the laboring process and delivery will take place in a negative pressure operating room.

COMPETENCE

Committed to their growth and support, professional societies worldwide have worked tirelessly on developing learning materials and resources for residents and fellows that are electronically disseminated and easy to obtain.

The American College of Obstetricians and Gynecologists (ACOG) has urged program directors to continue resident and fellow education through virtual learning whenever possible, and to attempt to create structured didactic remote learning to supplement clinical exposure during this time.[1]

The Council on Resident Education in Obstetrics and Gynecology (CREOG) of the American College of Obstetricians and Gynecologists (ACOG) has been active in sharing online material developed by certain residency programs with all the programs that fall under its umbrella.

These educational series, at times surgical videos and demonstrations, feature some of the most renowned educators to help foster remote learning among residents despite the disruption of their didactic lecture series. Other institutions have resorted to intensive simulation training as an alternate method of compensation. Finally, there has been a suggestion for limiting away rotations in the upcoming academic year to those applicants who have not been able to acquire this specific experience locally.[3]

In an effort to compensate for the loss in direct patient care, ACOG has also encouraged program directors to develop telehealth programs that involve residents and fellows.[1] This was, in fact, pursued at a number of Lebanese hospitals. Moreover, and also in an attempt to ensure competence of graduating residents, some institutions have elected to extend the academic year. For instance, the Executive Committee of a leading academic center has decided to extend the academic year by two months to be able to compensate for the lost training period. At another institution, residents with a cumulative absence above the maximum allotted per year – including both vacation and sick leave as well as days lost secondary to the uprising or corona – will have to make up these days prior to graduation. In addition, these residents were given the option to pursue an additional year of training without impacting the training of the more junior residents.

CERTIFICATION AND RECRUITMENT

Another issue that specifically pertains to graduating residents and fellows in the midst of the COVID-19 pandemic is the impact on their future endeavors,

Their absences due to COVID-19 illness or the need for quarantine have imposed the extension of their training in some instances. The lockdown in various countries and the focus on combating COVID-19 has affected the recruitment process of trainees after graduation. This was coupled with the challenge of an escalating economic crisis. Additionally, restricted travel and closed borders continue to threaten the future of graduates of Lebanese programs who have elected to pursue further training outside Lebanon in various countries across Europe and the Unites States. While virtual interviews were offered by some outside institutions, this was not a universal experience. Moreover, graduating trainees who

have sought international certification had to deal with cancelled examinations and difficulty traveling to examinations centers outside the country.

CONCLUSION

In the wake of the unprecedented cascade of events that Lebanon has struggled with in recent months, the healthcare sector was significantly impacted. The academic medical centers, with their residents and fellows, were not immune and the training of these young physicians was indeed jeopardized. Training programs were guided locally and internationally, and different measures were taken to ensure the safety of their trainees, to optimize their learning experience, and to safeguard their future as competent post medical graduates.

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COVID-19 PANDEMIC

STATEMENT OF THE LEBANESE PULMONARY SOCIETY, THE LEBANESE SOCIETY OF CRITICAL CARE MEDICINE & THE LEBANESE SOCIETY OF ANESTHESIOLOGY

http://www.lebanesemedicaljournal.org/articles/68(1-2)/pandemic13.pdf

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Abi Saleh W, Aoun-Bacha Z, Bou Khalil M, Bou Khalil P, Boulos R, Chami H, Diab Kh, Juvelikian G, Yazbeck P. Statement of the Lebanese Pulmonary Society, the Lebanese Society of Critical Care Medicine & the Lebanese Society of Anesthesiology. J Med Liban 2020; 68 (1-2) : 83-86.

ABSTRACT • COVID-19 has taken the whole world by surprise and overnight, we found ourselves at war with an invisible yet ruthless adversary. In Lebanon, representatives from the major medical societies at the forefront of the battle convened and drafted a document to serve as a roadmap towards tackling this pandemic. It involves diagnosis and early recognition of severity as well as potential treatment modalities, emphasizing the protection of healthcare personnel.

Keywords : COVID-19; management; statement; prevention

INTRODUCTION

COVID-19 is a highly transmissible viral illness of the Coronavirus family with relatively higher mortality in older individuals and patients with chronic disease. It has a particular predilection for the lungs. In severe cases multiorgan failure can also occur and might lead to death. [1,2]

TRANSMISSION

This disease is highly transmissible mostly through contact and droplets and could become airborne if nebulized.

PREVENTION OF TRANSMISSION

General recommended interventions

They include social distancing, frequent and thorough hand washing for at least 20 seconds with soap, hand rubbing with alcohol-based solution at a 60% to 70% strength, and frequent disinfection of high-touch surfaces.

Healthcare workers should wear gloves, face masks, eye shields and waterproof full body personal protective gowns when caring for patients with confirmed or suspected COVID-19.

Healthcare workers should additionally wear a N95 mask, preferably fitted, covered by a face shield to cover the whole face and an overall suit when caring for a confirmed COVID-19 patient receiving respiratory support (high flow oxygen, noninvasive or mechanical ventilation) and during aerosol generating procedures (nebulized therapy, bronchoscopy, intubation, suction).

Readiness of healthcare [2.3,4]

Safety of healthcare personnel is paramount. Ideally, every institution caring for COVID-19 should have a dedicated section for patients with coronavirus.

Personal protective equipment (PPE) includes long sleeved waterproof gown or overall suit, gloves covering the sleeve, shoe covers, protective shield or goggles, and mask N95 when performing procedures, in ICU rooms, operating rooms, and negative pressure rooms.

A proper decontamination of healthcare personnel upon removing their PPE is necessary for their own safety and the safety of their loved ones.

Ideally, critical patients should be placed in negative pressure rooms, and it is strongly recommended that intubation be performed in a negative pressure room.

Intubation should be performed via Rapid Sequence method, preferably without Ambu-bagging, preferably video assisted, with maximal barrier and airborne protection.

For severe cases, patients should be ventilated invasively to maximize their chances of recovery and minimize transmission to the surrounding.

In case of invasive mechanical ventilation, we recommend the following:

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– Use closed suctioning.
– Avoid circuit interruption.
– Avoid active humidification.
– Use properly placed bacterial and viral filters.

Avoid aerosolized treatments and use instead a dry powder inhaler (DPI) and a metered dose inhaler (MDI) with spacer (expand DPI and MDI).

Increase availability of critical care beds by restricting and postponing elective surgeries.

Noninvasive ventilation and high flow oxygenators should be avoided and kept as last resort if invasive ventilation is no longer available, as they may increase the risk of contamination.

As critical care beds become all occupied, the operating rooms can be used as critical care units.

PATIENT TRANSPORT

Avoid patient transport when it is possible. Nonintubated patients should wear a mask over their oxygen delivery service. All personnel should be wearing full PPE.

Hallways must be cleared.

Psychological support is strongly recommended to both patients and healthcare providers.[4]

PROPOSED PROTOCOL FOR DIAGNOSIS & TRIAGE OF SUSPECTED COVID-19 PATIENTS (Appendix)

Exposure history

This includes reviewing the history of travel or residency of the patient in a country or regionwith high COVID-19 exposure. It is also necessary to check whether the individual works in close proximity or lives in the same household as a COVID-19 patient..

Patients with a positive COVID-19 test, fever, cough and negative chest imaging can be discharged to home isolation if that is possible.

Triage of a suspicious case [2,3]

- Common symptoms of COVID-19 are: sore throat, fever, cough, and shortness of breath. Shortness of breath is a common indicator of more severe disease.
- A patient with known COVID-19 contact and/or with known travel to a high-risk area within the past 14 days with 2 out of 4 symptoms should be referred to a designated clinic.
- In case of shortness of breath or hypoxia, the patient should be directed to a designated Coronavirus Emergency Room.

Initial paraclinical assessment lab testing [2.3.5]

CBC, CRP, Chem 6 (basic chemistry). PCR (strongly recommended if available), chest X-ray.

A CT scan chest should be performed when there is high suspicion despite a normal chest X-ray.

Triage of patients [3,5]

Once a suspected case is confirmed by PCR or serology for COVID-19, we propose the following classification of severity:

1. Mild

Mild clinical disease with no evidence for pneumonia on radiography.

2. Moderate

Fever, respiratory symptoms, and pneumonia on radiography.

3. Severe

Patient exhibits any of the following:

- Tachypnea, RR > 30
- Room air SaO_2 < 93%
- PaO_2/FiO_2 < 300 mmHg
- Chest X-Ray or CT Scan of chest showing > 50% progression within 48 hours.

4. Critical [1]

Patient exhibits any of the following:

- Respiratory failure requiring mechanical ventilation
- Syncope
- Any other organ failure requiring care in a critical care..

TREATMENT [1,5]

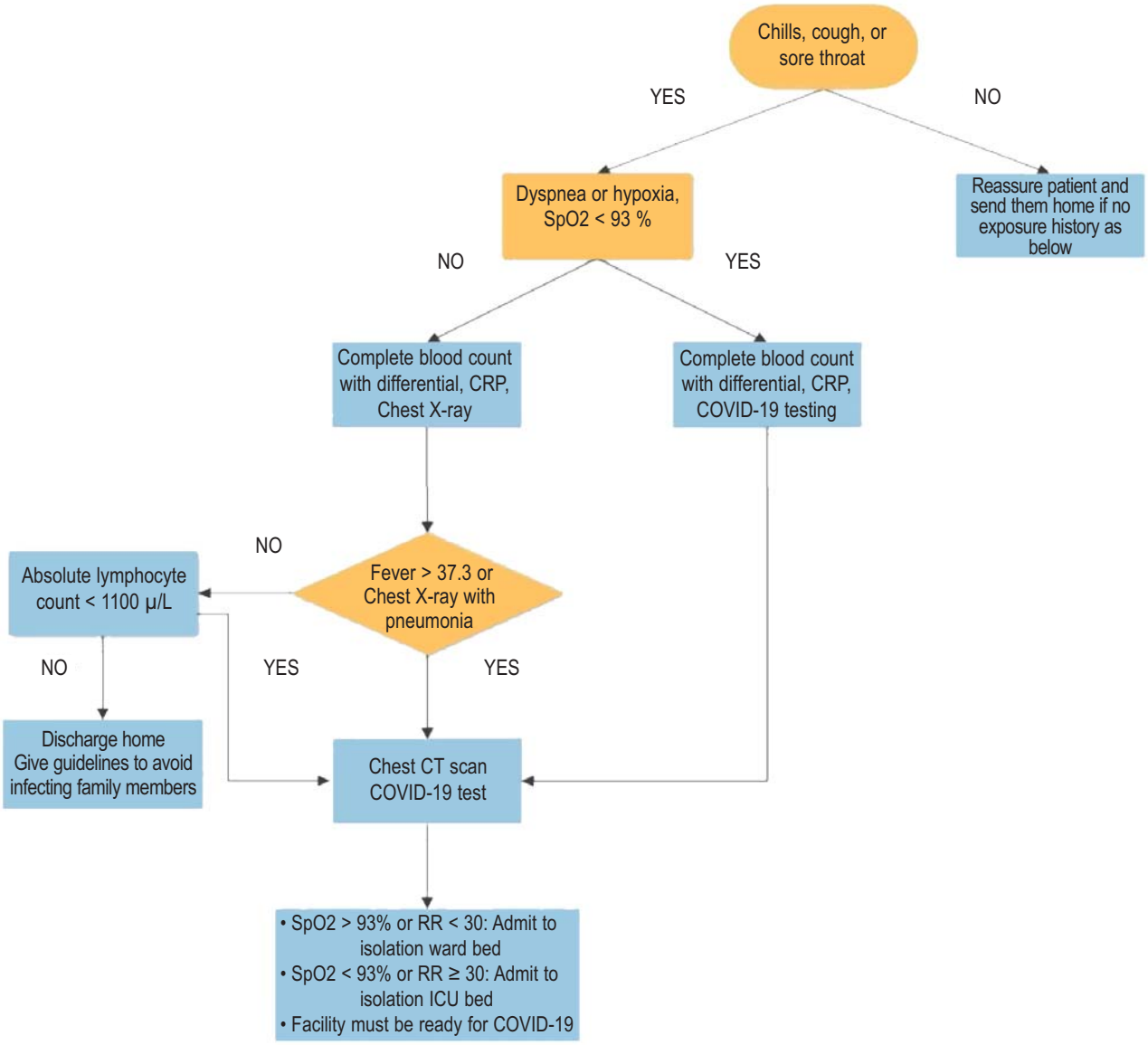
To date no pharmacologic intervention has been proven effective.

There is no strong evidence from randomized clinical trials for the below suggested COVID-19 therapeutic and diagnostic interventions. As such, all suggested diagnostic and therapeutic interventions in this document may be modified as new evidence emerges.

All interventions used in this document are considered investigational or for compassionate use. Decision to use any of the suggested interventions should be made while considering the patient's comorbidities, potential drug interactions, and sound medical judgement.

1. Systemic steroids: No proven benefit with potential harm. Avoid use unless indicated for another pre-existing condition.
2. Non-steroidal anti-inflammatory drugs: They should be avoided in patients with COVID-19 as they may worsen the outcome.
3. Fluid sparing strategy is recommended.
4. A multidisciplinary approach to pharmacotherapy is strongly recommended involving infectious disease consultants and other specialties as deemed appropriate.

APPENDIX
PROPOSED PROTOCOL FOR DIAGNOSIS AND TRIAGE OF SUSPECTED COVID-19 PATIENTS [9,10]



5. Potential treatments that can be considered after consultation with an infectious disease specialist:
   a. **Remdesivir: (Captisol)** [5.6]
      Remdesivir was proven efficient against Ebola, MERS, and SARSdiseases
      In the case of COVID-19, the treatment showed promising results in one in vitro study.
      The dosing used in this trial was 200 mgIV x 1 d, then 100 mg IV qD x 9 d.
   b. **Lopinavir/Ritonavir: (Kaluvia ou Kaletra)** [7]
      In JAMA a series of cases using Lopinavir to treat COVID-19 patients was published on March 3, 2020. The suggested dosage used in these cases was 400/100 mg x 14 d
   c. **Chloroquine (Nivaquine, Aralen)** [8]
      Anti-malarial medication [4,6,8]].
      Suggested dosing: 500 mg PO BID x 10 d.
   d. **Hydroxychloroquine** [4]
      After performing a trial, it was found that hydroxychloroquine is more efficient than chloroquine at inhibiting the SARS-CoV-2 virus in vitro.
   e. **Tocilizumab (Actemra)** [5,11]
      Tocilizumab is known to block the function-

ing of IL-6). Articles suggest that Tocilizumab could help in severe cases of COVID-19 where patients develop cytokine storm (which involves elevated levels of IL-6).

The suggested dosing determined from these trials is: 8 mg/kg in 100 mL of 0.9% NS IV over 60 min x 1.

f. **Favipiravir** [6]

The dosing suggested regarding the use of Favipiravir as treatment is: 1600 mg PO BID x 1 d, then 600 mg PO BID x 6 d.

ACKNOWLEDGEMENT

All authors have equally contributed to the manuscript.

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COVID-19 PANDEMIC

SURVEY OF COVID-19 PREPAREDNESS AMONG LEBANESE ICU PHYSICIANS

http://www.lebanesemedicaljournal.org/articles/68(1-2)/pandemic14.pdf

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On behalf of the Lebanese Society of Critical Care Medicine, the Lebanese Pulmonary Society & the Lebanese Society of Anesthesiologists COVID-19 task force

Chami HA, Abi Saleh W, Aoun-Bacha Z, Bou Khalil P, Chamandi S, Diab K, Juvelekian G, Yazbeck P, Kanj SS. Survey of COVID-19 preparedness among Lebanese ICU physicians. J Med Liban 2020; 68 (1-2) : 87-98.

ABSTRACT • Background : The rapidly spreading COVID-19 pandemic was associated with significant nosocomial transmissions and poses a risk to healthcare workers and hospitalized patients. We assessed intensive care units (ICU) resources, COVID-19 preparedness and the availability of personal protective equipment (PPE) to ICU practitioners in Lebanon. **Methods:** Between March 23 and 31, 2020, 250 ICU physicians working in Lebanon were surveyed on COVID-19 preparedness at their local hospitals, the availability of ICU resources, and adequate PPE. The survey was developed and administered by the Lebanese Society of Critical Care Medicine in collaboration with the Lebanese Pulmonary Society and the Lebanese Society of Anesthesiologists. **Results:** Eighty-nine ICU physicians working at 51 hospitals in all Lebanese regions completed the survey. The recommended PPE for ICU physicians (N95 masks, face shields and impermeable body-gowns) and the needed fitting and doning/doffing training were available to 34% of respondents. Dedicated wards and ICU for COVID-19 patients, negative pressure ICU rooms, video-laryngoscopes and COVID-19 testing were available on-site at 17% of respondents' hospitals. **Conclusions:** At the onset of the COVID-19 epidemic in Lebanon, the availability of recommended PPE to the surveyed ICU physicians in Lebanon and the available ICU resources and COVID-19 preparedness at their hospitals were limited.

Keywords : COVID-19; nosocomial transmission; personal protective equipment

INTRODUCTION

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)/COVID-19 is a highly transmissible respiratory virus that was first detected in China in December 2019 [1]. It spread rapidly to more than 200 countries resulting in a global pandemic with more than 2.8 million documented infections in 4 months [2].

The rapidly spreading virus caught public health authorities, hospitals and physicians by surprise and was associated with nosocomial transmissions posing a significant risk to healthcare workers (HCW) and other hospitalized patients [3-5]. The risk of transmission is especially concerning in confined spaces such as clinics, hospital rooms, and intensive care units (ICUs) where aerosol generating procedures are common.

Infection control recommendations and respiratory isolation directives of COVID-19 infected patients were published by the World Health Organization (WHO) [6] the Center of Disease Control [7] and the Surviving Sepsis Campaign [8]. Nevertheless, the rapid spread of the infection and the large numbers of affected individuals caused a shortage of personal protection equipment (PPE) in many hospitals across the world [6,9,10]. Although the virus is thought to mostly spread by droplets and contact with infected surfaces, the cited references to support the WHO recommendations have been questioned and there is a call for rigorous research to definitively answer the concern of airborne transmission even in scenarios when no procedures are performed [11].

The first case of COVID-19 infection was reported in Lebanon on February 20, 2020 and by April 28th more than 717 COVID-19 cases were diagnosed and 24 deaths reported [12]. However, the available local ICU resources and preparedness of Lebanese ICUs to face this epidemic and the availability of adequate PPE to healthcare providers in Lebanon was unknown. Therefore, the Lebanese Society of Critical Care Medicine (LSCCM) in collaboration with the Lebanese Pulmonary Society (LPS) and Lebanese Society of Anesthesiologists (LSA), surveyed Lebanese ICU physicians on COVID-19 preparedness at their hospital ICUs. This survey aimed to assess local ICU resources, COVID-19 ICU preparedness and the availability of adequate PPE to

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ICU practitioners in Lebanon, in order to inform the health authorities' efforts to face the COVID-19 epidemic.

METHODS

The network of 250 ICU physicians in Lebanon (including physicians in training) were surveyed on COVID-19 preparedness at their main hospital between March 23 and 31, 2020. The survey questionnaire was developed by a committee of 7 ICU experts (HAC, WAS, ZA, PBK, KD, GJ and PY) from 5 major Lebanese medical schools (American University of Beirut, Lebanese University, Saint Joseph University, Lebanese American University and University of Balamand). The committee was formed by the LSCCM in collaboration with the LPS and LSA and tasked to assess and enhance COVID-19 preparedness among Lebanese ICU specialists. The survey was translated into French and back-translated to English by experienced medical translators and was administered in both French and English and piloted in both languages among the committee members and corrected.

The questionnaire included 19 items assessing the availability of ICU resources at participants' hospitals, hospital locations, COVID-19 preparedness, and the availability of adequate PPE. ICU resources assessed included: number of ICU beds, ICU rooms, negative pressure ICU rooms, step-down beds, operating rooms, functioning ventilators and availability of transport ventilators and video-laryngoscopes.

COVID-19 preparedness included availability of on-site COVID-19 reverse transcriptase polymerase chain reaction (PCR) testing, a separate ward and a separate ICU for COVID-19 patients. Respondents were also surveyed about availability of PPE including: N95 masks, face shields, impermeable whole-body gowns, whole-body suits at their main hospital, and whether they were fitted for N95 masks and trained on wearing and re-moving PPE and whole-body suits (donning and doffing).

The questionnaire was distributed to the professional network and members of Lebanese ICU physicians formed by the three societies through electronic mailing and smartphone contact lists and administered using the open source online data collection tool Kobo Toolbox (www.kobotollbox.org Cambridge, MA). This survey was part of the three medical societies public health preparedness efforts, was anonymous and did not include personal identifiers or individual human subject data (demographics/readiness/knowledge, etc.) and therefore did not fit the "human subject research definition" to warrant IRB review.

Results are summarized using frequency and percentages for categorical variables, and sum total for continuous variables and are presented for all respondents and stratified by the five main regions: Beirut, Mount Lebanon, North, South and Bekaa. The results are reported by respondent and tallied by hospital. Discrepancy in binary responses between respondents from the same hospital were resolved by assuming lack of knowledge of availability of resources, while discrepancies in continuous variables were resolved by averaging the results. Agreement between respondents from the same hospital was assessed by measuring concordance.

RESULTS

Eighty-nine ICU physicians working in 51 different hospitals from 31 towns and all major cities and regions of Lebanon completed the survey (Table I). Twenty-one percent

TABLE I
RESPONDENTS' HOSPITALS DISTRIBUTION BY REGION AND TOWNS (N = 51)

Region	Frequency (%)
Beirut	**11 (21)**
Mount Lebanon	**19 (37)**
Aley/Baabda	
Baabda	1 (1.9)
Hadath	1 (1.9)
Haret Hreik	1 (1.9)
Chouf	
Ain w Zein	1 (1.9)
Siblin	1 (1.9)
Byblos/Keserwan	
Byblos	2 (3.9)
Jounieh	2 (3.9)
Keserwan	1 (1.9)
Ghazir	1 (1.9)
Adma	1 (1.9)
Maten	
Daher El Souwan	1 (1.9)
Jal el Dib	1 (1.9)
Zalqa	1 (1.9)
Bsalim	1 (1.9)
Mansouriye	1 (1.9)
Jdeideh	1 (1.9)
Sin El Fil	1 (1.9)
North	**8 (16)**
Tripoli	3 (5.8)
Zgharta	2 (3.9)
Koura	1 (1.9)
Halba Akkar	1 (1.9)
Batroun	1 (1.9)
South	**6 (12)**
Tyr	2 (3.9)
Saida	2 (3.9)
Bint Jbeil	1 (1.9)
Sarafand	1 (1.9)
Bekaa	**7 (14)**
Zahle	3 (5.8)
Chtoura	2 (3.9)
Bekaa	1 (1.9)
Baalbek	1 (1.9)

of respondents' hospitals were located in Beirut, 37% in Mount Lebanon, 16% in the North, 12% in the South and 14% in the Bekaa region. Sixty-five percent of respondents' hospitals were in urban areas and 35% in rural areas.

Personal protective equipment

Availability of the various PPE to respondents and at respondents' hospitals is presented in Figure 1 and availability of necessary PPE training and fitting in Figure 2. N95 masks were available to 87% of respondents (ranging from 71% in the South to 93% in Mount Lebanon), and in 87% of respondents' hospitals (from 60% in the South to 100% in Mount Lebanon) (Figure 1).

However, only 64% of respondents were fitted with N95 masks (from 55% in Mount Lebanon up to 86% in

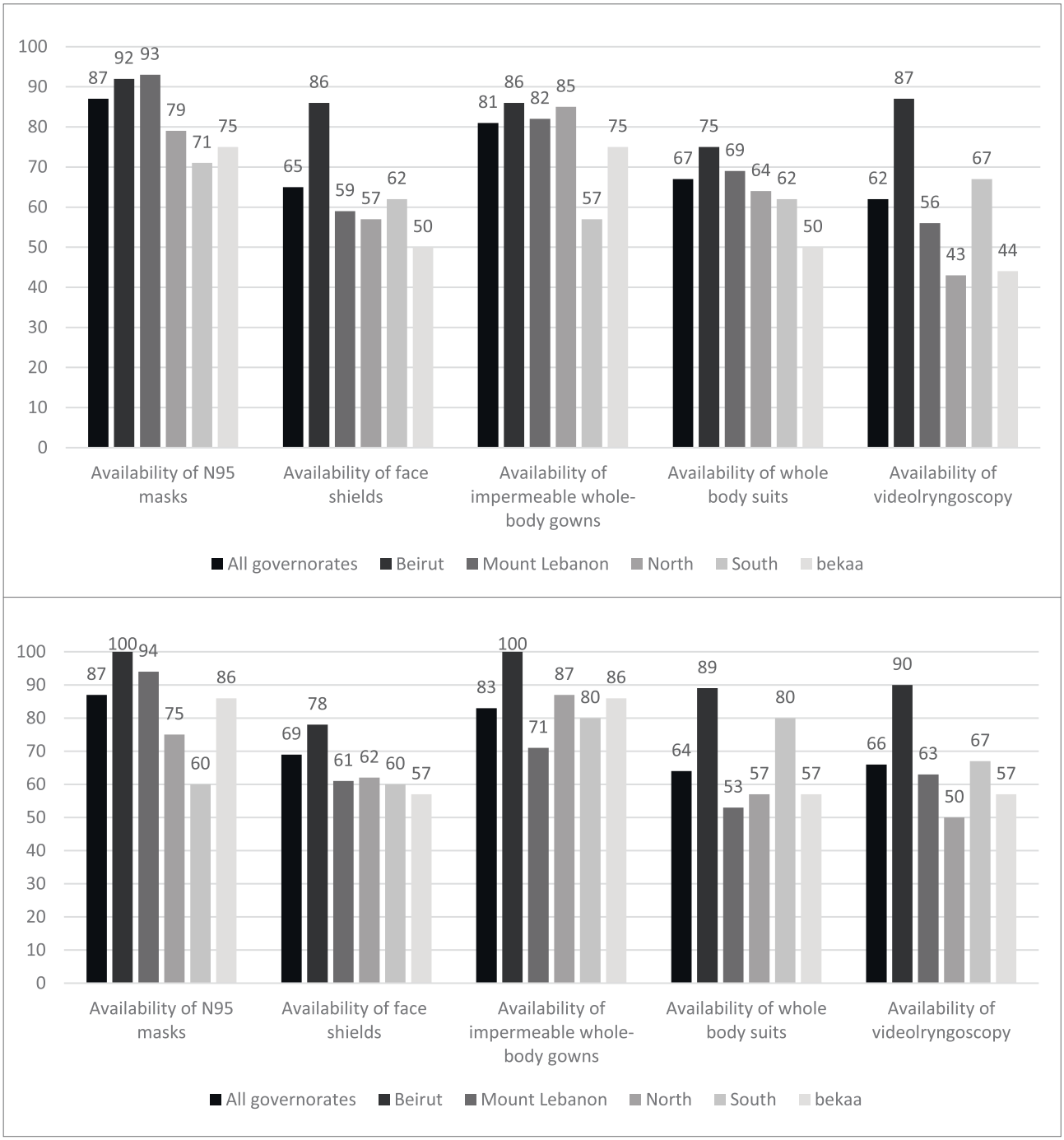

Figure 1. Availability of personal protective equipment to respondents (A, N = 89) and at respondents' hospitals (B, N = 51) by region.

the South) (Figure 2). Furthermore, face shields were available to only 65% of respondents (from 50% in Bekaa to 86% in Beirut) and in 63% of respondents' hospitals (ranging from 57% in Bekaa to 78% in Beirut).

Impermeable whole-body gowns were available to 81% of respondents (ranging from 57% in the South up to 86% in Beirut) and at 83% of respondents' hospitals (ranging from 71% in Mount Lebanon to 100% in Beirut). However, only 63% of respondents reported being trained on wearing and removing PPE (ranging from 57% in the South to 79% in the North). Similarly, whole-body suits were available to 67% of respondents (from 50% in Bekaa up to 75% in Beirut) and at 64% of respondents' hospitals (ranging from 53% in Mount Lebanon to 89% in Beirut). However, only 45% of respondents reported being trained on wearing and removing whole-body suits (from 33% in the South to 50% in Mount Lebanon).

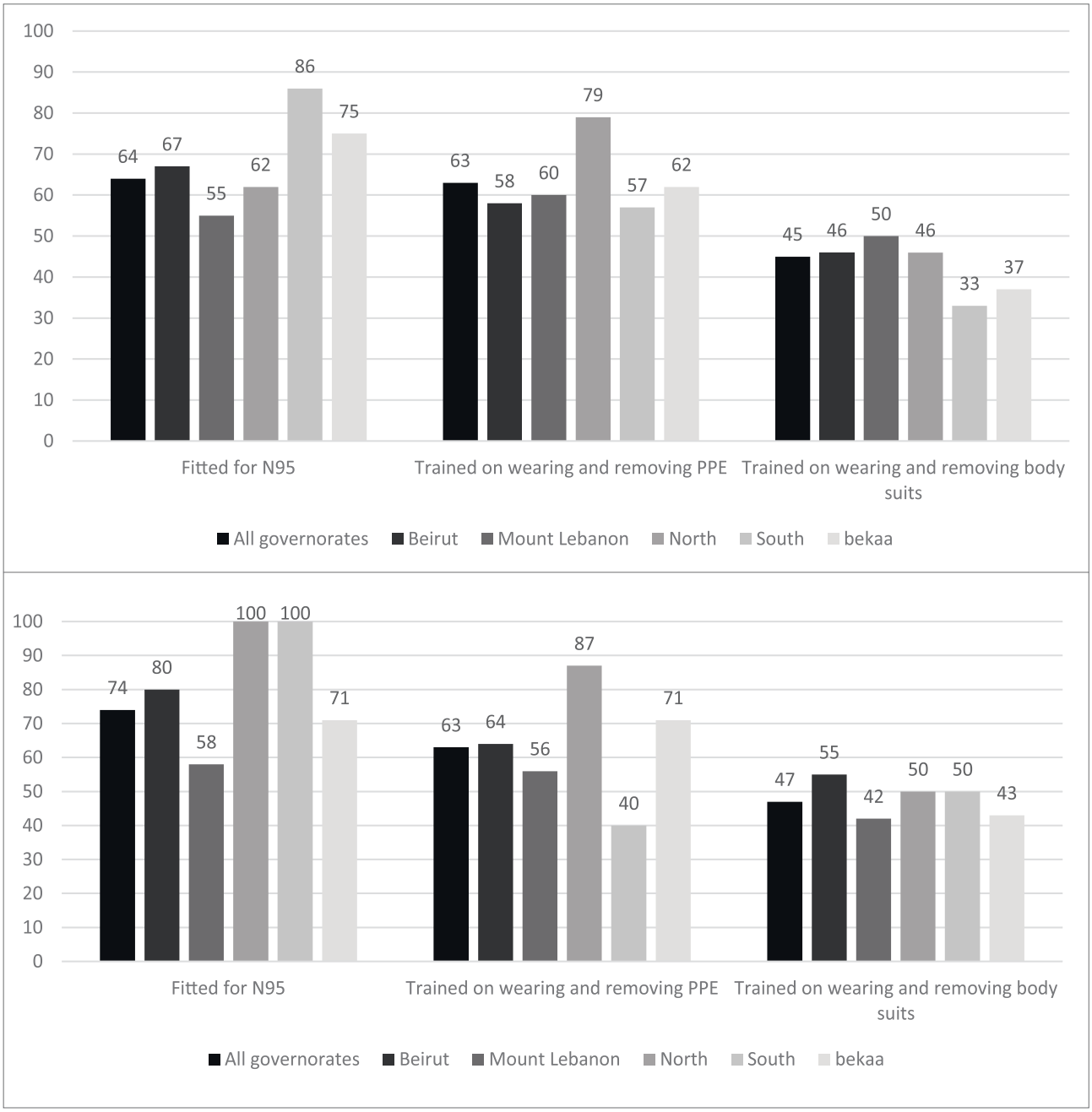

Figure 2. Personal protective equipment (PPE), fitting and training (%) among respondents (A, N = 89) and at respondents' hospitals (B, N = 51) by region.

All PPE recommended for ICU physicians including N95 masks, face shields and impermeable whole-body gowns were available to 60% of respondents (from 40% in the South to 75% in Beirut) and at 63% of respondents' hospitals (from 50% in North and South to 87% in Beirut (Figure 3). Both recommended PPE, N95 fitting and training on doffing and donning were available to 34% of respondents and at 43% of respondents' hospitals (from 42% in Bekaa to 75% in Beirut). Whole-body suits and training on whole-body suits were additionally available respectively to 54% and 29% of respondents and at 52% and 37% of respondents' hospitals.

Facility peraredness

COVID-19 facility preparedness is presenting in Figure 4. COVID-19 testing with reverse transcriptase PCR was

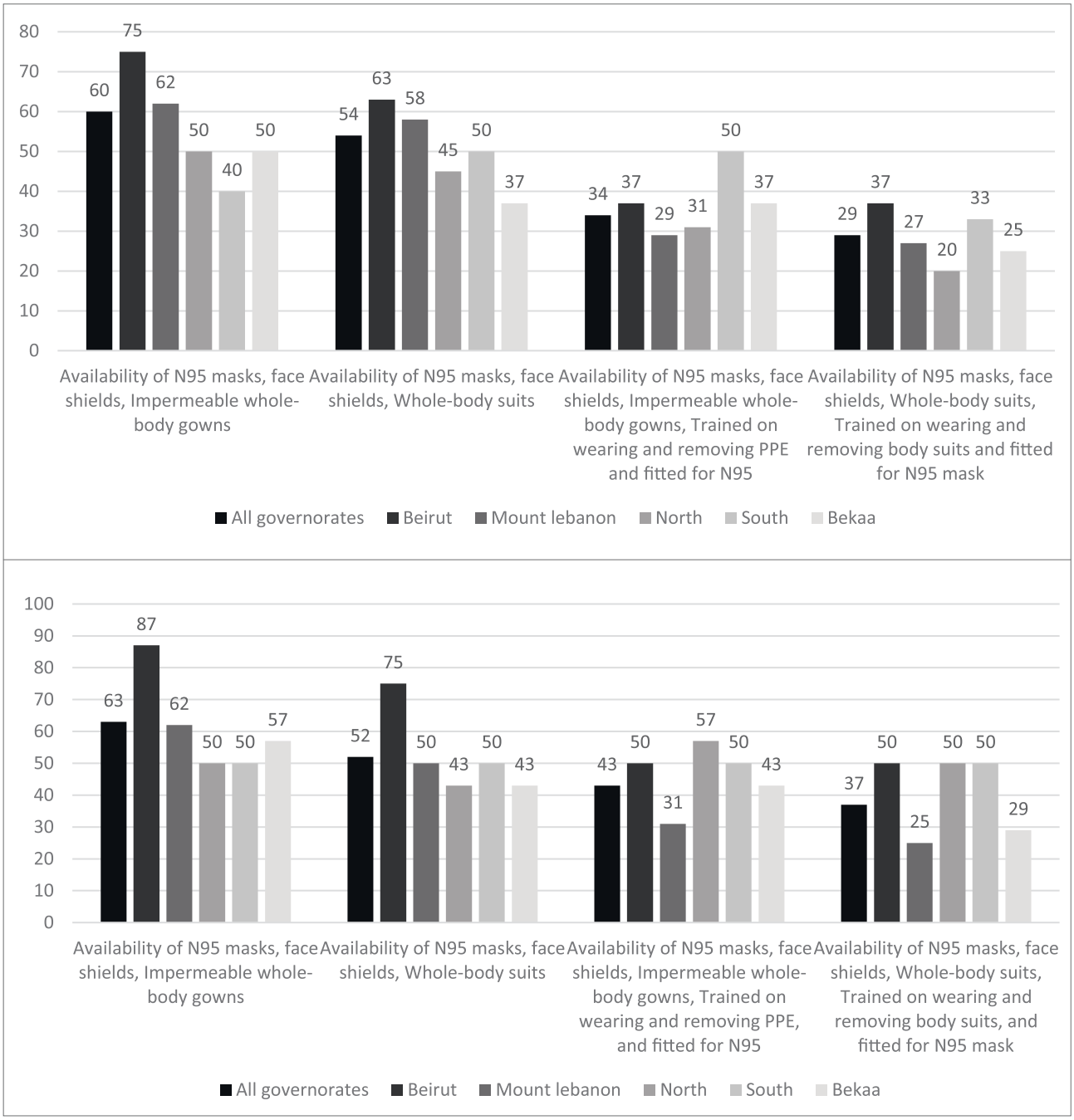

Figure 3. Availability of all recommended personal protective equipment (PPE), fitting and training (%) to respondents (A, N = 89) and at respondents' hospitals (B, N = 51) by region.

available on-site at 29% of respondents' hospitals (ranging from 14% in Bekaa to 64% in Beirut) (Figure 4). A dedicated ward for COVID-19 patients was available at 68% of respondents hospitals (ranging from 40% in the South to 100% in the North), while a dedicated ICU was available at 50% of respondents' hospitals (ranging from 17% in the South to 91% in Beirut). Negative pressure ICU rooms were available at 62% of respondents' hospitals (ranging from 50% in South, North and Bekaa to 73% in Beirut), while a video-laryngoscope was available at 66% of respondents' hospitals (ranging from 50% in the North to 90% in Beirut) and transport ventilators were available at 86% of respondents' hospitals (ranging from 83% in the North to 91% in Beirut).

Seventeen percent of respondents' hospitals met all these preparedness items, while none of the respondents'

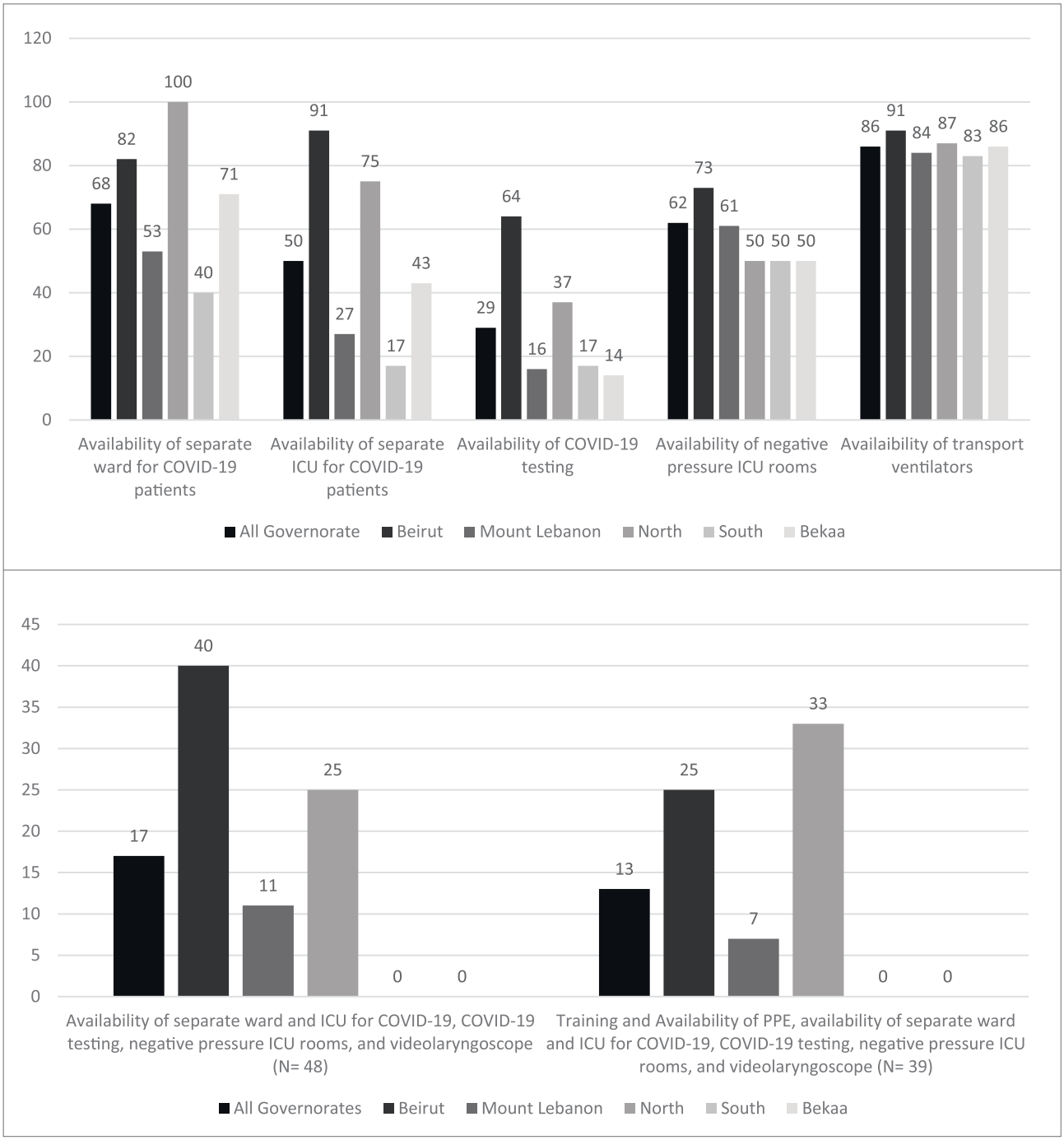

Figure 4. COVID-19 preparedness at respondents' hospitals (%) by region (N = 51)

hospitals in the South or Bekaa met all items and 13% of hospitals had additionally the recommended available PPE and training.

Agreement between respondents from the same hospital was high with an overall concordance rate of 89% (86% for questions addressing availability of PPE and training and 92% for questions addressing hospital preparedness).

ICU resources at the respondents' hospitals are presented in Figure 5. The estimated total number of ICU beds in the respondents' 52 hospitals was 748 beds in 465 ICU rooms, of which 110 were negative pressure ICU rooms with 611 functionnig ventilators (Figure 5). Additionally, the estimated number of operating rooms was 275 and the number of step-down beds was 147.

DISCUSSION

In this survey of ICU physicians practicing in Lebanon, the availability of PPE was limited and a substantial number were not fitted for N95 masks nor trained on using PPE. Moreover, the availability of on-site COVID-19 testing, dedicated ICU COVI-19 ICU and negative pressure ICU rooms were limited. Even basic whole-body impermeable medical gowns and face shields were not universally available to ICU practitioners. Resources were even more limited in hospitals located in regions away from the capital Beirut.

In addition to community transmission of COVID-19, the prospect of nosocomial transmission is important during this pandemic. In an early case series of 138 consecutive patients with confirmed COVID-19 who were hospitalized in January 2020 at a single center in Wuhan, China, 41% were presumed to have hospital-related transmission including hospitalized patients (12.3%) and HCW (29%) [3]. More than 2000 confirmed COVID-19 infections were reported among HCW in China by February 2020, the majority of whom were in Hubei [5] and the total number of infections among HCW in China is estimated at over 3,000 cases [13].

Nosocomial transmission could compound the impact of community transmission resulting in potential transmission to the vulnerable hospitalized patients as well as to other HCW, thus effectively reducing the healthcare work force due to illness and quarantine [13-14].

The WHO, CDC and Surviving Sepsis Campaign guidelines suggest wearing gloves, medical/surgical face masks, full-body impermeable gown and eye shields/goggles for HCW when providing usual care for non-ventilated COVID-19 patients or when performing non-aerosol generating procedures on mechanically ventilated COVID-19 patients [6-8].

In addition to wearing gowns, gloves and eyeshields, the Surviving Sepsis Campaign guidelines recommend that HCW wear a N95 respirator mask rather than a medical/surgical mask while perfoming aerosol generating procedures on COVID-19 ICU patients [8]. These guidelines also recommend performing those procedures in negative pressure rooms and suggest using a video laryngoscope rather than direct laryngoscopy while performing endotracheal intubation on COVID-19 patients. Indeed, negative pressure rooms are important, especially in the setting of ICU patients undergoing aerosolizing procedures as they help prevent the spread of respiratory viruses outside the room, thus decreasing the risk of aerosol transmission to other HCW and patients [8,11]. Furthermore, training on doning and doffing PPE is essential as the process can result in contamination especially when dealing with highly transmissible viruses such as COVID-19 [4, 10, 15]. While fitting for N95 was considered standard, the worldwide shortage of N95 during the COVID-19 epi-

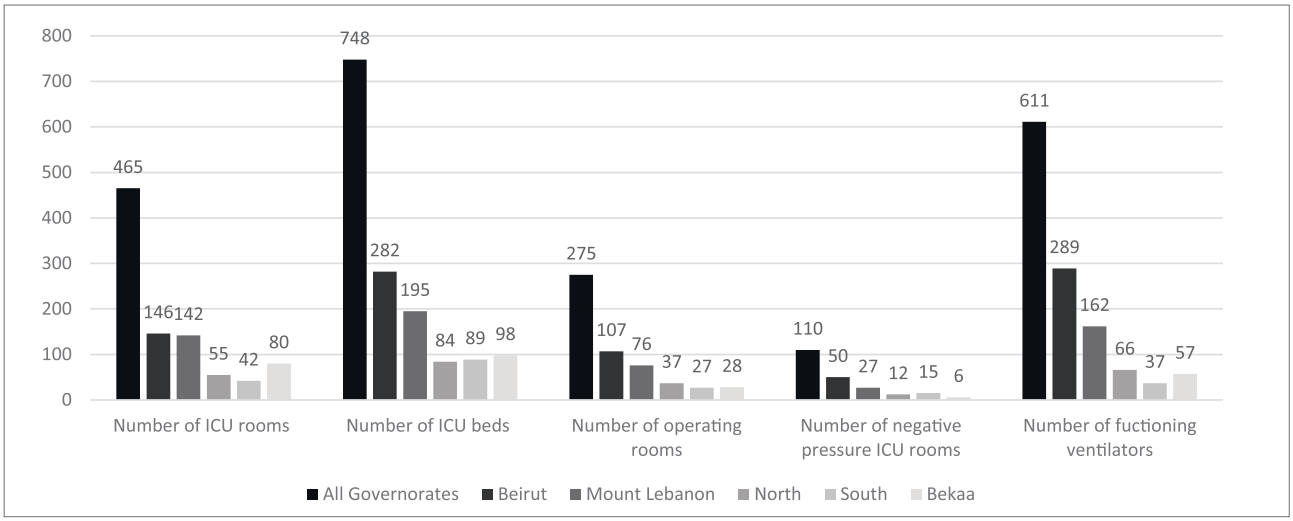

Figure 5. ICU resources at surveyed hospitals by region (N = 51)

demic forced HCW to wear various types of masks and that led to revision of guidelines to allow use of N95 masks regardless of standard fit testing and calling instead on fit checking with every mask use [15]. Finally, having rapid on-site COVID-19 testing is important for timely identification and isolation of COVID-19 patients, while having a dedicated ward and ICU for COVID-19 patients could help limit nosocomial transimission to other hospitalized patients.

This study has several limitations. The survey included respondents from 51 of 109 hospitals with ICUs in Lebanon [16]; however, the respondents covered the major hospitals with ICUs in Lebanon (Cf. Appendix). Furthermore, this survey was addressed to physicians and did not include administrative data; it therefore provides reasonable but not fully accurate estimates of the available ICU resources and equipments at the surveyed hospitals. Although there were some discrepancies among respondents from the same institution, concordance was high; furthermore, results were similar when responses were tallied either by respondents or by hospital. Finally, although PPE may be available at some hospitals, quantities/supplies could not be assessed in this survey of physicians and an assessment of the national stockpile was not possible at the time of this survey. The latter is important, as a limited stock and the disrupted supply chain due to the worldwide pandemic will make procuring PPE very challenging especially in a country going through a financial and economic crisis such as Lebanon [9].

Donations from private donors and from other countries will hopefully help ease the shortage. Lebanon has so far had a limited number of COVID-19 infected patients requiring ICU care [12]. At this point, it would be hard to predict how the epidemic will evolve in Lebanon and if new surges will occur again after a period of stability. Hospitals in all regions should work hard on acquiring needed PPE and improve HCW training on proper donning and doffing. Because of the limited manpower, various videos have been created by Lebanese academic centers in Arabic that could help achieve this goal.

In conclusion, while the COVID-19 epidemic poses a significant risk of transmission to HCW in general, the limited availability of PPE might make HCW in Lebanon especially vulnerable if the number of COVID-19 cases increases significantly and requires hospitals in many areas to care for such patients. In a resource-strained country going through a deep financial and economic crisis and a recent popular uprising, preparedness for the COVID-19 pandemic is even more challenging. After this survey was conducted, much effort has been invested in ensuring adequate PPE and training at several hospitals and by members of Lebanese medical societies, including LSCCM, LPS, LSA and the Lebanese Society of In-fectious Diseases and Clinical Microbiology. In addition, hospitals in Lebanon have been proactive in looking at various sources to procure PPE, including from local newly-established markets. Active training campaigns on the proper use of PPE for HCW are needed, in addition to using training videos when on-site training is not available. Protocols for sterilization of N95 masks are being assessed at various hospitals to address the shortage [17]. A follow-up survey to assess the progress of COVID-19 readiness at various hospitals will be informative to guide further efforts.

Acknowledgements
We are greatful to all physicians who agreed to complete the survey. We would also like to acknowledge the contribution of Sandra Kahwaji to data management and analysis.

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APPENDIX I LEBANESE HOSPITALS WITH ICU BY REGION

Hospital name	Number of respondents (%)	Respondents	Number of ICU beds*
Beirut	**25 (28)**	**11/17 (65)**	**80/105**
American University of Beirut Medical Center	5 (5.62)	Yes	9
Saint George Hospital University Medical Center	5 (5.62)	Yes	10
Hôtel-Dieu de France	4 (4.49)	Yes	12
Hôpital Libanais	3 (3.37)	Yes	8
Clinique Dr. Rizk	2 (2.25)	Yes	4
Clemenceau Medical Center	1 (1.12)	Yes	6
Al-Rassoul Al-Aazam Hospital	1 (1.12)	Yes	13
Al Zahraa University Hospital	1 (1.12)	Yes	8
Haddad Hospital for the Rosary Sisters	1 (1.12)	Yes	10
Rafik Hariri University Hospital	1 (1.12)	Yes	-
University Hospital	1 (1.12)	Yes	-
Makassed	0 (0.00)	No	5
Fouad Khoury Hospital	0 (0.00)	No	2
Sahel General Hospital	0 (0.00)	No	4
Trad Hospital & Medical Center	0 (0.00)	No	4
Bourj Hospital	0 (0.00)	No	6
Beirut General Hospital	0 (0.00)	No	4
North	**14 (16)**	**8/22 (36)**	**48/91**
Hôpital Albert Haykel s.a.l.	3 (3.37)	Yes	6
Mounla Hospital	3 (3.37)	Yes	8
Centre Hospitalier du Nord	3 (3.37)	Yes	5
Nini Hospital s.a.l	1 (1.12)	Yes	7
Hopital Al-Koura	1 (1.12)	Yes	10
El Youssef Hospital Center	1 (1.12)	Yes	5
Family Medical Center (FMC)	1 (1.12)	Yes	7
Batroun Hospital	1 (1.12)	Yes	-
Islamic Charitable Hospital	0 (0.00)	No	5
Dar El Chifaa	0 (0.00)	No	6

Al Salam, (La Paix)	0 (0.00)	No	6
Akkar Rahal	0 (0.00)	No	3
Al Bissar Hospital	0 (0.00)	No	4
El Kheir	0 (0.00)	No	4
New Hospital Mazloum	0 (0.00)	No	5
Hôpital Notre-Dame de la Paix	0 (0.00)	No	7
Hôpital Saydet Zgharta / HSZ	0 (0.00)	No	3
Orange Nassau Governmental Hospital	0 (0.00)	No	-
Menyeh Governmental Hospital	0 (0.00)	No	-
Tannourine Governmental Hospital	0 (0.00)	No	-
Halba Governmental Hospital	0 (0.00)	No	-
Tripoli Governmental Hospital	0 (0.00)	No	-
Mount Lebanon	**32 (36)**	**18/33 (55)**	**90/174**
Centre Hospitalier Universitaire – Notre-Dame de Secours	6 (6.74)	Yes	8
St Georges Hadath	3 (3.37)	Yes	2
Ain Wazein Hospital	3 (3.37)	Yes	11
Hôpital Notre-Dame Maritime	2 (2.25)	Yes	8
Hôpital Notre-Dame du Liban	2 (2.25)	Yes	7
Bhannes	2 (2.25)	Yes	4
Clinique du Levant	2 (2.25)	Yes	6
Hôpital Saint George - Ajaltoun	1 (1.12)	Yes	
Hôpital Monseigneur Cortbawi	1 (1.12)	Yes	4
St Louis	1 (1.12)	Yes	4
Keserwan Medical Center	1 (1.12)	Yes	4
St Joseph Hospital-Raymond & Aida Najjar Med Ctr	1 (1.12)	Yes	4
Abou Jaoude Hospital S.A.L	1 (1.12)	Yes	5
Arz hospital	1 (1.12)	Yes	3
Middle East Institute of Health	1 (1.12)	Yes	6
Bellevue Medical Center	1 (1.12)	Yes	8
Baabda Governmental Hospital	1 (1.12)	Yes	
Bahman Hospital	1 (1.12)	Yes	6
Siblin Governmental Hospital	1 (1.12)	Yes	
Hôpital Dr S. Serhal	0 (0.00)	No	9
Mount Lebanon Hospital	0 (0.00)	No	20
Hôpital Sainte Thérèse	0 (0.00)	No	7
Sacré-Cœur	0 (0.00)	No	7
Haroun	0 (0.00)	No	8
St Charles	0 (0.00)	No	6
Dar El Rahmeh	0 (0.00)	No	
Al-Hayat Hospital	0 (0.00)	No	5
Hôpital Hayek	0 (0.00)	No	2
Iklim Health Central Hospital	0 (0.00)	No	5
Medical 2000 Co. SARL Kamal Joumblat Hospital	0 (0.00)	No	6
Othman	0 (0.00)	No	9
Ftouh Kesrwan Governmental Hospital	0 (0.00)	No	-
Dahr El.Bachek Governmental University Hospital	0 (0.00)	No	-
Shahar Gharbi Governmental Hospital	0 (0.00)	No	-

South Lebanon	**9 (10)**	**6/23 (26)**	**39/85**
Jabal Amel	2 (2.25)	Yes	7
Hammoud Hospital - University Medical Center	2 (2.25)	Yes	17
Hiram Hospital	2 (2.25)	Yes	8
Ghandour Hospital	1 (1.12)	Yes	
Alaeddine Hospital	1 (1.12)	Yes	2
Labib Medical Center s.a.l.	1 (1.12)	Yes	5
Secours Populaire Libanais	0 (0.00)	No	-
Al-Raee Hospital	0 (0.00)	No	8
Kassab	0 (0.00)	No	2
Dalla'a General Hospital	0 (0.00)	No	8
Al-Janoub Hospital (Shuayb)	0 (0.00)	No	8
Ragheb Harb	0 (0.00)	No	6
Islamic Health Society Hospital	0 (0.00)	No	1
Jezzine Governmental Hospital	0 (0.00)	No	-
Najdeh	0 (0.00)	No	4
Meiss El Jabal Governmental Hospital	0 (0.00)	No	-
Tyr Governmental Hospital	0 (0.00)	No	-
Nabih Berry University Governmental Hospital of	0 (0.00)	No	-
Nabatie			
Marjayoun Governmental Hospital	0 (0.00)	No	-
Tibnin Governmental Hospital	0 (0.00)	No	-
Bint Jbeil Governmental Hospital	0 (0.00)	No	-
Saida Governmental Hospital	0 (0.00)	No	-
Lebanese Italian Hospital	0 (0.00)	No	9
Bekaa	**9 (10)**	**7/21 (30)**	**37/103**
Khoury General Hospital - Zahle - Doctors Center	2 (2.25)	Yes	10
El Bekaa Hospital	2 (2.25)	Yes	6
Farhat F.C.	1 (1.12)	Yes	-
Rayak Hospital	1 (1.12)	Yes	8
Chtoura Hospital	1 (1.12)	Yes	4
Rayan	1 (1.12)	Yes	3
Tal Chiha	1 (1.12)	Yes	6
Dr. Hamed Farhat Hospital	0 (0.00)	No	8
Al-Amal University Hospital	0 (0.00)	No	12
Dar El Hikmah	0 (0.00)	No	7
Doctors Hospital al Manara	0 (0.00)	No	4
El Assi	0 (0.00)	No	8
Ibn Sina	0 (0.00)	No	6
Libano-Français	0 (0.00)	No	8
Al Mortada Hospital	0 (0.00)	No	6
Taanayel Gen. Hosp.	0 (0.00)	No	4
Battoul	0 (0.00)	No	3
Rachaya Governmental Hospital	0 (0.00)	No	-
Hasbaya Governmental Hospital	0 (0.00)	No	-
Baalbeck Governmental Hospital	0 (0.00)	No	-
President Elias Harawi Governmental Hospital	0.(0.00)	No	-

*Source: Syndicate of hospitals in Lebanon. National Hospital Database Study 2016 (personal communication) www.syndicateofhospitals.org.lb

APPENDIX II CHARACTERISTICS OF RESPONDENTS' HOSPITALS BY REGION (N = 51)

	Number of respondents' hospitals surveyed	Estimated Total Sum (%)	Mean (S.D.)	Median	25th percentile	75th percentile	Minimum	Maximum
Number of adult ICU beds	**51**	**748**	**14.90 (9.80)**	**12**	**9**	**17**	**3**	**51**
Beirut	11	282 (37.70)	25.65 (13.74)	23.8	15	28	9	51
Mount Lebanon	19	195 (26.06)	10.60 (4.63)	11	8	13	4	22
North	8	84 (11.22)	10.52 (2.50)	10	10	11.83	6	14.5
South	6	89 (11.89)	14.83 (10.18)	11.5	10	21	3	32
Bekaa	7	98(13.10)	14.07 (5.54)	12.5	9	18	8	24
Number of ICU rooms	**51**	**465**	**9.17 (5.33)**	**8**	**5**	**12**	**1**	**25**
Beirut	11	146 (31.40)	13.28 (7.71)	14	6	21	2	25
Mount Lebanon	19	142 (30.53)	7.58 (3.86)	8	5	10	1	16
North	8	55 (11.80)	6.87 (3.22)	7	5	9.5	1	11
South	**6**	42 (9.03)	7.08 (3.16)	6.75	5	9	3	12
Bekaa	7	80 (17.20)	11.5 (3.98)	12	8	14	5	17
Number of negative pressure ICU rooms	**50**	**110**	**2.21 (3.05)**	**1**	**0**	**2.5**	**0**	**11.33**
Beirut	11	50 (45.45)	4.57 (4.70)	2	0	11	0	11.33
Mount Lebanon	18	27 (24.54)	1.50 (1.84)	1	0	2	0	6.5
North	8	12 (10.90)	1.56 (1.80)	1	0	3.25	0	4
South	6	15 (13.63)	2.50 (3.57)	1.5	0	2.5	0	9.5
Bekaa	7	6 (5.45)	0.85 (0.89)	1	0	2	0	2
Number of ICU and step-down beds	**51**	**895**	**17.57 (12.13)**	**13.16**	**10**	**23.8**	**3**	**58.4**
Beirut	11	315 (35.20)	28.66 (16.12)	24.32	15	43	9	58.4
Mount Lebanon	19	238 (26.60)	12.54 (5.67)	12	8	16	4	26
North	8	97 (10.83)	12.14 (3.55)	12.5	10	14.33	6	17.5
South	**6**	122 (13.63)	20.33 (17.50)	13	10	34	3	49
Bekaa	**7**	123 (13.74)	17.64 (8.67)	15	9	27.5	8	28
Number of operating rooms	**49**	**275**	**5.65 (3.16)**	**5**	**3**	**8**	**0**	**13**
Beirut	11	107 (38.90)	9.78 (2.35)	10	8	11	5	13
Mount Lebanon	17	76 (27.63)	4.50 (2.03)	4	3	6	2	9
North	8	37 (13.45)	4.62 (1.50)	5	3	5.5	3	7
South	6	27 (9.81)	4.58 (2.93)	4.25	2	5	2	10
Bekaa	7	28 (10.18)	4.07 (3.03)	3.5	3	5	0	10
Total number of functioning ventilators	**49**	**641**	**13.07 (12.81)**	**8**	**6**	**15**	**2**	**71**
Beirut	11	319 (47.30)	29 (18.30)	26	18	40	4	71
Mount Lebanon	18	162 (26.51)	9.01 (6.25)	7.5	6	9	2	28.5
North	8	66 (10.80)	8.20 (4.32)	7.83	4.5	10	4	17
South	5	37 (6.05)	7.40 (2.70)	7	6	9	4	11
Bekaa	7	57 (9.32)	8.14 (4.01)	7	6	12	3	15

In case of discrepancy between respondents working at same hospital, we reported the average number of answers.

COVID-19 PANDEMIC

ETHICAL CONSIDERATIONS IN RESPONSE TO THE COVID-19 PANDEMIC

http://www.lebanesemedicaljournal.org/articles/68(1-2)/pandemic15.pdf

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Daher M, Rouhana G, Souaiby N, Kallab K, Abou-Mrad F, Richa S. Ethical considerations in response to the COVID-19 pandemic. J Med Liban 2020; 68 (1-2) : 99-104.

INTRODUCTION

We are facing an unprecedented and devastating situation caused by the coronavirus spreading rapidly around the world, changing the way we work and live. In one way or another, we are all involved in confronting the COVID-19 pandemic.

The COVID-19 pandemic poses grave challenges for societies all around the world. Many lives have already been lost, and many more people fear for their own health and that of their loved ones.

Moreover, the economic impact of the pandemic has cost people their jobs and livelihoods, and started to impact people's wellbeing and mental health. The effects of this public health emergency will affect an entire generation.

On an another hand, the present situation should induce reflection. During this challenging pandemic, we are confronted with many ethical issues which need acceptable solutions. Human Rights (as stated in the Universal Declaration of the United Nations in 1948), are an important reference when elaborating these solutions.

It is important to ensure that the political strategy be founded on an interdisciplinary consensus between science, ethics, law, and society at large.

The key good solidarity and compliance from the society is to deliver clear and transparent information, based not only on scientific knowledge, but also rooted in the Human Rights.

We will be reviewing in this article the most prominent ethical considerations that can be met during the development of the COVID-19 pandemic.

AUTONOMY VERSUS SOLIDARITY IN THE CORONAVIRUS PANDEMIC

The current pandemic is an unprecedented challenge to our society and leads to serious ethical conflicts. While health policy makers work on securing an efficient health system during this pandemic, the major ethical issue is to engage the society in a process of responsibility and solidarity.

There is a conflict between two essential values: the respect of "Individual Rights" and the "Protection of society and the community". The physician's role here is essential. He must ensure that society is protected against epidemic spread, while insuring the protection of personal rights.

Whatever decisions will be taken, whatever their nature, human dignity has to be respected.

Some constraints on population and particular restrictions on individuals have to be taken; they should be decided and applied in conformity with a legitimate objective of general interest, without entailing unreasonable or discriminatory measures, and should be defined in the light of data acquired from science, particularly on their effectiveness.

When dealing with coronavirus, the watchword is solidarity more than autonomy. Policymakers must be aware of the severity of the restrictions implemented, how people can cope with them and for how long. Painful decisions, such as restriction of civil liberties, should be made by the organs mandated by the people to govern the healthcare system. For a better compliance from the population, it is necessary to mobilize Orders, Corporates, Syndicates, Political parties and others, to explain the measures applied.

Although the greatest attention must be paid to the goal of slowing considerably the spread of the coronavirus, decision makers should consider how to return orderly to a reasonably "normal" life as well as regular economic activities.

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In the name of solidarity, the best thing we can do to help each other during this public health emergency is to stay away from each other. Those of us with confirmed COVID-19, need to self-isolate. Those of us who have been exposed to a confirmed case of COVID-19, need to self-quarantine. Those of us who have been travelling, need to self-quarantine. All others, who are not essential workers, need to stay home as much as possible. If we have to venture out, we need to practice social distancing.

Social responsibility is a duty. One does not have the right to remain passive when faced to a threat to society and to remain confined to rigid laws far from social requirements.

RESPECT OF CONFIDENTIALITY & PRIVACY RIGHTS OF PATIENTS DURING COVID-19 CRISIS

Confidentiality and privacy are two of the six health universal rights. The four others are: right to access healthcare, right to information, right to nondiscrimination and right to self-decision making.

Confidentiality means protection of the personal information "that a patient reveals to a physician or to a health care provider but also what is heard, understood, seen or concluded by the physician".

Confidentiality has limits and legal derogations on how and when it can be disclosed to health authorities, a judge or a third party. According to the Lebanese Code of Ethics (Law 240 amended in october 2012, initially Law 288 of 1994, Article 7) confidentiality is a public matter. The physician is bound to this confidentiality at all times while taking into consideration some exceptions imposed by the law and public interest.

Privacy is the state of being free from being observed or disturbed by other people. The Lebanese Law 574 (2004) related to the patient's rights and informed consent, chapter 3, art. 12, stipulates that every patient under the care of a physician has the right to privacy on his/her life and all related information.

After the novel coronavirus (COVID-19) was declared a pandemic by the World Health Organization (WHO, March 11, 2020), it was considered as a serious danger to public health. In order to make people aware of this threat, some public health programmes carried information about person identity, affecting in many ways confidentiality and privacy.

To what extend should confidentiality and privacy be respected in COVID-19 pandemic?

According to the *British Council of Bioethics* (Re: Guide to the ethics of surveillance and quarantine for novel coronavirus), "the avoidance of significant harm to others who are at risk from a serious communicable disease may outweigh the consideration of personal privacy or confidentiality, and on this basis it can be ethically justified to collect non-anonymised data about individuals for the purpose of implementing control measures. However, any overriding of privacy or confidentiality must be to the minimum extent possible to achieve the desired aim. Liberty-infringing measures to control disease, such as quarantine and isolation, can be justified if the risk of harm to others can be significantly reduced."

In Lebanon, the declaration of COVID-19 cases is mandatory by decree decision of the Ministry of Public Health (MOPH). In a pandemic situation like the one we are facing with COVID-19 crisis, what is going to prevail: the values and ethical principles that are integral to the "Universal Declaration of Human Rights" or usefulness and efficiency as primary values for the good of the community?

In practice, the key element to consider is the good communication: Alarming statements issued by authorities scaring people to observe confinement as well as media breaking news lead to fear and stigmatization of COVID-19 pushing them to hide their illness. Consequences may be a miscommunication between healthcare providers and patients resulting in a delayed or missed care and treatment.

SHARED DECISION MAKING IN A PANDEMIC DILEMMA OF VENTILATOR ALLOCATION

COVID-19 is attacking the patient's era after the emergence of the notion of personalized medicine that influenced the development of healthcare facilities over the world (Iles, 2004), particularly the North countries. Medical decisions were initially guided by narrative-based medicine (NBM) where the patient narrated his/her symptoms and the healthcare professional (HCP) listened until a common story approved by the patient and understood by the HCP was formulated. The objectives of the consultation, the milieu and the dialog were the focus (Launer, 2002). Progress drove to privilege patients' choices and called upon the Law to protect these options leading to the patient's era, whereby move from NBM to shared decision-making (SDM) was realized over the last two decades. This entitled that HCPs introduce choices, discuss therapeutic options, and explore preferences to be honored by the actors and community (Elwyn et al., 2012). The problematic is whether this can be maintained during a pandemic. To answer we decided to reflect on a clinical complex situation that generated public and professional fears while facing COVID-19, specifically the dilemma raised by the allocation of ventilator.

The pandemic burdened medical resources calling for a rationing in the use of ventilators, particularly for dying patients (Truog et al., 2020). The most problematic was

mechanical ventilator (MV) which is not only rare but used for long periods by the same patient. The media, even in the Arab region, highlighted the issue disseminating confusion regarding access to intensive care unit (ICU) with comments like "first come, first served" or "the youngest will be served while the old rejected".

This aggravated social concerns affecting the preparedness to cope and inviting ethicists to explore the option of ventilating patients by Ambu bag when there is no ventilator. Ideas were raised just to empower communal solidarity without considering the dangers to the HCP bagging the patient, nor positive end-expiratory pressure (PEEP) that is mandatory in acute respiratory distress syndrome (ARDS) (synapse.aan.com/ethics).

Worldwide number of patients needing MV rose from 1.4 to 31 patients per devise. This worsened with restricted availability in respiratory therapists and trained critical care personnel leading to rationing (Emanuel et al., 2020).

Most of the rationing protocols encouraged saving most lives and maximizing improvements, thereby giving priority to patients having better chances to respond if treated. The idea "first come, first served" proposed for patients having similar prognosis is not acceptable in a pandemic because it affects the principle of justice and might lead to violent behavior. Therefore, random allocation should be encouraged.

Ceasing MV from one patient and making it available to another is possible through advanced patient's wishes and/or the person of trust or when treatment is judged futile by the physician under certain jurisdiction. This is socially accepted when the concept of futility is introduced in Biolaws. It is not the case in the Arab world where futility is not only legally prohibited but an additional parameter that weakens the social bond in the public health domain. A social cohesion is therefore a must (Abou-Mrad et al., 2014).

Good clinical practice guidelines highlighted the principles that should be honored by every physician, namely, beneficence, justice and embracing the vulnerable that is a quality determinant in healthcare (Abou-Mrad et al., 2014). The burden of MV withdrawal should not be left to the clinical physician because of its debilitating distress. Hence, a triage committee should be established to handle the decision, neutralize paternalism, and alleviate the clinician's emotional suffering.

This committee is invited to ration the decision, act as an independent body, and involve collectivity defined by those people who are concerned with the life and death of the patient but are confined and not able physically to assist their beloved. The benefits of such a committee that would act as an advisory body are tremendous in gaining public trust and confidence that is crucial to every health care system for the post pandemic period.

Two structures in hospitals could serve here: (i) the Institutional Review Boards and (ii) the palliative care groups.

The first, because of their independence and highest representativeness and the second offer support for cases where a prolonged time to death is expected. Advice from the two groups along clearly written protocols will provide a holistic approach to the enormous emotional, spiritual and ontological burden facing carers.

Returning to the initial hypothesis of whether SDM is maintained in a pandemic, we must keep in mind that it took decades for medicine to move from NBM to SDM. Pandemic has replaced SDM with community decision making (CDM) involving more actors and emphasizing the wellbeing of the population shifting more towards utilitarian ethics overcoming, in the depth of the western countries, the anglo-saxon approach in the patient's care.

What is reassuring with the elaboration of this triage independent committee, is that both models (utilitarian & anglo-saxon) and approaches (SDM & CDM) banned the clinician to decide solely on withholding or withdrawing, therefore rejecting the physician's paternalistic attitude,even in a pandemic, to continue honoring the principle of autonomy.

ADVOCACY FOR A GLOBAL ETHICS DURING THE PANDEMIC

Almost a hundred days after the start of the epidemic, it is a right and duty to ask ourselves if our actions and attitudes were compliant with ethical principles, knowing that previous experiences led to many recommendations. WHO (2007, Ethical considerations in the development of public health measures in the face of an influenza pandemic), the CCNE in France (Avis N° 106, Ethical questions raised by a possible influenza pandemic, February 2009), and World Medical Association (Notice N° 106, Ethical questions raised by a possible influenza pandemic, April 2019) are the most relevant.

Recently, on March 26, 2020, UNESCO and COMEST published a statement on COVID-19: "Ethical considerations from a global perspective", in order to learn lessons and enhance international cooperation.

The origin of the virus is still unclear. The alert made by a Chinese doctor was ignored for a while.

Some countries lacked transparency, others vigilance; football matches and election rounds were held despite the announced gravity, leading to a shortage of health resources and the painful sorting of patients to resuscitate. At the same time, barriers appeared between countries, and communities to stop the spread of the disease.

The lack of cooperation between countries for both either information sharing or resources is evident. Means of struggle are unequal to the disadvantage of the poor countries. The absence of a concerted international action has resulted in a "*chacun pour soi*" attitude (every man for himself). The behavior of European countries is an example. The specter of overpriced future treatments and vaccines haunts poor countries.

The great consequence is injustice. Who will pay the heavy price in human life and cost?

We are still not safe from a recrudescence of COVID-19, let alone subsequent epidemics. We must manage successive waves, sanction false news on social networks and address the root of the problem, including the relationship of humans to animals and or laboratory manipulations.

Strategy for global ethics is mandatory for the present and future. Any action on a planetary scale will have to respect human dignity, justice between countries and between individuals, solidarity, swift measures and efficiency; this is an ethical requirement, the choice of health and people's lives must take precedence over economy or politics. Context, whatever it is, cannot change ethical values, emergency only forces them to prioritize them provisionally.

Any plan should take advantage of the multiplicity and complementarity of resources across countries. The multilateral action advocated by WHO in 2007 must lead to a strong international treaty.

A sufficiently coercive treaty must include sanctions for countries and leaders who conceal information regarding the evolution and the treatment of the pandemic, sanctions for large companies breaching the main principles of ethics, notably justice, beneficence and non-maleficence. A treaty, which would allow access to research results to everyone and prevent states or commercial harmful exclusiveness.

This treaty must built structures of global governance, which, among other things, should ensure the necessary prioritization of needs on a global scale and coordination between member countries and ensure that governments respect ethical principles with regard to their citizens. Instead of narrow national interest, let us call for international cooperation and solidarity at all levels between international organizations, governments, and civil society. This should include an engagement from rich countries to provide significant help and assistance (technical and medical supplies) to poor nations confronted to this pandemic. It is never too late.

This is how, during such challenges, humankind can rediscover its solidarity, its values and reshape a culture worthy of the human person.

PSYCHOLOGICAL SUPPORT FOR PATIENTS & CAREGIVERS DURING COVID-19 PANDEMIC

The coronavirus crisis has highlighted a major anxiety generalized to the whole population, affected and not reached, and affecting even caregivers.

This irrational anxiety has generated the stigmatization of those affected and even of those caring for them. The health professionals' activity in a context of high and continuous demand has considerable impacts at different levels (physical, psychological and social). Thus, the risks these professionals are subjected to go far beyond the potential infection, and therefore they must be taken into consideration in the planning and implementation of specific strategies as a condition to ensure the safety of professionals, the full functioning of health institutions and the permanent care of patients at different stages of the disease. By fighting stress during this period, we significantly reduce stigmatization, which is one of the major ethical issues of this phase.

Coping with stress during the COVID-19 pandemic

It is normal to feel stressed, sad, confused, angry, or scared during a crisis. This can be completely normal. Time spent watching, reading or listening to news, which is a source of anxiety and distress, should be minimized and information sought only from reliable sources (such as the WHO), which could minimize anxiety. It is imperative not to use tobacco, alcohol or other drugs to manage negative emotions.

In the case of massive anxiety, it is important to benefit from the skills that anxious people have already used in the past and which helped them to manage life's difficulties.

It is also important to look for the positive and hopeful stories of people who have suffered from COVID-19. For example, stories of people who have recovered or knowing that the infection rarely affects children and young people. During isolation, it is important to participate in healthy activities as relaxation, such as mindfulness, meditation, prayer or physical activity.

Tips for better mental health for healthcare workers

Health professionals are key elements in any planning process to respond to a pandemic situation, fulfilling their different assistance tasks. We expect them to respond without restrictions, assuming those tasks as agents on the different fronts in which they are qualified and competent, within the limits of their technical and human capabilities. Among these tasks, caring for sick people severely affected by the disease is even more demanding.

It is normal to feel stressed and under pressure. This does not mean that a caregiver cannot do his job or that

he is weak, but that he must manage his own mental health and psychosocial well-being. He also needs to have enough rest between work periods, eating healthy food, practicing physical activity, setting aside time for relaxation, and staying in virtual contact with family and friends.

Being kept at a distance by one's own family or community due to stigmatization or fear could make the situation more difficult. It is imperative to get rid of the guilt of being able to infect your own family from the moment you take the necessary precautions. When you reach a state of emotional, physical, or mental fatigue, you need to know how to turn to others for help, reframe the way you see work, and seek the advice of a mental health professional.

Intervention strategies should be designed to reduce burnout and compassionate fatigue, as well as supporting patients' families to reduce the impact on their personal and family lives.

The current crisis has highlighted the solidarity that is extremely essential in this period. New human relationships will undoubtedly arise after the passage of the pandemic.

CONCLUSIONS AND RECOMMENDATIONS

The challenges and consequences of the COVID-19 pandemic affect every person and every region differently with their own vulnerability.

One of the major ethical issues during this pandemic is to engage society in a process of responsibility and solidarity. A good information and transparency will help citizens to accept and apply the different measures taken against the pandemic.

There is a place for ethical reflections in the management of severely diseased patients, the availability and distribution of resources, especially when they are limited. The local Ethics Committee can assist and support HCP to define their priorities in their care.

- Promote the triad of health, solidarity, equality: It is necessary to give priority to the respect of confidentiality and human dignity. Otherwise, the patient feels responsible towards the society.
- Ways out of the crisis: Prepare for the post-COVID-19 period by restructuring and reshaping society medically, legally, economically, politically and above all philosophically in order to rebuild society.

In this spirit we recommend that:

- Protection of human health be accorded a much higher priority in the system of values than economic interests.
- Saving lives is the most important and urgent goal. The public health emergency must not be abused to usurp power, or to permanently suspend the protection of rights and liberties.
- Once the crisis is over, countries should work together to implement lessons learned during COVID-19. A common strategy to deal with a pandemic and similar threats should be elaborated and implemented at the global level.
- States with sufficient resources for healthcare should share their resources with those who lack necessary resources in an attitude of solidarity. COVID-19 has shown, once more, that the most socio-economically deprived are most vulnerable to disease and illness.

We must live through this pandemic, and after it. We must face this situation with strength, care and solidarity.

ACKNOWLEDGEMENT

All authors have equally contributed to the manuscript.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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France: The French National Ethics Council

La contribution du CCNE à la lutte contre COVID-19: Enjeux éthiques face à une pandémie

Germany: Deutscher Ethikrat

Solidarity and responsibility during the coronavirus crisis

Greece: Hellenic National Bioethics Commission

The bioethical dimension of individual responsibility in response

to COVID-19 (coronavirus)

Luxembourg: Luxembourgish National Ethics Committee

Repères éthiques essentiels lors de l'orientation des patients dans un contexte de limitation des ressources thérapeutiques disponibles due à la crise pandémique du COVID-19

Mexico: National Bioethics Commission of Mexico

Statement: Bioethics in the face of the COVID-19 pandemic

Recommendations regarding the COVID-19 pandemic, from a bioethical approach

Portugal: National Ethics Council for the Life Sciences

CNECV Statement: COVID-19 Key Considerations

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Spain: el Comité de Bioética de España

Informe del Comité de Bioética de España sobre los aspectos bioéticos de la priorización de recursos sanitarios en el contexto de la crisis del coronavirus

The United Kingdom: The Nuffield Council on Bioethics

Ethical considerations in responding to the COVID-19 pandemic

Guide to the ethics of surveillance and quarantine for novel coronavirus

Statements by International Organizations

UNESCO International Bioethics Committee (IBC) and the UNESCO World Commission on the Ethics of Scientific Knowledge and Technology (COMEST)

Statement on COVID-19 Ethical Considerations from a Global Perspective

European Group on Ethics in Science & New Technologies (EGE)

Statement on European Solidarity and the Protection of Fundamental Rights in the COVID-19 Pandemic

Coronavirus Resources

- World Health Organization
- European Centre for Disease Prevention and Control
- United States Center for Disease Control
- United States Center for Disease Control: Travel Health Notices
- US Department of State: Travel Advisories
- National Institutes of Health
- City of Philadelphia Coronavirus Disease 2019 (COVID-19)
- Pennsylvania Department of Health Coronavirus Resources
- European Centre for Disease Prevention and Control Available at: https://www.ecdc.europa.eu/en/novel-coronavirus/event-background-2019
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COVID-19 PANDEMIC

MANAGEMENT OF LABOR AND DELIVERY UNITS DURING THE COVID-19 OUTBREAK
Report of 3 Cases at Rafik Hariri University Hospital, Beirut, Lebanon

http://www.lebanesemedicaljournal.org/articles/68(1-2)/pandemic16.pdf

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Chahine R, Khazaal J. Management of labor and delivery units during the COVID-19 outbreak. Report of 3 cases at Rafik Hariri University Hospital, Beirut, Lebanon. J Med Liban 2020; 68 (1): 105-108.

INTRODUCTION

The clinical implications of COVID-19 on infected persons range from mild self-limited respiratory tract infection to more severe pneumonia, multi-organ failure and death [1]. However, the full effect of this infection on pregnancy is still unknown, specifically its prevalence, morbidity, vertical and horizontal transmission and subsequently how to manage infected pregnant patients in labor, delivery and postpartum management [2,3]. Obstetrical services struggled in the early phase of the pandemic to design the best protocols for the care of these patients [5].

The Rafik Hariri University Hospital (RHUH) was designated as the first line COVID-19 hospital in Lebanon. Soon following the onset of the outbreak, and with lack of any international guidelines, the department of Obstetrics and Gynecology at RHUH developed its own algorithm for the management of pregnant women in labor with either confirmed or suspected COVID-19 infection (Figure 1).

We report the first three pregnant patients with suspected COVID-19 managed at RHUH.

CASE REPORTS

Case # 1

A 24-year-old woman, G3 P2 L2, presented at 36 weeks of gestation to the delivery suite in labor. She had two prior cesarean deliveries.

Initial screening for any symptoms or risk factors for COVID-19 – using the rapid assessment test (RAT) checklist (Figure 1) – revealed recurrent episodes of coughing, sore throat and dyspnea of two days duration. Patient was considered "at risk for COVID-19" and transferred to the special Corona Emergency Department (ED) where she was assessed by the corona and obstetrical teams. The transfer passageway was immediately disinfected by a specially trained team of janitors.

In the Corona Unit, she had regular uterine contractions and underwent a repeat cesarean section under strict personnel protective measures in the specially dedicated operating room inside the Corona Unit and gave birth to a live male newborn with an Apgar score of 8 [and 8] at 1 and 5 minutes respectively.

The newborn baby was transferred initially to a special isolation crib in the dedicated special Corona Unit, then transferred to an isolation room in NICU (Neonatal Intensive Care Unit) for respiratory distress. The mother was also transferred to the isolation area for further postoperative and medical care. The COVID-19 PCR test, 48 hours following delivery, was negative, so she was transferred to the regular obstetrical ward. The newborn baby also tested negative for the COVID-19 PCR. Mother and baby left hospital in good condition.

Case # 2

A 26-year-old female, G3 P2 A0 L2, at 35 weeks and 5 days of gestation, with previous two late preterm vaginal deliveries, presented to a hospital in South Lebanon with labor pain, and fever of 38.5°. She denied any respiratory symptoms or contact with suspected COVID-19 patients.

She was considered at risk for COVID-19 and was transferred to RHUH Corona ED unit and evaluated by the designated Corona obstetrical teams (one attending physician, the chief resident and a senior midwife). The cervix was 8 cm dilated and her temperature was 38.2° with no apparent focus of infection. A nasopharyngeal swab for PCR for COVID-19 was taken.

She progressed quickly and gave birth to a baby girl with an Apgar score of 9 and 10 at 1 and 5 minutes respectively. The patient and her baby were transferred to an isolation room in the Corona Unit awaiting the PCR result. The patient did not have any fever postpartum and remained clinically stable. The PCR test for her and her baby turned to be negative the following day.

The patient and her baby were discharged home on day two postpartum.

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Exposure risk (in the past 14 days prior to symptom onset)		**Clinical Signs and Symptoms** of respiratory infection	
• History of travel to areas with presumed ongoing community transmission of COVID-19 Like China, Iran, South Korea, North Italy, Singapore, Japan, Spain, France or any updated information added	☐	• Fever	☐
• Close physical contact in the past 14 days prior to symptom onset with a confirmed case of COVID-19	☐	• Cough (new or worsening)	☐
• Working in or attended a healthcare facility where patients with confirmed COVID-19 were admitted	☐	• Shortness of breath (new or worsening)	☐
		• Sore throat and/or runny nose	☐

Figure 1. Visual rapid assessment tests (RAT) checklist for acute respiratory illness during the COVID-19 pandemic [6] used by the Rafic Hariri University Hospital in Beirut, Lebanon.

Case # 3

A 28-year-old woman, G4 P1 A2 L1, at 29 weeks of gestation, known to have chronic hypertension post kidney transplant four years earlier and maintained on tacrolimus, azathioprine, prednisone, and bisoprolol followed outside the RHUH.

She was referred to our labor suite with high blood pressure reaching 160/95 mmHg, labor pain and a history of amniotic fluid leak of two days' duration. She was screened by RAT checklist. She was afebrile and denied any respiratory complaints or contact with any suspected COVID-19 patient. Her cervix was fully dilated with the fetus in frank breech presentation. Within few minutes of her presentation, she delivered vaginally a live baby boy, weighing 1365 g, Apgar 5 and 6 at 1 and 5 minutes respectively. The newborn baby was transferred to NICU.

One hour post delivery, the patient started coughing. Upon further questioning, she admitted having flu-like symptoms of few days' duration. She was labeled "at risk" for COVID-19 and transferred to the Corona Isolation Unit with her newborn following COVID-19 PCR testing, that proved to be negative 24 hours later. The newborn baby was then transferred from NICU isolation to the regular NICU and is still hospitalized till the date of writing this paper. The patient herself left the hospital on the third postpartum day in good condition.

DISCUSSION

The RHUH is one of the major tertiary teaching medical center in Beirut. As soon as the COVID-19 outbreak started in Lebanon, RHUH was designated by the Ministry of Public Health as the national COVID-19 hospital and a plan was designed for the management of suspected or confirmed COVID-19 pregnant women by the Department of Obstetrics and Gynecology.

The main hospital emergency department was transformed into a designated Corona-ED Unit. This ED consists of a triaging unit including a dedicated Computed Tomography scan and a separate operating room. The Corona-ED is separate from the rest of the hospital facilities (including corridors, elevators, etc.). On the other hand, special wards were converted to receive COVID-19 patients for isolation and treatment with separate access to the ED unit.

The Labor and Delivery Unit (L&D) at RHUH, in coordination with the infection control team, the nursing office and the hospital administration, designed special guidelines for the care of pregnant women presenting in labor during the COVID-19 outbreak. These included screening any patient presenting to the L&D, using the RAT recommended by many international organizations (Figure 1) [5], and assign a risk status for COVID-19 infection. Accordingly, every patient will be referred to either the regular L&D, or to the "Corona Unit" to be cared for. All pregnant women presenting to delivery suite and personnel will be wearing a surgical mask. All patients presenting to delivery suite will be screened at the door, their temperature taken, respecting the safety distance according to the recommended check list. The patient will be then classified as "low risk" or "at risk" for COVID-19.

In case the patient is known to have COVID-19 at our institution or referred from another one, she will be immediately directed to Corona-ED for further care.

The algorithm consists of the following steps according to three different scenarios (Figure 2):

1. SCENARIO 1: LOW RISK pregnant woman presenting to delivery suite: The patient will follow the routine obstetrical care inside the labor and delivery suite.
2. SCENARIO 2: AT RISK pregnant woman presenting to delivery suite:

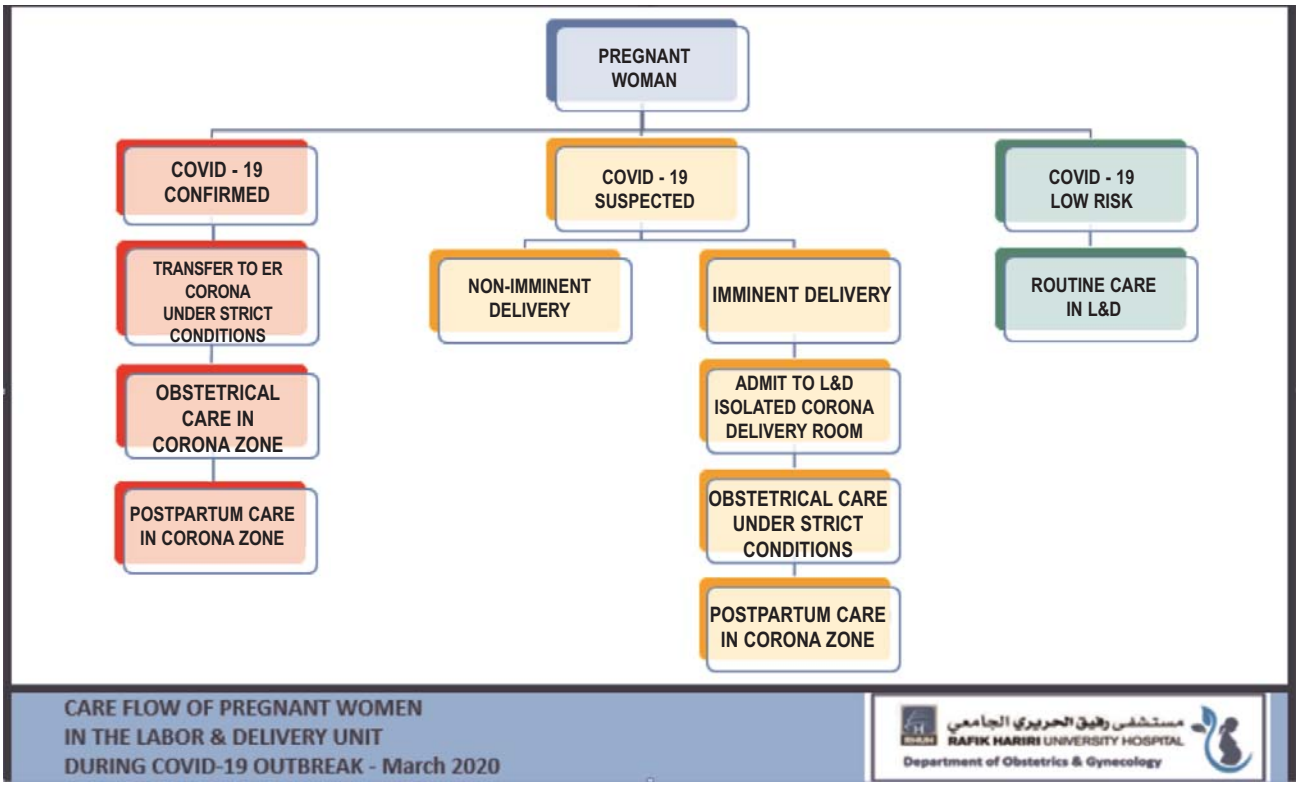

Figure 2. Care flow of pregnant women in the Labor and Delivery Unit during the COVID-19 outbreak at Rafic Hariri University Hospital in Beirut, Lebanon.

SCENARIO 2a: Patient with non-imminent delivery: The patient will stay outside the delivery suite and will be directly transferred to the Corona-ED via a specific passage way. The patient will be assessed by Corona and obstetrical teams, and managed or delivered inside the Corona Unit accordingly.

SCENARIO 2b: Patient with imminent delivery or complaints: The patient will be directed to a special isolation room created just outside the main delivery suite (the adjacent L&D conference room). This new room is appropriately equipped for vaginal delivery. An access to a special dirty room, special toilet and shower rooms were also assured. The patient will be managed by an assigned team (minimal number of personnel) under strict personal protective measures.

3. Scenario 3: CONFIRMED COVID-19 or symptomatic pregnant woman presenting directly to Corona-ED or transferred from another hospital: The patient will be directly managed in the Corona-ED zone where she will be assessed by Corona and obstetric teams. Either vaginal birth or cesarean section deliveries can be performed in the ED operating room.

The first patient (case #1) described belongs to scenario 2a; the patient presented to the delivery suite, was classified "at risk" according to the initial screening process (2 items on the RAT checklist). Therefore, she was transferred to Corona-ED where she was delivered by repeat tertiary cesarean section.

The second patient (case # 2) belongs to the scenario 3, where a suspected case (maternal fever) was referred from another hospital and was directly sent to Corona-ED. After initial assessment by both the Corona and the ob-stetrical teams, the patient was found to be in advanced stage of labor and soon delivered vaginally.

Both patients (cases #1 and 2) were kept in the isolation area of the Corona Unit until the PCR tests on both patients were negative and were transferred to a regular ward.

The third patient does not fit in any initially planned scenario (patient with preterm imminent delivery showing symptoms during the immediate postpartum period despite initial denial of any symptoms upon the screening process). Patients may deny symptoms for fear of rejection or stigmatization by the health care providers and centers.

Newborns of mothers either infected or suspected to have COVID-19 should be kept isolated in the NICU of the Corona Unit while waiting for the PCR results. Par-

turients will be encouraged to pump their breasts for milk expression.

The patient is allowed to keep her newborn with her during isolation and to breastfeed while respecting the required safety measures (mask wearing, hands and breast hygiene) [4].

Postpartum management of women with confirmed or suspected COVID-19 infection (herein considered as patient under investigation (PUI)) should be at the Corona isolation unit.

CONCLUSION

Although we did not encounter any patient with COVID-19 in Lebanon, all obstetrical units are encouraged to design special guidelines for the screening and the management of pregnant women with confirmed or suspected COVID-19. These guidelines are essential in the treatment of pregnant women and their newborn babies while protecting the health care workers.

The Ministry of Public Health in Lebanon has created a special COVID-19 committee to formulate guidelines to this effect and will be published separately in this issue.

Conflicts of interest

The authors declare no conflicts of interest.

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LETTER TO THE EDITOR

MUCH ADO ABOUT A VIRUS
COVID-19 Trigger of Scientific Curiosity and Medical Unity

http://www.lebanesemedicaljournal.org/articles/68(1-2)/letter1.pdf

Dear Editor,

Very few ever thought we would live to actually witness a catastrophic medical crisis affecting the whole world.

Learning how to protect one from the other, stigmatizing a neighbor with a cough or a sneeze, and counting the COVID-19 victims by the minute, the world watched this sanitary nightmare evolving on a television screen with a tsunami starting in Wuhan, Hubei Province, China, in December and reaching the Americas by the end of March.

Caught in the middle, the Lebanese saw their first cases hit the ground officially on March 1st. A remarkable effort ensued in our medical community. A swift organization was put in place by the Ministry of Health and Hariri Governmental Hospital to accommodate the first patients. Looking at projected numbers, it was clear that more hospitals and intensive care unit beds needed to be prepared to respond to the epidemic. The rule of thumb suggested that 80% of patients would require only outpatient care, and among the admitted ones, less than 10% would require intensive care. The whole health system, governmental and private, had to be restructured in a matter of days or short weeks.

The major private university hospitals were caught up in a paroxysm of preparedness for a virus that they hoped will never hit their door. Our institution, a private university hospital, volunteered to be at the frontline of this heroic battle. We were going from meeting to meeting until the wee hours of the night. Everything had to be thought of to care for the sick. One priority was to protect our healthcare workers; we doubled orders of personnel protective equipment, often having to resort to a growing black market. Facility organization had to be restructured: an isolated emergency room area, isolated elevator, isolated wards, and dedicated staff. Intensive care unit rooms had to be fitted with negative pressure. Extra respirators needed to be available in case of an overwhelming number of patients showing up. Benefactors were generous in helping provide much needed financial help.

While overwhelmed by the anticipated harms of COVID-19, we never stopped caring for patients affected by other pressing diseases during the pandemic, halting along the way all elective surgery and procedures. Physicians, students and nurses from all specialties got together to staff triage and flu clinics, isolation wards, and intensive care units. Medical specialists united and worked together like the fingers of one hand.

In our institution, healthcare workers and administrators gathered together to come up with impromptu decisions on urgent issues; from isolation, testing, hospital access control, to communication with media, and fundraising. Communication was made through a daily bulletin informing our community on the number of patients treated, recovered and deceased as well as pertinent decisions taken in our crisis group.

We created a task force grouping together biologists, pharmacists, anesthesiologists, specialists in infectious disease, immunology, pulmonary, critical care, and nurses. We had to deal with a disease with ever changing guidelines and soft-evidence-based therapy, making treatment protocols empirical and at times anecdotal. The medical literature from around the world had to be scrutinized. The Task Force treatment protocols were suggested by consensus among the group. Our goal was to give the benefit to the patient with the least harm. Various therapies were discussed and adopted at different stages of the disease: Hydroxychloroquine sulfate, lopinavir/ ritonavir, remdesivir, tocilizumab, statins, and zinc [1]. Remdesivir, a promising drug for severe cases was initially not available in Lebanon. For the first time in my career, I felt that we had to act before confirmatory science, which is not what we had been taught or instructed our students and residents so far. A fantastic number of studies initiated by young and senior investigators were hastily published. Over thirty studies and projects were brought forward to our university's medical ethics committee. We gathered weekly in a video conference to keep up with the flow. Turnaround for approval was kept very short, in line with the World Health Organization position of "*a moral obligation to conduct timely scientific research*" during an infectious disease outbreak [2].

Despite the present gloomy Lebanese socio-economic environment, our medical system's reactivity and preparedness avoided the worst. None of us can operate as an island, with this still young pandemic taking its course and no foreseeable vaccine in the near future. Going forward, we have to work together, coordinate our efforts, and share information. Our university's medical institutions brought the best to the frontline: initiative, expertise, solidarity and scientific output, put to the benefit of all, governmental and individual.

This virus has caused a long dynamic event that will require constant strategy adjustment and problem-solving at the national and local levels. Economic issues are heavily weighing on the sanitary crisis.

Pandemic or not, our vision of healthcare is changed forever.

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