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REVIEW ARTICLE

Palestinian strategies, guidelines, and challenges in the treatment and management of coronavirus disease-2019 (COVID-19)

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ABSTRACT

Background: Coronavirus disease-2019 (COVID-19) outbreak is a global concern and the World Health Organization (WHO) has declared it as a Public Health Emergency of International Concern. The Palestinian Authority (PA) has quickly and effectively responded to the outbreak of COVID-19, using an internationally and nationally coordinated, to contain the spread of the virus within the borders. The PA approaches are containment and suppression, which is designed to protect the citizens from infection while also mitigating the stress on the health care system. The PA immediately declared a State of Emergency when the first cases in Palestine were diagnosed on 5 March 2020 and launched robust national containment measures to encourage the citizens to protect themselves and follow the guidance. **Objectives:** There is currently no vaccine or effective treatment for COVID-19, the treatment is either supportive and/or the treatment of symptoms. Several strategies in the treatment of the disease were applied including medications. This review aims to summarize the different strategies, guidelines, challenges, and treatments used against COVID-19 worldwide and in Palestine. **Materials and Methods:** Different literature and guidelines among different databases were searched. Literature reviewing was conducted using the following search engines, Google Scholar, Medline, Pub Med, EMBASE, Web of Science, and Science Direct. Data also obtained from WHO and PA reports, and the published peer-reviewed articles of 2019-nCoV. The review focuses on the strategies, guidelines, therapeutics, challenges, and different approaches used in the treatment and management of the disease in Palestine and globally. **Conclusion:** The Palestinian Ministry of Health (MoH) strategies to end the COVID-19 pandemic were; slow and stop transmission; provide optimized care for patients; and minimize the impact of the epidemic on health systems, social services, and economic activity. Thus, proper management, right actions, and effective treatment of the disease should be considered to achieve these strategies. The biggest problem for PA to control and stop the outbreak of the disease is the different challenges which include; the Israeli military and economic control, uncontrol the borders, shortage of medical and financial resources, crowded cities and refugee camps, poverty, food insecurity, and the financial crisis. To date, there are no specific vaccines or medicines for COVID-19; and treatments are under investigation through clinical trials. However, an array of drugs approved for other indications, as well as multiple investigational agents, are being studied for the treatment of COVID-19; in several hundred clinical trials around the World. Treatment is essentially supportive and symptomatic.

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INTRODUCTION

Coronavirus disease-2019 (COVID-19) is a serious public health crisis threatening the world with extremely fast spread and mortality. The COVID-19 pandemic indisputably amounts to an unprecedented global public health challenge in the twenty-first century. It caused many consequences of socioeconomic, political, and public health worldwide. Many addressed the economic repercussions of the coronavirus, especially in the absence of confirmed news about the creation of an effective medical drug to combat it, as well as the close link between the global economy and the Chinese economy, which makes any tremors experienced by the latter with serious global consequences. Some have highlighted conspiracy theories related to the emergence of the virus and the rumors that spread fears, which in turn will reflect on the economy of countries. Although some warn of the impact of rumors, others have promoted a theory that corona is a "biological weapon." Coronaviruses are enveloped positive-sense RNA viruses ranging from 60 to 140 nm in diameter with spike-like projections on its surface giving it a crown-like appearance under the electron microscope; hence the name coronavirus. Four coronaviruses namely HKU1, NL63, 229E, and OC43 have been in circulation in humans and generally cause mild respiratory disease. The COVID-19 pandemic has exploded as cases have been identified as the cause of an outbreak of respiratory illness in Wuhan, Hubei Province, China at the beginning of December 2019. As of 31 January 2020, this epidemic had spread to 19 countries with 11 791 confirmed cases, including 213 deaths. The disease is transmitted by inhalation or contact with infected droplets and the incubation period ranges from 2 to 14 days or even more. The most common symptoms are fever, dry cough, and tiredness, whereas the serious symptoms are difficulty breathing or shortness of breath, chest pain or pressure, and loss of speech or movement. There are also less common symptoms such as; aches and pains, sore throat, diarrhea, conjunctivitis, headache, loss of taste or smell, and a rash on the skin, or discoloration of fingers or toes. The disease may progress to pneumonia, acute respiratory distress syndrome (ARDS), and multiorgan dysfunction especially in elderly people and those with comorbidities. However, symptoms of a coronavirus usually go away on their own and many people are asymptomatic. The virus is diagnosed in respiratory secretions by special molecular tests. In some cases, self-isolate to prevent the spread of infection is preferred and advisable. There is no specific treatment for disease caused by a coronavirus. However, many of the symptoms can be treated and therefore treatment based on the patients' clinical conditions. The World Health Organization (WHO) has declared it a Public Health Emergency of International Concern. By June 4, 2020, more than 6.5 million cases of COVID-19 have been reported globally, including >380,000 deaths. Cases caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections have been reported in more than 180 countries, including all 50 states of the United States.[1-3]

On February 22, 2020, the Palestinian Ministry of the Interior closed several restaurants in Palestinian cities as a result of the visit by a Korean delegation after some of its members were confirmed with the infection of the coronavirus 2019. The COVID-19 pandemic was confirmed to have spread to the West Bank on March 5, 2020 and the Palestinian MoH said the cases had first been detected at a hotel in the Bethlehem area, where a group of Greek tourists had visited the hotel in late February, with two later diagnosed with the virus. Although in the Gaza Strip, the first case was diagnosed in Gaza on March 21, and as of July 4, 2020, there were about 11 active cases and one death. On March 29, 2020, the Palestinian MoH confirmed 11 new cases in the West Bank, and on March 30 an additional 7 new cases were also confirmed. No new cases were reported for Gaza in this period. By March 30, 2020, the confirmed cases were 115 cases (West Bank 106 and Gaza Strip 9 cases). The highest cases were in Bethlehem (46 cases). By this time, the MoH has reported a total of 18 cases have recovered and one person had died. Most cases do not present clinical symptoms and none are critical. All new cases were under medical observation at designated health facilities and contact tracing was initiated for all cases. The East Jerusalem Hospital Network has also announced preparations for Jerusalem hospitals to deal with cases of COVID-19 that require clinical care. In the Gaza Strip, the local health authorities have expanded the laboratory monitoring process to include hundreds of samples for quarantine inmates and contacts of patients with COVID-19 in quarantine centers since the beginning of March 2020. In this period, more than 1760 people were in one of 25 designated quarantine facilities including at Rafah crossing quarantine center or at health facilities, schools, or hotels designated as quarantine facilities. The quarantine period was 2–3 weeks (21 days). Those coming from crossings at Rafah or Erez have been quarantined since March 15.

Home quarantine ended 26 March for those who entered Gaza 14 days prior. The MoH has limited public primary healthcare service delivery in the Gaza Strip, to 14 centers distributed across the five governorates, which provided essential services only, and one school per governorate was also assigned to serve as a triage center for respiratory cases. On 26 March 2020, the Palestinian Authority (PA) released the National COVID-19 Response Plan that outlined the strategic measures from several key sectors, including health, economy, and social protection to contain the outbreak.[4-6] As of April 23, a total of 480 Palestinians (including East Jerusalem) have been confirmed to have COVID-19, 319 in the West Bank, 17 in the Gaza Strip and according to the Palestinian MoH, another 144 known cases in East Jerusalem, although uncertainty remains over the figures due as East Jerusalem has been covered by the Israeli authorities. Four of these people (all in the West Bank) died and at least 92 have recovered as shown in Figure 1. Approximately 80% of people detected positive are below the age of 50, the vast majority of whom are asymptomatic. Although the apparent spread of the virus by this period was limited compared to other countries, this may reflect the limited testing capacity, with slightly over 26,000 samples were tested only. Figure 1 shows also quarantine centers, crossing points, and closed crossing points in this period. The PA was leading the efforts to contain the pandemic, in coordination with the Israeli authorities and international actors, primarily the WHO.[4-6]

Although on May 28, 2020, the pandemic cases were 5,868,922 and 360,476 deaths worldwide with a 6.14% mortality rate, and in Palestine, the pandemic confirmed cases were 570 with 4 deaths only. The disease spread extremely very fast as by the end of June (within only 1 month period), the cases have been nearly doubled as the coronavirus cases confirmed were 10,690,566, deaths 516,393 (8%), and recovered are 5,856,464 worldwide. The high incidence rate and cases were in the USA (2,751,571), then Brazil (1,426,913), Russia (654,405), India, UK, Spain, Peru, Chile, Italy, and Iran (230,211), respectively . In Palestine by this time, at the end of June, the reported cases were increased very sharply by about six times; as more than 3,095 cases were reported including East Jerusalem (337 cases), with 11 deaths. The highest cases (1947 cases) were in Hebron Governorate; with these confirmed cases Palestine ranked 97 among 215 countries that have coronavirus; with the highest outbreak rate in the world; compare to population number. The city of Hebron is the epidemic center, with 3,773 active cases as of July 8, 2020, and 15 deaths. The outbreak of the disease globally was continued raising very sharp as by July 11, 2020, the coronaviruses cases reported was 12,872,339 and the death cases were

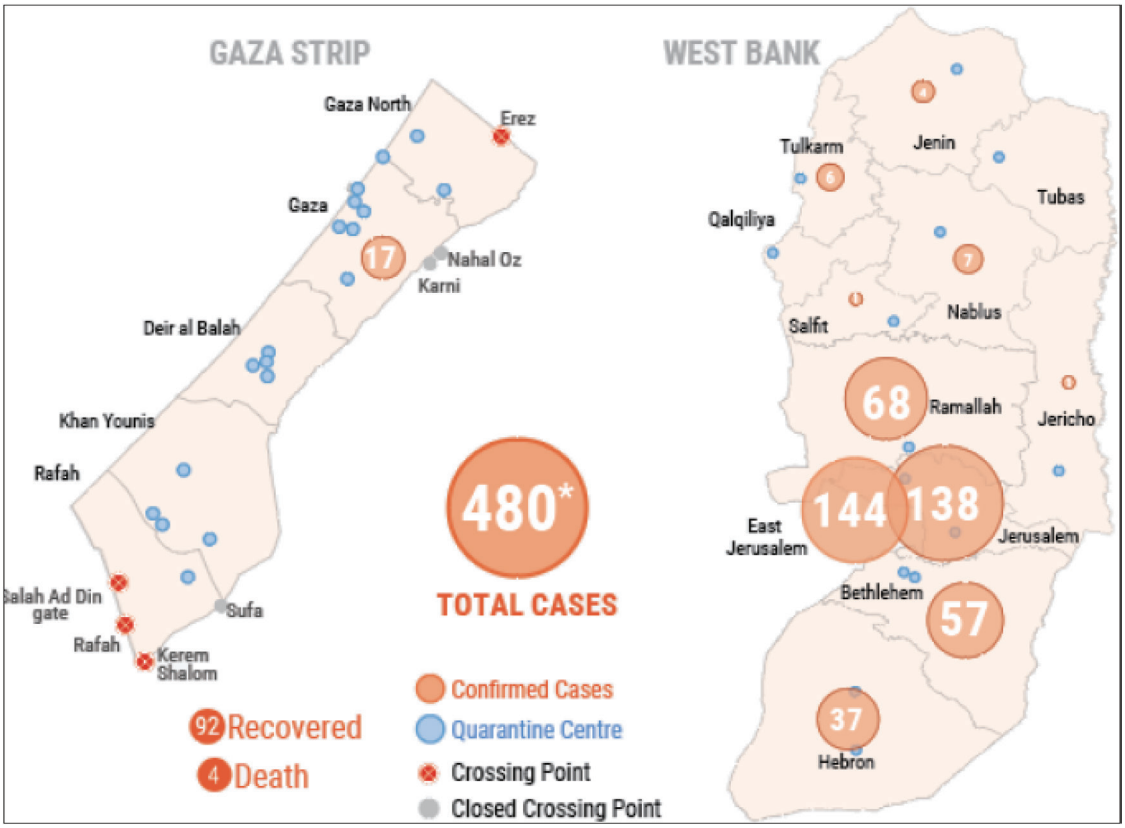

Figure 1: Coronavirus disease-2019 in Palestine by April 23, 2020

568,312, the increase rate of the new cases was ~8% and the rate death increased by 1.125%; within about 2 weeks period only, which considered high rates. The highest incidences by this time were in the USA with 3,356,242 reported cases, then Brazil (1,840,812), India (854,480), Russia (727,162), and Peru (322,710). In terms of the outbreak of the disease, the rank of the countries is changing every day, but the USA and Brazil remain and still rank first and second, respectively, for a while. In Palestine by July 11, 2020, the confirmed cases were 6688, and the death cases were 36, with an increased rate of 304%, which extremely very high and considered the highest worldwide. The highest cases were in Hebron Governorate (4620 cases), with about 70% of the total reported cases, with these confirmed cases Palestine ranked 87 among 215 countries that have coronavirus; with the highest outbreak rate in the world too; compare to population number. Within only 2 weeks period the Palestine rank changed from 97 to 87; however, if the outbreak in Palestine remains rising by the same rate, Palestine after a short period will be one of the top countries having the disease, if real and serious precautions did not apply especially the health recommendations, isolation and maintain social distance. The high outbreak of the disease in this region (Hebron Governorate), as 90% of infections have been caused by people meeting up with their families or attending wedding parties or funerals and failing to follow health recommendations and maintain social distancing according to Palestinian MoH officials.[4-6] (https://www.worldometers.info/coronavirus/). The number of people testing positive for COVID-19 continues to surge in the West Bank with an average of 396 new cases per day since July 1. On July 23, the occupied Palestinian territory (oPt) experienced a record number of confirmed cases in one day at 596. The WHO risk assessment remains very high for the oPt. The number of people testing positive for SARS-CoV-2 continues to increase. The total number of cases is 11,875 including 11,800 cases in the West Bank and 75 in the Gaza Strip, with three new cases reported in Gaza in this period. From July 1 (to July 23) the West Bank (including East Jerusalem) has averaged 396 cases per day, with 9,110 new cases and 61 fatalities. Most cases recorded are from Hebron (6,789), East Jerusalem (2,131), Jerusalem (784), Ramallah (654), Bethlehem (576), Nablus (339), and Qalqilya (143). Other governorates (Salfit, Tubas, Tulkarm, and Jenin) continue to record low case numbers. A total of 81 health workers are among those confirmed cases and 16 patients are in a serious condition, with four patients requiring mechanical ventilation (as of 23 July). By this period, the MoH reported a total of 3394 cases have recovered; 3326 in the West Bank (including 674 in East Jerusalem) and 68 in Gaza and seventy people have died, with an overall case fatality rate (CFR) of 0.59%. Less than half (47%) of all confirmed cases are male (4,388 cases) and about 81.6% of all cases (7,332 cases) are below the age of 50 years in the oPt, excluding East Jerusalem. A total of 172,382 laboratory samples have been tested for COVID-19 according to the MoH, with 13,634 samples tested in the Gaza Strip [Figure 2]. 23,261 Palestinians are in quarantine (home or facility-based) to prevent further spread of the disease. In the Gaza Strip, 259 people are in one of the key hospitals across the Gaza Strip on July 17. The Centers are designed to ensure that all suspected patients with COVID-19 are adequately assessed and managed, separate from other patients in emergency departments to ensure containment and prevent further spread of COVID-19. As of July 23 (noon), the PA MoH reported 2,131 COVID-19 cases in East Jerusalem. Three deaths have been reported (CFR: 0.14%) and 174 have recovered in the same period. As of July 20, 16 patients are being treated in three designated COVID-19 hospitals in East Jerusalem including five patients at Augusta Victoria Hospital, seven at St. Joseph Hospital, and four at Makassed Hospital. Over the past 2 weeks up to July 22, Makassed Hospital received 14 patients with COVID-19, discharged 12, and 2 have recovered. In these designated hospitals in East Jerusalem, 19 health workers have tested positive for COVID-19 and 35 are under quarantine (as of July 22).[4-6]

On August 3, 2020, 10:28 GMT the confirmed cases are 18,258,448, Deaths: 693,395, and Recovered: 11,460,069 worldwide. After about 3 weeks the number increased sharply by 5,386,109 cases, about 42% increased, which is high. The USA (4,813,984) and Brazil (2,733,677) are the highest in the world; ranked first and second with increased percentage ~43% and ~ 48.5%, respectively, within about 3 weeks only. It clear that the outbreak of the disease increased very fast globally. In Palestine, the cases also raised sharply; by ~136% increased within 3 weeks period too, the case increased from 6668 to 15780 cases, which extremely very high [Figure 3]; by this increased rate Palestine ranked 74 out of 215 countries have the disease. Figure 3 shows COVID-19 in oPt by August 2, 2020, cumulative confirmed, recovered and death cases, confirmed cases per day (since April to August 2020), confirmed cases by gender (March 5 to July 26, 2020), and confirmed cases by age in Palestine. Some data reported were included and some excluded East Jerusalem. (http://www.emro.who.int/pse/palestine-news/top-story.html). Table 1 shows cases for the top 30 countries including, other information such as daily new cases, total death, totally recovered, and a total test of each country. Although the actual and accurate causes and effective treatment of COVID-19 are still unknown or unavailable and the number of active cases of the infection is rising every

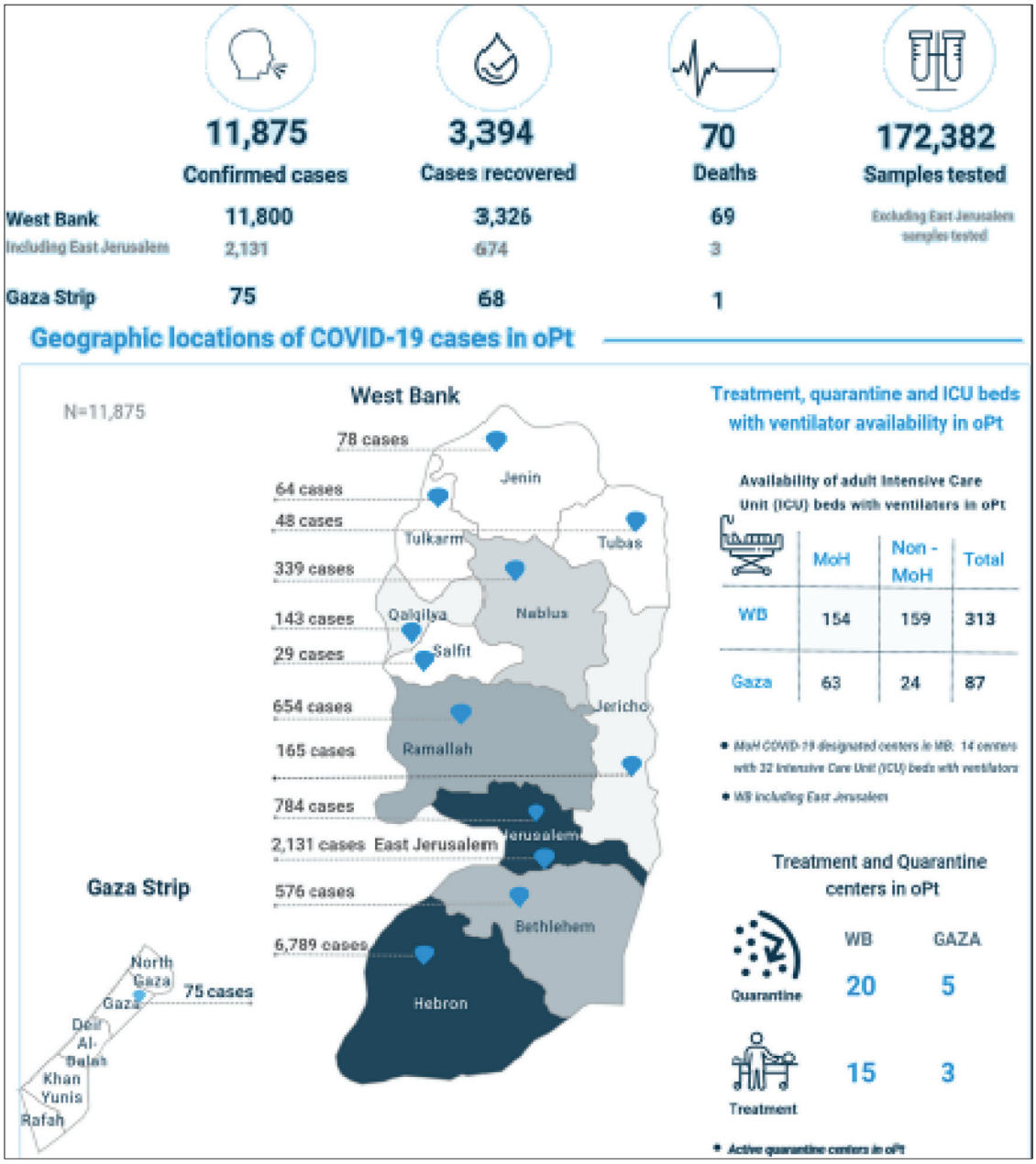

Figure 2: Geographic location of COVID-19 in Palestine by July 23, 2020 (excluding East Jerusalem)

day as mentioned, which rising panic and concern on public health worldwide. Prevention is still the best strategy to face this pandemic. These numbers are possibly an underestimate of the infected and dead due to limitations of surveillance and testing. It is though the SARS-CoV-2 originated from bats, the intermediary animal through which it crossed over to humans is uncertain. Pangolins and snakes are the current suspects.[7]

The onset and duration of viral shedding and the period of infectiousness are not completely defined. The estimated incubation period for COVID-19 is up to 14 days from the time of exposure or even more, with a median incubation period of 4 to 5 days.[8-10] The disease is transmitted by inhalation or contact with infected droplets. The spectrum of illness can range from asymptomatic infection to severe pneumonia with ARDS.[7] In a report of 1,482 hospitalized patients with confirmed COVID-19 in the United States, the most common presenting symptoms were cough (86%), fever or chills (85%), and shortness of breath (80%), diarrhea (27%), and nausea (24%).[11] Other reported symptoms have included, but are not limited to, sputum production, headache, dizziness, rhinorrhea, anosmia, dyspepsia, sore throat, abdominal pain, anorexia, and vomiting. Asymptomatic or pre-symptomatic individuals infected with SARS-CoV-2 may have viral RNA detected in

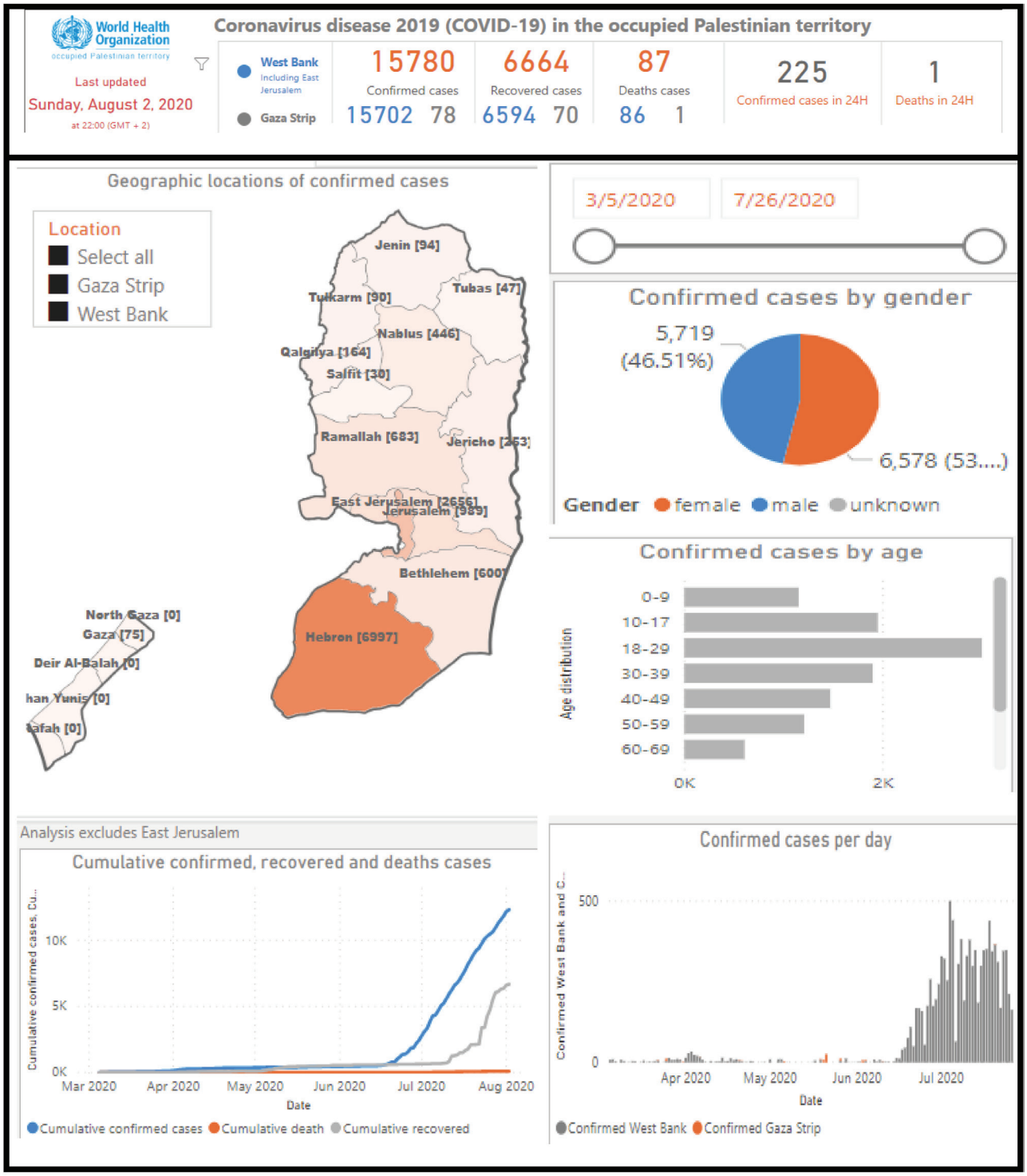

Figure 3: Coronavirus disease-2019 in Palestine

(Source: http://www.emro.who.int/pse/palestine-news/landing-page-for-covid19.html)

upper respiratory specimens before the onset of symptoms. Transmission of SARS-CoV-2 from asymptomatic individuals has been described.[12-14] The extent to which this occurs remains unknown. Individuals of all ages are at risk for infection and severe disease. The probability of fatal disease is highest in people aged ≥65 years and those living in a nursing home or long-term care facility. However, others at the highest risk for COVID-19 are people of any age with certain underlying conditions, especially when not well-controlled, including hypertension, cardiovascular disease, diabetes, chronic respiratory disease, cancer, renal disease, and obesity.[15-18]

Table 1: Reported cases and deaths by country as on August 3, 2020

S. no.	Country, other	Total cases	Total deaths	Total recovered	Active cases	Serious, critical	Total cases/ 1M pop	Deaths/1M pop	Total tests	Population
	World	18,258,448	693,395	11,460,069	6,104,984	65,759	2,342	89.0		
1	USA	4,813,984	158,375	2,380,548	2,275,061	18,623	14,536	478	59,936,833	331,176,957
2	Brazil	2,733,677	94,130	1,884,051	755,496	8,318	12,853	443	13,096,132	212,694,204
3	India	1,808,128	38,201	1,188,650	581,277	8,944	1,309	28	20,202,858	1,381,196,835
4	Russia	856,264	14,207	653,593	188,464	2,300	5,867	97	29,029,900	145,940,242
5	South Africa	511,485	8,366	347,227	155,892	539	8,615	141	3,036,779	59,373,395
6	Mexico	439,046	47,746	289,394	101,906	3,944	3,402	370	1,005,498	129,051,364
7	Peru	428,850	19,614	294,187	115,049	1,410	12,991	594	2,404,046	33,011,298
8	Chile	359,731	9,608	332,411	17,712	1,437	18,804	502	1,673,289	19,130,722
9	Spain	335,602	28,445	N/A	N/A	617	7,178	608	6,678,414	46,756,451
10	Colombia	317,651	10,650	167,239	139,762	1,493	6,237	209	1,647,396	50,930,338
11	Iran	312,035	17,405	270,228	24,402	4,104	3,711	207	2,534,658	84,085,874
12	UK	304,695	46,201	N/A	N/A	86	4,486	680	16,499,272	67,918,139
13	Pakistan	280,029	5,984	248,873	25,172	1,064	1,266	27	2,010,170	221,248,898
14	Saudi Arabia	278,835	2,917	240,081	35,837	2,011	7,999	84	3,432,354	34,859,989
15	Italy	248,070	35,154	200,460	12,456	42	4,103	582	6,916,765	60,453,535
16	Bangladesh	242,102	3,184	137,905	101,013		1,469	19	1,193,544	164,833,483
17	Turkey	232,856	5,728	216,494	10,634	582	2,758	68	4,885,916	84,418,418
18	Germany	211,462	9,226	193,600	8,636	261	2,523	110	8,006,135	83,808,340
19	Argentina	201,919	3,648	89,026	109,245	1,122	4,464	81	736,007	45,232,356
20	France	187,919	30,265	81,500	76,154	371	2,878	464	2,982,302	65,286,732
21	Iraq	129,151	4,868	91,886	32,397	498	3,205	121	1,029,159	40,296,137
22	Canada	116,884	8,945	101,574	6,365	2,253	3,095	237	4,143,459	37,771,409
23	Indonesia	113,134	5,302	70,237	37,595		413	19	1,537,413	273,776,774
24	Qatar	111,107	177	107,779	3,151	76	39,571	63	500,536	2,807,805
25	Philippines	106,330	2,104	65,821	38,405	351	969	19	1,563,278	109,706,778
26	Egypt	94,483	4,865	42,455	47,163	41	922	47	135,000	102,495,399
27	Kazakhstan	92,662	793	62,511	29,358	221	4,930	42	2,079,540	18,796,213
28	Ecuador	86,524	5,750	36,213	44,561	363	4,898	325	246,730	17,665,894
29	China	84,428	4,634	79,013	781	35	59	3	90,410,000	1,439,323,776
30	Sweden	80,422	5,743	N/A	N/A	37	7,959	568	810,356	10,104,909

Source: https://www.worldometers.info/coronavirus/

Common laboratory findings of COVID-19 include leukopenia and lymphopenia. Other laboratory abnormalities have included elevations in aminotransferase levels, include normal/ low white cell counts with elevated C-reactive protein (CRP), D-dimer, ferritin, and lactate dehydrogenase, X-ray, and computerized tomographic. The CT chest scan is usually abnormal and varies even in those with no symptoms or mild disease. Imaging may be normal early in infection and can be abnormal in the absence of symptoms.[19] Every year an estimated 290,000 to 650,000 people die in the world due to complications from seasonal influenza (flu) viruses. There are about 795 to 1781 deaths per day due to the seasonal flu. SARS (November 2002 to July 2003). The coronavirus that originated from China and spread to different countries; resulted in more than ten and a half million people infected; and with about more than half a million deaths; with a fatality rate of 8%, by end of June 2020. Thus, the rates of cases and death of coronavirus are most likely will be more than seasonal influenza viruses; especially the virus outbreak is rising sharply every day; thus, the fatality will higher. Treatment of the disease is essentially supportive; the role of antiviral agents is yet to be established. Prevention entails home isolation of suspected cases and those with mild illnesses and strict infection control measures at hospitals that include contact and droplet precautions. The virus spreads faster than its two ancestors the SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV) but has lower fatality till now. The global impact of this new epidemic is yet uncertain. Treatment is mainly supportive as no antiviral has been approved yet. Efforts are being made to find effective treatment and to reduce the virus outbreak. However, not much information is known about the virus causes, its survival period, methods of its spreading, biochemical and hematological disorders, its complications, its prevention, and treatments. Everyone talks about Covid-19, and wherever you look you find information about the virus and how to protect yourself from it. Knowing the facts is necessary to be adequately prepared to protect yourself and your loved ones. Unfortunately, much information is incorrect. The spread of misleading information during health crises leaves people unprotected and vulnerable to the disease and the spread of fear and stigma among them. Therefore, this review provides trustful information and data obtained from official reports and peer-reviewed journals. We mainly focused on the latest treatment and precautions of COVID-19 including the strategies, guidelines, and challenges against the disease globally and in Palestine. Slow and stop transmission; provide optimized care for all patients; and minimize the impact of the epidemic on health systems, social services, and economic activity are the main objectives for the management of the disease. More than 150 different drugs are being researched around the world. Most are existing drugs that are being tested against the virus. Here we also high light on the most important drugs used/or tested for the treatment of the disease and the disease complications. In Palestine, the treatment and management protocols of COVID-19 are similar to the strategies and protocols in the other countries which follow the guidelines of WHO.[5,7]

MATERIALS AND METHODS

The review discussed the different therapeutic strategies and drugs used for the treatment of COVID-19. Preciously, different literature and guidelines among different databases were searched, summarized, and discussed. The literature review was conducted using various search engines, Google Scholar, Medline, Pub Med, EMBASE, Web of Science, and Science Direct. Data also obtained from the WHO reports, and the published peer-reviewed articles of 2019 novel coronavirus (2019-nCoV). The initial terms "words" that match with the title or abstract or with the topic including 2019-nCoV, 2019 novel coronavirus, SARS, CoV-2, COVID-19, COVID-19, NCP, and novel coronavirus, PA, pneumonia were used in searching the databases. The further search was also carried out using the keywords, SARS-CoV, severe acute respiratory syndrome, MERS, MERS-CoV, Middle East respiratory syndrome, in combinations of with "pike protein, genome, reproductive number, incubation period, fatality rate, clinical characteristics, pathology, autopsy, protocols, guidelines, treatment, and prevention. Moreover, official documents that have been released by the WHO were accessed for up to date data on COVID-19.

RESULTS AND DISCUSSION

COVID-19 is a serious public health concern worldwide, particularly in conflict settings, which face fragility, governance, and significant deficits in resources. Although some countries of the Middle East and North Africa (MENA) region have the resources to respond effectively to the COVID-19 pandemic, other countries in the region have insufficient resources and capacity to fight this pandemic, especially those under protracted conflicts such as Syria, Iraq, Yemen, and Palestine. The COVID-19 crisis has revealed major gaps in the social and public health systems in these countries, such as social exclusion, inequalities, fragility, unpreparedness, underinvestment, and weakness in governance and cooperation. The political situation in Palestine threatens the health security of Palestinians in the time of the pandemic and the 72 year-long ongoing Israeli

control on Palestine is causing a dire humanitarian situation. The deteriorated living conditions in the West Bank, Gaza Strip and East Jerusalem including overcrowdedness, building restrictions, raids and arrests, home demolitions by Israel, absence of freedom of movement throughout Palestine, in addition to over 13 years of the siege on the Gaza strip, all impede Palestine's ability to control the spread of COVID-19. Moreover, the Water, sanitation, and hygiene (WASH) system infrastructure in Palestine has been destroyed as a result of Israel's regular attacks and its full control of all water resources in Palestine. The high levels of poverty and unemployment in Palestine (largely among refugees) means that they are unable to take necessary preventative measures against COVID-19. These humanitarian difficulties are expected to deteriorate further as a result of COVID-19. Local and international human rights and advocacy organizations must put pressure to end Israel's practices, mainly an immediate release of the imprisoned and besieged people who are at high risk. Palestinians are in a high need for financial and food support to alleviate the socioeconomic impacts of the pandemic and prevent any further economic collapses and food insecurity, especially among vulnerable populations including refugees and people in inaccessible areas. Although the political situation is complex and resources and capacities are limited, Palestine is outperformed many other countries in responding to COVID-19 especially at the beginning of the disease as the PA government was quick in imposing strict preventative lockdown measures. However, early relaxation of these measures could take away progress made and flare up the number of cases. Although authorities in the West Bank and Gaza Strip are following a restrict management approach to control COVID-19, their plans are still nonconsolidated. Yet, further coordinated efforts such as testing, tracing, public engagement, socioeconomic support packages are required for more efficient COVID-19 preparedness and response in Palestine. A more concise and unified response plan with a long-term vision including a robust exit strategy is essential for effectively combating the pandemic in Palestine. The response plan should include strategic directions; increased financial investments and efforts in strengthening the public health system's governance, capacity, and health research and surveillance. The emphasis on the importance of strengthening the national research system, improve the strategic components in all settings and conditions, and different novel means can help in building research capacity and emergency research of controlling the disease. Moreover, there is an urgent need to improve cooperation and collaboration between the different health actors in the West Bank, Gaza Strip, and East Jerusalem. This includes governmental, nongovernmental and private institutions and hospitals. Additionally, community participation and engagement in the response to COVID-19 are limited and need to be strengthened. Collective actions and investment strategy adopted by all state, nonstate actors, and regional and international humanitarian and development partners must become more efficient, systemic, and complementary to act into different trajectories which include; mobilizing all efforts and resources to the mitigation and containment measures to the COVID-19 pandemic; establishing a lockdown relaxation system conditional to local and national infection transmission rates; and re-thinking a post-pandemic strategy for strengthening the public health system taking into account health governance and policies, information system, advanced technologies, just resource allocation, and investment plans, health research system, and preparedness capacity.[4-6,20]

As the COVID-19 spreads, efforts are being made to reduce transmission *via* standard public health interventions based on isolation of cases and tracing of contacts. This contributes to reducing the size of the outbreak but cannot control the outbreak.[21] Other interventions that were recommended to reduce the outbreak include strengthening emergency departments, application of strict hygiene measures for the prevention and control of infection, and avoidance of close contact with patients suffering from respiratory tract infections. Efforts are being made to find drugs and vaccines that act against SARS-CoV-2 to control the outbreak of the virus (vaccine is under development). Supportive care is the main strategy for treatment; such as control fever, maintenance of hydration and nutrition, and oxygen therapy. Up to 76% of patients with COVID-19 require oxygen therapy. Some patients require endotracheal intubation such as patients with hypoxemic respiratory patients. Other patients require oxygen supplementation to maintain an oxygen saturation between 90%-96%. For patients who do not improve with oxygen therapy, high flow nasal cannula (HFNC) is recommended.[22-26] Thus, the first step is to ensure adequate isolation to prevent transmission to other contacts, patients, and healthcare workers. Mild illness should be managed at home with counseling about danger signs. The usual principles are maintaining hydration and nutrition and controlling fever and cough. Routine use of antibiotics and antivirals such as oseltamivir should be avoided in confirmed cases. In hypoxic patients, the provision of oxygen through nasal prongs, face mask, HFNC, or noninvasive ventilation is indicated. Mechanical ventilation and even extracorporeal membrane oxygen (ECMO) support may be needed. Renal replacement therapy may be needed in some. Antibiotics and antifungals are required if co-infections are suspected

or proven. The role of corticosteroids is unproven; although current international consensus and WHO advocate against their use, Chinese guidelines do recommend short term therapy with low-to-moderate dose corticosteroids in COVID-19 ARDS. Detailed guidelines for critical care management for COVID-19 have been published by the WHO. There is, as of now, no approved treatment for COVID-19.[23-26] Due to the characteristics of this virus, as it has a long incubation period, the infection can be transmitted to many people before symptoms appear, so preventive measures are very necessary, so prevention is very important. The greatest danger is the transmission of the virus to a healthcare worker as the virus has passed on to many of them, however, it is very important to follow a basic protocol to protect them and prevent the transmission of the disease to them and others by them. Those who deal with patients directly are isolated from others and do not deal with ordinary patients. The rooms and surfaces and equipment should undergo regular decontamination. To reduce the spread of the disease in geographical areas, each country quarantines travelers and people who dealt with the injured for 14 days to ensure that they are free of the virus and prevent its spread. As for society, the best ways to prevent coronavirus and other viruses are necessary to move away from crowded places, leave a safe distance between others and follow a healthy lifestyle that is mainly based on maintaining personal hygiene, eating healthy foods, good ventilation, sunlight penetration on all surfaces, adequate rest, using health masks and using sterilizers on an ongoing every 15-20min. People who already have a vitamin C deficiency are more likely and at risk to become infected with the virus. So vitamin C supplementation is very important for prevention according to many studies.[26-31]

Currently, no medication is proven to treat COVID-19 effectively, and no cure is available. Antibiotics aren't effective against viral infections such as COVID-19. The new coronavirus (COVID-19) is a virus and, therefore, antibiotics should not be used as a means of prevention or treatment. However, if the patient hospitalized for COVID19 he may receive antibiotics because bacterial co-infection is possible. There is no evidence that ibuprofen or other nonsteroidal anti-inflammatory drugs (NSAIDS) need to be avoided. Most patients have mild or no symptoms. However, mild cases are asymptomatic patients or patients with mild fever 37.5C°, cough, cold symptoms, nasal congestion, malaise, and without dyspnea, however, isolation of the patients is the most important care step for them and to others. The other approaches and strategies of the treatment depend upon the patient's situation and the symptoms. For example, if the patient has mild symptoms, it is recommended to stay at home for isolation of a period to avoid spreading the illness to others, as mentioned. If the patient is very ill, he may need to be treated in the hospital. Mild cases need supportive care and symptomatic treatment with antipyretic agents, if needed only, paracetamol is the first line and NSAIDs have caution in use, hydration and nutrition supplements should receive and ensure adequate calories intake. Frequent cough and fever monitoring. The organ function should routinely control, and any secondary infection should be prevented. All management is in their houses unless there are severe symptoms. If there is any development in the disease patient must refer to the healthcare center.[32,33] Patients with confirmed COVID-19 disease and develop severe symptoms that have respiratory distress (less than 30 breath/min), oxygen saturation less than 90%, cyanosis, and shock must receive oxygen therapy by including nasal catheter and mask oxygenation and nasal high-flow oxygen therapy. If possible, inhalation of mixed hydrogen and oxygen (H_2/O2: 66.6%/33.3%) can be applied to target more than 91% of oxygen saturation in nonpregnant adults and 92–95% to pregnant ones at room air. The nasal cannula is preferred for children with respiratory distress because it is better to tolerate. High flow nasal catheter or noninvasive mechanical ventilation is used when the respiratory distress does not relive after standard oxygen therapy. High flow nasal catheters consider safer than noninvasive ventilation because many scientists suggest that it may associate with the nosocomial transmission of the disease. About one third or two-third of critically ill-patients needs them. If the patient does not improve in time nearly 1–2 h invasive mechanical ventilation should be considered. The invasive mechanical ventilation used to avoid ventilator-induced lung injury while facilitating gas exchange *via* lung-protective ventilation. Patients with severe symptoms should be equipped with pulse oximeters, functioning oxygen systems and disposable, single-use, oxygen-delivering interfaces (nasal cannula, nasal prongs, simple face mask, and mask with reservoir bag), and should have regularly mentoring of the vital sign. In the case series of 99 hospitalized patients with COVID-19 infection from Wuhan, oxygen was given to 76%, noninvasive ventilation in 13%, mechanical ventilation in 4%, ECMO in 3%. Antiviral therapy consisting of oseltamivir, ganciclovir, and lopinavir-ritonavir was given to most patients (see later).[26,31,34] Patients with severe COVID-19 develop a systemic inflammatory response that can lead to lung injury and multisystem organ dysfunction, it has been proposed and/ or given a potent anti-inflammatory (corticosteroids), which might prevent or mitigate these harmful effects (see later). In Palestine, the treatment and management protocols of COVID-19 are similar to the strategies and protocols in other countries, especially those

who follow the guidelines of WHO. On March 26, 2020, the PA released the National COVID-19 Response Plan that outlined the strategic measures from several key sectors, including health, economy, and social protection to contain the outbreak. he MoH has implemented effective measures to ensure early detection and case management of any suspected COVID-19 case and so far have ensured that[4-6]:

- In the West Bank, quarantine and treatment facilities and emergency committees were established in key governorates.
- MoH has developed a new COVID-19 dashboard (in Arabic) to track cases: https://www.corona.ps/.
- A central operations room has been established at Prime Minister's office to coordinate activities, including contacts with media.
- Laboratory capacities of the MoH in Ramallah have been scaled up.
- Point of entry checks for incoming travelers are being conducted and isolation wards in health facilities have been established.
- Health workers are equipped and trained in the appropriate infection prevention and control measures and case management of potential COVID-19 cases across the oPt.
- The general public continues to be regularly updated, including advice on how to protect themselves.

In the Gaza Strip, there are always substantial capacity gaps including the procurement of essential medical supplies and equipment (such as lab testing kits), This may be due to the siege, economic and political situations. The COVID-19 response plan for the oPt presented the joint strategy of the humanitarian community to respond to the public health needs and immediate humanitarian consequences of the pandemic. The main goal of the Plan was supporting the efforts led by the PA to contain the pandemic and mitigate its impact. PA from time to time updated their plan according to the outbreak of the disease and all the plans provided an important bridge between the public health response and the broader socio-economic recovery plan. The primary focus was prevention, preparedness, and treatment of COVID-19, with the emphasis remaining on supporting the most vulnerable people. According to PA officials, the interventions will continue to be adapted as the situation evolves and understanding of the virus and how it spreads. PA urged the public to obtain the latest information on COVID-19 from key and trustful sources such as MoH and WHO, and follow and promote the recommended basic preventive and protective measures. Overall, the plans supported scaling up the test capacity and expand hospitals' capacity. Respiratory supported and intensive care treatment capacity was also scaled-up. Additionally, the plans targeted citizens with public health messages on preventive measures on how to effectively protect oneself from COVID-19 infection, and health workers also supported with infection prevention and control (IPC) measures, including personal protective equipment (PPE).[4-6] By June 2020, the MoH announced that Palestine entered a second wave of the coronavirus, and stressed the need for citizens to adhere to public safety measures, but pathologists and epidemiologists mentioned that was a continuation of the first wave and not considered a second wave, and it is obvious development after returning to normal life without taking any measures prevention and without commitment to instructions. The limitation of the disease outbreak at the beginning was due to the commitment by the citizens and the restricted follow-up by the government, so there were no infected cases recorded as this large number. But after the return to normal life without any regulation, it is natural for these cases to be recorded. Complete closure was at the beginning of the pandemic and by the end of May 2020, all facilities of life were comprehensively opened without any regulation. It seems to be that the secret to face this virus is regulation because closure is not a solution either, but the return of life to its nature must take place after taking measures. Thus, it was expected that a large number of cases will be recorded, because the number of contacts is large. MoH hoped that the increase would not be fast as in Hebron. The epidemiologists stressed that the citizens returned to normal life without taking the necessary measures such as masks, gloves, social distance, and sterilization, this gave chance for infected cases without any symptoms to transmit the virus, now the disease reached a stage that the source of the cases is unknown. Regarding the reasons for recording a large number of cases in Hebron, officials said it is obvious for this large number of cases to be recorded, as Hebron has a high population density (about a million) and it's close to the lands of the year 48, in addition to a large number of patients and hospitals and health centers, who did not adhere to the necessary procedures and health safety regulations.[4-6] Besides, the main reseason for the high outbreak of the disease in Hebron Governorate has been caused by people meeting up with their families or attending wedding parties or funerals and failing to follow health recommendations and maintain social distancing according to the Palestinian Ministry of Health (MoH) officials. The danger is not due to the unknown source of the infection, in the fact, anyone can be infected with the virus without he knows, so no precautions are taken because we and the patient do not know he is infected; although when we know someone is infected, we take the required precautions. However, if we do not know the source of the infection or infection, it

would not be prevented. Also, other reasons which increased the cases were the analysis of the random samples that showed cases that unknow before. As the elimination of the virus depends on the vaccine, the best solution until that time, adherence to public safety measures such as social separation, sterilization, and the wearing of masks. Others mentioned also that the high recorded infected cases were expected because limiting movement during the emergency period reduced the spread of the virus and upon returning to normal life and mixing without any safety measures increased cases. If the closure lasts for a full year, infections will be recorded after returning to normal life. Therefore, until the vaccine is reached, which will not take place in a short time, all must adhere to public safety measures and social distance to limit the spread of the virus. The general director of preventive medicine at the MoH stressed the need to commit to the instructions and protocols issued by the MoH to all institutions, to be able to coexist with the virus, reduce transmission and spread of the epidemic, and curb the second wave of the pandemic, which is recorded in steady numbers. He said that the indicators showed that the situation is a candidate for increasing casualties and this was what he warned about it during the past period. According to the indications, the situation is expected to deteriorate further. He also announced what determines the coming measures are the epidemiological situation, therefore all scenarios are open according to data that changes rapidly, and he hoped not to reach to raise recommendations to restrict movement. But, by the beginning of July 2020, a total closure to West Bank was approved by the government according to the emergency, to end the outbreak of the coronavirus in its second wave, as hundreds of infections daily were recorded, the process was similar to that imposed at the beginning of the disease's arrival in March, which includes preventing the movement of the population and closing the economic and commercial sectors, except the necessary services.[4-6] Hospitals and research labs all over the world are testing many different therapies on coronavirus-positive patients to find potential COVID-19 treatment. We highlight the medications, treatments, and management that have been applied to coronavirus. Table 2 summarizes the most important drugs used and/ or tested in treating COVID-19, including their rational use in the treatment of COVID-19, some other information was also included such as doses, methods of administration, and duration of treatment.[35-99]

In summary, patients with suspected or confirmed mild COVID-19 should be isolated to contain virus transmission according to the established COVID-19 care pathway. This can be done at a designated COVID-19 health facility, community facility, or at home (self-isolation). Patients with mild COVID-19 should be given symptomatic treatment such as antipyretics for fever and pain, adequate nutrition, and appropriate rehydration. Counsel patients with mild COVID-19 about signs and symptoms of complications that should prompt urgent care. Patients with suspected or confirmed moderate COVID-19 (pneumonia) should be also isolated to contain virus transmission. Patients with moderate illness may not require emergency interventions or hospitalization; however, isolation is necessary for all suspect or confirmed cases, and monitoring of signs or symptoms of disease progression for those patients is required. Severe patients should be equipped with pulse oximeters, functioning oxygen systems and disposable, single-use, oxygen-delivering interfaces (nasal cannula, Venturi mask, and mask with reservoir bag). Immediate administration of supplemental oxygen therapy to any patient with emergency signs and any patient without emergency signs and SpO2 < 90%; are recommended. Similar is recommended to those patients closely monitor for signs of clinical deterioration, such as rapidly progressive respiratory failure and shock, and respond immediately with supportive care interventions. Patients with COVID-19 and mild ARDS, a trial of HFNO, noninvasive ventilation – continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP); may be used. Prompt recognition of progressive acute hypoxaemic respiratory failure when a patient with respiratory distress and is failing to respond to standard oxygen therapy and adequate preparation to provide advanced oxygen/ventilatory support and the endotracheal intubation is recommended. Patients with ARDS, especially young children or those who are obese or pregnant, may desaturate quickly during intubation, implementation of mechanical ventilation using lower tidal volumes (4–8 mL/kg predicted body weight [PBW]) and lower inspiratory pressures (plateau pressure <30 cm H2O) are recommended. In adult patients with severe ARDS (PaO2/FiO2 < 150), prone ventilation for 12–16 hours per day is recommended. It is better to use a conservative fluid management strategy for ARDS patients without tissue hypoperfusion and fluid responsiveness. In patients with moderate or severe ARDS, a trial of higher positive end-expiratory pressure (PEEP) instead of lower PEEP is suggested and requires consideration of benefits versus risks. In COVID-19, we suggest the individualization of PEEP where during titration the patient is monitored for effects (beneficial or harmful) and driving pressure. In patients with moderate-severe ARDS (PaO2/FiO2 < 150); neuromuscular blockade by continuous infusion should not be routinely used. Disconnecting the patient from the ventilator, which results in loss of PEEP, atelectasis, and increased risk of

Table 2: The most important drugs used and/or tested in treating COVID-19[35-99]

Drug	Rationale use for COVID-19	Dosage	Conclusions
Antimalarial drugs chloroquine (CQ) and hydroxychloroquine (HCQ).[35-39] Used for treatment of malaria and autoimmune diseases (e.g., systemic lupus erythematosus and rheumatoid arthritis). No evidence of the efficacy in the prevention of COVID-19. They might block the production of pro-inflammatory cytokines (such as interleukin-6), thereby prevent ARDS. HCQ showed three times more potent than CQ in cytotoxic response and HCQ showed more efficacies in reducing viral nasopharyngeal carriage of SARS-CoV-2 in patients with COVID-19.	Have antiviral properties against various viruses, including coronaviruses. They intracellularly protonated and increase the pH of the cell, pH changes inhibit viral infusion with the cell membrane. They can also inhibit nucleic acid replication and appear to interfere with the terminal glycosylation of ACE2 receptor expression which prevents SARS-CoV-2 receptor binding and spread of infection. CQ has a potent cytotoxic response and inhibits viral replication. Used as a prophylactic as *in-vivo* models show high inhibition of viral spread before viral exposure	Oral; 500 mg of QC phosphate (300 mg QC) each time, 2 times/day; no more than 10 days and with a different regimen in several countries. Oral HCQ sulfate dosage used or being investigated in clinical trials: 400 mg once or twice daily for 5-10 days. Oral HCQ sulfate with azithromycin (France): 200 mg 3 times daily for 10 days with or without azithromycin (500 mg on day 1, then 250 mg once daily on days 2-5), FDA states that the dosage regimens of CQ and HCQ unlikely to have an antiviral effect in pts with COVID-19 based on a reassessment of *in vitro* EC50/EC90 data and calculated lung concentrations.	Efficacy and safety of CQ and HCQ for treatment or prevention of COVID-19 not established. No data to date indicating that *in vitro* activity against SARS-CoV-2 corresponds with clinical efficacy for treatment or prevention of COVID-19. QC suggested as a possible option and included in Chinese guidelines for the treatment of COVID-19. NIH COVID-19 Treatment Guidelines Panel recommends against the use of HCQ & CQ for the treatment of COVID-19. Emergency use authorization (EUA) for HCQ & CQ now revoked. Azithromycin has been recommended to use with HCQ to give a synergistic effect in treating COVID-19.
Data from a large, randomized, controlled trial showed no evidence of benefit in mortality or other outcomes such as hospital length of stay or need for mechanical ventilation for HCQ treatment in hospitalized patients with COVID-19. Only limited clinical trial data available to date to evaluate the use of HCQ & CQ for treatment or prevention of COVID-19. The majority of data to date involves use in pts with mild or moderate COVID-19; only limited clinical data on use in pts with the severe and critical disease. A small, randomized study in hospitalized adults in China compared CQ with lopinavir / ritonavir (Huang *et al*). Double-blind randomized phase 2b study in Brazil, (Borba *et al*). Many clinical trials of HQC were conducted in different countries as a single drug or combination and/or comparison of the other drugs.			
Antiviral drugs: remdesivir[35,36,40-42]: Broad-spectrum antiviral (nucleotide analog prodrug) with activity against various viruses, including coronaviruses. Metabolize the cell and tissue to activate the nucleoside triphosphate (GS-443902) which inhibits the viral RNA-dependent RNA polymerases in the viral infectious cycle cascade. May also involve lethal mutagenesis and chain termination of the virus. Initially, it is developed for the treatment of Ebola hemorrhagic fever, but it has no approval until now for any indications. Many viruses have resistance to these agents to result in exo-ribonuclease proofreading and removal; Remdesivir has the potential to avoid this. Pharmacokinetic data were available from evaluations for Ebola. Multiple international clinical trials were conducted and ongoing, the safety and efficacy of remdesivir for the treatment of COVID-19 are not yet established	*In vitro* evidence of activity against SARS-CoV-2 in Vero E6 cells. In Rhesus macaques infected with SARS-CoV-2, treatment with a 6-day regimen of IV remdesivir initiated 12 hours after virus inoculation was associated with some benefits (lower disease severity scores, fewer pulmonary infiltrates, lower virus titers in bronchoalveolar lavage samples) compared with vehicle control; remdesivir. Treatment did not reduce viral loads or infectious virus titers in nose, throat, or rectal swabs compared with vehicle control. *In vitro* activity against SARS-CoV and MERS-CoV; active in animal models of SARS and MERS; prevented MERS in Rhesus macaques when given before infection and provided benefits when given after animal already infected. NIH panel states that data are insufficient to recommend for or against the use of remdesivir for the treatment of mild or moderate COVID-19.	Optimal dosage and duration of treatment not known. EUA recommended loading dose of 200 mg by IV infusion on day 1, followed by maintenance doses of 100 mg by IV infusion once daily from day 2 for adults and children weighing 40 kg or more.; for children weighing 3.5 to less than 40 kg; loading dose of 5 mg/kg by IV infusion on day 1, followed by maintenance doses of 2.5 mg/kg by IV infusion once daily from day 2. Optimal duration of treatment not known; but for pts requiring invasive mechanical ventilation and/or ECMO, total treatment duration is 10 days and for those not requiring invasive mechanical ventilation and/or ECMO, total treatment duration is 5 days recommended. The recommended dose for another phase 3 clinical trials was 200 mg IV on day 1, then 100 mg IV daily on days 2-5 or 200 mg IV on day 1, then 100 mg IV daily on days 2-10.	Not commercially available; the most promising direct-acting antiviral (DAA) currently being investigated for COVID-19. Efficacy and safety of remdesivir for treatment of COVID-19 not established. FDA warns that concomitant use of remdesivir and CQ or HCQ is not recommended; there is *in vitro* evidence that CQ antagonizes intracellular metabolic activation and antiviral activity of remdesivir. In situations where remdesivir supplies are limited, the NIH COVID-19 Treatment Guidelines Panel recommends that remdesivir be prioritized for use in hospitalized patients with COVID-19 who require supplemental oxygen, but are not mechanically ventilated or on ECMO. NIH COVID-19 Treatment Guidelines Panel recommends the use of remdesivir for the treatment of severe COVID-19 in hospitalized patients who have oxygen saturation (SpO2) of 94% or lower on room air.
FDA issued a EUA on May 1, 2020, that permits the use of the drug for the treatment of COVID-19 only in hospitalized adults and children with suspected or laboratory-confirmed COVID19 who have severe disease.			

Table 2: Continued

Drug	Rationale use for COVID-19	Dosage	Conclusions
HIV protease inhibitors [Lopinavir (LPV), Atazanavir (ATV), Darunavir (DRV), Nelfinavir (NFV), Saquinavir (SQV), and Tipranavir (TPV),[43-49]]. NIH COVID-19 Treatment Guidelines Panel and Infectious Diseases Society of America (IDSA) recommends against the use of LPV/RTV or other HIV protease inhibitors for the treatment of COVID-19, except in the context of a clinical trial. clinical trials to date using LPV/RTV have not shown a clinical benefit in patients with COVID-19. Multiple international clinical trials were conducted and ongoing for the use of Lopinavir and Ritonavir, LPV/RTV with ribavirin and interferon β1b vs LPV/RTV alone, LPV/ RTV with or without Umifenovir (Arbidol®) and LPV/RTV vs chloroquine, LPV/ RTV vs hydroxychloroquine vs placebo, and DRV/ RTV in conjunction with chloroquine or oseltamivir) in treating the disease	LPV, NFV, SQV, and TPV: Some evidence of *in vitro* activity against SARS-CoV-2 in Vero E6 cells. LPV evidence also of *in vitro* activity against SARS-CoV-1 and MERS-CoV and some evidence of benefit in animal studies for the treatment of MERS-CoV. ATV: Some evidence that ATV alone or with ritonavir (ATV/RTV) has *in vitro* activity against SARS-CoV-2 in Vero E6 cells, human epithelial pulmonary cells (A549), and human monocyte. DRV: In one study, DRV with cobicistat had no *in vitro* activity against SARS-CoV-2 at clinically relevant concentrations in Caco-2 cells; in another study, high DRV concentrations were required for *in vitro* inhibition of SARS-CoV-2 in Vero E6 cells. LPV/RTV Clinical Experience (SARS and MERS): Evidence of some clinical benefit when used in conjunction with ribavirin and/or interferon.	Lopinavir/Ritonavir (LPV/RTV) oral; 200 mg/50 mg/capsule, 2 capsules each time, 2 times/day; no more than 10 days. Or LPV/ RTV (COVID-19): LPV 400 mg/ RTV 100 mg orally twice daily for 10- 14 days. LPV 400 mg/ RTV 100 mg orally twice daily with or without Umifenovir (Arbidol® 200 mg every 8 hours). LPV/RTV (COVID-19): LPV 400 mg/ RTV 100 mg orally twice daily for no longer than 10 days 13 with or without interferon (5 million units of interferon-α or equivalent twice daily given in 2 mL of sterile water by nebulization) and with or without ribavirin for up to 10 days. LPV/RTV (SARS): LPV 400 mg/ RTV 100 mg orally twice daily for 14 days with ribavirin. LPV/RTV (MERS): LPV 400 mg/RTV 100 mg orally twice daily with ribavirin (various regimens) and/or interferon-α; LPV 400 mg/ RTV 100 mg orally twice daily with interferon β1b (0.25 mg/mL sub-Q on alternate days) for 14 days	LPV/RTV: Efficacy for the treatment of COVID-19, with or without other antivirals, not established. Darunavir: Manufacturer states they have no clinical or pharmacologic evidence to support the use of DRV/ cobicistat for treatment of COVID-19 and there are no published clinical studies that have evaluated efficacy and safety of DRV, DRV/cobicistat, or the fixed combination of DRV, cobicistat, emtricitabine, and tenofovir alafenamide for treatment of COVID-19. Besides, initial unpublished results from an open-label, controlled study in China indicated that a 5-day regimen of DRV/cobicistat was not effective for the treatment of COVID-19. Atazanavir, Nelfinavir, Saquinavir, Tipranavir: No data to date to support use in the treatment of COVID-19. Only limited data on LPV/RTV used with or without interferon in pts with COVID-19 outside of clinical trials.
Ribavirin[50-52]: a prodrug of purine nucleoside analog (mimic the purine analog guanosine in RNA); broad-spectrum antiviral. Inhibit RNA synthesis of viruses. associated with hemolytic anemia, especially after taking a high dose (1-2 gm), which is needed for coronaviruses treatment. Ribavirin is a teratogen; contraindicated in women who are pregnant and in male partners of those pregnant women. In combination with other immunosuppressive therapies; azathioprine or IFN can lead to severe side effects.	Structural elements prohibit the subsequent addition of nucleoside analogs, effectively stop the synthesis of RNA. Used to treat HCV, RSV, hepatitis C, B, and respiratory viruses. Usually used in combination therapy to treat MERS-CoV and HCoV-OC43. Ribavirin and INF-α combination therapy are efficient in treating MERS-CoV. Patients treated with lopinavir/ritonavir had a lower risk of SARS and death. More studies about.	Intravenous infusion; 500 mg each time, 2 to 3 times/day in combination with IFN-α or lopinavir/ritonavir; no more than 10 days. Oral ribavirin has been dosed as a 4-gram loading dose followed by 1.2 grams every eight hours in two small studies for SARS. In the management of COVID-19, data is limited to ongoing studies using a dosing strategy of 400 mg by mouth twice daily for 14 days as a part of a combination regimen. However, Ribavirin side effects like anemia and myelosuppression, myelotoxicity, and pancytopenia limited its use	No effect to use Ribavirin as monotherapy, but it gives potential activity when combined with other anti-viral agents such as Lopinavir/Ritonavir or chloroquine analogs. Patients SARS treated with lopinavir/ritonavir had better outcomes as compared to those given ribavirin alone; because Lopinavir works by inhibiting the decomposition of gag-pol protein, while ritonavir works by inhibiting the decomposition of gag-pol protein precursor and inhibiting lopinavir metabolism, thus increasing its concentration.
Neuraminidase inhibitors[53-56]: Oseltamivir; Antivirals active against influenza viruses. No data to date support use in the treatment of COVID-19.	Neither oseltamivir nor zanamivir has shown inhibition of cytopathic effect against SARS-CoV *in vitro* cell culture.	The dosage of oseltamivir was 75 mg orally once or twice daily. Oseltamivir did not inhibit the replication of SARS-CoV-2 in infected Vero E6 cells *in vitro*.	Several clinical trials are currently looking at **Oseltamivir** in combination with other medications for coronavirus.

Table 2: Continued

Drug	Rationale use for COVID-19	Dosage	Conclusions
Favipiravir[57-61]: RNA-dependent RNA polymerase (RdRP)] has anti-SARS-CoV-2 activity. Favipiravir found to help to clear the virus faster than lopinavir/ritonavir (4 days vs. 11 days, respectively). Favipiravir may be effective against SARS-CoV-2. Multiple clinical trials initiated in pts with COVID-19 in China, Japan, USA, and other countries to evaluate favipiravir alone or in conjunction with other antivirals or other agents. Only very limited clinical trial data available to date to evaluate the use of favipiravir in the treatment of COVID-19. Data needed to substantiate initial reports of efficacy for treatment of COVID-19 and identify optimal dosage and treatment duration.	Broad-spectrum antiviral with *in vitro* activity against various viruses, including coronaviruses. *In vitro* evidence of activity against SARS-CoV-2 in infected Vero E6 cells reported with high concentrations of the drug. Licensed in Japan and China for the treatment of influenza. Not commercially available in the US. Efficacy and safety of Favipiravir for treatment of COVID-19 not established. Favipiravir is contraindicated in women with known or suspected pregnancy and precautions should be taken to avoid pregnancy during treatment with the drug. If Favipiravir is used in pts receiving acetaminophen, the maximum recommended daily dosage of acetaminophen is 3 g.	Some of one ongoing trial dosage: 1600 mg twice daily on day 1, then 600 mg twice daily thereafter for 7–10 or 14 days was used in several open-label COVID-19 studies in adults and adolescents ≥16 years of age in China. Or 1600 mg twice daily on day 1, then 600 mg twice daily for 6 –13 days or 1800 mg twice daily on day 1, then 800 mg twice daily for 9 –13 days for treatment of COVID-19 in adults. Or of 1800 mg twice daily on day 1, followed by 800 mg twice daily on days 2–10 for early treatment of suspected or confirmed COVID-19 in adults. Specifies a Favipiravir dosage of 1800 mg twice daily on day 1, then 1000 mg twice daily on days 2–14 for treatment of COVID-19 in adults.	Given the lack of pharmacokinetic and safety data for the high Favipiravir dosages proposed for the treatment of COVID19, the drug should be used with caution at such dosages. Favipiravir is associated with QT prolongation. Some have suggested close cardiac and hepatic monitoring during treatment, as well as monitoring of plasma and tissue concentrations of the drug and, if possible, the active metabolite. Some data suggest that favipiravir exposure may be greater in Asian populations. Early embryonic deaths and teratogenicity observed in animal studies. There are different dosage regimens in other trials.
Umifenovir (Arbidol®)[53-56]: Used to treat influenza. Broad-spectrum antiviral with *in vitro* activity against various viruses, including coronaviruses. inhibit SARS-CoV-2 *in vitro*	Although data limited, *in vitro* activity against SARS-CoV-1 and SARS-CoV-2 reported. Licensed in China, Russia, Ukraine, and possibly other countries for prophylaxis and treatment of influenza	Dosage recommended for treatment of COVID-19 in China: Adults, 200 mg orally 3 times daily for no more than 10 days	Not commercially available in the US. Included in some guidelines for the treatment of COVID-19. Efficacy for the treatment of COVID-19 not established.
Baloxavir[62-64], only limited clinical trial data available to date to evaluate the use of Baloxavir for treatment of COVID-19	Antiviral active against influenza viruses *In vitro* antiviral activity against SARS-CoV-2 shown in one trial.	Chinese trials specify an oral dosage of 80 mg on day 1 and day 4, and another dose of 80 mg on day 7 (as needed); not to exceed 3 total doses	No data to date support use in the treatment of COVID-19. Favipiravir was not good in helping patients recover, but, was better than Lopinavir/Ritonavir in clear the virus.
Galidesivir[53-56] : Used to treat influenza.	the new drug that is currently being developed for a variety of viral infections	Optimal dosage and duration of treatment not known	Not yet been approved for human use. Clinical trials are starting in Brazil
More evidence is needed before these drugs are recommended according to the National Health Commission (NHC) of China for provisional treatment of COVID-19			
Immunosuppressive Drugs Tocilizumab[34,65,66]: Used for the treatment of rheumatoid arthritis. Tocilizumab added to Lopinavir, methylprednisolone, and oxygen therapy in 20 patients with severe COVID-19 resulted in rapid reductions in fever in all patients, improvement in oxygenation for 75%, and facilitated discharged from the hospital in 95% of patients.	Recombinant humanized monoclonal antibody specific for the interleukin-6 (IL6) receptor; IL-6 is a proinflammatory cytokine. Tocilizumab may potentially combat cytokine release syndrome (CRS) and pulmonary symptoms in severely ill patients with COVID-19. The dosing of tocilizumab for COVID-19 is still not well established. intravenous tocilizumab 400 mg.	Tocilizumab is typically given IV to treat cytokine release syndrome (CRS) and in patients with COVID-19; however, the drug has been given subcutaneously in some patients. China recommends an initial dose of 4–8 mg/kg IV infused over more than 60 minutes. If the initial dose not effective may administer the second dose (in the same dosage as the initial dose) after 12 hours. No more than 2 doses should be given; the maximum single dose is 800 mg, maximum dose of 800mg.	In China, tocilizumab can be used to treat severely or critically ill patients with COVID-19 with extensive lung lesions and high IL-6 levels 2 NIH COVID-19. Treatment Guidelines Panel states that there are insufficient clinical data to recommend either for or against the use of tocilizumab in the treatment of COVID-1. The role of routine cytokine measurements (e.g., IL-6, CRP) in determining the severity of and treating COVID-19 requires further study.
Ruxolitinib[67-70]: Antineoplastic Agents; Janus kinase (JAK) 1 and 2 inhibitor; may potentially combat cytokine release syndrome (CRS) in severely ill patients. Limited published clinical trial evidence regarding efficacy and safety in patients with COVID-19.	Ability to inhibit a variety of proinflammatory cytokines, including interferon, has been raised as a possible concern with the use of JAK inhibitors in the management of hyper inflammation resulting from viral infections such as COVID19. Compassionate use of Ruxolitinib in combination with Eculizumab	Various dosages are being evaluated.; for example, 5 mg twice daily for 14 days with possible extension to 28 days and 5 or 15 mg twice daily (approximately every 12 hours). Severe reactions observed in some patients with COVID-19 following initiation of ruxolitinib. Multiple international clinical trials were conducted and ongoing, for the treatment of COVID-19	NIH COVID-19 Treatment Guidelines Panel recommends against the use of JAK inhibitors for the treatment of COVID19 except in the context of a clinical trial; the panel states that at present the broad immunosuppressive effect of JAK inhibitors outweighs the potential for benefit.

Table 2: Continued

Drug	Rationale use for COVID-19	Dosage	Conclusions
Baricitinib[71-73]: Antirheumatic Drug; Janus kinase (JAK) 1 and 2 inhibitors; disrupts regulators of endocytosis (AP2- associated protein kinase 1 [AAK1] and cyclin G associated kinase [GAK]), which may help reduce viral entry and inflammation; also may interfere with intracellular virus particle assembly. Currently, no known published controlled clinical trial evidence supporting efficacy or safety in patients with COVID-19	Inhibits JAK1 and JAK2- mediated cytokine release; may combat cytokine release syndrome (CRS) in severely ill patients. Ability to inhibit a variety of proinflammatory cytokines, including interferon, has been raised as a possible concern with the use of JAK inhibitors in the management of hyper inflammation resulting from viral infections such as COVID-19.	Therapeutic dosages of Baricitinib (2 or 4 mg orally once daily) are sufficient to inhibit AAK1. Dosage information is not yet available. NIH COVID-19 Treatment Guidelines Panel recommends dosage adjustment if Baricitinib is administered concurrently with a strong OAT3 inhibitor. Not recommended in patients with severe hepatic or renal impairment	Minimal interaction with CYP enzymes and drug transporters and low protein binding of Baricitinib allow for combined use with antiviral agents and many other drugs. NIH COVID-19 Treatment Guidelines Panel recommends against the use of JAK inhibitors for the treatment of COVID19 except in the context of a clinical trial.
Anakinra[74-78]; Antirheumatic Drug; Recombinant human interleukin-1 (IL-1) receptor antagonist. IL-1 levels are elevated in patients with COVID-19; anakinra may potentially combat cytokine release syndrome (CRS) symptoms in severely ill patients with COVID-19. Currently, no known published prospective clinical trial evidence supporting the efficacy or safety of anakinra for the treatment of COVID19. Encouraging preliminary results reported in China with another disease-modifying antirheumatic drug, tocilizumab.	Anakinra has been used off -label for severe chimeric antigen receptor T cell (CAR T-cell)-mediated cytokine release syndrome (CRS) and macrophage activation syndrome (MAS)/secondary hemophagocytic lymphohistiocytosis. IL-1 levels are elevated in patients with these conditions. Case reports and series describe a favorable response to anakinra in these syndromes, including survival benefit in sepsis and reversing cytokine storm in adults with MAS after tocilizumab failure.	Various dosage regimens are being studied. Trial protocol in Italy (COVID-19 with hyper inflammation and respiratory distress): 100 mg by IV infusion every 6 hours (total of 400 mg daily) for 15 days. Some studies underway in Europe are evaluating 100 mg given subcutaneously once daily for 10 or 28 days, respectively, or until hospital discharge. Anakinra is approved only for subcutaneous administration in the U.S. Numerous other clinical trials evaluating anakinra in the treatment of COVID-19 are planned or underway, mainly in Europe	NIH COVID-19 Treatment Guidelines Panel states that there are insufficient clinical data to recommend either for or against the use of anakinra in the treatment of COVID-19. Safety profile: Well established in adults with sepsis and has been studied extensively in severely ill pediatric patients with complications of rheumatologic conditions; pediatric data on use in acute respiratory distress syndrome/ sepsis are limited. Pregnancy: Limited evidence to date: unintentional first-trimester exposure considered unlikely to be harmful.
Sarilumab[78-80]: Antirheumatic Drug; based on encouraging results in China with a similar drug, tocilizumab, a large, U.S.-based, phase 2/3, randomized, double-blind, placebo-controlled, and adaptively designed study evaluating efficacy and safety of sarilumab in patients hospitalized with severe COVID-19	Recombinant humanized monoclonal antibody specific for the interleukin-6 (IL-6) receptor; IL-6 is a proinflammatory cytokine. Sarilumab may potentially combat cytokine release syndrome (CRS) and pulmonary symptoms in severely ill patients.	Dosage of 400 mg IV as a single dose or multiple doses (based on protocol criteria); the lower-dose (200-mg) treatment arm was discontinued following a preliminary analysis of study results. Multiple clinical trials to evaluate sarilumab for treatment of COVID-19 are registered at clinicaltrials.gov.	Currently, no known published clinical trial evidence supporting efficacy or safety in the treatment of COVID-19. NIH COVID-19 Treatment Guidelines Panel states that there are insufficient clinical data to recommend either for or against the use of sarilumab in the treatment of COVID-19. No new safety findings observed with use in patients with COVID-19.

Table 2: Continued

Drug	Rationale use for COVID-19	Dosage	Conclusions
Interferons (IFNs)[81-84]; Antineoplastic Agents and Immunomodulatory Agents. An endogenous protein released by the host cell in action of inflammation and infection. It stimulates the immune response against viral replication. INF-α broad-spectrum antiviral that is used in many viral infections. IFN-α and IFN-β are active *in vitro* against SARS -C0V-2 in Vero cells at clinically relevant concentrations; 1 *in vitro* study suggests SARS-CoV-2 is more sensitive than SARS-CoV-1 to IFN-α. lack of clinical benefit observed with the use of type 1 IFNs, generally in combination with ribavirin, for treatment of SARS and MERS.	*In vitro* studies indicate only weak induction of IFN following SARS-CoV-2 infection, and a possible role for IFNs in prophylaxis or early treatment of COVID19 has been suggested to compensate for possibly insufficient endogenous IFN production. IFN-α and IFN-β are active *in vitro* against MERS-CoV in Vero and LLCMK2 cells and rhesus macaque model of MERS-CoV infection; type 1 IFNs also active *in vitro* against SARS-CoV-1 in Vero, fRhK-4, and human cell lines; IFN-β is more active than IFN- α *in vitro* against SARS-CoV-1 and MERS-CoV. Efficacy and safety of IFNs for treatment or prevention of COVID-19 not established.	Various sub-Q dosages of IFN beta-1a and IFN beta-1b are being evaluated for the treatment of COVID -19. Chinese guidelines suggest IFN alfa dosage of 5 million units (or equivalent) twice daily *via* atomization inhalation for the treatment of COVID-19. IV IFN beta-1a did not reduce ventilator dependence or mortality in a placebo-controlled trial in patients with ARDS. IFN lambda is thought to provide important immunologic defense against respiratory viral infections. and may have less potential than type 1 IFNs to produce a systemic inflammatory response, including inflammatory effects on the respiratory tract;	NIH COVID-19 Treatment Guidelines Panel recommends against the use of IFNs for treatment of COVID-19, except in the context of a clinical trial, because no benefit was observed with the use of IFNs for treatment of other coronavirus infections (SARS, MERS), clinical trial results for treatment of COVID-19 are lacking, and toxicity of IFNs outweighs the potential for benefit. Interferon alfa via atomization inhalation is included in Chinese guidelines as a possible option for the treatment of COVID-19. Surviving Sepsis Campaign COVID-19 subcommittee states that there is insufficient evidence to issue a recommendation on the use of interferons, alone or in combination with antivirals, in critically ill adults with COVID-19.
COVID-19 Convalescent Plasma[85-91]; Plasma obtained from patients who have recovered from COVID-19 (i.e., COVID-19 convalescent plasma) that contains antibodies against SARS-CoV-2 may provide short-term passive immunity to the virus; theoretically, such immunity may prevent or contribute to recovery from the infection, possibly as the result of viral neutralization and/or other mechanisms. Efficacy and safety of COVID-19 convalescent plasma for the treatment of COVID-19 not established. Theoretically, convalescent plasma should be more effective if given during the early course of the disease. Logistics of obtaining, processing, storing, and distributing COVID-19 convalescent plasma evolving. FDA does not collect COVID-19 convalescent plasma and does not provide such plasma; healthcare providers and acute care facilities obtain COVID-19 convalescent plasma from FDA-registered establishments.	Convalescent plasma therapy has been used in the treatment of other viral diseases with various degrees of success. In patients with SARS-CoV1 infection, the use of convalescent plasma was reported to shorten the duration of hospitalization and decrease mortality. SARS patients who received convalescent plasma less than 14 days after onset of symptoms had better outcomes than those who received such plasma later in the course of the disease. Appropriate criteria for selection of patients to receive investigational convalescent plasma, an optimal time during the disease to receive such therapy, and appropriate dosage (e.g., volume, number of doses) not determined. Convalescent plasma is regulated as an investigational product. FDA guidance suggests that convalescent plasma be collected from individuals with laboratory-confirmed COVID-19 infection and complete resolution of symptoms for at least 14 days before donation.	Analysis of key safety indicators in 5000 adults who participated in a US FDA Expanded Access Program suggests that IV transfusion of COVID-19 convalescent plasma is safe in hospitalized patients with COVID -19; 31 however, potential risks associated with COVID-19 convalescent plasma therapy (e.g., the inadvertent transmission of other infectious agents, allergic reactions, thrombotic complications, transfusion-associated circulatory overload, transfusion-related acute lung injury [TRALI], antibody-dependent enhancement of infection) and steps to mitigate such risks not fully determined and require further evaluation. Although there is some evidence suggesting possible benefits of convalescent plasma in patients with COVID-19, available data to date are largely from case reports or series; confirmation from additional randomized controlled studies is required. There are no convalescent blood products currently licensed by the FDA.	NIH COVID-19 Treatment Guidelines Panel states that there are insufficient data to recommend for or against the use of convalescent plasma in pts with COVID-19. The Surviving Sepsis Campaign COVID19 subcommittee suggests that convalescent plasma not be used routinely in critically ill adults with COVID-19 because efficacy and safety not established and uncertainty surrounding optimal preparation of convalescent plasma. Optimal timing of donor plasma collection with recovery from COVID19, most appropriate methods of antibody testing, and minimum titers of SARS-CoV-2 antibody in convalescent plasma that may be associated with clinical benefits in pts with COVID-19 not determined. FDA issued a guidance for industry to provide recommendations to healthcare providers and investigators regarding administration and study of investigational COVID-19 convalescent plasma. Donation of the convalescent plasma guidelines and protocols should be followed.

Table 2: Continued

Drug	Rationale use for COVID-19	Dosage	Conclusions
Corticosteroids[26,92-98]; Patients with severe COVID-19 develop a systemic inflammatory response that can lead to lung injury and multisystem organ dysfunction. It has been proposed that the potent anti-inflammatory effects of corticosteroids might prevent or mitigate these harmful effects. different factors to consider in giving dexamethasone to patients with COVID-19 which include; review the patient's medical history and assess the potential risks and benefits of administering corticosteroids, monitor patients with COVID-19 for adverse effects (e.g., hyperglycemia, secondary infections) after administration dexamethasone, and review a patient's medication regimens to assess potential interactions as dexamethasone is a CYP3A4 inducer. When stopping corticosteroids taper down the dose, and monitor the recurrence of inflammation and the signs of adrenal insufficiency.	Inhaled corticosteroids may mitigate local inflammation and inhibit virus proliferation. There are currently no published studies specifically evaluating the use of inhaled corticosteroids in patients with COVID-19. A small case series from Japan observed possible clinical benefit in 3 patients with mild to moderate COVID-19 pneumonia following oral inhalation of ciclesonide; however, without a control group, it is not known whether the patients would have improved spontaneously. Adjunctive therapies for COVID-19, in the case of asthma exacerbation or COPD and septic shock, otherwise, it should be avoided due to the lack of effectiveness and possible harm including avascular necrosis, psychosis, diabetes, and delayed viral clearance; in addition to, higher risk of mortality and secondary infections. It isn't recommended using dexamethasone in patients with COVID-19 who do not require supplemental oxygen (AI).	The initial dosage of orally inhaled ciclesonide used in the published case series from Japan of 3 patients with COVID-19 pneumonia was 200 mcg 2 times daily. If necessary, the dosage was increased to 400 mcg 3 times daily. The authors suggested continued use of ciclesonide oral inhalation for about 14 days or longer. Clinical trials evaluating the use of inhaled corticosteroids (e.g., budesonide, ciclesonide) in patients with COVID-19 are being planned or underway, including the following trials registered at clinicaltrials.gov. recommended of dexamethasone is 6 mg per day for up to 10 days; in patients with COVID-19 who are mechanically ventilated (AI) and in patients with COVID-19 who require supplemental oxygen but who are not mechanically ventilated (BI).	NIH COVID-19 Treatment Guidelines Panel recommends that inhaled corticosteroids used daily for the management of asthma and COPD to control airway inflammation should not be discontinued in patients with COVID-19. The panel also states that no studies to date have investigated the relationship between inhaled corticosteroids in these clinical settings and virus acquisition, the severity of illness, or viral transmission. Currently, there is no clinical evidence supporting adverse or beneficial effects of premorbid use or continued administration of inhaled corticosteroids in patients with acute respiratory infections due to coronaviruses. Randomized controlled clinical studies are needed to assess the benefits of inhaled corticosteroids for the treatment of COVID-19 in patients with and without chronic respiratory conditions.
Miscellaneous Drugs[99-101]; *In vitro* study found that ivermectin can stop SARS-CoV-2 from replicating. Ivermectin, an FDA-approved anti-parasitic previously shown to have broad-spectrum antiviral activity in vitro. It inhibited the causative virus (SARS-CoV-2), as the single addition of the drug to Vero-hSLAM cells 2h post-infection with SARS-CoV-2 reduces the virus by about 5000-fold within 48h. Ivermectin, therefore, warrants further investigation for possible benefits in humans, and a lot more research is needed to see if the doses studied would be safe and effective against the virus in humans.[63] Researchers think that colchicine could work similarly to tocilizumab in patients with COVID-19 in that it might be helpful if the immune system becomes too activated and a cytokine storm occurs. A large clinical trial is currently running to see if colchicine; when given soon after a COVID-19 diagnosis, can lower the chances of hospitalization and death. One research investigated azithromycin in combination with hydroxychloroquine for COVID-19. They reported that 93% of patients cleared the virus after 8 days, but there was no control group; so we don't know if people would have cleared the virus on their own or due to the medications. There are also concerns about potentially serious side effects; when using azithromycin and HCQ.			

The optimal management of COVID-19 is evolving and updated quickly. However, many drugs are being under clinical trials to find drugs that are effective against the virus.

infection of health care workers is avoided. In patients with excessive secretions or difficulty clearing secretions, consider the application of airway clearance techniques. These should be performed only if deemed medically appropriate. Patients with ARDS in whom a lung-protective ventilation strategy fails; to achieve adequate oxygenation and ventilation, the ECMO is given. Recognize septic shock in adults when the infection is suspected or confirmed; vasopressors are needed to maintain mean arterial pressure (MAP) ≥ 65 mmHg AND lactate is ≥ 2 mmol/L, in the absence of hypovolaemia. Prevention of complications in hospitalized and critically ill patients with COVID-19; such as venous thromboembolism, low-molecular-weight heparin is used. For any other, clinically suspected; such as stroke, deep venous thrombosis, pulmonary embolism, or acute coronary syndrome, appropriate diagnostic and management pathways should proceed immediately.[78,81-85] There are three broad approaches of drugs being investigated for the treatment of CPVID-19; which include: antiviral drugs; that directly affect the coronavirus's ability to thrive inside the body, immunotherapies; drugs that can calm the immune system; patients become seriously ill when their immune system overreacts and starts causing collateral damage to the body, and antibodies; either from survivors' blood or made in a lab, that can attack the virus. WHO recommended that several medicines shouldn't be administered or taken as prophylaxis for COVID-19. These drugs include; chloroquine and hydroxychloroquine (+/– azithromycin), antivirals, (Lopinavir/ritonavir, Remdesivir, Umifenovir, Favipiravir), immunomodulators (Tocilizumabm, Interferon-β-1a), and Plasma therapy. WHO also against the routine use of systemic corticosteroids for the treatment of viral pneumonia. For the treatment of other acute and chronic infections in patients with COVID-19; WHO also against the use of antibiotic therapy or prophylaxis in suspected or confirmed mild COVID-19. Besides, antibiotics should not be prescribed in suspected or confirmed moderate COVID-19; unless there is clinical suspicion of bacterial infection. In suspected or confirmed severe COVID-19, the use of empiric antimicrobials to treat all likely pathogens are based on clinical judgment, patient host factors, and local epidemiology; this should be done as soon as possible (within 1 hour of initial assessment if possible); ideally, after blood cultures obtained first. Antimicrobial therapy should be assessed daily for de-escalation.[27,102-106] Caring for patients with suspected and confirmed COVID19; that have underlying noncommunicable diseases (NCDs); it is recommended to continue or modify their medicines; according to the patient's clinical condition. For example, antihypertensive drugs should not routinely be stopped in patients with COVID-19; but therapy may need to be adjusted; based on general considerations for patients with acute illness; with maintaining normal blood pressure and renal function. Careful consideration should be given to the numerous clinically significant side-effects of medications; that may be used in the context of COVID-19; as well as drug-drug interactions between medications; both of which may affect COVID-19 symptomatology (including effects on respiratory, cardiac, immune and mental and neurological function). Both pharmacokinetic and pharmacodynamic effects should be considered of the medications too.[102,107] The antiviral drug Remdesivir gained an emergency use authorization from the FDA on May 1, 2020, based on preliminary data showing a faster time to recovery of hospitalized patients with severe disease. However, Remdesivir is considering the most promising antiviral drug. Also, other antiviral agents, immunotherapies, and vaccines continue to be investigated and developed as potential therapies for COVID-19. Numerous collaborative efforts to discover and evaluate the effectiveness of antivirals, immunotherapies, monoclonal antibodies, and vaccines have rapidly emerged.

MANAGEMENT OF NEUROLOGICAL AND MENTAL MANIFESTATIONS ASSOCIATED WITH COVID-19

COVID-19 is associated with mental and neurological manifestations, including delirium or encephalopathy, agitation, stroke, meningoencephalitis, impaired sense of smell or taste anxiety, depression, and sleep disorders. In many cases, neurological manifestations have been reported even without respiratory symptoms. Anxiety and depression appear to be common amongst people hospitalized for COVID-19; with one hospitalized cohort from Wuhan, China; revealing over 34% of people experiencing symptoms of anxiety and 28% experiencing symptoms of depression. Series cases in France found that 65% of people with COVID-19 in intensive care units (ICUs) showed signs of confusion (or delirium), and 69% experienced agitation. Delirium, in particular, has been associated with increased mortality risk in the context of COVID-19. Moreover, there have been concerns related to acute cerebrovascular disease (including ischaemic and hemorrhagic stroke); in multiple case series from China, France, the Netherlands, and the United States of America. Case reports of Guillain-Barré syndrome and meningoencephalitis among people with COVID-19 have also been reported. It is recommended, in patients with COVID-19, that measures to prevent delirium, an acute neuropsychiatric emergency, be implemented; and patients be evaluated using standardized protocols, for the development of delirium. If detected, then immediate evaluation by a clinician is recommended to address any

underlying cause of delirium and treat appropriately, and providing basic mental health and psychosocial support (MHPSS) for all persons with suspected or confirmed COVID-19. Prompt identification and assessment for anxiety and depressive symptoms in the context of COVID-19 should be considered; and to initiate psychosocial support strategies and first-line interventions, for the management of new anxiety and depressive symptoms. Psychosocial support strategies as the first-line interventions for the management of sleep problems in the context of acute stress also needed.[105]

PREVENTIONS AND MANAGEMENT

Evidence has shown that the groups of people most vulnerable to the development of severe illness due to the COVID-19 are the elderly, and those suffering from hypertension, pulmonary and cardiovascular diseases, cancer, and diabetes. COVID-19 affects the global population in drastic ways; older people face a greater risk of developing severe illness because of underlying health conditions and many physiological changes that come with age; which shall lead to declines in intrinsic capacity, manifested as the following malnutrition, cognitive decline, depressive symptoms, and potential underlying health conditions. Early detection of inappropriate medication prescriptions is recommended to prevent adverse effects of drug or potential drug interactions with COVID-19 treatment. Importantly, studies give proof that the transmission of this virus from human-to-human; along with many exported instances across the world. The geriatric population and people who are under some diseases are at risk of infection of this virus and susceptible to serious outcomes; which can be associated with acute breathing distress syndrome (ADRs). The are several limitations such as; the virus outbreaks very fast; thus the actual and accurate causes and effective treatment of COVID-19 are still unknown or unavailable, and the number of active cases of the infection is rising every day. However, the information about the disease including the number of cases and death are changing every day sharply worldwide. The global impact of this new pandemic is yet uncertain. The numbers are possibly an underestimate of the infected and dead due to limitations of surveillance and testing. As at this time there are no approved treatments for this infection, prevention is crucial and important. Several properties of this virus and/ or lack of precise information; make prevention is difficult; mainly; nonspecific features of the disease, the infectivity even before the onset of symptoms in the incubation period, transmission from asymptomatic people, long incubation period, tropism for mucosal surfaces such as the conjunctiva, prolonged duration of the illness and transmission even after clinical recovery. Isolation of confirmed or suspected cases with mild illness at home is recommended. The ventilation at home should be good with sunlight to allow for the destruction of the virus. Patients should be asked to wear a simple surgical mask and practice cough hygiene. Caregivers should be asked to wear a surgical mask when in the same room as the patient and use hand hygiene every 15–20 minutes.[7,108] The greatest risk in COVID-19 is transmission to healthcare workers. In the SARS outbreak of 2002, 21% of those affected were healthcare workers. Almost more than 1500 healthcare workers in China have been infected with 6 deaths and about 600 US healthcare workers have died from COVID-19 (by the end of June). By May 6, the International Council of Nurses (ICN) reported that at least 90,000 healthcare workers had been infected and more than 260 nurses had died in the novel coronavirus pandemic. The physician in China; who first warned about the virus has died too. It is important to protect healthcare workers to ensure continuity of care and to prevent transmission of infection to other patients. Although COVID-19 transmits as a droplet pathogen and is placed in Category B of infectious agents (highly pathogenic H5N1 and SARS), by the China National Health Commission; infection control measures recommended are those for category A agents (cholera, plague). Patients should be placed in separate rooms or cohorted together. Negative pressure rooms are not generally needed. The rooms and surfaces and equipment should undergo regular decontamination preferably with sodium hypochlorite. Healthcare workers should be provided with fit-tested N95 respirators and protective suits and goggles. Airborne transmission precautions should be taken during aerosol-generating procedures such as intubation, suction, and tracheostomies. All contacts including healthcare workers should be monitored for the development of symptoms of COVID-19. Patients can be discharged from isolation once they are afebrile for at least 3 days and have two consecutive negative molecular tests at a 1-day sampling interval. This recommendation is different from pandemic flu where patients were asked to resume work/school once afebrile for 24 h or by day 7 of illness. Negative molecular tests were not a prerequisite for discharge.[7,108]

At the community level, people should be asked to avoid crowded areas and postpone nonessential travel to places with ongoing transmission. They should be asked to practice cough hygiene by coughing in sleeve/ tissue rather than hands and practice hand hygiene frequently every 15–20 min. Patients with respiratory symptoms should be asked to use surgical masks. The use of a mask by healthy people in public places has not shown to protect against respiratory

viral infections and is currently not recommended by WHO, but in most countries, they practice this. However, in China, the public has been asked to wear masks in public and especially in crowded places and large scale gatherings are prohibited (entertainment parks). China is also considering introducing legislation to prohibit the selling and trading of wild animals. The international response has been dramatic. Initially, there were massive travel restrictions to China, and people returning from China/ evacuated from China are being evaluated for clinical symptoms, isolated and tested for COVID-19 for 2 weeks even if asymptomatic. However, now with the rapid worldwide spread of the virus, these travel restrictions have extended to other countries. Whether these efforts will lead to the slowing of viral spread still uncertain.[72-75] Healthcare providers should take travel history of all patients with respiratory symptoms, and any international travel in the past 2 weeks as well as contact with sick people who have traveled internationally. They should set up a system of triage of patients with respiratory illness in the outpatient department and give them a simple surgical mask to wear. They should use surgical masks themselves while examining such patients and practice hand hygiene frequently. Suspected cases should be referred to as government-designated centers for isolation. Patients admitted with severe pneumonia and acute respiratory distress syndrome should be evaluated for travel history and placed under contact and droplet isolation; regular decontamination of surfaces should be done. They should be tested for etiology using multiplex polymerase chain reaction (PCR) panels; if logistics permit and if no pathogen is identified, refer the samples for testing for SARS-CoV-2. All clinicians should keep themselves updated about recent developments including the global spread of the disease. International travel should be avoided and people should stop spreading myths and false information about the disease and try to allay panic and anxiety of the public.[27,108,110,111] Physicians notice a septic shock in some adults when infected with COVID-19, the treatment goal is to maintain MAP ≥ 65 mmHg, lactate ≥ 2 mmol/L. In absence of hypovolemia, the child will suffer from a septic shock with hypotension when (systolic blood pressure [SBP] < 5th centile or >2 SD below normal for age) or suffers from two or more of the following: altered mental state; bradycardia or tachycardia (HR <90 bpm or >160 bpm in infants and HR <70 bpm or >150 bpm in children); prolonged capillary refill (> 2 sec) or feeble pulses; tachypnea; mottled or cold skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia or hypothermia. When lactate measurement isn't available blood pressure (i.e., MAP) and clinical signs of perfusion can be used to define shock.[112] Strategies for the resuscitation of adult and pediatric patients with septic shock include conservative fluid regimens, the crystalloid fluid which include normal saline and Ringer's lactate which is given as bolus infusion, hypotonic crystalloids, starches, or gelatins should not be used for resuscitation. Starches are associated with an increased risk of death and acute kidney injury. Gelatins are more expensive than crystalloids. Hypotonic solutions are less effective than isotonic at increasing intravascular volume. Treating Sepsis also suggests the use of albumin when patients require substantial amounts of crystalloids, but this recommendation is based on low-quality evidence.[113] In adults with septic shock 250–500 mL, the crystalloid fluid which includes normal saline and Ringer's lactate is given as rapid bolus in the first 15–30 minutes, in children10–20 mL/kg crystalloid fluid is given as a bolus in the first 30–60 minutes, check for signs of fluid overload after each bolus. Reduce or discontinue fluid administration; if there is evidence of no response by the patient to fluid loading; or if signs of volume overload appear on the patient (e.g., jugular venous distension, crackles on lung auscultation, pulmonary edema on imaging, or hepatomegaly in children); especially in patients with hypoxemic respiratory failure. Based on clinical response and improvement of perfusion targets additional fluid boluses may be given (250–500 mL in adults or 10–20 mL/kg in children). The Perfusion targets include MAP (> 65 mmHg or age-appropriate targets in children), urine output (> 0.5 mL/kg/hr in adults, 1 mL/kg/hr in children), and improvement of skin mottling and extremity perfusion, capillary refill, heart rate, level of consciousness, and lactate. Notice indices for volume responsiveness to fluid administration; these indices include passive leg raises, fluid challenges with serial stroke volume measurements, or variations in systolic pressure, pulse pressure, inferior vena cava size, or stroke volume in response to changes in intrathoracic pressure during mechanical ventilation. In pregnant women with sepsis and or septic shock, they may need to be placed in the lateral decubitus position to off-load the inferior vena cava to reduce the hypotension. Management of septic shock in adults includes administration of vasopressors, in case if fluid administration does not restore adequate perfusion. In adults, norepinephrine is the first-line agent; epinephrine or vasopressin are preferred as the second line over dopamine.if patients didn't respond to usual doses of norepinephrine consider adding vasopressin rather than further titrating norepinephrine. In children, epinephrine is considered the first-line agent, and norepinephrine may be added if necessary. The initial blood pressure target is around 65 mmHg. If signs of septic shock persist despite administration of fluids and vasopressors; the patient shall be given an inotrope agent such as dobutamine rather than further titrating norepinephrine.[112-116]

In Palestine; the president of PA declared a state of emergency the same day that the first cases were identified (in Bethlehem) on 5 March 2020. In the beginning, Palestine was one of the lowest rates of virus spread and almost no community transmission, with 84 active cases in the West Bank and the Southern Governorates (Gaza Strip) reported (by March 25, 2020). As the COVID-19 incidence increases around the world, the PA continued efforts to contain the virus to protect the citizens and contributed to the global effort to end the pandemic. On March 22, the PA rolled out stricter suppression measures in the West Bank, preventing movement between governorates, closing all nonessential facilities, and asking the people in the West Bank to stay at home for 14 days. However, Palestine faces significant challenges in this effort, including a severely under-equipped health sector and an existing fiscal crisis caused by the Israeli authorities withholding of revenue. The COVID-19 and the emergency measures that the PA is taking are and will continue to have a significantly negative impact on the economics, which led to, shrinking revenues (by at least 40%) that limit the ability to maintain the level of services and economic recovery. The approach of COVID-19 was to focuses on preparation, containment, and communication. The PA prepared an emergency response plan in late February and has worked with local and international partners to mobilize health professionals and facilities across the West Bank and equip them with training and the necessary protective gear, medical supplies, and medicine. Containing the virus outbreak was through testing and quarantining and restrictions on citizen movement. Individuals suspected to have COVID-19 are home quarantined until symptoms develop or they have a positive test. All in-coming travelers were placed in government quarantine for 2 weeks. Individuals with positive samples or symptoms are cared for in government hospitals. There are contact and trace units in each governorate. It was also launched a national coordinated communications campaign, passing public health and situation updates to citizens *via* national and local mechanisms on news, Facebook, and Twitter. The campaign includes a government COVID-19 tracking dashboard and collaboration with social media pages focused on tackling misinformation. The PA officials were twice-daily briefings through the national media, including updates on COVID-19 cases and government guidelines for citizens. The PA coordinated about COVID-19 with Jordan and Israeli authorities. Over weeks, the PA requested citizens comply with movement restrictions at the national and regional level, starting with the Bethlehem governorate, which had the first incidence of COVID-19. By 22 March, the following guidelines were taken[4-6]:

- Closure of all schools, universities and public parks for 30 days (from 5 March - 5 April);
- Closure of all borders (movement of goods is allowed);
- Government quarantine (14 days) and testing for all incoming travelers (from Ben Gurion airport);
- No movement between West Bank governorates;
- Palestinian laborers who travel to Israel for work are asked not to move between Palestine and Israel: this means that they should return to their homes (and remain in home quarantine for 2 weeks) or remain in Israel until the situation changes;
- No movement within all urban areas (except for exceptional circumstances), with all citizens, requested to remain with their homes for 14 days (from March 22);
- Closure of all stores, public institutions, and government offices, except for essential providers (pharmacies and food) and the Ministries of Health, Finance and Interior (for 14 days from 22 March);
- All citizens are asked to stay at home, except for essential activities and emergencies (for 14 days from 22 March).

These actions were also extended and the Emergency across the oPt was declared up to 4 May. In this context, it has scaled up restrictions on movement between cities, commercial activities, and public gatherings, along with a suspension of all educational activities. On 20 April, a series of relaxation measures aimed at allowing the resumption of certain economies were announced. Palestinians entering the oPt from Jordan, Egypt and Israel have been ordered by the Palestinians authorities to stay in mandatory quarantine. Although in the Gaza Strip this measure has been strictly enforced, with all incoming people being referred to designated facilities, implementation in the West Bank has been partially due to its porous boundary with Israel, raising concern about a potential spread of the virus by workers that have been returned from Israel.[4-6,20]

PALESTINIAN CHALLENGES

The Challenges of PA in the fight to contain the COVID-19 outbreak was, Israeli military and economic control, no control over borders, national resources (medical and financial), many population high-risk characteristics of (crowded cities and refugee camps, poverty, food insecurity, and NCDs), and fiscal crisis. The budget deficit restricted the ability to cover operating expenses, pay salaries and pensions, and maintain the social safety network. In the context of COVID-19, PA is not able to cover the full salaries to employees including health workers. Additionally, there are insufficient funds to cover the scheduled government transfers to the most vulnerable population, with greater numbers of Palestinians expected to need government

support due to the economic impact of COVID-19. The Gaza Strip is already in humanitarian and economic crisis. Thus, widespread incidence of the virus will be catastrophic in a population that is overcrowded, undersupplied, and in high poverty and food insecurity and ongoing closure of Gaza makes impossibility to freely mobilize the health resources if an outbreak of the disease. Across the oPt, the movement restrictions, closure of schools and growing unemployment is taking a toll on the most vulnerable. Service providers report that domestic violence affecting women and children is on the rise. Many families already live in poverty and the consequences of COVID-19 response measures have made it even harder for them to maintain their livelihoods and income. The Palestinian Ministry of Social Development (MoSD) estimates that at least 53,000 families across the oPt have fallen into poverty in recent weeks, due to the loss of a source of income. Without sufficient social protection and continuity of protection services for these vulnerable households, families risk plunging further into poverty and exacerbating already volatile family and community situations. The COVID-19 pandemic is characterized by the speed of its spread and difficulty to project how it will evolve at the country level. As a result, a mechanism to monitor the situation, needs and response are indispensable to rapidly adjust the interventions. The mandatory quarantine imposed by the PA to contain the virus, either home-based or at dedicated sites, has increased the risk of GBV including domestic violence affecting women and children, mental illness, and psychosocial deterioration. People with seeing, hearing, or mobility issues, already experience difficulty in accessing services and information in the oPt, now exacerbated as they seek to protect themselves from the outbreak. Many persons with disabilities depend on services that have been suspended and families report not having enough money to stockpile the specific food and medicine. Following the closure of education facilities in early March, 1.43 million children across the oPt need to continue distant learning and receive age-appropriate, awareness-raising messages around COVID-19.[4-6,20] In Palestine, not only the elderly and people suffering from hypertension, pulmonary and cardiovascular diseases, cancer and diabetes are the most vulnerable to the development of severe illnesses due to the COVID-19 but, also there are several others people were impacted by the COVID-19 outbreak, which includes:

- About 1,000 patients in Gaza cannot be referred to specialized treatment outside Gaza due to the crossing closure.
- More than 9,000 patients awaiting elective surgeries in Gaza (3,000 of which are urgent) that are postponed due to preparedness measures for the management of COVID-19 cases. Similarly, in the West Bank, over 4,000 elective surgeries per month are postponed.
- About 50,000 individuals seeking outpatient support. Currently, there are over 50,000 outpatient appointments per month in the MoH and more than 2,000 referrals per month to non-MoH for outpatient appointments from the West Bank. Most are affected by movement restrictions and health service re-prioritization.
- Pregnant and lactating women and children who might not be able to receive essential healthcare because of health service re-prioritization.
- Palestinian refugees, who live in one of the 19 overcrowded refugee camps, as well as Bedouin communities with inadequate living conditions most importantly, access to safe water and sanitation.
- Palestinians who are placed in quarantine facilities that may not be adequately prepared.
- Children in detention are vulnerable to infection due to confinement, and at risk of neglect and abuse due to movement restrictions affecting the ability to access essential services.

As the COVID-19 pandemic spreads, concerns are particularly serious in conflict and humanitarian settings. Tackling the pandemic in those countries is challenging due to the fragility of socioeconomic and health systems. Palestine is one of those countries that is facing compounding challenges, instability, fragility, living conditions, poverty, and mobility, all of which are caused by multifactorial etiology. The Pandemic shows triple tragedies; virus (COVID-19 pandemic), ongoing Israeli control (Politics), and Intra-Palestinian divide (Policies). Yet, Palestine's response to the pandemic is outperforming many countries in the region. The early preventative lockdown measures in the West Bank found effective and not overwhelming the already overstretched health system. Although in the Gaza Strip the response was slow, prisoners, laborers, besieged people, socioeconomic-disadvantaged classes, and refugees were put at additional high risk. Nonetheless, measures taken were unconsolidated in both regions largely due to the political factors. A little collaboration and inter-agency task forces in preparedness and response were observed, and the mechanisms and governance remain ambiguous. A consolidated and evidence-based nation-wide plan is required, whereby state and nonstate actors have a clear and transparent exit strategy. A new thinking approach to promote the public health system and evidence-informed policies in Palestine is an urgent national priority.[4-6,20] Despite these measures, the capacity of the Palestinian health system to cope with a potential surge in the number of people suffering from serious symptoms due to COVID-19 is impaired by a range of factors. The situation is of particular concern

in Gaza, where the health system has been undermined by the ongoing conflict between Hamas and Israel, the Israeli blockade, the internal Palestinian political divide, a chronic power deficit, and shortages in specialized staff, drugs, and equipment. In addition to capacity shortages, in the West Bank, vulnerable communities, particularly in Area C, continue to be affected by the Israeli authorities' destruction of property lacking building permits, as well as by Israeli settler violence, undermining their capacity to cope with the crisis. Several things should be emphasized which include; stope further transmission of COVID-19 across the oPt and reducing the demand for hospital critical care services and to avoid any overload of hospital care capacity, provide adequate care for patients affected by COVID-19 and to support their families and close contacts; and minimize the impact of the epidemic on the functional capability of the health system. Provide essential hygiene and disinfectant materials or cash for families and people at higher risk of being affected by COVID-19. Provide Non Food items (NFIs), such as bedding, cleaning, and hygiene materials to quarantine facilities. Improve hygiene conditions for families lacking basic facilities, such as latrines or kitchens, by providing appropriate hygiene materials, cleaning supplies, awareness materials, and technical consultancies and guidance. Contribute to mitigate the impacts of economic deterioration exacerbated as a result of the loss of income of the most vulnerable families by the provision of multipurpose cash or rental assistance. Distribute cleaning and hygiene packages to all schools in the oPt to prevent the spread of the pandemic before schools re-open. Rehabilitate the schools used as quarantine centers before re-open to ensure that they are back to normal status. Food support for most vulnerable households, including persons with disabilities, elderly and lactating and pregnant women, whose food security is directly affected by the virus outbreak. Clean and disinfected of all schools and public kindergartens in the oPt before re-opening.[4-6,20]

As there is currently no specific treatment for COVID-19, the most effective and impactful approach to protecting the population against the disease is containment measures, with a focus on early testing of all suspected cases, isolation and treatment of confirmed cases, contact tracing and quarantine arrangements, complemented by primary and community-based health initiatives with an emphasis on prevention and promotion of effective protection measures (hand hygiene and physical distancing). Efforts to scale up hospital preparedness and treatment capacity to manage an increase in demand for hospital-based patient care must continue. Strengthening the health care workforce and procurement of medicines, disposables, and equipment have been identified as the two crucial elements in fighting againstCOVID-19. The health workforce is the backbone of an effective health response and requires adequate technical support and protection. Therefore, it is important to mobilize further resources to provide adequate training health staff on most importantly clinical case management protocols and infection prevention and control policies. The unprecedented global demand for COVID-19 related materials, presents considerable challenges, particularly in the oPt. The approach, therefore, emphasizes a local procurement wherever possible, whilst maintaining quality control. The delays in global procurement serve to emphasize the need for a healthcare strategy that maximizes available resources and minimizes the consumption of currently limited materials. Therefore, PA recommended different strategies to be pursued which include; procurement and rational use of PPE, support quarantine facilities, enhance and rationalize laboratory testing, support case management of patients with COVID-19 who require hospital admission, enhance risk communication and community engagement and maintain core health services. As the COVID-19 continues to spread globally, vulnerable populations living in countries with weak health systems are at high risk of being hit the hardest. In conflict-torn countries and humanitarian settings, health and socioeconomic systems are already fragmented and overstretched to counter an outbreak. Furthermore, these settings suffer chronically from different forms of fragility, including weak health governance, high poverty and unemployment rates, high-density populations, and overcrowded refugee camps. They also suffer from poor access to essential WASH services, which are necessary for infection prevention and control. Health systems in these countries are ill-equipped and depleted by protracted conflicts and a large prevalence of co-morbidities such as NCDs according to WHO. All these factors increase the pandemics' transmissibility and high case-fatality and deter the COVID-19 preparedness and response modalities. The Middle East and North Africa (MENA) region is particularly experiencing multiple conflicts and political instabilities, which bring with them global health challenges. The impacts of devastating conflicts and political and social tensions in the region have been driving the emergence and spread of infections such as Cholera and COVID-19. The capacity to implement physical distancing and essential hygiene measures in conflict settings may prove unattainable. Humanitarian settings suffer from damaged health systems where they lack healthcare professionals, medicines, and equipment. Refugee camps and besieged areas also suffer from a lack of governance and access to essential needs and safe WASH services. The COVID-19 casualty and fatality rates are varied in the MENA region. According to

the WHO, more cases have been reported in conflict-free countries with strong health systems (e.g., Qatar) compared to conflict-affected countries with poor health systems (e.g., Yemen). This is largely attributed to insufficient surveillance and testing capacity in conflict settings. On the other hand, fatality cases are relatively low in Turkey, Palestine, and Iran and high in Algeria and Egypt, when compared to the rest of the region's countries. Fatalities were high in countries that have a high percentage of elderly people in the population, large population density, and those with weak testing, diagnostic, and treatment capacities. Despite this, the region's governments have taken various and different degrees of containment measures to mitigate the COVID-19 spread. These include complete or partial lockdown of cities and different levels of physical distancing and hygiene promotion activities. Some in conflict countries have ceased fire and eased political tension in line with the current situation, yet the Israeli occupation multiplied attacks on Palestinians and aborted measures to curb the COVID-19 spread. This public health crisis reveals major gaps in the political and social systems of countries facing conflicts in the MENA region, where vulnerability, disparity, unpreparedness, distrust, and injustice are evident from the lack of strategic and comprehensive policies, resources misallocation, and lack of investment in public health priorities. Therefore, there are serious concerns about the current MENA region's capacity that needs an immediate real investment to halt the spread of this pandemic. A group of global public health scholars from the MENA region and local researchers from Palestine who specialized in health systems, health policies, and the burden of diseases led this policy analysis. We explored and analyzed the health system's response to the COVID-19 pandemic with a focus on Palestine, based on published data. We explored and reported some policy failures and successes related to the COVID-19 health system response and some of the recommend potential public health solutions and alternatives were also discussed.[4-6,20] All infected patients should receive supportive care to help alleviate symptoms; and vital organ function should be supported in severe cases too as mentioned. In Palestine, the treatment and management protocols of COVID-19 are similar to the strategies and protocols in other countries especially those that follow the guidelines of WHO. The high outbreak of the disease in Hebron Governorate-Palestine has been caused by people meeting up with their families or attending wedding parties or funerals and failing to follow health recommendations and maintain social distancing according to the Palestinian MoH officials. However, isolation and other preventive and precautions are the most important ways in reducing the outbreak of the disease; which prevents the transmission of the virus to others. It is important to mobilize the community to combat rumors and misinformation.[4-6,20]

CONCLUSION

The MoH strategies to end the COVID-19 pandemic were; to stop the transmission of COVID-19 across oPt and reduce the demand for hospital critical care services and to avoid any overload of hospital care capacity; provide adequate care for patients affected by COVID-19 and to support their families and close contacts, and minimize the impact of the epidemic on the functional capability of the health system. The outbreak of the disease can be by applied health recommendations, isolation, and maintain social distance. PA strategies, guidelines, and protocols and plans against COVID-19 were similar to the other countries having the disease. But Palestine has different challenges and limitations in the treatment and management of the disease. The pandemic by COVID-19 is a very dangerous issue affecting people worldwide and still this pandemic is ongoing and no suitable treatments until now. Supportive treatment is still the main strategy in treating this disease; as no curative antiviral has been approved due to the lack of evidence and precise information. Isolating patients and other preventive and precautions are now the most important ways in reducing the outbreak of this virus; as these prevent the transmission of the virus to others or healthcare providers. However, there is an urgent need to develop targeted therapies. Understanding the disease and the different responses to this virus; could help to find immune-based therapeutics or/ and conventional medicines. It is important to have the latest information, but we must ensure that the information is coming from trustworthy sources. Thus, a variety of helpful resources related to COVID-19 treatments, management, and preventions have been collected. We explored and analyzed the health system's response to the COVID-19 pandemic including the challenges with a focus on Palestine.

Ethical policy and institutional review board statement

The identities of patients remained unknown and their identities remained confidential and only used for research purposes. The procedures were accomplished upon obtaining permission from the Ethical Committee of Hebron University.

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Conflicts of interest

There are no conflicts of interest.

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