Review Article

COVID -19 PANDEMIC: EMERGENCE AND EPIDEMIOLOGY

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ABSTRACT:
Novel corona virus emerged as 6th public health emergency of International concern. Since mid-Dec. 2019 several cases of pneumonia like illness were reported in central Chinese city of Wuhan but later the virus started spreading to other countries. On 11th Mar. 2020, World Health Organization (WHO) declared it as global "pandemic". On 26th feb. 2020, first two cases of COVID-19 were reported in Pakistan. COVID-19 causes common cold in humans and is transmitted in a similar fashion form person to person via respiratory droplets. Its clinical presentation is milder in children as compared to adults population, while gender distribution showed that men accounted for 60% of all COVID-19 patients. till date no specific vaccine is available for immunization of public mass. No specific antiviral treatment has yet recommended by WHO for COVID-19. However, health authorities have suggested isolation and symptomatic treatment for infected individuals. Due to non-availability of specific medication and vaccination for COVID-19, WHO has suggested that the best preventive strategy to combat this virus is to avoid its exposure. Uses of face masks, gloves, hand sanitizers, covering mouth and nose while coughing or sneezing and social distancing can reduce the risk of exposure to the virus. keeping in view the guidelines for prevention and control of COVID-19, government of Pakistan took many measures to stop the spread of virus i.e establishment of quarantine centers, testing facilities, designated hospitals, public awareness campaigns and implementation of lockdown. But besides all these efforts there are many challenges faced by government e.g misinformation, lack of public awareness, false interpretations and rumors has made it difficult to combat this pandemic in Pakistan.

Key Words: COVID-19, Pneumonia, Pandemic, Immunization

History of pandemics:

A disease outbreak/epidemic occurring worldwide or over a very wide area, crossing International boundaries and usually affecting a large number of people is termed as a pandemic.[1] The first-ever recorded pandemic was "the plague of Athens", more than 2000 years ago, which lasted from 430 to 426 BC.[2] The plague remains the most devastating pandemic in history, that affected social and economic conditions of the society.[3] Smallpox pandemic was a second with an estimate of 56 million casualties.[4] Other notable pandemics in human history include cholera, typhoid, and influenza outbreaks affecting millions of people across the globe.[5]

Emergence of Wuhan Epidemic: COVID-19:

First manifested as a suspicious case of pneumonia in Wuhan, Hubei province of China, the novel Corona Virus emerged as the 6th Public Health Emergency of International concerns[6] resulting in more than 43000 deaths across a stretch of 28 countries by 11th Feb 2020.[7] Therefore, by March 2020, this ambiguous global crisis was declared a pandemic.[8]

Since December 2019, an alarming acceleration was noticed in the cases of corona virus-infected pneumonia in Wuhan.[9] Initial, 41 cases reported with respiratory symptoms, had a history of exposure in the Huanan seafood market where in addition to seafood and chicken, other wild animals were also sold. The Huanan Seafood market of Southern China was allegedly held responsible for coronavirus outbreak. Based on the clustering of cases in Huanan seafood

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market among old men brought an assumption that coronaviruses have 96% of the genetic makeup similar to bats.[10]

The government sealed the Wuhan market in an attempt to contain the disease but failed to put the rising number of cases to a halt. Evidence of the human to human spread was spotted when the hospital staff contracted COVID-19, setting up the globe on high alert. The Chinese Government continued intensive surveillance and epidemiological analysis in an attempt to follow up on the emerging cases of coronavirus by placing Wuhan and neighboring cities under quarantine to limit the spread of infection. All schools, colleges, factories, and airports were sealed. All social gatherings and International travel were banned.[11] During the outbreak, an additional lookout for the Chinese officials and researchers was the New Year Holiday that expected a massive flow of population across the country. [12] China felt the initial blow of the COVID-19 epidemic with its peak in mid-February, the country's daily report exceeded 5,000 cases per day. As of June 15, 2020. Chinese health authorities had acknowledged over 83,181 cases and 4,634 deaths – most of them being bagged by the province of Hubei.[13]

COVID 19: Public health emergency of International concern to Pandemic:

By the end of December 2019, WHO was informed about 27 cases of " atypical pneumonia" in Wuhan city by higher authorities of China.[14] By the 20th of January 2020, Wuhan confirmed 258 individuals had tested positive for COVID-19 along with six deaths.[15] As COVID-19 has deemed an emergency epidemic by 22nd of January, rapid response by the Wuhan local government was shown and the lockdown was imposed throughout the municipality by 23rd of January, 2020.[16,17] Lockdown measures including public transport within and out the city halted, businesses shuttered, jobs suspended, schools closed and strict stay at home ordered. Aiming to localize, isolate, and monitor the epidemic, a key measure that was taken to report and streamline the epidemic data was to electronically notify the National infectious disease system (NIDS).[18] Doctors would notify every suspected and confirmed case to construct a daily statistical report of COVID-19 in each area.[17] After the celebrations of the new year and movement of a large population, the virus then started spreading to other countries too. The first case reported outside China was in Thailand on 13th January 2020.[19] With the emergence of a large number of cases Internationally, WHO declared this outbreak as a "Public health emergency of International concern" by the end of January 2020. On 11th February 2020, a new name "**COVID-19**" was announced by WHO.[20] The panic started to kick in as the disease started spreading to various parts of the world, confirmed cases were reported in a large number of countries covering gulf area and Asian region by the end of February-2020.[21] Soon, on 11th March-2020, WHO declared it as a **global pandemic**.[22] After China, the virus hit European countries causing a huge number of fatalities, more than 50,000 cases were reported in Italy by 21st Mar-20.[23] It then spread across France, Spain, and the UK. After Europe, the wave hit the United States of America resulting in a great number of mortalities, New York City was worst hit by the outbreak with 30,856 deaths up to date.[24]

Globally, 8,175,482 cases were confirmed with 443,730 deaths and 3,956,263 recovered till 17th June-2020. Highest number of cases reported in US (2,137,731) followed by Brazil, Russia and India.[25] The Americas region is most affected in the world with 3,841,609 cases and 203,574 deaths, followed by Europe (2,434,184 cases/ 188,779 deaths), Eastern Mediterranean (796,759 cases/ 17,558 deaths), South-East Asia (486,673 cases/ 13,409 deaths), Western Pacific (199,922 cases/ 7,228 deaths) and Africa (181,903 cases/ 4,235 deaths) respectively.[26]

COVID -19 in Pakistan:

By February 24, WHO had reported cases in many other countries such as Japan, United

States, Thailand, Denmark, Ireland and subsequently declared that this virus has affected 196 countries around the globe.[27] WHO attributed the main reason of spread as trade with China and International traveling across the globe.[28] At that time of crisis, Pakistan was surrounded by two neighboring countries infected with COVID-19, including China, from where this disease arose and had the highest number of deaths and Iran.[29] On 26th February 2020, the first two cases of COVID-19 were reported in Karachi and Islamabad. The number of cases reached 20 within the first 15 days. All the cases had a history of International traveling.[30] By March 26th, 2020, 1179 cases were confirmed in Pakistan with 9 deaths.[31] On Monday, April 6th, 2020, there were a total of 3277 confirmed positive cases among which 18 were critical and 50 mortalities happened. The highest number of cases appeared in the Punjab province (1493) followed by Sindh.[32] On 15th May 2020. WHO declared total 4,628,785 COVID positive cases and on the same day, situation of Pakistan reflected 38,799 confirmed cases with 834 deaths with 28.05% (n = 10,880) recoveries.[33]

Epidemiology of coronavirus:

Agent: International Committee on Taxonomy of Viruses has named this virus as novel coronavirus,2019 as it was a new addition in coronaviruses family. The disease was termed as COVID-19. World Health Organization announced this name on 11th February, 2020.[34] This is a single-stranded RNA virus with a crown-like structure. The majority of the viruses in this family infect animals. Till today, there are only seven identified species that can infect humans. This noval coronavirus has been found with genetic material similar to bats.[35]

Source of Infection:

It is estimated that 2% of the infected population with COVID-19 presents as asymptomatic carriers and 5-10% of the infected population presents with respiratory signs & symptoms.[35] Respiratory droplets, nasal secretions, salivary secretions are a potential source of infection. Respiratory droplets less than 5-8 microns generated by coughing, sneezing, and talking of infective cases play a significant role in maintaining the chain of transmission of infection.[36] According to the World health organization, asymptomatic cases play a significant role in the generation of a propagated epidemic caused by this virus.[37] Contamination of fomites and surfaces with infected droplets can also be a source of infecting susceptible individuals. A close distance of 6 feet and 1.8 meters with an infected individual is a risk factor for contracting the disease.[38]

Route of transmission:

COVID-19 is a highly contagious disease and has multiple characteristics different from other infectious diseases.[39] Human-to-human transmission has been evidenced by respiratory droplets, close contact, and fomites. Evidence for vertical transmission is still lacking.[40]

Incubation period:

The range of incubation periods varies from day one to 24 days with a mean of 3 days. and the meantime from symptom onset to fatality is 14 days and the median latency is 4 days.[41] The period from the onset of COVID-19 symptoms to death ranged to an average of 14 days.[42]

Period of communicability:

COVID-19 is highly infectious. Studies have shown that infective case can communicate this virus to others even in their incubatory phase. It has been estimated that transmission to susceptible hosts can occur even five days before the development of symptoms in the infective case.[43] On average, each patient of COVID-19 transmits the infection to an additional 2.2 individuals.[44]

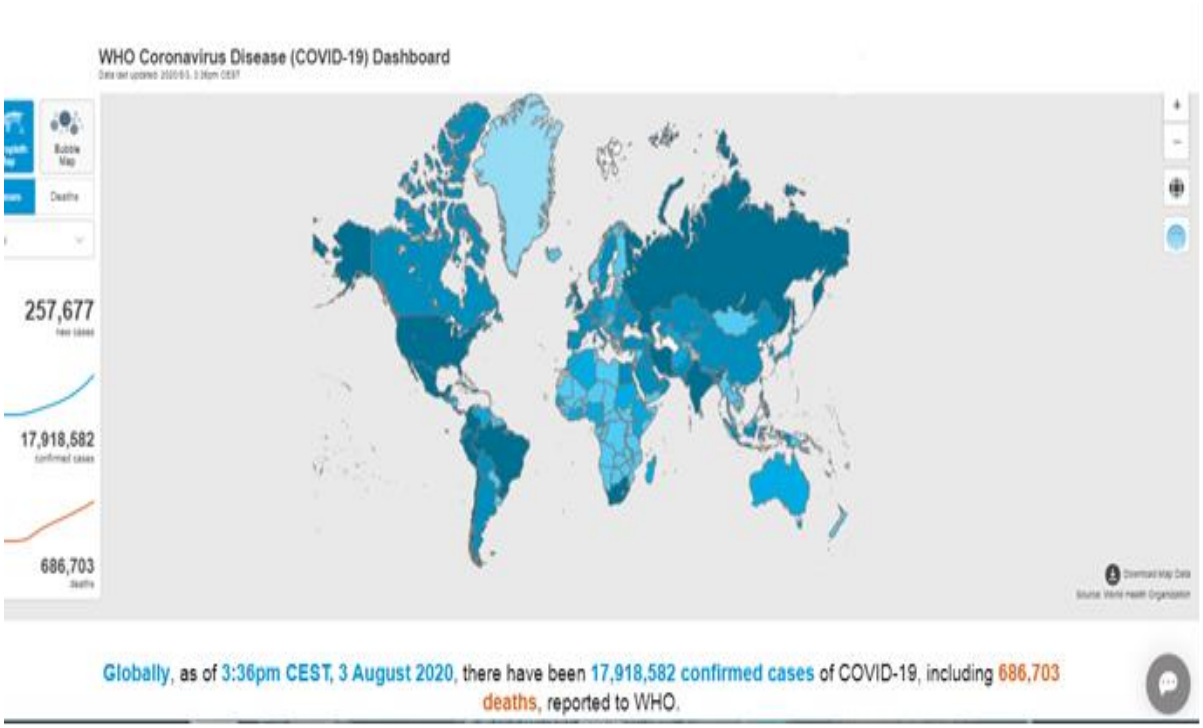
Secondary attack rate:

The risk of transmitting the infection to household contacts was reported between 12.4% [45] to 16.3%[46] in studies conducted in

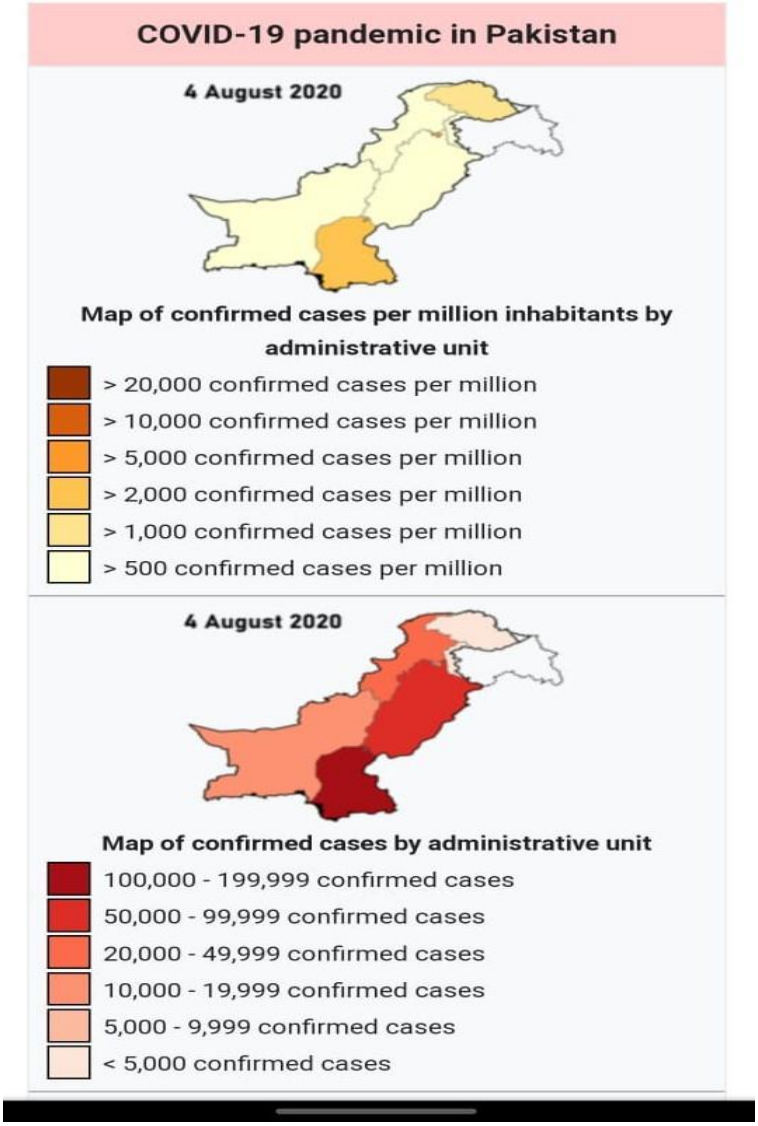
China. Secondary attack rate was highest in spouses with 27.4% and lowest in children 4%.[47]

Geographical distribution worldwide:
According to sources of WHO, accessed on 3rd August 2020, 17,918,582 confirmed cases have been reported globally. The maximum number of cases has been reported from the United States of America which is 4,582,276 whereas the minimum number of cases (only 3) has been reported in Anguilla. Till date, Brazil has 2,707,877, India 1803,695, Iran 309,437, Spain 288,522 cases are among the countries who have reported maximum cases.[48]

Geographical distribution in Pakistan:
Worldwide COVID 19 trackers showed on 6th August that Number of cases in Pakistan were 281,836. Maximum cases till that date were reported in Sindh (122,373), followed by Punjab (93,847). The number of cases in KPK were 34,359 and only 11, 793 cases were reported in Baluchistan.[49]



Figure–1: Worldwide cases of COVID 19 and their distribution



Figure–2: Pakistan cases of COVID 19 and their distribution

Age distribution:

COVID-19 is milder in children as compared to the adult population.[50] Among hospitalized patients, the average age has been reported between 49-56 years.[51] The majority of deaths are in the elderly population who are 60 years and above.[52] In Pakistan, it has also been observed that the elderly are more prone to infection than younger people, and also accompanied by the increased mortality rate due to a decrease in immunity.[41] Elderly people are most prone to SARS-CoV-2 and the maximum number of deaths are reported in the elderly population of more than 75 years[19] and most of the patients who died had comorbidities usually cardiac diseases or a history of prior surgery.[53]

Gender distribution:

Gender distribution shows men accounted for 60% of COVID-19 patients.[54] Even in data of hospitalized cases, the predisposition of male gender was observed ranging from 54 to 73% of cases.[51] The older men are more prone to infectious diseases with low immunity and poor resistance to infections. The COVID-19 associated mortality has shown a pattern of higher mortalities in males than females in China and Italy.[41] Another study shows that women are less susceptible to viral infection than men because of the protection of X chromosome.[55]

Risk factors:
Male gender and old age are risk factors for COVID-19 infection.[41] Associated comorbidities such as hypertension, diabetes, cardiovascular disease, and respiratory disease are now known factors to show more susceptibility towards COVID-19 infection and even high mortality associated with this infection.[55] Low immune status, high LDH, and d-dimers were found with increased susceptibility for COVID-19 too. Body in a state of stress and poor nutritional status favored coronavirus infection.[56]

Vaccine:
Till date, no vaccine is available for immunization of the mass public. Field trials have been conducted. WHO and many International agencies are trying to formulate vaccines against COVID-19 and these are awaited in the market.

Herd Immunity:
Centre for disease control (CDC) defines herd immunity as the immunity developed by a fraction of the population to indirectly offer immunity to those individuals who cannot get vaccinated and are immune-compromised.[57] Herd immunity depends upon the number of active cases, subclinical cases, vaccination of population, structure, and movement of population. In the absence of vaccine and restriction of movement in population, the most important factor to produce herd immunity is the number of individuals infected with this disease. WHO recommends that for a population to develop herd immunity, a minimum of 60% of the population should be immune to stop transmission to a susceptible population. This is supported by a recent study conducted in the United States concluded that almost 50% to 60% of the population is supposed to be immune for herd immunity to work for those susceptible to coronavirus.[58] A recent study conducted in Japan hypotheses that the S type of the virus is capable of inducing herd immunity whereas the L type of the virus replicated increasingly having a high morbidity and mortality rate so does not produce the desired number of immune individuals to stop the chain of transmission. A study conducted in India (May-2020) concluded that the virus needed to stay for a long period in a particular geographical area to reach the desired herd immunity threshold value and that subsequently decrease the mortality rate.[59] Another recent study in China concluded that South Korea had 1% of their population infected with the virus and this was less than what they needed for the herd immunity to work in their population.[60] The role of herd immunity and its level is still debatable at the level of the World Health Organization.

Sign and symptoms:
Transmission of the novel coronavirus occurs through respiratory droplets and aerosols from coughing and sneezing.[61] The virus uses the ACE-2 receptor to enter the bronchial cells and thus it is postulated that the virus can infect extrapulmonary tissues that express the angiotensin-converting enzyme (ACE-2) receptor.[62]
Symptoms appear 2-14 days after exposure to the virus.[63] The clinical features of the disease vary from individual to individual. Signs and symptoms range from being asymptomatic or mild to causing acute respiratory distress syndrome (ARDS) and multiorgan failure and ultimately death.[19,64] Symptoms most commonly seen in patients with mild disease are fever which is variable in degree and unresponsive to antipyretics, cough which in most cases is dry cough but may also be productive in a subset of patients and shortness of breath. Relatively uncommon symptoms include headache, nasal congestion, sore throat, and myalgia.[63,64] A small proportion of patients also have ocular findings consistent with viral conjunctivitis.[65] A fraction of patients also report with loss of smell and taste, often being very first apparent symptom.[66-68] As the disease progresses, those patients with co-morbidities develop pneumonia and/or acute respiratory distress syndrome (ARDS).

Pneumonia presents with fever, hypoxia, oxygen saturation levels below 90%, respiratory distress and tachypnoea.[64] Bilateral ground-glass opacities or consolidation were found in X rays of infected patients.[69]

In addition to respiratory symptoms, patients testing positive for the coronavirus also have gastrointestinal symptoms such as anorexia, nausea, vomiting, and diarrhea being the most common. GI symptoms in these patients are relatively uncommon as compared to respiratory symptoms but are present. Even though, these manifestations can be extremely uncomfortable and inconvenient for the patient they do not cause any change in the clinical outcome of the patient.[70] Fecal samples in a subset of patients with GI symptoms show the presence of viral RNA which may also indicate fecal-oral transmission (need more evidence) and causation of GI symptoms.[71] Some degree of liver damage in a minute percentage of patients is also evident by the presence of abnormal liver function tests (LFTs). Clinically significant liver dysfunction is a rare occurrence.[72]

Causes of death in critically ill patients in addition to respiratory failure also include multi-organ damage and failure, to name a few, the heart, kidney, and the haematolymphoid systems.[73] Patients with renal damage or renal failure are found to have oliguria, proteinuria, haematuria, hypoalbuminemia, elevated serum creatinine, and elevated blood urea nitrogen.[74,75] Due to the high grade systemic inflammatory response of the body, the incidence of cardiovascular injury is high. Patients developing complications of cardiovascular diseases such as acute myopericarditis left ventricular (LV) dysfunction and pericardial effusion have a poor prognosis.[76,77] Critically ill patients are also at the risk of developing coagulopathies. The pro-inflammatory state of the body results in abnormal coagulation parameters. Disseminated intravascular coagulation (DIC) and venous thromboembolic events are common coagulopathies seen in these patients.[78,79] The pro-inflammatory state results in fulminant and fatal hypercytokinemia with multiorgan failure and eventually death.[64]

Treatment:

Coronavirus disease 2019 (COVID-19) can range from mild disease to severe respiratory failure and may require Intensive Care Unit admissions. There is no specific treatment for the COVID-19 available as of yet so WHO emphasizes treatment as supportive and symptomatic. The treatment is mainly symptomatic and oxygen therapy, the latter being mainly required in severe cases.[80] Because there is no prior experience of therapy, the current treatment of novel-n COV is based on a limited number of therapeutics and pharmacological preparations. WHO and CDC are working hard to support randomized and non-randomized control trials to find out options for treatment.[81]

Patients having fever must be treated with antipyretic drugs. The most commonly used drugs for this purpose include Ibuprofen (orally 5-10mg/kg every time) and Acetaminophen (orally 10-15mg/kg every time). WHO encourages the intake of fluids, multivitamins as immunity boosters. Patients require increased protein and nutritional support while isolated in hospital wards or at home. So, to boost the immunity of the patients, a protein-rich diet and multi-vitamins particularly vitamin C should be an essential part of the daily diet. However, those who are unable to take it orally should be supported with high protein/low glucose formulas parenterally.[82]

Remdesivir has been found effective in patients of coronavirus. Remdesivir exhibits broad-spectrum antiviral activity against RNA viruses. The dose under investigation for the treatment of COVID-19 is 200mg intravenously (IV) on day 1 and then followed by 100mg IV daily for up to 10 days, infused over 30-60 minutes.[83] Immediate oxygen therapy must be provided in severe cases either by oxygen mask or nasal catheter.[84]

In COVID-19 patients with decreased arterial oxygen partial pressure leading to severe hypoxia and tachypnoea, acetazolamide has been found effective in the regard that it improves minute ventilation and also decreases elevated lactate dehydrogenase levels caused by hypoxia. Other drugs such as nifedipine and phosphodiesterase inhibitors can also be used for the same purpose.[85] Patients with severe pneumonia (also seen in patients infected with novel coronavirus) have activated platelets and clotting factors which can further complicate the condition. So, aims are at assessing the efficacy of anti-thrombotic treatment including aspirin and low-molecular-weight heparin (LMWH). However, aspirin has been found effective in patients with severe pneumonia.[86]

Chloroquine and hydroxychloroquine have also been found effective in the treatment of infected patients at early stages. WHO has banned its trial due to complications faced in patients but recently has permitted its reuse in clinical trials.

WHO RECOMMENDATIONS FOR PREVENTION:

As there is no vaccine currently available for COVID-19, the best prevention is to avoid exposure to the virus. Use of face masks and gloves, hand sanitizers, covering mouth and nose with a flexed elbow while coughing and sneezing and avoiding contact with the infected person while maintaining proper distance as well as refraining from touching nose, eyes, the mouth can reduce the risk of exposure. [87] According to WHO, personal protection equipment (PPE) should be used where there is a high risk of infection.[88]

Temporary isolation areas should be formed for suspected cases and the surfaces that are frequently in contact with the patient must be disinfected regularly.[89] Active corona patients should be kept in strict isolation for two weeks until the lab tests return to be negative.[90] Travelers from other countries who develop symptoms either during travel or within 14 days of their return should seek medical attention. Complete isolation for 14 days should be practiced after traveling.[91,92] Screening tests should be done at the point of entry and free testing for maximum health coverage to avoid an outbreak in migrants and refugees.[93] Neonates born to COVID positive mothers should be quarantined as they can be the carrier since vertical transmission is not yet ruled out.[94] Media Tools should be used for health education empowerment to practice preventive measures at the global level.[95] Telemedicine to be used for decreasing patient overload in the hospitals for avoiding transmission.[96] Cancellation of mass gatherings, closing public transports, dismissal of educational institutes, and workplaces shall be conducted. [32]

Efforts of Government of Pakistan:

The government of Pakistan took many measures to stop the spread of viruses e.g establishment of quarantine centers, testing facilities, designated hospitals, public awareness campaigns, implementing lockdown, and social distancing.[97] Moreover, the government of Pakistan has established a COVID-19 relief fund for the public.[98] Isolation wards were established all over Pakistan and there are designated hospitals for the treatment of Corona patients.[99] All schools, colleges, and universities were closed on 13th March 2020 to avoid the further spread of the virus. Daily wage labor is the most vulnerable part of Pakistan's population. Pakistan's labor force comprises of 72.5 million people. As a developing country, it was not possible for the government to support the daily basic needs of all wagers. Thus, a partial lockdown was implemented by the government.[100,101] The government of Pakistan laid stress on the community for social distancing and self-isolation to stop the spread of the virus.[102] After the declaration of the corona outbreak as a Public Health Emergency of International Concern (PHEIC) by the WHO, the Government of Pakistan issued a National Preparedness and Response Plan for COVID-19. This included Guidelines/SOPs

for different sectors to comply strictly to reduce the spread of this disease.[103] Besides all these efforts, there were many challenges faced by the Government of Pakistan. Misinformation, lack of public awareness, false interpretations, and rumors made it difficult to combat this pandemic.[104] A critical time for all the stakeholders of the government to establish an efficient control system to combat COVID-19 with community participation and multisectoral coordination is required.[30] Large masses of Pakistan are not well aware of the gravity of the situation because of illiteracy. Moreover, many doctors and patients are losing their lives to face the challenge.[105,106] Being a propagated epidemic and human to human transmission, social distancing, home quarantine, isolation of cases are the most effective measures to combat this pandemic.

AUTHOR'S CONTRIBUTION:

KN: Literature search and write up of WHO recommendations for prevention
LJ: Literature search and write up of treatment
MUZ: Literature search and write up of sign and symptoms
IM: Finalization of write up, supervision and critical analysis
KN: Literature search and write up of epidemiology of coronavirus
MS: Literature search and write up of public health emergency of international concern to pandemic
NF: Literature search and write up of herd immunity
RS: Literature search and write up of emergence of Wuhan epidemic
MM: Literature search and write up of COVID-19 in Pakistan
DA: Literature search and write up of history of pandemics

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