Coronavirus (Covid-19) Pandemic: Outbreak, Current Scenario, and Impact on Human Physiology In Pakistan

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ABBREVIATIONS:

1. COVID-19: Coronavirus disease 2019
2. SARS-CoV2: Acute respiratory syndromecoronaviruses 2
3. SARS-CoV: Severe acute respiratory syndrome coronavirus
4. MERS-CoV: Middle East respiratory syndrome coronavirus
5. H1N1: Hemagglutinin Type 1 and Neuraminidase Type 1
6. H5H1: Hemagglutinin Type 5 and Neuraminidase Type 1
7. MHS: Ministry of Health Services
8. OPDs: Out-Patient Departments
9. ARDS: Acute respiratory distress syndrome
10. 1ORF1: The open reading frame
11. PCR: Polymerase chain reaction
12. MM: Molecular mass
13. ACE-2: Angiotensin-converting enzyme-2
14. GSK: Glaxo Smith Kline
15. RdRp: RNA-dependent RNA polymerase
16. KPK: Khyber Pakhtunkhwa
17. AJK: Azad Jammu and Kashmir
18. ICT: Islamabad
19. GB: Gilgit-Baltistan
20. ARDS: Acute respiratory distress syndrome
21. IL-6: Interleukin 6
22. CRP:C-Reactive Protein
23. NDMA: The National Disaster Management Authority
24. NIH: National Institute of Health
25. ssRNA: single-stranded RNA
26. WHO: World Health Organization

Abstract

Coronavirus that is also known as COVID-19 disease is produced by SARSCoV-2. This causative agent is highly contagious and can cause potentially fatal pneumonia worldwide with serious public health concerns. In the beginning among infected individuals, most of them were those who were mainly shown to the wet animal market in a big city of China known as Wuhan. So, it was suggested that this was almost certainly the zoonotic source of COVID-19illness. The transitional source of origin and their mode of transmission to humans were not known obviously. Conversely, from human to human rapidly transformation have been confirmed generally. Currently, there is no availability of FDA approved clinically antiviral drugs and/or vaccines to be used against the COVID-19. Afterward, SARS-CoV and MERS-CoV, the occurrence of SARS-CoV-2 has been manifested as the third sketch of an enormously pathogenic coronavirus into human population globally. In this review, we provide a brief overview of the history of COVID-19 in Pakistan up-to 18th weeks after beginning, current situation, epidemiology, and its impact on the human population. Moreover, we focused on physiological variation during the incubation period, genome analysis of SARS-CoV2, supportive treatment approaches, and safety measures in the Pakistani population, which may be supportive for combating the risk of COVID-19 epidemic. We also reviewed the future approaches for the development of therapeutic interventions and vaccines to cope with the COVID-19 epidemic.

Keywords: Coronaviruses; COVID-19; Pakistan; current situation; human physiology; diagnosis; treatment

Introduction

Coronaviridae is a family of coronaviruses which belong to the order of Nidovirales. The crownish appearance of spikes on the virus' surface; therefore, it was known as a coronavirus [1]. The diameter of coronaviruses is approximately 65-125 nm and the capsid material of corona is containing a single-stranded RNA. The sub-categories of coronavirus are including alpha [α], beta [β], gamma [γ] and delta [δ] coronavirus. The genomic sequence of SARS-CoV-2 has shown a 99% similarity to the genome of SARS-CoV. Historically, SARS-CoV and MERS-CoV, H1N1, and H5N1 influenza-A are the main known epidemics causing acute respiratory distress and lung injury that can lead to pulmonary failure and leading to mortality and morbidity [2, 3]. Coronaviruses were considered to infect only animals until 2002, when the world seen a SARS CoV's disease caused by SARS-CoV, in Guangdong, China [4, 5]. SARS was ultimately controlled utilizing rapid isolation of patients; strict execution of infected person to quarantine along with their associates, inter-connecting of all person to person transmission is controlled, and all these precautionary measures successfully and efficiently eliminated the risk of SARS-CoV [6]. Recently during the last quarter of 2019, coronavirus which was named as novel coronavirus SARS-CoV-2, occurred in Wuhan, China, that have killed over a large population due to rapid spread of coronavirus infection [7]. To date 12 April 2020, COVID-19 is affecting 214 countries and territories all around the world. There are still a lot of un-known mechanisms associated with the COVID-19 outbreak; all these are causing severe illness and even subsequently several deaths, have been reported in China, the USA, Spain, Italy, Pakistan, and other worldwide countries [8]. In this mini-review, we analyzed a brief overview about the history of COVID-19 new confirmed cases and death cases according to per weeks in Pakistan, Current situation of COVID-19 in Pakistan and countries comparison analysis of COVID-19 outbreak. Moreover, focused on physiological variation during different stages of incubation periods and WHO supportive treatment strategies and safety measure during SARS-CoV2 viral replication cycles, which may be supportive for combating the risk of COVID-19 epidemic. We also reviewed the future approaches for development of therapeutic interventions and vaccines to cope with the COVID-19 epidemic.

Emerging and current scenario of COVID-19 in Pakistan

New confirmed cases of COVID-19 per weeks in Pakistan

In Pakistan, after the detection of the first 2 cases of COVID-19 on 26 Feb 2020 in Sindh Province, the number of coronavirus infected patients were gradually increased up to 8th

weeks. In 1st week, 4 cases of COVID-19 were reported in Sindh, in 2nd week, by the Ministry of Health Services (MHS) total 15 no. of COVID-19 cases in different provinces and cities of Pakistan such as 10 cases in Sindh, 1 case in Balochistan, 2 cases in both Gilgit-Baltistan (GB) and Islamabad (ICT) were reported. In 3rd week, the no. of new reported cases were increased up-to 219 in different provinces and cities of Pakistan such as in Punjab, Sindh, Balochistan, KPK, GB, and ICT are 26,158,14, 17,1 and 3 cases respectively. In 4th week, total 762 new confirmed cases were reported in Punjab, Sindh, Balochistan, GB, KPK, ICT, and AJK are 270, 241, 100,78, 61,11 and 1 respectively, in 5th week, total 1039 no. of cases were reported in the different large area of cities such as in ICT and GB; the announced confirmed cases of COVID-19 are 38 and 103 and in provinces such as Punjab, Sindh, KPK and Balochistan are 412, 263, 175 and 43 cases of coronavirus were reported respectively, in 6th week the outbreak of novel coronavirus were increased gradually and new reported cases in 6th week are reached up-to digit 1,322. In the 7th week total of 1,915 new cases of COVID-19 were reported in provinces and different cities in Pakistan such as Punjab, Sindh, KPK, Balochistan, AJK, GB, and ICT are 915, 532, 336, 35, 27, 22 and 48 respectively. Similarly, in 8th weeks total of 3786new cases were reported in Punjab, Sindh, KPK, Balochistan, ICT, GB, and AJK are 1383, 1535, 505, 255, 54, 49 and 5 respectively. In the week 9th total of 5114 confirmed new cases were reported in Sindh, Punjab, KPK, Balochistan, ICT, Gilgit-Baltistan, and AJK are 2338,1499,793,420,103,47 and 14 respectively. At the end of 18th weeks (26 June 2020) total no of 209,337 confirmed cases of COVID-19 were reported in Pakistan **(Figure. 1A)** [9-11].

Death cases of COVID-19 per weeks in Pakistan

The first death case was reported in 4th week, Pakistan, a total of 7 no. of death cases were reported in this week, 3 in KPK and 4 death cases were declared in Punjab, Sindh, Baluchistan, and GB. Similarly, in the 5th, 6th, 7t, 8th, and 9th weeks, the reported deaths were steadily increased up-to 19, 31, 50,102, 118 respectively. At the end of the 18th weeks; a total of 4304 cases of death cases were announced **(Figure. 1B)** [10, 12].
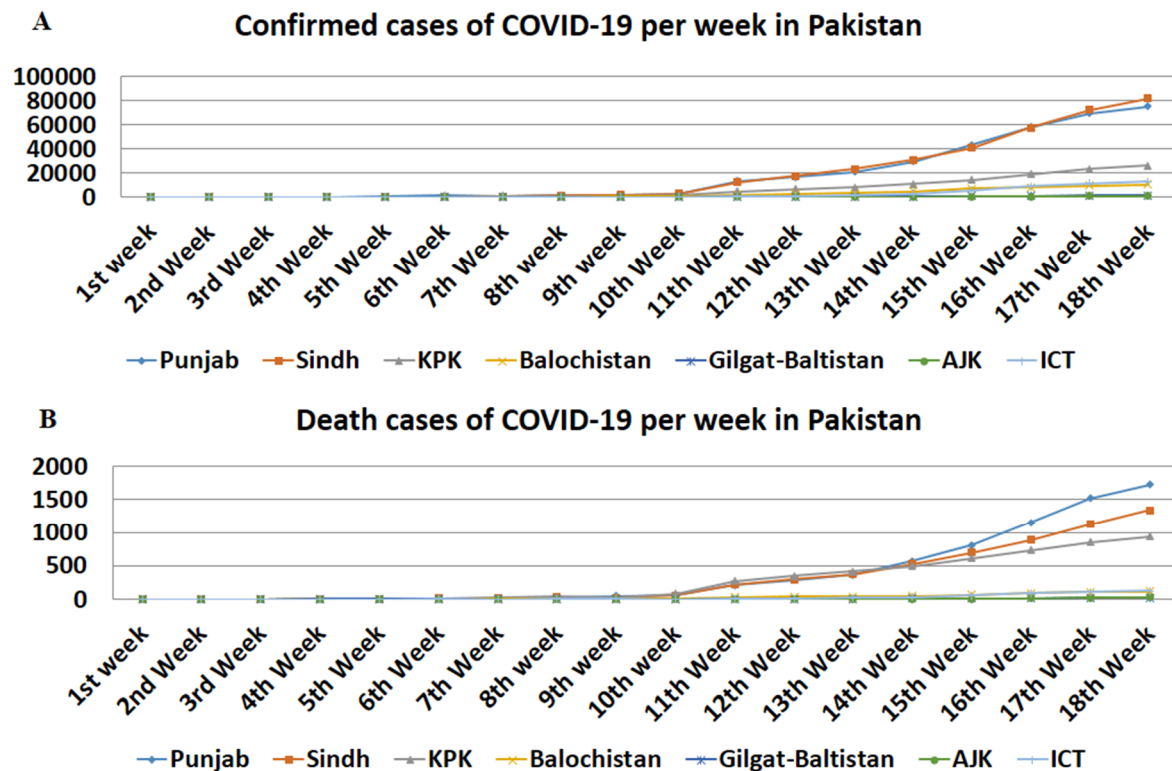
Figure 1: (A) and (B) represent that the new cases and death cases of COVID-19 up-to 10th weeks in Pakistan respectively. Blue, red, green, purple, froze, orange and sky-blue lines were shown in the cases of COVID-19 in Punjab, Sindh, KPK, Baluchistan, GB, AJK, and IST respectively. The upward movement of these lines represents that increase in number and also death rate of COVID-19 cases according to weeks.

Beginning and pathway analysis of Coronaviruses's transmission

Human diseases are transmitted due to interactions of host and environmental factors (droplet, polluted air, etc.). Although few diseases are mainly genetic in origin and nearly all disease consequences occur from an interaction of several parameters such as environmental, behavioral, genetic factors are responsible to extents of variations in different diseases/infections. Various underlying protocols are mainly responsible for the transmission of infections. Hence in the current review, we also discuss the approaches of infection origin and their mode of transmission. Coronavirus infection-19 is an extremely pathogenic and contagious viral disease. Previously, chines people were infected with a respiratory virus causing SARS in 2003, Guangdong province, China. People infected with SARS-CoV developed symptoms of pneumonia along with alveolar damage in the lungs that led to ARDS[13]. Secondly, a decade later, several peoples in Saudi Arabian were inspected to be

diseased with another kind of coronavirus in 2012. The isolated virus belonged to the class of coronaviruses and entitled to the MERS-CoV. The MERS-CoV infection causes a minor upper respiratory tract injury and leads to the progression of severe respiratory infection/disease [14]. Currently, in December 2019, the Chinese government informed the World Health Organization about numerous cases of pneumonia along with unaware etiology. The transmission of COVID-19 is based on huge numbers of the Chinese population in Wuhan city, China. In the human seafood market, where the animals such as frog, bats, birds, rabbits, snake, and marmots were frequently been sold and it is proposed that all these are the probably belong to the zoonotic origin of coronaviruses. The first report recognized that few species of bats and snakes which could be a potential source of coronaviruses. Only α and β sub-categories of coronaviruses can cause disease in humans, the feeding of infected animals mainly bats, and snakes are the main sources of food for chines peoples. And this route is the main source of virus transmission from animal to human due to close contact with the infected person; the virus is also transmitted to healthy people**(Figure 2).**Various surveys have recommended that human to human contact mainly by sneezing and coughing is a possible route for COVID-19 infection transmission [15].
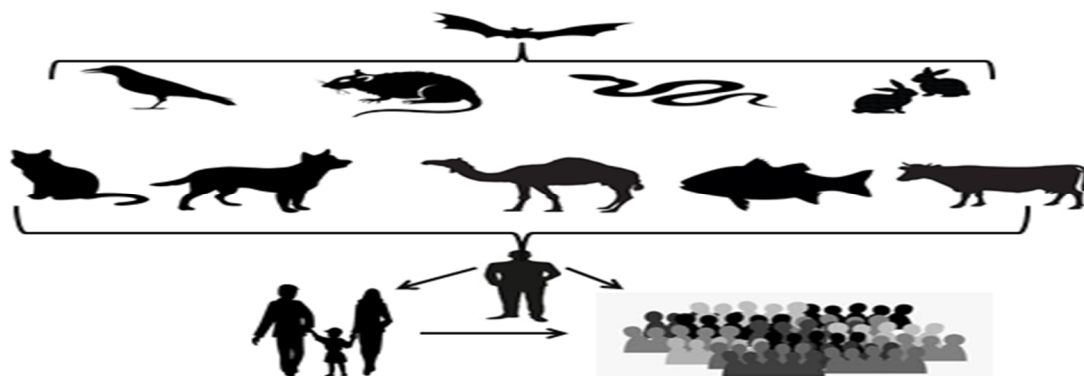

Figure 2: Suspected ways of SARS CoV-2 outbreak transmission from bats to humans

Approved Diagnostic test for COVID-19 in Pakistan

On 12 March 2020, The National Institute of Health in Pakistan has recommended Reverse transcriptase, Polymerase chain reaction (RT-PCR) test for batter diagnosis and detection of SARS-CoV2. In different cities across the country, different laborites have established with RT-PCR system that facilitates the free test for COVID-19. Up to 18-weeks, till 30 June

2020, in Pakistan; total1283092 number of tests were conducted for COVID-19 detection and about 20, 9336were reported as positive respectively **(Figure. 3)**. The ratio of confirmed cases of COVID-19 was progressively increasing in different provinces of Pakistan, such as in Punjab, Sindh, KPK, Baluchistan, ICT, Gilgit-Baltistan, and AJK are 36.06%, 39.16%, 12.47%, 4.98%, 6.70%, 0.70%, and 0.50% respectively (**Figure. 4**). The NDMA works with the NIH to increasing the research laboratories for detection of COVID-19 from 15 to 50, in edict to boost the research quality. The new research laboratories will be established in distinct cities all over the country. Similarly, Pakistan is starting a training program for paramedics and laboratory staff to resolve the shortfall. NDMA will recruit 100 molecular-biological laboratory technicians [10, 16-18].
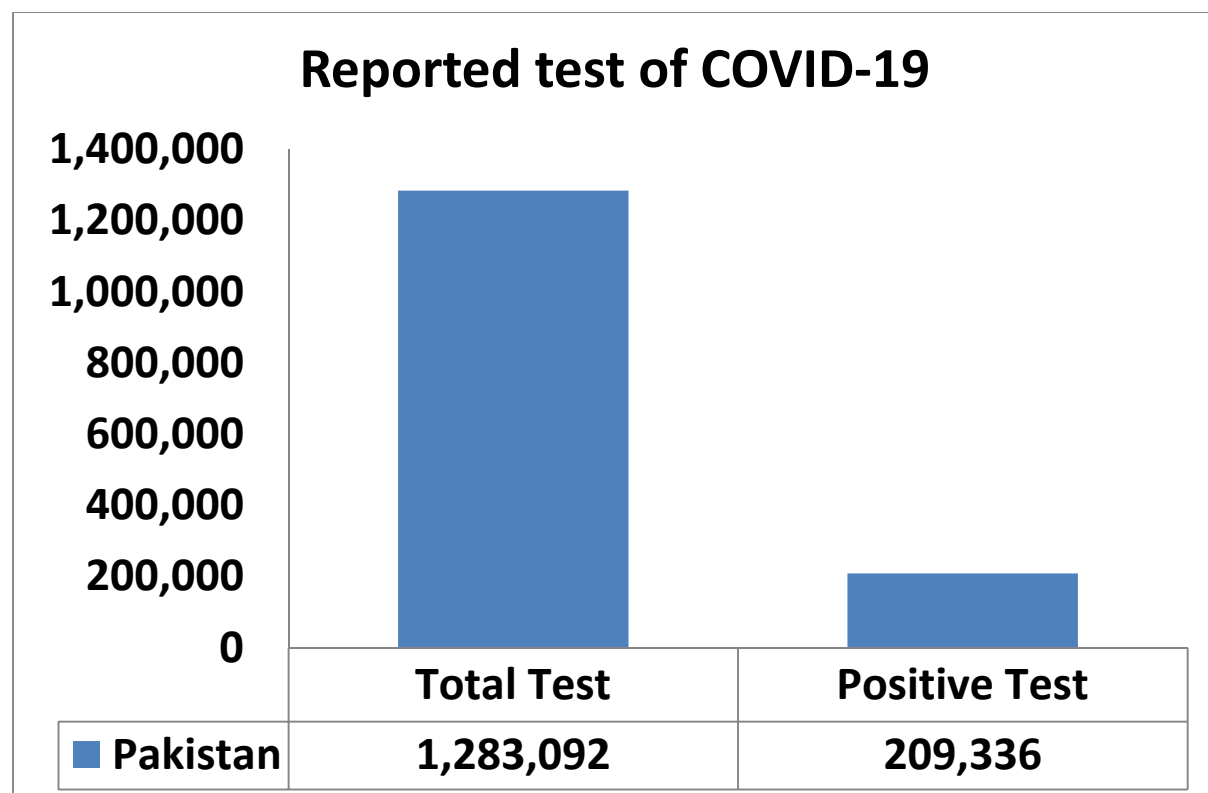

Reported test of COVID-19

	Total Test	Positive Test
■ **Pakistan**	**1,283,092**	**209,336**

Figure 3: Represent that the analysis of COVID-19 reported test in Pakistan
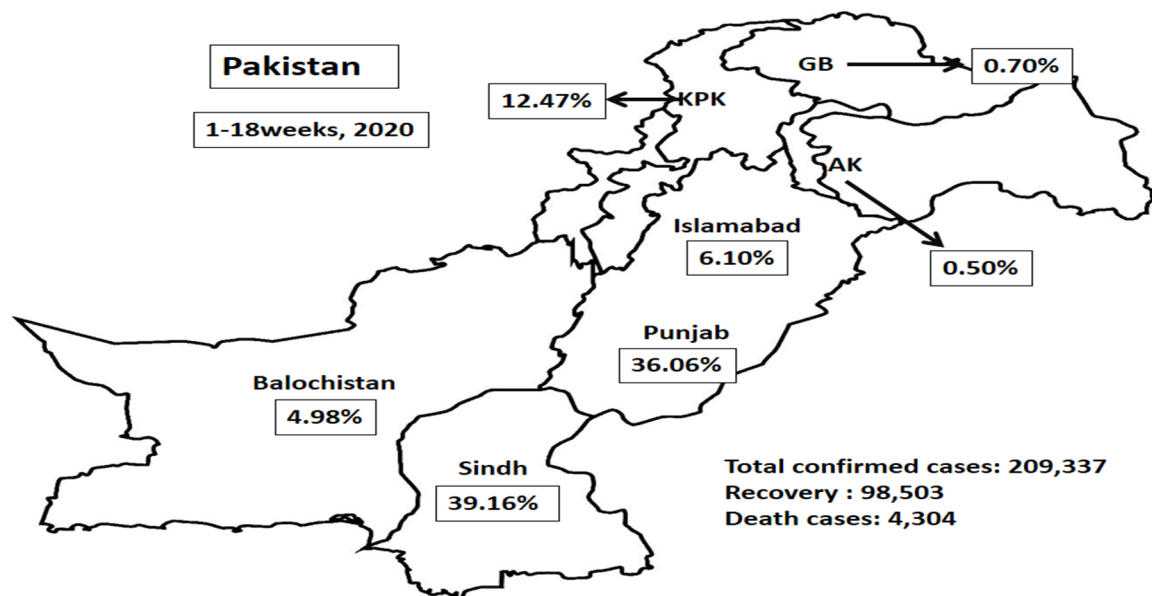
Figure 4: Current scenario of COVID-19 in Pakistan

COVID-19 Impact on human physiology

The incubation duration of COVID-19 is nearly $5^{1/2}$ days and the symptoms of COVID-19 exhibit after the incubation period. The approximate duration from the appearance of the symptoms to death can range from 0 to 14 days [19].Mainly the duration is dependent on the patient's immunity and age. The impact of COVID-19 on human physiology was appearing in the forms of influenza, runny nose, coughing, fever, headache, dyspnea, diarrhea, shortness of breath and lymphopenia [20-24].Medical features exposed by a CT-scan of the chest were symbolized as pneumonia, contrariwise others infrequent sorts such as acute cardiac injury and acute respiratory distress syndrome prevalence; that led to death **(Figure.5)** [25, 26].
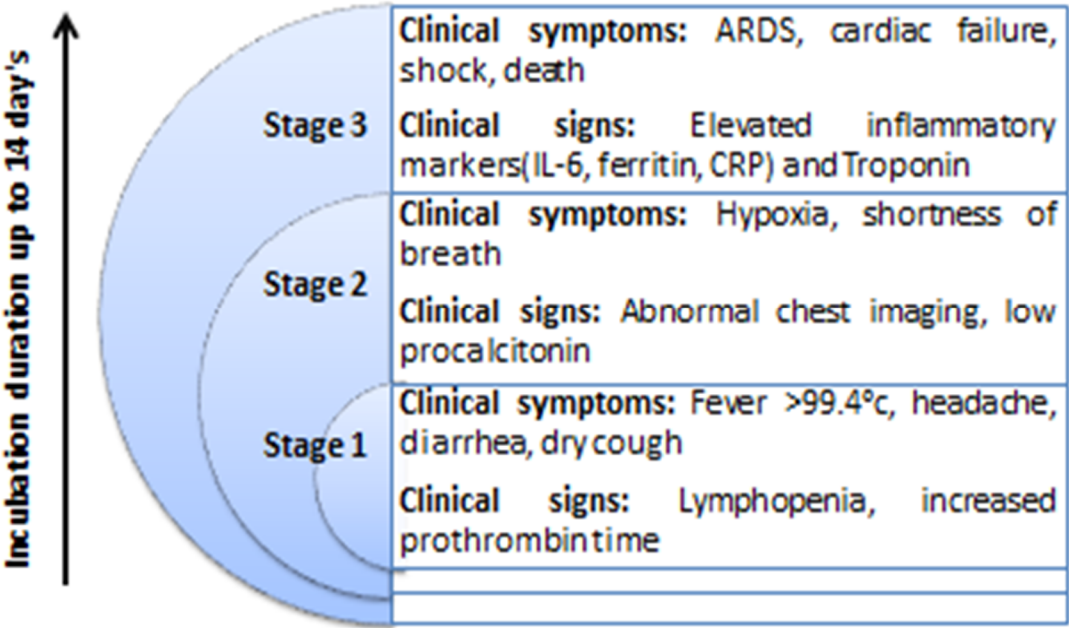
Figure 5: Represent the clinical sign and symptoms of COVID-19 infection at different stages during their incubation period of viral infection (27).

Structure and Genomic analysis of SARS CoV-2

The genomic sequence of the SARS-CoV-2 has been reported having more than 80% similarity to the previously detected human coronaviruses SARS-CoV [28]. The genome of SARS-CoV-2 comprises of10 open reading frames (ORFs). In SARS-CoV-2the biggest genes which encode the proteolytic processing (pp1ab) protein and 15 naps (non-structural proteins) for viral replication is ORF1ab gene [29, 30]. In SARS-CoV and MERS-CoV, two pp1a and pp1ab polyproteins are translated into seventeen non-structural proteins (nsp1-nsp16), which form the transcriptase complex of viral replicas that initiates viral transcription and replication [31, 32]. Similarly, SARS-CoV-2 ORFs on the 1/3 of the genome encode four core structural proteins such as spike (S), membrane (M), nucleocapsid (N), and envelope (E) proteins that may be involved in viral replication [33, 34]. Accordingly, some previous investigations and few current studies showed that COVID-19 's genomic research associates the β-coronavirus genus **(Figure. 7)** [35, 36].
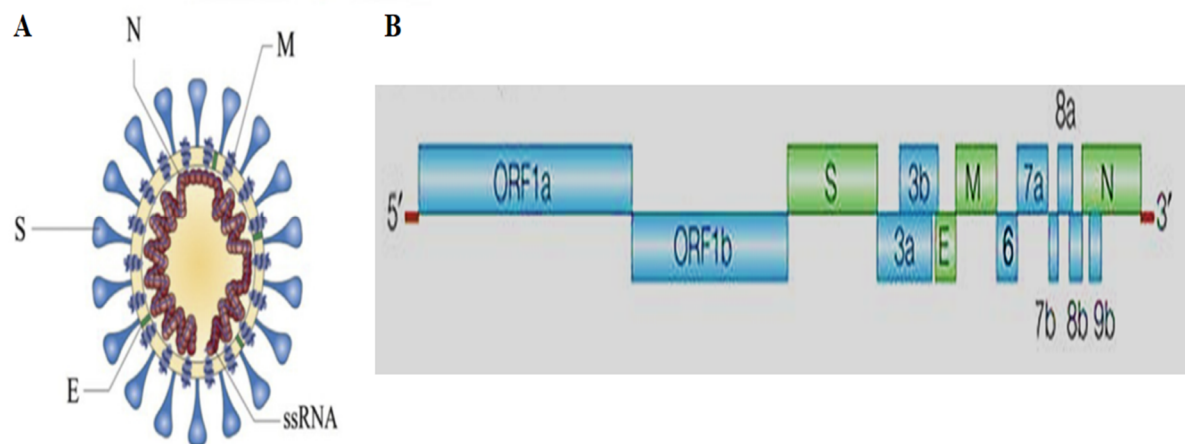
Figure 6:(A) Representing coronaviruses type enveloped and 100-160 nm diameter spherical particles. They contain a ssRNA genome 26-32 kb in size. **(B)** Reflect all the SARS-CoV2 genome sequences. In SARS-CoV-2, ORF1a / b encoded polyproteins that are two-thirds of the 5- terminal genome, forming the transcriptase complex of viral replicas. The four major structural proteins, Bolt, shell, nucleocapsid and membrane encoded by the other one-third ORF genome, and some accessory proteins (37).

Supportive treatment and preventive measure against COVID-19 in Pakistan

There is no availability of vaccine and approved anti-viral drugs against COVID-19 worldwide. Specialized Department of Health and Medical Education, Government of Punjab, Pakistan, is providing supportive management for PCR-positive COVID-19 infected patients which included, oxygen saturation and inhalation, vitals monitoring, supportive management by carefully use of I/V fluid. The WHO has announced the largest global trial that would help to manage coronavirus infections. According to such a trial report, few anti-viral drugs were recommended to treat corona-viral infected ill patients. Included anti-malarial drug such as chloroquine / hydroxyl chloroquine have observed to act against COVID-19 infection and seems to decline the period of viral infection by inhibiting viral entry and endocytosis, Lopinavir and Darunavir have shown an effect to inhibits 3–chymotrypsin-like protease enzyme during proteolysis of viral RNA and Ribavirin is another anti-viral drug that has an act to inhibit viral RNA-dependent RNA polymerase (RdRp) during the translation process and inhibit RNA replication **(Figure.7)** [38-40].
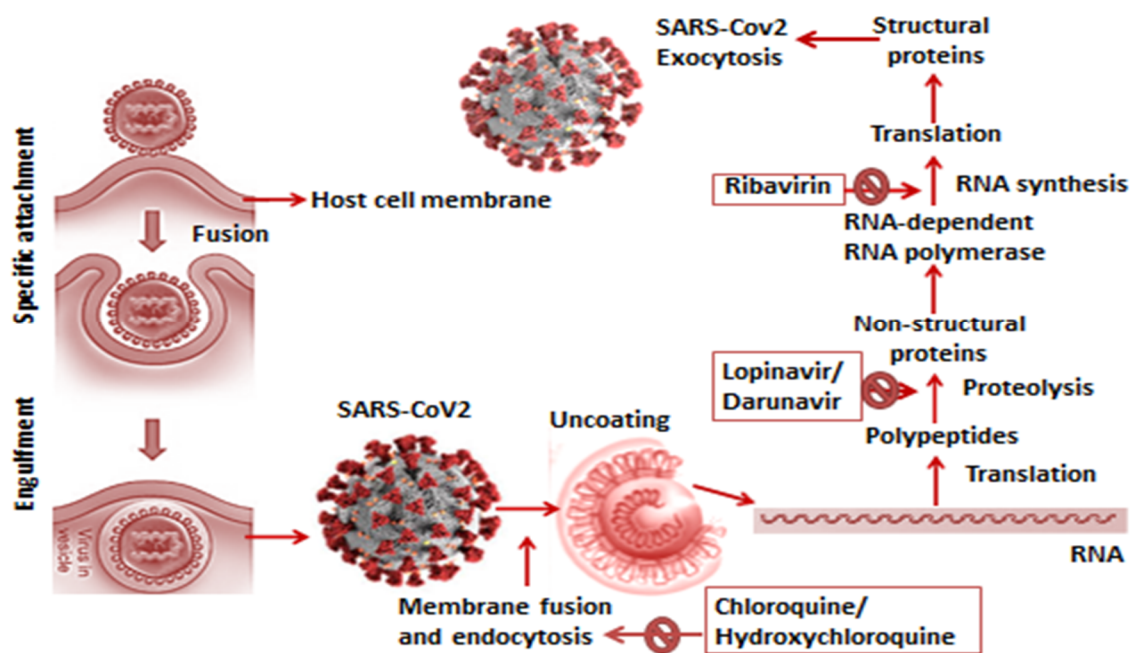
Figure 7: Represent the mood of action of treatment strategies being announced by WHO and their interaction with different steps in the coronavirus replication cycle (41).

Outcomes of continuing clinical trials are impatiently awaited. For preventive measures were essentially required to use gloves, eye protection, hand sanitizer, and N95 respirators for patients for medical staff along with all populations for safety, and also plenty of water and organ juice intakes are played a significant role for boosting up human immunity.

Future Prospects

Furthermost importantly working on human COVID-19 targeting antiviral drugs and vaccines should be designed that could be used against viral epidemics. Many companies such as Inovio California, Cancino Bio China, Pfizer & Biotech, Sanofi and GSK are working to effectively develop the vaccine against SARS-CoV-2. Researchers are working hard to advance / develop the required successful therapeutic approaches to manage the novel COVID-19. The transmission of COVID-19 influences the population, so if we adopt aggressive preventive measures, we can safe several human lives. A government recommended guideline should be practiced, diminishing the transmission from one person to another of COVID-19 and regulates the viral epidemic. The exact diagnosis will help to

monitor the rapid spread of the infection in the early stages of the epidemic [42]. Pakistan and all other countries will adopt primary anticipatory, control and preventive measures explicitly focusing on travel screening to regulate the further transmission of the outbreak of SARS-CoV2 [43].

Conclusion

China faced to COVID-19 in December 2019 and has been confirmed to clear the spread of coronavirus approximately after 5-months; few other countries such as South Korea has been capable enough to manage the outbreak of COVID-19, but numerous developing countries mainly Pakistan has not been well-off. The pandemic of COVID-19 is looking more catastrophic and disaster effect than the 2nd World War. Pakistan would extremely be affected by COVID-19 outbreak and mainly impact on the socio-economic situation in different fields/sectors. In this review, we concluded the coronavirus epidemic up-to 18 weeks (30-June, 2020) in Pakistan and their outbreak was gradually increased in different provinces of Pakistan. The large no. of COVID-19 cases was seen in Sindh. Similarly, overall, about 2.06% of death ratio due to COVID-19 in Pakistan was reported. COVID-19 mortality rate accordingly to area division progressively increased in-order such as in Punjab, Sindh, Balochistan, Gilgit-Baltistan, and ICT are 2.28%, 1.64%, 1.90%, 2.62%, and 1.00% respectively. The mortality rate was highly testified in KPK about 3.58% and test conductance rate was reported fewer in KPK, this situation should be noticeable. Appropriate implementation of preventative measures and control of the COVID-19 outbreak now-a-day become a challenging phase for the Pakistan population.

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Author's Contributation

All authors contributed equally to this work.

Conflict of interest

The authors declare no conflict of interest.

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