Review Article

Coronavirus (COVID-19) pandemic: Outbreak, current scenario and impact on human physiology in Pakistan

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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 24th 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.

Abbreviations

COVID-19: Coronavirus Disease 2019; SARS-CoV2: Acute Respiratory Syndrome Coronaviruses 2; SARS-CoV: Severe Acute Respiratory Syndrome Coronavirus; MERS-CoV: Middle East Respiratory Syndrome Coronavirus; H1N1: Hemagglutinin Type 1 and Neuraminidase Type 1; H5H1: Hemagglutinin Type 5 and Neuraminidase Type 1; MHS: Ministry of Health Services; OPDs: Out-Patient Departments; ARDS: Acute Respiratory Distress Syndrome; 1ORF1: The Open Reading Frame; PCR: Polymerase Chain Reaction; MM: Molecular Mass; ACE-2: Angiotensin-Converting Enzyme-2; GSK: Glaxo Smith Kline; RdRp: RNA-dependent RNA polymerase; KPK: Khyber Pakhtunkhwa; AJK: Azad Jammu and Kashmir; ICT: Islamabad; GB: Gilgit-Baltistan; ARDS: Acute Respiratory Distress Syndrome; IL-6: Interleukin 6; CRP: C-Reactive Protein; NDMA: The National Disaster Management Authority; NIH: National Institute of Health; ssRNA: single-stranded RNA; WHO: World Health Organization

Introduction

Viruses can lead to dangerous lives; they threaten people and

cause irreparable damage to them. The world is unlikely to learn to deal with the virus strain when another appears and poses a threat to future humanity. A similar situation arose when a new strain of novel Coronavirus (CoV) that hasn't been there before was previously identified in people reported in December 2019 [1]. Coronaviruses are the largest among RNA Coronaviridae, Roniviridae and Families Arteriviridae. Coronaviridae is not segmented; 3'-polyadenylated and 5'-encapsulated positive single-stranded RNA viruses cause various respiratory diseases in people [2]. The coronaviruses' diameter is approximately 65-125 nm and the capsid material of the corona contains 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 major known epidemics causing acute respiratory distress and lung injury, leading to pulmonary failure and mortality, and morbidity [3,4]. Coronaviruses were considered to infect only animals until 2002 when the world has seen a SARS CoV disease caused by SARS-CoV in Guangdong, China [5,6]. SARS was ultimately controlled utilising 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 [7]. 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 the rapid spread of coronavirus infection [8]. On Mar 30, 2021, COVID-19 is affecting 219 countries and territories all around the world. There are still many un-known mechanisms associated with the COVID-19 outbreak; all these are causing severe illness. Even subsequently, several deaths have been reported in China, the USA, Spain, Italy, Pakistan, and other worldwide countries [9]. In this mini-review, we analysed 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 detecting the first 2 cases of COVID-19 on Feb 26, 2020, in Sindh Province, the number of coronavirus infected patients was gradually increased up to the 8th weeks. In 1st week, 4 cases of COVID-19 were reported in Sindh, in 2nd week, by the Ministry of Health Services (MHS), a total of 15 no. of COVID-19 cases in different provinces and cities of Pakistan such as 10 cases in Sindh, 1 case in Baluchistan, 2 cases in both Gilgit-Baltistan (GB) and Islamabad (ICT) were reported. In the

3rd week, the no. of new reported cases was increased up-to 219 in different provinces and cities of Pakistan such as in Punjab, Sindh, Baluchistan, KPK, GB, and ICT are 26,158,14, 17,1 and 3 cases respectively. In the 4th week, a total of 762 new confirmed cases were reported in Punjab, Sindh, Baluchistan, GB, KPK, ICT, and AJK are 270, 241, 100,78, 61,11 and 1 respectively, in 5th week, a total of 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 Baluchistan are 412, 263, 175 and 43 cases of coronavirus were reported respectively, in 6th week the outbreak of novel coronavirus were increased gradually. New reported cases in the 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, Baluchistan, AJK, GB, and ICT are 915, 532, 336, 35, 27, 22, and 48 respectively. Similarly, in the 8th week total of 3786 new cases were reported in Punjab, Sindh, KPK, Baluchistan, ICT, GB, and AJK are 1383, 1535, 505, 255, 54, 49, and 5, respectively. In week 9th, 5114 confirmed new cases were reported in Sindh, Punjab, KPK, Baluchistan, ICT, Gilgit-Baltistan, and AJK 2338,1499,793,420,103,47 and 14, respectively. Similarly, at the end of the 31st weeks (Oct 6, 2020) total no of 315,727 confirmed cases of COVID-19 was reported in Pakistan. Similarly, at the end of 36th weeks (end of October 2020) total no of 333,970 confirmed cases of COVID-19 was reported in Pakistan (Figure 1) [10-12].

Death cases of COVID-19 per weeks in Pakistan

The first death case was reported in the 4th week, Pakistan, a total no. 7 death cases were reported in a week, 3 in KPK and four 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. Similarly, at the end of the 31st week, a total of 6523 death cases were announced. Similarly, at the end of the 36th week, a total of 6823 death cases were announced (Figure 2).

The effectivity of the COVID-19 situation comparatively significantly distinct in a different province of Pakistan (Table 1). The highest COVID-19 cases were reported in Sindh province, while the lower COVID-19 cases were reported in AJK [13,14].

Beginning and pathway analysis of Coronaviruses' transmission

Human diseases are transmitted due to interactions of host and environmental factors (droplets, polluted air, etc.). Although few diseases are mainly genetic in origin and nearly all disease consequences occur from an interaction of several environmental, behavioral, and genetic factors, genetic factors are responsible for 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 transmission mode. Coronavirus infection-19 is an extremely pathogenic and contagious viral disease. Previously, Chinese people were infected with a respiratory virus causing SARS in
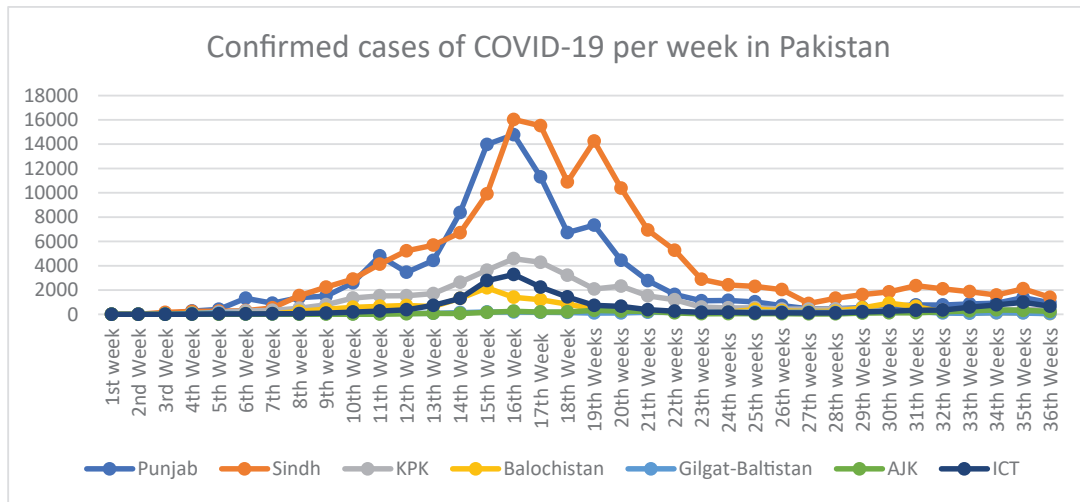
Figure 1: Represents that reported new cases of COVID-19 up-to 36th weeks in Pakistan, respectively. Blue, red, green, purple, froze, orange and sky-blue lines were shown in the cases of COVID-19 in Punjab, Sindh, KPK, Baluchistan, GB, AJK, and IST, respectively. According to weeks, these lines' upward movement represents an increase in the number and death rate of COVID-19 cases.
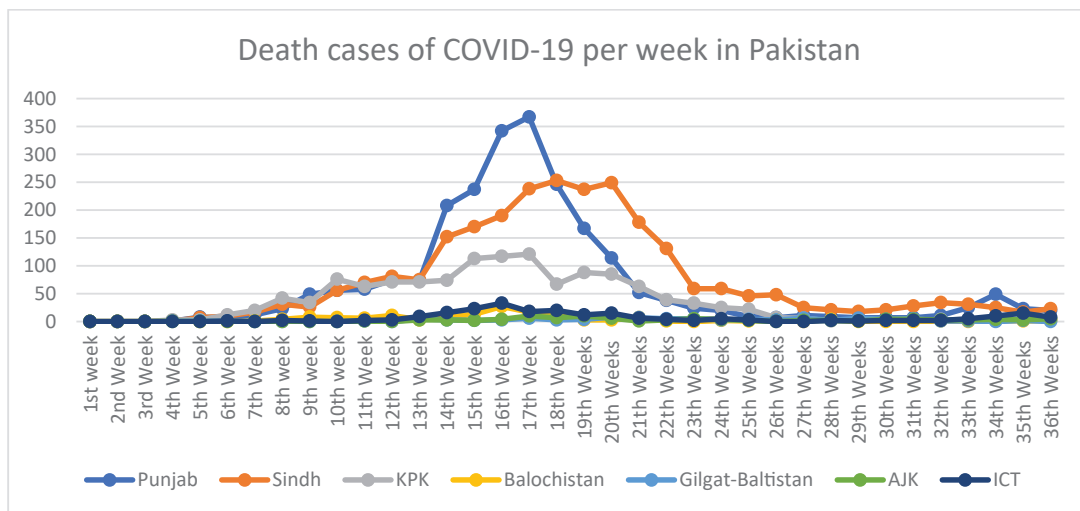

Figure 2: Represents that reported death cases of COVID-19 up-to 36th weeks in Pakistan, respectively. Blue, red, green, purple, froze, orange and sky-blue lines were shown in the cases of COVID-19 in Punjab, Sindh, KPK, Baluchistan, GB, AJK, and IST, respectively. According to weeks, these lines' upward movement represents an increase in the number and death rate of COVID-19 cases.

Table 1: The statistics of COVID-19 in a different province of Pakistan.

Province	Confirmed cases	Deaths
Punjab	104271	2362
Sindh	145851	2627
KPK	39564	1277
Baluchistan	15920	151
AJK	4133	92
ICT	19970	222
Gilgit Baltistan	4261	92

2003 in Guangdong province, China. People infected with SARS–CoV developed pneumonia symptoms and alveolar damage in the lungs that led to ARDS [15]. Secondly, a decade later, several Saudi Arabian peoples were inspected to be diseased with another kind of coronavirus in 2012. The isolated virus belonged to the class of coronaviruses and was entitled to the MERS–CoV. The MERS–CoV infection causes a minor upper respiratory tract injury and leads to severe respiratory infection/disease [16]. In December 2019, the Chinese government informed the World Health Organization about numerous pneumonia and unaware aetiology cases. 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 frogs, bats, birds, rabbits, snakes, and marmots were frequently sold, and it is proposed that all these probably belong to the zoonotic origin of coronaviruses. The first report recognised that few bats and snakes could be a potential source of coronaviruses, but claims are still under discussion and require more subnational research to prove it [17-19]. 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 food sources for Chinese 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 3). Various surveys have recommended that human-to-human contact, mainly by sneezing and coughing, is a possible route for COVID-19 infection transmission [20].

Approved diagnostic test for COVID-19 in Pakistan

On Mar 12, 2020, The National Institute of Health in Pakistan had recommended Reverse transcriptase, Polymerase chain reaction (RT-PCR) test to better diagnose and detect SARS-CoV2. Different countries across the country have established with RT-PCR system that facilitates the free test for COVID-19 (Table 2). Up to 18-weeks, till Jun 30, 2020, in Pakistan, a total of 3,702,607 tests were conducted for COVID-19 detection, and about 315,727 were reported as positive, respectively (Figure 4). 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 5). The NDMA works with the NIH to increasing the research laboratories for detection of COVID-19 from 15 to 50 in mandate to boost the research quality. The new research laboratories will be established in different 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 [21,22-24].

Impact of COVID-19 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 symptoms' appearance to death can range from 0 to 14 days [25]. 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, diarrhoea, shortness of breath, and lymphopenia [26-30]. Medical features exposed by a CT-scan of the chest were symbolised as pneumonia, contrariwise others infrequent sorts such as acute cardiac injury and acute respiratory distress syndrome prevalence; that led to death (Figure 6) [31,32].

Structure and genomic analysis of SARS CoV-2

The genomic sequence of the SARS-CoV-2 has been reported to have more than 80% similarity to the previously detected human coronaviruses SARS-CoV [34]. 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 are the ORF1ab genes [35,36]. 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 viral replicas that initiate viral transcription and replication [37,38]. Similarly, SARS-CoV-2 ORFs on the 1/3 of the genome encodes four core structural proteins such as spike (S), membrane (M), nucleocapsid (N), and envelope (E) proteins that may be involved in viral replication [39,40]. Accordingly, some previous investigations and few current studies showed that COVID-19's genomic research associates the β-coronavirus genus (Figure 7) [41,42].

Supportive treatment and preventive measure against COVID-19 in Pakistan

There is no availability of vaccines and approved antiviral drugs against COVID-19 worldwide. Specialized Department of Health and Medical Education, Government of Punjab, Pakistan,
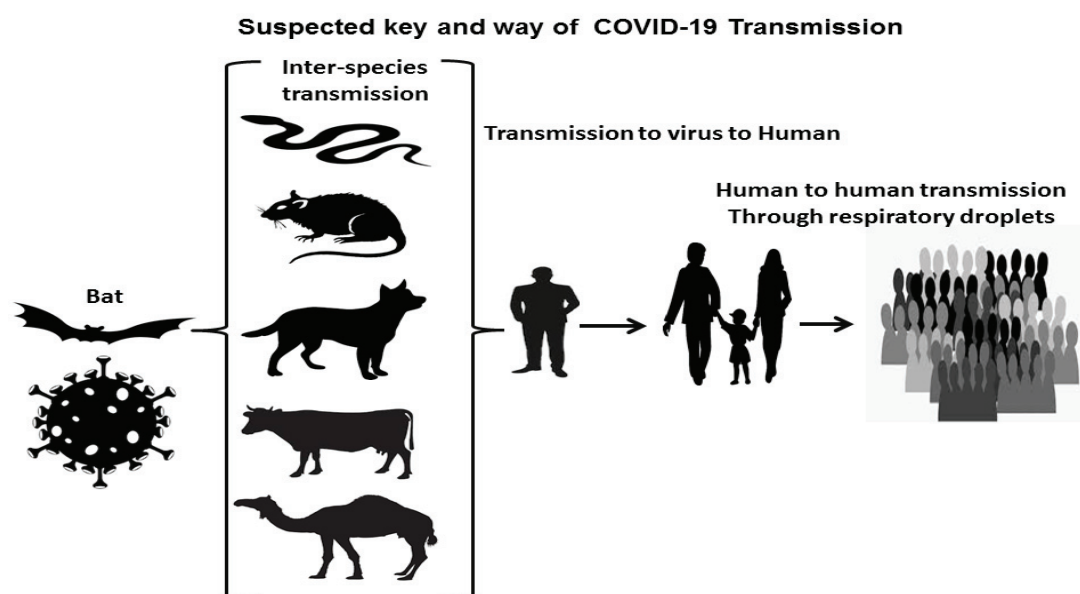

Figure 3: Suspected ways of SARS CoV-2 outbreak transmission from bats to humans.

Table 2: The COVID-19 test facilities in different laborites at distinct areas of Pakistan.

Sr.no	Province	City	Functional Lab/Category
	Punjab	Faisalabad	Public
1			Allied hospital
			Private
2			Abwa Hospital & Research Centre
		Lahore	Public
3			Punjab Forensic Science Auth Lab
4			Punjab AIDS Control Program incl Hepatitis Lab
5			Jinnah Hospital
6			CAMB
7			Lahore General Hospital
8			PKLI
9			Lahore TB Program
10			UVAS
11			IPH Lahore
			Private
12			Chughtai Lab (Pvt)
13			Shaukat Khanum Memorial Hospital (Pvt)
14			Zeenat Lab (Pvt)
15			Bahria Intl Hospital (Pvt)
16			University of Lahore (Pvt)
		Multan	Public
17			Nishtar Medical College
18			Private
19			Multan TB Program
		Rawalpindi	Public
20			Rawalpindi Medical University
21			Benazir Bhutto Hospital (BBH) Rawalpindi
			Private
22			Bahria Intl Hosp (Pvt)
23			Al-Khidmat Foundation Lab (Pvt)
24			Citi Lab (Pvt)
		Bahawalpur	Public
25			Civil Hospital
		Wazirabad	Public
26			Trauma Centre THQ
		DG Khan	Public
27			DHQ DG Khan
	Federal	Islamabad	Public
28			PIMS
29			National Institute of Health
			Private
30			Excel Labs
31			Akbar Niazi Teaching Hospital
32			Maroof Hospital
33			Shaafi Hospital
34			Nayyab
35			Kulsum Intl Hosp
36			Biogene
37			MedAsk
	Sindh	Karachi	Public
38			Liaqat National Hospital
39			Dow University
40			PCMD Karachi University
41			Civil Hospital
42			Jinnah PG Medical Institute
43			Civil Hospital North Karachi
			Private
44			Indus Hospital (Pvt)
45			Chughtai Lab
46			Hashmanis
47			Essa Lab
48			Ziauddin Hospital
49			Advanced Lab
		Hyderabad	Public
50			LUMHS
		Sehwan	Public
51			SASIMS
		Sukkur	Public
52			Gambit Institute
		Larkana	Public
53			Larkano Lab
	Baluchistan	Quetta	Public
54			Bolan Medical College
55			Regional Blood Centre (RBC)
56			Fatima Jinnah Hospital
		Taftan	Public
57			Mobile Diagnostic Unit
	Gilgit-Baltistan	Gilgit	Public
58			DHQ
		Chalas	Public
59			Chalas (TB Lab)
		Skardu	Army
60			CMH (Army)
	AJK	Muzaffarabad	Public
61			Abbas Institute of Medical Sciences
		Mirpur	Public
62			DHQ
		Rawlakot	Public
63			CMH
	KP	Peshawar	Public
64			Khyber Medical University
65			Khyber Teaching Hospital
66			Hayatabad Medical Complex
67			Leady Reading Hospital
68			Private
69			RMI
70			IDC
71			NWGH
		Abbottabad	Public
72			Public Health Lab Ayub Teaching Hospital
73			Private
74			Shaheena Jameel Hospital
		DI Khan	Public
75			Mufti Mehmood Memorial Teaching Hospital
		Mardan	Public
76			Mardan Medical Complex
		Bannu	Public
77			Khalifa Gul Nawaz Teaching Hospital
		Sawat	Public
78			Saidu Sharif Medical College Hospital
			Private
79			Anwar Lab

provides supportive management for PCR-positive COVID-19 infected patients, including oxygen saturation and inhalation, vitals monitoring, and supportive management use of I/V fluid. (Table 3). In Pakistan, there are different strategies followed to overcome the effect of COVOD-19. The government focuses on wearing a mask when you go to outside homes, social places, and marketplaces. During this should people maintain the stay 6 feet away/ social distance in the market or crowded places. While during daily life, people should wash their hands with hand sanitisers properly.
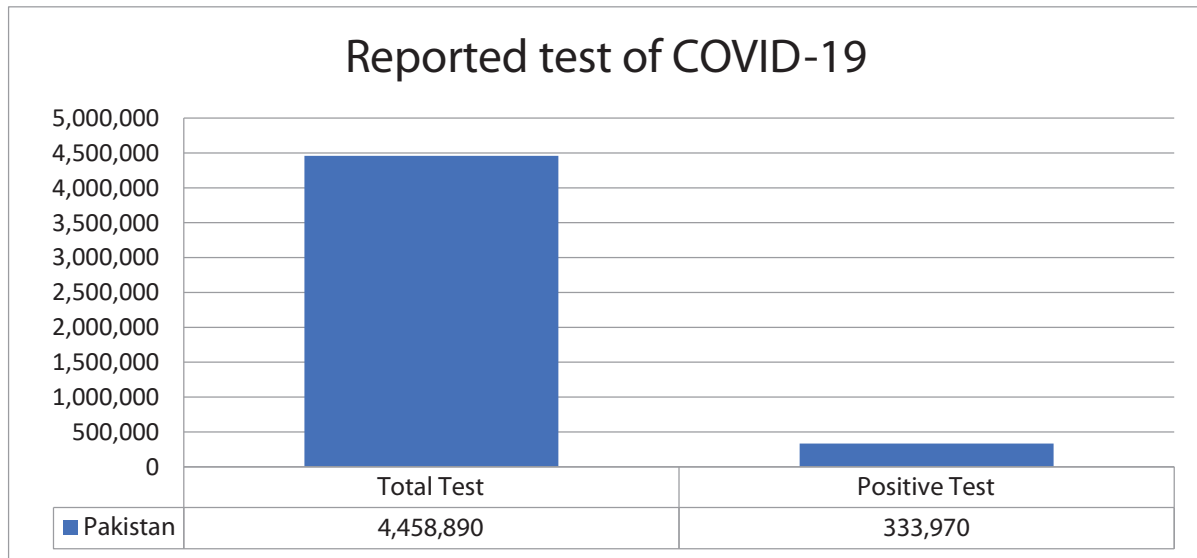
Figure 4: Represent that the analysis of COVID-19 reported test in Pakistan.
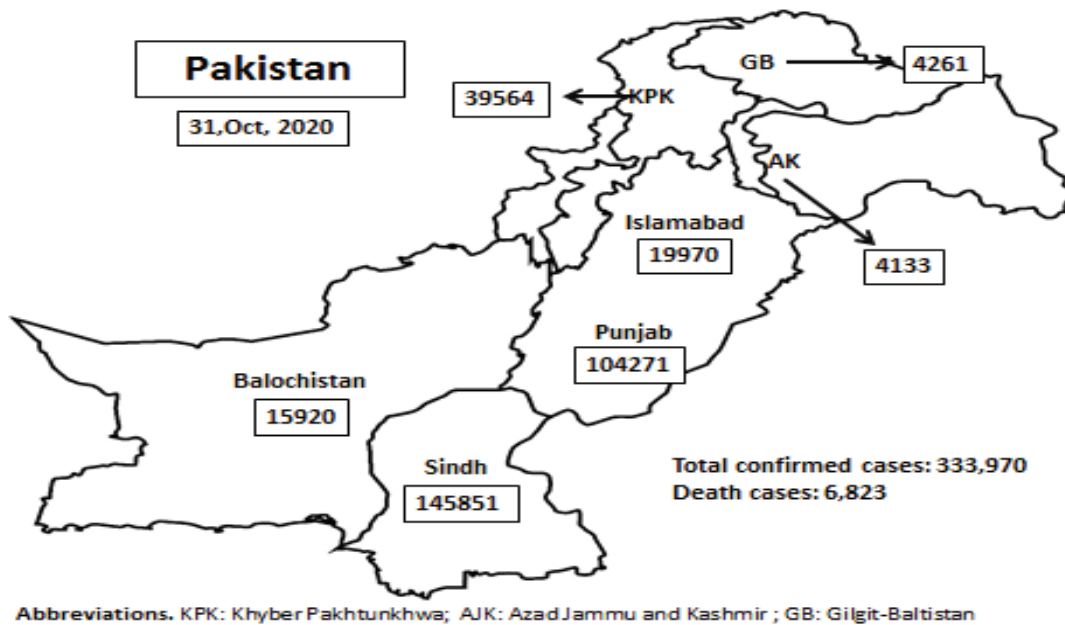

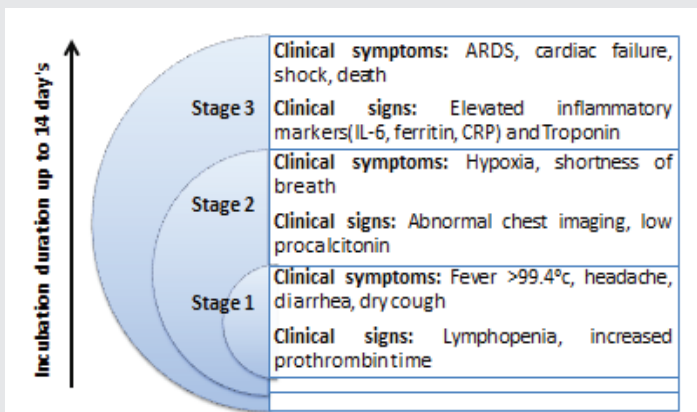**Figure 5:** The Current scenario of COVID-19 in Pakistan.

Figure 6: Represent the clinical sign and symptoms of COVID-19 infection at different stages during their incubation period of viral infection [33].
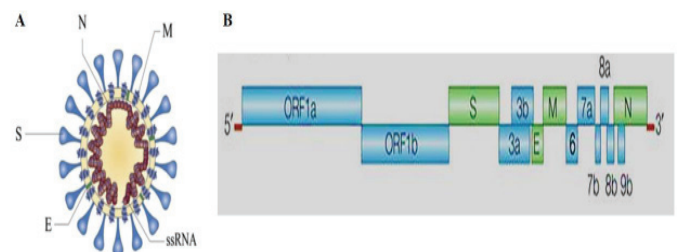

Figure 7: Representing coronaviruses type enveloped and 100-160 nm diameter spherical particles. They contain an ssRNA genome 26-32 kb in size. **(B)**Reflect all of the SARS-CoV2 genome sequences. In SARS-CoV-2, ORF1a / b encoded polyproteins are two-thirds of the 5- 5-terminal genome, forming the viral replicas' transcriptase complex. The four major structural proteins, Bolt, shell, nucleocapsid, and membrane encoded by the other one-third ORF genome and some accessory proteins [43].

The government of Pakistan also initiates the vaccination in different trials. In the first phase, the vaccination was used by premedical's staff, and in the second phase, the older adults whose age was more than 65 were vaccinated without any cost. In the third phase, the government will use the vaccination for more than 40 years. So, using these strategies government of Pakistan is trying to combat the COVID-19.

Drug availability

At the onset of the pandemic, no new COVID-19 therapeutics or vaccinations were eligible. Several treatments are being tested, including remdesivir and favipiravir, but their antiviral effectiveness is unknown. During the 2014 Ebola virus outbreaks, convalescent plasma was recommended as an alternative therapy. In 2015, a guideline for using convalescent plasma to treat the Middle East respiratory syndrome coronavirus was developed. Other viral infections, such as SARS-CoV, avian influenza, and H1N1 influenza, were treated similarly, indicating that transfusion of convalescent plasma was successful. In previous studies, most patients obtained convalescent plasma from a single transmission [44].

Furthermore, hydroxychloroquine is another treatment for Covid-19, according to the researcher. In vitro, it has antiviral activity against SARS-CoV-2. In ICU Covid-19 patients, the Surviving Sepsis Campaign recommendations stated that there was inadequate data to prescribe antiviral drugs and hydroxychloroquine. Furthermore, the usage of two separate dosing regimens for these medications has little impact on chronically ill patients' results [45].

Patients who are seriously ill with COVID-19 are being handled with convalescent plasma, according to recent research. Within days after receiving convalescent plasma, viral load decreased, and these patients' health outcomes increased,

as shown by lower body temperatures and improved chest imaging. Nine days after consuming plasma, four patients on mechanical ventilation no longer needed it (Yeh, et al. 2005) (Figure 8) [44-46]. Outcomes of continuing clinical trials are impatiently awaited. Self-protection from COVID-19 was confirmed by using gloves, glasses, hand sanitiser, and N-95 masks. Also, plenty of water and organ juice intake played a significant role in boosting human immunity.

Future prospects

Furthermost importantly, working on human COVID-19 targeting antiviral drugs and vaccines should be designed to be used against viral epidemics. Many companies such as Inovio California, Cancino Bio China, Pfizer & Biotech, Sanofi, and GSK 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. COVID-19 vaccinations have been provided to millions of citizens in the United States, and they have undergone the most rigorous safety testing in the country's history. To ensure that COVID-19 vaccinations are secure, this surveillance requires both existing and new protection monitoring systems. The European Medicines Agency (EMA) has licensed these

Table 3: Potential Antiviral Drugs Under Evaluation for the Treatment of COVID-19.

| Sr.no	Antiviral drugs	Duration/Effects
1	Remdesivir	5-10 days
2	Chloroquine	600 mg twice daily for ten days
3	Hydroxychloroquine	In combination with azithromycin to better manage COVID-19
4	Lopinavir	Under clinical trial but used against COVID-19
5	Ritonavir	Under clinical trial but used against COVID-19
6	Ivermectin	Under clinical trial but used against COVID-19
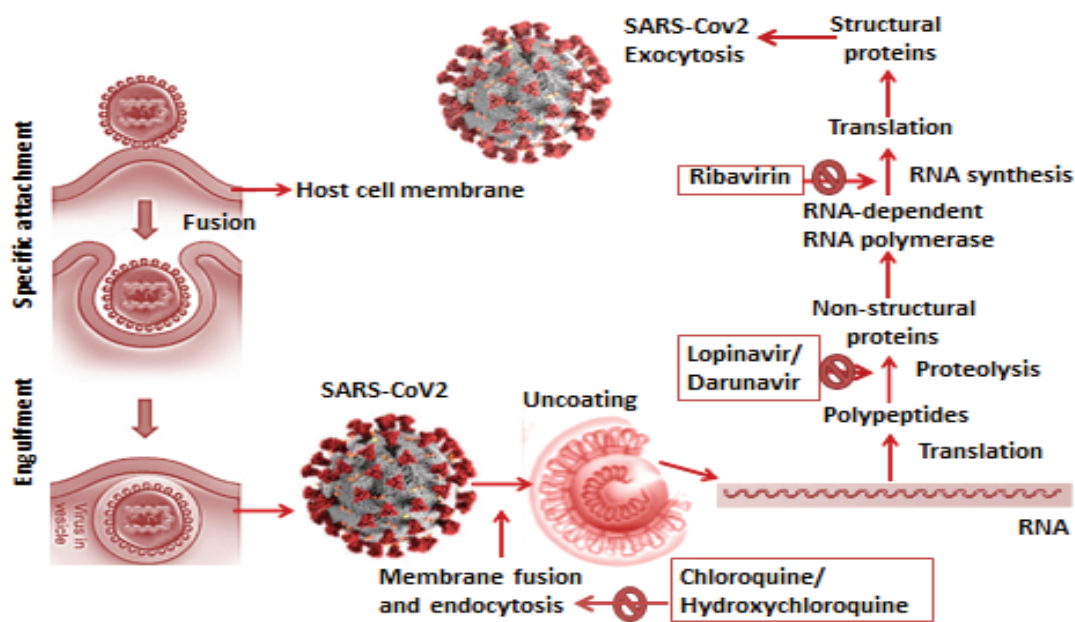
Figure 8: The mood of action of treatment strategies is announced by WHO and their interaction with different steps in the coronavirus replication cycle [47].

vaccinations, which has previously only authorised vaccines from Pfizer/BioNTech, Moderna, and AstraZeneca. According to forecasts, the Covid-19 vaccine could decrease morbidity and mortality rates while also enhancing health outcomes in efficacy and safety management. Lockdown, mask wear, social distance, exact evaluation, proper treatment, and vaccine are only a couple of the precautionary steps that the government can take to minimise the danger of Covid-19. The transmission of COVID-19 influences the population to save several human lives if we adopt aggressive preventive measures. A government recommended guideline should be practised, diminishing the transmission from one person to another of COVID-19 and regulates the viral epidemic. The exact diagnosis will help monitor the rapid spread of the infection in the early stages of the epidemic. 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.

Conclusion

China faced COVID-19 in December 2019 and has been confirmed to clear the spread of coronavirus approximately after months; few other countries, such as South Korea, have 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 be affected by the COVID-19 outbreak and mainly impact 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. A large no. of COVID-19 cases was seen in Sindh.

Similarly, overall, about 2.06% of the 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, Baluchistan, 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 contributions

All authors have contributed significantly to this for the conception, design, analysis and Data interpretation, review and approval of the final version of the manuscript and agree to be responsible for its content.

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