

IT'S ALL ABOUT COVID-19: A REVIEW OF PATTERN OF WAVES IN PAKISTAN, DRUGS AND VACCINATION PROGRAMS

Marvi Shaikh^{1,2}, Naseem Aslam Channa², Sadia Qamar Arain³, Ghulam Mujtaba Junejo³ Ali Muhammad Shahani², Mehnaz Shaikh¹

¹Department of Biochemistry, Indus Medical College, University of Modren Sciences, Tando Muhammad Khan, Sindh, Pakistan, ²Institute of Biochemistry University of Sindh, Jamshoro, Pakistan, ³Department of Biochemistry, Shah Abdul Latif University, Khairpur, Sindh, Pakistan
³Diagnostic Research Laboratory, Liaquat University of Health Sciences Jamshoro, Sindh, Pakistan.

Correspondence:

Prof. Dr. Naseem
Aslam Channa
Institute of Bio-
chemistry,
University of
Sindh, Jamshoro,
Sindh, Pakistan

Email: na-channa2000@gmail.com

DOI:
10.38106/LMRJ.2022.4.4-08

Received: 06.10.2022
Accepted: 23.12.2022
Published: 31. 12.2022

Key Words: COVID -19, waves, current scenario, Pakistan, Vaccination, SARS-CoV-2

INTRODUCTION

Coronaviruses are members of the Coronaviridae family of Nidoviruses, which includes the coronaviruses and Toroviruses genera. Coronaviruses are a type of "infectious bronchitis virus." In December 2019 (1) and January 2020, the first few COVID-19 infected patients were reported, and the disease was speedily spread around the globe. Given its origin in Corona virus family and first reported in 2019 it was identified as COVID-19 (2). Since its inception in a wholesale seafood market in Wuhan, a central city in the People's Republic of China (PRC), 2019 new coronavirus (SARS-CoV-2) spread to more than 215 countries and territories (2). The emergence and re-emergence of human coronaviruses (CoVs) always caused a new global threat (3). COVID- 19) is a viral infection that emerged as a new worldwide public health crisis (4, 5). It is highly contagious causing severe acute respiratory syndrome which can be lethal (4). On January 30, 2020, the World Health Organization (WHO) designated the COVID 19 outbreak as the Sixth public health emergency services (SPHEC) (6). This was not the first time the coronavirus had spread. The outbreak of severe acute respiratory syndrome coronavirus (SARSCoV) and the outbreak of Middle East respiratory syndrome coronavirus (MERSCoV) are two previous outbreaks of coronavirus (7). It's an emerging worldwide menace, and the WHO has described it as a pandemic, offering multi-pronged strategies to the states around the world. The WHO had issued a warning about

the pandemic's speeding up, noting that it took sixty-seven days to reach 100,000 cases from the first-reported case, eleven days to reach the second 100,000 cases, 4 days to reach the third 100,000, and only two days to reach the fourth 100,000 cases(8).

The first case of COVID-19 was certified by Pakistan's Ministry of Health on February 26, 2020 (9) and since then, the disease has been spreading across the country. It has entered through the pilgrims who were coming from Iran , Saudi Arabia (10) and from other countries where they were trapped, owing to the surging case the only panacea was lockdown and social distancing, the other measures were futile and fruitless (11). On March 24, 2020, the government instituted a countrywide lockdown that lasted more than a month(12).

In Pakistan, there were 295,849, confirmed coronavirus infections and 6,294 deaths(13). Adult male patients (age ranged 34-59 years) were most commonly infected with SARSCoV2 (14, 15). The virus was more likely to infect those with chronic comorbidities including cerebrovascular and cardiovascular diseases, as well as diabetes mellitus (16). Adults over 60, as well as those with cardiovascular and neurological diseases, and diabetes, have the highest prevalence of severe disease and it was also linked with high mortality. There have been less COVID-19 cases reportedly among children under the age of 15(17, 18). There were no cases in children under the age of 15 years in a study of 425 COVID-19 patients published on January 29 in Wuhan China (19). However, by January 2020, 28 pediatric patients have been reported. Infected children show an extensive range of clinical symptoms, albeit majority have minimal symptoms without fever and pneumonia and had a good prognosis. (20).

The purpose of this review was to highlight COVID-19 waves with drugs, immunization programs, treatment options, and Pakistan's current COVID-19 condition.

METHODS

This narrative review including studies and reports published since first report of COVID-19 (i.e. 2019) till January 2022. The study was conducted by searching websites including scientific direct, Google scholar, PubMed, and Scopus databases for published papers presenting data in first to fifth waves, medicines tried and recommended, immunization program offered for COVID-19 in Pakistan. The key words "coronavirus," "wave", "drugs", "therapy", "vaccine", and "current scenario" were used in conjunction with the disease key words for the respective searches. The first author evaluated the titles and abstracts of 70 publications found and finally 43 were including for qualitative synthesis of this review. All authors reviewed 43 studies to confirm selection. The results were obtained from nominated studies underwent a descriptive outline of the assertion of evidence. Inappropriate literature, which included case studies of COVID-19, short communications articles studies that do not cover any of the above-mentioned items were excluded from the study. Only full-text articles were used to extract data. Because of the enormous number of submissions found in the published articles, the Google Scholar search was limited to titles only.

RESULTS

First Wave of COVID-19

In Wuhan, China, on December 29, 2019, an outbreak of pneumonia linked to the novel coronavirus of 2019 (2019-nCoV) was confirmed; affecting patients' lower respiratory tracts, and was linked to a local human South China seafood market. The name 2019-nCoV has been changed to extreme Acute respiratory syndrome coronavirus 2 at this time (SARS-CoV-2) (21). The first wave of COVID-19 began in late May 2020, peaked in mid-June with all-time highs in daily new confirmed cases and daily new mortality counts, and then ended in mid-July. The initial wave had a low fatality rate and passed quickly after peaking, with case and death rates rapidly declining. Following the initial wave, Pakistan's

COVID-19 situation stabilized, with daily new death tolls dropped and testing positivity rates in the country stabilized at low levels. The first wave of illness was extremely unpredictable and imaginary owing to the obscurity of origin and inception, mode of infectivity, transmission, and possible treatment options. On February 26, 2020, Pakistan testified its first case of intense acute respiratory syndrome coronavirus 2, a traveller from Iran, almost two months after the first case in Wuhan, China.

Despite having the world's 5th largest population, Pakistan had only the twenty ninth -maximum loss of life toll (round 23,087) and the 29th maximum range of cases (at approximately 1,011,708). However, the rapid response of all countries, including that of Pakistan, had helped to reduce the worrying prevalence of COVID19. Pakistan was fairly successful in directing the disease's spread during the first wave. Patients were also managed through quarantine and isolation centers, as well as COVID19 high-dependency units and critical care units. To advise and support the District COVID19 Command and Control Centers, Provincial and National COVID19 Command and Control Centers (NCOCs and PCOCs and) were established (22).

Second Wave of COVID-19

The second-wave pandemic poses an immediate threat to society, gargantuan human toll and terrible economic consequences. Traditionally, the dynamics of disease diffusion have shown using compartmental or complex network diffusion techniques (23). In early November 2020, the second wave of countries commenced. This wave stood low in strength and mostly affected areas of Pakistan were Sindh southern areas. It peaked around mid-December 2020. Nonetheless, a second wave of the disease emerged, this time with a more limited transmission and toxicity.

Third Wave of COVID-19

Testing positivity rates, as well as daily new confirmed cases and deaths, increased during the world's thirdwave, which began in mid-March 2021. The thirdwave mostly affected the provinces of Khyber Pakhtunkhwa and Punjab. In late April 2021, this wave peaked, after which positive rates, everyday new cases, and mortality dropped.

As of January 27, 2021, a new SARS-CoV-2 strain developed in the United Kingdom (UK) (24) and has been discovered in more than 64 countries, including Pakistan (25). This SARS-CoV-2 variation was shown to be related to a higher risk of death. When compared to other versions, with an average of 100 patients dying every day in Pakistan. The ten cities of Pakistan including Lahore, Faisalabad, Muzaffarabad, Bahawalpur, Hyderabad, Multan, Islamabad, Peshawar, Swat and Rawalpindi, were placed under firm lockdown until April 11, 2021.

The provincial administration was directed to strictly implement Standard Operating Procedures (SOPs). One thing that the first and third waves had in common was the time of beginning which was spring (from March till the end of April). It could lead to the creation of a theory that pollens play a crucial role in SARS-CoV-2 viral transmission (9), but surely confirmed seasonal association.

FourthWave of the COVID-19

The emergence of Delta variant, a type of the virus initially found in the neighboring India, raised fear of a fourth wave of coronavirus in Pakistan (26). This number was significantly greater than it was in June (where they reported 1,200 daily new cases). Preventive measures were put in place in May, and the cases gradually started to decline as patients recovered (27). On August 20, 2021, the nationwide count of active COVID-19 cases reached 88,209, one of the highest during the fourth wave of the pandemic, with 3,974, more persons tested positive for the fatal virus and 3,122 recovered, from the disease, in the preceding 24 hours. According to the latest information from the NCOc, 66 corona

patients had died in 24 hours, 58 of them were receiving treatment in hospitals and six of whom died in their individual quarantines or homes. Punjab was the state having most deaths, followed by Sindh (28).

Fifth Wave of the COVID-19

The fifth wave showed most cases reported in Karachi, the positive ratio increased from 2% to 6% over a period of three days (29). The Health Ministry in the South Asian country recorded over 500 new infections during a span of 24 hours. The wave was confined on 2nd January 2022. The country's overall caseload increased to 1,296,527, with 594 new infections, bringing the infection rate up from 0.6% to 1.3% (30). Nevertheless, five waves of COVID-19 have been witnessed in Pakistan, but the case rate and mortality remained lowered as compared to other countries.

2. Drugs and vaccination programs

There was no vaccination for COVID-19 as of June 17, 2020, but multiple medications such as Tocilizumab, Nirmatrovir lyophilized and Azithromycin, Remdesivir lyophilized and Dexamethasone were offered used to treat the condition empirically. As a result, the only way to keep the virus from spreading was to practice social distancing and self-isolation. After considering the established quality and safety requirements, the Drug Regulatory Authority of Pakistan (DRAP) approved Hydroxychloroquine as the first drug to treat COVID-19 patients. Then, in clinical trials, a combination of medicines (Chloroquine and Azithromycin) was proven to be effective against COVID-19 (31). Convalescent plasma therapy was later approved for the treatment of severely ill COVID-19 patients. A probationalary at Agha Khan Hospital in Karachi, Pakistan, found Tocilizumab, an anti-interleukin-6 receptor monoclonal antibody, to be effective (32), The Federal Government, on the other hand, did not adopt this procedure as a feasible treatment for COVID-19 patients. Supportive care, mechanical breathing, and Extracorporeal oxygenation are still the most important therapeutic option for medical experts, according to numerous sources from around the world and in Pakistan.

Anti-inflammatory drugs, Antiviral, and anti-parasitic; interferon therapy; hyper-immunoglobulin; convalescent plasma therapy; oligonucleotide-based therapies; and, occasionally, mesenchyme stem cell, and RNA interference therapy are among the therapeutic alternatives being studied and employed (33, 34). After the development of a corona vaccine, pandemic would be curbed and alleviated, Russia gave the world a ray of hope. Within 15 weeks of the corona virus outbreak, Russia released the first applicable vaccination (Sputnik- V) in this hope (35). From February to August 2020, Clinical data was collected retrospectively from 1812 confirmed COVID-19 patients admitted to four major tertiary referral hospitals in Pakistan. Monthly distributions of different medications given to COVID-19 patients (n=1562) in Pakistan during the 1st wave of the pandemic (May-July 2020) (36). Covid-19 and its related symptoms were cured by 19 drugs. Ceftriaxone and Azithromycin were mostly used ones. Anticoagulants such as heparin and Enoxaparin Sodium and steroids such as Hydrocortisone were also among the 5 most frequently used drugs (37, 38). In early February 2021, Pakistan began spreading out COVID-19 vaccine across the country. China has sent vaccines to the country, including CanSino and Sinopharm vaccines, as well as vaccines as part of the COVID-19 Vaccines Global Access (COVAX) initiative (22). However, 7 vaccines approved for use in Pakistan (Table.1) (38):

Vaccine adoption and hesitation among the general public and health-care personnel are critical factors in containing the (COVID)-19 pandemic. While there is evidence of vaccine un-availability all over the world, a total of 130,958,324, vaccine doses had been provided as of August 26th 2022, and 72 percent of Pakistanis had been infected at least once. Assuming that each individual requires two doses, this would be enough to vaccinate 48.4 percent of the country's population (39).

Table 1. Vaccines approved for use in Pakistan.

RNA	Moderna Spikevax	Approved in 85 countries 60 trials in 22 countries
RNA	Pfizer/BioNTech Comirnaty	Approved in 142 countries 73 trials in 26 countries
Non Replicating Viral Vector	CanSino Convidecia	Approved in 10 countries 13 trials in 6 countries
Non Replicating Viral Vector	Gamaleya Sputnik V	Approved in 74 countries 24 trials in 7 countries
Non Replicating Viral Vector	Oxford/AstraZeneca Vaxzevria	Approved in 138 countries 62 trials in 30 countries
Inactivated	Sinopharm (Beijing) Covilo	Approved in 91 countries 26 trials in 12 countries
Inactivated	Sinovac CoronaVac	Approved in 55 countries 37 trials in 9 countries

Pakistan's current scenario

The Omicron wave continues to subside globally. Based on vaccination, previous infection, and the current wave of Omicron, we estimate that 57% of the population is immune to Omicron (40). According to WHO, confirmed cases of COVID-19 were 1,567,893, reported in Pakistan from (3rd January 2020 to 26th August 2022), with 30,569 deaths and 1,528,145 are recovered (Fig-2) (41). Sindh province of Pakistan is more prone to COVID-19 as compared to other provinces. Province wise cases of COVID-19 in Pakistan shown in (Table 2) (42).

Table-2 Province wise cases of COVID-19 in Pakistan (42).

PROVINCE	CONFIRMED CASES	DEATHS	RECOVERIES
SINDH	593,120	8,225	567,237
PUNJAB	520,440	13,605	491,786
BALUCHISTAN	35,935	378	35,108
KPK	223,249	6,347	212,886

CONCLUSION

The current review has found that strict observation about the COVID-19 waves and a current scenario that help to build national policies reshape their strategies according to the forecasted situation for effective control of disease during this winter. A vaccine is available for everyone to halt the virus surging in the world, and despite Pakistanis' relatively good response to vaccination, issues negatively influencing their intention must be addressed quickly to control the pandemic. Measures to address public acceptability, trust, and anxiety about the safety and benefit of licensed vaccines are required. It may not be until the second or third week of January 2022 that we have enough evidence to alter our severity assessment.

ETHICAL CONSIDERATION: Not applicable

FUNDING SOURCE: This study required no additional funding

CONFLICT OF INTEREST: Authors declare no conflict of Interest

REFERENCES

1. Abadie A. Poverty, political freedom, and the roots of terrorism. *American Economic Review*. 2006;96(2):50-6.
2. Yang X, Yu Y, Xu J, Shu H, Liu H, Wu Y, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory Medicine*. 2020;8(5):475-81.
3. Noreen N, Dil S, Niazi S, Naveed I, Khan N, Khan F, et al. COVID 19 pandemic & Pakistan; limitations and gaps. *Global Biosecurity*. 2020;1(4).
4. Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. *Journal of advanced research*. 2020;24:91.
5. Abdolvahab MH, Moradi-Kalbolandi S, Zarei M, Bose D, Majidzadeh-A K, Farahmand L. Potential role of interferons in treating COVID-19 patients. *International immunopharmacology*. 2021;90:107171.
6. Bilgin S, Kurtkulagi O, Kahveci GB, Duman TT, Meryem B, Tel A. Millennium pandemic: A review of coronavirus disease (COVID-19). *Experimental Biomedical Research*. 2020;3(2):117-26.
7. Zhou P, Yang X-L, Wang X-G, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *nature*. 2020;579(7798):270-3.
8. Zhu H, Wei L, Niu P. The novel coronavirus outbreak in Wuhan, China. *Global health research and policy*. 2020;5(1):1-3.
9. Kamran K, Ali A. Challenges and Strategies for Pakistan in the Third Wave of COVID-19: A Mini Review. *Frontiers in Public Health*. 2021;9.
10. Mubeen SM, Kamal S, Kamal S, Balkhi F. Knowledge and awareness regarding spread and prevention of COVID-19 among the young adults of Karachi. *J Pak Med Assoc*. 2020;70(5):S169-74.
11. Abid K, Bari YA, Younas M, Tahir Javaid S, Imran A. <? covid19?> Progress of COVID-19 Epidemic in Pakistan. *Asia Pacific Journal of Public Health*. 2020;32(4):154-6.
12. Transmission. CDC. 2021.
13. Ocha W. Gold rush abroad: The trajectory of Singapore-based Thai transsexual (male to female) sex workers in global sex tourism. *ASEAS-Austrian Journal of South-East Asian Studies*. 2020;13(1):123-41.
14. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The lancet*. 2020;395(10223):497-506.
15. Chang D, Lin M, Wei L, Xie L, Zhu G, Cruz CSD, et al. Epidemiologic and clinical characteristics of novel coronavirus infections involving 13 patients outside Wuhan, China. *Jama*. 2020;323(11):1092-3.
16. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The lancet*. 2020;395(10223):507-13.
17. Bai Y, Yao L, Wei T, Tian F, Jin D-Y, Chen L, et al. Presumed asymptomatic carrier transmission of COVID-19. *Jama*. 2020;323(14):1406-7.
18. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *Jama*. 2020;323(11):1061-9.

-
19. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. *New England journal of medicine*. 2020.
 20. Shen K-L, Yang Y-H. Diagnosis and treatment of 2019 novel coronavirus infection in children: a pressing issue. *Springer*; 2020. p. 219-21.
 21. Rasheed Qureshi S, Hussain Memon N, Qamar Arain S, Shah Nizamani G, Ali Abbasi M, Hussain Laghari A, et al. Seroprevalence of Anti-SARS-CoV-2 Antibodies in COVID-19 Patients in Hyderabad, Sindh. 2021.
 22. Imran M, Khan S, Khan S, Uddin A, Khan MS, Ambade P. COVID-19 situation in Pakistan: A broad overview. *Respirology (Carlton, Vic)*. 2021.
 23. Cacciapaglia G, Cot C, Sannino F. Second wave COVID-19 pandemics in Europe: a temporal playbook. *Scientific Reports*. 2020;10(1):15514.
 24. Volz E, Mishra S, Chand M, Barrett JC, Johnson R, Geidelberg L, et al. Transmission of SARS-CoV-2 Lineage B. 1.1. 7 in England: Insights from linking epidemiological and genetic data. *MedRxiv*. 2021:2020.12. 30.20249034.
 25. Umair M, Ikram A, Salman M, Alam MM, Badar N, Rehman Z, et al. Importation of SARS-CoV-2 variant B. 1.1. 7 in Pakistan. *Journal of Medical Virology*. 2021.
 26. Delta variant hits Pakistan amid 4th COVID wave worries. 2021.
 27. GlobalData Epidemiologist Report: India sees Covid downturn as Pakistan suffers fourth wave. *pharmaceutical technology* 2021.
 28. Covid-19 4th wave intensifies. 2021.
 29. Omicron-driven fifth COVID-19 wave spreading at a great pace in Pakistan: NCOC 2022.
 30. Pakistan faces 5th wave of COVID-19. 2022.
 31. Mallhi TH, Ahmad A, Butt MH, Misbah S, Khan YH, Alotaibi NH. Chloroquine and hydroxychloroquine in COVID-19: practice implications for healthcare professionals. *Journal of the College of Physicians and Surgeons--Pakistan: JCPSP*. 2020;30(10):124-8.
 32. Ahmed K, Shahid S, Nawaz N. Impacts of climate variability and change on seasonal drought characteristics of Pakistan. *Atmospheric research*. 2018;214:364-74.
 33. Park YJ, Farooq J, Cho J, Sadanandan N, Cozene B, Gonzales-Portillo B, et al. Fighting the war against COVID-19 via cell-based regenerative medicine: lessons learned from 1918 Spanish Flu and other previous pandemics. *Stem cell reviews and reports*. 2021;17(1):9-32.
 34. Siam M, Banna H, Nishat NH, Ahmed A, Hossain MS. Stopping the COVID-19 pandemic: a review on the advances of diagnosis, treatment, and control measures. *Journal of Pathogens*. 2020;2020.
 35. Callaway E. Outrage Over Russia'S Fast-Track Coronavirus Vaccine. *Nature*. 2020:334-5.
 36. 7 Vaccines Approved for Use in Pakistan. *COVID 19 vaccine tracker*.
 37. Akhtar H, Akhtar S, Rahman F-U, Afridi M, Khalid S, Ali S, et al. An overview of the treatment options used for the management of COVID-19 in Pakistan: retrospective observational study. *JMIR Public Health and Surveillance*. 2021;7(5):e28594.
 38. vaccinator c. 7 Vaccines Approved for Use in Pakistan. 2022; Available from: <https://covid19.trackvaccines.org/country/pakistan/>. REUTERS. 2022.
 40. COVID-19 Results Briefing. IHME. 2021.
 41. WORLD HEALTH ORGANIZATION. 2022.
 42. Pakistan Cases Details. Government of Pakistan.