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Coronavirus diseases (COVID) - 19: Epidemiological trends and the emergence of omicron in Pakistan (2019–2022)

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Abstract: Background: In February 2020 Pakistan reported its 1st case of coronavirus disease (COVID-19) which can be distinguished from other respiratory-related disease by causing due to SARS-CoV-2 (severe acute respiratory syndrome-coronavirus 2), a special variant. Emerged from Wuhan, China in December 2019 the corona virus rapidly evolved into a global pandemic which caused acute respiratory syndrome (ARDS). Pakistan experienced multiple waves since 2020 throughout 2022. **Objectives**: The study aims to provide epidemiological trends of COVID-19 in Pakistan from 2019 to 2022, with its primary emphasis on Omicron variant. The study assesses different indicators like change in the public health response in the quarantine and public health measures. Clinical characteristics were compared among original virus and Omicron, disease severity trends and limitations in national surveillance that affect data interpretation during Omicron phase was also important part of this study. **Methods**: The data was collected from the WHO COVID-19 dashboard, Pakistan's National Command and Operation center (NSOC) reports and peer reviewed literature covering 2019-2022 using narrative approach including three analytical snapshots during the fifth wave (14 January, 14 April and 14 June 2022).For greater coverage a refined search strategy with Boolean combinations along with targeted searches with additional key words on Google scholar was employed for systematic identification and to add Pakistan specific clinical and epidemiological data. The method facilitated the reliable analysis of case trends, mortality patterns and public health responses **Results**: showed that National data from the fifth wave shows significant case increases in January 2022, followed by decreases in cases and deaths by April, with lower severity and mortality compared to earlier waves. As the cases fluctuate, trends were re-evaluated in June. Decrease in severe complications was observed, hence Pakistan transitioned from severe restrictions to only focused prevention. Most limitations were lifted for individuals who were vaccinated and schools were re-opened with observance of pre-cautionary measures. However, Omicron was highly transmissible, but it led to very reduced complications and deaths in Pakistan even in its dominant period. The virus is mutated continuously and developed mutated and highly transmissible form, Omicron. **Conclusion**: Available evidence suggests that, compared to earlier variants, Omicron shows few clinical presentations. The principal limitations of the present study include reliance on national reporting systems with potential under-reporting, variability in testing intensity and limited subvariant-level resolution.

Keywords: COVID-19, Epidemiology, Omicron, Pathophysiology, Symptoms and Complications

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INTRODUCTION

Coronaviruses are a diverse family of RNA viruses to infect mammals and birds, primarily causing respiratory and gastrointestinal diseases (Balasuriya *et al*., 2022). Few human coronaviruses have been identified over the past decades, but prior to the 2000s, none initiated severe illness and were therefore thought unimportant pathogens in human virology. SARS-CoV-2 is among seven coronaviruses that cause severe infections. The situation changed intensely with the emergence of severe acute respiratory syndrome (SARS-CoV) in 2002–2003, followed by Middle East respiratory syndrome (MERS-CoV) in 2012 both zoonotic viruses linked to animal reservoirs such as bats, civet cats and camels (Ng & Hiscox, 2020).

In December 2019, the third novel SARS-CoV-2 was identified in Wuhan, China in December 2019 and igniting global health crises due to its rapid human-to-human transmission (Del Rio & Malani, 2020). The first case of SARS-CoV-2 was recorded on February 26th, 2020, in Karachi, Pakistan after which the virus spread nationwide (Abid *et al*., 2020). World Health Organization defined on March 11, 2020, it as COVID-19, or coronavirus disease 19, a universal pandemic, which caused the disturbance of normal economic, social and political conditions across the world (Chetty *et al*., 2020).

Although most individuals experience mild disease and recover without complications, patients with co-morbidities and advanced age may develop a severe type of COVID (Kim *et al*., 2020). Approximately (5%) may

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progress to an acute respiratory distress syndrome (ARDS), a life threating condition associated with high mortality (Aslan *et al*., 2021). Treatment strategies have largely been supportive. Antiviral drug remdesivir shows significant in vitro activity against SARS-CoV-2 but limited definitive clinical evidence at the time of early research (Sanders *et al*., 2020).

Scientific understanding of SARS-CoV-2 continues to change as research increases on its epidemiology, genetics and clinical manifestations. Randomized clinical Trials (RCTs) were started to identify effective treatments that manage the condition without incurring organ damage with several treatments option utilizations. One strategy to discover a solution is to reassess the existing marketed medications by studying their pharmacological effects in COVID patients to speed up clinical studies (Sultana *et al*., 2020). The scientific understanding of the virus's epidemiology, genetics and clinical symptoms is changing frequently. (Hu *et al*., 2021). Rapid sequencing of the viral genome accelerated timely diagnosis and vaccine production, aiding significantly to global disease-control approaches. (Del Rio & Malani, 2020). COVID-19, beyond its biological impact, also exerts significant psychological, social and economic challenges due to lockdowns, mobility restrictions and prolonged isolation (Fegert *et al*., 2020). The current study utilizes data from WHO dashboards, NCOC reports and published research to deliver an updated understanding of COVID-19's evolution in the country.

MATERIALS AND METHODS

A narrative literature search was conducted using the databases PubMed, WHO resources (including the WHO COVID-19 dashboard), NCOC (Pakistan's National Command and Operation Centre) situation reports/dashboards and Google Scholar (Heath *et al*., 2022).

Eligibility criteria

Inclusion criteria

The inclusion sources included the reported epidemiological trends such as cases, deaths, recoveries, test positivity for Pakistan; described clinical presentation or complications of COVID-19 along with Omicron; or summarized policy and public-health measures relevant to Pakistan (Bergeri *et al*., 2022).

Exclusion criteria

Exclusion criteria included duplicate reports, preprints lacking methodological detail and articles that were irrelevant to Pakistan or to Omicron-related differences (Ejaz *et al*., 2022).

Data extraction

Two independent reviewers screened the collected data on chronological trends in cases, deaths and recoveries (Zhang *et al*., 2022). National-level snapshots from the National Command and Operation Centre (NCOC) were extracted at three time points-14 January 2022, 14 April 2022 and 14 June 2022-to characterize the fifth wave and subsequent epidemiological trends in Pakistan. Any discrepancies between reviewers were resolved through consensus and the findings were systematically organized. The data from mentioned resources was collected from the period of 2019 till 2022, consistent with emergence of SARS-CoV-2 and the Omicron-dominant period in Pakistan, between 5 and 14 January 2023, using predefined Boolean combinations including ("COVID-19" OR "SARS-CoV-2") AND ("Pakistan") AND ("epidemiology" OR "clinical characteristics") and ("Omicron") AND ("Pakistan") AND ("variant of concern" OR "fifth wave"). Google Scholar searches used additional keyword strings such as **"**COVID-19 Pakistan fifth wave" and "Omicron epidemiology Pakistan" to widen coverage. WHO and NCOC dashboards were specifically asked for national case trends on 14 January, 14 April and 14 June 2022, aligning with the study's analytic time points. All retrieved records went through a three-step screening protocol beginning with title screening, followed by abstract evaluation and finally full-text review. Using both automatic and manual screening any duplication in record was removed. This refined search is transparent, reproducible and aligns the study with established standards for narrative evidence synthesis of PRISMA guidelines. As figure 1, PRISMA flow diagram is illustrated, it summarizes number of records identified across databases, duplicates removed, records screened, full texts assessed for eligibility and studies finally included in synthesis.

A total of 1278 records were initially identified through searches conducted in PubMed, WHO COVID-19 resources, NCOC dashboards and Google Scholar, using combinations of keywords related to "COVID-19," "SARS-CoV-2," "Omicron," "Pakistan," "epidemiology," After removing 1147 duplicate records, 131 records remained for title and abstract screening. Studies relevant to COVID-19 epidemiology, clinical presentation, or complications in Pakistan were considered for further evaluation. Articles lacking Pakistan-specific data, clinical or epidemiological relevance, or preprints with insufficient methodological detail were excluded during the screening stage, resulting in 84 full-text articles assessed for eligibility. Following full-text review, 23 sources met the predefined inclusion criteria and were included in the final synthesis. (Vosoughi *et al*., 2022).

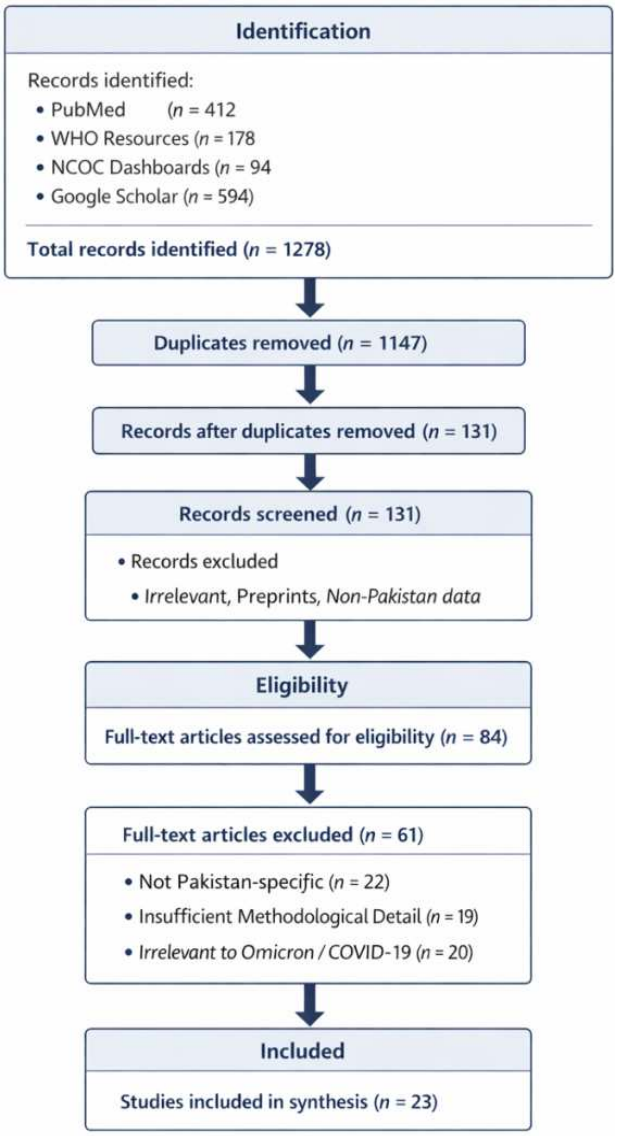


Fig. 1: Prisma flow diagram of the literature search.
Note: PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses; NCOC = National Command and Operation Center. Records were identified through PubMed, WHO resources, NCOC dashboards and Google Scholar. After removal of duplicates, records were screened for relevance. Studies were excluded if they were irrelevant, preprints, non-Pakistan data, lacked sufficient methodological detail, or were not directly related to Omicron/COVID-19. A total of 23 studies were included in the final synthesis.

Quality Considerations and Risk of Bias

Quality Considerations and Risks of Bias were thoroughly evaluated that arising from under-reporting, reporting delays, variability in testing intensity and limited subvariant-level resolution. Evidence from peer-reviewed journals was prioritized and dashboard data (WHO/NCOC) were used (Hu *et al*., 2021).

Results: Change in public health interventions and policy response in Pakistan

Pakistan initially implemented strict public-health measures to control COVID-19 (Binte Aamir *et al*., 2022). These actions included COVID 19 testing policies, developing isolation and quarantine policies, consistent mask mandates, phased school closure and reopenings, organized national communication efforts and effective vaccination campaign (Chohan, 2022).

COVID-19 testing policies

Pakistan implemented structured testing policies, relying primarily on molecular tests, serum tests and antigen tests. Testing data collected through national dashboards (e.g., WHO and NCOC) were incorporated into epidemiological analyses, encouraging policy decisions like easing restrictions after declining case severity (Zaidi & Hussain, 2022).

Isolation and quarantine strategies

Pakistan's early isolation policies involved strict isolation and quarantine measures during the previous COVID-19 waves, even though public resistance was common. Several steps were taken to improve public understanding and acceptance of these measures (Hussain *et al*., 2022).

Mask policies

Initially mask mandates were key interventions during the pandemic. People had to wear masks in public places, and this rule was enforced widely (Grigsby-Toussaint & Shin, 2022). In 2022, although the government reduced restrictions due to a decline in severe cases, mask usage continued to be recommended in crowded settings in Pakistan (Salman *et al*., 2022).

Closure and reopening of educational institutions

Educational institutions underwent several closures and reopening cycles depending on wave intensity (Jahan *et al*., 2022).

NCOC communication strategies

It delivers real-time data, reporting public advisories, operational guidance and dashboards that communicate nationwide epidemiological updates and policy decisions (Abbas & Mannan, 2022b)

Vaccination campaign

The vaccination program in Pakistan played a crucial role with contribution to 13 billion doses administered globally and a 95.8% recovery rate (Hayat *et al*., 2022). Effective vaccination reduces ICU admissions, complications and fatalities as a preventive measure (Rahmani *et al*., 2022). Public awareness campaigns continuously highlight the role of vaccination as an important protective measure. The government favoring vaccinated individuals and emphasizing the strategic importance of vaccination and reducing Vaccines hesitancy (Peters, 2022).

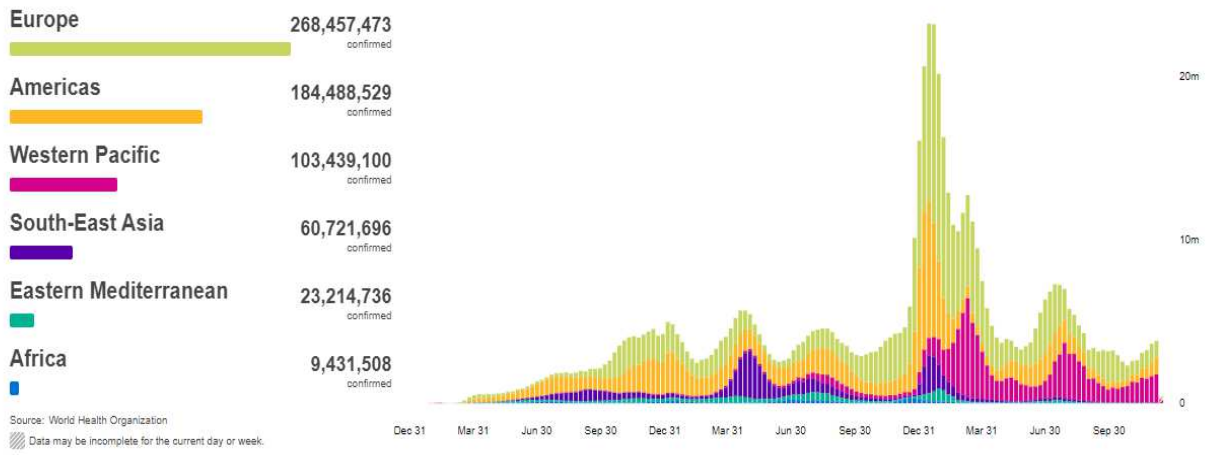


Fig 2. COVID global burden in world 2022 (WHO) (https://covid19.who.int/region/emro/country/pk).

Note: The figure presents the regional distribution and temporal trend of confirmed COVID-19 cases reported by the World Health Organization. The highest cumulative case burden was observed in Europe, followed by the Americas and Western Pacific. The stacked bar chart illustrates changes in reported cases over time across the six WHO regions. Data may be incomplete for the current day or week. Source: World Health Organization.

Table 1:
COVID cases status in Pakistan till 14th January 2022

	Confirmed Cases	Active Cases	Deaths	Recoveries
AJK	34,726	44	749	33,933
Balochistan	33,682	49	367	33,266
GB	10,437	8	186	10,243
Islamabad	110,243	1,432	967	107,844
KPK	181,996	687	5,952	175,357
Punjab	450,686	7,343	13,085	430,258
Sindh	494,064	16,865	7,693	469,506
Total	1,315,834	26,518	29,009	1,260,307
Total	1,315,834	26,518	29,009	1,260,307

Table 2:
COVID cases status in Pakistan till 14th April 2022

	Confirmed Cases	Active Cases	Deaths	Recoveries
AJK	43,303	18	792	42,493
Balochistan	35,481	2	378	35,101
GB	11,722	27	191	11,504
Islamabad	135,141	72	1,023	134,046
KPK	219,308	445	6,322	212,541
Punjab	505,528	1,249	13,559	490,720
Sindh	576,469	7,633	8,097	560,739
Total	1,527,952	9,446	30,362	1,488,144
Total	1,527,952	9,446	30,362	1,488,144

Table 3:
COVID cases status in Pakistan till 14th June 2022

	Confirmed Cases	Active Cases	Deaths	Recoveries
AJK	43,375	19	793	42,563
Balochistan	35,487	2	378	35,107
GB	11,726	30	191	11,505
Islamabad	135,153	15	1,023	134,115
KPK	219,448	80	6,323	213,045
Punjab	505,570	1,243	13,559	490,768
Sindh	576,669	1,333	8,097	560,775
Total	1,527,998	9,368	30,363	1,468,267
Total	1,527,998	9,368	30,363	1,488,267

Fig. 3, 4 & 5 compare new COVID 19 cases on daily basis for the one month at three selection points i.e., December21-January 2022: March-April,2022 & May-June 2022 respectively. The comparison reveals that after an initial increase in newer instances, daily reporting of cases was decreased in April 2022 while re-increased in June 2022 (https://covid.gov.pk/stats/pakistan). Overall, Tables 1–3 demonstrate a distinct three-phase pattern: showing rapid surge in mid-January, with significant decline by mid-April, and mild resurgence by mid-June.

Results of epidemiology of COVID-19

As of statistics for the month of 20th December 2022, 649 million confirmed COVID-19 cases and 6.65 million reported deaths had been reported worldwide with the higher prevalence observed in Europe as per WHO (Figure 2). Approximately 13 billion doses of vaccine had been administered to population worldwide (https://covid19 .who.int/). In Pakistan, COVID-19 was transmitted to 1,574,965 from 3rd January 2020 till December 2022.The patient recovery rate was found to be 95.8% within two years of this pandemic despite of higher prevalence (https://covid19.who.int/region/emro/country/pk). These data emphasize not only the massive scale of the pandemic but also the level of international vaccination efforts.

The fifth wave and emergence of omicron in Pakistan

Pakistan experienced its fifth wave of COVID-19 between January and February 2022, with highly transmissible Omicron variant. The assessment of severity and progression of disease during this period was done by collecting retrospective epidemiological data at three points: 14 January 2022, 14 April 2022 and 14 June 2022. These data were retrieved from the National Command and Operation Centre (NCOC) database.

Key findings from national data

The findings support public health planning and future pandemic preparedness, sum up the adaptations in Pakistan's health system regarding involvements, surveillance and vaccination efforts during the fifth wave.

As of the 14th of January 2022, Pakistan reported 26,428 active cases (2.2% positivity rate). Highest number of confirmed cases and 7,693 deaths. In the preceding two years, highest number of confirmed cases and 7,693 deaths because of COVID-19 complications. Gilgit-Baltistan reported the lowest mortality among all regions. Tables 1, 2 and 3 show the number of cases reported in different provinces at selected data points, i.e., 14th January 2022, 14th April 2022 and 14th June 2022. The data from 14th January to 14th April 2022 revealed that there was a decline in the death rate of patients and an increment in the recovery rate of COVID-19 patients. Furthermore, it has been noticed that the number of new cases were surged in January 2022, but there was a decline in the number of cases reported in April 2022, implying that the spread seems to be less significant. The data up to 14th June 2022 revealed that now there was again surged in COVID-19 cases along with decline in mortality rate.

This progression shows dynamic epidemiological landscape during the Omicron wave; it shows change in burden of disease in Pakistan from high transmission to manageable severity due to immunity and public-health awareness. Omicron's emergence was characterized by high transmission and short incubation period as shown in Figure 3. The data shows sudden shift from relatively stable transmission patterns of earlier months to steep incline during January 2022.

Figure 4 illustrates decrease in daily cases as compared to January. This decline aligns with decreased clinical severity of Omicron, immunity of the population (vaccination and prior infection) and relaxation of transmission dynamics. During this period, the epidemiological curve of Pakistan significantly flattened, this shows effective control of the fifth wave. However, re-emergence of cases was also reported as shown in Figure 5, that might be due to continued spread of Omicron sub-variants.

However, cases increased in June again, but severity did not rise proportionally, this reflects Omicron's milder clinical profile.

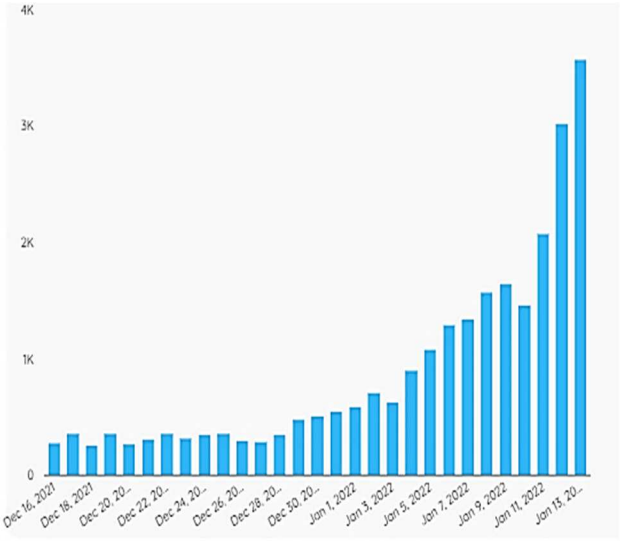


Fig. 3: New Daily COVID cases in Pakistan; 16th December to 14th January, 2022.

Note: The figure shows the daily number of reported COVID-19 cases from December 2021 to January 2022. A modest increase is visible in late December, followed by a pronounced surge in January 2022, with the highest number of daily cases recorded in mid-January. This pattern suggests a rapid escalation in transmission during the study period.

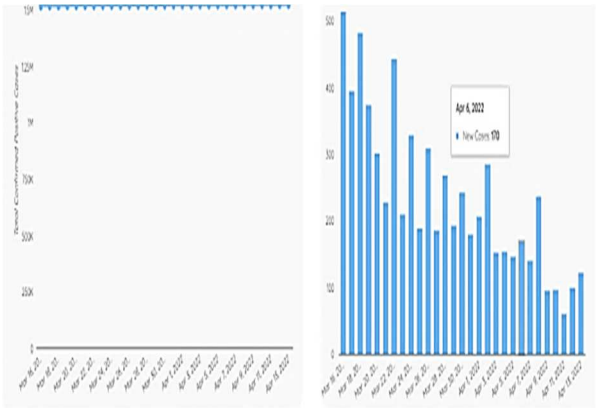


Fig. 4: New Daily cases in March-April 22 in Pakistan.

Note: The figure shows the daily number of newly reported COVID-19 cases from March to April 2022. A generally decreasing trend is observed over time, although minor fluctuations are present. Case counts were higher in mid-March and declined gradually by mid-April 2022, reflecting a reduction in disease transmission during the observed period.

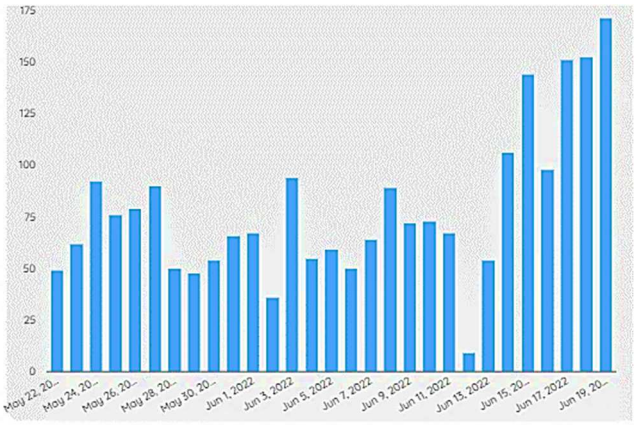


Fig. 5: New Daily cases in May-June 22 in Pakistan.
Note: The figure shows the daily number of newly reported COVID-19 cases from May to June 2022. Daily counts fluctuated at moderate levels during late May and early June, followed by a marked rise in the second half of June. The peak observed near 19 June 2022 suggests a renewed increase in transmission during the study period.

Figure 6 shows a sharp increase in active cases, paralleling the spike in cases shown in Figure 3. The rapid rise highlights Omicron's highly infectious nature and a swift turnover of cases during the early part of the fifth wave. Despite the dramatic rise in infections, the mortality rate remained stable around 2%, underscoring: omicron's reduced virulence, the protective effect of vaccination and Improved clinical management, Mortality stability during a case surge is a key indicator of decoupling between infection levels and severe outcomes. Followed by January's peak in active number of cases, significant decline in active cases was reported by early April, it reflects decreased viral transmission and stabilized national condition as shown in Figure 8. Figure 9 illustrates decline in mortality rate which is continuous. it is attributed to milder symptoms of Omicron, high recovery rates and increased vaccination coverage. This downward trend also illustrates Omicron's low pathogenicity as compared to earlier other variants like Delta. Figure 10 shows slight resurgence of active cases like Figure 5 but active hospitalization remained low, recovery rates remained high and severe complications continued to decline. The slight resurgence represents continuous spread of Omicron's sub-variants rather than emergence of new waves. Mortality rate of May-June 2022 is shown in Figure 11. Even with rising number of cases, mortality remained low (~2%). This reduced mortality shows declined virulence of Omicron and improved immunization of population. Figure 12 shows daily death numbers till June 14, 2022. The overall downward trend shows decreased clinical severity, better disease management, reduced progression to ARDS or pneumonia during the Omicron period.

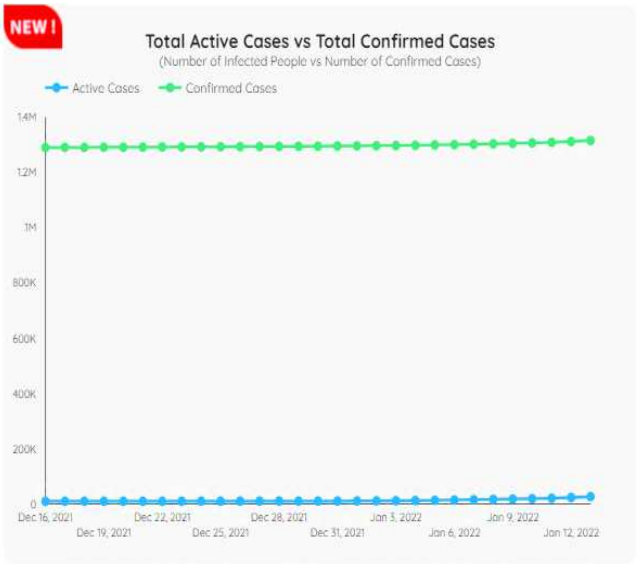


Fig. 6: Active cases comparison in Pakistan

(16th December 2021-14th January 2022)

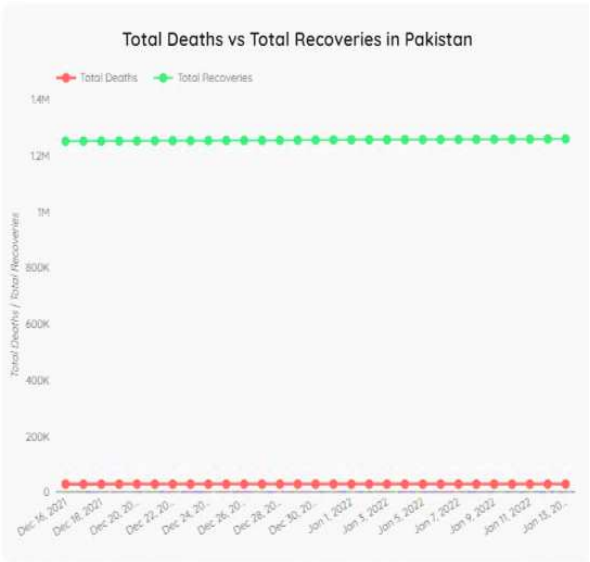


Fig. 7: Mortality rate COVID in Pakistan

(16th December 2021-14th January 2022)

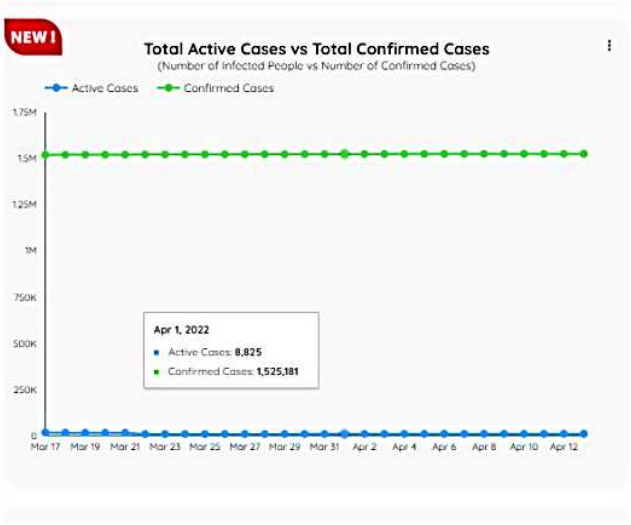


Fig. 8: Active cases comparison in Pakistan

17th March 2022-14th April 2022)

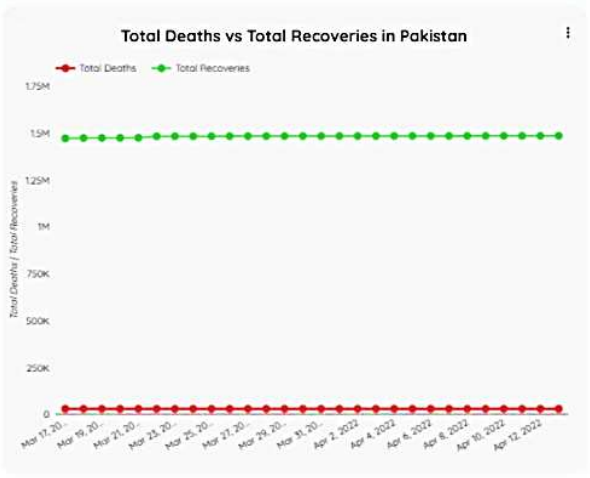


Fig. 9: Mortality rate of COVID in Pakistan

17th March 2021-14th April 2022)

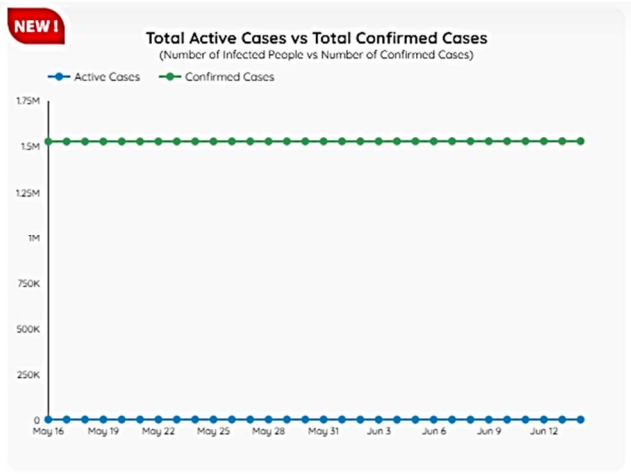


Fig. 6 note: Note: The figure compares total active COVID-19 cases with total confirmed cases in Pakistan from 16 December 2021 to 14 January 2022. Total confirmed cases remained substantially higher than active cases throughout the observed period.

Fig. 7 note: Note: The figure compares total deaths and total recoveries due to COVID-19 in Pakistan from 16 December 2021 to 14 January 2022. Total recoveries remained markedly higher than total deaths during the study period.

Fig. 8 note: Note: The figure compares total active COVID-19 cases with total confirmed cases in Pakistan from 17 March 2022 to 14 April 2022. Confirmed cases continued to remain considerably higher than active cases throughout the observed period.

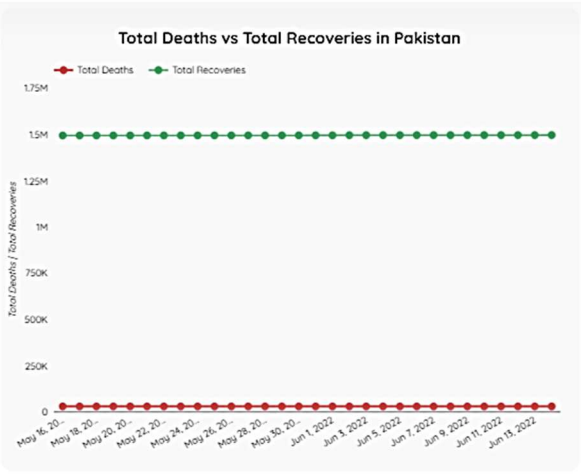


Fig. 9 note: Note: The figure compares total deaths and total recoveries due to COVID-19 in Pakistan from 17 March 2022 to 14 April 2022. Total recoveries consistently exceeded total deaths during the study period.

Fig. 10 note: Note: The figure compares total active COVID-19 cases with total confirmed cases in Pakistan from 16 May to 14 June 2022. Confirmed cases remained substantially higher than active cases throughout the observed period.

Fig. 11 note: Note: The figure compares total deaths and total recoveries due to COVID-19 in Pakistan from 16 May to 14 June 2022. Total recoveries remained markedly higher than total deaths across the study period.

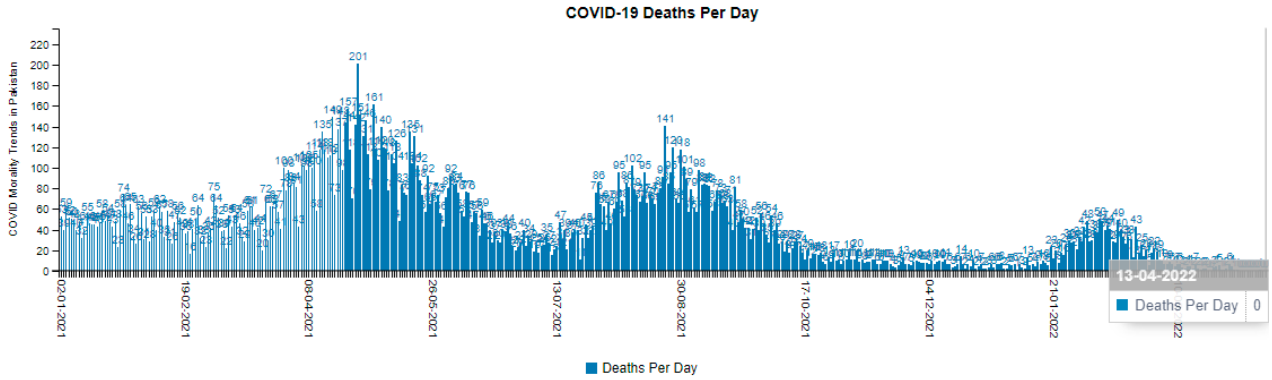


Fig. 12: Deaths per day by COVID-19 in Pakistan

Note: The figure presents the temporal trend of daily COVID-19 mortality in Pakistan. Daily deaths reached their highest levels during major waves in 2021, after which a gradual decline was observed. By early 2022, mortality had decreased considerably, approaching negligible levels by April 2022.

Table 4: Comparation of the Study Variables

Variable	Description	Analytic Relevance to Study
Case Counts	Daily or monthly confirmed COVID-19 cases	Indicates transmission intensity across waves; identifies Omicron surge patterns
Deaths	Laboratory-confirmed COVID-19 fatalities	Measures severity; evaluates reduction in mortality during Omicron wave
Recoveries	Number of patients clinically recovered	Helps determine resolution trends and healthcare burden
Active Cases	Total ongoing infections	Tracks wave peaks (Jan 2022) and declines (Apr 2022)
Positivity Rate	Percentage of positive tests out of total tests	Indicates viral prevalence and adequacy of testing
Testing Policies	PCR, antigen, serological test availability & criteria	Influences detection rates and quality of national surveillance
Hospitalizations / ICU Burden	Number of severe cases requiring care	Evaluates severity differences between Omicron and earlier variants
Vaccination Coverage	Population receiving full or booster doses	Explains reduced severity and mortality during Omicron period
Symptoms Profile	Upper vs. lower respiratory symptoms	Distinguishes Omicron clinical presentation vs. original SARS-CoV-2
Variant Characteristics	Genomic mutations in spike, RBD, NTD	Determines transmissibility, immune escape, and severity
Public Health Restrictions	Lockdowns, masking, quarantine, school closures	Provides context for observed epidemiological shifts
Policy Relaxation Status	Lifting restrictions post-March 2022	Correlates with decreases in severe outcomes
Geographical Data	Provincial breakdown (Punjab, Sindh, KP, etc.)	Compares regional trends across Tables 1–3
Wave-Specific Time Points	14 Jan, 14 Apr, 14 Jun 2022 snapshots	Enables structured wave progression analysis
Global Comparisons	WHO data on worldwide cases/deaths	Positions Pakistan's patterns within global Omicron trends

Comparison of study variables

Table 4 shows comparative analysis of study variable of present study. This comparative analysis shows progression of COVID 19 pandemic in Pakistan during Omicron's dominant phase. Cases counts and positive rates demonstrated a sharp rise in January 2022, which shows Omicron's high transmission, which followed by decline in cases in April and mild appearance by June, as documented in national NCOC data. Active cases followed this trend, with rise in January and decline by April, while recoveries increase throughout study period continuously. This data also indicates improved clinical outcomes. Mortality remained constant and stable at approximately 2%. It supports the evidence that despite rapid spread, Omicron only caused milder disease. Clinical variables further reinforced this pattern: symptoms profiles changed from lower respiratory infections shown in SARS-CoV-2 strains to upper respiratory tract infection during Omicron, which led to reduced hospitalization and ICU burden.

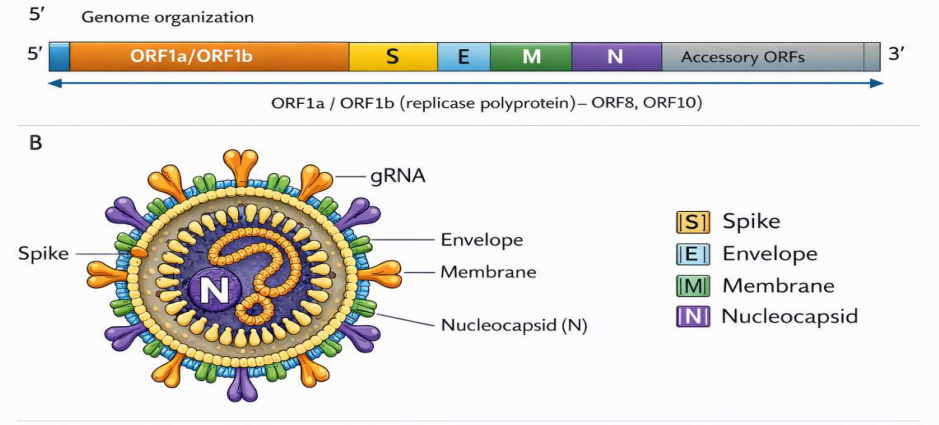


Fig. 13: Genomic Organization of Original SARS COV-2 (Hu et al., 2021)

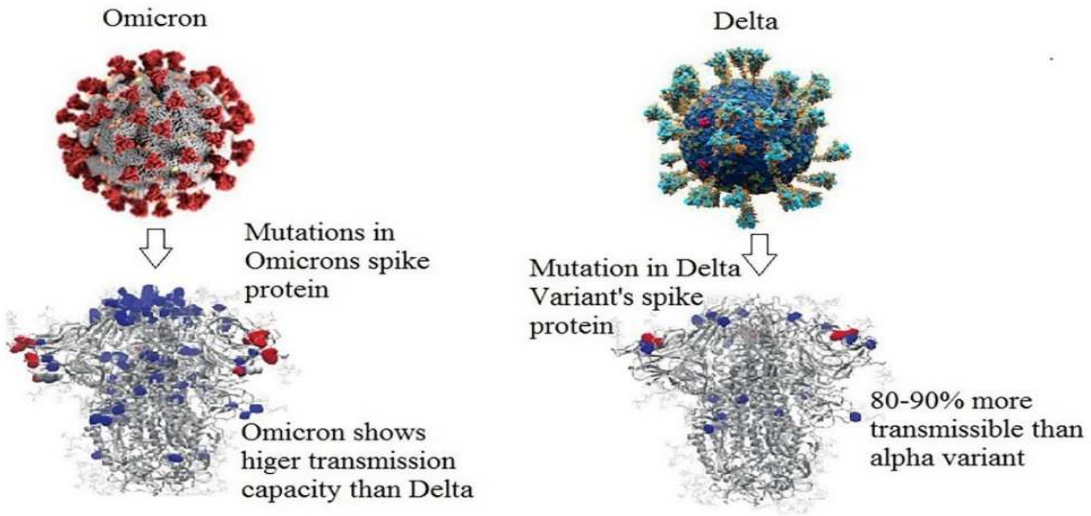


Fig. 14: Structural and mutation comparison between original SARS-CoV-2 and Omicron variants(Md. Rabiul Islam et al., 2022)

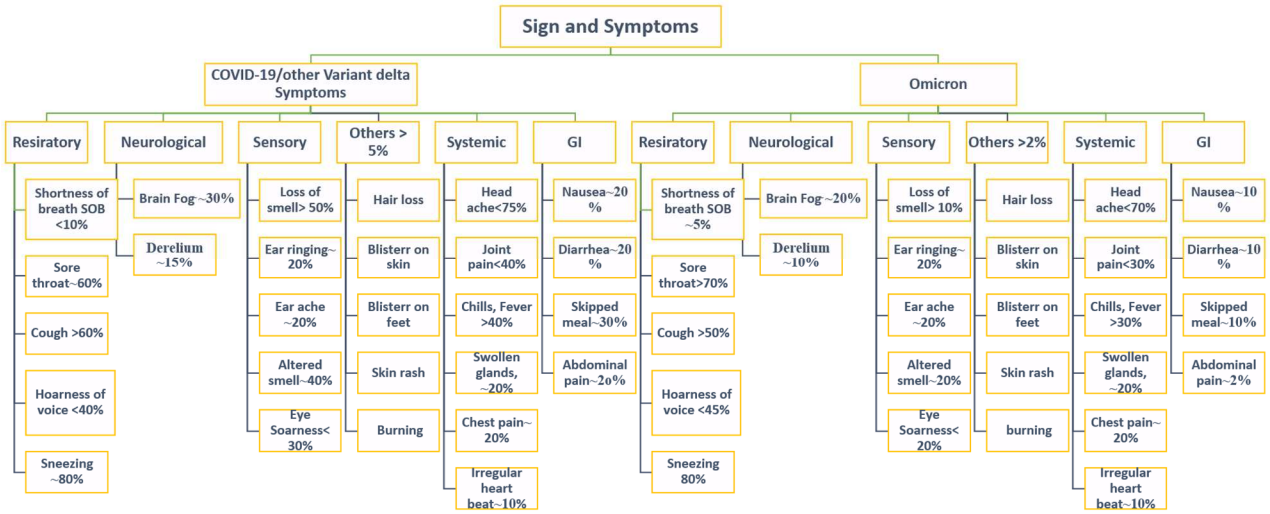


Fig. 15: Difference of Sign and symptoms of diseases induced by SARS CoV-2 and Omicron (Menni et al., 2022).

Variant-specific characteristics including extensive spike protein mutations and enhanced immune escape explained both the heightened transmissibility and the decoupling between infection and severe disease. Public-health variables also played a significant role; changes in testing policies, continued vaccination efforts and calibrated non-pharmaceutical interventions helped shape the observed epidemiological patterns. The national policy adaptation of relaxation in restrictions aligned with declining outcomes of the disease. Collectively, these variables provide understanding of Pakistan's pandemic trajectory, highlighting how biological properties of Omicron variant increased population immunity and responsive public health strategies led to reduced severity while managing transmission.

National response and relaxation of restrictions

During the first two years of the pandemic, Pakistan implemented strict public health measures, including nationwide lock down, closure of all educational institutions, markets and suspensions of outdoor social gatherings to stop the spread of COVID-19. However, following a sustained decline in severe cases after February 2022, the Pakistan government's policy on rigorous lockdown was altered (Noreen et al., 2021). After 16th March 2022, National Command and Operation Centre (NCOC) of Pakistan, lifted most restrictions for vaccinated individuals. Schools and other educational institutes were reopened with alternate classes schedules. Public events were allowed with standard precautions. Consequently, after noticing a continuous decrease in mortality and severity of diseases, Pakistan's regular social and economic conditions were restored completely in March 2022.

Difference between omicron and original SARS-CoV-2

Omicron differs sharply from earlier SARS-CoV-2 variants such as Delta across multiple biological and clinical dimensions (Guo *et al*., 2022). It carries more than 30 mutations in the spike protein, particularly clustered in the receptor-binding domain, enhancing its attachment to ACE2 receptors and enabling significant immune escape, which results in more frequent reinfections and breakthrough infections despite prior immunity or vaccination. These mutations also contribute to its markedly increased transmissibility, with Omicron spreading three to five times faster than Delta due to its high viral load in the upper respiratory tract and a short incubation period of only two to three days (Kumar *et al*., 2022). Unlike earlier variants that affected the lower lungs and caused severe pneumonia, Omicron affects the lower lungs much less, leading to milder illness with fewer hospitalizations, ICU cases and deaths (Trunfio *et al*., 2022).

Clinically, earlier variants commonly produced high fever, shortness of breath and loss of smell or taste, whereas Omicron predominantly causes upper-airway symptoms such as sore throat, hoarseness, cough, headache and joint or muscle pain, with sensory loss being far less common (Bouzid *et al*., 2022). Altogether, Omicron's extensive mutations, rapid spread, strong immune-escape potential, milder severity and altered symptom profile set it apart as a uniquely behaving variant among previous SARS-CoV-2 strains. The original SARS-CoV-2 strain that initiated COVID-19 had a comparatively stable genome whereas it involves fewer mutations and created infections that repeatedly involved the lower respiratory tract. It often leads to severe disease, hospitalization and higher mortality (Telenti *et al*., 2022). Figure 12 shows the Genome of original SARS-CoV-2.

The Omicron variant represses a higher number of mutations as compared to prior strain, especially in the spike protein, with the receptor-binding and N-terminal domains, that results in significantly altered spike structure and function (Ou *et al*., 2022). These mutations increase Omicron's ability to bind to the ACE2 receptor and escape neutralizing antibodies generated by former infection or vaccination, resulting in significantly increased transmissibility (Kudriavtsev *et al*., 2022). However, despite its rapid spread, Omicron generally causes milder clinical disease compared to the original strain, with reduced lung involvement and lower rates of severe outcomes, especially among vaccinated individuals (Nealon & Cowling, 2022). Omicron relies on endosomal entry pathway instead of TMPRSS2-mediated fusion for cell entry, hence it differs from original virus, therefore it affects tropism and pathogenicity. That shift from original SARS-CoV-2 variant to Omicron variant reflects the transition of disease towards high transmission and immune escape but reduced severity. Structural and mutation difference between SARS-CoV-2 and Omicron variants is illustrated in Figure 14. As Omicron variant possesses high number of spike protein mutations especially in RBD and NTD region, it leads to high transmission, enhanced immune system invasion compared to the original strain. Figure visualizes the extensive spike protein mutations in Omicron, especially in Receptor-Binding Domain (RBD) and N-terminal Domain (NTD). These mutations enhance immune escape, ACE2 binding affinity and Transmissibility

Key differences between SARS-CoV-2 and Omicron variants lie in their clinical presentation, transmissibility and overall disease severity (Arabi *et al*., 2020). Manifestation of original SARS-CoV-2 variant was fever, cough and shortness of breath, it mainly caused lower respiratory tract infection that led to severe pneumonia and increased risk of hospitalization and mortality. However, Omicron variant was mainly involved with upper respiratory tract symptoms such as sore throat, hoarseness, headache, cough and muscle or joint pain, while the classis loss of smell or taste is less frequent which is frequently seen in earlier strains (Ekroth *et al*.,

2022). As compared to earlier strains, Omicron variant rarely progressed to severe pneumonia, or acute respiratory distress syndrome, that results in milder clinical course for most patients. These distinct differences in symptoms and severity reflect Omicron's altered tissue tropism, which favors the upper respiratory tract, as well as improved population immunity from vaccination and prior infections. The transmission dynamics and severity have shifted from early SARS-CoV-2 to Omicron. It highlights faster spread, shorter incubation, lower lung involvement and reduced mortality (Andre *et al*., 2023). These graphical comparisons reinforce the narrative that the fifth wave's burden was largely transmission-heavy but severity-light. There are various mutations in viral genomes and in the spike protein that enhance ACE2 binding affinity and immune escape potential, enabling rapid spread across the population (Tian *et al*., 2022). This aligns with the observed sharp rise in national case counts during January 2022, where Pakistan experienced a steep surge in infections associated with Omicron's shorter incubation period and greater upper-respiratory tract tropism. In contrast, the original SARS-CoV-2 displayed slower transmission kinetics and greater lower-respiratory tract involvement, frequently progressing to severe pneumonia, hypoxemia and ARDS features that were significantly reduced during the Omicron-dominated period (Fan *et al*., 2022).

DISCUSSION

COVID 19 emerged in Wuhan, China in December 2019 and it appeared to be as a challenge to health crisis around the globe (Hu *et al*., 2021). Lockdown and social distancing were the front-end measures that were undertaken during that time especially for the patients suffering from disease. In Pakistan, SARS-CoV-2 transmitted via all three main routes of transportation i.e., sea, land and air (Noreen *et al.,* 2021). Molecular, serum and antigen tests were used as major tests for detection and surveillance of the disease (Rasool *et al*., 2022). These tests were selective and odd and relied upon population or on severity of infection. In 2022, active COVID 19 cases declined, but the cause remained unidentified (Abbas & Mannan, 2022a). Till date, researchers and scientists are putting numerous efforts to understand causative factors and preventive measures of the disease. It was a huge administrative issue for Pakistan to overcome COVID 19 pandemic (Raza *et al*., 2022). After the emergence of Omicron, lockdown policies were relaxed and several public awareness campaigns were launched regarding hygiene, focus on usage of mask in crowded places, social distancing and vaccination of the population (Hussain *et al*., 2022).

As per WHO data, there were more than 649 million confirmed cases of 6.65 million deaths reported worldwide by December 2022. As per the figure, Europe reported the highest number of cases prevalence, reflecting both extensive community transmission and stronger diagnostic and surveillance capacity. Despite many cases around the world, global use of almost 13 billion vaccines helped decouple number of infections from serious consequences during Omicron period. This means that even though many people were getting infected fewer people were getting severely ill. Trend of disease spread in Pakistan shows similar transmission patterns in the context of global trends. However, viruses spread more easily but caused less severe illness cases.

Following COVID 19, several variants of COVID virus evolved including Alpha, Beta, Gamma, Delta and Omicron. Among these, Delta variant was linked to greater transmissibility, greater viral load and high rates of re-infection (Andre *et al*., 2023). Whereas emergence of Omicron was also considered as highly transmissible and life threatening (Tian *et al*., 2022). In December 2021, Omicron was confirmed in United States, Canada and rest of the world. Omicron was concerned as novel variant of concern (VOC) because of its highest number of mutations, which is principal antigenic target of antibodies generated by infections or vaccination (Md Rabiul Islam *et al*., 2022). Omicron has numerous changes in spike protein (34-50) throughout its spike protein, it affects all parts of spike proteins and can alter how antibodies recognize the virus (Guo *et al*., 2022). Among these mutations, 15 mutations were observed in the receptor-binding domain (RBD) of the virus (De Marco *et al*., 2022). Scientists assumed that Omicron might have mutation that may help it to escape the vaccines, which caused concerns worldwide (Khan *et al*., 2022). Even a single change in virus amino acid can affects its ability to avoid the immune system, making development of vaccines more difficult (Bhattacharya *et al*., 2021).

Many of these mutations change how a virus interacts with binding sites where antibodies normally bind, some also change shape of spike protein making it difficult for antibodies to recognize the virus. Overall, these mutations in Omicron spikes cause more resistance for antibodies to neutralize the virus (Chatterjee *et al*., 2023). There is mixed data available regarding how vaccines are effective against Omicron, this variant is expected to spread rapidly around the world and to affect both vaccinated and unvaccinated population (Lu *et al*., 2022). Third dose (booster) of mRNA vaccine was found to be more effective for its neutralizing potential. Furthermore, Omicron variant was found to be replicated less effectively than Delta variant (Bowen *et al*., 2022). Importantly, antiviral drugs molnupiravir and remdesivir were found to be effective against Omicron variant (Jeong *et al*., 2022). With Omicron variant as the number of cases increased, question arose whether a natural infection

should be considered as vaccine dose. A study revealed that, people who were previously infected with SARS-CoV-2 developed stronger immune response even after a few vaccine doses (Bates *et al*., 2022). A debate has also been discussed whether term "fully vaccinated" covers initial two and third booster dose of vaccine. This term is important where proof of vaccination is required such as foreign travel, dining, joining indoor events, or meeting official requirements. The CDC defines "fully vaccinated" as two weeks after the receiving the Johson & Johnson/Janssen single-dose vaccination or the second dose of an mRNA vaccine. However, many institutions, sports organizations and places like the state of New Mexico consider one as fully vaccinated after completing primary doses with booster dose (Del Rio & Malani, 2020).

According to a new study, effectives of vaccine is much lower against symptomatic infections caused by Omicron than many other previous variants (Gardner & Kilpatrick, 2021). Early research studies conducted based on data collected from pharmaceutical companies used computer models to estimate how well COVID 19 vaccines worked after two doses against symptomatic Omicron infection whether form Pfizer/BioNTech or Moderna. These studies showed than efficacy of vaccines dropped to 30% for Omicron variants compared to around 87% against other variants. Another research study was conducted to investigate variations in symptoms, prevalence, risk of hospitalization among the vaccination population. It was identified that Omicron variant shows lower mortality rate and duration of infections is also lower than previous variants (Menni *et al*., 2022).

Using the ZOE COVD app that was undertaken in the United Kingdom research was also carried out to look for change in complaints based on self-reporting of individuals. Individuals described their weight, BMI, age, condition and vaccination status. Loss of smell was a less frequent symptom. However, throat infection/sore throat was more common condition in patients infected with Omicron strain which has lesser risk of hospitalization and shorter length of symptoms (Lo *et al*., 2021).

Another study revealed that German individuals who were partially or fully vaccinated along with booster doses with SARS-CoV-2 mRNA vaccine were still infected with Omicron variant. However, infection was mild. This showed that current mRNA vaccine was not fully able to prevent Omicron infection (Kuhlmann *et al*., 2022). More detailed clinical data is required to clearly define whether vaccines remain as integral preventive measures or booster dose is still necessary.

Across three stages (14 January, 14 April and 14 June 2022), the pattern of COVID 19 cases showed three phase trajectories. In January, cases rose very rapidly due to highly contagious and transmissible Omicron variant. In April both cases and deaths dropped significantly. In June slight increase in cases was identified possibly due to spread of number of Omicron sub-variants. Importantly with these fluctuations, there was no similar increase in severe illness or death. This supports the interpretation that Omicron caused less severe infection despite its higher transmission.

Clinical symptoms caused by Omicron variant were much different from original SARS-CoV-2 variant and Delta variant. Earlier variants mainly caused lower respiratory tract disorders like pneumonia, lack of oxygen and higher risk of ICU admissions and death. On the other hand, Omicron variant mainly caused upper respiratory tract symptoms such as sore throat, hoarseness, cough, headache, myalgia), with lower frequency of anosmia/ageusia (loss of smell/taste) and fewer patients reported severe pneumonia and acute respiratory distress syndrome (ARDS). These differences are mainly due to mutations in virus spike proteins, which explain how virus enters cells and how its severity is generally lower.

Public health policy in Pakistan updated along with these epidemiological changes. During early critical symptom days extreme non-pharmaceutical interventions (NPIs) such as lockdown, school closures, mask mandates and isolation or quarantine protocols were implemented. After February 2022, where cases continued to decline, many restrictions for vaccinated people were removed by Mid-March 2022. Schools and public events reopened with mandatory precautions. Alongside, national vaccination campaign along with global vaccination efforts helped reduce ICU admissions and deaths. This marked a transition from strict restrictions to targeted preventive measures.

Some important implications are obtained from these findings. First, future preparations for flexible and data-based measures that can be more restricted when cases surge and relaxed when cases decline. Second, as Omicron is continually mutating to new sub-variants, surveillance systems should monitor routine data and combine it with genetic engineering to better track and understand the changes. Third, immunization by vaccination and clear public communications can be essential tool to reduce risk for future waves and can protect healthcare system. Booster dose can be necessary for high-risk patients.

However, these findings must be considered with certain limitations. This data mainly comes from WHO and NCOC databases, difference in testing might indicate that certain cases were not reported especially in certain regions. Availability of limited data about certain sub-variants also makes it harder to link trends with specific strains. However, stable death rates during Omicron

period might be due to its lesser severity and missed or delayed reporting of mild symptoms. These limitations highlight the need for better and more consistent data collection, improved testing and stronger integration of genetic and epidemiological data for future studies.

Novelty of this article lies in its data that is specific to Pakistan, combining information on epidemiological patterns, clinical characteristics, symptoms changes, public health responses and Omicron related differences during 2019-2022 period. Unlike global studies, this article brings national data from WHO dashboard, NCOC reports and Pakistan based research to give a complete picture of fifth wave and emergence of Omicron variant.

This study summarizes that although the Omicron variant rapidly transmitted, but Pakistan experienced less severe cases, lesser hospitalization and mortality and improved recoveries. Mainly manifestation of variants were symptoms of upper respiratory tract. This article also explains how government eased restrictions, reopened schools, restored normal activities and continued vaccination that helped the country to manage fifth wave more effectively.

CONCLUSION

Fifth wave in Pakistan reflected global epidemiological dynamics, a rapid increase in transmission, followed by a sharp decline and mild re-emergence. The convergence of Omicron's biological properties, expanding vaccination coverage and calibrated public-health measures likely underpins this pattern. To manage subsequent variants while minimizing social disruption, investment in surveillance quality, genomic resolution and adaptive response capacity will be essential.

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Authors' contributions
Shahana Wahid: Conceptualization, Methodology, Investigation, Writing of Original Draft, Review & Editing. Azra Riaz: Supervision. Shumaila Qadir: Data Curation. Nausheen Hameed Siddiqui: Review & Editing. Zainab Fazal Haq: Investigation, Writing sections of Original Draft.

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Limitations of the study
This study has some limitations like rapidly evolving nature of COVID 19 and summarized data that does not portray recent developments. This study relies on national reporting systems such as WHO and NCOC dashboards.

Future research
Future research on COVID 19 in Pakistan should focus mainly on improving quality of surveillance system by integrating genomic sequencing with epidemiological monitoring to detect variants more effectively. Key areas include enhancing data collection, standardizing reporting and boosting testing to reduce under-reporting. Health strategies should move to targeted interventions only instead of strict lockdowns to combat Omicron type variants. Additionally, studies should evaluate the long-term effects of COVID-19 waves on healthcare capacity and vaccination behaviors and multidisciplinary research could provide insights into transmission dynamics and public compliance.

Note: The data described in the article was valid during the period of publication. However, as evidence related to COVID-19 is constantly changing, critics are recommended to access the official site of Pakistan destined for COVID-19 and the official website for the World Health Organization (WHO), for most up-to-date data.

***Abbreviations*:** ACE2, Angiotensin-converting enzyme-2; AKI, Acute kidney injury; ARDS, Acute respiratory distress syndrome; BMI, Body mass index; CKD, Chronic kidney disease; COVID, Coronavirus disease; hrACE2, Human recombinant angiotensin-II receptor blockers; ICU, Intensive care unit; MERS-CoV, Middle East respiratory syndrome coronavirus; NCOC, National Command and Operation Centre; NTD, N-terminal domain; nsps, Non-structural proteins; ORFs, Open reading frames; RBD, Receptor-binding domain; RAS, Renin–angiotensin system; RCTs, Randomized clinical trials; RTC, Replication–transcription complex; SARS-CoV-2, Severe acute respiratory syndrome–coronavirus-2; sgRNA, Sub-genomic RNA; SOB, Shortness of breath; TMPRSS2, Transmembrane protease serine-2; VOC, Variant of concern; WHO, World Health Organization

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