

## Review Article

## Wrestling with Time: from Pandemic to Endemic Are We Heading to the Beginning of an End

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### Abstract

On 30th January 2020, the World Health Organization (WHO) announced COVID-19 outbreak as the sixth public health emergency of international concern (PHEIC), and on March 11, 2020, the WHO declared COVID-19 as pandemic naming the corona virus disease (COVID-19) and the virus that causes it. SARS-CoV-2 has recently emerged as a global threat, directly affecting human life owing to its morbidity and mortality and indirectly, due to the enormous economic and psychological impact produced by social isolation, the most effective measure so far. From March 2020 to early 2022, many variants of SARS-CoV-2 have been identified driving different waves of COVID-19. Every single day we hear about some new variant with more rapid transmission rate and more severity. Currently the world is facing another wave of covid-19 because of omicron variant which was initially said to be milder disease intensity variant but highly transmissible. Experts were of the opinion of building herd immunity and getting covid-19 limited to some specific areas in the form of a milder ENDEMIC disease in future with variants like omicron. But every single day, exploding surge in omicron cases n mortalities make us all question the concept of pandemicity to endemicity. Meanwhile all we can do to lessen the burden caused by COVID -19 is to vaccinate more n more people, booster doses and to take help of some new antiviral drugs with proven efficacy along with social distancing and mask wearing.

**Key words:** SARS-CoV-2, different waves of covid-19 in Pakistan, covid-19 from pandemic to endemic.

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### Introduction

The human race has always been at the verge of some pandemic. Major pandemics and epidemics such as plague, cholera, flu, severe acute respiratory syndrome, coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) have already burdened humanity. A novel coronavirus (CoV-19) began to circulate people of Wuhan, China, around December 2019, the impact of which was poorly understood at that very time, which later on spread rapidly worldwide in 209 countries of America, Europe, Australia and Asia including Pakistan. Since then, this “severe acute respiratory syndrome corona virus 2” (SARS-CoV-2), has made an appearance as the source of a global pandemic, with nearly 379 million confirmed cases reported worldwide and over 5.69 million fatalities as of end January 2022<sup>1</sup>, while figure increasing rapidly with every single wave. The ubiquity and detrimental impact of SARS-CoV-2 across the globe has established it among the most notorious pandemics that have ever been recorded

in human history.

The earliest disclosure of a cluster of an atypical pneumonia, later known as SARS-CoV-2, dates from late December 2019, which was linked to people who visited the Huanan seafood and wildlife market in Wuhan city, Hubei, China.<sup>2,3</sup> Study of nucleotide sequences of SARS-CoV-2 genomes led to the opinion that the virus might have emerged as early as October 2019, a couple of months before its first detection.

SARS-CoV-2 is linked to the subgenus Sarbecovirus of the genus Betacoronavirus, and phylogenetic analysis demonstrated that it is more associated with two bat-SARS-like coronaviruses (88% identity at nucleotide level) than to the human SARS-CoV and MERS-CoV (79 and 50%, respectively).<sup>4,5</sup> There were conspiracy theories too claiming that it could have been deliberately created in the laboratory.

Lamentably, several aspects of the pandemic showed that the current outbreak is not a single event, nor will

it be the last of its kind. First, outbreaks of coronavirus infection have occurred frequently over the last two decades, although previous outbreaks remained relatively isolated at the regional level. These incidents include the first SARS outbreak in 2003 and the Middle East respiratory syndrome (MERS) in 2012, both of which induced severe human diseases.<sup>6,7</sup> Many outbreaks are still appearing in different parts of the world.

This covid-19 pandemic was not unpredictable; in fact, it was anticipated by many<sup>8,9</sup> and we had at least two “rehearsals”, SARSCoV in 2002/2003 and MERS-CoV in 2012, that affirmed the risk and harm of coronaviruses jumping from animals to humans.<sup>10</sup>

Since the outbreak of the novel coronavirus, people have been combating the ever-expanding list of symptoms, long term complications and the effects of different COVID mutations in and around the world. The recent surge in coronavirus cases is evident from the risks posed by the new evolving mutations, traced in various parts of the world. Not only is the severity of the symptoms alarming, but the increase in transmissibility of the infection is of more concerning with every single mutation.

COVID-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes. With the onset of the novel corona virus, people have been experiencing different and varied type of symptoms. Although the list has continued to increase and expand, the most common symptoms remain to be the same. Most classic symptoms of COVID-19 are;<sup>11</sup>

- Dry cough
- Sore throat
- Headache
- Runny and stuffy nose
- Chest pain and shortness of breath
- Fatigue
- Gastrointestinal infection
- Loss of sense of smell and taste

Clinical manifestation of COVID-19 can vary from very mild to moderate or severe and critical disease, with patients requiring mechanical ventilation. Asymptomatic cases are there too, and asymptomatic and pre-symptomatic patients play an important role in disease spread.<sup>12,13</sup> The median incubation period is 4 days with almost 95% of symptomatic cases showing symptoms at 11 days.<sup>11,12</sup> In 80% of persons, the disease is mild to moderate in intensity, presenting with a flu-like syndrome with resolution of symptoms in 10–14 days. The Kawasaki syndrome has been described in children and adolescents.<sup>14</sup> Twenty percent of patients present severe symptoms requiring hospitalization and about 5% will evolve to critical illness and intensive care

unit (ICU) admission, the majority of them with acute respiratory distress syndrome (ARDS), requiring mechanical ventilation. Renal failure occurs in 30% of critically ill patients, most of them require hemodialysis.<sup>15,16</sup>

Case fatality rate varies between 1–6% but in patients requiring mechanical ventilation, mortality can be as high as 61%.<sup>11,15</sup> Median time for hospital admission is 7 days usually and for ICU admission, 9.5 days.<sup>15,16</sup>

### **Situational and Statistical Analysis of Different Variants of SARS COV-2:**

Viruses are programmed to change and evolve through mutations. According to the World Health Organization (WHO), "When a virus replicates or makes copies, it changes a little bit, which is normal for a virus. These changes are called “mutations”. A virus with one or more new mutations is referred to as a “variant” of the original virus."

Multiple variants of the SARS-COV-2 virus have been circulating in and around the world. According to the Centre for Disease Control and Prevention (CDC), three classifications of COVID-19 variants are being monitored, namely variant of Interest (VOI), Variant of Concern (VOC), and Variant of High Consequence (VOHC). So far many strains have been defined<sup>17</sup>:

- Alpha (B.1.1.7 and Q lineages)
- Beta (B.1.351 and descendent lineages)
- Gamma (P.1 and descendent lineages)
- Epsilon (B.1.427 and B.1.429)
- Eta (B.1.525)
- Iota (B.1.526)
- Kappa (B.1.617.1)
- 1.617.3
- Mu (B.1.621, B.1.621.1)
- Zeta (P.2)
- Delta (B.1.617.2 and AY lineages)
- Omicron (B.1.1.529 and BA lineages)

Given the recent rise in the number of COVID cases and the prevalence of complications in not just the most vulnerable, but also in younger individuals, is an indication that the newer COVID variants pose greater risks to people's health and are associated with an increased risk of death compared to the original strain.

While SARs-COV-2 is a highly infectious disease, the different mutations have made it more transmissible. Many countries have experienced multiple waves of covid-19. Empirical Data show that characteristics varied between waves. Being the world's 5th-most-populous country, Pakistan has so far recorded the world's 29th-highest death toll (at approximately 29,330) and 29<sup>th</sup>-highest number of confirmed cases (at approximately 1,436,413). However, this number does not

include undercounting of COVID-19 infections in the country.<sup>18,19</sup> Pakistan so far has experienced four different waves of COVID-19 and currently facing fifth wave in view of omicron variant.

**First Wave**

The nation's first wave of COVID-19 began in late March 2020, peaked in mid-June when daily number of new confirmed cases and deaths soared high, this wave ended in mid-July. The first wave was marked by a low death rate and which began to drop very quickly after a short time peak. Most of the patients were with mild illness with a very little chunk of moderate severity illness patients. Fever and respiratory tract infection along with loss of smell and taste turned to be the predominant symptoms of that wave. Only little number of cases had severe disease leading to ARDS. Major risk sources were close contact with a previously confirmed patient and international travelling and trading.

After the first wave, situation improved with decline in daily deaths and positivity ratio because of strict lockdown policy, halting the transmission rate.

**Second Wave**

Cases and deaths started rising again in late October 2020 and peaked in mid-December 2020, culminating in the country's second wave mainly affecting Sindh and later on other provinces with a peak in mid-December 2020. The country battled this wave by using "smart lockdowns" and enforcing SOPs. Major risk was local transmission in this wave.

**Third Wave**

The country's third wave began in mid-March 2021, when positivity rates and new death number began to skyrocket. The third wave mainly affected the provinces of Punjab and Khyber Pakhtunkhwa. This wave peaked in late April 2021. Main risk sources were close contact with a previously confirmed patient, active and community surveillance, and cluster communities. Meanwhile, Vaccination drive started from early February.

**Fourth Wave**

In mid July 2021, there were Concerns of a fourth wave of coronavirus in Pakistan amid the emergence of the Delta variant a double mutant highly transmissible strain, the fastest, fittest and most formidable version of the coronavirus, first identified in neighboring India leading to a shot up in positivity ratio to 9% in May from 2% and 4% hitting Sindh and Punjab. Earlier it was classified as a "variant of interest" but later announced to be a "variant of concern" by the WHO because of easy transmission, more severe illness, reduced neutralization by antibodies or reduced effectiveness of treat-

ment and vaccines. The situation deteriorated in few weeks with more spread and mortalities, despite an expedited nationwide vaccination drive.

**Fifth Wave**

Currently Pakistan is facing a fifth wave of coronavirus omicron driven, spreading at a great pace amid surging infections across the country which started in late December 2021 since then cases are on rise, predominantly affecting Sindh and Punjab province with overall positivity ratio towering to 10 percent these days. The strain was first detected in southern Africa and Hong Kong in November, with the first known case in Pakistan identified last month in a woman who had no travel history outside the country.

A retrospective multi-centered study in Pakistan in April 2021 revealed the median age of infected individuals was 34 years. The adult age group (19–59 years) was affected more with predominance in males (80.9%) as compared to females (19.1%). 20 Commonest comorbidities were Hypertension, diabetes, cardiovascular conditions. The percentage mortality was 2.50% with the highest mortality among elders. In addition, differences in age range and severity of the disease have been reported—severe cases have affected more patients younger than 3 years and older than 60 years compared with previous waves.

**Pakistan Statistics**

Pakistan statistics of covid 19- to date showed:<sup>21</sup>

- CONFIRMED CASES 1,442,263
- DEATHS 29,372
- RECOVERED 1,312,819
- TOTAL TESTS 25,194,561
- Critical cases: 1590
- CRITICAL CASES 1,559

**Province wise Cases**

| Province    | Confirmed Cases |
|-------------|-----------------|
| SINDH       | 546,141         |
| KPK         | 197,937         |
| PUNJAB      | 483,779         |
| ISLAMABAD   | 129,758         |
| BALUCHISTAN | 34,557          |
| AJK/GB      | 39,323/10,768   |

**Future of Pandemic**

Two interconnected variables that are a key to project the future of the pandemic are immunity and viral evolution. People do develop a detectable IgG but it is

still not known whether this denotes some immunity and, if it does, for how long. There is some evidence that re-infection is unlikely, at least in the short term.<sup>22</sup> More data is needed to prove that the presence of IgG is indeed a correlate of immunity for SARS CoV-2. Every day a new variant origin with consumption of immunity imparted by vaccination or re-infection in previously treated patients reveal little value of Immunity imparted by IgG. Even if antibodies wane, protection may remain through cellular memory and fast regain of antibodies production upon exposure, as observed in other viral infections. In this scenario, sero-prevalence rates will indicate the actual risk for a population, and above a level of infection, estimated as 60–70%, the herd immunity may ensue.<sup>23</sup>

Viral evolution correlates with immunity in the context of viral escape and replication. The optimistic scenario is one where immune response to SARS-CoV-2 would be long lasting and, in populations with high sero-prevalence, new cases will be rare and self-contained, while the pessimistic one is where immunity lasts for only a few months, as seen for other human corona viruses.<sup>24</sup> and thus we will continue to witness periodic outbreaks, as the majority of the population remains susceptible.

Identifying asymptomatic and pre-symptomatic carriers that are contacts of index cases is clearly the strategy that reduces the rate of new infections.<sup>25</sup> Meanwhile, there are great expectations for a definite solution represented by an effective vaccine.

Many Countries are currently at different stages of the epidemic. With time it became more evident which approaches work better. Social isolation is extremely efficient in flattening the curve of the disease but it is inequitable in the long run. An effective vaccine is the only solution along with social distancing.

### Vaccine Statistics of Pakistan

Vaccination drive started in early February 2020 with an aim to combat the ongoing covid-19 strikes. Since then an effective vaccination expedition is going on. Recent statistics show 89.3 M people are fully vaccinated showing a chunk of 38% vaccinated population only:<sup>21</sup>

**First Dose:** 106,328,291

**Fully Vaccinated:** 83,275,083

**Booster Doses Vaccinated:** 2,666,553

**Total Doses Administered:** 178,996,974 ~almost 181million

With omicron rates soaring, you may find yourself dejectedly asking if this pandemic is ever going to end. Experts agree on that it will end. According to them we're not going to totally eradicate Covid-19, but we will see it moving from pandemic phase to endemic

phase where cases will be confined to a particular geographical location with constant presence in low numbers in that specific are. Its prevalence and impact will decrease to relatively manageable levels, so it might ends up more like the flu than a world-stopping disease.

For an infectious disease to be classed in the endemic phase, the rate of infections has to be stabilized across years, rather than showing big, unexpected spikes as Covid-19 has been doing. "A disease is endemic if the reproductive number is stably at one," Boston University epidemiologist Eleanor Murray explained. "That means one infected person, on average, infects one other person".<sup>26,27</sup>

We're nowhere near that right now. The outlook is more uncertain now because of highly contagious omicron variant and exploding cases because of it across the globe. And how should omicron is shaping our lives? A major concern of the time is: Does omicron push endemicity farther off into the future? Or could it actually speed up our path to herd immunity by swiftly infecting people and imparting immunity because of its milder nature and highly transmissible rate or is it just a misnomer?

Angela Rasmussen, a virologist at the University of Saskatchewan in Canada explained "It's really hard to say right now." Because endemicity isn't just about getting the virus's reproductive number down to one, but there are other factors that come into play, too: What's the rate of hospitalizations and deaths? Is the health care system overburdened to the point that there's a precipitous space or staffing shortage? Are there treatments available to reduce how many people are getting seriously ill? In general, a virus becomes endemic when we (health experts, governmental bodies, and the public) collectively decide that we're okay with accepting the level of impact the virus has — that in other words, it no longer constitutes an active crisis but with surge in covid cases drive by omicron variant, we are still in crisis mode. "So much depends on the burden it'll place on the health care system and that's going to be different from community to community. Definitely it has the potential to delay endemicity."<sup>26</sup> Rasmussen said:

A senior epidemiologist in Delhi<sup>28</sup> gave the similar statement that COVID-19 is heading towards an endemic stage. Favoring the concept of herd immunity he added that "Looking at the COVID-19 vaccination status and the natural infection, we can say that very soon, the majority of us will be getting an infection. And then this virus will convert into the endemic virus. The overall severity is less so the majority of us will get this infection. Based on the current scientific evidence, we can see those who recovered from the COVID they are the best-

protected person as of now, then the second-best protective person is those who had the vaccination.”

“The pandemic will end when the world chooses to end it. It is in our hands. We have all the tools in our hand but the world has not used those tools well. With almost 50,000 deaths a week, the pandemic is far from over” said by dr. Tedros WHO chief in a recent summit.<sup>27</sup>

Even though omicron so far seems to result in milder disease than previous variants but it does have the potential to delay endemicity. The high number of infection by omicron is building up population-level immunity. That’ll be crucial in terms of muting future waves. In addition to that, vaccinations and boosters are also contributing to “a significant immunity wall that’s being built,” said Joshua Michaud, associate director for global health policy at the Kaiser Family Foundation. There could be another variant which could evade immunity down the road”.<sup>28</sup>

The key determinant of when the pandemic ends is how long it will take to vaccinate the people around the world. Currently, we’re not pacing fast enough to starve the virus of opportunities to mutate into something new and serious.

Though we’re in much better shape now, than we were at the start of the pandemic. We’ve discovered a lot more information about how Covid-19 works. We’ve manufactured effective masks, vaccines, boosters, treatments, and rapid tests. But we need to pace up the vaccination expedition.

Almost two years into the Covid-19 pandemic, an end might finally be in sight.

Experts say that Covid will likely lose its “pandemic” status sometime in 2022, due largely to better global vaccination rates and developments of drugs for Covid. Eventually it will become endemic fading in severity and folding into the backdrop of regular, everyday life. Various strains of influenza have followed a similar pattern over the past century or more, from the Spanish flu pandemic of 1918 to the swine flu pandemic in 2009.<sup>29</sup>

Covid will probably remain dangerous once the pandemic ends — much like the flu, which killed as many as 62,000 people in the U.S. between October 2019 and April 2020, according to the Centers for Disease Control and Prevention.<sup>29</sup>

Endemic illnesses are always circulating throughout parts of the world, but tend to cause milder illness because more people have immunity from past infection or vaccination. You might get a cough and sniffles,

Like other respiratory viruses, there will be season of the year e.g fall and winter months when Covid infections peak —meaning Covid and flu seasons will be

concurrent. In addition to usual seasonal flu, wearing a mask during AND TO STAY AT HOME could become the norm in Covid season. If you’re up-to-date on your vaccinations, you’ll be protected enough to prevent severe illness or hospitalization.

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