Review Article

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Omicron variant in COVID-19 current pandemic: a reason for apprehension

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Abstract: COVID-19 emerged in Wuhan, China, but was caused by the original coronavirus, severe acute respiratory syndrome associated coronavirus-2 (SARS-CoV2). In early 2020, there was a widespread breakout of cases well over world, resulting in an epidemic that rapidly escalated to become a pandemic. This abruptly shook the global healthcare system. The emergence of the alpha, beta, and delta SARS-CoV-2 were associated with new waves of infections, sometimes across the entire world but until this month i.e., between Nov-Dec, 2021, Delta variant reigned supreme until the emergence of a newer variant i.e., Omicron (B.1.1.529) of SARS-CoV-2. Delta had 13 mutations. Of these, nine are in the spike protein, the protrusion on the surface of the virus that helps it latch onto human cells. Specifically, two are in a molecular hook, called the "receptor-binding domain". Omicron, a creation caused by monstrous mutations. At least 32 mutations are in the spike protein and 10 in the receptor-binding domain. was designated a COVID-19 variant of concern (VoC) by the World Health Organization (WHO) on 26th November 2021. Structurally, the omicron variant has shown too mutated at antibody binding sites which would leverage them for escaping the possible immune response by the body. We don't yet know much about the other alterations and how they might affect the virus's behavior. Omicron COVID-19 strain after identifying individuals with symptoms that were not the same as those seen in the Delta form. People with night sweats have also been reported. The new omicron variant has more mutations than the prevailing rampant delta virus. This makes the newer variant more transmissible, better able to evade itself from various vaccines readily available in the current scenario. These overall increases in the percentage changes in a single day cases of COVID-19 reported cases can be attributed to the beginning of third wave or can be speculated as newer surge of omicron variant cases. Yet another new variant has been detected in France with 46 mutations and 37 deletions in its genetic code, many affecting the spike protein. 'B.1.640.2' is the current nomenclature for this variation.

Keywords: COVID-19; delta variant; omicron variant; perspective; symptoms.

Background

The original coronavirus, severe acute respiratory syndrome associated coronavirus-2, was responsible for the development of COVID-19, which first appeared in Wuhan, China (SARS-CoV2). An epidemic that quickly escalated into a pandemic in early 2020 as a result of a global outbreak of cases that occurred on a large scale. This abruptly jolted the global healthcare system. Isolation of patients, quarantine, masking, social distancing, sanitizer use, and complete lockdown were all vital health-care procedures for everyone. With the 'new normal' and vaccination programmes, the number of cases and recovered patients began to rise months later. The relaxation of constraints during the plateau phase resulted in a resurgence of incidents, which affected people with greater ferocity and vengeance around the beginning of April 2021. Since COVID-19 virus originally surfaced in December 2019, and since then, numerous variants have evolved. The emergence of the alpha, beta, and delta SARS-CoV-2 were associated with new waves of infections, sometimes across the entire world but until this month i.e. between Nov-Dec, 2021, Delta variant

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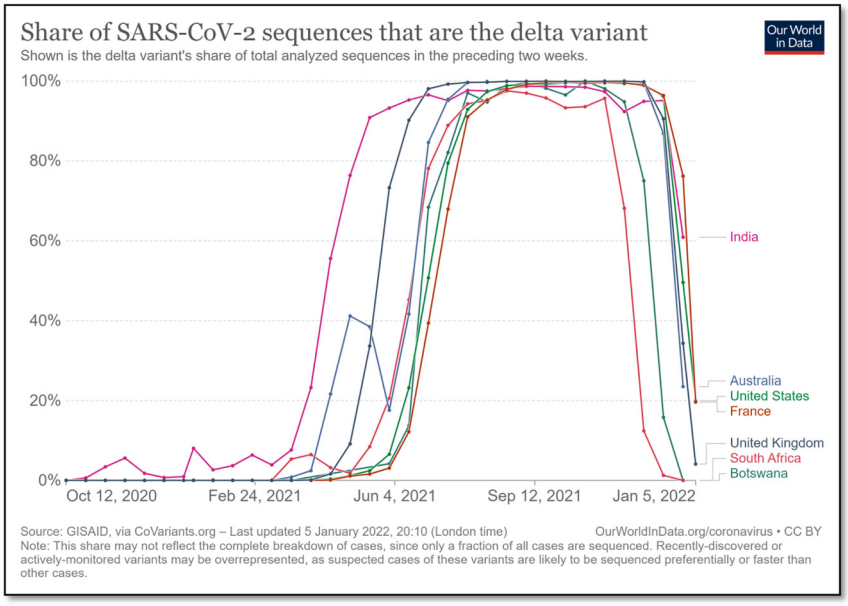

Figure 1: Share of SARS-CoV-2 sequences that are delta variant.

reined supreme until the emergence of a newer variant i.e., Omicron (B.1.1.529) SARS-CoV-2 (Figure 1).

Delta

There were 13 mutations. Nine of these are found in the spike protein, a protrusion on the virus's surface that aids in the attachment of the virus to human cells. According to Suresh K of Penn State University, who researches viral evolution, two are specifically in a molecular hook called the "receptor-binding domain," enabling it to adhere to cells more firmly. Many of the most successful mutations found in earlier variants, including Delta, it possesses changes found nowhere before. The effect of the delta variant can be seen considerably showing as an upsurge in the spread of the variant all throughout the second half of the year 2021 which later shows a substantial decrease toward the month of December.

It has been a quite a long time for the virus to be lingering around. But as the fall of the delta variant did give us some breathing space which was suddenly interrupted by a sudden emergence of newer COVD-19 variant i.e. Omicron. The variant (B.1.1.529 SARS-CoV-2 variant) was first found in a specimen collected on November 9, 2021, and reported to the World Health Organization (WHO) on November 24, 2021 [1]. Two days later, the WHO named the variant Omicron and classified it as a *Variant of Concern (VOC)*, because of increasing detections in South Africa and large number of mutations in immunogenic regions of the spike protein [1]. In addition to increasing cases in South Africa, the new variant may have been prevalent in other locations in southern Africa. Omicron has the most mutations of any variant of SARS-CoV-2, the virus that causes COVID-19. We still have to learn how those genetic changes behave.

Omicron

It is a creation caused by monstrous mutations. The spike protein has at least 32 mutations, and the receptor-binding domain has 10 mutations. The emergence of Omicron in the USA began with a case being found in San Francisco, followed by several others in New York, Minnesota, and Colorado the following day. This acts as a warning that Delta is not the end game [2] (Figure 2).

THE omicron variant, which was designated a COVID-19 variant of concern (VOC) by the World Health Organization (WHO) on 26th November 2021, has triggered travel restrictions, a race to accelerate booster vaccination programmes and renewed calls to address vaccine inequity. According to the WHO on 29 November, omicron poses a "very high" risk globally, and preliminary evidence suggests that it might be a more transmissible variant, which could lead to surges of infection [3].

By November 30, 2021, over 11 countries had reported 34 detections of the Omicron variant, with the first reports of international importations coming 35 from Hong Kong, Israel, Japan, and France [4]. Three days later, it was reported in 36 additional countries [4]. As of December 2, 2021, more than 50 countries had enacted border controls to slow the global spread of Omicron [5]. For example, Japan and Israel closed

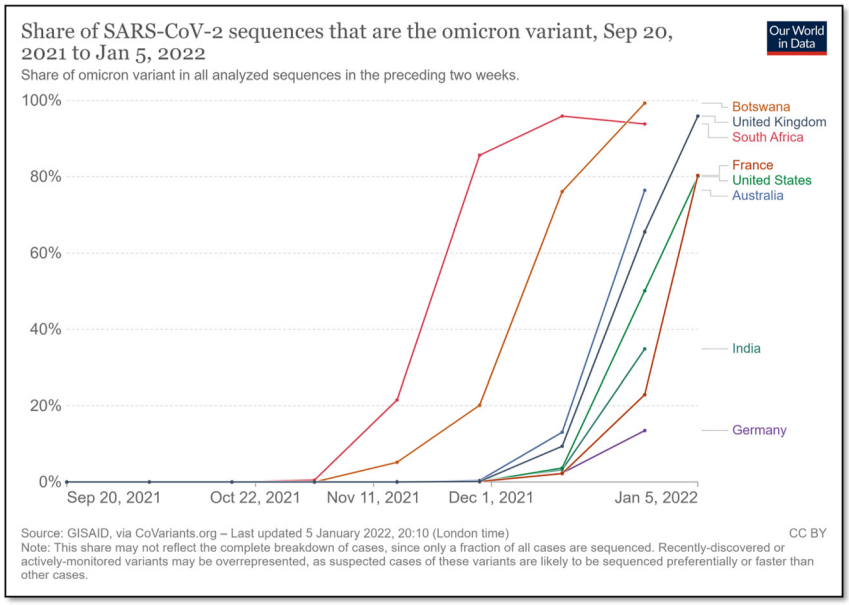

Figure 2: Share of SARS-CoV-2 sequences that are Omicron variant.

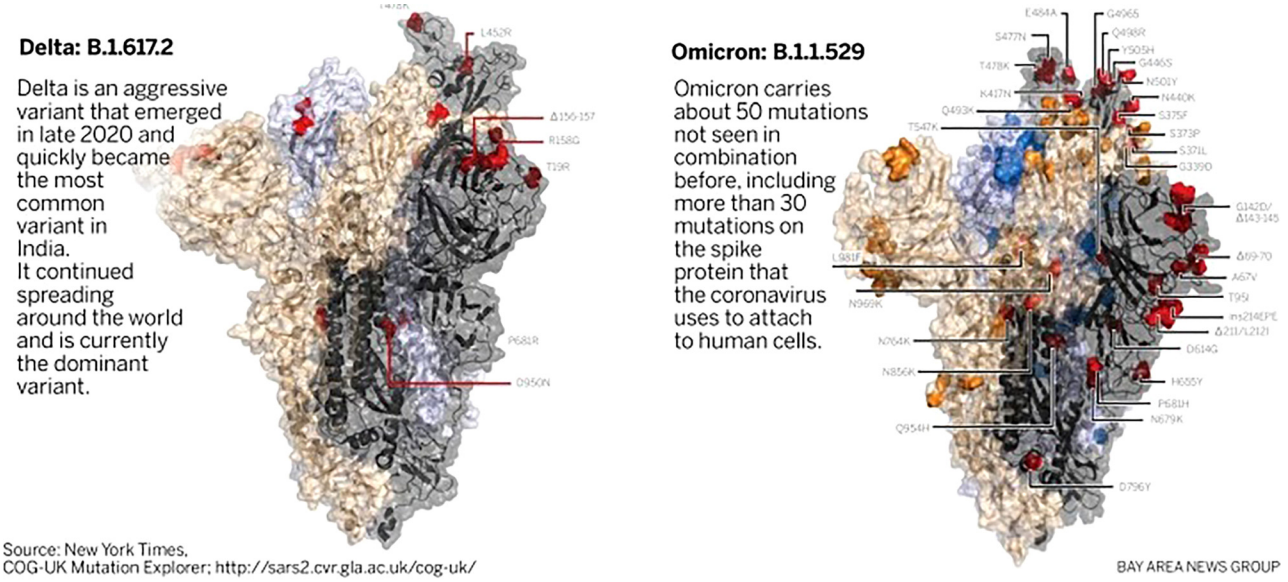

Figure 3: Structural comparison of the delta variant and the omicron variant.

their 38 borders to all foreign travelers [5]. The Omicron variant might have been spreading cryptically in these and other countries before the WHO declaration, undetected because of limited viral sequencing capacity.

What are these diverse mutations doing? It is still too early to tell whether they'll make Omicron worse than Delta. According to Kristian Andersen, an infectious disease specialist at Scripps Research, the combination of mutations rather than any single mutation alone is what really matters in this case. The spike protein has so many mutations, which can make the variant's capacity to infect cells and elude immunity stronger. Mutations known are: D614G"Doug", N501Y"Nelly", E484K"Eek", (COG-UK) are few to name (Figure 3).

The new omicron variant has more mutations than the prevailing uncontrolled delta virus. This makes the newer variant more transmissible, better able to evade itself from various vaccines readily available in the current scenario.

Structurally, the omicron variant has shown too mutated at antibody binding sites which would leverage them for escaping the possible immune response by the body. It has shown further more than 50 mutations including 26–32

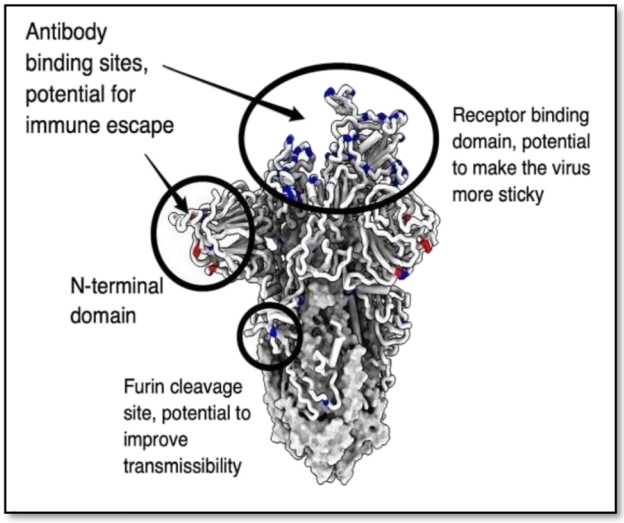

Figure 4: Omicron variant – Structural changes.

mutations on the spike proteins. These include newer amino acids being substituted or deleted or newly inserted [1, 4–8]. As a result, we don't yet know much about the other alterations and how they might affect the virus's behavior (Figure 4).

Mutations

The significant and decisive mutations in spike protein are G339D, S371L, S373P, S375F, K417 N, N440K, G446S, S477 N, T478K, E484A, Q493R, G496S, Q498R, N501Y, and Y505H [7]. These amino acid S371L substitutions occur in the Receptor Binding Domain (RBD). Interestingly, this variant carries mutations found in other variants of concern (VOC); it has the deletion at spike position 69–70, similar to the Alpha variant that leads to the S gene dropout or S gene target failure [9]. It in addition has three key mutations similar to those found in Beta and Gamma variants that confer immune escape [9]. Furthermore, it has a range of close mutations to the furin cleavage site similar to those present in the Delta variant [9]. Based on these mutations, it is thought that the Omicron variant may have similar characteristics to all other variants, at least at the molecular level [9, 10].

It is currently too early to remark on the variant's infectivity and its effects on vaccine efficacy/effectiveness based on actual scientific evidence. Because the Omicron's alterations are identical to those seen in other varieties, it is most likely very contagious and contagious. D614G, N501Y, and K417N spike protein polymorphisms are contemplated to make the virus more infectious [11]. Similarly, the H655Y, N679K, and P681H mutations (also present in Alpha and Delta versions) may augment virus transmission [9]. Antibodies developed in response to a natural infection have a low titer and dissipate quickly. Based on these assumptions, it is more likely that the omicron form will cause more reinfections. The antibodies produced for the natural infection are generally low in titer and dissipate quickly resulting more likely cause more reinfections with the omicron variant.

Signs and symptoms

A wide spectrum of illnesses and symptoms are brought on by COVID-19. It has been established that the majority of infections are asymptomatic or oligosymptomatic. Since the commencement of the outbreak, infected, asymptomatic individuals have been documented to transmit COVID-19. Some common symptoms observed during COVID-19 infections, but these differed from variant to variasnt. In the first wave of COVID-19, the only symptoms were fever, a persistent cough, and anosmia with augesia, but in the second wave, other symptoms like conjunctivitis, skin rashes, sore throats, diarrhoea, headaches, fatigue, and myalgia emerged along with discoloration of the finger and toes, dry mouth, and tongue [12]. Some of the changes so observed in symptoms pertaining to delta and omicron variant have been tabulated below in Table 1.

Dr. Angelique Coetzee, the chair of the South African Medical Association, was one of the first to suspect the Omicron COVID-19 strain after identifying individuals with symptoms that were not the same as those seen in the Delta form. Seven patients at her private clinic reported symptoms such as excessive weariness, moderate muscle aches, scratchy throat, and dry cough, according to her. Unlike other versions, they showed no loss of smell or scent, according to Dr. Coetzee. People with night sweats have also been reported by doctors in South Africa, where the variant was first discovered. Night sweats occur when you sweat so much that your night clothes and bedding are soaked wet [13].

Indian perspective: indian case scenario

On November 23, 2021, the first confirmed case of Omicron was detected in India. By 5th Jan 2022, there were 2,630 Cases of omicron confirmed. There were one death due to omicron was confirmed from Rajasthan. By the time, around 853 million people got vaccinated of first dose and 620 millions of second dose. Most of the Omicron cases seen in

Table 1: Common symptoms observed in Delta variant infection and Omicron variant infections.

Symptoms	Delta variant	Omicron variant
Fever	Common	Common
Tiredness/Fatigue/Exhaustion 	Sometimes	**Common**
Cough	Common	Common
Aches and pains 	Sometimes	**Common**
Running nose	Rare	Rare
Scratchy throat 	Sometimes	**Common**
Headaches	Sometimes	Common
Night sweats 	Rare	**Common**
Diarrhea	Rare	Rare

the state of Maharashtra (797) leads the country wide count and is closed followed by Delhi (465), Rajasthan (236), and Kerala (234). The number of Covid-19 cases in India is increasing at an exponential rate, allegedly powered by Omicron variant and noting that the R naught value, which indicates the spread of the infection, is 2.69, up from 1.69 at the peak of the pandemic's second wave. The rate of hospitalization is rather low. It is nearly 3.7 percent in Delhi and 5% in Mumbai. In comparison, the hospitalization rate was close to 20% last year. The rise in cases during the Omicron wave was not followed by a concurrent spike in hospital admissions, as was the situation during the Beta and Delta waves. When compared to Delta, these preliminary national data imply that Omicron is related with reduction in the likelihood of COVID-19 hospitalization [14].

The percentage changes notified by the government can be seen in various states with more active cases of COVID-19 being reported from Maharashtra seconded by West Bengal (Figure 5). Cities around the country are seeing a dramatic increase in the number of cases Over 15,000 cases were reported in Mumbai, the biggest single-day increase since the epidemic began in March 2020. On 5th Jan 2022, the number of Covid-19 cases in Delhi more than doubled, with 10,665 new cases reported. Pune, too, had a six-fold increase in the previous week, rising from 477 on December 30 to 2,813 on 5th Jan 2022. These overall increases in the percentage changes in a single day cases of COVID-19 reported cases can be attributed to the beginning of third wave or can be speculated as newer surge of omicron variant cases in these states which need to be confirmed by genetic sequencing.

Vaccination

SARS-CoV-2 mutation vaccines may still provide sufficient protection (Figure 6). The effect of the omicron variant on current vaccines should be evaluated as soon as feasible because the most of vaccines rely on SARS-CoV-2 spike proteins to activate immune cells. Most vaccines require two or three doses to stimulate acquired immunity. Later exposure to SARS-CoV-2 and its variants may have induced antibodies against the SARS-CoV-2 that resulted in protective antibodies and memory cells [15]. In a recent preliminary evaluation of a phase II or phase III research conducted by Pfizer, a novel COVID-19 oral antiviral candidate PF-07321332 (Paxlovid) shrunk the risk of hospitalization or death by 89% in contrast to the placebo. PF-07321332 is intended to block the activity of the SARS-CoV-2-3CL protease, an enzyme that participates in

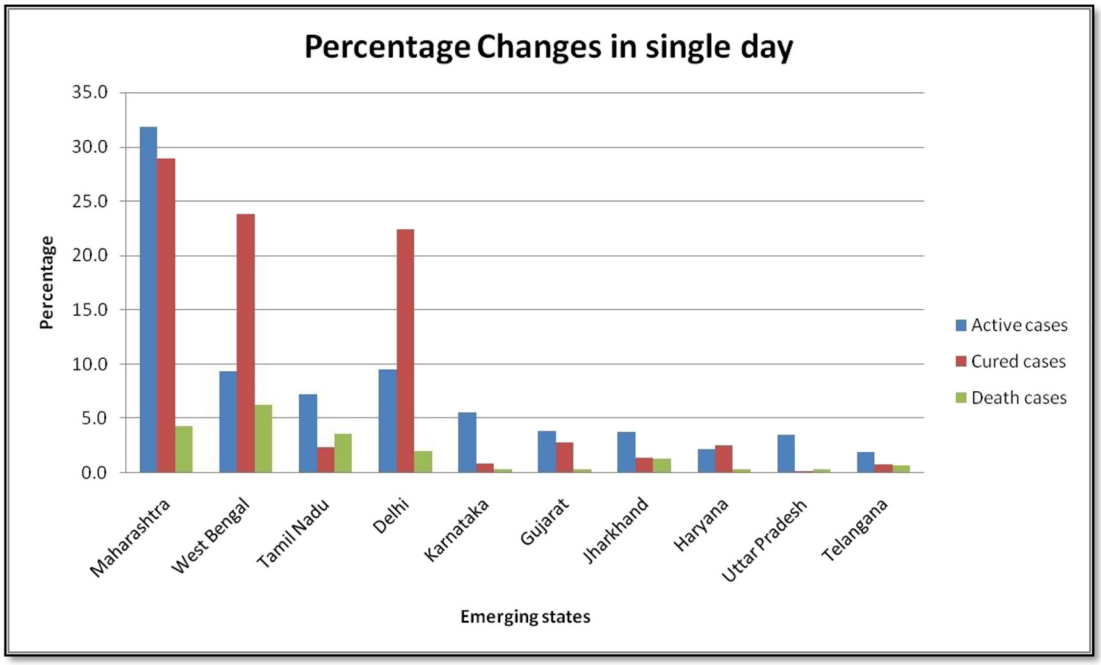

Figure 5: Percentage changes in a single day in cases across India.

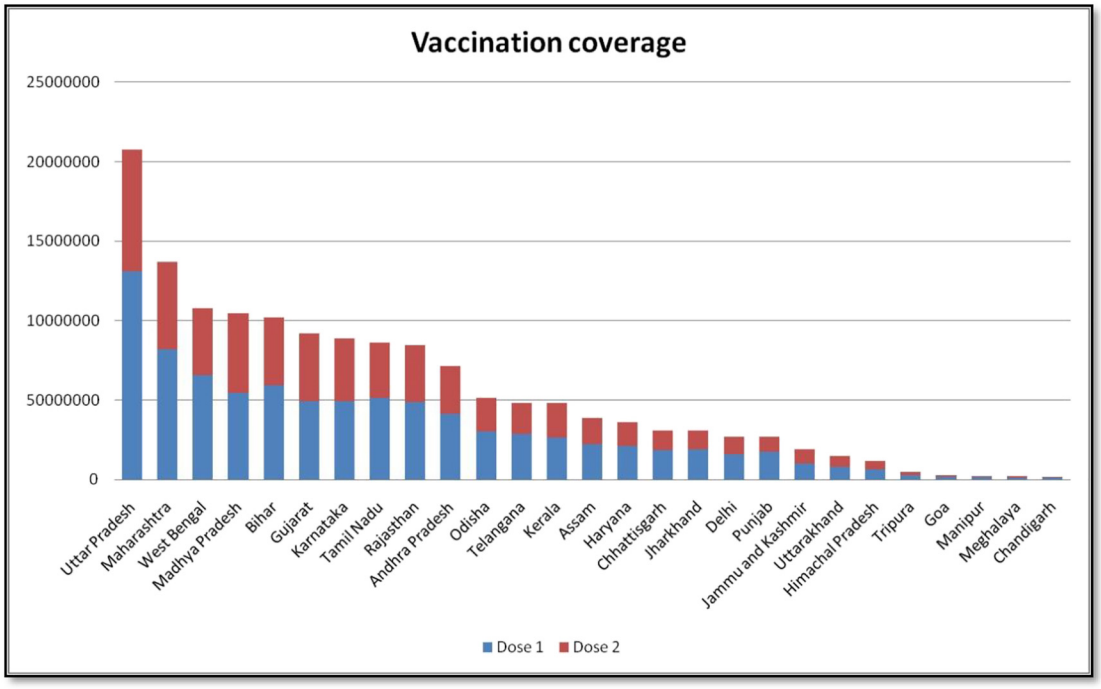

Figure 6: Vaccination drive in India.

virus replication. Prior to viral RNA replication, during a step of proteolysis, it prevents viral replication [16]. In order for PF-07321332 to stay active and sustain high concentration for a longer period of time to attack the virus, co-administration with a low dose of ritonavir may slow down the metabolism or breakdown of the drug [17]. However, the unvaccinated populations are most susceptible to the Omicron variant.

Preparedness

The World Health Organization recommends the following priority actions: increased surveillance to ascertain early warning systems are in position, including numerous indicators such as the virus's doubling rate, case incidence, and test positivity proportion. We need to do studies to increase our capability to understand transmission characteristics, vaccine effectiveness, severity, and the efficiency of public health and social measures against Omicron where expertise exists and in coordination with the international community.

Public health authorities should ramp up their efforts to hasten the implementation of the COVID-19 vaccination in all eligible groups, with a focus on those who are most at risk [18], for serious disease who remain unvaccinated or are not yet fully vaccinated which comprise of older adults, health care workers and those with any underlying conditions putting them at risk of severe disease and death. WHO advises that countries should continue to apply an evidence-informed and risk-based approach when implementing international travel measures in accordance with the WHO's interim guideline published in July 2021 [19].

New variant

Further novel variant has been uncovered in France, with 46 mutations and 37 deletions in its genetic code, several of which have an impact on the spike protein. 'B.1.640.2' is the current nomenclature for this variation. As a team from the Méditerranée Infection University Hospital Institute (IHU) in Marseilles, France, was the first to divulge the variant in a pre-print submitted to MedRxiv on December 29,2021, it has been designated the "variant IHU" [20].

Conclusions

The rampant increase in number of cases globally, is a cause of concern. Mortality rate though low, the new VoC i.e., Omicron is highly transmissible but gives the impression to be less infective. This still need to be studied under longer term review of these newer variants. The vulnerable group of population needs to be protected by the means of vaccination which can only be achieved by the governing authorities. All the needs to pondered upon as there might be many more mutations lurking around. Maybe this is the beginning of the third wave and are we really prepared for the occurrence of the same. Hence, keeping in mind the apprehension of the third wave, globally we need to get together and put up a battle against the COVID-19. Or this can be well thought-out as natural response to the prevailing infection and being projected as a nature's own response to the prevalent pandemic.

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