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## Omicron variant: Current insights and future directions

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### ABSTRACT

The global COVID-19 outbreak has returned with the identification of the SARS-CoV-2 Omicron variant (B.1.1.529) after appearing to be persistently spreading for the more than past two years. In comparison to prior SARS-CoV-2 variants, this new variant revealed a significant amount of mutation. This novel variety may have a greater rate of transmissibility which might impede the effectiveness of current diagnostic equipment as well as vaccination efficacy and also impede immunotherapies (Antibody / monoclonal antibody based). WHO designated B.1.1.529 as a variant of concern on November 26, 2021, identified as Omicron. The Omicron variant transmission method and severity, on the other hand, are well defined. The global spread of Omicron, which has now seized many nations, has resulted in numerous speculations regarding its origin and degree of infectivity. The following sections will go over its potential for transmission, omicron structure, and impact on COVID-19 vaccines, how it is different from delta variant and diagnostics.

### 1. Introduction

The coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that emerged from Wuhan, China in December 2019 posed a significant threat to the global public health (Yang et al., 2020; Guan et al., 2020). COVID-19 causes a variety of symptoms, including fever, dry cough, and shortness of breath, muscle pain, fatigue, sore throat, and anosmia. After emerging of Covid-19, various mutations occur in the virus resulting in various mutant strains like alpha, beta and delta variants. About 23 months since the first reported case of COVID-19, on 24 Nov 2021, a new SARS-CoV-2 variant of concern (VoC), omicron was reported in South Africa. B.1.1.529 was discovered in specimens taken in Botswana on November 11, 2021, and in South Africa on November 14, 2021 (Organization WHO, 2021a). Based on the recommendation from World Health Organization's Technical Advisory Group on Virus Evolution, World Health Organization assigned variant B.1.1.529 as a variant of concern (VOC) on November 26, 2021, and named the strain Omicron. The Omicron variant is a highly divergent variant with a large number of mutations, including 26–32 in the spike protein, some of which are concerning and may be linked to humoral immune escape potential and increased transmissibility and it is considered as the most mutated strain among SARS-CoV2, including VOCs and VOIs. Four structural proteins—Spike (S), Envelope (E), Membrane (M), Nucleocapsid (N)

proteins, and nonstructural proteins (NSPs) (NSP3, NSP4, NSP5, NSP6, NSP12, NSP1)—all have the amino acid alterations of the Omicron variant (Gu et al., 2021). The Omicron variant had been identified in 89 countries across all six WHO regions as of December 16, 2021. B.1.1.529 had spread to 105 countries as of January 10, 2021. According to the WHO, as of November 28, 2021, there is no indication that the symptoms associated with Omicron are unique from those linked with other variants. The condition's severity, as well as its specific indications and symptoms, are yet unclear (WHO, 2021). The Omicron variation has been detected in 188 nations as of 31 March 2022 and had already become the dominant strain on a worldwide scale, contributing for 99.7% of registered sequences from 23 February to 24 March 2022 (Guo et al., 2022). Four sub lineages of the Omicron variety have emerged: BA.1, BA.1.1, BA.2, and BA.3. The most prevalent Omicron variants in circulation are BA.1, BA.1.1, and BA.2. S-gene target failure may be used to determine the Omicron BA.1 variant, commonly referred to as the original form. BA.1.1 is a sub-lineage of BA.1 with an R346K alteration in the spike protein. Notably, the fraction of BA.2, which does not produce SGTF, is increasing, and the Omicron BA.2 variants has become prominent in several nations, including Denmark, India, Norway, and Singapore, indicating that it may have a selection advantage over the Omicron BA.1 variant. According to one epidemiological research conducted in Denmark, the effective reproduction number of BA.2 was approximately 1.26 times more than that of BA.1 (Guo et al., 2022).

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Although BA.1 is expanding more quickly than BA.2, BA.2 has gained ground in a number of countries from January 2022. The BA.2 lineage's spike protein has a different genetic sequence than the BA.1 lineage, indicating that it may give stronger immunological tolerance to antibodies (Yamasoba et al., 2022a; Wang et al., 2022; Desingu et al., 2022). As more data becomes available, our understanding of the Omicron variant continues to evolve. There is strong evidence that Omicron has a significant growth advantage over Delta. In countries with documented community transmission, it spreads significantly faster than the Delta variant, with a doubling time of 1.5–3 days. Omicron is rapidly spreading in countries with high levels of population immunity, and it is unclear how much of the observed rapid growth rate can be attributed to immune evasion, intrinsic increased transmissibility, or a combination of the two. However, based on current data, Omicron is likely to surpass Delta in the case of community transmission.

The Omicron variant of SARS-CoV-2 infects cells that depend on its obligatory receptor-angiotensin-converting enzyme 2 (ACE2) (Guo et al., 2022). The S1 and S2 subunits, as well as furin protease cleavage sites, are present in the SARS-CoV2 spike protein. The N-terminal domain (NTD) and receptor-binding domain make up the S1 subunit (RBD). The receptor-binding motif (RBM) directly interacts with the angiotensin-converting enzyme-2 (ACE2) receptor on the surface of human cells, mediating viral invasion and determining the virus's transmissibility (Lu et al., 2020; Pachetti et al., 2020; Ye et al., 2021). Furthermore, the spike protein is the primary target of elimination for convalescent plasma, vaccinations, and monoclonal antibodies (mAbs) (Lan et al., 2020; Hoffmann et al., 2022). Adaptive mutation of the SARS-CoV2 genome can alter the virus's infectivity, immune evasion, and phenotypic features (Tian et al., 2021; Harvey et al., 2021; Volz et al., 2021). The discovery of the Omicron variety has raised severe concerns regarding enhanced infectivity, immune escape capabilities, and the potential of reinfection (Islam et al., 2022). From April 2022 and onward, the fifth wave in South Africa was quickly started by the two new Omicron lineages (BA.4 and BA.5), which now account for more than half of all sequenced cases (Tegally et al., 2022). The BA.4 and BA.5 lineages were confirmed for the first time in samples taken in South Africa in January and February of 2022. Ever since, these lineages have also been uncovered in other regions of the world, and they are now recognized in several nations. While this has been happening, several new sub variants/sub-lineages of Omicron have appeared, some of which, primarily BA.2.11 (France), BA.2.12.1 (USA), and BA.4/5 (South Africa), are currently displacing BA.2 in a number of nations (Yamasoba et al., 2022a, 2022b). The number of BA.4 and BA.5 cases is increasing globally, according to GISAID. By the end of April 2022 in South Africa, the percentages of sequences for BA.4 and BA.5 had reached 35% and 20%, respectively. As of May 8, 2022, according to the ECDC, BA.5 accounted for 37% of positive cases in Portugal. According to these growth rates, the Omicron lineages BA.4 and BA.5 may be more transmissible than other Omicron lineages (ECDC, 2022b; Tegally et al., 2022). South Africa reports the majority of these instances, although BA.4 has also been found in Austria, the UK, the USA, and Denmark, while BA.5 has been found in Germany, Portugal, the UK, and the USA. Due to the projected greater transmissibility of these variations, there may be a considerable overall rise in COVID-19 cases in the future (ECDC, 2022b). These two sub-lineages (BA.4 and BA.5), which were previously classified as variants of interest (VOI), have recently been reclassified by ECDC as variants of concern (VOC) (ECDC, 2022a).

In addition to these, SARS-CoV-2 recombinant/hybrid forms (XD, XE, and XF) have been discovered, with XE (BA.1/BA.2 recombinant form) encountering the greatest threat to human health worldwide during the ongoing COVID-19 pandemic (Basky and Vogel, 2022; Chakraborty et al., 2022; Mohapatra et al., 2022a, 2022b, 2022c; Rahimi and Abadi, 2022). The Institute Pasteur in France has likewise acknowledged and validated the XD variant (AY.4/BA.1), and the genome sequence has been sent to GISAID. The VOCs Delta (AY.4) and Omicron BA.1 were recombined to create the XD lineage, which is

regarded as a recombinant lineage (Chakraborty et al., 2022). Two more SARS-CoV-2 recombinant variants, XE and XF, were also verified in addition to this recombinant variation (XD). The two Omicron sister variations, Omicron BA.1 variant and Omicron BA.2 variant, which are recombinant genomic elements, gave rise to the recombinant XE variant. Similarly, the recombinant XF variant was constructed by combining the recombinant genomic components of two variants: The Delta variant and the Omicron BA.1 variant. (Chakraborty et al., 2022).

We will go over the omicron's overall structure and how it differs from prior variants like delta, as well as the many diagnostic procedures available and whether the antibodies produced by existing vaccines are effective enough to neutralize the omicron's function. Also, we will discuss the possible future direction to mitigate the spreading of the Omicron variant.

## 2. Omicron: Emergence, pathogenic evolution

Omicron strains initially emerged in late September or early October, indicating that it is expanding more gradually than is currently thought (Kupferschmidt, 2021a; Quarleri et al., 2021). Although that indicates that this mutant has supplanted older variants in South Africa, nonetheless, any findings might be inaccurate assuming that the viral profile rose with the spike in the number of patients and remained mostly limited to the Omicron infected regions. Preliminary findings from a clinical investigation in South Africa suggested that the Omicron version would indeed be able to evade immune responses and have a greater transmissibility, which might have serious repercussions (Cele et al., 2021). Coronaviruses (CoVs) are unlike other RNA viruses in that they are extremely adaptive to shifting ecological niches owing to excessive mutation rates triggered by a number of circumstances (Banoun, 2021). The genome is spiced up by the unique manner of viral replication, which is handled by the "copy-choice" technique and viral recombination (Terada et al., 2014). Template swapping, which occurs at numerous places and resulting in the creation of new viruses, is one method that has been found in Feline Coronavirus Type II Strains. That resulted from a twofold recombination event between Feline Coronavirus Type I and Canine Coronavirus (Herrewegh et al., 1998). It is evident that CoVs may recombine amid two distantly related parent viruses, and that the offspring produced may differ from the parent in cell culture and receptor utilization (Terada et al., 2014). It is plausible that the appearance of VOC is related to the dissemination of multiple strains. It's reasonable to assume that this Omicron variety acquired up at least one mutation from yet another virus, perhaps one that induces the cold, that enables it bypass the host immune system and proliferate more efficiently whilst generating a modest form of the disease (Lapid N, 2021). In general, fitness and virulence traits of viruses are thought to be linked, however major discrepancies have been documented. Viral fitness and virulence, on either hand, are modulated by complicated cell specificities, viral-host interactions, and virus-virus interactions. Viral quasispecies, which are well-defined mutants originating from the complicated mutation-selection process, are constantly present and relatively abundant in a host cell niche due to immunological stresses, changing environment, or simply error-prone replicating machinery (Furió et al., 2012). Omicron is said to have improved fitness, as indicated by its great transmissibility (WHO, 2021b). Mutations are prevalent in viruses, and SARS-CoV-2 is no exception; nonetheless, the scientific community's primary worry stems from the greater ratio of mutations found in the Omicron variant's genome (Kupferschmidt, 2021b). The Omicron variant's sequence analysis revealed that mutagenic impact is higher on S1 than on S2, and it is free of backbone hydrogen bonds, increasing mutability (Penner, 2021). The phylogenetic study Omicron variant was analysed using two separate models, the Kimura model and the Jukes-Cantor model, although the results of both models were different. When using the Kimura model, it was discovered to form a novel monophyletic clade distinct from previous SARS-CoV-2 variations, although the Jukes-Cantor model demonstrated

a strong link between alpha and Omicron variants (Kandeel et al., 2022; Du et al., 2022; Lennerstrand et al., 2022). There are four possible theories/hypotheses about Omicron's origin, including VOC (Sun et al., 2022; Naveca et al., 2021). First, it is thought that the virus began propagating and changing in a restricted group of humans, where it evolved rapidly to become extremely distinct from other versions, furthermore it spread to the rest of the population (Wild, 2021). SARS-CoV-2 infection was also reported to have lasted more than six months in a patient with advanced Human Immunodeficiency Virus (HIV) who had failed antiretroviral therapy. Apart from that, it was discovered that the E484K alteration, which is linked to immune escape, and the N501Y substitution, which is linked to most VOC, have emerged, bolstering the concept of intra-host evolution of VOCs in the same patient (Kupferschmidt, 2021c). Alternatively, as in the case recounted, the virus might have lingered in an immune-compromised person for a longer length of time (Karim et al., 2021). It's safe to assume both mRNA- and non-mRNA-based vaccines had a role in the onset of Omicron variants in a chronically infected COVID-19 patient, permitting the virus to expand and transform while gaining the capacity to evade the body's immune response (Li, X., 2021). Another reason for the high mutation rate might be because immunological pressure varies between species, which could contribute to the increased mutation rate. It should be emphasized that animals have been infected with SARS-CoV-2 developing variations, including the delta form (Bonilla-Aldana, 2021; Karikalan et al., 2021). Another argument is that if an immune system is compromised with two coronaviruses, coupling is conceivable, and Omicron may have acquired so many mutations. Recombination events between SARS-CoV-2 types are visible, despite the theory's pessimism (Le Page, M., 2021). Wei et al. has offered a notion of Omicron genesis in mice. Further research, comparative analysis of molecular mutation spectra from multiple host species and then molecular docking, indicated that pre-epidemic Omicron mutations in the Spike protein were incredibly homologous to the mutations seen in mouse-adapted SARS-CoV-2. Per the result of this research, the forebear of Omicron may have hopped from humans to mice, gained mutations quickly that allowed the virus to infect mice, and then jumped back into humans, indicating an inter-species phylogenetic projected path to be aware of the current Omicron variant infestation (Wei et al., 2021).

### 3. Structure of Omicron

Omicron is unlike any other variety currently in circulation in terms of structure. In comparison to the original Wuhan strain, the variation has 60 mutations (50 non-synonymous, 8 synonymous, and 2 non-coding) and some of which have alarmed researcher (Hurst, 2021). The mutations in the variation are extraordinarily numerous, with several of them being unique (Torjesen et al., 2021). At least 50 amino acid mutations and about 10 non-amino acid-altering changes have been found in Omicron, some of which may be in regulatory regions (Hoffmann et al., 2022). At the time of the Omicron variant's discovery, a considerable proportion of them affected the spike protein targeted by most COVID-19 vaccines. The spike protein, which is the principal antigenic target of antibodies produced by infections and many extensively used vaccinations, has 32 mutations. Many of the alterations had never been seen before in any other strain (Cookson and Barnes, 2021; Callaway, 2021). In comparison to the original virus, the variation has 30 amino acid modifications, three small deletions, and one short insertion in the spike protein, 15 of which are in the receptor-binding domain (residues 319–541). In addition, it has a number of deletions and alterations in other genomic areas. There are also three mutations at the furin cleavage site in this variation (Hanage, W., 2021). Substitutions of Key Amino Acids in Spike Protein are A67V, del69–70, T95I, del142–144, Y145D, del211, L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F (Science Brief, 2021). Five sub-lineages of

Omicron have been discovered by the scientists. The standard sub-lineage is now known as BA.1 /B.1.1.529.1, while the other two are known as BA.2 /B.1.1.529.2 and BA.3 /B.1.1.529.3 and the most recent sub-lineage are name as BA.4 and BA.5. The variant may also be immune to cell-mediated immunity, according to computational modeling (Callaway, 2021). With the exception of a few East African strains (A.30 and A.23.1), Omicron is derived from the first major variety of SARS-CoV-2, which we call The Triad and others call D614G. Many of the most concerning mutations reported in earlier variants of concern are detected in Omicron, as well as many unique mutations in both the S and non-S proteins (Hoffmann et al., 2022). Omicron has a large number of previously known mutations in different VOCs, and several other proteins vital for viral replication, such as NSP12 and NSP14 (Gao et al., 2022). Mutations in Spike proteins are thought to have improved the Spike's ability to bind to the ACE2 receptor on host cells (Kupferschmidt, 2021b). There are ten synonymous mutations in Omicron that do not result in an amino acid change. Except for C241U, all 10 synonymous alterations in Omicron are unique. However, by changing the structures and crucial recognition sequences in viral RNA essential for replication, transcription, and translation, such modifications may disrupt what are known as cis-acting regulatory sequences (Hoffmann et al., 2022). According to one of the research findings, current neutralizing antibodies will still attach to the Omicron variant's altered spike protein. However, as compared to the reference RBD structures, it appears that Omicron's RBD has a low propensity for neutralizing antibodies. This finding implies that antibodies produced by vaccinations or a past infection may offer some protection against Omicron (Ford et al., 2022). Accessory proteins are mostly immunological regulators; however, Omicron has no mutations in this area, which is unusual given that proteins like Orf8 and Orf6 are frequently heavily altered, possibly indicating Omicron's selection pressures (Hoffmann et al., 2022). The number of nucleotide alterations in the Omicron genome was in the following order when compared to other variants: SARS-CoV-2 USA isolate > Mu variant > Beta variant > Delta variant > Gamma variant > Alpha variant > Omicron variant, with 141, 140, 138, 132, 130, and 109 mutations, respectively. The Alpha variant has the maximum identity percentage (99.63%) with the Omicron version when compared to other variants, followed by Gamma and Mu variants (99.56%). Interestingly, upon genome alignment with other viruses, the Omicron variant had the most gaps, ranging from 43 to 63 (Kandeel et al., 2022). Fig. 1 illustrates the structural lineages of omicron.

The efficiency with which the Omicron variety can spread from person to person is yet unknown. The differences in the spike protein suggest that the Omicron variant is more extremely contagious than the COVID-19 virus, but it's impossible to say if it's more transmissible than Delta (Science Brief, 2021). Because the Omicron variant's effective (instantaneous) reproduction number is 3.19 (95% CI 2.82–3.61) times greater than the Delta variant's, a substantial increase in Omicron instances is likely in the near future due to its significant advantage of increased transmissibility (Ito et al., 2022). In vitro evidence provided by Chinese scientist shows that mutations at the N440K, T478K, and N501Y locations confer ten times and two times increased infectivity to Omicron, respectively, when compared to the original SARS-CoV-2 variation and Delta variant (Chen et al., 2022). The Omicron strain might be ten times more contagious and twice more infectious than the Delta variant, according to an artificial intelligence (AI) model that was developed and verified with a large number of experimental data point (Chen et al., 2022). However, several mutations in the Omicron variant have been discovered that aid the virus's transmission rate, and a few of them are described: The N501Y mutation is thought to be located at RBD, which could aid in achieving stronger binding to host cells, resulting in increased transmission and infectiousness (Kazybay et al., 2022). While doing in vitro evolution tests, it was observed that the combination of mutations Q498R and N501Y dramatically improved the binding affinity to ACE2 (Zahradník et al., 2021). Moreover, High transmissibility has been linked to the N679K, N501Y, P681H, N679K,



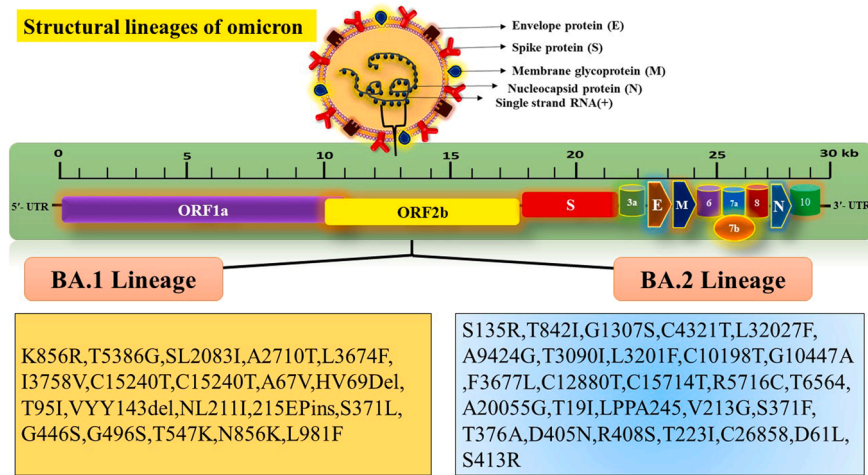


Fig. 1. Illustrate the structural lineages of omicron; B1 and B2 lineages are showing different mutations in their genomic structure respectively.

and D614G mutations (Hodcroft, 2021). Spike cleavage has been observed to be enhanced by P681H, which could assist transmission. This mutation is found in Alpha, but a different mutation (P681R) is found in Delta (Gong et al., 2021). Plenty of the evidence suggests that the Omicron form has a higher transmissibility potential. Currently, there is no evidence that the symptoms associated with Omicron are distinct from those associated with other variations. According to a report by the African Medical Association, although Omicron is seven times more contagious than the Delta form, the number of reported cases and deaths in Africa has continued to fall, and those infected with Omicron have shown no signs of serious illness.

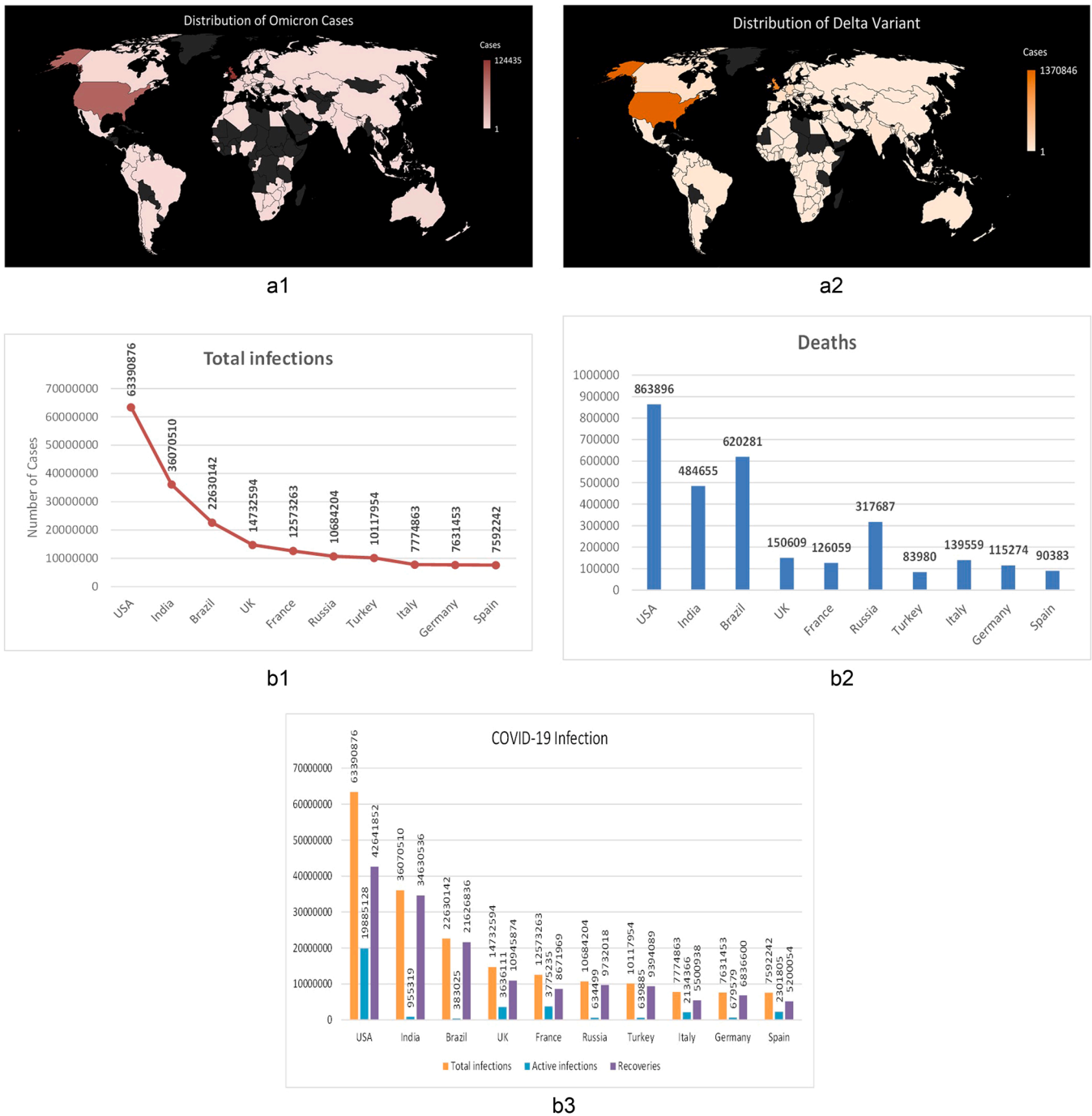
L452R and F486V mutations in the S-protein RBD have caused modifications in the structure of the more recent BA.4 and BA.5 lineages compared to BA.1 (Omicron). Except for the inclusion of the 69–70 deletion, F486V, and L452R, the BA.4 and BA.5 S-proteins are identical to BA.2 (Omicron) (H. Tegally et al., 2022). Compared to BA.2, both of them have the amino-acid changes L452R, F486V, and R493Q in the S-protein RBD. The BA.4 and BA.5 lineages have the infection-causing F486V mutation in S-proteins. (Mohapatra et al., 2022a, 2022b, 2022c).

The XD variant incorporates genetic components from the Delta and Omicron BA.1 variant. The XD variation includes the genetic components ORF1a and ORF1b from the Delta variant, as well as the spike protein from the Omicron BA.1 variant. The other genetic components of the XD (E, M, ORF6, ORF7a, ORF7b, ORF8, N, 3UTR) are derived from the Delta variant (Chakraborty et al., 2022). Approximately 1–21463 bp of the genomic material are incorporated from the Delta variant, according to researchers. The Omicron BA.1 variant's genomic segment from 21643 base pairs to 25581 base pairs is also integrated (spike protein region). Again, the genomic element is from the Delta variation from 25581 bp to the terminal. But it has been noted that the new mutation is present in XD (E172D). The genomic region of NSP2 has the E172D mutation. However, it has been shown that the NSP6 protein-coding genomic area of the XE variant contains up to 11,537 bp of genomic elements from the Omicron BA.1 variant. The recombinant XE variant comprises genomic elements from the Omicron BA.2 variant after the 11,537 bp location of genomic elements. The genetic components of NSP1 to NSP3 from the Delta variant are present in the XF version. The genetic component of the Omicron BA.1 variant is included in the following section of the XF variant. The initial portion of the genomic element of the Delta variant is recorded up to 5386 base pairs, while the recombinant XF variant incorporates genomic elements from the Omicron BA.2 variant following the 5386 base pair location of genomic elements. Therefore, as compared to the Delta variation, the XF variant has more genetic components from the Omicron BA.1 variant. (Chakraborty et al., 2022). The characteristics of these recombinant

variants, such as their interaction properties (for example, the interaction between the RBD of S-glycoprotein and the hACE2 receptor, which explains the infectivity), molecular determinants involved in the creation of recombinant lineage, and epidemiological information to develop suitable prevention and control strategies to stop the pandemic, all require further study. Fig. 2a.1, Fig. 2a.2 shows 'choropleth distribution' of omicron and delta variant cases respectively. Fig. 2b.1, b.2 and b.3 shows covid-19 cases, deaths, recoveries in most impacted countries as of jan.12, 2022.

#### 4. Omicron variant v/s delta variant

It is critical to comprehend and investigate the differences as well as similarities between these two variants in order to fully understand and gain insightful knowledge about the mechanism by which they infect the host, so that doctors and researchers can devise new strategies to prevent infection and reduce infection rates. In South Africa, the novel Omicron variant appears to have quickly displaced older variants, but this phenomenon could be skewed by the fact that virus characterization has increased in tandem with the number of cases and is still mostly concentrated on the Omicron variant's emerging area. This novel variety included 50 mutations overall, including 32 alterations to the S protein, according to the first genome-sequencing data received from Botswana. Many of the modifications have been discovered in Delta. The receptor-binding domain (RBD) of the S protein is the part of the protein that target significantly to human ACE2 receptors. Omicron and the Delta variant share two of the three RBD mutations. The first, a lysine to asparagine alteration at position 417 (not found in all Delta sequences but common in the Beta version), has been linked to S protein structural changes that may aid in immunological escape. The second mutation, a threonine to lysine substitution at position 478, is likely to boost the residue's electrostatic potential and steric interference, perhaps increasing RBD binding affinity and allowing immunological escape. The third RBD mutation, which is prevalent in Delta but not in Omicron, is a leucine to arginine substitution at position 452, which is designed to affect affinity for ACE2 receptors expressed on the surface of a range of human cells, as well as the lungs (Sanchez et al., 2021). The SARS-CoV-2 spike protein must be cleaved twice by host proteases that hydrolyze peptide bonds at certain amino acid sequences in order to gain cellular entrance. A Furin cleavage site is also one of those sites, and it's essential for pre-activated viral particles to be produced throughout replication and before splitting from an infected cell. When compared to the Alpha form, the Delta S protein contains a mutation (P681R) at a Furin cleavage site that separates the spike 1 (S1) and S2 subunits, which improves SARS-CoV-2 fitness. Increased transmissibility may also be



**Fig. 2.** a.1 ‘Choropleth distribution’ of omicron variant cases worldwide. This depicts the global spread of omicron, with the darker shades of red representing the more contaminated areas and the lighter shades of red representing the less affected areas (John, 2022). Fig. 2 a.2 ‘Choropleth distribution’ of delta variant cases worldwide. The darker hues of orange signify more contaminated locations, while the lighter colours reflect less contaminated areas, depicting the global spread of delta (John, 2022). Fig. 2 b (1,2,3) Covid-19 cases, deaths, recoveries in most impacted countries as of Jan.12, 2022. Number of coronavirus (COVID-19) cases, death and recoveries among the most impacted countries worldwide as of January 12, 2022. Graph(2b.1) depicts the overall number of covid infected cases, mostly in the most affected areas. The death cases caused by the covid infection are depicted in graph (2b.2) (John, 2022).

linked to a cluster of mutations at the S1-S2 Furin cleavage site in the Omicron form (H655Y, N679K, and P681H). In addition to the mutations listed above, there are a few others that are exclusively seen in the Omicron version and not the Delta form. The Omicron variation has a 3-amino-acid deletion in ORF1a at L3674-, S3675-, and G3676- (also identified as a loss in NSP6 from 105 to 107). This mutation may aid in innate immune evasion by impairing the ability of infected cells to destroy viral components, according to some theories (Benvenuto et al., 2020; Pang et al., 2021).

Finally, the Omicron variation has two additional mutations in the nucleocapsid (N) protein, R203K and G204R (48). RBD T470-T478 loop and Y505 as viral factors for particular identification of SARS-CoV-2 RBD by ACE2 were discovered in a prior investigation (Xu et al., 2021). In Delta and Omicron variations, T478 mutation is the observed in both of the variant (Kumar et al., 2022b). In terms of physical protein parameters, the Delta variant comprises 1271 and the Omicron variant contains 1270; however, due to loss in sequence, both the Delta and Omicron variants have a few fewer residues than the wild type. The

Omicron variation is projected to have an alkaline pI in the current studies, but the Delta and Wuhan-Hu-1 variants are expected to have an acidic pI (Kumar et al., 2022b). The amino acid profile of the Omicron variant is higher than that of the Delta variant in the mentioned amino acid compositions: Arginine (Arg), Lysine (Lys), Aspartic acid (Asp), as well as Glutamic acid (Glu), suggesting that the Omicron does have more charged residues that play a role in the formation of salt bridge and that charged residues are subjected to a greater extent. When compared to the Delta variation, the higher amino acid composition of Phenylalanine (F) and Isoleucine (I) in the Omicron spike protein implies that the Omicron spike protein contains more hydrophobic amino acids, which may be attributable to its position inside the protein core. In contrast to the Delta form, the amino acid composition of Omicron variant is deficient in polar amino acids such as asparagine (N), glutamine, and glutamine (Q). Omicron RBD contains a lot of non-polar amino acids such leucine (L), phenylalanine (F), and proline (P) (Ortega et al., 2020). Omicron contains a higher percentage of alpha-helix structure than Delta variation, but less prolonged strand and random coil structure (Kumar et al., 2022b). It has already been suggested that an increase in alpha-helices indicates that alpha helices are more resistant to mutations than beta strands (Abrusán and Marsh, 2016). Omicron, on the other hand, has a somewhat higher random coil composition (Zhang et al., 2021). Fig. 3 (a, b, c) shows the comparison of spike protein structures between Alpha (B.1.1.7), Delta (B.1.617.2) and Omicron Variant (B.1.1.529) respectively. Viral pathogenicity and infectivity are connected to disordered regions of viral proteins. The Omicron variant, as per the prediction, has a less disordered region than the Delta variant and the wild type (Kumar et al., 2022b). Data from PredyFlexy confirmed that residues I921, S980, V1187, F1218, and I1219 are significantly changeable in the Delta variation, whereas residues I920, S979, V1186, F1217, and I1218 are particularly flexible in the Omicron form (Kumar et al., 2022b). This demonstrates that Omicron may have the highest transmissibility of the current SARS-CoV-2 strains. Additionally, Omicron replicates more than 70 times quicker in the human bronchus than the Delta variation, which may help to explain why Omicron may spread more quickly between humans than other variants. When compared to other VOC, Omicron has a lot of information, yet it's still scarce. A retrospective analysis of suspected reinfections among South Africans reveals a temporally juxtaposed Omicron emergence with a higher risk of reinfection, which was not seen in previous waves associated with Beta or Delta variants, implying that the Omicron variant is linked to a unique ability to overcome natural immunity from prior infection (Pulliam et al., 2021). Table 1 shows the different mutation at different region of the Alpha (B.1.1.7), Delta (B.1.617.2) and Omicron Variant (B.1.1.529) (COVID et al., 2021). The difference between symptoms of the omicron variation and other COVID-19 variants is still unclear, but the CDC just prepared a briefing with the most commonly reported symptoms, which can be seen here. They include cough, fatigue, congestion and runny nose (Stanford, 2022). Fig. 4 shows overall mutation list in Alpha (B.1.1.7), Delta (B.1.617.2) and Omicron Variant (B.1.1.529).

##### 5. Omicron variant's impact on currently available laboratory diagnosis

Using cutting-edge technologies, an incredible number of innovative diagnostic tests for COVID-19 have been designed. Molecular or nucleic acid amplification tests (e.g., PCR tests) that detect viral RNA; antigen tests that detect viral proteins (e.g. nucleocapsid or spike proteins); and serology tests that detect host antibodies in response to infection, vaccination, or both are all relevant to patient management and pandemic control. Table 2 shows various types of tests used to diagnose covid 19. Molecular tests can amplify viral RNA, making it possible to identify viral infection. These tests are also known as "nucleic acid amplification assays" (NAATs). The first step is to take a sample from a person who may be infected mouth or nose, where the virus may be

present. If SARS-CoV-2 is present in the sample, a molecular diagnostic method can locate millions of copies of viral genetic material. The secretions of the nasopharyngeal surfaces, which are most likely to transmit the virus, must be collected in order to do molecular testing. The majority of COVID-19 assays that are now available or being developed employ oral or nasopharyngeal tissues to facilitate testing. Viral RNA can be found if someone is infected. There are several molecular diagnostics available, and some of them deliver results more quickly than conventional PCR-based methods. Rapid molecular diagnostics, like LAMP, increase the genetic material in the patient sample, making them extremely sensitive while also being very specific. Identifying DNA or RNA pathogens and amplifying a section of the pathogen's genome are the fundamental steps in all of these methods. Provide an output measurement indicating how much amplified genetic material is present in the sample, if any. Deletion 69–70, a minor deletion mutation in BA.1, modifies the spike protein's structure and makes it possible for it to evade detection by the PCR test. As a result, the test result for Omicron is uncertain (Kumar et al., 2022a). The strain can be identified by various specialised tests, but the BA.2 sub-variant lacks this omission mutation, and even though the test is Omicron, the results will be inaccurate with other strains, particularly the Delta variation in standard PCRs (Fonager et al., 2022). It is thought that omicron's unique traits may influence testing procedures, and this distinguishes omicron from seasonal coronaviruses and SARS-CoV, which has significant implications for diagnostic strategies. However, it is unclear whether or not the existing test methods are accurate in detecting Omicron variant. There is no evidence that the PCR test cannot be used to detect omicron variants, and no other diagnostic approach has been introduced yet, therefore it's best to stick with the present test, which is the PCR. However, there are several key caveats: not every RT-PCR can detect omicron, which is also not the only variation sensitive to detection. Fig. 5 shows the workflow of PCR for detection of Omicron. To screen SARS-CoV-2, researchers must identify specific sections in the virus's genetic coding that do not change fast over time but have features that allow it to be recognized. According to one of the Indian scientists, COVID-19 test kits contain two or more sets of primers that bind the virus's genetic elements at two or more locations in the RNA sequence. It is done in order to improve detection and reduce the likelihood of false positives. The N, E, RdRP, and S genes are used in conjunction. As a result, the test's effectiveness will be entirely dependent on the primer we choose. And also mentioned that genome sequencing is the only way to confirm if a person is infected with omicron or not, because RTPCR will help to screen out the existence of virus in the sample. Along with that it is also stated that a mutation in any of the proteins against which the primers are generated can influence the testing kit's efficacy, but that it is extremely rare for both sites to be lost owing to mutation. As one of the three target genes, the S gene dropout or S gene target failure was not observed and suggested as a marker for this variation. It also suggests that RT-PCR with an SGTf (spike gene target failure) can be used to detect for omicron in a preliminary manner. Unfortunately, the primers for the bulk of kits used in India are not publicly revealed, so we can't be positive that all of the available RT-PCR kits will give us highly effective outcomes while screening for omicron variant. RT-PCR tests already take up to 24 h to furnish the results. Further to confirm the presence of omicron variant, one has to sequence the virus which is time consuming as well as expensive. It is very important to develop a set of primers that are specific for omicron by using whole genome sequencing of the SARS-CoV-2 virus which will make the detection of the omicron variant considerably easier for the diagnosis. It will also save time and be a more cost-effective technique than conducting two rounds of confirmation tests. To ensure sustained efficient primer binding in currently circulating variations, manufacturers and laboratories should examine the choice of diagnostic targets on a regular basis. This has significant implications, particularly in an emerging circumstance like the spread of a novel VOC like Omicron. Due of intellectual property considerations, firms rarely or never release specific information about their assays'

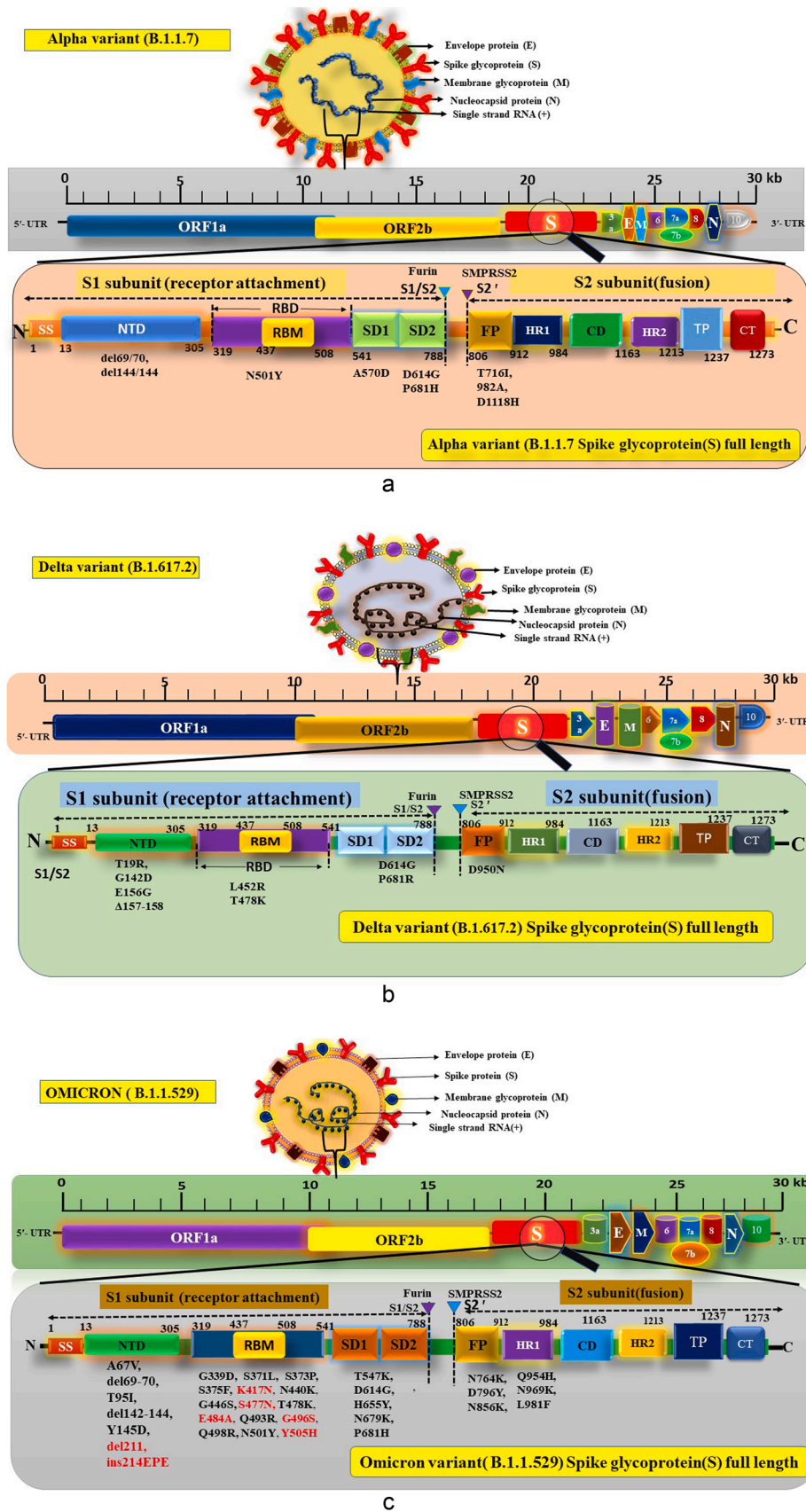


Fig. 3. (a,b,c) Diagrammatic representation of SARS- CoV 2 variants- Alpha (B.1.1.7), Delta (B.1.617.2) and Omicron Variant showing the comparison of spike proteins structural mutations. The spike proteins possess two different subunits- S1 and S2 where S1 is receptor attachment subunit and S2 is fusion subunit and the cleavage site for Furin and TMPRSS2. It mediates the attachment of virus to the host cell. TMPRSS2 helps in activation of spike proteins.



**Table 1**

Shows the different mutation at different region of the Alpha (B.1.1.7), Delta (B.1.617.2) and Omicron Variant (B.1.1.529).

GENE	ALPHA VARIANT (B.1.1.7)	DELTA VARIANT (B.1.617.2)	OMICRON VARIANT (B.1.1.529)			
			BA.1 LINEAGE	BA.2 LINEAGE	BA.4 LINEAGE	BA.5 LINEAGE
ORF1ab	T1001I, A1708D, I2230, del3675/3677, P314L	A1306S, P2287S, V2930L, T325S, T3255I, T3646A, P314L, G662S, P100L, A1918V, sp4: V167L, RdRp: P323L, RdRp: G671S, nsp13: P77L	K856R, S2083I, del2084/2084, A2710T, T3255I, P3395H, del3674/3676, I3758V, P314L, I1566V	S135R, T842I, G1307S, L3027F, T3090I, L3201F, T3255I, P3395H, del3675/3677, P314L, R1315C, I1566V, T2163I	nsp1: S135R, Del141–143, nsp3: T842I, G1307S, nsp4: L3027F, T3090I, 3CL:T3255I, P3395H, nsp6: del 3675–3677, RdRp: P4715L, nsp13: R5716C, nsp14: I5967V, nsp15: T6564I, T223I	nsp1: S135R, nsp3: T842I, G1307S, nsp4: L3027F, T3090I, 3CL:T3255I, P3395H, nsp6: del 3675–3677, RdRp: P4715L, nsp13: R5716C, nsp14: I5967V, nsp15: T6564I,
SPIKE	del69/70, del144/145, N501Y, A570D, D614G, P681H, T716I, 982 A, D1118H	T19R, G142D, E156G, del157/158, L452R, T478K, D614G, P681R, D950N	del69/70, T95I, G142D, del143/145, N211I, del212/212, G339D, S371L, S373P, S375F, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, D796Y, N856K, Q954H, N969K, L981F	T19I, L24, del25/27, G142D, V213G, G339D, T376A, 371 F, 373 P, 375 F, T376A, D405N, R408S, K417N, N440K, L452R, S477N, T478K, E484A, F486V, Q498R, N501Y, Y505H, D614G, H655Y, N679K, K417N, N440K, 477 N, T478K, E484A, Q493R, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K, T223I	T19I, LPPA24–27S, Del 69–70, G142D, V213G, G339D, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440K, L452R, S477N, T478K, E484A, F486V, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K	T19I, LPPA24–27S, Del 69–70, G142D, V213G, G339D, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440K, L452R, S477N, T478K, E484A, F486V, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K
ORF3a	–	S26L	–	T223I	–	T223I
E	–	–	T98I	T9I	T9I	T9I
M	–	I82T	D3G, Q19E, A63T	Q19E, A63T	Q19E, A63T	D3N, Q19E, A63T
ORF6	–	–	–	D61L	D61L	–
ORF7a	–	V82A, T120I	–	–	–	–
ORF7B	–	T40I	–	–	L11F	–
ORF8	Q27, R52I, Y73C, S84L	S84L, del119/120	S48L	S84L	S84L	S84L
N	D3L, R203K, G204R, S235F	D63G, R203M, G215C, D377Y	P13L, del31/33, R203K, G204R	P13L, del31/33, R203K, G204R, S413R	P13L, 31–33del, P151S, R203K, G204R, S413R	P13L, 31–33del, R203K, G204R, S413R

diagnostic targets. Diagnostic laboratories are currently having difficulty detecting the new Omicron VOC. The diagnostic performance of available PCR assays is currently unknown, as all information accessible at this early stage is based on businesses’ in silico analyses.

To check for SARS-CoV-2 infection, antigen-detecting diagnostic tests identify viral proteins in saliva or upper respiratory sample. In comparison to NAATs, the use of antigen-detecting rapid diagnostic tests (Ag-RDTs) may be a more effective strategy for SARS-CoV-2 screening. Ag-RDTs are most effective in patients with high viral loads early in their illness and would be most accurate in regions with less than 5% SARS-CoV-2 prevalence. With limited transmission, Ag-RDTs have a low positive predictive value. As a result, in these circumstances, NAATs are

advised for initial testing or the verification of positive Ag-RDT findings. Ag-RDTs that satisfy the minimal performance criteria of 80% sensitivity and 97% specificity are advised by the WHO (Mak et al., 2020). The analytical sensitivity of the 10 antigen kits did not significantly differ between the delta and omicron forms, according to a recent research testing ten commercially available COVID-19 antigen assays. According to earlier research on the sensitivity of antigen kit assays, all ten kits found Delta at 6.50 log10 copies/mL (Ct 25.4) and Omicron at 6.39 log10 copies/mL (Ct 25.8) respectively. At the lowest dilution concentrations (5.23 log10 copies/mL, Ct28.8 and 5.33 log10 copies/mL, respectively), neither Delta nor Omicron could be found in any of the ten kits. This outcome is in line with other research proving the reliability of

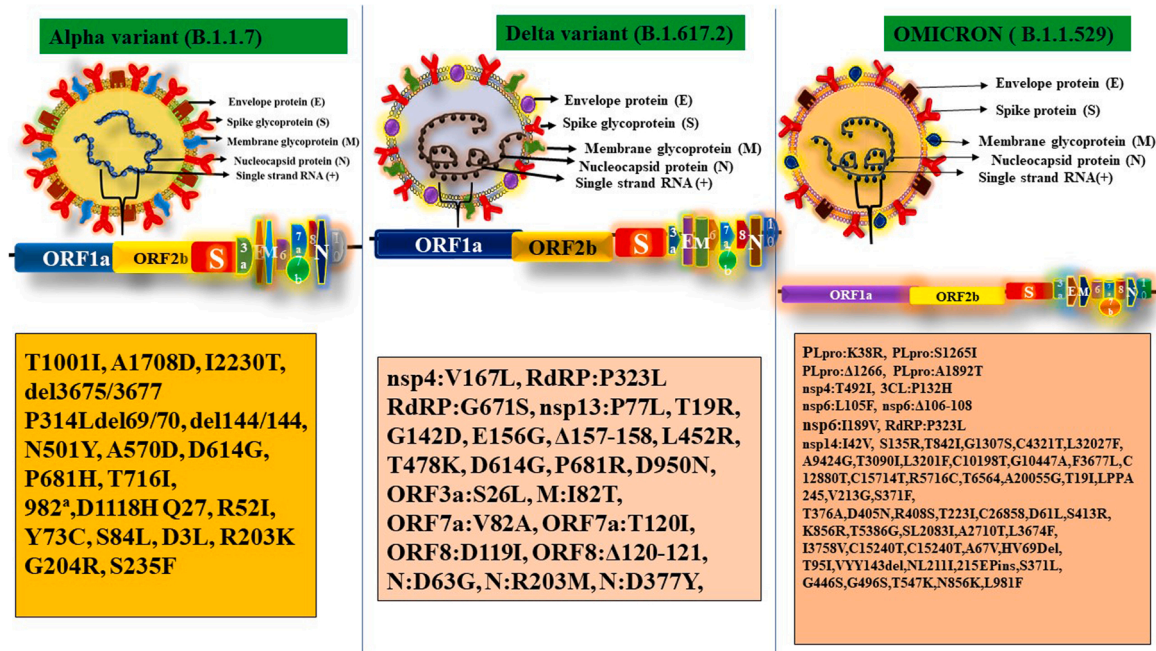


Fig. 4. Overall mutation list in Alpha (B.1.1.7), Delta (B.1.617.2) and Omicron Variant (B.1.1.529).

Table 2

List of Diagnostic test available for SAR-CoV-2 infected patients and their efficiency.

Type of the Test	Molecular test	Antigen rapid detection Test	Combination of molecular test, rapid antigen test, antibody test	Repeat molecular or antigen rapid detection test with the help of a lower respiratory tract specimen and antibody test
Biological specimen	Nasopharyngeal or nasal swab	Nasopharyngeal swab or nasal swab	Nasopharyngeal or nasal swab	Sputum, blood, bronchi alveolar lavage or tracheal aspirate
Principle	To screen out the presence of viral RNA.	Helps to detect the presence of viral protein.	This test is used, if both the molecular test as well as rapid antigen test shows negative result.	For clinical diagnosis
Efficiency	The sensitivity and specificity of this test are considered to be highly commendable for detecting the viral RNA for clinical diagnostic.	Can provide result within half-an hour. Require a minimum training.	Highly sensitive, it can provide result within 30 min if rapid-antibody is employ otherwise it will take 24 h.	If the antibody test is positive, you can use it to make a diagnosis of a previous or recent infection.
Drawbacks	Not a cost-effective test, can take longer time to obtained result. Require skills technician.	Poor test quality, test is not much reliable, Sensitivity is comparatively lesser then the molecular test.	Antibody test can produce false positive result	Antibody test can produce false positive result

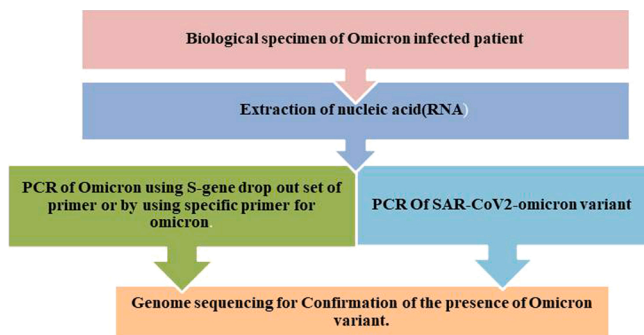


Fig. 5. shows the workflow of PCR for detection of Omicron.

antigen testing for SARS-CoV-2 variants (Bekliz et al., 2022; Bekliz et al., 2021)

NGS sequencing techniques have swiftly become the preferred method for a variety of virological applications, such as the discovery of novel viruses. This approach is crucial for figuring out where SARS-CoV-

2 came from. Academics may presently use the majority of coronavirus and SARS-CoV-2 genomes discovered using NGS in their research on the origins of SARS-CoV-2. (Chen et al., 2021). The method of choice today for locating, categorising, and monitoring SARS-CoV-2 variants is sequencing (Izquierdo-Lara et al., 2021). Sequencing takes longer than other genotyping techniques, like PCR, and requires specialised tools and interpretation. PCR approaches are less costly, more practical, and quicker than sequencing for SARS-CoV-2 genotyping, despite the fact that they only target preselected mutations. These methods could make it easier to find variants since variations spread throughout populations over time, especially in environments with limited resources (Fontanet et al., 2021). The sensitivity for detecting spike mutations was 98.7% and 100%, respectively, for the Allplex SARS-CoV-2 Master Assay and Variants I Assay when the results of 115 samples were compared using NGS as the reference (Fu et al., 2022). An accurate diagnosis for Omicron was made during the SARS-CoV-2 genomic surveillance in the state of Georgia using a combination of the Spike SNP PCR test (2 h and 12 min of run time) and genome sequencing and lineage classification (72 h). The test was furthermore able to differentiate between the other VOCs and Omicron owing to the SNP analysis, and it may be further

changed in accordance with the needs to identify new mutations if necessary (Sexton et al., 2022). Following the WHO's instructions, Omicron was found in an airplane wastewater sample using the CDC N1, CDC N2, and del (69–70) RT-qPCR tests. Sequencing later verified the presence of Omicron with the BA.1 sub-lineage (Ahmed et al., 2022).

When deciding which test to utilize in which situation, it's important to think about the goal of the test and the resources available, as well as the test's accuracy, accessibility, affordability, and the speed with which answers are needed. Molecular tests, with their excellent sensitivity and specificity, are the test of choice for COVID-19 case detection. Test sensitivity may be a secondary concern to frequency of testing and time to result when screening asymptomatic illnesses in communities to break the chain of transmission. Testing strategies should also be established to help with global surveillance of SARS-CoV-2 genetic sequences and to ensure links that can quickly detect changes in infectiousness, pathogenicity, or both on a worldwide scale. The global epidemic must serve as a wake-up call for countries to implement a diagnostic and surveillance system that ensures the integrity of a healthcare system, with relevant technologies at every level, as well as data communication, so that clinicians and policymakers have more tools and resources to exercise precision medicine and early warnings of potential outbreaks are investigated quickly. Therefore, on December 20, 2021, the WHO Regional Office for Europe and the European Center for Disease Prevention and Control (ECDC) released the first update to their methodologies and strategies for identifying and characterising SARS-CoV-2 variants. (ECDC, 2021).

## 6. Will the impact of Omicron be the same as other variants or worse?

The emergence of COVID in 2019 has wreaked havoc around the world. It has put human lives at danger, disturbed livelihoods, and impacted trade, the economy, and business around the world. Because the global economy is heavily interconnected and associated with global supply, the world economy has entered a massive recession with an unprecedented economic crisis and massive disruptions as a result of the pandemic. Because of its contagious nature, practically everyone in the country backed a lockdown to prevent it from spreading. South Asian countries, in particular, have had to deal with a more difficult scenario as a result of their vast population, poor health facilities, high poverty rates, low socio-economic status, and failure to take other necessary measures to contain the pandemic. South Asian countries have implemented strict lockdowns to prevent the virus from spreading, affecting the lives and livelihoods of millions of people in the region. Due to pandemic, India is likewise in the midst of a major crisis. This region has megacities such as Delhi and Mumbai, which have extraordinarily high population densities. Because this region's economy is already insecure, the majorities of its population has few resources and are ill-equipped to deal with the repercussions of a pandemic, as a result of which they have suffered greatly (ICIMOD, 2020). During COVID, India had to deal with major macroeconomic issues such as near-recession, with a sluggish GDP growth rate of 4.7% in 2019, the lowest since 2013 (according to official statistics), high unemployment, a decline in core sector industrial output the worst in 14 years, stagnancy in private sector investment, and a drop-in consumption expenditure for the first time in decades (Dev et al., 2020). A huge sector of India was already in economic hardship as a result of demonetization in 2016 and GST in 2017, and the situation has exacerbated as a result of the pandemic (Mehta, P, 2020). Aviation, transportation, travel, and tourism are among the worst-affected industries worldwide, not only in India. The amount of money lost in this industry will be determined by the intensity and duration of the crisis.

Huge problems have arisen as a result of the rural healthcare system's inability to handle the pandemic and its transmission, particularly in northern states with high population density, including a doctor shortage, a lack of full-fledged healthcare facilities, and a scarcity of

beds per thousand people, among other things. Cancer patients, transplant patients, and cardiovascular patients all suffered considerably as a result of the pandemic, as they were unable to access health care facilities and, more importantly, hospitals were overloaded by COVID afflicted people. In addition to the health and financial issues, lockdown has led in mass unemployment, the failure of many businesses, a loss of revenue, increased inequality and poverty, deaths, decreased mobility, and so on. The impact on people's mental health is enormous. From the old to the young, the wealthy to the poor, everyone was touched. As a result of the worldwide pandemic, anxiety, concern, despair, fury, dread, and other health issues have occurred (Mehta, 2020). The COVID19 pandemic has had a worldwide impact unlike any other, but India, as a developing country, is expected to be disproportionately affected in every industry. Agriculture and related industries have been impacted disproportionately hard, with horticulture and poultry suffering the most. The agriculture business, on the other hand, is seen as a bright spot and is projected to be less affected than other industries. ED visits, hospital admissions, and the daily seven-day moving average of COVID-19 cases increased dramatically over the Omicron period, according to the current study. ED visits, on the other hand, fell during the last week of January 15, 2022, and were followed by a slowdown of hospitalization and daily case rates. In comparison to the Winter 2020–2021 season, the daily number of cases, ED visits, hospital admissions, and mortality increased by 219%, 137%, 31%, and – 46% during the Omicron period. In comparison to the Delta era, these changes were 386%, 86%, 76%, and – 4%, respectively. The key question now is whether omicron will have the same consequence as of the other previous variants of COVID-19 that had sent the country into the dark ages since the emergence of COVID-19? Will the post-COVID effect of the omicron infected patient going to be the same as the other variants? During the first pandemic, there was no vaccine available; but, now that the bulk of the population has been fully vaccinated, could we hope that immunization will provide some protection against omicron? How much would Omicron be able to weaken the protection provided by existing Covid-19 vaccines if we already have protection? It is very difficult to predict whether omicron will have the same effect as other variables. It is critical to have a thorough understanding of the severity of omicron as well as the mortality rate in order to comprehend. We believe it is too early to suggest what impact omicron will have on social and economic issues, as well as what health crises we will confront. We should adopt the bare minimum of efforts to restrict the spread of omicron so that the country does not suffer the same issue as the former variants. For example, Masks are needed in enclosed places on public transit vehicles travelling into, within, or out of the country, and initiatives to educate travelers are aimed at reducing omicron transmission and promoting safer global travel.

## 7. Vaccines efficacy updates

New SARS-CoV-2 variants were expected to emerge. As a result, scientists have advocated for close international monitoring to determine the need for vaccination boosters and redesign (Torales et al., 2020). Even those who had received the complete course of vaccinations experienced SARS-CoV-2 reinfections due to the Delta form, which was linked to breakthrough infections. However, the majority of breakthrough infections either had no symptoms or only produced minor symptoms. The development of Omicron, which has more than 30 mutations that may impair the S protein, has raised new concerns about the effectiveness of vaccines. A persistently infected COVID-19 patient who received an mRNA- or non-mRNA-based vaccine may have given rise to Omicron, which allowed the virus to modify and mutate in order to evade the immune response. The global panic caused by the Omicron variant prompts the scientific community to investigate how much this new variant could undermine existing vaccines and monoclonal antibodies. The mutations on the Omicron variant are widely distributed on SARS-CoV-2 proteins. The main focus, however, is on the S protein

receptor-binding domain (RBD) mutations, which are being studied to determine the potential impact on infectivity and antibody resistance caused by this new variant. The reason for this is that the S protein receptor-binding domain facilitates the binding of the S protein to the host angiotensin-converting enzyme 2 (ACE2), which facilitates virus entry into host cells and viral infection initiation. As a result, the effectiveness of vaccines currently in use that were created utilising the S protein of earlier viral strains has been questioned. Furthermore, the reproductive number (RO), which is 2.5, 7, and > 10 for the wild-type virus, the Delta variant, and the Omicron variant, respectively, provides further evidence of the increased transmissibility of the Delta and Omicron variants (Burki TK, 2021). Various studies have found that the binding free energy between the S protein receptor-binding domain and angiotensin-converting enzyme 2 is directly proportional to the virus's ability to cause infection (Farooqi et al., 2021; Li et al., 2005; Qu et al., 2005; Song et al., 2005; Hoffmann et al., 2020). Antibodies that bind to the S protein receptor-binding domain weaken the bond between S protein and angiotensin-converting enzyme 2 and thus directly neutralize the virus (Walls et al., 2020; Wang et al., 2020; Yu et al., 2020; Li et al., 2021). Omicron is roughly four times as infectious as the wild-type and Delta pseudoviruses, respectively, and continues to rely on the human ACE2 receptor for host cell entrance, according to in vitro infectivity assays. Antibodies produced in response to virus infection are mostly based on the aforementioned fact, which is why any change in the S protein receptor-binding domain may affect the efficacy of existing vaccines and monoclonal antibodies. Some scientists used a validated topology-based artificial intelligence (AI) model called TopNetmAb (Li et al., 2021; Chen et al., 2020, 2021a) to predict the binding free energy changes of S and angiotensin-converting enzyme 2/antibody complexes induced by mutations on the S protein receptor-binding domain of the Omicron variant and discovered that Omicron may be over ten times more contagious than the original SARS-CoV-2 and about twice as infectious as the D virus. Furthermore, Omicron has a high potential to disrupt the binding of most 132 antibodies to the S protein, owing to receptor-binding domain mutations K417N, E484A, and Y505H, indicating that it is a more potent vaccine break through than the Delta variant (Chen et al., 2021b). Scientists discovered that Omicron receptor-binding domain mutations K417N, E484A, and Q493R may significantly reduce the efficacy of the Eli Lilly mAb cocktail. Omicron RBD mutations E484A, Q493R, and Q498R may disrupt the cell Trion antibody Regdanvimab. Rockefeller University mAbs may also be disrupted by the Omicron RBD mutation E484A (Chen et al., 2022). Furthermore, scientists predicted that existing neutralizing antibodies will still bind to the mutated spike protein of the Omicron variant (Ford et al., 2022). However, it appears that Omicron's receptor-binding domain has a lower affinity for neutralizing antibodies when compared to the reference receptor-binding domain structures. This finding suggests that antibodies elicited by vaccines or a previous infection may offer some protection against Omicron. Studies on antibody concentrations following two doses of vaccination with vaccines from Astra Zeneca, Pfizer-BioNTech, and Moderna have shown reductions in neutralizing antibody titers against the Omicron variant compared to those against earlier variants or the original strain of the virus by 5.3–6.2, 11.4–, 20–, 25–, 29.8–, 41–, and 49–84 times (Wilhelm et al., 2021, Cele et al., 2021, Dejnirattisai et al., 2022, Doria-Rose et al., 2021). In addition, BioNTech and Pfizer announced on December 8 that a three-shot course of their COVID-19 vaccine could neutralize the new Omicron variant in a laboratory test, an early indication that booster shots may be required to protect against infection from the newly identified variant. They claimed that two doses of the vaccine resulted in significantly lower neutralizing antibodies, but that they could still protect against severe disease (Pfizer, 2021). In fact, the titers of neutralising antibodies against the Omicron variant fell below the detectable threshold in the sera of several subjects who had two vaccinations. Therefore, the neutralising antibody titers against some SARS-CoV-2 VOCs are lower than those against the vaccination strain. This is

significant since neutralisation and effectiveness against viral variations are related. 54 Additionally, a number of studies have demonstrated that 3–8 months following vaccination, antibody levels begin to decline (Khoury et al., 2021a, 2021b; Israel et al., 2021). According to recent US research, vaccine efficacy against symptomatic infection caused by the Omicron variant is expected to be significantly lower than against previous variants (Gardner and Kilpatrick, 2021). South African researchers published a contradictory report, claiming that a cluster of Omicron variant infections occurred in a group of German visitors who had received full primary vaccination series and booster doses of SARS-CoV-2 mRNA vaccines and experienced breakthrough infections with the Omicron variant (Kuhlmann et al., 2021). Vaccine efficacy is measured quickly after vaccination and six months later in studies. With the help of their previously established model, David Khoury et al. estimated that six months after primary immunization, vaccine efficacy against Omicron has decreased to 7.5%, 28.1%, and 40.4% protection against symptomatic infection for Covishield, BNT162b2 (Pfizer BioNTech), and Moderna vaccines, respectively, and 36.7%, 70.9%, and 81.1% protection against severe symptoms for the same three vaccines (Khoury et al., 2021a, 2021b). They discovered that adding a third booster dose to an existing mRNA vaccine might enhance Omicron efficacy to 86.2% for symptomatic infection and 98.2% for severe infection. Emerging research on the loss of neutralization against the Omicron variation demonstrates significant neutralizing response escape, but suggests that boosting with existing vaccines that target ancestral spike protein could provide high levels of protection against symptomatic and severe infection. Alexandra B Hogan et al. calculated that neutralizing antibody titres for Omicron are 4.5-fold lower than the Delta variant using an immunology model and population-level vaccine efficacy data (Hogan et al., 2022). If neutralizing antibody titers decay at the same rate following boosting as they did after the primary course, vaccine efficacy against severe disease for the Pfizer-BioNTech booster will drop from 96.5% against Delta to 80.1% against Omicron by 60 days post boost, and from 97.6% against Delta to 85.9% against Omicron if neutralizing antibody titers decay at half the rate observed after the primary course. Another study found that after the second and third doses of vaccination, the risk of hospitalization for Omicron patients is lower, with an 81% (77–85%) reduction in the risk of hospitalization after three doses compared to unprotect Omicron cases. Apart from aforementioned studies, there are several reports which showed the effect of Vaccine booster dose efficacy of different vaccines on omicron (Andrews et al., 2022; Munro et al., 2021a, 2021b; Nemet et al., 2022; Barda et al., 2021; Edara et al., 2022). The connection between the S protein and the ACE2 receptor is affected by modifications to the S protein, according to Dawood (2022). Additionally, he claimed that compared to the wild-type strain, Omicron activates the immune system more. Omicron's numerous S protein mutations are to blame for both the diminished ability of the vaccine to prevent infection and the escape from antibody neutralization (Dawood, 2022; Keeton et al., 2022) evaluated both vaccinated (with Ad26. CoV2. S or BNT162b2) and unvaccinated convalescent COVID-19 patients' capacity for adaptive responses, such as those involving T cells, to respond with the Omicron S protein. According to the study, the size of the T cell reaction to Omicron was comparable to that against Delta and Beta. The most effective strategy for containing this continuing pandemic will be to produce vaccinations that are secure and efficient against SARS-CoV-2 and its VOCs. One of the main areas of focus for the creation of vaccine candidates is the RBD of the S protein. (Mohapatra., et al., 2022d). In this regard, Wang et al. (2022a,b,c) reported the development of a self-adjuvanting lipoprotein compound containing the RBD and -galactosylceramide (GalCer), which elicits a powerful invariant natural killer T cell response. This conjugate also promotes potent immunisation against SARS-CoV-2 VOCs (Wang et al., 2022a). Additionally, all VOCs, including Delta and Omicron, were effectively cross-neutralized by the conjugate vaccination. Therefore, the creation of diverse subunit vaccines will benefit from research work.



Despite the fact that the clinical symptoms were mild to moderate, three doses of mRNA vaccines may not be enough to prevent infection and symptomatic illness with the Omicron variant. Furthermore, two Singaporeans were infected by the omicron variant despite receiving COVID-19 booster shots, indicating its high virulence and uncertain immunological trajectories (Fortune, 2021). At present, it seems that omicron has a potential to alter immunological responses. It is ascertaining to tell how well vaccination or previous infection with SARS-CoV-2 safeguards against omicron infection. Several Omicron mutations seem to impair T cells' ability to recognize and attack infected cells. In case, Omicron can avoid neutralizing antibodies, it does not preclude the probability that immune responses provoked by vaccination and subsequent infection may provide no or limited protection against omicron variant. According to immunological research, low concentrations of neutralizing antibodies may shield against extreme COVID-19 infections. The level of protection against Omicron provided by existing vaccines and subsequent infections will be an important aspect of the research. People who have been exposed to SARS-spike CoV-2's protein on multiple occasions, whether it is through infection or a booster dose, are very highly probable to have neutralizing antibodies against Omicron (Cele et al., 2021; Wilhelm et al., 2021; Devlin and Kollwe, 2021). Despite the fact that new data is being generated on a daily basis, the scientific community requires time to complete studies and interpret the results. T cell immunity decline, which is mostly brought on by immunological fatigue and memory deficits. Focus is returned to antibody-facilitated immune responses as T cells are important in the adaptive immunological responses to SARS-CoV-2 infection (Iqbal, 2020). It was also discovered that the conserved viral proteins (Orf3, Orf6) influence T cell responses, which has an impact on IFN- $\gamma$  activation. The virus reproduces without restriction in the infected cells as a result (Guihot et al., 2020).

In the wake of the circulation of Omicron SARS-CoV-2 Variant of Concern, the Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) advocates for globalized access to existing COVID-19 vaccines for primary series as well as booster doses, in the order to diminish the emergence and impact of new VOCs. COVID-19 vaccines must meet the following criteria: be based on strains that are genetically and antigenically similar to the circulating SARS-CoV-2 variant(s); be more effective in protecting against infection, thus reducing community transmission and the need for stringent and broad-reaching public health and social measures; evoke broad, robust, and long-lasting immune responses in attempt to lessen the need for invasive and long-term public health and social measures; along with the reduce need for successive booster doses. COVID-19 vaccine makers are encouraged to create and share data on the efficacy of existing and Omicron-specific COVID-19 vaccines, including the breadth, magnitude, and durability of humoral and cell-mediated immune responses to variations via monovalent and/or multivalent vaccines. To meet the task of continuing to produce the best possible vaccines in a timely manner, WHO and its expert groups, the TAG-CO-VAC, regulatory authorities, and COVID-19 vaccine makers must maintain a constant flow of information and collaboration. On behalf of its Member States, WHO is committed to supporting this effort.

## 8. The necessity of booster dosages to combat Omicron

Humoral immunity prevents viral attachment and prevents virus penetration into host cells during the immune-pathogenesis of SARS-CoV-2 infection by neutralising certain antibodies (Kaplonek et al., 2021). The appearance of the Omicron variant has highlighted the significance of COVID-19 booster injections. Omicron mutations cause neutralising antibody titers to escape and confer, whereas mutations in immunodominant epitopes are less likely to affect T cell responses, leading to the superiority of the mRNA vaccine against SARS CoV-2 variants. Neutralizing antibody titers are typically weaned after a few months of vaccination (Cohen et al., 2022). According to some recent

reports, heterologous vaccination or the third dose may spur the immune system or cross-reactivity of neutralising antibodies against new SARS-CoV-2 variants; thus, various researchers have investigated the potential implication of the third booster heterologous vaccination for effective immunity against the VOC Omicron. Individuals who were fully vaccinated and received a booster dose had a tenfold reduced chance of developing COVID-19 than residents who had just received the primary immunisation series or were unvaccinated (Tanne et al., 2021). In the weeks following booster delivery, booster shots provide 70–75% protection against symptomatic infection, according to the UKHSA (UK Health Security Agency). SARS-CoV-2 variants of concern and variants under investigation in England SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 31. 2021 Dec 10). Planas et al., (2021ab) discovered that Sera from prior COVID-19 convalescent patients had little or no neutralising activity against Omicron, but a booster with BNT162b2 can generate neutralising antibodies against the Omicron variant. Lee et al. (2022) discovered recently that heterologous vaccination with ChAdOx1 followed by BNT162b2 results in an immunological response comparable to homologous BNT162b2 immunisation. It was discovered that heterologous boosting produces a more potent immune response than homologous boosting in a recent phase 4 single blind randomised research (Clemens et al., 2022). According to Geurtsvan Kessel et al. (2022) BNT162b2 booster vaccination partially restored neutralisation of the Omicron variant after two mRNA-1273 immunizations or Ad26. COV.2 priming, though the neutralising antibody titers against this variant were still up to 17-fold lower than those against the wild-type virus. In participants who received two doses of the CoronaVac vaccine, omicron neutralisation was undetectable; however, as compared to two doses of mRNA immunisation, it rose 1.4-fold following the delivery of the BNT162b2 dosage. Despite this increase, the Omicron and Delta variants had neutralising antibody titers that were 7.1 and 3.6 times lower than those of the original strain's ancestor, respectively (Mohapatra et al., 2022e). Independent of the type of primary immunisation, people who received mRNA booster shots (BNT162b2 or mRNA-1273) had higher frequencies of Omicron RBD-binding B cells and higher levels of Omicron RBD-specific IgG1 antibodies compared to people who received booster shots using inactivated viral vaccines. Therefore, after receiving the initial two doses of the mRNA vaccine, people are more likely to be protected against SARS-CoV-2 infection, including the Omicron variant (Zhang et al., 2022). In addition, the quantity of a third shot (booster dose) has a beneficial impact on neutralising antibody titers. For example, the currently approved 50 g booster with mRNA-1273 increased neutralising antibody levels against Omicron by roughly 37-fold in comparison to pre-boost levels, while a 100 g dose of mRNA-1273 increased neutralising antibody levels by roughly 83-fold. Studies on the effectiveness of two vaccine doses and booster doses showed the necessity of a booster dosage to provide protection against serious disease even in vulnerable groups, such as those over 60 (Patalon et al., 2022, Barda et al., 2021) AstraZeneca, Johnson & Johnson (Janssen), Curevac, Moderna, Pfizer, Novavax, and Valneva participated in the Cov-boost experiment to validate the safety, immunological response, and adverse effects of several COVID-19 vaccines. Booster dosages are secure and efficient, although the degree of the antibody increase varies widely (Munro et al., 2021a, 2021b, Mahase, 2021b). Wearing the mask and receiving the third dose of the booster vaccination are both necessary precautions against the severity and fatality caused by COVID-19, and they may also be the best ways to stop the formation of new variations (Rathinasamy et al., 2022, Mohapatra et al., 2022a, 2022b, 2022c).

## 9. Effect of Omicron variant on current monoclonal antibody therapies

In the RBD area, a key target for neutralising antibodies, Omicron possesses 15 replacements. The RBD's RBS-A, RBS-B, RBS-C, CR302, and S309 are just a few of the antigenic locations where any of these

mutations may be found (Yuan et al.,2021). Omicron could thus be resistant to one or more monoclonal antibodies that aim to bind to these locations. In terms of medicine, the FDA has authorised the emergency use of a combination of LY-CoV016 and LY-CoV555 (bamlanivimab) (etevimab). According to a computer investigation, insertions and deletions in the N3 and N5 domains of the spike protein prevent neutralising antibodies from attaching to the protein (NABs) (Andreano et al., 2021b). In an investigation, Andreano et al. (2021b) extracted serum from 10 volunteers who had received the BNT162b2 mRNA vaccination. In the experiment, researchers made an effort to assess the viral neutralisation by B cells against various VOCs and the antibody response produced against vaccinations at the cellular level. Nearly 3000 of the 6000 cells that were sorted could make monoclonal antibodies (MAbs) against the S protein. The Wuhan-born SARS-CoV-2 virus was neutralised by antibodies from more than 400 cells. Variants, however, displayed varying levels of neutralisation and eluded neutralisation. Both beta and gamma versions have been observed to be resistant to the neutralisation of LY-CoV 016 (due to K417 N/T) and LYCoV 555 (due to E484K) (Starr et al., 2021). Prior research has linked mutations at positions 484 and 417 with immune evasion (Zimmerman et al.,2022). Since Omicron has been confirmed to carry the mutations E484A and K417N, it is also likely to be resistant to both antibodies. Nine mAbs that are currently in development for therapy or have received clinical approval entirely failed to neutralise Omicron (Taylor et al., 2021, Planas et al., 2021b). Omicron neutralisation was investigated on a group of anti-RBD mAbs intended for clinical use, including S309 (the parent mAb of sotrovimab), COV2-2196, COV2-2130 (father mAbs of AZD8895, AZD1061), REGN10933, REGN10987, LY-CoV555, LY-CoV016 and Celltrion (CT-P59). While combinations of COV2-2196 and COV2-2130 or S309 were only marginally effective against Omicron in Vero-TMPRSS2 and Vero-hACE2-TMPRSS2 cells, LY-CoV555, LY-CoV016, REGN10933, REGN10987, and CT-P59 mAbs were utterly ineffective (VanBlargan et al., 2022). Only two monoclonal antibodies have been discovered to date to be efficient neutralising agents against Omicron (IC50: Vir-7831, 0.181 ng/L; DXP-604, 0.287 ng/mL) (Cao Y et al.,2021). Additionally, an in vitro examination of the authentic Omicron virus revealed that, while Omicron was impervious to casirivimab and imdevimab, both could successfully inhibit Delta infection (Wilhelm et al.,2021).

## 10. What is the impact of the Omicron variant as well COVID on children?

The most pressing question on our mind right now is probably how omicron will affect the child if they become sick. The delta variety, as we witnessed throughout the summer, produced a significant increase in infections among youngsters, as well as an increase in hospitalizations (CDC. Centers for Disease Control and Prevention., 2021). Even if they are vaccinated or have no symptoms, experts at the Centers for Disease Control and Prevention (CDC) believe that anyone infected with Omicron can spread the virus to others. Given the current distribution of the Omicron type, there's a good chance you'll get exposed if you're out in public. Considering Omicron is extremely contagious, COVID19 is infecting an increasing number of people. This involves children, who are already at a risk of becoming infected if they are not vaccinated. As the number of incidents grows, so does the number of children hospitalised with COVID19. With the Omicron spike, the rate of new COVID19 hospitalizations in children hit an all-time high. The number of hospitalised children infected with COVID-19 reached its highest point since the outbreak began. The spike was particularly noticeable in children aged 4 and younger, according to data issued by the Centers for Disease Control and Prevention - an age group that is currently not eligible for immunization. As of January 1, 2022, more than 4 in 100, 000 children under the age of 5 were hospitalised with COVID-19, which is more than double the rate recorded a month ago and more than three times the rate of children under the age of 5 being hospitalized this time

last year. 8.5 million Children have tested positive for COVID-19 since the outbreak began. According to data provided by the US Centers for Disease Control and Prevention, 305 children were hospitalised with Covid-19 on any given day during the week ending Dec. 26. While Spinner sees no evidence that the Omicron variant causes more severe disease in children than prior variants, he also sees no indication that it causes less severe disease. While the Delta variant infected more youngsters than earlier forms, the Omicron variant appears to be far more dangerous. Children are an obvious target for the virus, according to Dr. Juan Salazar, physician in chief at Connecticut Children's Medical Center in Hartford, who told CNN. It's having an impact on bigger communities, and it's clearly having an impact on children in ways we haven't seen in the previous year. It is critical to determine whether the epidemic is influencing the minds and behaviors of children. Social and economic gaps play a definite impact in who is most affected during the pandemic, as they do in many other facets of health. Early evidence suggests that wearing masks hasn't had a harmful impact on children's emotional development. However, prenatal stress may play a role in some changes in brain connection (Melinda, 2022).

As India, like other countries, reports COVID-19 infection in children, the Union Health Ministry, in collaboration with the All India Institute of Medical Sciences (AIIMS) in Delhi, regional and state centers of excellence, and the Indian Medical Association, stated, "It is important for us to understand that children are not like adults, and we cannot translate what we do in adults to children." They must be considered as distinct entities." "There has also been a lot of concern regarding the severity of disease in children during this current wave, with reports from hospitals in the United States reporting that they are seeing an increase in the number of children hospitalised. It is critical to comprehend how the current Omicron is functioning in terms of children. The fear has always been that the younger children are not being vaccinated, and as a result, they are contracting more serious diseases. Children are affected by Omicron; however, it is a mild condition remarked by doctor. Even though youngsters are more frequently afflicted, according to Head, Professor, Pediatric Intensive Care Unit, more data is needed to determine if the infection rate is increasing or not. Although there does not appear to be a significant increase in the proportion, absolute numbers are likely to rise as the cumulative or total number of cases in the country rises. Simultaneously, the subject of why children are less frequently and seriously affected was raised. They are more resistant to the virus. Furthermore, if the lungs are injured, the better regeneration potential of the juvenile alveolar epithelium will aid in a faster and more complete recovery. Furthermore, risk factors such as comorbidities, such as smoking and diabetes that we see in adults and the elderly are apparently less prevalent in children. As a result of all of these variables, children suffer from less serious illnesses.

With the introduction of COVID-19 vaccines for children aged 5-11 and teens aged 12-15; parents may rest assured that their children will be protected against COVID-19. As a result, many of us have been wondering if the discovery of omicron may make these vaccines less effective. Are the children protected against the Omicron Variant if he or she has been vaccinated? Pfizer revealed preliminary laboratory data on how their vaccination performed against omicron on December 8, 2021. When comparing the omicron version to the original COVID-19 strain, the company discovered that neutralizing titers (antibody concentrations) were lower. When serum antibodies of persons who had received two doses of Pfizer's vaccine were evaluated, this drop was most obvious. People who had received three doses of the vaccination still exhibited significant neutralizing titers, which was encouraging. Because changes in the omicron variety did not disrupt 80% of spike protein epitopes [molecules to which antibodies attach], two vaccination doses would still provide protection against more severe disease. Indeed, experts believe that omicron is two to three times more likely than delta to spread, but they don't know why. The variety is also better than earlier ones in evading antibodies developed by past illnesses and immunizations, which could explain why it is more contagious.

However, experts believe that the enhanced transmissibility of the variant is the reason for more children being hospitalised with this variant. Each new variation, such as Omicron, has its own contagiousness and pathogenicity characteristics (harmfulness). Each kind can have a different impact on the immune system, influencing the efficacy of infection vaccinations. Researchers are still attempting to find out how the Omicron variant operates and how it responds to an individual's immunity. We still don't know the extent of Omicron's effects. This variety, according to some studies, may cause less lung damage and has a lower risk of hospitalisation. While this is good news, catastrophic disease is still a possibility, especially for those who have risk factors. It's too early to tell if Omicron produces more severe sickness in children than other coronaviruses. Vaccination is still the most effective way to protect children and families from COVID19. The COVID19 vaccine is a safe and effective way to protect from serious illness. If you suspect you've been exposed to the virus, attempt to restrict your exposure before seeing them, wear masks in public, and get tested. Finally, remember to check in with yourself and your children emotionally as you seek to maintain your family physically well.

## 11. Future directions

The WHO classification of Omicron as a variant of concern has revealed significant emerging issues and flaws in global COVID-19 response and control efforts. Unvaccinated people are now more likely to have severe illnesses that require hospitalization. Till now, limited information is known regarding Omicron's infectivity, vaccine breakthrough, antibody resistance, and the effectiveness of ongoing booster doses. Based on previous experiences with other variants, we believe that only time and surveillance will provide us with more information on the transmissibility, vaccine efficacy, and severity of the disease caused by this new variant. According to studies, Omicron may be ten times more contagious than the original SARS-CoV-2 and about twice as infectious as the Delta virus. These findings highlight the need for updated vaccines to protect humanity from the monstrous Omicron Variant attack. Till then, prevention of spreading of this variant should be the primary focus of authorities. At present situation, it seems that spreading of omicron variant is not so easy due to its high contagious nature. And in the near future, many other variants of covid 19 can also be discovered. So, here are some directions which should be following by everyone.

### 11.1. Preventive measures

COVID-19 pandemic is likely to take several months; so public need to follow social distancing and improving hygienic practices. Each and every one should follow the actions that help to prevent the spread of omicron, as well as other coronaviruses variant. Everyone should get vaccinated and wear a face mask even after fully vaccination. These kinds of practices will be effective in delaying the onset of wide community transmission, reducing peak incidence and its impact on public services (Wilder et al., 2020). Prompt diagnosis, thorough surveillance, and monitoring of the new SARS-CoV-2 mutations are necessary (Rahimi et al., 2021; Raman et al., 2021; Khan et al., 2022). The safety precautions put in place during the early waves of SARS-CoV-2, such as quarantine, the use of masks and other high-tech protective gear, alongside appropriate hygiene practices, need to be regularly followed up on (Dhama et al., 2021; Zhou et al., 2021). Much of the research should focus on drug repurposing, which involves using medications that have already been created, tested for safety and efficacy, and are currently being used to treat one condition to treat SARS-CoV-2. This is in addition to creating therapeutics to combat the emerging variants (Dhama et al., 2020). Drugs for Omicron can be delivered successfully using nanosystems as a therapy alternative (Kaushik, 2021). Another example of utilising nanotechnology to combat the greater transmissibility of Omicron is nano-neutraceuticals, which take the form of

nanosystem-based masks, gloves, and disinfectants (Dubey et al., 2022). Additionally, bioinformatics and AI may be utilised to enhance computer simulations and assess the effectiveness of potential medications against SARS-CoV-2 (Tiwari et al., 2022). In order to effectively combat the virus, new antiviral medications need to be created in light of the several mutations of the Omicron variant. These particular medications, such as Paxlovid and Molnupiravir, have lately demonstrated strong effectiveness against Omicron (Mohapatra et al., 2022a, 2022b, 2022c). Despite being a novel virus, the SARS-CoV-2 has showed variant polymorphism, making therapeutic optimization challenging. But biotechnology experts look at every aspect of bioinformatics to build a viable treatment based on cutting-edge antiviral medications, antibodies, CRISPR-Cas, and vaccinations (Mujawar et al., 2020, Paliwal et al., 2020). Another strategy for treating COVID-19 infection is strengthening immunity or orienting it through food. Innovative treatments to cure COVID-19 infection and boost the immune system and organs affected by the SARS-CoV-2 virus may be developed by examining the properties of nanomedicine (Weiss et al., 2020).

### 11.2. Diagnosis

Besides, hygiene practices and social distancing, Antibody testing has to be implemented on a large scale to identify who is already immune to the virus. The effect of temperature, season, and humidity on COVID-19 also has an impact on the COVID-19 outbreak; however, results from other parts of the world are awaited (Chan et al., 2011; Shi et al., 2020). Genome sequencing could also be a good option to know exactly the omicron cases and also effective in keeping eye on new variants of Covid-19 but genome sequencing should be done on a minimum of 5% of total positive cases. There are also certain limitations of genome sequencing like high cost, time consuming, and very low number of genome sequencing labs especially in India. Government should take steps to mitigate these limitations so that frequency of genome sequencing can be improved. Previous research has demonstrated a correlation between rising Omicron infections and rising spike gene failure rates in PCR assays. Improving diagnostic precision, ensuring prompt isolation and treatment of infected individuals, and stopping the cycle of Omicron mutations are therefore imperative. The novel Omicron variant is linked with unique issues compared to prior variants, including greater transmissibility, infectious rate, and immune evasion. It has also demonstrated partial resistance to natural immunological antibodies, monoclonal antibodies, and vaccine-induced antibodies. Due to these difficulties, new technologically based approaches to combat and eliminate the virus are required. Nanofiber swabs are an example of a quicker test that may be used to diagnose SARS-CoV-2 infection (Mostafavi et al., 2022). Correct diagnosis of Omicron patients is the first step towards effective treatment. The most effective diagnostic methods for finding Omicron variants associated with the S-protein are PCR and antigen COVID-19 testing. Omicron-specific quick testing kits, however, call for significant effort because these tests are expensive and time-consuming (Cao Y et al., 2022). An additional method of quick diagnosis involves using nanoparticles to isolate RNA or DNA from biological components using a magnetic field. These SARSCoV-2 nano-enabled sensors successfully detected a very low viral concentration. Numerous effective biomarkers, such as antibodies, CRISPR/Cas, and segment-specific DNA/RNA, have been investigated to identify SARS-CoV-2 in real samples in addition to the intelligent nanosystem (Phan et al., 2022). Modern SARS-CoV-2 biosensors that specifically target the spike protein ought to work. Omicron has more mutations at the spike protein than other variants, therefore to diagnose a large population and determine if COVID-19 infection is caused by Omicron, a suitably planned and high-throughput validation of current diagnostic techniques must be carried out (Vernet-Crua et al., 2021). A TaqMan SARS-CoV-2 mutation panel molecular genotyping test was created by (Neopane et al., 2021) and was able to distinguish between variants B.1.617.2 (Delta), B.1.1.7 (Alpha), B.1.526 (Iota), B.1.351



(Beta), P.1 (Gamma), P.2 (Zeta), B.1.617.1 (Kappa), and B.1.427 (Epsilon). The test is very helpful in the current situation and may be utilised for epidemic control and surveillance. However, there are still obstacles to overcome before the testing kit can be developed quickly enough to meet the broad demands of the pandemic.

### 11.3. Vaccines

The difficulty with the vaccination campaign is that ethnic minority groups and poorer groups are less likely to get vaccinated (Rae, 2021). People living in low-income and less developed nations should be a top priority topic for mass immunisation since vaccination has been shown to be highly successful in the treatment of COVID-19 and to prevent high burden of disease severity (Nainu et al., 2020; Liu et al., 2021; He et al., 2021). High-income and more developed nations can manage a fully organised and focused campaign of mass vaccination assistance. To promote vaccination equity and worldwide access, vaccines must be given to those living in low-income nations. The longer vaccine disparity exists, the more opportunities the virus will have to spread, mutate, and adapt (Vaughan, 2021). It is necessary to develop improved methods for creating superior vaccine candidates with a longer shelf life, greater stability, and convenience of vaccination, such as an oral or nasal vaccine (Snehota et al., 2021). Currently, many mRNA-based vaccines may be effectively designed to meet the pace of emerging variants when there is a high requirement to protect the population from emerging SARS-CoV-2 VOCs and VOIs; however, there is a quest to develop a much more experimental one-shot universal vaccine that can protect people for their entire lifetime (Li, 2021).

Vaccine rich countries in collaboration with pharmaceutical companies are developing strategies to deliver a booster dose. More prosperous countries must remember the WHO slogan, "none of us is safe until all of us are safe." Debates are ongoing about the efficacy of existing vaccines against omicron but we should also focus on the point that months are needed before a new vaccine is developed and approved. Scientist are also discussing if booster dose can be an option to counter the omicron effect. Even in some countries like Israel are already vaccinated their population with booster dose. Israel also approved 4th covid vaccine shot to prevent their population from omicron (116). Bivalent vaccine can also be a better approach against omicron. Scientists also developed four distinct recombinant vesicular stomatitis virus (rVSV)-based bivalent vaccines against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and influenza virus (Hassan et al., 2020). This variant has more advanced immune evasion than the previous ones as a result of the many mutations described in Omicron, which makes it partially resistant to monoclonal antibodies, vaccine neutralizing antibodies, and antibodies made from natural immunity. According to recent findings, natural and vaccine-induced immunity will respond differently in the event of an Omicron infection. Six months following immunization, a decline in serum neutralizing antibodies has been noted in several investigations. Adding a booster at the same time can increase or restore the vaccine's efficacy to its initial level (Bekliz et al., 2022; Hoffmann et al., 2022; Planas et al., 2021a; Fabricius et al., 2021). The importance of a third vaccination with BNT162b2 is emphasised, due to at least 100 factors high neutralisation efficacy after a third shot against the omicron variant (Nemet et al., 2021); and other researchers have obtained similar results (Garcia-Beltran et al., 2021), who confirmed that the vaccine's ability to protect against infection is compromised (Cele et al., 2021). All of the findings point to the necessity of booster dosages in promoting Omicron neutralisation (Garcia-Beltran et al., 2021; Natario, 2021; Barda et al., 2021). Although homologous or heterologous vaccination with protein subunit vaccine (ZF 2001) increases neutralisation against the Omicron and the sera from patients who received two doses of inactivated whole-virion vaccinations (BBIBP-CorV) revealed lower neutralisation by Omicron (Wang et al., 2022). In a sample of 292 people, homologous boosting with the BBIBP-CorV vaccine 9 months after the two dose immunisation regimen

showed that Omicron was neutralised in 78.08% of patients (Yu et al., 2022). However, this enhanced defence against Omicron may wane more quickly than it did against Delta, with a 15–25% decline in defence after ten weeks following the booster (Mahase, 2021a). According to the data, even if boosting with a third dosage increased the neutralisation capacity, Omicron is the most resistant to neutralisation when compared to other VOCs, and the boosting was unable to elicit a significant reaction in pregnant women who had received the vaccine. The results point to significant variation in the size and range of Omicron's neutralising reactions among various populations (Sievers et al., 2022). There was no measurable Omicron neutralisation after 2 doses of heterologous immunisation with the CoronaVac vaccine, but when it was enhanced with BNT162b2, it demonstrated 1.4-fold greater neutralisation than after 2 doses of the mRNA vaccine (Pérez-Then et al., 2022).

## 12. Discussion

Since November, 2021 omicron variant emerged as a new public health threat due to its highly contagious nature. At this point of the pandemic, the Omicron strain is supercharging the booster debate, and bivalent vaccines. The people who have travelled to high-risk countries or those who have been in touch with a person or symptomatic healthcare worker or patients with severe respiratory disease should be compulsory tested. Lockdown is not the only solution to prevent the spreading of virus, in order to do so proper and adequate testing should be done. In order to reduce the number of new cases, screening, infection prevention and control, quarantine of sick people, and precautionary self-isolation of contacts are essential. The emergence of a new, potentially more dangerous variant serves as a sobering reminder that the world is still in the grip of a pandemic, and that the world is extremely vulnerable to another SARS-CoV-2 outbreak. Given various similarities between documented mutations in B.1.1.529 and the Delta variation, we expect that the immune responses produced by currently available vaccines will be effective in fighting against this variant. The degree of protection provided by these vaccines against Omicron is now the subject of research. As a result, worldwide immunization is essential; otherwise, the threat of new and more severe SARS-CoV-2 subtypes will always be present. As a result, we must continue to exercise extreme vigilance in our social gatherings and ensure that everyone who is eligible is vaccinated, including the third and/or booster doses.

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### Data Availability

No data was used for the research described in the article.

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### Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

### Author contributions

Dr. RR and Prof. NKG contributed to the concept. Dr. RR, Mr. RK, Mr. RSH and Ms. DB wrote the manuscript. Dr. RR, Mr. RK and Mr. RSH edited the Manuscript. The final version of the manuscript was read and approved by all authors.



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