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EPIDEMIOLOGY, MUTATIONS AND IMPACT OF NEW OMICRON VARIANT (B.1.1.529): A REAL GLOBAL THREAT OF COVID-19 PANDEMIC

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ABSTRACT: The recent emergence of the Omicron variant (B.1.1.529) of SARS-CoV-2 has added alarm to the eternal flame of the global COVID-19 pandemic. Omicron was first identified in Botswana in November 2021. The omicron is thought to be at least three times more infectious than the previous variants. Omicron can cause diseases varying from asymptomatic, mild, and severe infection and people have died from omicron in a second pandemic wave that occurred in March-May 2021. This variant has been detected in more than 77 countries worldwide as per WHO until January 2022. The spike protein is the target of most COVID-19 vaccines and is what the virus uses to unlock access to our body's immune cells, many of which (69–70del (deletion), T95I, G142D/143–145del, K417N, N679K, T478K, N501Y, N655Y, and P681H) overlap with Alpha, Beta, Gamma, or Delta variants. Some spike protein mutations include A67V, Δ69-70, T95I, G142D/Δ143-145, Δ211/L212I, ins214EPE G339D, S371L, S373P, S375F, *etc*. Remarkable mutations in the furin cleavage site may increase transmissibility and replication as in Alpha (P681H) and Gamma (H655Y, N679K) and affect the binding affinity of ACE-2 receptor. Though, after many ongoing mutations and adaptation, omicron can efficiently breach the host immunity, leading to prolonged, severe infection, causing more mortality and rapid spread. There is still substantial uncertainty based on ongoing genomic changes, the effectiveness of current and upcoming vaccines, and treatment against omicron. Thus omicron has forced on the world a chance to explore the intricacies of the complex immunological mechanism.

INTRODUCTION: Coronavirus is one of the major pathogen of 21st century that primarily target the human respiratory system. Previous outbreaks of coronaviruses include; severe acute respiratory syndrome-corona virus-2(SARS-CoV-2) and the Middle East Respiratory Syndrome- coronavirus (MERS-CoV), which have been previously characterized as agents of important public health threat [1].

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These patients were epidemiologically linked to the seafood and wet animal wholesale market in Wuhan, Hubei Province, China [2]. The first sequenced confirm case of the Omicron variant was reported from Botswana on 11 November 2021. A few days later, one more genetically sequenced patient was reported from the china city, Hong Kong, who had recently traveled from South Africa, as shown in **Table 1** [3].

On subsequent days several sequences of omicron have been reported from South Africa. The new variant was associated with an absence of S-gene on a specific polymerase chain reaction (PCR) assay because of a 69–70 deletion, similar to the alpha variant of coronavirus [4]. The earliest known case of Omicron in South Africa was a patient

diagnosed with COVID-19 on 9, November 2021. However, it is possible that there were many unidentified cases in several countries across the world [5]. In South Africa, 280 COVID-19 cases per day in the week before the first detection of Omicron cases increased to around 800 cases per day in the following week, partly attributed to increased awareness and timely surveillance diagnosis of sequencing and global concern [6]. COVID-19 cases were increasing in the Gauteng, South Africa; the early doubling time in the fourth wave is higher than that of the previous waves of the COVID-19 pandemic, as shown in **Fig. 1** [7].

TABLE 1: SEQUENCE OF OMICRON VARIANT DETECTED IN REFERENCE TO TIME IN WORLD AND INDIA

Date	Counties	Number of cases and history of travel
24 November 2021	South Africa in Gauteng province and Botswana	Two cases reported
26 November 2021 WHO designated named (B.1.1.529) Variant of Concern	Netherland, Israel, Hongcong, Belgium	New cases were reported in four countries
27 November 2021	Australia, Czech Republic, Italy, Germany, England	Travel related cases in this county first detect omicron cases
28 November 2021	Denmark, Austria	Travel-related cases
29 November 2021	Canada, Sweden, Spain, Switzerland	Travel-related cases
30 November 2021	France, Japan, and Portugal	First detected transmission-related case
1 December 2021	Brazil, South Korea, Norway, Saudi Arabia	Travel-related cases
2 December 2021	India & many other counties in the world	Two cases detected Karnataka:66 year old South African Bangalore:46 year doctor with no travel history
4 December 2021	India & many other counties in the world	Gujarat:72-year-old NRI man Maharashtra:32-year-old man
5 December 2021	India	New Delhi capital detected first case of omicron variant
6 December 2021	India	Two more cases were detected in Mumbai
8 December 2021	India and Globally	Total 23 cases were reported in India, and omicron was spread in more than 50 counties across the world
10 December 2021	Europe	180 additional SARS-CoV-2 Omicron cases have been confirmed in the European Union and European
	India	Economic Area (EU/EEA), an overall total of 582 confirmed cases 32 cases of the new variant of concern omicron have been detected
14 December 2021	UK, China India	UK confirms 1st Omicron death, First case of omicron detected in China Totally of the cases of the new variant in India reached [38]

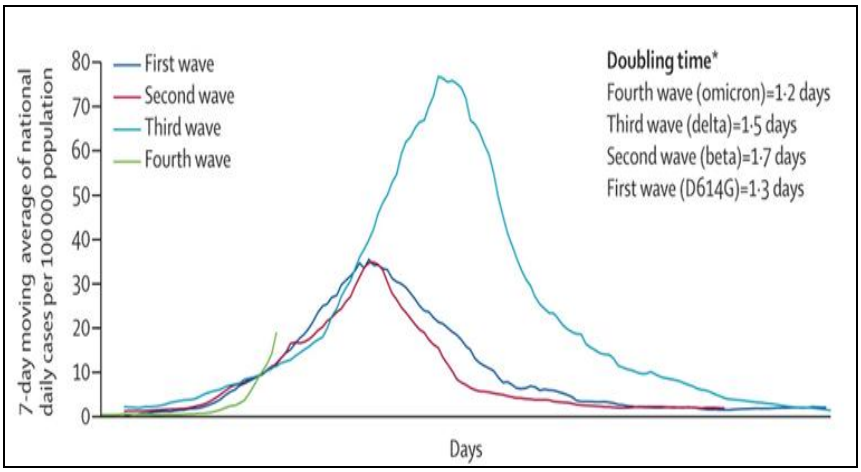

FIG. 1: SARS-COV-2 CASES IN FIRST, SECOND, THIRD, AND FOURTH WAVES, GAUTENG PROVINCE, SOUTH AFRICA

More than 77 countries have currently reported genetically sequenced cases of the Omicron variant. Omicron has a family of SARS-CoV-2 variants belonging to Pango lineage, *i.e.,* B.1.1.529 as a variant of concern, next-strain clade 21K, and is characterized by 30 amino acid changes due to mutations, three small deletions and one small insertion in the spike protein gene causing immune escape mechanism and increased transmissibility as compared to the Beta and Delta variant of SARS-CoV-2 and the *R*-value is above 2.0 [5, 8].

Review: The Omicron variant has many mutations; due to these mutations, this new variant is gaining utmost importance in the COVID-19 pandemic. Initial evidence suggests that there is an increased risk of re-infection with omicron as compared to other SARS-CoV-2 variants. The number of cases of omicron appears to be increasing in almost all countries globally and as of now, even remote location counties have also reported omicron.

Current SARS-CoV-2 PCR diagnostics continue to detect omicron based on the fact that after major mutation in the S (spike) gene, one of the three target genes is not detected (absence of S gene or target failure), and this can, therefore, be used as a marker for omicron, pending for sequencing confirmation [9]. This variant has been detected faster than previous surges in COVID-19 infection, suggesting that this variant may have a high rate of *in-vitro* propagation using the above principle [10].

TABLE 2: WHO DESIGNATED SARS-COV-2 VARIANTS OF CONCERN (VOCS) [8, 22, 23]

WHO designation (Date of Designation)	Pango lineage	GISAID clade	Nextstrain Clade	Additional amino acid changes monitored	Country of origin of first documented samples
ALPHA (18 December 2020)	B.1.1.7	GRY	20I (V1)	+S:484K +S:452R	September 2020 United Kingdom,
BETA (18 December 2020)	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	May 2020 South Africa
GAMMA (11 January 2021)	P.1	GR/501Y.V3	20J (V3)	+S:681H	November 2020 Brazil
(DELTA) 11 May 2020	B.1.617.2	G/478K.V1	21A, 21I, 21J	+S:417N +S:484K	October 2020 India
(OMICRON) 26 November 2021	B.1.1.529	GR/484A	21K	E484A N440K S477N S/D796Y	South Africa, Hong Kong, Belgium, Israel, Europe, Asia Now >60 countries have been affected so far. (10 December 2021)

Omicron has around more than 50 mutations, among which the majority of mutations (32 mutations) are seen in the spike protein. The viral spike protein is present on the virus's surface that mediates viral attachment to the host cell through the angiotensin-converting enzyme 2 (ACE-2) receptor, thereby making viral entry into the host cell. So, it acts as the prime target of neutralizing antibodies to the virus. The spike glycoprotein has two subunits, the S1, and S2, which mediate ACE-2 attachment and membrane fusion, respectively, to facilitate viral entry into the target host cell.

These two subunits require cleaving by a host furin enzyme and then showing non-covalent interactions in further pathogenesis. Major mutations on the spike protein are A67V, Δ69-70, T95I, G142D/Δ143-145, Δ211/L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, H655Y, N679K, P681H, N764K, , N969K, L981F T478K, E484A, Q493K, G496S, Q498R, N501Y, Y505H, T547K, D614G, D796Y, N856K, Q954H. Some of these mutations are identified in Omicron and other VOCs and may be associated with immune escape mechanism, enhanced transmissibility *via* inducing cell fusion, and susceptibility to treatment [11, 12]. Three important mutations around the furin cleavage site may increase transmissibility and replication as it is also found in Alpha (P681H) and Gamma variants (H655Y, N679K) [13].

It has been observed that there are six mutations detected in the N-terminal domain, which may be associated with evasion of antibody neutralization by innate, vaccine-based, or monoclonal-based antibodies, as shown in **Fig. 2**. The spike protein is the target of most COVID-19 vaccines. It is what the virus uses to unlock access to our body's immune cells, many of which (69–70del (deletion), T95I, G142D/143–145del, K417N, N679K, T478K, N501Y, N655Y, and P681H) overlap with Alpha, Beta, Gamma, or Delta variants [14]. Some of these mutations are also found in Alpha (Δ69-70),

Delta (T95I, G142D/Δ143-145), as well as other mutations, which are not yet found in a variant of concerns (VOCs) (A67V, Δ211/L212I, ins214EPE). Three mutations of the cell surface receptor binding domain, T478K (Delta), N501Y (Alpha, Beta, and Gamma), and Q498R (not previously reported in any VOCs), may increase the binding affinity with ACE-2 receptors on host cells and further enhance immune escape mechanisms [15]. Importantly, the effects of most of the remaining genomic mutations are not fully known, resulting in uncertainty about how the combination of deletions and mutations will affect pathogenesis and susceptibility to natural and vaccine-mediated immunity [16].

Outside of the surface spike protein, the nsp6 deletion Δ105-107 (Alpha, Beta, and Gamma) may be associated with further evasion of innate immunity, leading to enhanced transmissibility as seen in Omicron [17]. Further, two mutations of the nucleocapsid, R203K and G204R (Alpha and Gamma), may be an important factor causing increased infectivity in Omicron [18, 19].

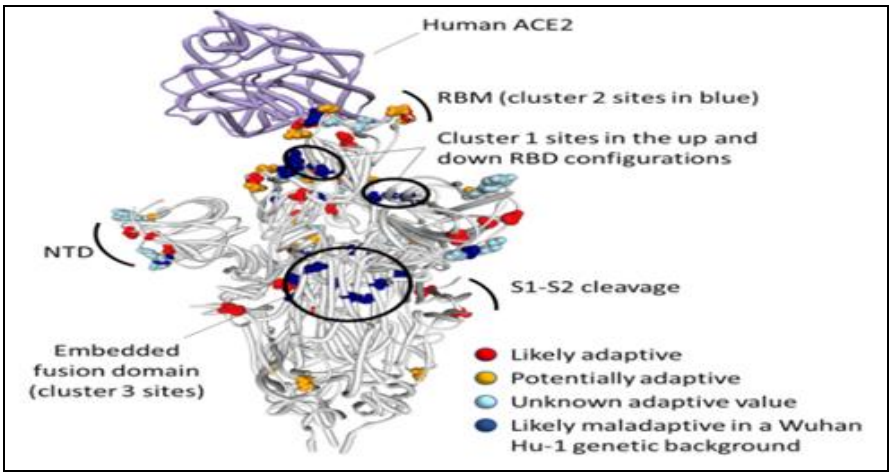

FIG. 2: THREE DIMENSIONAL SARS-COV-2 SPIKE TRIMER HAVING DISTRIBUTION OF OMICRON AND AMINO ACID REPLACEMENTS

Clinical Features and Diagnosis of Omicron: The main concern about omicron includes whether it is more infectious or severe than other VOCs and whether it can be prevented by ongoing vaccination[7]. Although, the clinical as well immunological data are not yet available to large multicentric research to provide definitive evidence about the transmissibility, severity, and immune escape mechanism of the new Omicron [20]. In the first few omicron cases, patients reported general fatigue, body aches, a mild headache, and a scratchy throat rather than the usual "sore throat".

The common clinical features include fatigue, body ache, headache, fever, myalgia, malaise, and muscular pain. Among pulmonary involvement, cough, scratchy throat, shortness of breath, and pneumonia may be present. Extra-pulmonary characteristics like abdominal pain, nausea, and vomiting, diarrhea may occur. While other patients began reporting similar symptoms (unusual among alpha and Delta variants), it raised the suspicion of a new variant [21]. The major clinical manifestations of the omicron variant are those of a "mild infection rather more severe symptoms as observed in 2nd pandemic wave caused by previous variants. The SARS-CoV-2 virus has mutated over time, resulting in genetic variation in circulating strains throughout the COVID-19 pandemic. There are many types of diagnostic tests available to diagnose a suspected case of SARS-CoV-2, including molecular, antigen, and serological tests.

These tests are affected by viral mutations differently due to each test's inherent principle, design and differences in sensitivity and specificity. Now usually, molecular tests target single or combination of different genes like E (envelop), N(nucleoprotein), S, and RdRp (RNA dependent RNA polymerase) genes. However, most tests are now testing the S-gene because there is an S-gene dropout or S-gene failure target failure. So if that happened, then by proxy, we can say by default, we can say that this is omicron, and such sample should be tested for either variant-specific PCRs in the S gene of SARS-CoV-2 or whole genomic

sequencing. For omicron confirmation, genomic sequencing is essential to confirm whether it is the Omicron variant or not [22].

Working Definition: A SARS-CoV-2 variant that meets the definition of a variant of interest (VOI) and, through a comparative assessment, has been demonstrated considering the degree of global public health significance with one or more changes [23, 24].

- Increase in transmissibility or detrimental change in COVID-19 epidemiology; OR
- Increase in virulence or change in severity and clinical presentation; OR
- Changes in the effectiveness of public health and social measures; OR
- Role and effectiveness of available diagnostics, vaccines, and treatments

Variants of Concern (VOC): Some virus variants because they spread more easily and may cause severe diseases and might be able to escape from the body's immune response. This help in the identification of mutational changes in both assembled genome sequences and raw intra-patient, as shown in **Table 2** [25].

Transmission of Omicron: Omicron virus can spread through direct exposure to infected human-to-human more rapidly from person to person than other variants.

The replacement of Delta by Omicron as the predominant variant in South Africa raises concerns that the Omicron variant may be more transmissible than Delta, but due to the low number of cases in the world caused by Omicron [26]. Further, a few studies are documented to date, making it difficult to estimate Omicron transmissibility, as shown in **Fig. 3**.

Analysis of the changes in the spike protein indicates that the Omicron variant is likely to have more transmissible than the original SARS-CoV-2 virus, if it is more infectious than Delta variant [27].

a. N501Y increases binding to the ACE-2 receptor, which could increase the combination of N501Y and Q498R may increase the binding affinity of receptor binding domain, resulting in more transmission; however, other substitutions in the Omicron spike protein are expected to decrease binding to ACE-2. The receptor binding affinity needs to be assessed using the full spectrum of spike protein substitutions [28].

b. H655Y is proximal to the furin cleavage site and may increase spike cleavage, aiding further transmission.

c. N679K is proximal to and adds to the polybasic nature of the furin cleavage site, which may also increase spike cleavage and could aid transmission.

d. P681H has been shown to enhance spike cleavage, which could aid transmission. This mutation is found in Alpha, and an alternate mutation at this position (P681R) is also found in Delta variant [27].

Severity of Omicron Infection: It is not yet clear whether infection with omicron causes more severe disease than infections with other variants, including Alpha, Beta, and Delta variants. Initial data suggest increasing rates of hospitalization in South Africa, but this may be due to increasing overall numbers of people becoming infected rather than a result of specific infection with Omicron [29]. Currently, no large studies suggest that symptoms associated with omicron are different from those of other variants. Initially reported infections were among university students, younger individuals who tend to have more mild disease, but understanding the level of severity of the Omicron variant will take days to several weeks. All variants of SARS-CoV-2, including the Delta variant that is still dominant worldwide, can cause severe disease or death, particularly for the most vulnerable people. Thus, prevention is always key factor [30].

Impact of Omicron: The new Omicron variant of SARS-CoV-2poses risks to the global economic growth, travel industry, and inflation outlook of the global market, as concerns mount about the variant's health risks and several countries have imposed new travel restrictions. So, restricting over-travel will negatively impact direct and indirect economic and social consequences on health systems, especially recently in South Africa and its neighbouring countries, which are only just

starting to recover from the devastating effects of several lockdowns over the past 2 years. This is all the more important when the economy is fragile, suffering inflation and currency deflation and their hospitals lack funds to operate efficiently for control of such new variant [31].

Impact of Omicron in India: On 5 December 2021, the fifth Omicron case was detected in India. The Indian government monitors the situation closely and issues suitable guidelines from time to time. Meanwhile, the scientific and medical community is geared up for developing and deploying diagnostics, carrying out genomic surveillance, generating evidence about viral and epidemiologic characteristics, and developing therapeutics [32]. A total of 2,135 cases of the Omicron variant of coronavirus have been detected across the country. The fatality count increased to 4, 82, 551, with 354 more people succumbing due to the deadly contagious disease. The rapid surge in the daily number of COVID-19 infections, comparable to the global trends, strongly suggests the dominance of the Omicron variant in infections in India. The logarithmic regression suggests the early growth rate of infections in the third wave is nearly four times that in the second wave [33].

Global Impact of Omicron: Vaccination against SARS-CoV-2 successfully reduces deaths, hospitalizations, and transmission worldwide, despite the emergence and continued dominance of the Delta variant of the SARS-CoV-2 strain. Due to the ongoing active circulation of the Delta variant, global countries are urged to give priority to the vaccination of individuals initially targeted by COVID-19 vaccination programs that remain unvaccinated or not yet fully vaccinated by a minimum of two doses [34]. It is also possible that the Omicron variant causes a prolonged infection within apparent symptoms and consequently confers virus spread to more people. The high clinical data should be available in the next few weeks. The second question is whether the mutations in viral Nsp12-RdRp and Nsp14-Exo confer a higher mutation rate in the Omicron variant. Through mutations, substitutions, and adaptation, viral variants can efficiently evade the host immunity, resulting in prolonged infection and virus spread to others. The third question is whether the current vaccines, which are entirely based on the original SARS-CoV-2 strain, are protective against this new variant [35].

This information could be quickly obtained by examining neutralization antibodies against an Omicron pseudovirus or an authentic infectious clone. It is noted that all four early Botswana Omicron variant patients were fully vaccinated, indicating a possible vaccine escape. It is currently unknown to what extent the Omicron variant affects the vaccine effectiveness of the COVID-19 vaccine licensed in the world. Various developed countries are currently finalizing a protocol to investigate SARS-CoV-2 outbreaks in semi-closed settings, including those related to the Omicron variant, to assess vaccine effectiveness. India and the rest of the world plan to publish the protocol during the first half of December 2021to to combat this new variant. It has been highlighted that countries should consider a booster dose for those aged 40 years and above, first targeting the most vulnerable front line workers and the elderly and then expanding to all adults aged 18 years and above at least six months after completion of the primary vaccination. Booster doses will increase immunity in the high-risk population and sustain transmission control beyond the immediate impact of non-pharmaceutical interventions, which will be particularly important in previewing the emergence of more transmissible variants with potentially reduced vaccine effectiveness [36].

Future Impact of Omicron Variant: Globally, scientists tracking the evolution of SARS-CoV-2 are looking for two broad categories of changes to the virus. One makes it more infectious or transmissible by replicating it more quickly so that it spreads more easily through coughs, sneezes, and wheezes. The other enables it to overcome a host's immune response. When a virus first starts spreading in a new host, the lack of pre-existing immunity means there is little advantage to be gained by evading immunity, as shown in **Table 3** [36]. One important question is still not fully explained. A heavily mutated variant such as omicron could have arisen because the virus began circulating and mutating, where it would have had an opportunity to change dramatically. It could then have been introduced, with its numerous mutations, into the larger population, where it was able to travel into different human groups and countries.

As growing evidence points towards large numbers of people becoming infected with omicron across the globe, there are additional concerns that omicron is just the starting point for more variants to emerge - potentially maintaining its high levels of transmissibility but with maybe greater virulence. Of most concern is that, as new variants like omicron appear, there is a broadening of the groups at risk of serious disease after infection. Each new variant deriving from omicron could challenge the efficacy of any cumulative, existing immunity to infection we have obtained from vaccines or previous infections, slowing down how quickly we can emerge from the pandemic [37]. A worrying possibility is whether the profile of the groups at risk from infection was to change. For instance, children are relatively spared from severe disease after infection with other variants, and hopefully, this remains the case with the Omicron variant. Nevertheless, if the susceptibility of young children were to change, it would alter how we approach the control of SARS-CoV-2 infections. The key point is that just because the virus has followed a particular pattern before, it does not mean this will be followed in the same way in the future [38].

Scientists have warned of a lethal variant called '*NeoCov'* that requires only one mutation to infiltrate human cells. According to a study by Chinese researchers, it is a type of corona virus, NeoCov, which spreads among bats in South Africa, may pose a threat to humans in the future if it mutates further. *NeoCov* carries the combination of (the MERS-CoV mortality rate (where one in every three infected persons may die) and the current SARS-CoV-2 coronavirus with a high transmission rate [39].

TABLE 3: WHAT WE KNOW ABOUT INFECTION AND SPREAD OF OMICRON WITH IMPORTANT QUESTIONS AND THEIR POSSIBLE ANSWERS [34]

S. no.	Query/Question	Answer
1	How easily does omicron spread	Omicron variant likely will spread more easily than the original SARS-CoV-2 virus and how easily omicron spreads compared to Delta remains unknown CDC expects says that anyone with Omicron infection can spread the virus to others, even if they are vaccinated or don't have symptoms
2	Will Omicron cause more severe illness than other variants	More data are needed to know if Omicron infections, and especially re-infections and breakthrough infections in people who are fully vaccinated, cause more severe illness or death than infection with other variants
3	Will vaccines work against Omicron variant	Current vaccines are expected to protect against severe illness, hospitalizations, and deaths due to infection with the Omicron variant However, breakthrough infections in people who are fully vaccinated are likely to occur. With other variants, like Delta, vaccines have remained effective at preventing severe illness, hospitalizations, and death Recent emergence of omicron further emphasizes the importance of vaccination and boosters
4	Will treatments work against Omicron variant	Scientists are working to determine how existing treatments for COVID-19 work. Based on the changed genetic make-up of omicron, some treatments are likely to remain effective while others may be less effective
5	Role of current vaccine available for SARS-CoV-2 against Omicron	Researchers are still unclear about the effectiveness of vaccines against this variant because this variant displays multiple mutations that might resist neutralization

Role of Available Vaccines over Next Covid-19 Pandemic Wave: A healthy person has many immune cells called CD4+T cells, which stimulate another type of immune cell called natural killer (NK) T cells. In healthy people, who get COVID-19 infection, these NK T cells destroy the virus-infected cells. But in immune-compromised people having low numbers of CD4+T cells, "the virus establishes a persistent infection" because of a lack of killer-T-cell responses, as shown in **Table 3** [40].

However, their immune systems produce some other immune cells called B cells that trigger an antibody response, which "results in an arms race between the virus and host antibodies". The B-cell response does not create enough antibodies because of the weak response to clear the virus completely. Consequently, the genetic sequence for the virus's spike protein undergoes pressure to mutate to a large extent to escape the effect of antibodies [41].

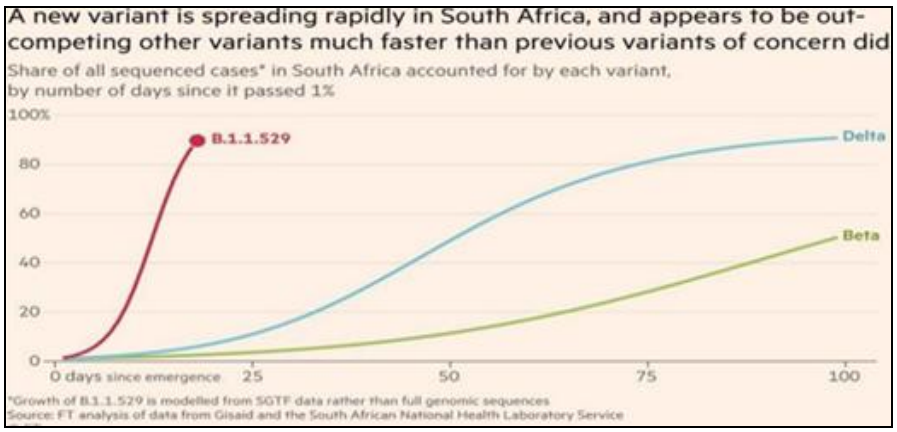

FIG. 3: COMPARATIVE TRANSMISSIBILITY OF OMICRON, ALPHA AND DELTA VARIANT OF COVID-19

So, the first and biggest gains a new virus will make tend to come through enhancements to infectivity or transmissibility [11]. The Omicron variant has a lot more mutations on the spike proteins. Having more mutations on the spike protein confers a great advantage to it. It can attach itself much more firmly to the human cells. In India, we have had substantial exposure to the delta variant (March-June 2021) in the second wave. Therefore, the immunity developed against the delta variant would carry over, to some extent to this variant as well. We need to study how much of our existing immunity, particularly of our vaccines, is working against this new Omicron variant [42].

Regardless of the outcome, it seems prudent to immediately jumpstart the production of a vaccine against this new variant. Numerous pharmaceutical companies have wasted no time and announced plans to develop vaccines against the new variant. Governments should join forces with vaccine companies to develop an efficient strategy to best deal with this rapidly emerging medical urgency [35].

Two doses of existing COVID-19 vaccine protocols laid by many countries are not enough to stop the infection of Omicron. That's why scientists from the United Kingdom have already warned and suggested a third dose/booster of the vaccine at the earliest. Early analysis of Omicron and Delta cases showed that the vaccines were less effective at stopping the spread of new variants. But a third booster prevents around 75% of people from getting any COVID-19 symptoms [43]. The primary community control measures available were containment through isolation of those who had symptoms consistent with SARS and quarantining contacts, which might be incubating the disease. There is still substantial uncertainty surrounding the biological characteristics of the Omicron variant (particularly severity), the effectiveness of existing vaccines and available treatments, and the efficacy of infection control measures like COVID-19 appropriate behaviour for suppressing transmission of Omicron variant. In populations with high levels of immunity, it is clear that the Omicron variant has the potential to cause significant disruption, particularly if it exhibits higher levels of immune escape even after vaccination.

It remains unclear, whether the Omicron variant will outcompete with pre-existing variants in other settings with lower levels of existing immunity where there is inherent lower transmissibility than that of the current Delta and Delta plus variant [44]. However, vaccination remains one of the most effective protection tools against SARS-CoV-2, including for the 99.9% of Delta strains currently representing the COVID-19 disease burden in Ontario. Global efforts to optimize vaccination coverage, especially in low to middle-income countries with limited resources to prevent and control SARS-CoV-2 transmission, are also a key measure to combat newer VOCs spread as each transmission event plays an important role in fostering mutations that leads to development of further new variants [19]. In a small-scale study, those who have received Ad26. COV2.S or Sputnik V or BBIBO-CorV vaccines did not show any neutralizing activity against Omicron S protein. Those who received mRNA-1273, BNT162b2, and AZD1222 showed 33-, 44- and 36-fold decrease, respectively, in neutralizing activity against the omicron S protein. Prior infection in vaccinated individuals showed a less pronounced 5-fold

decrease in neutralizing activity. Furthermore, broadly neutralizing *mAbs* that recognize conserved epitopes among SARS-CoV-2 variants and other sarbecoviruses may contribute to controlling the pandemic and curtailing future sarbecovirus zoonotic spillovers [45]. The re-infection with SARS-CoV-2 seems unlikely, although reported now a day, taking into consideration on level and duration of viral neutralizing antibody, duration from past infections, the type of specimen, testing methods, and the presence of fecal viral RNA without replication [46].

Containment through isolation of an infected person who had symptoms consistent with SARS-CoV-2 and quarantining contacts who might be incubating the disease is the primary community control measure available to combat the existing and a new variant like Omicron [47].

Even though most of the measures have been focused on adults, we must not forget the devastating effect of the COVID-19 pandemic on children globally. Despite children being considered to be at lower risk of mortality than adults, children are still suffering from milder, post-infectious complications of COVID-19 such as multisystem inflammatory syndrome and breathing difficulties. The long-term effects of COVID-19, especially newer variants, are also still unraveling [48].

CONCLUSIONS: The extrapolations based on known mutations and preliminary observations, which should be interpreted with caution, indicate that omicron might spread faster and might escape immune mechanisms, especially from antibodies, more readily than previous variants, thereby increasing cases of re-infection and cases of mild breakthrough infections in people even who are vaccinated by two doses. Based on data from various scientific studies, it was observed that vaccinated people are likely to have a lower risk of severe disease of COVID-19 from the new Omicron variant.

There is optimism that vaccines will keep many people out of the hospital, even if more do get COVID-19 infection. However, an Omicron wave could be problematic, even if it will be milder. A large and sudden wave could lead to everyone who is still vulnerable needing hospital care at the same time. So, a combination of targeted pharmaceutical agents, a preventive approach of booster/third dose vaccination, and public health measures are expected to remain an effective strategy to combat the devastating pandemic.

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CONFLICTS OF INTERESTS: The authors declare no conflicts of interest.

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