

## OMICRON SUB-VARIANTS: IS THE WORLD GOING TO WITNESS ANOTHER WAVE?

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### ABSTRACT

Omicron, the new 'Variant of Concern' of SARS-CoV-2, is rapidly evolving into new sub-variants or sub-lineages (BA.1, BA.2 etc.). These sub-variants have higher transmissibility, decreased vaccine effectiveness and increased risk of re-infection. As a result, many nations across the globe are reporting surge in infections which is a matter of concern. Understanding Omicron and its sub-variants is vital for development of public health policy and preventing disease transmission. The present paper throws a spotlight on the newly detected sub-variants of Omicron as reported in ongoing researches which are available only in pre-print form and also the importance of a booster dose of the vaccine. Information regarding recent research on a new nasal vaccine formulation, which may be effective against the new variants, is also highlighted in the paper.

**Key words:** *Omicron, sub-variants, transmission, vaccine, genome*

### INTRODUCTION

'Omicron' (B.1.1.529), a recent variant of COVID-19, first detected on November 9, 2021, has been designated as 'Variant of Concern' (VOC) by World Health Organization (WHO) [12]. Since its detection, Omicron has been sequenced all over the world and appears to be responsible for driving several outbreaks of SARS-CoV-2 or causing existing outbreaks to accelerate. Recently, on the basis of computational analysis, it was divided into three sub lineages (BA.1, BA.2 and BA.3). BA.1 and BA.2 are more dominant as they have the ability to overcome the defences of even highly immune individuals and it has been reported that sub lineage BA.1 has spread to more than 130 nations [6, 7].

After several weeks of declines, reported cases of COVID-19 are once again increasing globally. Covid cases have surpassed 500 million as new infections are occurring at a rapid rate in many countries of Europe and Asia because of sub variant BA.2 [4]. The recent surges in China and record infections in Europe

are as a result of rise of BA.2. It has been called as the 'stealth variant' as it is harder to track as compared to other variants. Highest average number of new cases have been reported from South Korea with more than 1,82,000 cases being reported on daily basis. Cases are also rising in smaller South Asian countries like Thailand, Taiwan and Bhutan. China is witnessing its worst Covid outbreak since the emergence of the virus in Wuhan in 2019, with its major financial capital, Shanghai reporting more than 25000 cases per day [3]. Apart from Shanghai, 18 other provincial-level regions on the mainland saw new local COVID-19 cases. India is also witnessing sharp rise in daily cases especially in its capital city, New Delhi. Revised COVID protocols are being framed in the national capital as new infections are surging at the state and the national level due to Omicron sub-variants.

### Recombinants of Omicron

As a result of genetic selection, viruses naturally evolve and are continuously changing. They have the ability to undergo minor genetic changes through

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mutation, as well as major genetic changes through recombination [14]. When an error is incorporated in the viral genome, it leads to mutation and recombination occurs when two viruses infect the same host cell and exchange genetic information, which creates a novel virus. Recombinants can surface when the same person (or animal) is infected by more than one variant at the same time ('co-infection'). This allows the variants to interact during replication, mixing their genetic material and forming new combinations. Three SARS-CoV-2 recombinant variants with evidence of person-to-person transmission have been reported: XD (AY.4/BA.1 recombinant, where AY.4 is Delta), XE (BA.1/BA.2 recombinant) and XF (another AY.4/BA.1 recombinant) [14].

### **Risk of re-infection with BA.1 and BA.2**

BA.2 differs from BA.1 in its genetic sequence, including some amino acid differences in the spike protein and other proteins. It has been shown that BA.2 has a growth advantage over BA.1 [12]. Studies are ongoing that are evaluating the risk of re-infection with BA.2 compared to BA.1. Re-infection with BA.2 following infection with BA.1 has been documented; however, initial data from population-level re-infection studies suggest that infection with BA.1 provides strong protection against re-infection with BA.2, at least for the limited period for which data are available. As Omicron has the ability to cause so many infections over a short period of time, many more people are being hospitalized than at any other time in the pandemic.

### **WHO tracks two new sub-variants (BA.4 & BA.5)**

The WHO recently said that it was tracking two new Omicron sub-variants BA.4 and BA.5 to assess whether they are more infectious or dangerous [2]. The immune escape properties of these two new sub-variants are being studied by various clinical, epidemiological and immunological methods by leading researchers in South Africa, which was the first country to report Omicron. Oliveira and his team are conducting one of the world's strongest genomic surveillance programmes for SARS-CoV2. It is reported that there were several abnormal SARS-CoV2 genome sequences with notable mutations that encode its spike protein. By the first week of April, it was found that BA.4 and BA.5 sequences comprised around 50% of the roughly 500 genomes sequences in South Africa. Immune escape potential of these sub-variants is being studied by immunologists by exposing samples of BA.4 and BA.5 to blood drawn from people infected with COVID-19 and people who have been vaccinated.

### **Booster vaccine dose**

Boosters for COVID-19 vaccines may be required because the first dose can only unreliably activate the body's immune system, and the second provides consistent protection against COVID-19. Immunity is better three months after the Moderna vaccine and six months after Oxford shots, but this immunity lasts only for few months after the vaccination. Furthermore, since coronavirus is rapidly mutating into new variants like the Omicron, our immune cells may not identify the mutated virus, and thus, we may need a booster vaccine shot to tackle new strains [8, 11]. The children and younger students are not vaccinated yet in India as only very recently COVID-19 vaccination has been announced to be started for 15–18 years age group from January 3, 2022, so as to avoid Omicron infection to this younger category [10].

### **Omicron as a natural vaccine**

Some researchers have asserted that Omicron can provide natural vaccination while others have refuted this claim. Omicron may act as a vaccine because it allows a large number of people to effectively develop herd immunity against the Omicron, halting transmission in the same way that vaccination develops herd immunity [5]. This variant has the potential to enhance immunity in individuals without causing major sickness. Omicron is similar to live attenuated vaccines in certain ways as it causes milder infection and triggers a strong immune response against viruses. Immunity developing in vaccinated persons (infected with Omicron) can be paired with immunity against the previous variant to generate a threshold level of herd immunity, allowing 70–90% of people to be recovered from or vaccinated against COVID-19. Also, according to some scientists, considering Omicron as a natural vaccine is a perilous idea [5]. It creates complacency and is based more on pandemic fatigue and incapacity to do more than on current data and that Omicron is not a vaccine; no matter how light it may be, because this variant has resulted in deaths and hospital admissions worldwide.

### **Nasal Omicron vaccine booster**

Current vaccination modalities provides less protection against contracting and transmitting the Omicron variants compared with earlier variants, it still provides some protection, especially after the third or fourth booster dose. A recent research published in a reputed journal described an ultra-effective nasal vaccine booster that potently induced the extraordinary high-level of neutralizing antibody in pre-vaccinated mice [9]. This particular vaccine booster is composed of a recombinant receptor binding domain of SARS-CoV-2 spike (either wild-type or omicron) fused with a domain of SARS-CoV-2 nucleoprotein. In the absence of adjuvants, a single intranasal administration of the

booster significantly induced systemic and mucosal antibody responses in pre-vaccinated mice and also minimizes the chances of irritation or allergy to the mucosa. Most importantly, the single dose nasal vaccine booster (omicron version) potently enhanced the neutralizing activity against authentic SARS-CoV-2 omicron virus infection. However, these nasal protein boosters warrant further studies and clinical trials in humans before being successfully applied to human populations.

#### Aircraft wastewater sampling for new variants

A recent study detected the presence of Omicron variant in aircraft wastewater sample from a flight arriving in Northern Territory of Australia by using RT-qPCR assays per guidance from the WHO [1]. The sequencing of nasopharyngeal swab of one of the patients infected with SARS-CoV-2 resulted in the detection of Omicron VOC. It is difficult to identify all COVID-19 positive cases among arriving passengers by doing only pre-flight testing of clinical samples, therefore under these circumstances, post-flight testing of passengers may be beneficial when potentially more-infectious variants are predicted to be emerging globally, and quarantine measures may be necessary when new variants cause increase disease severity. Further studies are needed to identify other suitable sample matrices such as air sampling or surface swab sampling to determine whether these are more appropriate than wastewater.

#### Ukraine war and COVID-19

There is a well-established link between war and disease outbreaks extending back centuries. It challenges every public health program existing in the country. It limits the availability of medical care for those who might be seriously ill, and often fosters COVID-19 transmission when so many people are crowded into bomb shelter locations, trains and refugee processing facilities. Ukraine was struggling to control the pandemic even before the Russian invasion. Vaccination campaigns in Ukraine were much slower as compared to other neighbouring European countries [15]. Till the end of February 2022, only 35% of its population had been vaccinated. Since the war began, COVID testing has decreased as health care facilities have been destroyed and Russian attacks have cut off humanitarian aid routes. The millions of refugees who are crossing Ukrainian border and entering surrounding European countries will need treatment for their medical problems including COVID 19. These countries should be well prepared to handle the demands on their health systems as many European countries are already witnessing spurge in cases caused by Omicron sub-variant BA.2.

## CONCLUSION

As the whole world was advancing towards normalcy after three waves of the pandemic, COVID-19 cases are again beginning to rise owing to Omicron and its new sub-variants. The newly detected sub-variants of Omicron are more transmissible and have the potential for immune escape. Booster shots of the vaccine can provide some amount of protection from the new sub-variants. Research is being conducted on new nasal vaccine formulations that can effectively neutralize the new variants, however human trials of these vaccine candidates are still in nascent stage. Populations experiencing pandemic fatigue could possibly ignore reports of new outbreaks, relaxing preventative behaviours and leading to additional transmissions. We should realize the fact that pandemic is not yet over. We should not lower our guard and there is an urgent need to increase public communications to adhere to mask-wearing especially by vulnerable populations. At the individual level, people need to do self-assessment of risk and follow Covid-appropriate behaviour accordingly.

#### Conflict of interest

*The Authors declare no conflict of interest.*

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