CHAPTER 1

OMICRON: IS THE END OR A NEW BEGINNING?

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INTRODUCTION

Seen for the first time on November 9, 2021 in South Africa, the Omicron variant of the novel coronavirus causing COVID-19 rapidly spread all over the world and became the predominant variant. The Who announced Omicron variant as the variant of concern on November 21, 2021. Since that time, many countries implemented restrictions and travel bans to and from several African countries, while continuing vaccination programs in the meanwhile.

Unlike the Dalta variant which has 8 mutations, a total of 32 mutations occurred in the Omicron variant with most important ones being in the spike protein, through which the virus is attached to ACE2 to enter the body. Preliminary studies have compared Omicron with deltah variant and found that Omicron has the advantages of replication, escape protection by previous infections or vaccination and disease severity compared to the Delta variant.

It seems that the Omicron is confined to the upper respiratory tract and it has low effects on small airways of the lungs. This leads to less hospitalization, ICU stays and mortality. However, its rapid spread increases the burden on both health care staff and health related costs. This chapter begins with the emergence and spread of the Omicron variant and continues with epidemiology and clinical presentation. Respiratory symptoms are specifically addressed and the Omicron variant is compared with Delta variant. In addition, antibody resistance and vaccine efficiency issues are also discussed.

THE EMERGENCE AND SPREAD

The first known confirmed Omicron case was from a specimen collected on November 9, 2021. The World Health Organization (WHO) declared Omicron, a novel severe acute respiratory syndrome coronavirus variant (B.1.529) as a variant of concern (VOC) on November 26, 2021 (1). A virus is classified as VOC based on the evidence of an increase in transmissibility, significant reduction in

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neutralization provided by antibodies produced by previous infections or vaccination (2). According to this announcement made by the WHO in six languages, in recent weeks there has been a steep increase in infections, coinciding with the detection of the B.1.1.529 variant. Omicron harbors as high as 32 several mutations in the spike protein, which is the attachment site of the virus to the body and the primary target of both infections and vaccinations. The number of variations was only 5 in the Delta variant (3).

Upon the announcement by the WHO, many countries have enacted travel restrictions in order to prevent rapid spread of the Omicron variant. This global panic caused by the emergence of the new Omicron variant has prompted the scientific community to immediately investigate how much Omicron could undermine monoclonal antibodies and the existing vaccines. These attempts will of course take a few weeks to come out. Artificial Intelligence (AI) programs analyzing the existing big data to draw estimations have been effectively used to achieve this purpose. On the other hand, some governments immediately responded the emergence of Omicron with issuing bans against South Africa, which sequenced the Omicron for the first time, and some other African countries despite warning from the WHO against these bans (4). The WHO stated that by restricting travel from these areas, the economic status of these countries will be harmed, and in turn this will results in a decrease in their ability to combat the pandemic.

The COVID-19 Data Explorer on Our World in Data (5) shows an uneven global distribution of SARS-CoV-2 variants. Accordingly, some countries such as Hong Kong and Denmark have sequenced at least half of their cases for mutations, while most countries have sequenced zero cases, suggesting the presence of global blind spots for emergence of the Omicron. Remarkably, only 0.8% of the cases have been sequenced in South Africa (4). Increasing global spread of the new variants requires international collaboration and sharing of expertise and resources.

EPIDEMIOLOGY

The alarming increase in COVID-19 cases in South Africa due to the Omicron variant has raised questions that this variant has enhanced immune evasion and transmissibility. These increased immune evasion, transmissibility and escape from neutralizing antibodies are caused by a high number of mutations, especially those on the spike protein of the virus (6). Following the first cases in South Africa, the Omicron spread to nearby countries including Botswana, Zimbabwe, Swaziland, Mozambique and Namibia very quickly. Following travel restrictions from South Africa by many countries; Hong Kong, Israel, Belgium, Egypt, Sri

Lanka Malaysia and India reported new COVID-19 cases due to the Omicron variant (7). As of January 5, 2022, it has been reported by 76 countries. At the end of December 2021, Omicron accounted for the majority of newly diagnosed COVID-19 in the USA (8).

The emergence of Omicron in South Africa is mainly caused by its insufficient vaccination rate with only 24.6% of the population being fully vaccinated compared to the world rate of 42.7%. What is worse, the rest of Africa has much lower vaccination rates as low as <0.1% in the Democratic Republic of Congo (9).

Omicron has a high capacity of reinfection that may affect patients infected by COVID-19 previously. In addition, many Omicron patients were found to be young patients and even those at the school age (10). On the other hand, the Omicron variant is yet to be fully understood and researchers all over the world continue to conduct research in order to increase their understanding and insight to the Omicron and share data timely (2). The clinical characteristics and severity of infection with the Omicron will become better understood as new cases are identified and investigated.

CLINICAL PRESENTATION

Majority of early reports on the clinical features of Omicron are in the form of anecdotal statements. According to these reports, most patients infected with the Omicron are young adult patients with mild clinical symptoms that do not require hospital stay or critical care. Reinfections in some of these patients suggest the possibility of lesser protection against prior COVID-19 infection. As data accumulates from all around the world regarding high-risk patients subgroups, including unvaccinated, boosted and previously infected patients, clinical profile of Omicron will be gradually determined (11).

Omicron is known to infect younger people compared to the previous variants. Although signs and symptoms of Omicron are similar to those of the other variants, preliminary reports from various regions of the world have reported milder symptoms. In a study by Meo et al. from Saudi Arabia (12), the most common clinical symptom of the Omicron variant was reported as fatigue followed by body ache, headache, fever, generalized myalgia, malaise and muscle pain. Pulmonary characteristics include cough, scratchy throat and shortness of breath. Pneumonia may also be seen. Ekstrapulmonary symptoms include abdominal pain, nausea/vomiting and diarrhea (12). In a more recent study by Kim et al. with 40 Omicron patients from Korea (13), 52.5% of the patients were symptomatic and the most common presentation symptoms were reported in order of frequency as sore

throat, fever, headache, cough, sputum, runny nose, myalgia, fatigue and loss of taste and smell. The longest symptom duration was found as 5-10 days with runny nose followed by 7-9 days with sore throat and 5-8 days with cough. Pulmonary involvement was found only in 6 (15%) patients. In these patients, lung infiltrations were detected with chest X-rays or CT scans (13).

It has been reported that one of the mutations of the Omicron leads to "S gene target failure", suggesting that one of the many areas of the gene that are targeted by PCR testing will give a false negative result (14). However, the WHO reported that this new variant is still more or less being caught by PCR sufficiently (15).

RESPIRATORY SYMPTOMS OF OMICRON (2469)

Experimental and clinical studies have shown that Omicron has less impact on the lower respiratory tract, leading to milder disease. It has been shown in recent ex vivo studies that replication of the Omicron variant was higher in the human upper respiratory tract as compared to the small airways of the lungs (16). Consistently with the animal experiments, these findings support the opinion that disease caused by infection with the Omicron variant may be confined to the large airway (17).

It has been postulated that a feeble attack of the Omicron on the lungs could make it less dangerous. In an animal study, the concentration of the virus was 10 times lower in the animals injected with the Omicron variant compared to those infected with the other variants (18). Similarly, McMahan et al. and Bentley et al. also noted that Omicron was found at reduced levels in lung tissue compared to the other variants (19, 20). In addition, it was found that Omicron variants replicate more readily in the upper airways compared to the lungs. However, the immune response of the host plays an important role in the severity of disease.

OMICRON VS DELTA

The Omicron variant has 32 mutations with some of them being on the spike protein. The Delta variant has a total of 8 mutations. An illustration of the mutations of Delta and Omicron variants is presented in Figure 1.

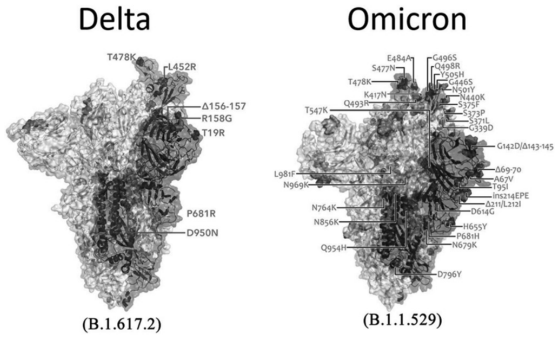

Figure 1. Mutations on the Delta and Omicron variants (image source: Modified from COVID-19 Genomics UK Consortium). COVID-19, coronavirus disease 2019

Accumulating evidence suggests that Omiceron is superior over the Delta variant in terms of replication. Omicron escapes from humoral immunity resulting from infections and/or vaccinations to a greater extent compared to the previous variants. On the other hand, Omicron seems to cause milder disease (Figure 2).

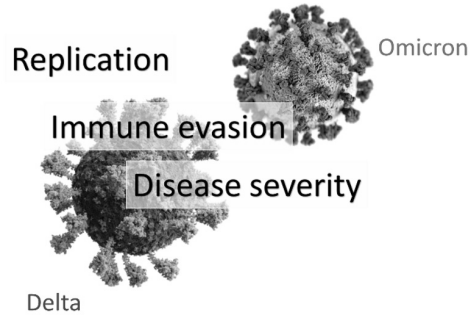

Figure 2. Differential characteristics of the Omicron variant compared to the Delta variant.

REPLICATION

The rate of replication is higher in the Omicron (World Health Organization. Enhancing Readiness for Omicron (B.1.1.529): Technical Brief and Priority Actions for Member States. December 10, 2021. https://www.who.int/publications/m/item/enhancing-readiness-for-omicron-(b.1.1.529)-technical-brief-and-priority-actions-for-member-states (Accessed on December 13, 2021). According to the United Kingdom Health Security Agency, the rise in cases due to Omicron was considerably higher than that caused by Delta (21). The replication advantage of Omicron may be its ability to evade immunity. In vitro studies have reported

that replication of Omicron preferably occurs in nasal epithelial cells and bronchial tissue (22).

IMMUNE EVASION

Escaping from humoral immunity, Omicron causes a higher risk of reinfection in patients previously infected by different variants. In a study from South Africa, reinfection/primary infection rate was reported to be higher with the Omicron at the time of the emergence compared to the Delta variant (0.25 vs 0.09) (23). In another case-control study from Qatar, a history of prior infection was correlated with an 85-90% lower risk of infection Delta, but only a 56% lower risk with Omicron (24). Rössler et al. reported that serum samples collected from vaccinated individuals neutralized the Omicron varian to a much lesser extent compared to d-the Delta variant (25).

DISEASE SEVERITY

The risk for developing severe disease has been reported as lower in the Omicron variant compared to the other variants of coronavirus (26, 27). In their study, Abdullah et al. from South Africa reported that the rate of in-hospital death (1 vs 4.5%), rate of stay in the ICU (4 vs 21%) and length of hospitalization (4 vs 8.8 days) were significantly lower during the Omicron surge compared to the Delta surge (28). An analysis study from England, reported the risk of hospital admissions with Omicron was approximately one-third of that of the Delta variant (29). The decreased risk for devere disease with Omicron may partially be due to immunity gained from prior infection or vaccination. However, lower viral levels of the lung tissue and milder clinical features suggests that the Omicron variant may cause milder disease by itself. Nevertheless, despite the risk for severe disease being lower in this variant, increased hospital presentations and excess burden on health care systems remain a big challenge.

In a study by Joseph et al. from the USA, data of 52297 cases with Omicron variant and 16982 cases with Delta variant were analyzed. Hospital admission occurred in 0.5% of the patients with Omicron and 1.3% cases with Delta variants. Zero cases with Omicron infection and 11 cases with Delta infection received mechanical ventilation during the follow-up period. The length of stay in hospital was lower by 69.6% in patients with the Omicron variant (30). In the same study, Omicron variant infections were associated with 52%, 53%, 74% and 91% reduction in hospitalization, symptomatic hospitalization, ICU admission and mortality, respectively.

INFECTIVITY AND TRANSMISSIBILITY

Infectivity

The infectivity of the novel coronavirus is mainly determined by the binding affinity of receptor-binding domain (RBD) and ACE2 complex. angiotensin-converting enzyme 2. However, the furin cleavage site also plays an important role in infectivity (31). Having three mutations at the furin cleavage and 15 mutations on the RBD suggests that infectivity of the coronavirus has significantly increased by the Omicron. Mutations in the virus to strengthen its ACE-RBD binding affinity or escape from antibody protection enhance its evolutionary advantages at the RBD (32). In the Omicron variant, multiple RBD mutations enhance the effective infection pathway. The mutation of a hydrophilic amino acid to a hydrophobic amino acid might alter the interaction between human ACE2 and RBD.

The percentage of Omicron infectivity reached approximately 90% in 25 days in South Africa (33). The early doubling time was calculated as 1.2 days for the Omicron, and 1.5 days for the Delta variant (34). Each variant has been subjected to a linear regression analysis to compare with the wild type. As a result, the Gamma variant had similar infectivity rates to the wild type and the Beta variant was less infectious, while the Delta variant's infectivity was 2 folds higher compared to the wild type. Infection rates were four times higher in Omicron variant thani n the wild type and twice higher than in the Delta (34). These results indicate that spike sequence affects infectivity and the Omicron variant exhibits more effective ACE2-mediated infection compared to the wild type and other variants.

Transmissibility

There is still no sufficent data on the infection rate of Omicron in order to analyze and estimate its transmissibility. The Omicron variant carries some spike mutations that could be involved in increased transmissibility. This was supported by the rapid replacement of the Delta variant by Omicron as the dominant variant first in South Africa, and then in the rest of the world. There are several mutations in the Omicron that overlap with those in the alpha, beta, gamma and delta variants of concern (VOCs) such as 69–70del, N501Y, N655Y, N679K, T95I, K417N, T478K, G142D/143–145del and P681H (34). Most of the identified mutations in the Omicron variant accumulate in the spike, facilitating transmission. These mutations are known to increase transmissibility, binding affinity and escape from antibody protection (35). Unfortunately, the effects of most of the Omicron mutations are not known at the time of this chapter. Therefore, the impact of Omicron on transmissibility is a concern.

ANTIBODY RESISTANCE

A large number of mutations identified in the Omicron variant, including multiple mutations to the receptor binding domain (RBD) of the spike protein, are associated with reduced antibody response. Accumulating evidence suggests an antibody escape of the Omicron variant in the vaccinated people, although the booster doses increased the antibody titers (36).

The resistance to various antibodies used for the treatment of COVID-19 suggests that spikes of the Omicron variant can also escape from antibodies induced by infections or vaccination. In a study investigating whether the Omicron spike can be inhibited by soluble ACE2, which is under investigation for the treatment of COVID-19. Soluble ACE2 inhibited virus entry driven by the Omicron variant. In the same study, the Omicron variant was demonstrated to be fully resistant against neutralization by several antibodies used for the treatment of COVID-19, including bamlanivimab, etesevimab, and imdevimab, and largely resistant against casirivimab (37). Similarly, Wilhelm et al. reported that the currently used monoclonal antibodies casirivimab and imdevimab failed to neutralize the Omicron variant (36). Liu et al. reported that sera collected from convalescent patients and vaccines showed significant reduction in neutralizing activity against the Omicron variant (38). These findings support the emerging clinical data on the Omicron variant showing a high rate of reinfections (23).

VACCINE BREAKTHROUGH

Immune escape potential of the Omicron variant was predicted from the genomic data as subsequently supported by the increased incidence of reinfections and breakthrough infections (23). This situation has resulted in the intensification of vaccine programs, including booster doses in an attempt to overcome rapid spread of this new variant. With the spreading of the virus from South Africa where it was seen for the first time, to neighboring countries and subsequently all over the world, rate of reinfections and vaccine breakthrough infections began to rise. Kuhlmann et al. reported that mild-to-moderate course of the disease suggests that full vaccination followed by a booster dose protects against severe disease caused byu Omicron. But long term sequels of the COVID-19 can not be ruled out. The authors concluded that there is a need for updated vaccines to provide better protection against the Omicron variant and underlined that non-pharmacological measures such as mask, hygiene and social distancing must be maintained (39).

CONCLUSION

The Omicron variant of the novel coronavirus seems to replicate more rapidly, escape from immunity and cause milder disease compared to the other variants. Studies in the literature on the Omicron variants are yet very limited with many of them in the preprint stage. However, with the limited data at hand, at least rapid replication and milder disease due to the Omicron are almost definitely well-established. In addition, it is now almost certainly known that the effect of this variant on the lungs is limited. As data accumulate in the relevant literature, more detailed information could be obtained about the impact of this (new, but perhaps not the last) variant of the virus.

Keywords: COVID-19, coronavirus, delta variant, omicron variant, ACE2, infectivity, transmissibility, antibody, immunization, neutralization, vaccine, vaccination, vaccination breakthrough, variant, South Africa, WHO, spike, spike protein, affinity, antibody resistance

REFERENCES

1. (WHO) 2021. Classification of Omicron. https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern (Access Date: 29/01/2022).
2. Musa SS, Gyeltshen D, Manirambona E, et al. The new COVID-19 omicron variant: Africa must watch its spread! Clin Epidemiol Glob Health. 2022 Jan-Feb;13:100961. doi: 10.1016/j.cegh.2022.100961. Epub 2022 Jan 13.
3. Kumar S, Thambiraja TS, Karuppanan K, et al. Omicron and Delta variant of SARS-CoV-2: A comparative computational study of spike protein. J Med Virol. 2021 Dec 15. doi: 10.1002/jmv.27526. Epub ahead of print.
4. The Lancet Infectious Diseases. Emerging SARS-CoV-2 variants: shooting the messenger. Lancet Infect Dis. 2022 Jan;22(1):1. doi: 10.1016/S1473-3099(21)00770-2. Epub 2021 Dec 9.
5. (Our World in Data) 2021. The COVID-19 Data Explorer. https://ourworldindata.org/search?q=coronavirus+data (Access Date: 30/01/2022).
6. Kannan S, Shaik Syed Ali P, et al. Omicron (B.1.1.529) – variant of concern – molecular profile and epidemiology: a mini review. Eur Rev Med Pharmacol Sci. 2021 Dec;25(24):8019-8022.
7. (Omicron). 2021. Omicron. https://www.cdc.gov/media/releases/2021/s1126-B11-529-omicron.html (Access Date: 29/01/2022)
8. (Covid Data Tracker) 2021. https://covid.cdc.gov/covid-data-tracker/#variant-proportions (Access Date: 30/01/2022).
9. Callaway E. Heavily mutated Omicron variantputs scientists on alert. Nature.2021;600(7887):21. doi:10.1038/d41586-021-03552-w
10. Nealon J, Cowling BJ. Omicron severity: milder but not mild. Lancet. 2022 Jan 19;399(10323):412–3. doi: 10.1016/S0140-6736(22)00056-3. Epub ahead of print.
11. Ingraham NE, Ingbar DH. The omicron variant of SARS-CoV-2: Understanding the known and living with unknowns. Clin Transl Med. 2021 Dec;11(12):e685. doi: 10.1002/ctm2.685.
12. Meo SA, Meo AS, Al-Jassir FF, et al. Omicron SARS-CoV-2 new variant: global prevalence and biological and clinical characteristics. Eur Rev Med Pharmacol Sci. 2021 Dec;25(24):8012-8018.
13. Kim MK, Lee B, Choi YY, et al. Clinical Characteristics of 40 Patients Infected With the SARS-CoV-2 Omicron Variant in Korea. J Korean Med Sci. 2022 Jan 17;37(3):e31.

14. Torjesen I. Covid-19: Omicron may be more transmissible than other variants and partly resistant to existing vaccines, scientists fear. BMJ. 2021 Nov 29;375:n2943.
15. (WHO) 2021. Update on Omicron. https://www.who.int/news/item/28-11-2021-update-on-omicron (Access Date: 29/01/2022).
16. Chan MCW, Hui KPY, Ho J, et al. SARS-CoV-2 Omicron variant replication in human respiratory tract ex vivo. ResearchSquare 2022; doi: 10.21203/rs.3.rs-1189219/v1.
17. Garcia-Beltran WF, St Denis KJ, Hoelzemer A, et al. mRNA-based COVID-19 vaccine boosters induce neutralizing immunity against SARS-CoV-2 Omicron variant. medRxiv [Preprint]. 2021 Dec 14:2021.12.14.21267755. doi: 10.1101/2021.12.14.21267755.
18. Diamond M, Halfmann P, Maemura T, et al. The SARS-CoV-2 B.1.1.529 Omicron virus causes attenuated infection and disease in mice and hamsters. Res Sq [Preprint]. 2021 Dec 29:rs.3.rs-1211792. doi: 10.21203/rs.3.rs-1211792/v1.
19. McMahan K, Giffin V, Tostanoski LH, et al. Reduced Pathogenicity of the SARS-CoV-2 Omicron Variant in Hamsters. BioRxiv [Preprint] doi: https://doi.org/10.1101/2022.01.02.474743
20. Bentley EG, Kirby A, Sharma P, et al. SARS-CoV-2 Omicron-B.1.1.529 Variant leads to less severe disease than Pango B and Delta variants strains in a mouse model of severe COVID-19. BioRxiv [Preprint] doi: https://doi.org/10.1101/2021.12.26.474085
21. SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 31. December 10, 2021.https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1040076/Technical_Briefing_31.pdf (Access Date: 29/01/2022).
22. Peacock RP, Brown JC, Zhou J, et al. The SARS-CoV-2 variant, Omicron, shows rapid replication in human primary nasal epithelial cultures and efficiently uses the endosomal route of entry. Unpublished. https://www.biorxiv.org/content/10.1101/2021.12.31.474653v1.full.pdf (Access Date: 30/01/2022).
23. Pulliam JRC, van Schalkwyk C, Govender N, et al. Increased risk of SARS-CoV-2 reinfection associated with emergence of the Omicron variant in South Africa 2021-12-01. Unpublished. https://www.medrxiv.org/content/10.1101/2021.11.11.21266068v2.full.pdf (Access Date: 29/01/2022).
24. Altarawneh H, Chemaitelly H, Tang P, et al. Protection afforded by prior infection against SARS-CoV-2 reinfection with the Omicron variant. Unpublished. https://www.medrxiv.org/content/10.1101/2022.01.05.22268782v1.full.pdf (Access Date: 29/01/2022).
25. Rössler A, Riepler L, Bante D, et al. SARS-CoV-2 Omicron Variant Neutralization in Serum from Vaccinated and Convalescent Persons. N Engl J Med. 2022 Jan 12:NEJMc2119236. doi: 10.1056/NEJMc2119236.
26. Maslo C, Friedland R, Toubkin M, et al. Characteristics and Outcomes of Hospitalized Patients in South Africa During the COVID-19 Omicron Wave Compared With Previous Waves. JAMA. 2021 Dec 30:e2124868.
27. Wolter N, Jassat W, Walaza S, et al. Early assessment of the clinical severity of the SARS-CoV-2 omicron variant in South Africa: a data linkage study. Lancet. 2022 Jan 19;399(10323):437–46. doi: 10.1016/S0140-6736(22)00017-4. Epub ahead of print.
28. Abdullah F, Myers J, Basu D, et al. Decreased severity of disease during the first global omicron variant covid-19 outbreak in a large hospital in tshwane, south africa. Int J Infect Dis. 2021 Dec 28;116:38-42. doi: 10.1016/j.ijid.2021.12.357.
29. (Omicron Severity Update) 2021. Technical Briefing. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1044481/Technical-Briefing-31-Dec-2021-Omicron_severity_update.pdf (Access Date: 30/01/2022).
30. Lewnard JA, Hong VX, Patel MM, et al. Clinical outcomes among patients infected with Omicron (B.1.1.529) SARS-CoV-2 variant in southern California. 2022 Jan 11. medRxiv preprint doi: https://doi.org/10.1101/2022.01.11.22269045
31. Zhang L, Mann M, Syed Z, et al. Furin cleavage of the sars-cov-2 spike is modulated by o-glycosylation. Proceedings of the National Academy of Science of the United States of America,

118(47):e2109905118, 2021.
32. Rui Wang, Jiahui Chen, Yuta Hozumi, et al. Emerging vaccinebreakthrough SARS-CoV-2 variants. arXiv preprint arXiv:2103.08023, 2021.
33. He X, Hong W, Pan X, et al. Omicron variant: Characteristics and prevention. MedComm (2020). 2021 Dec 16;2(4):838–45. doi: 10.1002/mco2.110. Epub ahead of print.
34. Karim SSA, Karim QA. Omicron SARS-CoV-2 variant: a new chapter in the COVID-19 pandemic. Lancet. 2021;398(10317):2126-2128.
35. Harvey WT, Carabelli AM, Jackson B, et al. SARS-CoV-2 variants, spike mutations and immune escape. Nat Rev Microbiol 2021; 19: 409–24.
36. Wilhelm A, Widera M, Grikscheit K, et al. Reduced Neutralization of SARS-CoV-2 Omicron Variant by Vaccine Sera and monoclonal antibodies. 2021; medRxiv preprint doi: https://doi.org/10.1101/2021.12.07.21267432
37. Hoffmann M, Krüger N, Schulz S, et al. The Omicron variant is highly resistant against antibody-mediated neutralization: Implications for control of the COVID-19 pandemic. Cell. 2021 Dec 24:S0092-8674(21)01495-1. doi: 10.1016/j.cell.2021.12.032.
38. Liu L, Iketani S, Guo Y, et al. Striking Antibody Evasion Manifested by the Omicron Variant of SARS-CoV-2. Nature. 2021 Dec 23. doi: 10.1038/s41586-021-04388-0. Epub ahead of print. PMID: 35016198.
39. Kuhlmann C, Mayer CK, Claassen M, Maponga T, Burgers WA, Keeton R, Riou C, Sutherland AD, Suliman T, Shaw ML, Preiser W. Breakthrough infections with SARS-CoV-2 omicron despite mRNA vaccine booster dose. Lancet. 2022 Jan 18:S0140-6736(22)00090-3. doi: 10.1016/S0140-6736(22)00090-3. Epub ahead of print.