Omicron SARS-CoV-2 Variant of Concern: A Review on its Transmissibility, Immune Evasion, Reinfection, and Severity

Md Mohsin (✉ mmohsin@isrt.ac.bd)

University of Dhaka <https://orcid.org/0000-0001-7257-6015>

Sultan Mahmud

University of Dhaka <https://orcid.org/0000-0003-0757-7630>

Short Report

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Abstract

Background: Omicron, the new Covid-19 variant, has already become dominant in many countries and is spreading at an unprecedented speed. The objective of this study was to review the existing literature on Omicron's transmissibility, immune evasion, reinfection, and severity.

Method: A literature search was performed in "PubMed", "Web of Science", "Scopus", "ScienceDirect", "Google Scholar", "medRxiv", and "bioRxiv". Data were extracted from articles that reported at least one of transmissibility, immune evasion, reinfection, and severity related to Omicron.

Findings: We found that Omicron spreads faster than any other previous variants. This higher transmissibility can be ascribed to its more extraordinary ability to evade immunity developed by both vaccinations and previous infections. However, we found that infections by Omicron are significantly less severe compared to infections by Delta and other previous variants. We observed a significantly lower incidence of hospitalization, intensive care unit, and mechanical ventilator use, a shorter median hospital stay, and lower fatality rates in Omicron infections than Delta and other variants.

Conclusion: Omicron might be less severe than other VOCs. However, its immune evasiveness and faster spread pose an enormous threat to the global healthcare system.

Introduction

WHO identified B.1.1.529 as a variant of concern (VOC) on 26 November 2021, following advice from the WHO's Technical Advisory Group on Virus Evolution [1]. The variant that was first detected in South Africa was named Omicron. Omicron is a highly divergent variant with a large number of mutations, including 26–32 mutations in the spike protein, several of which are likely connected with humoral immune evasion and increased transmissibility [2]. For a variety of reasons, the total risk associated with Omicron remains exceptionally high. To begin, the global danger of COVID-19 is quite high overall. Second, current data indicate that Omicron outperforms other variants (Delta) in terms of growth, resulting in the rapid community spread [2]. The quick increase in cases may result in an increase in hospitalizations, place a strain on health care systems, and result in severe morbidity, particularly among vulnerable populations.

Rapid transmission of the Omicron variant generated the fourth wave of SARS-CoV-2 infections in South Africa, with daily diagnosed illnesses exceeding totals recorded in the country during all preceding periods [3]. As of January 2022, the Omicron variant had spread widely around the world, including the United States, where the Omicron variant was believed to be responsible for 95% of all SARS-CoV-2 illnesses detected during the week ending January 1, 2022 [4].

The overall threat posed by Omicron is highly dependent on four critical factors: (i) how transmissible the variant is; (ii) how well vaccines and prior infection protect against infection, transmission, clinical disease, and death; (iii) how virulent the variant is in comparison to other variants; and (iv) how well

populations recognize these dynamics, perceive risk, and adhere to control measures, including public health and social measures[2].

To find answers to the above questions, extensive research is required. As of now, very few studies have been conducted on transmissibility, immune evasion, reinfection, and severity of the Omicron variant. This study aims to review the existing literature on the topic.

Method

A literature search was performed in "PubMed", "Web of Science", "Scopus", "ScienceDirect", "Google Scholar", "medRxiv", and "bioRxiv" using the following key words: "SARS-CoV-2", "coronavirus", "COVID-19", "Omicron", "Transmissibility", "Immune Evasion", "Reinfection", and "Severity" to find articles published in 2021 and 2022. We checked the reference lists of all studies identified by the above methods. Data were extracted from articles that reported at least one of Omicron's transmissibility, immune evasion, reinfection, and severity.

Review Findings

Transmissibility

This is not easy to quantify how contagious Omicron is. One of the world's leading infectious disease experts, Dr. Antonio Fauci, says, "Omicron, with its extraordinary, unprecedented degree of efficiency of transmissibility, will ultimately find just about everybody" [5]. On January 10, 2022, the U.S reported a record 1.35 million new coronavirus infections, almost five times higher than the peak points of all other waves [6]. Almost similar patterns were observed in many countries in Europe. Such an unprecedented increase in cases might be attributed to the latest Covid variant Omicron, either due to its greater transmissibility or other factors.

In Norway, a study found that among 117 participants in a party, 74% got infected with Omicron. In the party, there was one participant from South Africa (the country where Omicron was first detected and later spread) [7]. Among the partygoers, about 96% were fully vaccinated. The study concludes that Omicron is highly contagious even among vaccinated people.

Researchers in Denmark analyzed the transmission of Omicron and Delta variants among household members (11,937 households) and determined that Omicron was approximately 2.6 times (95%-CI: 2.34-2.90) to 3.7 times (95%-CI: 2.65-5.05) more infectious than the Delta variant among vaccinated and boosted individuals [8]. However, among unvaccinated people, Omicron was only 1.17 times (95%-CI: 0.99-1.38) more infectious than the Delta, which was statistically insignificant.

Immune Evasion and Reinfection

The most significant matter about the new variant is whether it can evade immunity developed by vaccinations and previous infections. Several studies have been found in the literature that inspected the

evasion ability of Omicron compared to other variants. Between November 30, 2021 and January 1, 2022, one study in the United States investigated clinical and epidemiologic data from cases testing positive for SARS-CoV-2 infection inside the Kaiser Permanente Southern California healthcare system. The study included 52,297 cases of SGTF (Omicron) infection and 16,982 cases of non-SGTF (Delta [B.1.617.2]) infection [9]. The adjusted odds of having previously been infected with SARS-CoV-2 were 4.45 (95% CI: 3.24-6.12) fold greater in individuals with Omicron variant infections than in cases with Delta variant infections. Likewise, the adjusted odds of receiving any vaccine series (1, 2, or 3 doses of BNT162b2/mRNA-1973, or Ad.26.COV2.S with or without a booster dose of any vaccine) were significantly greater (2-6 times) in cases with Omicron variant infections than in cases with Delta variant infections.

Lyngse and his colleagues, in a large-scale study in Denmark, found that among vaccinated people, Omicron was 2.6-3.7 times more infectious than the Delta variant. However, they found no significant difference in transmissibility for the two variants among unvaccinated people [8]. They summarize that the Omicron VOC's rapid spread can be attributed to its immune evasiveness, rather than an inherent increase in fundamental transmissibility.

Pullium et al. conducted a study in South Africa with routine surveillance data of 2,796,982 persons who tested positive for SARS-CoV-2 in a laboratory at least 90 days prior to 27 November 2021 to examine reinfection risk. The analysis found that, in contrast to the Beta and Delta, the Omicron variant of SARS-CoV-2 demonstrates substantial population-level evidence for evasion of immunity from prior infection [10].

Reduced neutralization of the Omicron variant has been seen in investigations using plasma specimens from persons who received the entire (two- or three-dose) mRNA vaccination series [11] and from patients who had previously been infected with SARS-CoV-2 [12]. Besides, several early observational studies revealed that COVID-19 vaccinations were substantially less efficacious in preventing Omicron variant infection [13]–[15].

Researchers from the University of Edinburgh, UK, found that the Omicron variant had a 10 times greater risk of reinfection than the Delta variant [16]. Also, Brandal et al. demonstrate that Omicron has a more remarkable ability to evade immunity developed by vaccines. They showed 74% of people got infected in a party where 96% of party participants were fully vaccinated for SARS-CoV-2 [7].

Severity

The severity for Covid-19 is measured through the requirement of hospital admission, length of hospital stay, the requirement of ventilators, the time required to recover, mortality, etc. There is some unanimity regarding the severity of the new Omicron variant per the existing literature we have found. The Southern California study that included 52,297 cases of SGTF (Omicron) infection and 16,982 non-SGTF (Delta) infection reported a significantly decreased risk of severe clinical outcomes and shorter lengths of stay in the hospital [9]. Hospitalizations of Omicron and Delta variant infections occurred in 235 (0.5%) and 222

(1.3%) cases, respectively. Throughout the follow-up period, zero instances of Omicron variant infection required mechanical ventilation, compared to 11 cases of Delta variant infection ($p < 0.001$). In addition, the median length of stay in the hospital was 3.4 (2.8-4.1) days shorter for hospitalized individuals with Omicron variant infections than for hospitalized cases with Delta variant infections, indicating a 70% (95% CI: 64.0-74.5%) reduction in hospital length of stay.

Researchers in South Africa assessed the clinical severity of the SARS-CoV-2 Omicron variant using nationwide data. After adjusting for confounding variables, they found that persons with Omicron (SGTF) infection had an 80% lower risk of hospitalization than those without Omicron infection (aOR 0.2, 95% CI: 0.1-0.3) [3]. Moreover, compared to earlier Delta infections, after adjusting for risk factors for severe disease, those infected with Omicron had a 70% decreased risk of severe disease (aOR 0.3, 95% CI: 0.2-0.5).

The study in Scotland conducted by researchers from the University of Edinburgh indicates that when compared to Delta, Omicron is related with a two-thirds reduction in the probability of COVID-19 hospitalization [16]. They also found that while vaccination provides the best protection against Delta, the third/booster dose provides significant protection against the risk of symptomatic COVID-19 infection in Omicron when compared to ≥ 25 weeks after the second vaccine dose [16].

Clinical characteristics of 466 patients infected with Omicron variant admitted to a large hospital in Tshwane, South Africa, were compared to 3962 hospital admissions from earlier waves. Deaths and ICU admissions were 4.5% vs 21.3% ($p < 0.0001$) and 1% vs 4.3% ($p < 0.0001$) for the Omicron and preceding waves, respectively; length of stay was 4.0 days vs 8.8 days [17].

A study conducted in England observed a reduction in the risk of hospitalization for Omicron infections when compared to Delta infections during the study period (Dec 1 to Dec 14, 2021). The magnitude of the reduction varied according to the inclusion criteria for cases and hospitalization, ranging from 20–25% when any hospitalization is used as the endpoint to 40–45% when hospitalizations lasting 1 day or more is used [18].

A retrospective cohort study (Omicron cohort and Delta cohort) was carried out using electronic health record (EHR) data from 577,938 first-time SARS-CoV-2 infection patients in the United States [19]. After adjustment for demographics, socioeconomic determinants of health, comorbidities, medications, and immunization status, the 3-day risks in the Emergent Omicron cohort were consistently less than half of those in the Delta cohort: Emergency Department (ED) visit: 4.55% vs. 15.22% (risk ratio or RR: 0.30, 95% CI: 0.28-0.33); hospitalization: 1.75% vs. 3.95% (RR: 0.44, 95% CI: 0.38-0.52); ICU admission: 0.26% vs. 0.78% (RR: 0.33, 95% CI: 0.23-0.48); mechanical ventilation: 0.07% vs. 0.43% (RR: 0.16, 95% CI: 0.08-0.32) [19].

Discussion

Amidst an unprecedented surge in Covid-19 cases globally, presumably due to the emergence of the new variant Omicron, we conducted a rapid review of the existing knowledge on the variant's transmissibility, immune evasion, reinfection, and severity. We found that the Omicron variant can spread faster than any other previous variants. However, researchers argue that the faster transmission might happen due to Omicron's strong ability to evade immune response induced by vaccinations and previous infections [8]. In this rapid review study, we found that Omicron has several times higher odds of infecting fully vaccinated and previously infected people compared to Delta and other variants, and this is consistent among other studies [7], [9], [11], [12], [16]. One study also found no significant difference in the risk of infections among unvaccinated people when they compared the Omicron variant with Delta [8].

Although Omicron showed a greater ability to evade immunity developed by vaccinations and previous infections, we found significantly reduced severity in Omicron infections. Almost all the studies we reviewed consistently reported a considerably lower risk of requiring hospital admission, ICU, and mechanical ventilators, shorter median stay at the hospital, and lower mortality rates among Omicron infections compared to Delta and other variants [3], [9], [16]–[19]. Also, we found that though Omicron has a greater ability to escape immunity developed by vaccines, booster/third doses are still significantly effective in protecting from symptomatic Covid infections [16].

A team of researchers in Hong Kong compared the replication competency and cellular tropism of all Covid variants in ex vivo explant cultures of human bronchus and lung. They demonstrated that Omicron replicated more rapidly in the bronchus than any other SARS-CoV-2 strain but less efficiently in the lung parenchyma [20]. This finding might be a probable reason for reduced severity in Omicron infections. Identical findings were found in an animal trial as well [21].

This timely review study accumulates available information on Omicron, the new emerging variant of Covid-19. It summarizes quantitative data on popular questions on Omicron: transmissibility, immune evasion, reinfection, and severity. However, there are some limitations of the study. There was a scarcity of literature on the new variant of Covid-19. All the studies our data based on are from only Europe, America, and South Africa. Importantly, most of the studies cited in this review are not yet peer-reviewed.

Our review concludes that Covid-19 infections associated with the Omicron variant are less severe than other variants of concern. However, findings of Omicron variant infections being more transmissible and immune evasion following prior infection and vaccination are worrying [9]. The rapid spread of the Omicron variant over a short time has resulted in extraordinary COVID-19 outbreaks in some parts of the world. Even though Omicron is less severe than non-Omicron variants, due to high infection rates and immunity escape, Omicron might overburden healthcare systems worldwide. The usual prevention methods such as vaccination, masking, and suitable infection mitigation strategies are highly recommended for curtailing transmission, reducing morbidity and death, and easing the load on health systems across the world. However, the findings of this study should be interpreted with caution because of the lack of peer-reviewed content the study is based on.

Declarations

Author Contributions

MM initiated and designed the study. Also, MM extracted data, wrote, proofread, and prepared the manuscript. On the other hand, SM conceptualized the study, searched the literature, screened relevant articles, and extracted data. Besides, SM wrote, proofread, and edited the manuscript.

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