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Omicron Threat or Boon to Global Health Systemic Review

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ABSTRACT

With a rising number of coronavirus Omicron cases reported across the whole world, starting a third wave of the pandemic in India, the chances are high that it will soon replace Delta as dominant global variant. The trend was already visible in the U.S. where Omicron has taken over Delta as the dominant strain. Omicron is nearly four to five times more infectious than Delta. That is because of mutations in the spike protein which make it easier for the cells to be attacked. Omicron is spreading with faster pace with very little consequences, except for the elderly population and those with comorbidities. Omicron will take a big toll on the vulnerable population with comorbid diseases. Meanwhile, it is a burden as it is causing devastating infections across the world, the World Health Organization has warned that Omicron should not be dismissed as "mild" variant. Increased transmission may lead to more hospitalizations which can lead to increase strain on frontline workers and health care systems and can result in more deaths. While people who recover from coronavirus disease 2019 may develop some natural immunity to the virus, how well the individual is protected from future genetic mutation of coronavirus is still a big question. The definitive evidence for increased remission and immune evasion and vaccine effectiveness is still awaited. This article will highlight few aspect of Omicron including increased transmission, immune evasion, hospitalization, mortality, vaccine effectiveness, and therapeutic drugs effective against the disease.

Keywords: Hospitalization, Immune evasion, Natural immunity, Omicron

INTRODUCTION

The current global epidemiology of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is characterized by the predominance of the Omicron variant on a global scale, rapid decline in the prevalence of the Delta variant, and low-level circulation of Alpha, Beta, and Gamma variant. Omicron cases are increasingly being reported from countries outside of South Africa including the U.S., Europe, and India.

OMICRON: AN OVERVIEW

On November 26, 2021, the World Health Organization (WHO) designated the variant B.1.1.529 as variant of concern (VOC), following advice from the WHO's Technical Advisory Group on Virus Evolution. The variant was given the name Omicron. Omicron is a highly divergent variant with a high number of mutations, including 26 to 32 mutations in the spike protein, some of which are associated with humoral immune escape potential and higher transmission. The Omicron variant comprises four lineages including B.1.1.529, BA.1, BA.2, and BA.3.[1]

The Omicron variant of coronavirus disease 2019 (COVID-19) has been called a VOC by WHO based on the evidence that it has several mutations that may have an impact on how it behaves. There is consistent evidence that Omicron is spreading significantly faster than the Delta variant

in countries with documented community transmission, with a doubling time of 2 to 3 days.[2]

Omicron has a substantial growth advantage over Delta, and it is rapidly replacing Delta globally. There is now significant evidence that immune evasion contributes to the rapid spread of Omicron. While the BA.1 lineage has previously been the most dominant, recent trends from India, South Africa, the United Kingdom, and Denmark suggest that BA.2 is increasing in proportion. Drivers of transmission and other properties of BA.2 are under investigation but remain unclear to date.[3]

OMICRON SPREAD OF INFECTION

As of January 20, 2022, the Omicron variant has been identified in 171 countries. The variant has rapidly outpaced Delta in most countries, driving an upsurge of cases in all regions. During week 2, the South-East Asia and the Eastern Mediterranean regions reported the highest increases in case incidence of 145 and 68%, respectively. The large increase in the South-East Asia region is mainly driven by the increase in the number of cases in India which reported 1,594,160 new cases compared with 638,872 cases the previous week (a 150% increase). In the Eastern Mediterranean region, the highest numbers of new cases were reported from Morocco (46,104 vs. 31,701 new cases, a 45% increase), Lebanon (45,231 vs. 38,112 new cases, a 19% increase), and Tunisia (39,487 vs. 13,416 new cases, a 194% increase).[3]

OMICRON RATE OF TRANSMISSION

Experimental evidences are suggestive of 70 times faster replication of Omicron in human bronchus while 10 times slower in human lung tissue that probably results in low disease severity. Despite presenting low disease severity, its higher transmissibility might present a threat for comorbid patients.[4]

OMICRON DIAGNOSIS

Polymerase chain reaction (PCR) tests that include multiple gene targets, as recommended by the WHO, are unlikely to be significantly affected and should continue to be used to detect SARS-CoV-2 infection, including the Omicron variant.[3] The Indian Council of Medical Research has approved a testing kit for detection of Omicron variant of the SARS-CoV-2 coronavirus. The kit will be used to confirm Omicron in patients with its S-Gene Target Failure (SGTF) strategy.[5] Suspected and probable cases of Omicron infection should be confirmed by gene sequencing. Both targeted sequencing of the spike gene (using Sanger sequencing or next-generation sequencing) or whole-genome sequencing are appropriate to confirm the presence of Omicron.[3]

Reinfection and transmission

More than 90% of newly sequenced infections in South Africa now involve the Omicron variant, and has displaced Delta. Omicron also appears more capable than Delta of penetrating the immune defenses of the previously infected. In the third (Delta) wave, the previously infected ran only 40% as much risk as the never infected. But in the current wave, new cases are 73% as common among the previously infected as among the never infected. The protection against severe symptoms requiring hospital admission has stood up better, at 70% in the current wave compared with 93% in the last.[6]

A recent U.K. study suggests rapid growth of the frequency of the Omicron variant relative to Delta, with the exponential growth rate of its frequency estimated to be 0.34/day (95% confidence interval [CI]: 0.33–0.35) (2.0-day doubling time) over the study period from both SGTF and genotype data. The distribution of Omicron by age, region, and ethnicity currently differs markedly from Delta, with 18- to 29-year-olds, residents in the London region, and those of African ethnicity having significantly higher rates of infection with Omicron relative to Delta. There is a strong evidence of immune evasion, both from natural infection, where the risk of reinfection is 5.41 (95% CI: 4.87–6.00)-fold higher for Omicron than for Delta, and from vaccine-induced protection.[7]

A South African study at Centre for Respiratory Diseases and Meningitis, National Institute for Communicable Diseases (NICD) of the National Health Laboratory Service, Johannesburg, reveals that proportion of SGTF infections increased from 3% in early October (week 39) to 98% in early December (week 48).[8]

The effectiveness of previous infection in preventing reinfection was estimated to be 90.2% (95% CI: 60.2–97.6) against the Alpha variant, 85.7% (95% CI: 75.8–91.7) against the Beta variant, 92.0% (95% CI: 87.9–94.7) against the Delta variant, and 56.0% (95% CI: 50.6–60.9) against the Omicron variant.[9]

Hospitalization and mortality

This South African study by Wolter et al reveals that among 1,142 hospitalized individuals, 1,037 (90·8%) had accumulated an in-hospital outcome by December 21, 2021. After controlling for factors associated with severe disease, individuals with SGTF infections diagnosed between October 1 and November 30, 2021, had a significantly lower odds of severe disease than did those with Delta variant infections diagnosed between April 1 and November 9, 2021 (adjusted odds ratio [aOR] 0.3, 95% CI: 0.2–0.5). Individuals with SGTF versus non-SGTF infections had an 80% lower odds

of being admitted to hospital. When compared with Delta variant infections, SGTF (SARS-CoV-2 Omicron variant using SGTF) infections were associated with a 70% lower odds of severe disease. The odds of severe disease varied geographically and was higher among individuals aged ≥ 60 years (aOR 11.5, 95% CI: 2.8–47.0), compared with individuals aged 19 to 24 years.[8]

The U.K. study also reveals hospitalization and asymptomatic infection indicators were not significantly associated with Omicron infection, suggesting at most limited changes in severity compared with Delta.[7]

A recent South African study at a tertiary care academic hospital, Tshwane District Hospital, reveals that peak bed occupancy was about half that of the third (Delta) wave suggesting a lower rate of hospital admissions relative to the number of cases in the Omicron wave compared with previous waves. Fewer intensive care unit (ICU) admissions and deaths and a shorter length of hospital stay indicate decreased severity of disease caused by the Omicron variant. A third of deaths resulted from a cause other than COVID-19, and there were no pediatric deaths related to severe COVID-19 disease. For the Omicron and previous waves, deaths and ICU admissions were 4.5 versus 21.3% ($p < 0.00001$) and 1 versus 4.3% ($p < 0.00001$), respectively; length of stay was 4.0 versus 8.8 days, and mean age was 39 versus 49.8 years.[10]

A prospective study at the Institute of Liver and Biliary Sciences, New Delhi, India, where respiratory specimen from all reverse transcription PCR confirmed positive cases between November 25 and December 23, 2021, reveals that out of the 264 cases included during the study period, 68.9% ($n = 182$) were identified as Delta and its sublineages, while 31.06% ($n = 82$) were Omicron with BA.1 as the predominant sublineage (73.1%). Most of the Omicron cases were asymptomatic ($n = 50$, 61%) and not requiring any hospitalizations. A total of 72 (87.8%) cases were fully vaccinated. Note that 39.1% ($n = 32$) had a history of travel and/or contacts while 60.9% ($n = 50$) showed a community transmission. A steep increase in the daily progression of Omicron cases with its preponderance in the community was observed from 1.8 to 54%.[11]

A similar trend was observed at Netcare Group private hospitals in South Africa with younger patients having fewer comorbidities, fewer hospitalizations and respiratory diagnoses, and a decrease in severity and mortality. Patients hospitalized during wave 4 were younger (median age, 36 years vs. maximum 59 years in wave 3; $p < 0.001$) with a higher proportion of females. Significantly fewer patients with comorbidities were admitted. In wave 4, the proportion presenting with an acute respiratory condition was lower (31.6% in wave 4 vs. maximum 91.2% in wave 3, $p < 0.001$). Of 971 patients admitted in wave 4, 24.2% were vaccinated, 66.4% were unvaccinated, and vaccination status was unknown for 9.4%. The proportion of patients requiring oxygen therapy significantly decreased (17.6% in wave 4 vs. 74% in wave 3, $p < 0.001$) as did the percentage receiving mechanical ventilation. Admission to intensive care was 18.5% in wave 4 versus 29.9% in wave 3 ($p < 0.001$).[12]

Vaccine efficacy

A Danish observational cohort study of 188,980 SARS-CoV-2 positive individuals during November to December 2021 compared the risk ratio (RR) of admission for Omicron compared with Delta infection and stratified by vaccination status and found that Omicron was associated with an adjusted RR of hospitalization of 0.64 (95% CI: 0.56–0.75) compared with Delta infection. RR was 0.57 (95% CI: 0.44–0.75) among cases with none or one vaccination, 0.71 (95% CI: 0.60–0.86) among two-dose vaccinated, and 0.50 (95% CI: 0.32–0.76) among three-dose vaccinated. Similarly, Omicron had lower risk than Delta.[13]

This Scottish study reveals that relative to ≥ 25 weeks post-second vaccine dose, the third/booster vaccine was associated with a 56% (95% CI: 51, 60) reduction in the odds of developing symptomatic disease with S gene negative 2 or more weeks after booster, among those aged 16 to 49 years. For individuals aged ≥ 50 years the corresponding reduction was 57% (95% CI: 52, 62). The third/booster dose is associated with substantial additional protection within 2 weeks of this additional dose, compared with two doses of vaccine received 25 or more weeks ago. This protection is greatest for Delta, but still substantial for Omicron.[14]

European Union/European Economic Area countries' update suggest that there is growing evidence for significantly lower vaccine effectiveness against Omicron infection and symptomatic disease after primary vaccination compared with the Delta variant, but with the booster dose increasing vaccine effectiveness. The data on hospitalization is still limited but suggests that protection against severe disease is higher than against infection and mild disease, although lower than the protection against the Delta variant.[15]

This South African study provided the effectiveness of a homologous Ad26.COV.2 vaccine boost given 6 to 9 months after the initial single vaccination series during a period of Omicron variant circulation. Vaccine effectiveness for hospitalization increased over time since booster dose, from 63% (95% CI: 31–81%) to 84% (95% CI: 67–92%) and then 85% (95% CI: 54–95%), 0 to 13 days, 14 to 27 days, and 1 to 2 months postboost.[16]

This Canadian study reveals that effectiveness of two doses of COVID-19 vaccines against infection (irrespective of symptoms or severity) is substantially lower for Omicron than Delta, and that vaccine efficacy (VE) against Omicron infection was only 37% ≥ 7 days following a third dose. We also observed negative VE against Omicron among those who had received two doses compared with unvaccinated individuals.[17]

Pharmaceutical measures

WHO continues to work with researchers to understand the effectiveness of therapeutics against the Omicron variant. Interleukin-6 receptor blockers and corticosteroids are expected to remain effective in the management of patients with severe and critical disease, since they mitigate the host inflammatory response to the virus.

Molnupiravir is a nucleoside analog, which means it mimics some of the building blocks of ribonucleic acid (RNA) and leads to the introduction of copying errors during viral RNA replication. If anything, the Omicron variant might be more susceptible than previous SARS-CoV-2 lineages to Molnupiravir given a large number of mutations it already carries in its spike protein. As such, Omicron may be more easily sent into "mutational meltdown."[18]

Paxlovid (PF-07321332) is a protease inhibitor targeting the 3CLpro SARsS-CoV-2 protease (gene NSP5) reducing the ability of the virus to replicate in host cells. A recent preprint presented in vitro data suggesting that the efficacy of specific Mpro inhibitors such as PF-07321332 is not compromised in current COVID-19 variants.[19]

Remdesivir directly inhibits the SARS-CoV-2 replication inside infected cells by targeting the viral RNA polymerase. Studies by Gilead suggest that it will continue to be active against the new omicron variant.[20]

Sotrovimab retained activity against Omicron but with a threefold lower potency in neutralization as measured by EC50.[21]

OMICRON QUARANTINE MEASURE

For people who are unvaccinated or are more than 6 months out from their second messenger RNA dose (or more than 2 months after the J&J vaccine) and not yet boosted, Centers for Disease Control and Prevention now recommends quarantine for 5 days followed by strict mask use for an additional 5 days. The change is motivated by science demonstrating that the majority of SARS-CoV-2 transmission occurs early in the course of illness, generally in the 1 to 2 days prior to onset of symptoms and the 2 to 3 days after.[22]

Hybrid immunity

Hybrid immunity is effective in preventing the spread of the Omicron, a variant of coronavirus, according to the findings of the study conducted by a team led by a Kerala doctor Dr. Padmanabha Shenoy. As more than 70% of Indians were infected with Delta during the second wave and India has vaccinated 95% of eligible population, at least with one dose, so close to three-fourths of India's population has hybrid immunity. This hybrid immunity wall is the reason India had a relatively minor third wave. About 65% of patients, who had received a single dose of Covishield following an infection, were able to neutralize Omicron.[23]

Omicron natural vaccine

Most Omicron cases have been reported as "mild" and some virologists claim that it could lead to natural immunity and that the new variant could act as a "natural vaccine." Omicron does not pose any dangers to healthy people. Post-Omicron infection, it could boost the immunity without causing a serious illness.

Targeted interventions should be planned for high-risk individuals with comorbidities like people who are older, who have compromised health conditions, or who have not been vaccinated or in fragile state.

The definitive evidence for increased remission, immune evasion, vaccine effectiveness, drug efficacy on Omicron, and mortality is still awaited. Omicron will provide a natural immunity to healthy people but Omicron can take a big toll on the vulnerable population with elderly and comorbid diseases. Therefore, it is essential to wear mask properly covering both mouth and nose, people get the vaccine when available to them, and continue to follow COVID protocol on preventing the spread of the virus including physical distancing more than 1 m, regular hand washing, high nutritious diet, and keeping indoor areas well ventilated.

Conflict of interest

None declared.

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