Transmission dynamics and mutational prevalence of the novel Severe acute respiratory syndrome coronavirus-2 Omicron Variant of Concern

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Abstract

The novel Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) variant, Omicron (PANGO lineage B.1.1.529) is being reported from all around the world. The WHO has categorized Omicron as a Variant of Concern (VOC) considering its higher transmissibility and infectivity, vaccine breakthrough cases. As of January 6, 2022, Omicron has been reported in at least 149 countries. Therefore, this study was planned to investigate the transmission dynamics and mutational prevalence of the novel SARS-CoV-2 Omicron variant. The transmission dynamics and Omicron SARS-CoV-2 divergence was studied using GISAID and Nextstrain which provides information about the genetic sequences, epidemiological, geographical, and species-specific data of human, avian, and animal viruses. Further, the mutation prevalence in spike glycoprotein of Omicron was studied, and the frequency of the crucial mutations was compared with the other prevalent VOCs. The transmission dynamics suggest that the Omicron was first identified in South Africa and then it was reported in the United Kingdom followed by the United States and Australia. Further, our phylogenetic analysis suggests that Omicron (BA.1) was clustered distinctly from the other VOCs. In the Spike glycoprotein, the Omicron (B.1.1.529) demonstrates critical 32 amino acid changes. This study may help us to understand mutational hotspots, transmission dynamics, phylogenetic divergence, effect on testing and immunity, which shall promote the progress of the clinical application and basic research.

KEYWORDS

COVID-19, Delta, Omicron, B.1.1.529, receptor-binding domain, SARS-CoV-2, Variants of Concern

1 | INTRODUCTION

The world is facing the recurrent emergence of Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) variants.¹ So far, at least 312 million cases and 5.5 million fatalities have been documented globally. Since January 2021, many SARS-CoV-2 variants have emerged and transmitted across several countries. According to the WHO, SARS-CoV-2 variants have been categorized based on the transmission ability, infectivity, and diagnostic and immune escape ability. SARS-CoV-2 variants are categorized as Variant of Concern (VOC), Variant of Interest...
2. Transmission dynamics of Omicron

To study the transmission dynamics of Omicron, we used GISAID (https://www.gisaid.org/). GISAID provides information about the genetic sequences, epidemiological, geographical, and species-specific data of human, avian, and animal viruses. The transmission lines were analyzed to understand the transmission dynamics of Omicron in various countries.14,15

2.1 Transmission dynamics of Omicron

To determine the Omicron SARS-CoV-2 divergence, we employed the Nextstrain, which offers the most recent worldwide genomic sequencing of the SARS-CoV-2 data as soon as it is released by GISAID (https://www.gisaid.org/). Phylogenetic tree analysis was performed to observe the mutational divergence of Omicron SARS-CoV-2 in the unrooted tree.16

2.2 Phylogenetic analysis of Omicron

To determine the Omicron SARS-CoV-2 divergence, we employed the Nextstrain, which offers the most recent worldwide genomic sequencing of the SARS-CoV-2 data as soon as it is released by GISAID (https://www.gisaid.org/). Phylogenetic tree analysis was performed to observe the mutational divergence of Omicron SARS-CoV-2 in the unrooted tree.16

2.3 Mutation prevalence of Omicron versus other VOCs

To determine the mutation prevalence in spike glycoprotein of Omicron, we have analyzed the frequencies of amino acid substitutions reported on SARS-CoV-2 (hCoV-19) Mutation Reports (https://outbreak.info/compare-lineages?pango=Alpha%26gene=S%26threshold=0.2). The frequency of the crucial mutations was compared with the other prevalent VOCs.17

2.4 Statistical analysis of mutational prevalence

To identify the most significant mutations in the Omicron, we have taken 60,410 Omicron sequences and performed the $\chi^2$ test analysis where the prevalence of specific mutation was considered as the observed value and the expected value was considered to be 100. If the null hypothesis is true, the observed and expected frequencies will be close in value and the $\chi^2$ statistic will be close to zero. If the null hypothesis is false, then the $\chi^2$ statistic will be large.

3 RESULTS AND DISCUSSION

3.1 Transmission dynamics of Omicron

Omicron-specific cases increase exponentially and spread worldwide within days of initial identification.18 Transmission dynamics showing the widespread transmission of novel SARS-CoV-2 Omicron (Figure 1A). The transmission dynamics suggest that the Omicron was first identified in South Africa (Figure 1B) and then it was reported in the United Kingdom (Figure 1C) followed by the United States (Figure 1D). Subsequently, the cases were reported from various countries (Figure 1E). As of December 28, 2021, globally the total number of Omicron cases is 53,695 and the highest number of Omicron cases have been identified in the United Kingdom (34,573), USA (83,111), and in Denmark (2,092), South Africa (16,432), Australia (859), Belgium (609), Canada (586), and in Switzerland is (471), and so on. Considering the rapid transmission of Omicron in a short span of time, the Omicron is expected to be more transmissible than other VOCs.19,20 The temporal change in the number of Omicron cases in a population was measured with or without pre-existing immunity.

3.2 Phylogenetic analysis of Omicron

To study the evolutionary links between the Omicron variant and the recently emerged SARS-CoV-2 variants, we have analyzed the
phylogenetic data based on the genomic sequencing of SARS-CoV-2. When the phylogenetic tree is plotted in unrooted style, the divergence between SARS-CoV-2 variants is obvious. We have found that the Omicron (BA.1) was clustered distinctly from the other VOCs producing a monophyletic clade (Figure 2A), based on the recent submission of continent wise Omicron genomic data (Figure 2B). Omicron is distinct from other SARS-CoV-2 VOCs because of mutations in the spike suggesting that Omicron formed a new emergent group that was not originating with other variants. Mutations in the spike protein, and more specifically in receptor-binding domain (RBD) cause the SARS-CoV-2 variant’s critical infectivity and antibody resistance, which may affect COVID-19 transmissibility, infectivity, neutralizing antibody escapes, and vaccination breakthrough cases.22 Alpha, Beta, Gamma, and Delta are four VOCs, and Eta, Iota, Kappa, and Lambda are four VOIs that are now in use across the world.23 In terms of immune evasion and transmission, Alpha, Beta, and Delta variants of SARS-CoV2 had a large effect globally, with Delta quickly replacing other variants to prevail globally, including in South Africa.24

3.3 | Mutations in Omicron SARS-CoV-2

The SARS-CoV-2 spike glycoprotein interacts with human ACE2 receptors for attachment and internalization.25 For emergency use, most medicines and vaccinations authorized have been developed to counteract the spikes and ACE2 interactions to prevent attachment.26,27 Apart from the mutations in the spike glycoprotein, Omicron variant mutations are found in many different SARS-CoV-2 proteins, particularly NSP3 (K38R, ΔA1265, A1892T, L1266I), NSP4 (T492I), NSP5 (P132H), NSP6 (I189V, Δ105-107), NSP12 (P323L), NSP14 (I42V), nucleocapsid protein, envelope protein, and membrane protein. In the S protein receptor-binding domain (RBD) alterations are being studied for their possible influence on antibody resistance and infectivity.
3.4 | Mutation in the RBD of Omicron and its implication

In the spike glycoprotein, the variant of Omicron includes 32 amino acid alterations, three minor deletions in the N terminus domain (NTD), three deletions in Omicron spike that is, Δ143–145, Δ69–70, and Δ211, and one minuscule insertion in spike at 214 positions, that is, ins214EPE, with 15 mutations occurring in the receptor-binding domain (RBD). Mutations are referred to as Δ69–70, Ala67Val, Thr95Ile, Δ143–145, Δ211, Gly142Asp, ins214EPE, Leu212Ile, Gly339Asp, Ser373Pro, Ser371Leu, Lys417Asn, Ser478Asp, Thr478Lys, Tyr505His, Asn501Y, Asp614Gly, Thr547Lys, Asn679Lys, His681His, Asn764Lys, Pro681His, Asn856Lys, Asp796Tyr, Asn969Lys, Gln954His, Leu981Phe. The RBD has 15 of these changes (residues 319–541) [17,25,28].

Prominently, the 15 RBD mutations are as G339D, S371L, S373P, S375F, K417N, N440K, G440K, G446S, S477N, T478K, E484A, Q493R, G496S, N501Y, and Y505H (Figure 2C). Because of its RBD mutations N440K, T478K, and N501Y, Omicron may be nearly 10 times more transmissible than the original SARS-CoV-2. Because of its RBD mutations K417N, E484A, and Y505H, the Omicron has a higher potential to impact the interaction of most 132 antibodies with the S protein, indicating that it has a higher vaccination escape capacity than the Delta variant. K417N, which is also part of the Beta variant that arose in South Africa, produces the most substantial breakdown of recognized antibodies amongst the 15 RBD mutations. E484A is another mutation that has a significant impact on several known antibodies. The variant has several changes and deletions in additional genomic locations. Nonstructural protein modifications (NSP)3 as Lys38Arg, SΔ1265, Ala1892Thr; Leu1266Ile and NSP4 as Thr492Ile; NSP5 as Phe132His; NSP6 as Ile189Val; Δ105–107, NSP12 as Pro323Leu; NSP14–Ile42Val; membrane (M) as Gln19Glu, Asp3Gly, Ala63Thr; envelope (E) as Thr9Ile nucleocapsid (N) as Gly204Arg, Δ31–33, Pro13Leu, Arg203Lys. In contrast to other common VOCs, such as Delta (B.1.617.2), Omicron has a high mutation rate. Moreover, such Omicron alterations may be associated with increased infectivity, higher viral binding affinity, and antibody evasion.
To observe the mutational prevalence of Omicron, we have compared the prevalence of crucial mutations observed in the Omicron in comparison with the other VOCs. Our analysis suggests that the prevalence of the mutation in RBD as K417N, N440K, and G446S is 22.53%, 25.08%, and 25.73% with $\chi^2$ test values are 60.01, 56.11, and 55.14, respectively. Similarly, one another mutation in spike observed as N764K exhibits 55.77% prevalence with $\chi^2$ test values of 19.55 among the Omicron genome sequencing data submitted.
(Table 1). These data suggest that these mutations are not prevalent in Omicron.

4 | CONCLUSIONS AND FUTURE PERSPECTIVES

The WHO has categorized the COVID-19 Omicron variant as a variant of concern, based on evidence that it has various alterations that might affect its transmissibility and pathogenicity, vaccine effectiveness, and monoclonal antibody-mediated protection. The specificity and efficacy of the variant monitoring system, as well as infectious preventive measures in each nation, are critical for efficient prevention and therapeutic management of Omicron. The most efficient way for COVID-19 protection and control has already been demonstrated via vaccination. Live attenuated vaccines, replicating and non-replicating viral vector vaccines, DNA/RNA vaccines, and protein-subunit vaccines are the major types of vaccines that are currently available for human use. The 32 amino acid alterations in the spike protein of Omicron, which include three modest deletions and one short insertion, some of which are concerning and may be related to humoral immune escape potential and higher transmissibility. These alterations may increase the potential to escape existing immunizations. Our findings show the transmission dynamics of the novel SARS-CoV-2 Omicron which shows that it's highly transmissible. Moreover, the mutational comparison of Omicron's spike glycoprotein with other VOCs of SARS-CoV-2 helps us to better understand the worldwide transmissibility, pathophysiology, and the development of efficient prevention and treatment strategies toward novel SARS-COV-2 variants.

ACKNOWLEDGMENTS

The authors are grateful to the Vice Chancellor, King George's Medical University (KGMU) Lucknow, for the encouragement for this study. Ahmed S. Abdel-Moneim also acknowledges the support of Taif University Researchers Supporting Project No. TURSP-2020/11. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Shailendra K. Saxena conceived the idea and planned the study. Swatantra Kumar, Saniya Ansari, and Shailendra K. Saxena collected the data, devised the initial draft, reviewed the final draft, and contributed equally to this study as the first author. Shailendra K. Saxena, Saniya Ansari, Swatantra Kumar, Janusz T. Paweska, Vimal K. Maurya, Anil K. Tripathi, and Ahmed S. Abdel-Moneim finalized the draft for submission. All authors read and approved the final version of the manuscript.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article.

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How to cite this article: Saxena SK, Kumar S, Ansari S, et al. Transmission dynamics and mutational prevalence of the novel Severe acute respiratory syndrome coronavirus-2 Omicron Variant of Concern. J Med Virol. 2022;94:2160-2166. doi:10.1002/jmv.27611