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META-ANALYSIS

Clinical outcomes of the omicron variant compared with previous SARS-CoV-2 variants; meta-analysis of current reports

Mohsen Karbalaei, Masoud Keikha

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Mohsen Karbalaei, Department of Microbiology and Virology, School of Medicine, Jiroft University of Medical Sciences, Jiroft, Iran

Masoud Keikha, Department of Microbiology and Virology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Corresponding author: Masoud Keikha, PhD, Doctor, Instructor, Teaching Assistant, Department of Microbiology and Virology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. masoud.keykha90@gmail.com

Abstract

BACKGROUND

Omicron (B.1.1.529) is a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant of concern; however, there is no comprehensive analysis regarding clinical features, disease severity, or clinical outcomes of this variant.

AIM

To compare the clinical characteristics of infection with omicron and previous variants of SARS-CoV-2.

METHODS

We searched major international databases consisting ISI Web of Science, PubMed, Scopus, MedRxiv, and *Reference Citation Analysis* to collect the potential relevant documents. Finally, clinical features, *e.g.*, death rate, intensive care unit (ICU) admission, length of hospitalization, and mechanical ventilation, of infection with SARS-CoV-2 omicron variant compared with previous variants were assessed using odds ratio and 95% confidence intervals by Comprehensive Meta-Analysis software version 2.2.

RESULTS

A total of 12 articles met our criteria. These investigated the clinical outcomes of infection with omicron variant compared with other variants such as alpha, beta and delta. Our results suggested that ICU admission, need for mechanical ventilation, and death rate were significantly lower for omicron than previous variants. In addition, the average length of hospitalization during the omicron wave was significantly shorter than for other variants.

CONCLUSION

The infectivity of omicron variant was higher than for previous variants due to

several mutations, particularly in the spike protein. However, disease severity was mild to moderate compared previous variants.

Key Words: SARS-CoV-2; COVID-19; Omicron; Infectious disease

Core Tip: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) omicron (B.1.1.529) is a variant of concern that was first identified on 24 November 2021 as a new global threat. However, due to the lack of comprehensive statistical analysis, clinical characteristics and disease outcomes of infection with omicron variant have remained unknown. Hence, the comparison of clinical profile between cases infected with this new variant and previous variants will lead to the establishment of a strategy regarding appropriate management and global control of this variant.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a global pandemic that first emerged from Wuhan, China in December 2019. According to the World Health Organization (WHO), so far > 378 million cases, as well as 5.67 million deaths have occurred due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection[1]. On 24 November 2021, the Network for Genomics Surveillance in South Africa (NGS-SA) reported a new variant of this virus from Gauteng Province, named omicron (B.1.1.529); the new variant was confirmed by WHO on 25 November 2021[2,3].

The omicron variant rapidly replaced the previous variants in South Africa and spread to other countries, so it quickly became a dominant variant. In the USA, approximately 95% of all new cases of COVID-19 were diagnosed as being caused by the omicron variant by January 2022[4,5].

The genome of this variant contains 26–32 mutations in the spike gene as well as 45–52 amino acid substitutions. these mutations are associated with increases in viral characteristics such as transmissibility, immune escape, and S gene target failure (SGTF). SGTF is due to the 69 to 70 deletion in the S gene of B.1.1.7[6-8]. Early studies have shown the inefficacy of current vaccines (vaccination schemes and booster doses) and the higher rate of re-infection with the omicron variant[9,10]. Based on animal model findings, the severity of symptoms as well as the viral load of the omicron variant were lower compared to the previously reported variants of SARS-CoV-2[11,12]. Clinical reports from Scotland, England, Canada, and the USA have also confirmed animal experiments[13-16]. However, the fourth global wave of COVID-19 caused by the omicron variant was not associated with increased hospitalization or death in comparison with previous SARS-CoV-2 variants[17].

Understanding the clinical characteristics, susceptibility factors, and immune response against the new SARS-CoV-2 variants could be useful strategies in managing these viruses and development of novel treatment options. In this study, we evaluated the clinical severity of SARS-CoV-2 omicron variant compared with previous variants.

MATERIALS AND METHODS

We searched global databases such as ISI Web of Science, PubMed, Scopus, MedRxiv, and Reference Citation Analysis (https://www.referencecitationanalysis.com/) using MeSH keywords such as "Omicron", "COVID-19", "SARS-CoV-2", "Disease severity", "Variant of concern", "ICU", "Intensive care unit", and "fourth wave". We retrieved all potential studies related to the clinical severity of SARS-CoV-2 omicron variant regardless of language and publication date. All eligible documents were carefully screened; required data including mean age, immunization status, mortality rate, intensive care unit (ICU) admission, length of hospitalization, and mechanical ventilation are summarized in Table 1. We also reviewed the bibliography of documents to avoid missing relevant articles. Finally, the severity of COVID-19 caused by omicron compared with previous SARS-CoV-2 variants was evaluated using odds ratio (OR) and 95% confidence interval (CI). We used a random-effect size due to the presence of significant heterogeneity (I^2 index and Cochrane *P* value test). Data were pooled using

Table 1 Characteristics of included studies

First author	Country	Mean age		Immunization		Death rate		ICU admission		Length of stay		Ventilation		Number of cases		Ref.
		Omicron	Previous variants	Omicron	Previous variants	Omicron	Previous variants	Omicron	Previous variants	Omicron	Previous variants	Omicron	Previous variants	Omicron	Previous variants	
Abdullah	South Africa	39	49.8	NA	NA	4.5%	21.3%	1%	4.3%	4	8.8	NA	NA	466	3962	[18]
Cloete	South Africa	4.2	NA	NA	NA	4	NA	7	NA	3.2	NA	7	NA	6287	NA	[19]
Christensen	USA	44.3	50.0	2497	101	38	170	NA	NA	3.2	5.1	49	144	4468	3149	[20]
Davies	South Africa	NA	NA	HR:0.41, 95%CI: 0.29-0.59		HR: 0.27, 95%CI: 0.19-0.38		NA	NA	NA	NA	NA	NA	5144	11609	[21]
Goga	South Africa	33	55	NA	NA	NA	NA	3%	16%	3	6	0.2%	8%	17650	22888	[22]
Lewnard	USA	NA	NA	6,981	784	1	12	4	20	5.5	15.8	0	11	52297	16982	[23]
Iuliano	USA	NA	NA	NA	NA	1854	1924	24776	24774	3	5	358	503	48238	25873	[24]
Maslo	South Africa	36	53	235	NA	27	520	180	1104	3	8	16	431	971	2628	[25]
Santos	Portugal	37.1	43.4	295	201	0	26	0	17	3.7	8.6	NA	NA	6581	9397	[26]
Torjesen	UK	NA	NA	NA	NA	NA	NA	9.9%	14%	1.7	6.6	2%	5.8%	NA	NA	[27]
Wang	USA	36.4	36.1	2.4%	3.1%	23	30	0.26%	0.78%	NA	NA	0.07%	0.43%	14054	563884	[28]
Wang	USA	1.49	1.73	NA	NA	NA	NA	0.14%	0.43%	NA	NA	0.33%	1.15%	7201	63203	[29]

ICU: Intensive care unit; NA: Not available; HR: Hazard ratio; CI: Confidence interval.

Comprehensive Meta-Analysis software version 2.2 (Biostat, Englewood, NJ, USA).

RESULTS

A total of 12 studies investigated the clinical outcomes of infection with SARS-CoV-2 omicron variant compared with other variants such as alpha, beta and delta (Figure 1). Eligible studies were performed in South Africa, USA, Portugal and UK from 2021 to 2022[18-29]. We pooled the data of 887 132 cases with positive PCR test for SARS-CoV-2, including 163 457 cases positive for omicron variant, as well as 723 675 cases positive for other variants.

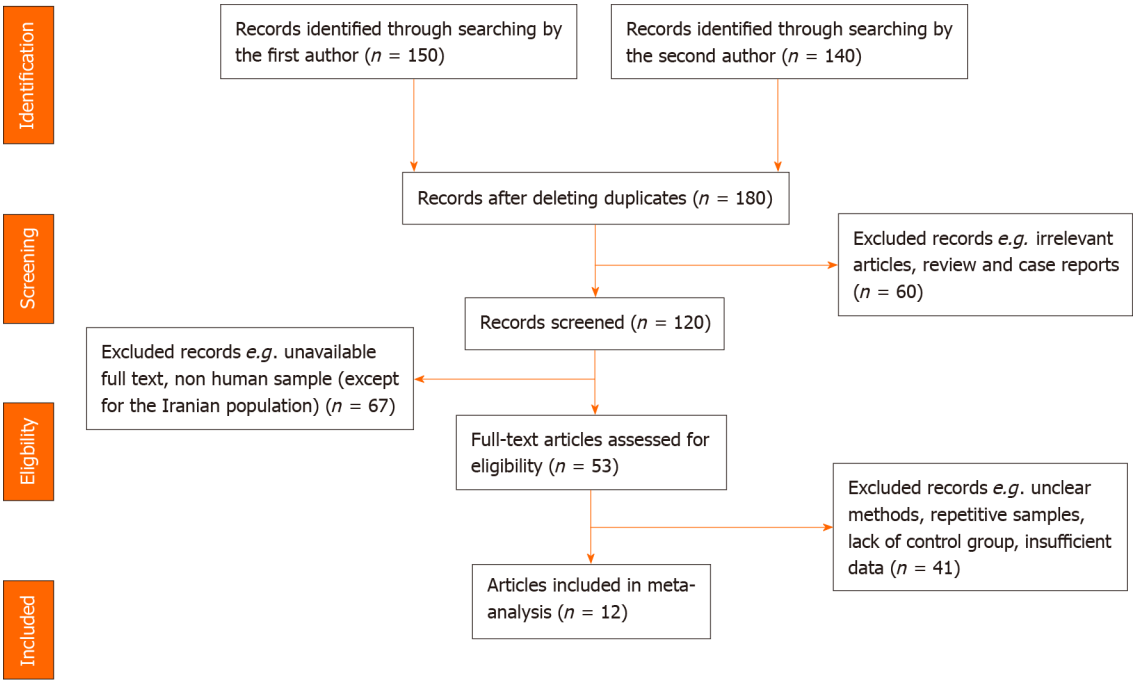

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Figure 1 Flowchart of literature search and study selection process.

The mean age of patients infected with omicron variant was 28.93 ± 15 years. The frequency of events such as ICU admission, need for mechanical ventilation, and death rate for omicron variant was 0.8% (95% CI: 0.2%–3.7%; I^2: 99.89; P = 0.01; Egger's P = 0.01; Begg's P = 0.29), 0.2% (95% CI: 0.1%–0.5%; I^2: 95.75; P = 0.01; Egger's P = 0.16; Begg's P = 0.26), and 0.4% (95% CI: 0.1%–1.0%; I^2: 98.47; P = 0.01; Egger's P = 0.01; Begg's P = 0.45), respectively. The average length of hospitalization for omicron was significantly less than for other variants (3.36 ± 1 d *vs*. 7.98 ± 3 d; P < 0.05). The incidence of omicron infection among fully vaccinated individuals was 12.9% (95% CI: 5%–27%; I^2: 99.89; P = 0.01; Egger's P = 0.22; Begg's P = 0.40). the current findings revealed that the severity of infections caused by omicron was less than for previous infections caused by alpha, beta, and delta variants. The current findings are consistent with similar reports[30,31]. In comparing the fourth wave of COVID-19 caused by the omicron variant with previous waves, it should be said that the mean age for patients infected with omicron was ~13 years (28.93 ± 15 years), which was less than that for other variants (41.29 ± 17 years). There was a significant reduction in ICU admission (OR: 0.18; 95% CI: 0.094–0.37; P = 0.01; I^2: 99.05; P = 0.01; Egger's P = 0.2; Begg's P value: 0.07) (Figure 2). Our results suggested a significant reduction in the need for mechanical ventilation (OR: 0.135; 95% CI: 0.05–0.31; P = 0.01; I^2: 97.24; P = 0.01; Egger's P = 0.12; Begg's P = 0.26) among omicron cases (Figure 3). The mortality rate also declined among patients infected with omicron variant (OR: 0.17; 95% CI: 0.06–0.46; P = 0.01; I^2: 98.32; P = 0.01; Egger's P = 0.44; Begg's P = 0.71) compared with previous variants (Figure 4).

DISCUSSION

We found that the severity of COVID-19 caused by the SARS-CoV-2 omicron variant was significantly less than for previous variants; however, there was significant heterogeneity that could be due to differences in several factors such as study design, geographical region, time for assessment of clinical outcomes, and diverse conditions of included cases; publication bias was also significant. Recently, Zhao *et al*[32], showed that the omicron variant is less dependent on the TMPRSS2-mediated entry pathway, which leads to less-efficient replication and decreased viral load within the lungs. In addition, the omicron variant is more susceptible to interferons than other variants are, especially the delta variant [33]. Similar evidence could be a reasonable explanation for the lower severity of COVID-19 with the omicron variant, as confirmed by numerous observational studies[15].

The omicron variant nucleotide sequence has several mutations, especially 32 single substitutions in the spike protein that cause resistance to neutralizing antibodies, as well as inefficiency of current vaccines[34-36]. We revealed that omicron variant causes less severity of COVID-19 than previous variants; however, heterogeneity and publication bias were significant in our estimations (Figure 5). Further studies need to confirm the present findings.

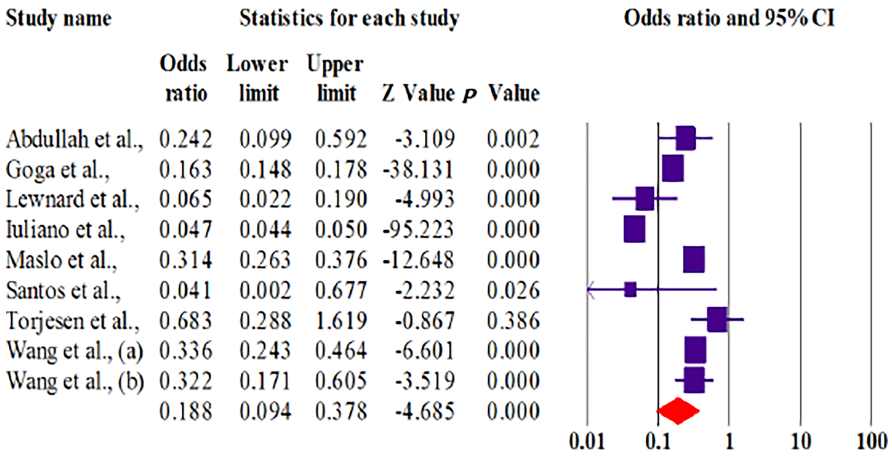

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Figure 2 Forest plot of the meta-analysis on intensive care unit admission for patients infected with severe acute respiratory syndrome coronavirus 2 omicron variant.

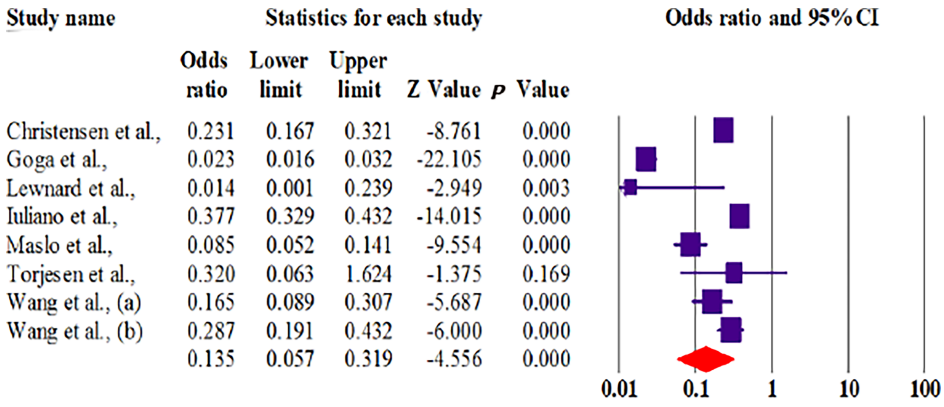

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Figure 3 Forest plot of the meta-analysis for need for mechanical ventilation in patients infected with severe acute respiratory syndrome coronavirus 2 omicron variant.

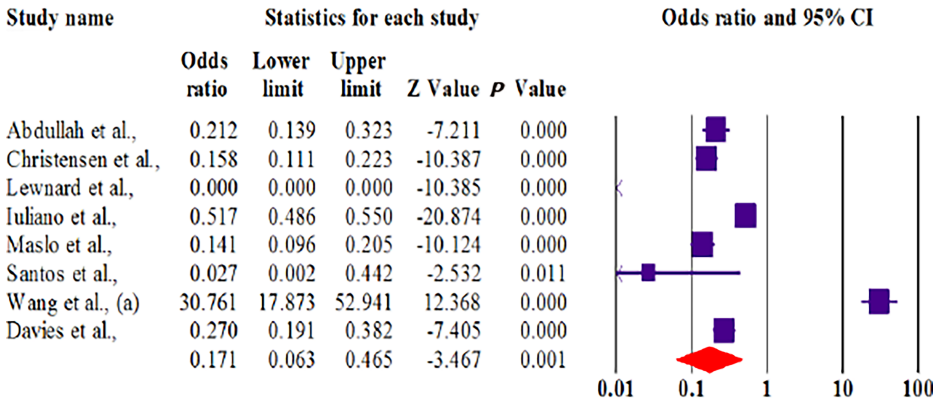

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Figure 4 Forest plot of meta-analysis of risk of mortality in patients infected with severe acute respiratory syndrome coronavirus 2 omicron variant.

CONCLUSION

A new global increase in COVID-19 has been accompanied by the emergence of the SARS-CoV-2 omicron variant that is associated with less disease severity, as well as fewer ICU admissions, shorter

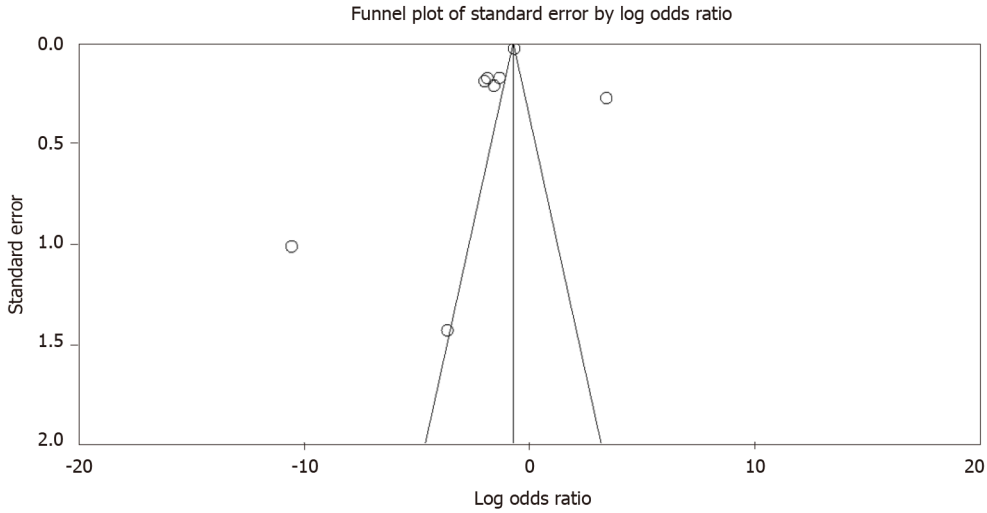

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Figure 5 Funnel plot of meta-analysis of disease severity of patients intfected with severe acute respiratory syndrome coronavirus 2 omicron variant compared with previous variants.

hospitalization, and lower mortality rate. Nonetheless, there is limited information about the effect of omicron on children, pregnant women, and immunodeficient individuals. Overall, omicron has been considered as the most contagious SARS-CoV-2 variant that affects children and young adults more than other groups. Continuation of the current situation can have deadly consequences for these age groups.

ARTICLE HIGHLIGHTS

Research background

Omicron (B.1.1.529) is a new variant of concern of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); however, there is no comprehensive analysis regarding clinical features, disease severity, and clinical outcomes of infection with this variant.

Research motivation

There is insufficient evidence regarding clinical characteristics, standard therapeutic regimen, and efficacy of currently available vaccines against the omicron variant.

Research objectives

This study was a comprehensive review and statistical analysis to compare the clinical characteristics of infection with the omicron and previous variants.

Research methods

We searched major international databases consisting ISI Web of Science, PubMed, Scopus, and MedRxiv to collect the potential relevant documents. Finally, clinical features, *e.g.*, death rate, intensive care unit (ICU) admission, length of hospitalization, and need for mechanical ventilation of patients infected with omicron variant compared with previous variants, were assessed.

Research results

Twelve articles met our criteria. These studies investigated the clinical outcomes of infection with SARS-CoV-2 omicron variant compared with other variants such as alpha, beta and delta. Our results suggested that ICU admission, need for mechanical ventilation, and death rate were significantly lower for omicron than previous variants. In addition, the average length of hospitalization during the omicron wave was significantly shorter than for other variants.

Research conclusions

The infectivity of the omicron variant was much higher than for previous variants due to the presence of several mutations, particularly in the spike protein. However, disease severity was mild to moderate disease compared with previous variants.

Research perspectives

We revealed that the disease severity of infection with omicron was lower than for previous variants. However, this variant was more contagious. Nevertheless, further investigation with larger samples is needed to confirm the present findings.

FOOTNOTES

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ORCID number: Mohsen Karbalaei 0000-0001-9899-2885; Masoud Keikha 0000-0003-1208-8479.

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