WHO Global Clinical Platform
for COVID-19

Data for public health response

Severity of disease associated with Omicron variant as compared with Delta variant in hospitalized patients with suspected or confirmed SARS-CoV-2 infection

World Health Organization

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Abbreviations

CI	confidence interval
CRF	case record form
ECMO	extracorporeal membrane oxygenation
HIV	human immunodeficiency virus
HR	hazard ratio
ICU	intensive care unit
IQR	interquartile range
OR	odds ratio
PCR	polymerase chain reaction
SARS-CoV-2	severe acute respiratory syndrome corona virus 2
SGTF	S-gene target failure
TAG-VE	Technical Advisory Group on SARS-CoV-2 Virus Evolution (WHO)
TB	tuberculosis
VOC	Variant of Concern
WHO	World Health Organization

Background

Globally, as of 23rd May 2022, there have been over 522,000,000 confirmed cases and more than 6.2 million deaths from COVID-19 *(1)*. On 25 November 2021, South Africa reported the detection of a new variant (B.1.1.529) of severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) after a sharp increase in cases in Gauteng province with the unique finding of S-gene target failure (SGTF) on polymerase chain reaction (PCR) testing. This new variant of SARS-CoV-2 was notable for having numerous mutations, with many in the spike protein, leading to concerns of increased transmissibility and antibody escape *(2)*. The Technical Advisory Group on SARS-CoV-2 Virus Evolution (TAG-VE) of WHO convened on 26 November 2021 and designated B.1.1.529 a new Variant of Concern (VOC) and assigned the nomenclature Omicron *(3)*.

One of the key questions as Omicron variant emerged was how it affected severity of disease. Early on, data suggested that although Omicron variant may have increased transmissibility, it caused less severe disease than the Delta variant *(4–6)*. There were also data to suggest that Omicron variant may have reduced proclivity to damage the lungs based on animal studies and increased tropism for the upper airway *(7,8)*. However, significant uncertainty exists on the true severity and outcomes from Omicron variant due to a variety of reasons – the limited amount of data available and, crucially, challenges in disentangling the protective effects of prior infection (with different variants) and vaccination *(9,10)*. Recent trends from Hong Kong SAR, China, show that in populations with suboptimal pre-existing immunity, Omicron variant can lead to substantial mortality and morbidity *(11)*.

Omicron variant is now the dominant global SARS-CoV-2 variant and has replaced Delta variant *(12)*. Understanding the true severity of a VOC has several important implications – in planning the public health response, in resource allocation, in providing clinical guidance and designing clinical management protocols and, more broadly, regarding the nature of public health messaging.

Since May 2020 and throughout the pandemic, many countries and research networks around the globe have contributed anonymized individual patient-level clinical data of hospitalized COVID-19 patients to the WHO Global Clinical Platform *(13)*. To determine the severity associated with Omicron SARS-CoV-2 infection, we compared clinical severity and outcomes during a period of Omicron variant circulation with a period of Delta variant circulation in a subset of cases submitted to the WHO Global Clinical Platform.

Objectives of the analysis

1. Describe the clinical characteristics and key outcomes for hospitalized patients with COVID-19 during the Omicron period compared with the Delta period.
2. Assess the difference in severity between hospitalized patients during the "Omicron period" compared with the "Delta period".

Methods

Data sources

Anonymized individual-level data from patients admitted to hospitals with COVID-19 in South Africa and submitted to the WHO Global Clinical Platform were used to identify the eligible study sample. Two options exist to contribute date to the platform: 1) use of the WHO case record form (CRF), which exists in both paper-based and electronic formats; and 2) data entered into a local system or database. For locally entered data (as in this report), relevant variables were mapped and aligned to the WHO CRF data dictionary and transferred to the WHO Clinical Platform hosted on REDCAP.

Inclusion criteria

All patients hospitalized with suspected or confirmed COVID-19 symptoms to a health care facility in the South African provinces of Eastern Cape, Free State, Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga, North West, Northern Cape and Western Cape between 2 August 2021 (week 31) and 3 October 2021 (week 39) [Delta period] or 15 November 2021 to 16 February 2022 [Omicron period] were included in the analysis.

Disease severity was categorized as critical, severe or non-severe where:

- critical included those “ever on invasive ventilation” during hospitalization or “ever on oxygen and on high-flow nasal oxygen”, or “ever extracorporeal membrane oxygenation (ECMO)” or “admitted to intensive care unit (ICU)”;
- severe included those if “ever on oxygen only”;
- non-severe if none of the above conditions were met.

Statistical analysis

We compared patient and clinical characteristics, disease severity and outcomes of patients admitted during the Delta period with those admitted during the Omicron period. Records with missing data were excluded when determining distributions across outcome levels. Observations with missing values for death or discharge outcomes and severity classification were excluded from analysis.

We used multivariable logistic regression models using generalized estimating equations to compute odds ratios (ORs) of severe or critical illness for Omicron compared with Delta patients. In addition, we developed a proportional hazards model to estimate the hazard ratio (HR) of in-hospital mortality for the Omicron period compared with Delta. For the time-to-event model data were right censored at 28 days. Additionally, we assumed that patients discharged before 28 days were considered to be alive for at least 28 days.

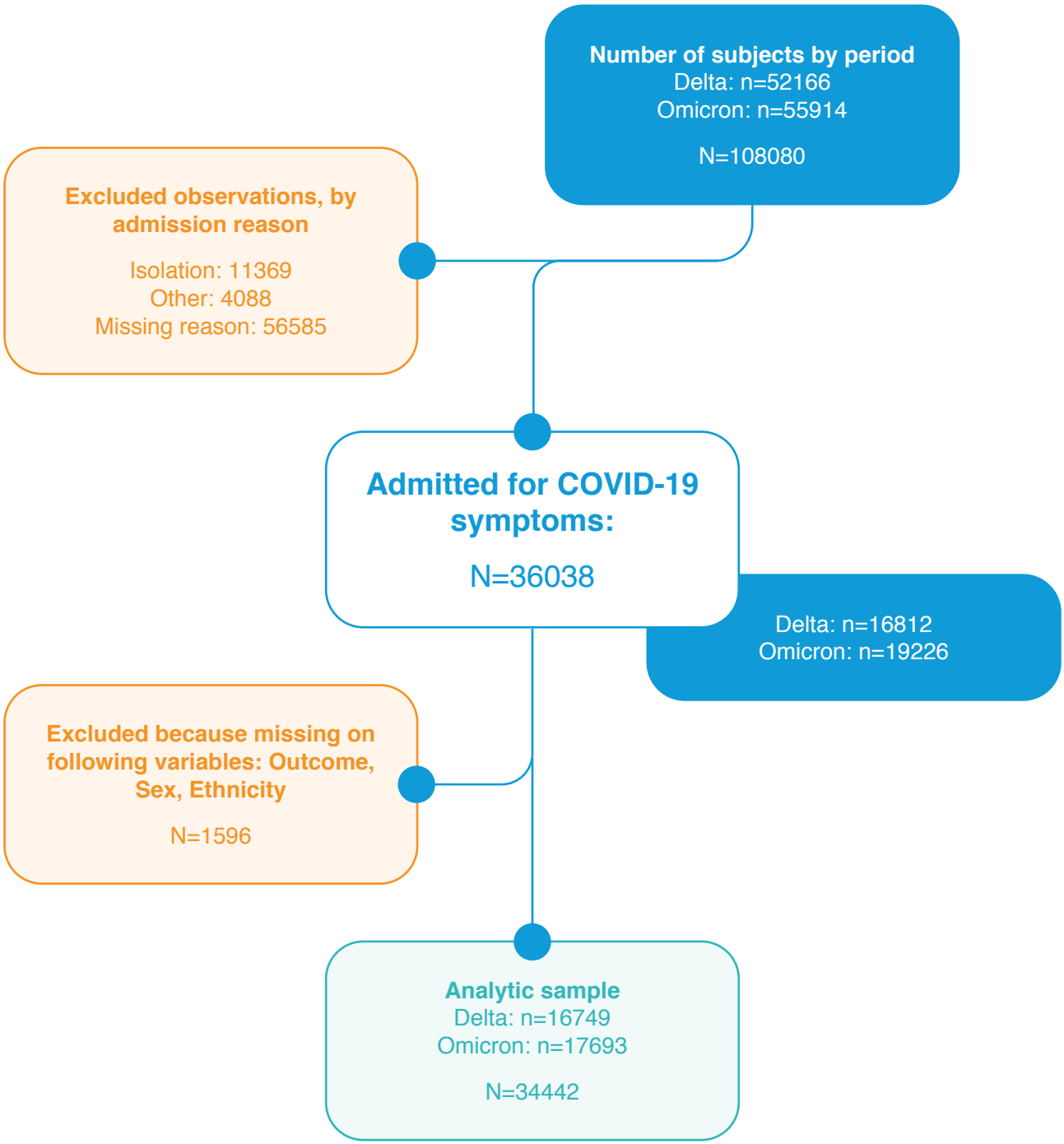
Age and sex were included in the models as a priori confounders. Other covariates that were considered for inclusion in the models were self-reported vaccination status, number of underlying conditions (none, one or more), public or private sector, ethnic group and self-reported COVID-19 reinfection. Included covariates were retained in the final model if they were found to be significant at $p < 0.05$ level. All models included provinces as random effect to account for potential heterogeneity in patient care. We also undertook a sensitivity analysis by excluding patients that were not vaccinated to test the consistency of the primary results.

All analyses were conducted in SAS version 9.4 (Copyright © 2016 by SAS Institute Inc., Cary, NC, USA) or R version 4.1.1 (R Core Team 2021. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/).

Results

For this report, we included data on 17 693 patients from the Omicron period and 16 749 patients from the Delta period, data extracted on 16 February 2022. Fig. 1 lists the flow of participants through the analysis.

Figure 1 Flow of participants through the analysis



Key characteristics and outcomes

Table 1 lists the key characteristics of the two groups. The median age (IQR) of the Omicron cohort was 41 years (28,62) and for Delta, was 52 years (36,66). Close to 60% of the population in both groups were female. 28.1% of Omicron patients had severe disease as compared with 49.2% of the Delta cohort. Similarly, 3.7% of the Omicron cohort and 7.7% of the Delta cohort had critical disease.

Table 1 Baseline characteristics of the included population

Variable	Omicron (n=17 693)	Delta (n=16 749)	P value[a]
Age - median (IQR)	41 (28,62)	52 (36,66)	< 0.0001
Sex (n and %)			0.0005
Male	7500 (42.4%)	6792 (40.6%)	
Female	10 193 (57.6%)	9957 (59.5%)	
Key underlying conditions (n and %)			
Diabetes	1629/7573 (21.5%)	2648/8752 (69.7%)	< 0.0001
Hypertension	3196/8322 (38.4%)	4632/9668 (47.9%)	< 0.0001
Chronic heart disease	315/6431 (4.9%)	396/7138 (5.6%)	0.0899
Chronic lung disease	178/6326 (2.8%)	127/7018 (1.8%)	0.0001
Chronic kidney disease	142/6318 (2.3%)	186/7034 (2.6%)	0.1392
Malignancy	58/6249 (0.9%)	79/6968 (1.1%)	0.2439
HIV	1982/6665 (29.7%)	1592/7132 (22.3%)	< 0.0001
Current smoking	523/4492 (11.6%)	383/5462 (7.0%)	< 0.0001
Current or past TB	559/6081 (9.2%)	389/6875 (5.7%)	< 0.0001
Asthma	383/6537 (5.9%)	399/7206 (5.5%)	0.4159
Vaccination status (n and %)			
Yes	16 71(9.4%)	734 (4.4%)	
Unknown/No	16 022 (90.6%)	16 015 (95.6%)	
Severity (n and %)			< 0.0001
Non-severe	12 082(68.3%)	7207 (43.0%)	
Severe	4964 (28.1%)	8248 (49.2%)	
Critical	647 (3.7%)	1294 (7.7%)	

a Chi-Square test for categorical variables and Wilcoxon rank sum for continuous variables.

Table 2 lists the key outcomes by variant period. 15% of the Omicron cohort and 28% of the Delta cohort died during their hospital stay. Median (IQR) length of stay was 6 days (3,10) in the Omicron group and 7 days (3,10) in the Delta group.