SARS-CoV-2 Alpha Variant Infection

Subjects: Pathology
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The ongoing global coronavirus-19 disease (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), poses major challenges to health systems worldwide. While the majority of infected people have mild to moderate symptoms, some patients develop acute respiratory distress syndrome (ARDS) requiring intensive care treatment and mechanical ventilation.

Keywords: SARS-CoV-2 virus variant ; Alpha variant ; COVID-19 ; intensive care medicine ; mortality

1. Introduction

SARS-CoV-2 is a positive-sense single-stranded RNA virus whose genome is of a low stability and is thus more prone to mutation accumulation, with approximately 9.8 × 104 substitutions/site yearly [1][2][3][4]. By the beginning of May 2021, there had been more than 1.4 million sequences reported, and among them, 3913 major representative variant genomes that have been identified and included in the global SARS-CoV-2 sequence database operated by Global Initiative on Sharing Avian Influenza Data (GISAID). Not all genetic mutations lead to variation in major proteins and/or alter virus infectivity. In the meantime, several mutations of SARS-CoV-2 have emerged . These genetic variants affect the course of the disease by altered virulence, susceptibility to immune response and transmissibility. Four of these variants are classified as variants of concern (VOC) by the World Health Organization (WHO): Alpha variant/Lineage B.1.1.7 (first detected in the UK) [5], Beta variant/Lineage B.1.351 (first detected in South Africa) , Gamma variant/Lineage P.1 (first detected in Brazil)[6][7] and Delta variant/Lineage B.1.617.2 (first detected in India) [8]. The current spike gene mutations account for most of the clinically influential VOC.

To date, the pandemic has evolved in waves with rapidly increasing infections and deaths in most countries. These waves led to various measures, such as lockdowns, mandatory masks and others, which consequently resulted in decreasing infection rates.

In Germany, the second COVID-19 wave in the autumn of 2020 was still caused by the SARS-CoV-2 wild-type (WT), but the Alpha variant successively superseded the WT and constituted the predominant COVID-19 pathogen from March 2021 onwards. The SARS-CoV-2 Alpha variant (lineage B.1.1.7) was first detected in the UK in September 2020 [5] and was shortly after named the Alpha variant. The Alpha variant has an N501Y mutation: at the 501 residue, asparagine N has been replaced with Y tyrosine, and K417N, lysine K, has been replaced with asparagine N. Evaluations[9] of the Robert Koch Institute illustrated a continuous increase in the proportion of infections with the Alpha variant up to more than 90% at the end of April 2021 [10]. Previous studies described the Alpha variant as being significantly more contagious. Evidence suggests that the VOC Alpha increased the transmissibility rate by ~50%, especially in younger age groups and children[11]; however, data regarding the severity of disease when compared to the SARS-CoV-2 WT are inconclusive [12][13][14][15][16][17]. At present, very limited data are available regarding the course of patients requiring admission to intensive care units (ICU) and the impact of the Alpha variant on ICU mortality[17].

Therefore, the aim of this study was to analyze the outcome and clinical course of patients with Alpha variant SARS-CoV-2 infections in the ICU of a maximum care hospital in Germany and to compare it to patients with WT infections.

2. Results

2.1. Baseline Characteristics of Full Patient Population (n = 160)

One hundred and sixty patients who were admitted to our ICU were included in this analysis. Of those, 80 patients each tested positive for the Alpha variant and WT. Male patients accounted for 59 of 80 cases (74%) in the Alpha variant group and 57 of 80 cases (71%) in the WT group (p = 0.073). The median age was 55.5 years (range 13–83) in the Alpha variant group and 62.5 years (range 16–87) in the WT group. Despite the lower median age, the patients in the Alpha variant group had slightly higher rates for chronic respiratory and cardiovascular disease compared to the patients in the WT group. None of the differences in pre-existing conditions between the Alpha variant and the WT group reached statistical significance (**Table 1**).

Table 1. Baseline patient characteristics of both the full patient population as well as the matched-pair analysis. No significant differences were identified between the SARS-CoV2 Alpha variant group and the SARS-CoV2 wild-type group.

#: matching criteria (sex, age).

	Full Patient Population (*n* = 160)			Matched-Pair Analysis (*n* = 116)		
	Alpha Variant (*n* = 80)	Wild Type (*n* = 80)	*p*	Alpha Variant (*n* = 58)	Wild Type (*n* = 58)	*p*
Age (median, range)	55.5 (13–83)	62.5 (16–87)	0.073	61 (26–83) #	62 (25–85) #	0.917
Males	59/80 (74%)	57/80 (71%)	0.860	43/58 (74.1%) #	43/58 (74.1%) #	1
Diabetes	25/80 (26%)	21/80 (31%)	0.601	20/58 (34.5%)	14/58 (24.1%)	0.308
Chronic respiratory diseases	13/80 (16%)	10/80 (13%)	0.653	9/58 (15.5%)	4/58 (6.9%)	0.238
Cardiovascular disease	44/80 (55%)	40/80 (50%)	0.635	30/58 (51.7%)	30/58 (51.7%)	1
Oncologic/hematologic disease/immunosuppressive medication	11/80 (14%)	16/80 (20%)	0.399	9/58 (15.5%)	12/58 (20.7%)	0.630
Liver disease	8/80 (10%)	4/80 (5%)	0.369	5/58 (8.6%)	3/58 (5.2%)	0.717

3.2. ICU Procedures and Outcomes in Full Patient Population (n = 160)

In total, 61 of the 80 patients (76%) in the Alpha variant group and 52 of the 80 (65%) patients in the WT group required mechanical ventilation (MV) during their ICU stay (p = 0.165). The median duration of MV was 16 days (range 2–61) in the Alpha variant group and 14 days (range 1–55) in the WT group (p = 0.814). Among ICU survivors, the median duration of ventilation was 11 days (range 3–61) in the Alpha variant group (n = 23) and 12 days (range 1–55) in the WT group (n = 18) (p = 0.814). Overall, 6 of the 80 patients (8%) in the Alpha variant group and 14 of 79 patients (29%) in the WT group received extracorporeal membrane oxygenation (ECMO) therapy (p = 0.365). In total, 17 of 77 patients (22%) in the Alpha variant group and 23 of the 80 patients (29%) in the WT group required renal replacement therapy (RRT) (p = 0.365). Data regarding ECMO and RRT could not be obtained for one and three patients, respectively.

Overall, 41 of the 80 patients (51%) in the Alpha variant group and 35 of the 80 patients (44%) in the WT group survived the ICU stay (p = 0.429). The data showed that 33 of the 75 patients (44%) in the Alpha variant group and 34 of the 80 patients (43%) in the WT group survived the hospital stay (p = 0.872); no data regarding the hospital survival could be obtained for five patients in the Alpha variant group. In total, 36 of 71 patients (51%) in the Alpha variant group and 36 of 79 patients (46%) in the WT group were still alive 28 days after initial admission to the ICU (p = 0.624); no data on 28-day survival could be obtained for nine patients in the Alpha variant group and one patient in the WT group. **Table 2** and **Figure 1** show the data regarding the ICU stay and outcomes in the Alpha variant and WT group, both for the full patient population and the matched-pair analysis.

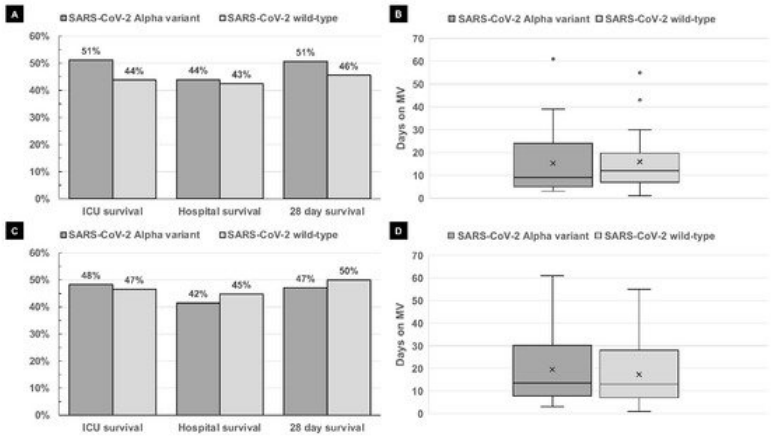

Figure 1. (**A**) ICU survival, hospital survival and 28-day survival in the full patient population in the SARS-CoV-2 Alpha variant group and SARS-CoV-2 wild-type group (n = 80 each). (**B**) Duration of mechanical ventilation (MV) in days of the entire patient population in the SARS-CoV2 Alpha group and SARS-CoV2 wild-type group (n = 80 each); X = mean; line inside the box marks the median; the bottom and top of the box correspond to the upper and lower quartiles, respectively; upper and lower whiskers correspond 1.5 times the interquartile range. (**C**) ICU survival, hospital survival and 28-day survival of the matched-pair analysis in the SARS-CoV-2 Alpha variant group and SARS-CoV-2 wild-type group (n = 58 each). (**D**) Duration of mechanical ventilation (MV) in days of the matched-pair analysis in the SARS-CoV-2 Alpha variant group and SARS-CoV-2 wild-type group (n = 58 each); X = mean; line inside the box marks the median; the bottom and

top of the box correspond to the upper and lower quartiles, respectively; upper and lower whiskers correspond to 1.5 times the interquartile range. No significant differences were detected between the SARS-CoV-2 Alpha variant group and the SARS-CoV-2 wild-type group in any of the illustrated analyses.

Table 2. Outcome and ICU-specific therapies both in the full patient population as well as in the matched-pair analysis (sex, age). No significant differences were identified between the SARS-CoV2 Alpha variant group and the SARS-CoV2 wild-type group. MV = mechanical ventilation; NIV = non-invasive ventilation; HFNO = high-flow nasal oxygen.

	Full Patient Population (*n* = 160)			**Matched-Pair Analysis (*n* = 116)**		
	Alpha (*n* = 80)	**Wild Type (*n* = 80)**	***p***	**Alpha (*n* = 58)**	**Wild Type (*n* = 58)**	***p***
ICU survival	**41/80 (51%)**	**35/80 (44%)**	**0.429**	**28/58 (48%)**	**27/58 (47%)**	**1**
Hospital survival	**33/75 (44%)**	**34/80 (43%)**	**0.872**	**22/53 (42%)**	**26/58 (45%)**	**0.848**
28-day survival	**36/71 (51%)**	**36/79 (46%)**	**0.624**	**24/51 (47.1%)**	**29/58 (50%)**	**0.848**
Mechanical ventilation	**61/80 (76%)**	**52/80 (65%)**	**0.165**	**45/58 (78%)**	**38/58 (66%)**	**0.217**
Duration of mechanical ventilation (days) (median, range)	**16 (2–61)**	**14 (1–55)**	**0.814**	**16 (2–61)**	**14.5 (1–55)**	**0.694**
Duration of mechanical ventilation of ICU survivors (days) (median, range)	**11 (3–61) [*n* = 23]**	**12 (1–55) [*n* = 18]**	**0.814**	**13.5 (3–61) [*n* = 28]**	**13 (1–55) [*n* = 15]**	**0.694**
Duration of NIV/HFNO in patients with no MV (days) (median, range)	**6 (2–14) [*n*= 16]**	**5.5 (1–20) [*n* = 16]**	**0.934**	**5 (2–9) [*n* = 11]**	**4 (1–13) [*n* = 11]**	**0.844**
ECMO	**6/80 (8%)**	**14/79 (18%)**	**0.059**	**10/58 (17%)**	**6/58 (10%)**	**0.420**
Renal replacement therapy	**17/77 (22%)**	**23/80 (29%)**	**0.365**	**13/56 (23%)**	**17/58 (29%)**	**0.526**

4. Conclusions

In summary, mortality among patients with severe COVID-19 treated in the ICU remains high. Recently, more younger patients have required intensive care treatment. Whether the reasons for this development are changes in the transmissibility due to viral variants, the advancing vaccination campaign, and/or the virus spread in a younger segment of the population remains uncertain. At present, the impact of SARS-CoV-2 variants on the severity of the disease as well as on ICU mortality has not been elucidated. However, in the present age- and sex-matched analysis, no significant differences with respect to clinical course and mortality in intensive care units between the SARS-CoV-2 Alpha variant and the SARS -CoV-2 WT were detected.

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