The SARS-CoV-2 B.1.1.7 variant and increased clinical severity – the jury is out

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Dear Editor,

Frampton et al. demonstrate an increased viral load, but not severity of disease or 28-day mortality in hospitalised patients infected by the B.1.1.7 variant of the SARS Cov-2 virus.[1] In contrast, we found slightly different results when assessing the risk of morbidity and mortality in a matched case-control study of 60 patients – 30 hospitalised by infection with the B.1.1.7 variant and 30 patients by non-B.1.1.7 variants. Cases were matched for admission period and age band. Clinical severity scores, requirement for ventilation, treatments received and 28-day mortality were compared between groups from anonymised retrospective data, using Wilcoxon rank sum and Chi-squared or Fisher's exact tests.

Our findings (Table 1) showed consistent and rational evidence that patients infected with the B.1.1.7 variant developed more serious disease - higher clinical severity (e.g., higher NEWS value, lower ROX index), higher levels of supplemental oxygen requirement and mechanical ventilation, more often received approved treatments for SARS CoV-2 infection (e.g., dexamethasone, remdesivir and tocilizumab) and more serious clinical outcomes (i.e., higher 28-day mortality, WHO clinical progression scale). Although our results show a tendency towards severe disease with B.1.1.7 infection , it is likely that our study was under-powered as statistical significance was only achieved for more patients requiring dexamethasone in the B.1.1.7 variant group. Nevertheless, they echo the findings of Challen et al., who studied a younger population with likely less comorbidity and found a 64% increase in 28-day mortality following community infection with the B.1.1.7 variant (control group, 0·26%; B.1.1.7 variant group, 0·41%).[2]

We believe that the identification of any increased morbidity and mortality risks caused by SARS-CoV-2 variants of concern requires adequately powered studies utilising a combination of community and hospital PCR swabs, examination of disease severity using more detailed clinical severity scores with physiological measures and the impact of viral load, novel treatments and vaccinations. For the purposes of future case-control studies, we estimate a post-hoc sample size of 234 patients in each group is required for an effect size of +11·4% on 28-day mortality for a baseline of 20·7% at 80% power with 5% significance. We propose the jury for mortality risk for B.1.1.7 infections currently requires more time and data for its final deliberation.

References

1. Frampton D, Rampling T, Cross A, et al. Genomic characteristics and clinical effect of the emergent SARS-CoV-2 B.1.1.7 lineage in London, UK: a whole-genome sequencing and hospital-based cohort study. Lancet Infect Dis. 2021 Apr 12:S1473-3099(21)00170-5.
2. Challen R, Brooks-Pollock E, Read JM, Dyson L, Tsaneva-Atanasova K, Danon L. Risk of mortality in patients infected with SARS-CoV-2 variant of concern 202012/1: matched cohort study BMJ 2021; 372 :n579.

Table 1. Summary of results between cases of SARS-Cov-2 infection with B.1.1.7 variant compared to non-B.1.1.7 variants.

	n	Infection with B.1.1.7 variant	n	Infection with a non-B.1.1.7 variant	p-value
Demographics					
Date of first positive PCR swab	30	03/12/20 – 20/12/20	30	10/10/20 – 20/12/20	
Age (years)		77 (59-88)		79 (59-87)	0·976
Male sex (%)		50%		60%	0·436
Number of comorbidities		2 (1-3)		2 (1-3)	0·845
White ethnicity (%)		26/30 (87%)		30/30 (100%)	
Clinical severity scores					
National Early Warning Score 2 (NEWS2)*:					
At presentation	30	4 (2-7)	30	2.5 (1-6)	0·135
Maximum value	30	6 (4-8)	30	5 (3-9)	0·345
ROX index:					
At presentation	30	20 (15-26)	30	24 (15-27)	0·371
At maximum F_iO_2	25	15 (11-21)	26	18 (13-26)	0.341
Sequential Organ Failure Assessment (SOFA) score:					
At presentation	30	3·0 (2-7)	30	3·5 (2-6)	0·858
At maximum F_iO_2	30	5·5 (2-7)	30	5·0 (2-7)	0·566
4C Mortality Score:					
At presentation	30	12·0 (9·0-14·8)	30	10·5 (9·0-14·0)	0·568
At maximum F_iO_2	30	12·5 (8·3-14·0)	30	11·5 (9·0-13·0)	0·463
Maximum ventilatory support received	30		30		0·265
Mechanical ventilation		10·0%		3·3%	
Non-invasive ventilation		0·0%		3·3%	
Standard oxygen therapy		60·0%		46·7%	
No supplemental oxygen required		30·0%		46·7%	
Treatment received					
Dexamethasone	18	13 (72·2%)	24	10 (41·7%)	0·049**
Remdesivir	14	2 (14·3%)	22	1 (4·6%)	0·547
Anticoagulation	24	4 (16·7%)	30	8 (26·6%)	0·380

Tocilizumab	28	1 (3·6%)	28	0 (0·0%)	1·000
28-day mortality (95% confidence interval)	28	32·1% (17·9-50·7%)	29	20·7% (9·8-38·4%)	0·326
Patients with a severe clinical outcome (%)[$] [$] WHO scale by day 14 after symptom onset or after first positive SARS-CoV-2 PCR of at least 6 or patient death within 28 days.		11/30 (36·7%)		8/30 (26.7%)	0·405

Unless stated, all results are the median (interquartile range).
F_iO_2 = fraction of inspired oxygen)
* The NEWS2 score was not calculated at maximum F_iO_2.
** indicates a statistically significant result.