Dysfunctional neutrophil response in COVID-19 infection vary by subtype

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Background

The global COVID-19 pandemic has significantly evolved since first identified in November 2019. Viral antigenic shift has seen the emergence of several new strains leading to spikes in infection. Transmissibility has increased with each emerging strain, corresponding with a decrease in overall mortality. We have previously demonstrated dysfunctional neutrophil responses in COVID-19 patients compared to community acquired pneumonia control.[1] Here we aimed to correlate strain severity with change in underlying neutrophil function.

Methods

Patients were recruited between January 2021 and May 2022 from the Queen Elizabeth Hospital in Birmingham. Patients

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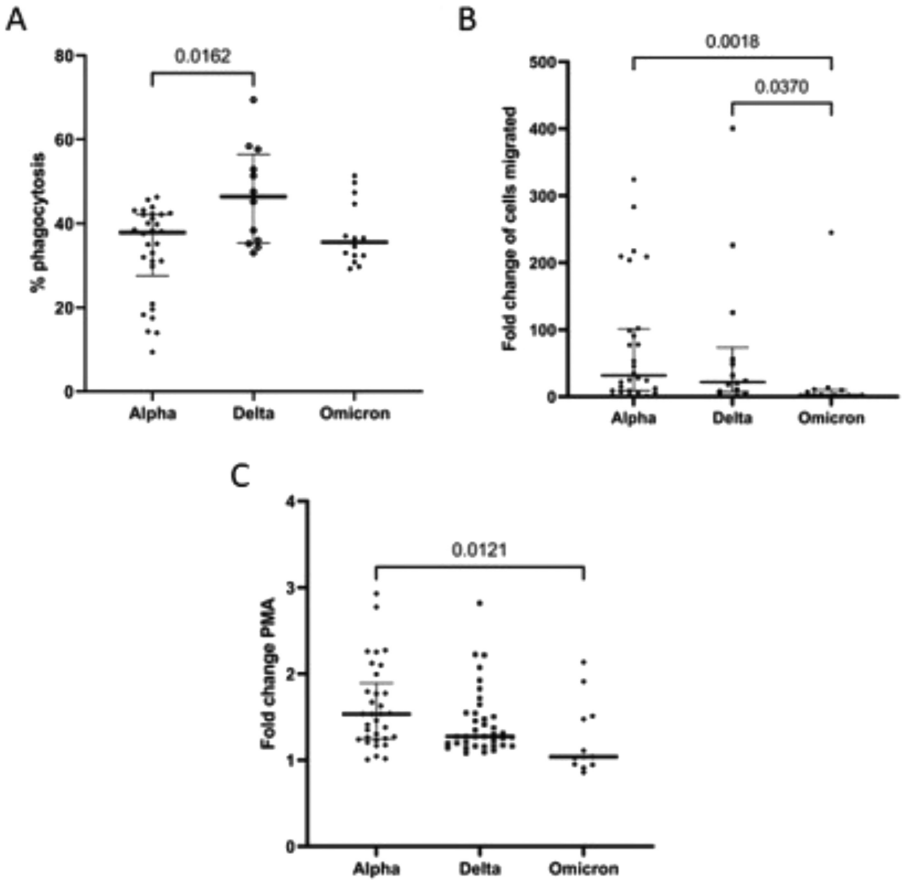

Fig 1. Variations in neutrophil function and phenotype between variants of COVID-19 infection.

were recruited if not admitted to the ITU. 33 patients presented infection with alpha COVID-19, 13 delta COVID-19 and 14 omicron COVID-19 infections. Neutrophils were isolated from whole blood. Phagocytosis of labelled *Streptococcus pneumoniae*, transwell migration towards IL-8, neutrophil extracellular trap (NETosis) formation and surface extracellular marker expression were analysed.

Results

There were no significant differences in demographics between patients recruited for different variants. Patients infected with the alpha variant had significantly raised CRP compared to omicron patients ($p=0.0427$). Phagocytosis was significantly increased between alpha and delta variants (Fig 1A). Transwell migration was significantly reduced in omicron patients compared to the other variants (Fig 1B). There was reduction in neutrophil extracellular trap in omicron patients compared to alpha variant patients (Fig 1C). Compared with alpha patients, neutrophils from omicron patients had reduced expression of CD10 ($p=0.0004$), CD54 ($p=0.0015$), CD62L ($p=0.0013$) and CD11c ($p<0.0001$). CXCR2 expression was higher in neutrophils from omicron patients ($p=0.0001$), while there was no difference in CD11b, CXCR4, PD-L1 and CD66b expression.

Discussion

Our results showing changes in neutrophil function and phenotype differ between variants of COVID-19 infection, potentially reflect viral evolution. This change in neutrophil function may contribute to the evolving clinical phenotype observed in patients. Our population of ward-based COVID-19 patients represents the majority of inpatient hospital burden where early intervention may prevent clinical deterioration. Targeting neutrophil function may be an effective way of improving infection outcome in the future.

Reference

1 Belchamber K *et al*. Altered neutrophil phenotype and function in non-ICU hospitalised COVID-19 patients correlated with disease severity. *medRxiv* 2021:2021.06.08.21258535.