represents in healthy newborns, whether it is related to changing pulmonary vascular resistance, changes in intracardiac or extracardiac shunts, fluid shifts, or all of these processes in concert.

With respect to the statistical analyses performed and our sample size, we created our hypothesis regarding differences in BNP trajectory based on our clinical experience and performed exploratory analyses based on this hypothesis. It is our practice to conduct power analyses in the context of negative findings to ensure that we have not encountered false-negative results. In the receiver operating characteristic curve analyses, we identify robust findings in the accuracy of BNP for prediction of clinical outcome during weeks 3 through 5, with cut-off values that maximize the percent correctly classified, and sensitivity and specificity without bias toward either measure. Despite our sample size, the positive findings for these weeks negates the potential for false-negative results. We are overall reassured that our findings are robust to multiple different analytic approaches.

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Coronavirus disease 2019, multisystem inflammatory syndrome in children, apolipoprotein E4, and race

To the Editor:

Kaushik et al presented a series of 33 children from New York City hospitals diagnosed with multisystem inflammatory syndrome in children (MIS-C); 81% had antibodies to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] Similarly, Carter et al, reported on a series of 25 children diagnosed with MIS-C from the United Kingdom; 68% were SARS-CoV-2 seropositive.[2] The children in both groups exhibited a cytokine profile consistent with a robust innate immune response. At the same time, emerging evidence suggests the hypothesis that the apolipoprotein E4 (apoE4) genotype can predict coronavirus disease 2019 (COVID-19) severity in adults.[3,4] Accordingly, we propose the hypothesis that the apoE4 genotype may identify children at increased risk of developing MIS-C from SARS-CoV-2 infection.

Classically, the apoE4 genotype has been associated with cardiovascular disease and Alzheimer's disease[5]; however, it has also been associated with an enhanced in vivo innate immune response.[6] Notably, individuals of African descent may have twice the frequency of the ε4 allele (30%-40%) compared with those of European or Asian descent,[7] and therefore, they may be more likely to exhibit a stronger innate immune response to the SARS-CoV-2 infection.

In the series presented by Carter et al, the children who were SARS-CoV-2 seropositive exhibited more severe disease; 8 of 9 black children compared with 5 of 10 white children in the series were SARS-CoV-2 seropositive.[2] Of 21 patients with a depressed systolic ventricular function in the report by Kaushik et al, 11 were black and 1 white (Table 4).[1] This suggests an overrepresentation of black children diagnosed with MIS-C from severe SARS-CoV-2 infection.

Therefore, as seen with adults, the apoE4 genotype may identify children at a greater risk of severe SARS-CoV-2 infection; and in particular, MIS-C.

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