How does COVID-19 Associated Coagulopathy relate to severity of illness?

Introduction

Thromboembolic events in children have been on the rise – over the last two decades the rate of venothromboembolism (VTE) in hospitalized patients has increased by 211%.[1] Significant morbidity (such as stroke, pulmonary embolus, infection) and mortality has been associated with thrombotic events in children. While there is no single reason why the rate of VTE is on the rise, the incidence continues to increase despite efforts to prevent thrombotic events from occurring[1]

Acute COVID-19 infection and Multisystem Inflammatory Syndrome in Children (MIS-C) associated with previous COVID-19 infection were both quickly identified to increase a patient's risk of thrombosis.[4] Increased risk for thrombosis is a result of immune-thrombotic phenotype called COVID-19-associated coagulopathy (CAC)[5]. CAC typically presents with extremely elevated D-dimer, modest decrease in platelet count, mild prolongation of prothrombin time and elevation of fibrinogen. One cohort study showed the incidence of thrombosis in MIS-C patients to be as high as 6.5% and in symptomatic COVID-19 patients to be 2.5% - both of which are higher incidences of thrombosis than previously reported for both non-critically ill and critically ill children[2,6]. When the MIS-C patients were further stratified by age, the cohort of patients > 12years had a thrombotic event incidence of 19%.[2]

No clear recommendations exist to risk stratify pediatric patients with COVID-19 or MIS-C based on risk of a thrombotic event to determine need for prophylaxis. Some experts have recommended an assessment of severity of illness while others advised to follow laboratory markers (such as c-reactive protein or CRP) or a combination of the two[3,4]. Of note, in the initial cohort study, 71% of the thrombotic events identified happened despite thromboprophylaxis indicating persistent gaps in understanding severity of coagulopathy in children with acute COVID-19 or MIS-C.[2]

Methods

Data was collected through a retrospective chart review of all Acute COVID-19 and MIS-C patients admitted to St. Christopher's Hospital for children from April 2020 to April 2022. Patients were excluded if they had been receiving anticoagulation therapy for any reason prior to admission. If they did not receive any lab-work associated with their admission, they were excluded from the laboratory analysis.

Results

A total of 209 patients were included in the study, 128 with Acute COVID-19 and 82 with MIS-C. 72 Acute COVID-19 patients had mild disease (admitted with COVID-19), 23 had moderate disease (an O2 requirement without an ICU stay), and 32 had severe disease (required an ICU stay). 64 MIS-C patients had moderate disease (admitted with MIS-C), and 17 had severe disease (required an ICU stay). Mean difference between d-dimer values between mild,

moderate, and severe Acute COVID-19 patients was not statistically significant with a $p = 0.109$ using an ANOVA test. Mean difference between d-dimer values between moderate and severe MIS-C patients was statistically significant with a two sided $p < 0.001$ using an independent t-test. D-dimer and CRP values in Acute COVID-19 had a correlation of $r = 0.453$ with a $p < 0.001$; in MIS-C they had a correlation of $r = 0.210$ with a $p = 0.062$.

Conclusions

Severity of illness using our designation was not statistically significant for severity of coagulopathy in Acute COVID-19 patients but was significant in MIS-C patients. Additionally, CRP was significantly correlated with severity of coagulopathy in Acute COVID-19 patients but not MIS-C patients.

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