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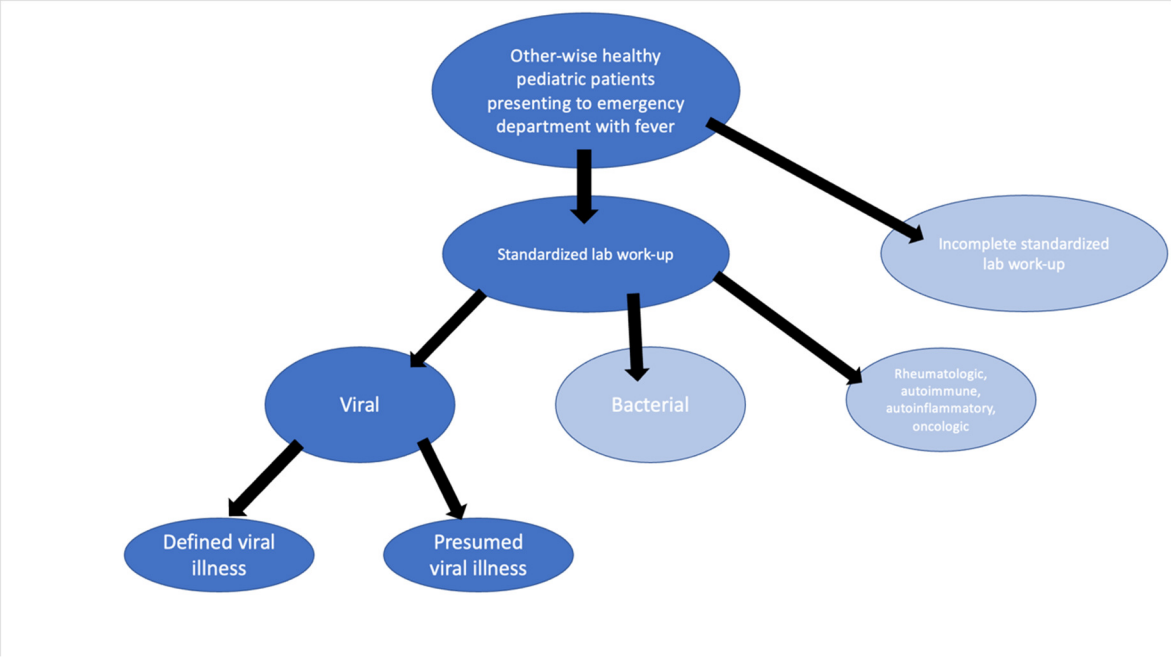
Aim:
To define the laboratory profile of non-traditional biomarkers of inflammation in febrile pediatric patients presenting to the emergency department with a viral illness

Background:
Fever is among one of the most common chief complaints in the pediatric emergency department (ED).[1] Pediatric fever typically signifies systemic inflammation that is usually associated with an infectious etiology, most commonly viral infection.[2] For patients presenting with fever who undergo a laboratory evaluation, typical biomarkers of inflammation typically obtained include white blood cell count, c-reactive protein, erythrocyte sedimentation rate, and procalcitonin.[3] With the emergence of multi-system inflammatory syndrome in children (MIS-C), clinicians in EDs have also frequently obtained a host of non-traditional biomarkers of inflammation and end-organ involvement in children with fever, most of whom do not have MISC. These non-traditional biomarkers include fibrinogen, d-dimer, ferritin, lactic acid dehydrogenase (LDH), and interleukin 6 (IL-6), as well as cardiac biomarkers BNP or NT-pro-BNP and troponin. There is little prior data regarding the spectrum of values of these non-traditional biomarkers in children with typical febrile illnesses due to viruses. Therefore, we have a unique opportunity to define an expected laboratory profile of non-traditional biomarkers in this patient population. This data could allow clinicians to use these non-traditional markers to aid in diagnosis and possibly trend values for those admitted to the hospital in order to track disease course.

Study design: Retrospective review

Study subjects:
Otherwise healthy children 2 months to 20 years of age presenting to the ED with fever who had laboratory evaluation for MIS-C. We excluded patients who were ultimately diagnosed with MIS-C, Kawasaki disease or rheumatologic processes, auto-immune, auto-inflammatory, or oncologic conditions during that emergency department visit. We also excluded patients with known or presumed bacterial infection. We studied patients with defined viral illness (by laboratory diagnosis) and presumed viral illness (by clinical diagnosis).



Main outcomes/measurements:

- Spectrum of laboratory values including ferritin, fibrinogen, d-dimer, pro-BNP, and troponin in patients with defined/presumed viral illness.
- Mean and standard deviation of each biomarker for our cohort
- Expected standard deviation from normal laboratory values established by our institution's laboratory that can be expected in this cohort of patients

Methods:

We conducted a retrospective study of children presenting to the ED who were evaluated for MIS-C during the SARS-CoV-2 period between 4/15/20-10/31/2020.
Eligible children were identified by retrospective review of children presenting to the ED for evaluation of fever during the study period and for whom a NT-pro-B-type Natriuretic Peptide (NT-pro-BNP) or troponin was performed. During this time period, our hospital guidelines recommended the use of specific laboratory tests, including NT-pro-BNP and troponin, for all children being evaluated in the ED for MIS-C. Inclusion criteria included previously healthy patients, age 2 months-20 years, and emergency department diagnosis of presumed virus (either by confirmatory laboratory test or clinical diagnosis). Institutional review board approval was obtained with a waiver of written informed consent.

Laboratory values for fibrinogen, d-dimer, ferritin, LDH, IL-6, troponin, and pro-BNP will be collected for each patient. We will aim to create a normal distribution of values for each biomarker. The range of normal values as defined by our institution's laboratory will serve as the control group. We will then use the mean for each biomarker and compare the mean of the control group and perform an unpaired t-test between the two groups.

Limitations:
Our study only includes the subset of patients who underwent complete laboratory evaluation for MIS-C. We do not include all patients who present to the emergency department with the very common chief complaint of fever due to viral illness. Most patients who present to the emergency department with fever due to viral illness did not meet the clinical picture of MIS-C as defined by the clinician, and therefore did not undergo this laboratory evaluation. Consequently, we are only able to define the spectrum of laboratory values in patients who had a similar enough phenotype to those patients with MIS-C to be deemed by clinicians eligible to undergo the complete standardized MIS-C laboratory work-up. Furthermore, there is variation by emergency department clinician as to which patients undergo the complete work-up, and therefore who is included as our study subjects.

References:

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