ORIGINAL RESEARCH

Exploring inflammatory markers and clinical associations in pediatric sars-cov-2 infection

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Received: 24 October, 2023 Accepted: 28 November, 2023

ABSTRACT

Background and Objectives: The emergence of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to a global pandemic, resulting in significant and far-reaching consequences on life worldwide. Notably, the introduction of new viral variants has brought about clinical manifestations in the paediatric population, some of which exhibit a severe progression. This study aimed to identify essential laboratory parameters crucial for the delineation of an effective therapeutic approach in paediatric patients. **Methods:** A cohort of 73 paediatric patients meeting the inclusion criteria was selected for this study. Following confirmation of the COVID-19 diagnosis, a thorough analysis of laboratory parameters was conducted, and their correlation with the severity of the illness was examined. **Results:** Thrombocytopenia, leukocytosis, and lymphopenia demonstrated significant associations with the severity of the disease. Furthermore, vigilant monitoring of D-dimer values was undertaken due to its high correlation with an unfavourable prognosis and the development of a severe form of the disease. **Conclusion:** This study underscores the utility of D-dimer values and a complete blood count as indispensable parameters in the evaluation of COVID-19 in children. These findings contribute valuable insights into potential avenues for effective therapeutic interventions.

Key Words: Child, SARS-CoV-2, leukocytosis, D-dimers, COVID-19.

INTRODUCTION

Clinically, COVID-19 presents with a spectrum of symptoms, with fever and respiratory manifestations being the most prevalent. While approximately one-third of cases are asymptomatic, the remaining cases are categorized as mild, moderate, severe, or critical. In comparison to adults, pediatric patients generally exhibit milder forms of COVID-19 [1]. However, studies suggest a more pronounced deterioration in children than initially reported and expected. Clinical presentations in most pediatric cases align closely with those observed in adults. Less frequently reported signs in the literature include crepitations, sputum, abdominal pain, lymphadenopathy, cyanosis, and hypoxemia [2-5]. Additionally, rare complications such as purpuric rashes, multisystem inflammatory syndrome in children (MIS-C), and chilblain-like lesions (CLLS) have been documented [6-10].

In conjunction with clinical manifestations, a comprehensive assessment of laboratory markers is imperative, reflecting changes based on the context and the progression of the inflammatory process. Patients infected with SARS-CoV-2 typically exhibit elevated levels of D-dimers, C-reactive protein, white blood cells, neutrophils, and lymphocyte count [28]. A meta-analysis conducted by Qui et al. (2021), encompassing 37 articles and 2,874 children with COVID-19, identified lymphopenia, leukopenia, elevated C-reactive protein, increased alanine transaminase, and leukocytosis with elevated aspartate aminotransferase as the most frequently altered laboratory markers. D-dimer elevation was reported in 11 studies [11].

MATERIAL AND METHODS

An observational study was conducted within the paediatricunit of a tertiary care hospital in India, involving the selection of 73 cases for study inclusion. The inclusion criterion centred on the confirmed diagnosis of COVID-19, with the exclusion of cases presenting oncological and haematological comorbidities.

Virus diagnosis entailed the identification of the antigen (utilizing a rapid test) or the ribonucleic acid (RNA) [Real-time polymerase chain reaction (RT-PCR) assay] of SARS-CoV-2. All specimens were procured within the initial two hours of hospital admission, employing a Rapid Antigen kit for SARS-CoV-2 antigen detection.

The automated Haematology Analyser was used for the measurement of a complete blood count from venous blood samples. Furthermore, D-dimers in plasma samples were scrutinized using an automated analyser.

In the classification of severe forms of COVID-19 in children, distinct categories were delineated as follows: the asymptomatic form involves the identification of viral antigen or RNA SARS-CoV-2 in the nasopharyngeal sample. The mild form is characterized by general and/or respiratory tract features without pulmonary involvement. The moderate form encompasses general and/or respiratory tract manifestations, combined with pulmonary involvement (either clinical or imaging), and requires an oxygen saturation (SpO2) of ≥94% on room air. Finally, the severe form is defined by oxygen saturation (SpO2) level below 94% on room air, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) less than 300 mm Hg, a respiratory rate exceeding 30 breaths per minute, or lung infiltrates exceeding 50%. These distinctions serve as valuable parameters for the comprehensive evaluation and categorization of severe COVID-19 cases in the paediatric population.

RESULTS

Table 1 outlines the clinico-demographic parameters of the study participants. The mean age is reported as 6.80 ± 3.87. The gender distribution shows the number and percentage of male and female participants, providing insights into the composition of the study population. Additionally, the table presents the prevalence of specific clinical features such as fever, hepatomegaly, and splenomegaly.

Table 2 in the results section of the research article provides an overview of the laboratory parameters of the study participants. The table includes various hematological and biochemical markers along with their respective mean values and standard deviations.

Table 1: Clinico-demographic parameters of study participants

Parameter	n	%
Age (Mean ± SD)	6.80 ± 3.87	
Male	33	45.21
Female	40	54.79
Fever	57	78.08
Hepatomegaly	27	36.99
Splenomegaly	24	32.88

Table 2: Laboratory parameters of study participants

Parameter	Mean ± SD
Hemoglobin	8.71 ± 1.91
Total Leukocyte Count (TLC)	13389.44 ± 7062.57
Neutrophil Count	60.18 ± 14.94
Lymphocyte Count	31.92 ± 13.08
N/L Ratio	2.50 ± 1.72
COVID IgM	142.30 ± 514.31
Platelets	134748.57 ± 122675.42
D-Dimer	3504.94 ± 2593.77

DISCUSSION

During the years of the COVID-19 pandemic, pediatric patients initially received insufficient attention. However, the emergence of more Variant of Concerns (VOCs) made it inevitable to focus on the specificities of pediatric cases. The COVID-19 pandemic continues to pose a significant threat, and there remains a substantial need for further research to comprehensively understand the extent of this virus and its implications and manifestations in pediatric patients [1].

Paraclinical markers, such as NLR, leukocyte counts, and neutrophils, along with the inflammatory syndrome, serve as early indicators to identify the etiologies of various infectious diseases. Leukopenia has been documented in cases of severe coronavirus infection in humans, contrasting with common human coronaviruses that cause flu-like symptoms. Notably, in this study, individuals above 12 years old exhibited leukopenia, potentially influenced by the onset of puberty. The existing literature lacks sufficient information regarding the role of leukopenia as a prognostic factor for pediatric patients [12-13].

NLR is considered indicative of an unfavorable outcome in pediatric patients. A retrospective study by Ciccullo et al. in March 2020, involving 74 patients with COVID-19, revealed that a median NLR value of approximately 4.5 was correlated with illness

severity and poor outcomes. In this study, NLR values above 3 were predominantly observed in the group aged above 12 years, a variation dependent on individual factors and possibly linked to the onset of puberty. NLR serves as a parameter through which clinicians can assess the body's stress at a given moment [13-15].

Lymphopenia is commonly observed in viral infections due to the virus's impact on the immune system and the destruction of CD4+ cells, leading to reduced cytokine levels that protect against various pathogens [48]. However, a study by Guang et al., involving 66 cases, reported no significant changes in lymphocytic values for prognosis or differentiation between mild, moderate, or severe illness [16]. Discrepancies between this study and Guang et al.'s study may be attributed to the small number of patients and age differences.

The present study identified neutropenia at an increased rate of 17.5%, exceeding the approximately 7.6% rate reported in the medical literature for neutropenia in COVID-19 pediatric patients. Neutrophilia was prevalent, especially in patients aged above 12 years, although it was not correlated with the disease form. Elevated D-dimer values were statistically significantly more prevalent in the age group above 12 years, with minor differences from other age groups. However, this difference might also be attributed to the dynamic nature of puberty [17-19]. Strengths and weaknesses of the study can be discussed. A limitation is the absence of an examination of the effect of different viral variants on the monitored laboratory parameters. Future research should consider a larger cohort from various hospitals and include the identification of virus variants. Such studies could establish distinct blood panels for each variant, aiding in determining the risk of severe disease with potential future complications.

CONCLUSION

COVID-19 continues to pose a significant health challenge, necessitating extensive research and the development of protocols. In light of this, the current study suggests the monitoring of D-dimers, neutrophils, platelets, and lymphocytes as essential elements in determining the prognosis of the disease. Notably, Neutrophil-to-Lymphocyte Ratio (NLR) emerges as a potential predictor of a poor prognosis.

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