

Original Research Article

CONCURRENT SCRUB TYPHUS AND COVID-19 INFECTION IN PAEDIATRIC PATIENTS: A DIAGNOSTIC PUZZLE

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ABSTRACT

The pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has brought to light a novel condition known as multisystem inflammatory syndrome in children (MIS-C). In regions with developing healthcare systems, pediatricians need to be vigilant regarding the resemblances between MIS-C and other tropical fevers, including scrub typhus. It is imperative not only to remain alert in order to differentiate and exclude tropical diseases but also to administer appropriate treatments such as steroids or immunomodulatory medications. This concern is heightened as the exclusive use of steroids or immunomodulatory treatment, in the absence of detecting rickettsial or bacterial infections through cultures and serology, can potentially lead to fatal outcomes.

Key Words: Child, Scrub typhus, severe acute respiratory syndrome, COVID 19.

1. INTRODUCTION

Scrub typhus is a febrile infection induced by *Orientia tsutsugamushi*, a gram-negative coccobacillus, transmitted via the bite of an infected larval trombiculid mite. This infection has been documented globally, including in India [1-4], primarily during the summer and autumn in rural areas. A crucial aspect of diagnosis involves distinguishing it from other endemic febrile illnesses, aligning with compatible clinical signs, symptoms, laboratory findings, and epidemiologic indicators, such as recent exposure to areas where chiggers are suspected.

The disease's histological hallmark is lymphohistiocytic vasculitis, characterized by extensive vascular dysfunction and endothelial damage. In recent times, a severe condition known as multisystem inflammatory syndrome in children (MIS-C) has been identified among patients who tested positive for coronavirus disease-2019 (COVID-19) (via PCR or serology) or exhibited epidemiological linkages to COVID-19 [5-7]. MIS-C seems to result from an

exaggerated immune response linked to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), presenting symptoms such as persistent fever, hyperinflammation, and complications affecting the cardiac, gastrointestinal, renal, hematologic, dermatologic, and neurologic systems. This study delves into the clinical characteristics, laboratory data, and treatment management of pediatric scrub typhus patients exhibiting as MIS-C in an Indian hospital.

2. MATERIAL AND METHODS

A comprehensive investigation was conducted on children admitted to the PICU of a tertiary care teaching hospital in central India. The cohort presented with unexplained fever and symptoms indicative of multisystemic involvement. The diagnostic protocol included testing for COVID nucleic acid amplification tests (NAAT) and serological assessments for COVID, scrub typhus, dengue, typhoid, as well as malaria. Additionally, blood and urine cultures were performed to identify bacterial infections.

Retrospective analysis was carried out on the hospital records of patients meeting the criteria of positive Scrub IgM ELISA serology, coupled with symptoms, signs, and laboratory markers consistent with systemic hyper inflammatory disease. This investigation aims to shed light on the clinical characteristics, laboratory findings, treatment strategies employed, and the ultimate outcomes of pediatric patients facing the dual challenge of unexplained fever and multisystemic involvement in the specified timeframe and geographical location.

3. RESULTS

Table 1 presents the clinico-demographic characteristics of the study participants. A total of 73 individuals were enrolled, with 40 (54.79%) being female and 33 (45.21%) male. The prevalence of fever was observed in 57 participants, accounting for 78.08% of the cohort. Additionally, hepatomegaly and splenomegaly were noted in 27 (36.99%) and 24 (32.88%) participants, respectively. The average age of the study population was calculated as 6.80 years, with a standard deviation (SD) of 3.87.

Table 2 outlines the laboratory parameters assessed in the study participants. 43 individuals (58.90%) tested positive for Scrub Typhus. The mean concentration of COVID IgM was determined to be 142.30 units, providing insights into the immune response among the participants. Hematological parameters revealed an average hemoglobin level of 8.71 ± 1.91 g/dL. Neutrophil and lymphocyte counts were recorded at $60.18 \pm 14.94\%$ and $31.92 \pm 13.08\%$, respectively. The neutrophil-to-lymphocyte (N/L) ratio was calculated as 2.50 ± 1.72 , offering valuable information on the inflammatory status. Total leukocyte count (TLC) exhibited an average value of 13389.44 ± 7062.57 cells/mm³. Platelet count, a crucial indicator, displayed a mean value of 134748.57 ± 122675.42 /mm³. D-Dimer, a marker of coagulation activation, was recorded at 3504.94 ± 2593.77 ng/mL

Table 1: Clinico-demographic parameters of study participants

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

Table 2: Laboratory parameters of study participants

Parameter	Mean \pm SD
Scrub Typhus Positive	43 (58.90%)
COVID IgM	142.30 \pm 514.31
Hemoglobin	8.71 \pm 1.91
Neutrophil Count	60.18 \pm 14.94
Lymphocyte Count	31.92 \pm 13.08
N/L Ratio	2.50 \pm 1.72
Total Leukocyte Count (TLC)	13389.44 \pm 7062.57
Platelets	134748.57 \pm 122675.42
D-Dimer	3504.94 \pm 2593.77

4. DISCUSSION

According to early reports of SARS-CoV-2 patients, the sickness was more common and severe in elderly persons and people with comorbidities compared to children [8]. However, incidences of severe multisystem hyper inflammatory syndrome in children were shortly reported from a number of countries [6]. The World Health Organization (WHO) provided a case definition for MIS-C which include patients under 19 years of age with ≥ 3 days fever, laboratory evidence of inflammation, and involvement of two or more organ systems (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic, or neurological), with positive testing for SARS-CoV-2 indicating current or recent infection or COVID-19 exposure; and no other alternative plausible diagnoses [9]. With the ongoing COVID-19 pandemic, clinicians have been on the lookout for MIS-C; and in countries like ours, many tropical infections such as scrub typhus, leptospirosis, malaria, dengue, Kawasaki syndrome, and toxic shock syndrome have been close differential diagnoses in the initial 2–3 days when laboratory investigations for alternative diagnosis are not available.

In central India, postmonsoon months always see a spike in cases of scrub typhus among adults and children. Few critically sick children presented in shock with multiple organ dysfunction syndrome (MODS) and during the initial 2–3 days satisfied the case definition of MIS-C pending IgM enzyme linked immunoassay (ELISA) report for scrub typhus. We treated these children according to MIS-C protocol in addition to antibiotics for tropical infections including scrub. Recently, a case report of dengue presenting as MIS-C has also been published; therefore, tropical fevers in children should always be its close differential [10-12].

The presence of SARS-CoV-2 antibodies in scrub typhus patients might be attributed to community transmission of COVID infection. Given the likelihood of children harboring asymptomatic infections during the peak of the COVID pandemic, they may now exhibit serological evidence. This poses a concern, as relying solely on steroid or immunomodulatory treatment in the absence of detecting rickettsial or bacterial infection through cultures and serology can lead to fatal outcomes [9].

It is imperative to exercise vigilance in ruling out tropical infections and implementing appropriate treatment strategies, including the judicious use of steroids or immunomodulatory drugs in such patients. Historically, scrub typhus patients have presented with shock and multiple organ dysfunction syndrome (MODS), yet the hesitation to administer steroids and

immunomodulatory treatment for associated hyperinflammation persisted due to concerns about exacerbating the infection.

Within this study, we observed a favorable prognosis in scrub typhus patients exhibiting hyperinflammation when a treatment regimen combining steroids and intravenous immunoglobulin (IVIg) was employed in conjunction with doxycycline. In light of these encouraging findings, we advocate for the initiation of randomized controlled trials to establish the definitive role of steroids and immunomodulatory treatment in enhancing the outcomes of children with scrub typhus and presenting with hyper inflammation.

5. CONCLUSION

We observed a positive prognosis in individuals with scrub typhus and hyperinflammation when a therapeutic regimen combining steroids and IVIg was implemented alongside doxycycline. In light of these encouraging findings, we advocate for the initiation of randomized controlled trials to establish a conclusive understanding of the definitive role played by steroids and immunomodulatory treatment in enhancing the outcomes of children affected by scrub typhus and presenting with hyper inflammation.

6. REFERENCES

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