DOI: 10.7860/IJNMR/2022/53265.2340

Original Article

Paediatrics Section

Cutaneous Manifestations among Hospitalised COVID-19 Infected Children from Northern India: A Cross-sectional Study

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ABSTRACT

Introduction: Novel Coronavirus Disease-2019 (COVID-19) is caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). Besides the systemic manifestations, mucocutaneous involvement has also been reported with COVID-19. Reports suggest that the mucocutaneous manifestations may differ in children and adult patients.

Aim: To describe the prevalence and characteristics of cutaneous manifestations among COVID-19 infected children.

Materials and Methods: This descriptive cross-sectional study was undertaken in Shaheed Hasan Khan Mewati, Government Medical College and Hospital, Nuh, Haryana, India. Total 50 SARS-CoV-2 positive children, admitted during the study period (between July to December, 2020) and fulfilling inclusion criteria were screened for mucocutaneous manifestations. Findings were recorded on a predesigned proforma. The data was statistically analysed and significant association between findings was recorded.

Results: Total 50 (4.56%) children out of 1095 were positive for SARS-CoV-2 by Reverse Transcription Polymerase Chain Reaction (RT-PCR) test and were admitted in Isolation Ward. Male to female ratio was 3:2 in present study. Four children had cutaneous manifestation: maculopapular rash (3/50) and urticarial lesions (1/50). All four patients had mild to moderate severity of disease. None of the patient had mucosal involvement.

Conclusion: Appearance of dermatological findings among 8% of COVID-19 positive children warrants that all COVID-19 positive children should be screened for cutaneous findings.

Keywords: Coronavirus disease-2019, Maculopapular rash, Neonates, Urticarial lesions, Vasculopathic

INTRODUCTION

Novel COVID-19 is caused by SARS-CoV-2. The clinical spectrum of SARS-CoV-2 infection appears to be wide, encompassing asymptomatic infection, mild upper respiratory tract illness and severe viral pneumonia with respiratory failure and even death [1,2].

The viral S protein of SARS-CoV-2 interacts with Angiotensin-Converting Enzyme 2 (ACE-2) receptors which is most abundant on alveolar type II cell leading to pharyngeal congestion, pulmonary rales with or without pneumonia other then alveolar cells. The ACE-2 is also found on apical membranes of nasal, oral, nasopharyngeal and oropharyngeal mucosal epithelium, endothelial cells of blood vessels and heart, renal tubules and enterocytes in small intestine, contributing to development of extra pulmonary symptoms [1,2]. Besides the systemic manifestations, skin involvement has also been reported as a part of this viral infection. Various studies and case reports about dermatological manifestations among adults suffering from COVID-19 have been described in literature though data about skin manifestations related to COVID-19 in paediatric patients is comparatively scarce [3-6].

From the beginning of the COVID-19 pandemic, it has become evident that the clinical spectrum of disease in children is different from those seen in an adult which is usually milder in course. The possible mechanism could be the innate immune cells in children are in more activated state following initial antigen stimulation (infections or vaccination) leading to enhanced transcription of Interleukin (IL)-1β, IL-6 and Tumour Necrosis Factor--α genes). In addition, presence of cross-reactive antibodies (CR3022) following coronavirus infection (as upper respiratory infection in children) targeting highly conserved domain of SARS-CoV-1 and SARS-CoV-2 and good regenerative capacity of alveolar cells in children [7].

Most of the published articles are in form of case reports or case series mentioning various skin lesions like chilblain-like acral lesion, erythema multiforme, urticaria etc [8,9]. This cross-sectional study tried to analyse and describe the appearance of the rash in paediatric patients who have been hospitalised at tertiary care hospital for the treatment of COVID-19 disease.

MATERIALS AND METHODS

A descriptive cross-sectional study was conducted between July to December, 2020 at Shaheed Hasan Khan Mewati, Government Medical College, Nuh, Haryana, India. Approval of Institutional Ethics Committee was obtained for conducting this study with IEC no: EC/OA-15/2020.

Inclusion criteria: All children with RT-PCR positive for SARS-CoV-2 were studied and all neonates who tested positive for SARS-CoV-2 infection during birth admission or were readmitted anytime in the neonatal period were also included in the study.

Exclusion criteria: Children presenting with congenital or pre-existing dermatosis were excluded.

The present study included all the SARS CoV-2 positive children those who were admitted within the study duration. Children who needed admissions during study period were 1095, among which fifty (4.56%) were positive for SARS-CoV-2 RT-PCR test.

Study Procedure

As per institutional protocol, derived from national guidelines [10], every child requiring admission was tested for SARS-CoV-2 by RT-

PCR (nasopharyngeal or oropharyngeal swab). The SARS-CoV-2 positive children were examined, categorised and managed as per degree of disease severity (asymptomatic/mild/moderate/severe/critical) based on standard guidelines [10]. The presenting sign/symptoms and the median age were recorded. Nutritional assessment was done with help of various anthropometric parameters- height, weight.

Baseline laboratory parameters (complete haemogram and C-reactive protein) and imaging studies were evaluated and repeated as required. Complete dermatological evaluation for the patients was done by dermatologist. Varied morphology of skin eruptions, time of onset, location and pattern of evolution were recorded. Clinical photography of significant findings was done with due precautions to avoid risk of transmission of SARS-CoV-2 through the device.

All children admitted were managed as per the hospital protocol. General supportive therapy, active control of fever, respiratory support with oxygen and/or ventilation (if needed), management of shock, and active monitoring of organ system dysfunctions was done. The children were monitored daily for changes in disease severity. Discharge protocol from hospital was as per guidelines of Ministry of Health and Family Welfare, Directorate General of Health Services, India [11]. The duration of hospital stay and outcome was evaluated.

STATISTICAL ANALYSIS

The data were analysed using the Statistical Package for Social Sciences (SPSS) software version 25.0. Numerical data were presented as number and Standard Deviation (SD); and categorical data were presented as number and percentage. The level of significance, wherever applicable, was taken as p-value<0.05.

RESULTS

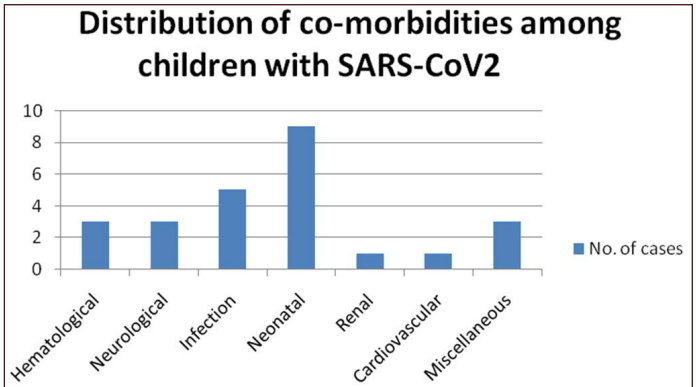
In the present study 30 (60%) were males and 20 (40%) were females with ratio of 3:2. The median (IQR) age was three years among the paediatric age group and two days in neonates. Among 29 children, severe malnutrition was seen in 10 (34.4%), moderate to mild malnutrition in 14 (48.3%) while only 5 (17.2%) had weight for age within normal range.

The most common systemic symptom was respiratory distress 24 (48%) followed by fever 19 (38%). On basis of standard guidelines criteria, 18 (36%) were asymptomatic, 13 (26%) were in mild, 18 (36%) in moderate and 1 (2%) in severe category [Table/Fig-1]. None of the children developed Paediatric Inflammatory Multisystem Syndrome temporally associated with COVID-19 (PIMS-TS) which is also known as “Multisystem Inflammatory Syndrome in Children” (MIS-C).The associated co-morbidities like haematological (n=3), neurological (hypoxic ischaemic encephalopathy, Old chiari malformation) (n=3), infectious (n=5), neonatal conditions (perinatal asphyxia, neonatal sepsis and transient tachypnoea of newborn) (n=9), renal (nephrotic syndrome) (n=1), cardiovascular (congenital heart disease) (n=1) and miscellaneous (oraganophosphorus poisoning, turpentine oil poisoning and airway obstruction) (n=3) in COVID-19 patients are described in [Table/Fig-2].

Among 50 SARS-CoV-2 positive children, 4 (8%) were found to have dermatological manifestations. Total 3 (6%) had maculopapular rash and 1 (2%) had urticarial lesions [Table/Fig-3]. Trunk was the most frequently affected area 4 (8%) followed by the extremities 2 (4%). Palms/soles were spared in all patients. None of patients showed mucosal signs and symptoms. No vasculopathic lesions were present. None of the patient had any pre-existing dermatoses and any associated co-morbidity. The evolution of maculopapular rash was on day 2 of fever in 3 (6%) patients whereas urticarial rash appeared at the time of onset of fever. The maculopapular rash was centripetal at onset and then spread to the extremities whereas urticarial lesions were present all together on trunk and extremities.

Parameters	Number of children n (%)
Male	30 (60%)
Female	20 (40%)
Age	
<1 month	21 (42%)
1 month to 1 year	10 (20%)
>1-5 years	12 (24%)
>5-10 years	4 (8%)
>10-15 years	3 (6%)
Contact with patients of COVID-19	4 (8%)
COVID-19 disease severity	
Asymptomatic	18 (36%)
Mild	13 (26%)
Moderate	18 (36%)
Severe	1 (2%)
Cutaneous manifestation	
Maculopapular rash	3 (6%)
Urticaria	1 (2%)
No cutaneous manifestation	46 (92%)
Clinical presentation	
Respiratory distress	24 (48%)
Fever	19 (38%)
Cough	3 (6%)
Sore throat	7 (14%)
Myalgia	4 (8%)
Seizures	6 (12%)
Loss of smell/taste	3 (6%)
Diarrhea	2 (4%)
Headache	2 (4%)

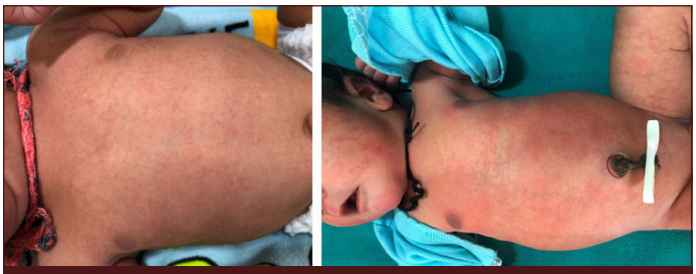
[Table/Fig-1]: Epidemiological and clinical characteristics of children with SARS-CoV-2 infection.



[Table/Fig-2]: Distribution of co-morbidities among children with SARS-CoV-2 infection (N=29).

Among patients having dermatological findings, two each had mild and moderate COVID-19 disease. The presence of dermatological manifestations did not show any significant association between mild, moderate and severe cases (p-value=1.0). Though, dermatological

manifestations of COVID-19 were not seen in any of neonate, three out of 21 neonates developed dermatoses which were diagnosed as miliaria rubra, milia and erythema toxicum neonatorum respectively [Table/ Fig-4].



[Table/Fig-3]: Maculopapular rash on the trunk in a child with SARS-CoV-2 infection. **[Table/Fig-4]:** Erythema toxicum neonatorum in a child with SARS-CoV-2 infection. (Images from left to right)

The median duration of RT-PCR negativity was five days (range, 3-15 days). The median (range) length of hospital stay was nine days (4-17 days). A 19 (38%) patients needed Intensive Care Unit (ICU) admission of which 10 (52%) were neonates. There were 2 (4%) deaths attributed to COVID-19, one was 1-year-old infant and another was 2-days-old neonate.

DISCUSSION

The COVID-19 has become a pandemic since its origin from Wuhan, China in December 2019. The disease principally affects the respiratory tract with clinical presentation ranging from common cold to severe pneumonia. Reporting of extra pulmonary involvement started with surge in cases across the world. Dermatological manifestations of COVID-19 can present in varied form, most commonly includes exanthematous and urticarial eruptions, followed by livedo, petechiae, vesicular and vasculopathic eruptions [3].

The clinical course, presentation and outcome is usually milder in children compared to adults. The possible factors could be early isolation, strong innate response due to live vaccines, high ACE-2 expression, good lung regeneration capacity and absence of ageing related co-morbidities could explain overall less severity and early recovery of COVID-19 compared to older patients [7]. In a study by Rao S et al., 12.8% children were tested positive for COVID-19 among a sample size of 969 children whereas Bustos-Cordova et al., reported a positivity rate of 54% among 92 children [12,13]. The positivity rate in present study was 4.56%. Asymptomatic children in present study were 36% which is higher than previous studies: 21.7% in Rao S et al., 4.4% in Dong Y et al., and 23% in a meta-analysis by Meena J et al., [12,14,15]. Higher percentage (58%) of asymptomatic children has also been reported [16]. Severe disease was found in only 2% of children in present study which is similar to that seen in a study from China [17]. Remarkably higher percentage (26%) of severe disease among children has also been reported [12].

Skin expressions are becoming a common manifestation of the disease with prevalence ranging from 0.2-45.7 [4,5,18,19]. Mucocutaneous findings in children have varied prevalence and features among different studies [20-23]. A systematic review found that skin lesions were present in only 0.25% paediatric patients in 119 published studies [20]. The reported prevalence is much higher in studies by Andina-Martinez D et al., (42%) and Rekhtman S et al., (42%)) [21,22]. Swann OV et al., reported rash in less than 15% of the children [23]. In present study, 8% of COVID-19 confirmed children showed dermatological manifestation. The most common finding in present study was maculopapular rash. Bursal Duramaz B et al., also reported maculopapular rash to be the only cutaneous manifestation among three of the 20 COVID-19 patients [24]. All three patients started with rash on their faces and continued on extremities whereas in present study rash appeared first on trunk and then involved extremities. Similar pattern of progression was noted in adults as reported in a study by Dalal A et al., [5]. No significant association was found between dermatological finding and disease severity in present study which is similar to observations made by Bursal Duramaz B et al., [24]. Onset of maculopapular rash was noted at the beginning of disease in all three of present study patients.

Urticaria is a common dermatological finding in COVID-19 adult patients [6]. Morey-Olivé M et al., reported a case of a 3-month-old girl presented with fever and pruritic urticarial rash of four days duration who was SARS-CoV-2 positive [25]. We also found one case with urticarial lesions (without any concomitant history of drug intake). Possible mechanism of urticarial rash might be due to nonimmunological activation of mast cells via complement or vasculitis as SARS-CoV-2 virus binds ACE-2 receptors on blood vessels. Though, histopathological findings of urticarial rashes in children have not been published but in adults, it reveal perivascular infiltrates of lymphocytes, eosinophils and upper dermal oedema and vacuolar-type interface dermatitis with occasional necrotic keratinocytes [26].

Various authors have reported cutaneous manifestation like chill-blain like lesions, erythema multiforme like lesion, varicella like exanthema, kawasaki disease like presentation and oral apthous ulcers which were not seen in any of present patients [27-30]. Thrombotic occlusive vascular manifestations like livedo reticularis, digital ischemic necrosis or digital acral ulceration which are marker of severe disease weren't seen in our study probably due to lesser number (only single patient) of patients in severe category of disease. Death reported by Rao S et al., was 11.4% which is higher than in present study (4%) which can be explained as more children were having severe disease in their study [12].

The present study highlights that mucocutaneous involvement among Indian children with COVID-19 are not very common and manifests in the form of maculopapular rash and urticarial lesions. As paediatric COVID-19 is considered milder compared to adults, so children may be otherwise asymptomatic and the dermatological manifestation may be the first sign of infection so it is particularly important to be aware of these manifestations as part of the clinical picture of the disease.

Limitation(s)

This study was limited by a small sample size, lesser number of patients in the severe category of the disease and lack of histology.

CONCLUSION(S)

The dermatological findings encountered in form of maculopapular rash and urticaria among admitted COVID-19 children warrants that all COVID-19 positive children should be screened for cutaneous findings. Moreoever, dermatological findings could aid a general physician or dermatologist in recognising the early cases and helps in limiting the community spread. More detailed analytical studies with larger sample size are advocated for generating further evidence for prevalence of mucocutaneous findings and their histopathological correlation among COVID positive children.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Nov 25, 2021
- Manual Googling: Feb 28, 2022
- iThenticate Software: Apr 14, 2022 (24%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Nov 24, 2021**
Date of Peer Review: **Jan 04, 2022**
Date of Acceptance: **Mar 09, 2022**
Date of Publishing: **Jun 30, 2022**