

Original Research Article

Retrospective study on mucocutaneous manifestations due to COVID-19 in paediatric age group in a tertiary care centre in Southern India

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ABSTRACT

Background: COVID-19 virus is known to cause wide variety of mucocutaneous manifestations. The inflammatory response of body plays a crucial role in SARS-CoV-2 induced lung injury. These cytokines arriving at the skin and reaching various cells of cutaneous immune system can cause dermatological lesions described during COVID-19 infection. The primary aim of this study is to characterize the diversity of cutaneous manifestations due to COVID-19 in pediatric age group.

Methods: The study was an observational study done on paediatric COVID cases aged less than 12 years who were admitted in COVID isolation ward of Institute of Child Health, Rajiv Gandhi Government General Hospital. This study was conducted for 3 months from August 2020 to October 2020.

Results: A total of 191 swab-confirmed cases of COVID-19 aged less than 12 years were recruited in the study. Out of 191 cases, 19 had dermatological manifestations (10%). The most common type of dermatological manifestation noted in our study was maculopapular rash (N=8), followed by purpura (N=4), urticarial (N=3), angular cheilitis (N=2), palmar erythema (N=1), purpura with palmar erythema occurring together (N=1). Time latency between onset of first COVID symptom and occurrence of cutaneous lesion was 1 to 7 days.

Conclusions: A total of 191 swab-confirmed cases of COVID-19 aged less than 12 years were recruited in the study. Out of 191 cases, 19 had dermatological manifestations (10%). The most common type of dermatological manifestation noted in our study was maculopapular rash (N=8), followed by purpura (N=4), urticarial (N=3), angular cheilitis (N=2), palmar erythema (N=1), purpura with palmar erythema occurring together (N=1). Time latency between onset of first COVID symptom and occurrence of cutaneous lesion was 1 to 7 days.

Keywords: COVID-19, Mucocutaneous, Multisystem inflammatory syndrome in children, Kawasaki

INTRODUCTION

In December 2019, a novel infectious agent named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified in Wuhan city in China.¹ This pathogen was called coronavirus disease 2019 (COVID-19) and by 15th February 2020, it rapidly spread throughout China and across the world, until a pandemic condition was announced by WHO on March 11, 2020.²

Decreased ACE 2 function can cause dysfunction of renin-angiotensin system (RAS) and intensification of inflammation, vascular permeability, and neutrophil accumulation. Rapid viral replication causes cellular apoptosis and triggers a cascade of inflammatory reactions and increase in cytokines/chemokines. The inflammatory response of body also plays a crucial role in SARS-CoV-2 induced lung injury.^{3,4} These cytokines arriving at the skin and reaching various cells of

cutaneous immune system can cause dermatological lesions described during COVID-19 infection.⁵

Multisystem inflammatory syndrome in children (MIS-C) is a newly recognised multiorgan disease presumed to be a delayed immune mediated complication of SARS-CoV-2 infection seen in children, adolescents and young adults.⁶ MIS-C results from abnormal immune response to virus, with some similarities to Kawasaki disease. It can be associated with life-threatening organ dysfunction requiring complex multidisciplinary care and hence early recognition is important in order to prevent complications and serious sequelae.^{7,8} Dermatological manifestations in COVID-19 patients include morbilliform, pernio-like, urticarial, macular erythema, vesicular, erythema-multiforme like, and purpura.⁹ MIS-C cases have skin rash, bilateral non purulent conjunctivitis or mucocutaneous inflammatory signs.⁷ This study throws light on the diversity in cutaneous manifestations due to COVID-19 in paediatric age group.

METHODS

The study was an observational study done on paediatric COVID cases aged less than 12 years who were admitted in COVID isolation ward of institute of child health, Rajiv Gandhi government general hospital. This study was conducted for 3 months from August 2020 to October 2020. All children were examined only after taking consent from the parents/guardians

Inclusion and exclusion criteria

Inclusion criteria were cases aged less than 12 years admitted in COVID isolation ward and cases whose parents/guardians gave consent for participation. The exclusion criteria were cases above 12 years of age, previous history of skin diseases, history of drug intake in the recent past and history of systemic diseases affecting the skin, and cases whose parents/guardians did not give consent for participation.

Procedure

Detailed clinical history including basic demographic details, history of presenting complaints, treatment history, past history and personal history. Any child with history of skin diseases or history of drug intake in the past 2 weeks was excluded from the study.

A thorough dermatological examination was conducted to record the morphology and the sites affected like skin, mucosa, scalp, hair, nails and palms/soles. All the cases included were confirmed cases of COVID-19 by swab RT-PCR technique. All the cases were observed from the day of admission till discharge for occurrence of skin lesion and symptoms pertaining to skin lesions like itching, pain and burning sensation. Also a note on treatment given and use of oxygen support was made.

The study also included a series of 6 cases of MIS-C, admitted in paediatric ICU.

Cases were diagnosed as MIS-C based on the WHO criteria.¹⁰ The criteria were age 0 to 19 years, fever for ≥ 3 days, clinical signs of multisystem involvement (at least 2 of the following): rash, bilateral non purulent conjunctivitis, or mucocutaneous inflammation signs (oral, hands, or feet), hypotension or shock, cardiac dysfunction, pericarditis, valvulitis, or coronary abnormalities (including echocardiographic findings or elevated troponin/BNP), evidence of coagulopathy (prolonged PT or PTT; elevated D-dimer), acute gastrointestinal symptoms (diarrhoea, vomiting, or abdominal pain), acute gastrointestinal symptoms (diarrhoea, vomiting, or abdominal pain), no other obvious microbial cause of inflammation, including bacterial sepsis and staphylococcal/streptococcal toxic shock syndromes, evidence of SARS-CoV-2 infection (any one of the following-positive SARS-CoV-2 RT-PCR, positive serology, positive antigen test, contact with an individual with COVID-19).

Statistical analysis

The data collected was entered in MS Excel. Values were expressed in the form of descriptive statistics like mean and graphs.

RESULTS

A total of 191 swab-confirmed cases of COVID-19 aged less than 12 years were recruited in the study. There were 99 male and 92 female children. Most common age groups were 2 to 3 years and 9 to 10 years, and mean age was found to be 5.100 ± 3.74 . Out of 191 cases, 48 had history of contact with an index case (25.13%). COVID symptoms occurred in these patients as follows; fever (N=107, 56.02%), cough (N=80, 41.88%), sore throat (N=59, 30.89%), rhinorrhoea (N=32, 16.75%), dyspnoea (N=24, 12.56%), headache/myalgia (N=20, 10.47%), nausea/vomiting (N=21, 11%), diarrhoea (N=19, 10%).

Out of 191 cases, 19 had dermatological manifestations (10%). The most common type of dermatological manifestation noted in our study was maculopapular rash (N=8), followed by purpura (N=4), urticarial (N=3), angular cheilitis (N=2), palmar erythema (N=1), purpura with palmar erythema occurring together (N=1). The time latency between onset of first COVID symptom and onset of cutaneous lesions is given in (Table 1). The sites affected is as shown in (Figure 1). Clinical pictures have been shown in (Figure 2).

Maculopapular rash occurred in 5 male and 3 female children (N=8, 42%). Mean age affected was 5.06 years (range=6 months to 8 years). The mean time taken for the lesions to disappear was 5.25 days (range=3 to 7 days). 2 of these children were on oxygen support. Other

symptoms noted in these patients were itching (N=4), burning (N=1).

Table 1: Time latency, in days, between onset of first COVID symptom and occurrence of cutaneous lesion.

Parameters	Maculopapular rash	Purpura	Urticarial	Angular cheilitis
Mean (days)	3.25	3.5	2.6	6.5
Range (days)	1-7	3-5	2-4	6-7

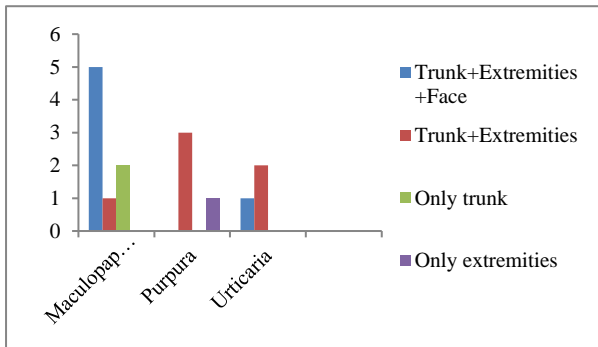


Figure 1: Site involvement of mucocutaneous lesions in paediatric COVID-19.

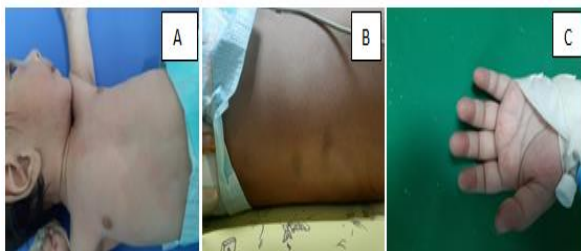


Figure 2: Various dermatological lesions in COVID-19 (A) macular rash; (B) purpuric rash; and (C) palmar erythema.

Purpura occurred in 1 male and 3 female children (N=4, 21%). Mean age of affected was 5.75 years (range= 3 to 8 years). Lesions disappeared in 1 week in one patient and was present even at the time of discharge in 2 children. One child died on day 4 of admission. 2 of these children were on oxygen support. Other symptoms like itching or burning were absent. Urticaria was present at time of examination in one child and history suggestive of urticarial was present in 2 other children, 1 male and 2 female children (N=3, 16%). Mean age affected was 8 years (range= 5 to 11 years). Lesions disappeared after half an hour to 2 hours. Other symptoms like itching (N=3) and burning (N=1) were absent. Angular cheilitis was present in 2 male children (N=2, 11%) affecting mean age of 8 years. Lesions were present even at time of discharge, that is, 11 days after the onset of first COVID symptom. Pain and burning sensation was noted in both these patients. Palmar erythema was present in one 3-year

old female child that occurred 3 days after the onset of first COVID symptom, disappeared in 5 days. Purpura on trunk and palmar erythema was noted in one 3-year old female child that was on oxygen support. Purpura occurred on 4th day and palmar erythema on 5th day after the onset of COVID symptoms. Purpura was present over trunk and extremities. These lesions were present at the time of death (10th day after onset of COVID symptoms). The clinical manifestations of six MIS-C cases have been tabulated in (Table 2) and clinical pictures in (Figure 3).



Figure 3: Mucocutaneous manifestations in MIS-C (A) skin rash over face; (B) skin rash over upper limb; (C) cheilitis; (D) periorbital puffiness; and (E) edema of hands.

DISCUSSION

This study highlights the various cutaneous manifestations of COVID-19 in pediatric age group, admitted in a tertiary care centre in South India. Previous case series have documented various skin lesions like pernio-like lesions, erythematous macules or papules, urticarial rashes, morbilliform, varicelliform, petechial, papulosquamous eruption, livedo reticularis; like rashes, retiform purpura, acro-ischemic lesions which are of serious concern.¹¹⁻²⁰

Dermatological lesions can be classified as either inflammatory (morbilliform, maculopapular, vesicular, urticarial) or vascular (chilblain-like, purpura, petechiae, livedoid).²¹ The reports of cutaneous manifestations in COVID-19 came initially from Italy since it was the first European country to be affected heavily by the pandemic during first wave. The cutaneous manifestations of COVID-19 in children differs from those of adults in the fact that lesions such as maculopapular rash, urticarial or vesicular rashes can occur in all ages, whereas manifestations like erythema multiforme, chilblains, and cutaneous manifestations of MIS-C are seen frequently in children and young patients. First and the most common cutaneous manifestation of COVID-19 in children was found to be chilblain lesions.²² In our study maculopapular rash was found to be the most common cutaneous manifestation. In a study from Thailand, it was found that urticaria was the most common skin lesion

observed in contrast to pseudo-chilblain that was commonly reported from cold and temperate countries. It is speculated that the host factors, environment and

different strains of viruses may be the reason for this difference.³

Table 2: Clinical manifestations of multisystem inflammatory syndrome in children (MIS-C).

Parameters	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age in years	3	3	5	7	8	12
Sex	Female	Female	Male	Male	Female	Male
Skin rash	+	+	+	+	--	--
Conjunctivitis	+	+	+	+	+	--
Oral mucosal changes	+	+	+	+	+	+
Periorbital puffiness	+	+	--	+	+	--
Edema of hands/feet	+	+	--	+	+	--
Fever	+	+	+	+	+	+
Irritability/lethargy	+	+	--	+	+	--
Labored breathing	+	--	--	+	+	--
Elevation of d-Dimers/inflammatory markers	+	+	+	+	+	+
ECHO changes						
Left ventricular systolic dysfunction	+	--	--	+	--	+
Coronary artery dilation	--	--	+	--	--	--
Ground glass opacity of chest X-ray	+	--	+	--	+	--

In a review article by Kaya et al it is stated that frequency of cutaneous manifestations in COVID-19 is between 1.8% and 20.4%. The lesions were located in trunk and extremities with mean duration of few days, with some lasting as short as 20 minutes to as long as 4 weeks. The mean latency time in majority of cases was 1 to 14 days. But in some patients lesions appeared 2-5 days even before the onset of COVID symptoms.²⁴ In our study none of the cutaneous lesions occurred before the onset of COVID symptoms.

According to study published by Mirza et al the average age for adult patients with cutaneous manifestations was found to be 34.2 years and for paediatric patients was 12.9 years. A slight female preponderance was noted in both paediatric and adult population. Average latency from onset of COVID-19 symptoms to cutaneous lesions was 1.5 days and 7.9 days in paediatric and adult age groups respectively. Average time of resolution of cutaneous lesions for paediatric and adult patients was 5.8 days (1-14 days range) and 8.5 days (1-21 days range) respectively.²⁵

In a prospective study conducted in Spain, it was found that pseudo-chilblain lesions occurred later in course of the disease and was associated with less severe COVID-19 infection. Whereas vesicular lesions happened to occur in intermediate disease severity and urticarial/maculopapular lesions in more severe COVID-19 disease. Livedoid/necrotic lesions occurred in severe disease with transient livedo occurring in patients not requiring hospitalization.²⁶ In our study, 2 children that died due to COVID-19 had purpuric rashes. During the initial phase of COVID-19 pandemic, children were presumed to be spared of the COVID related morbidity and mortality until case series from the United States and

Europe raised concerns regarding the hyperinflammatory process in children associated with COVID-19, now defined as MIS-C.²⁷ This syndrome that mimics Kawasaki disease manifests 2-4 weeks after COVID-19 exposure affecting multiple organ systems. The most common symptoms at presentation being fever, rash and oral mucosal changes, gastrointestinal symptoms, vasodilatory shock. The pathophysiology behind multi-organ system damage is thought to be multifactorial, like, low cardiac output state, edema, inflammation, vasculitis, microthrombus.²⁸ Mucocutaneous manifestations in MIS-C can be diverse with scarlatiniform rashes, morbilliform rashes, urticarial, reticulated eruptions, periorbital erythema and edema, palmoplantar erythema, lip erythema, lip cracking, conjunctival injection.²⁹

An article published by Naka et al which is a review of 13 case series from European countries and United States, describes the muco-cutaneous manifestations seen in MIS-C. The most common dermatological presentations are; non specific eruption, dry and red lips, other mucosal changes, hand/feet erythema and edema. The percentage of children affected by MIS-C who developed mucocutaneous manifestations included- conjunctivitis 27% to 93%, changes in oral mucosa 25% to 87%, skin eruption 47% to 81%, hand/feet erythema and edema 27% to 68%. This article also mentions that skin manifestations of MIS-C are more common in children of younger age group and decreases with age.³⁰ There have also been reports of acral gangrene, owing to severe hypoperfusion, in children of MIS-C.³¹ In an article published by Abrams et al., it was found that cardiac artery abnormalities were noted more frequently in patients with mucocutaneous manifestations and conjunctival injection.³² In our study, oral mucosal changes and conjunctivitis were the most common mucocutaneous manifestations seen in MIS-C. Coronary artery dilation

was present only in 1 child that had angular cheilitis and conjunctivitis.

Limitations

The relation between type of cutaneous manifestations and the severity or outcome of the disease could not be assessed due to small sample size. Also this study was done only during the first wave of COVID-19 which affected very small percentage of paediatric population compared to adults. Follow up of the cases was not done and hence total duration of skin lesions for some cases could not be noted.

CONCLUSION

This wide diversity of mucocutaneous manifestations in COVID-19 pandemic is gaining attention since they might be useful in early diagnosis and triage and risk stratification. Kawasaki disease like features in a paediatric patient during this pandemic should provoke the minds of paediatricians and dermatologists to consider the diagnosis of MIS-C, thereby enabling early treatment and prevention of complications.

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