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REVIEW ARTICLE

Skin Manifestations In Children With COVID-19: A Literature Review

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Coronavirus Infections, Skin Manifestations, Pediatrics.

Abstract

Objectives: Perform a literature review to correlate data on dermatological manifestations in pediatric patients with coronavirus disease 2019 (COVID-19). **Methods:** A systematic literature review was performed, selecting articles involving COVID-19 and dermatological manifestations in pediatric patients, in databases such as PubMed, The New England Journal of Medicine, The British Medical Journal and The Lancet. **Results:** Studies indicate that the SARS-CoV-2 virus (severe acute respiratory syndrome coronavirus 2) can cause dermatological manifestations, like macules, papules, rash, hives, erythema and oral mucositis. Skin involvement by COVID-19 in children may be associated with multisystemic inflammatory syndrome, in which there is an abnormal immune response associated of cytokines and activation of macrophages, which can justify the changes in the skin. **Conclusion:** Cutaneous manifestations, although unspecific, are important for the identification of the disease in pediatric patients and better control of the spread of infection to the population.

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INTRODUCTION

Coronavirus Disease 2019 (COVID-19), a condition caused by a new type of coronavirus called SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2)[1], was first detected in the city of Wuhan, China, in December 2019. COVID-19 was described as a global public health emergency in January 2020 and has since propagated to all continents.[2]

The country with the most cases of the disease today is the United States, with more than two million individuals tested positive for COVID-19, of which 4.2% are children; a small portion of the individuals with the disease requires hospitalization or intensive care.[1] According to the World Health Organization (WHO), Brazil ranks second in number of infected individuals, with approximately 1.2 million cases; two percent of the pediatric patients with COVID-19 in Brazil have developed severe acute respiratory syndrome (SARS).[3]

Coronaviruses are a group of RNA viruses that cause respiratory infection in a variety of animals. Seven coronaviruses are known to infect humans. In the last 20 years, two viral epidemics associated with severe acute respiratory syndrome (SARS) were recorded, one in Hong Kong, China, in 2003, and one in Saudi Arabia involving the Middle East respiratory syndrome-related coronavirus (MERS-CoV) in 2012.[4]

Evidence suggests that COVID-19 originated from zoonotic transmission of SARS-CoV-2 occurred in a seafood and wet animal wholesale market.[5] The disease is transmitted via respiratory droplets or direct contact with infected individuals. Incubation takes about four days and the main symptoms are fever and coughing.[1] Symptoms affecting other organs and the skin have been described.[6]

OBJECTIVES

This systematic review was designed to collect and correlate data from the literature about skin manifestations of COVID-19 in pediatric patients and share the findings with healthcare workers to potentially help them diagnose individuals in the early stages of involvement and curb the spread of the disease.

METHODS

This systematic review included articles published in 2020 in PubMed, The New England Journal of Medicine, The British Medical Journal, and The Lancet. The searches included keywords “Coronavirus Infection,” “Skin Manifestations,” and “Pediatrics” and their equivalents in Portuguese.

Thirty-two articles came out in the first search; 16 were excluded for not covering skin manifestations in pediatric patients (aged 0-18 years) or for not addressing the subject of the review. After the 16 papers were read, two were excluded for not answering questions inherent to the objectives of this study. Fourteen articles were included in the review.

RESULTS

The review featured eight articles reporting the cases of children tested positive for COVID-19 with skin manifestations alone or skin and other alterations combined.

Nearly all patients were tested for COVID-19 based on nasopharyngeal swab specimens analyzed via reverse transcription-polymerase chain reaction (RT-PCR). The exception was the study by Mazzota et al.[11], which was affected by an acute nationwide RT-PCR test kit shortage. (Table 1)

DISCUSSION

Adults and children with COVID-19 experience similar symptoms, despite variations in the frequency with which they occur.[7] Children usually do not develop severe symptoms. Skin manifestations are important in the identification of pediatric patients with the disease and in controlling the spread of COVID-19 in the population.[8]

Several unspecific skin manifestations such as maculae, papules, rash, urticaria, and erythema have been described in adults and children alike. These lesions are usually found in the feet and hands, in asymptomatic patients, and in individuals with few COVID-19 symptoms.[6]

COVID-19 has been associated with multisystem inflammatory syndrome in children (MIS-C). Knowledge of the risk factors, pathogenesis, clinical progression, and treatment of MIS-C is still limited. It has been suggested that MIS-C results from anomalous immune response to the virus and bears similarities with cytokine release syndrome, Kawasaki disease, and macrophage-activation syndrome. A finding that supports this hypothesis is that MIS-C has been associated with immune deregulation occurring after acute infection, as many affected children present negative RT-PCR tests for SARS-CoV-2 infection but positive serology.[10]

The skin manifestations described for MIS-C include erythematous and polymorphous light eruption, erythema and/or hand and foot skin thickening, oral mucositis, and conjunctivitis. Less frequent lesions such as papulosquamous eruption, erythema multiforme, petechiae, and gangrene have been reported.[10]

In a prospective study carried out in Spain with 375 patients, Galvan et al.[3] described five different patterns of skin manifestation caused by SARS-CoV-2. The patterns involving acral sites include erythema and edema, vesicles and/or pustules; vesicular and monomorphic lesions; urticaria; maculopapular rash; livedo or necrosis. Lesions such as vesicles and pustules (pernio-like lesions) affect younger patient with mild COVID-19 symptoms.[3]

Guarneri et al.[13] reported the cases of three pediatric patients with skin manifestations tested positive for SARS-CoV-2 infection. The patients aged 14-18 years had mild COVID-19 symptoms and presented with skin lesions lasting for 7-21 days. The lesions were described as purple erythema,

Table 1. Articles describing skin manifestations of children with COVID-19.

Author/ Journal	Country	Sex	Age	Symptoms	Skin Manifestations
Parri *et al*.[8] *New England Journal of Medicine*	Italy	M	2 months	Coughing, dysphagia, and hyporexia	Rash
Genovese *et al*.[9] *Pediatric Dermatology*	Italy	M	2 months	Coughing, dysphagia, and hyporexia	Rash
Guarnieri *et al*.[13] *The Lancet Infectious Disease*	Italy	M	14 years	None	Purple, erythematous lesions and maculopapular rash
Guarnieri *et al*.[13] *The Lancet Infectious Disease*	Italy	M	14 years	None	Necrotic-like purple, erythematous lesions
Guarnieri *et al*.[13] *The Lancet Infectious Disease*	Italy	M	18 years	Fever	Dermatophytosis
Morey-Olivé *et al*.[14] *Anales de Pediatria*	Spain	M	6 years	Fever and symptoms consistent with cholestatic liver disease	Maculopapular rash
Morey-Olivé *et al*.[14] *Anales de Pediatria*	Spain	F	2 months	Fever	Acute urticaria
Mazzotta e Troccili[11] *Dermatol. Pediatrica*	Italy	M	13 years	Fever, muscle pain, and headaches	Itchy purple, erythematous lesions, and crusts
Aghdam *et al*.[12] *Infectious Diseases*	Iran	M	15 days	Fever, lethargy, dyspnea, no coughing	Livedo reticularis

Legenda: M = Masculino; F = Feminino.

maculae, papules, and crusts, primarily involving the feet. Acute ischemic acral manifestations associated with SARS-CoV-2 infection are different from the characteristic lesions seen in acrocyanosis, erythema pernio, and vasculitis, and may represent a consequence of a thrombotic pattern of disease caused by hyperinflammation, coagulation disorders, and endothelial damage.[13]

The patient described by Genovese et al.[9] had mild symptoms of the disease and varicella-like papulovesicular lesions. The lesions developed three days after the onset of coughs and resolved within seven days. Other skin manifestations, pain or pruritus were not associated with exanthema, thus ruling out the possibility of the lesion stemming from prior infection or insect stings. Besides, the early appearance of papulovesicular lesions is indication that the patient may have COVID-19.[9]

One of the patients described by Morey-Olivé et al.[14] had non-pruritic erythematous maculopapular eruption that resolved spontaneously after five days. Another patient had itchy urticaria with fever lasting for five days and requiring treatment.[14]

According to published evidence, the skin manifestations seen in individuals with COVID-19 are similar to the lesions described in patents with other viral diseases. It cannot be stated that the extent of these lesions correlates with the severity of disease. In addition to acute phase exanthema, recent reports of acral lesions and dermatophytosis should also be considered, since they might be associated with late manifestations of an inflammatory process tied to the disease or microthrombotic events occurring in the immune phase of infection.[14]

CONCLUSION

Pediatric patients with COVID-19 account for a small proportion of the population with the disease. In these individuals, symptoms are usually mild and of shorter duration. Skin manifestations may exist, but are unspecific and do not correlate with typical patterns of the disease. A clear association between skin manifestations and COVID-19 has not been established.

The literature on the subject is scarce, since few studies about pediatric cases of COVID-19 have been published. More research is needed so that the disease and its manifestations are comprehensively understood.

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