

Oral and cutaneous manifestations of covid-19 in pediatric patients

Manifestações bucais e cutâneas da covid-19 em pacientes pediátricos

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ABSTRACT

COVID-19 began in December 2019 in Wuhan City, China, and on March 11, 2020 it was classified by the World Health Organization as a pandemic. It is an asymptomatic infection that can progress to severe respiratory conditions. In adults, it is more prevalent, but is also observed in children, with the occurrence of extra respiratory symptoms, such as oral and cutaneous manifestations. This literature review aims to report the oral and cutaneous manifestations of COVID-19 in pediatric patients. The bibliographic search strategy was carried out in the PubMed, SciELO and Bireme databases on August 1, 2020, using MeSH Terms "COVID-19"; "Child"; "Oral Manifestations"; "Skin Manifestations"; "Ageusia"; "Dysgeusia" and corresponding Decs, and also manual search, without language restriction. The stages of search, screening, selection, evaluation of studies and data extraction were performed by four independent reviewers. Nine studies that met the eligibility criteria were identified. The most cited oral and cutaneous manifestations were, respectively, taste dysfunction in adolescents and erythematous eruption in extremities and trunk. Health professionals should be aware of these manifestations, however, this is a recent theme in the literature, and more careful studies with greater strength of evidence still need to be performed.

Indexing terms: Coronavirus Infections. Child. Oral manifestations.

RESUMO

A COVID-19 iniciou em dezembro de 2019, na cidade de Wuhan na China e em 11 de março de 2020 foi classificada pela Organização Mundial de Saúde como pandemia. Trata-se de uma infecção assintomática que pode evoluir para quadros respiratórios graves. Em adultos é mais prevalente, mas também é observada em crianças, com ocorrência de sintomatologias extra respiratórias, como as

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manifestações bucais e cutâneas. Esta revisão de literatura objetiva relatar as manifestações bucais e cutâneas da COVID-19 em pacientes pediátricos. A estratégia de busca bibliográfica foi realizada nas bases de dados PubMed, SciELO e Bireme em 01/Agosto/2020, utilizando MeSH Terms "COVID-19"; "Child"; "Oral Manifestations"; "Skin Manifestations"; "Ageusia"; "Dysgeusia" e Decs correspondentes, e ainda busca manual, sem restrição de idiomas. As etapas de busca, triagem, seleção, avaliação dos estudos e extração dos dados foram realizadas por quatro revisores independentes. Foram identificados nove estudos que atenderam aos critérios de elegibilidade. As manifestações bucais e cutâneas mais citadas foram, respectivamente, a disfunção gustativa em adolescentes e a erupção eritematosa em extremidades e tronco. Os profissionais de saúde devem ficar atentos às referidas manifestações, entretanto, trata-se de um tema recente na literatura, estudos mais criteriosos, com maior força de evidência ainda precisam ser realizados.

Termos de indexação: Infecções por coronavírus. Criança. Manifestações bucais.

INTRODUCTION

In the city of Wuhan in China, in December 2019, the spread of the disease began, which would become a pandemic, caused by SARS-CoV-2, a pleomorphic RNA virus with a microscopic crown shape. The disease that was named by the World Health Organization (WHO) as COVID-19 spread rapidly around the world [1], reaching 187 countries from December 2019 to July 2020 [2]. In Brazil, until August 3, 2020, the number of confirmed cases was 2,733,677 and deaths from the disease, 94,104 [3].

The clinical picture can manifest itself with symptoms ranging from an asymptomatic infection to severe respiratory implications, and may have extra-respiratory manifestations, affecting the cardiovascular, gastrointestinal, renal, hepatobiliary system, endocrinological, dermatological and nervous system, eyes and conjunctiva [4,5]. Initially, COVID-19 was more prevalent in adults with non-specific symptoms such as fever, cough, myalgia, dyspnea and diarrhea [6,7]. However, it can also be observed in children, being evident the severity of the disease in term or preterm babies [8]. Among the extra-respiratory manifestations that have been described as important symptoms of COVID-19 are the possible cutaneous and oral manifestations, among them the decrease or loss of taste (ageusia) [5]. These signs and symptoms represent a challenging differential diagnosis.

Thus, knowing what the literature reports, identifying what can assist dentist in understanding the symptoms of the disease, becomes relevant so that everyone can be attentive during their clinical practice regarding coping with COVID-19. This study aims to carry out a review of the literature on oral and skin manifestations in pediatric patients diagnosed with COVID-19.

METHODS

The literature review was carried out based on the formulation of the following guiding question: Can

oral and skin manifestations be observed in children and adolescents diagnosed with COVID-19?

The bibliographic search was conducted on August 1, 2020 in the databases National Library of Medicine National Institutes of Health (PubMed), Scientific Electronic Library Online (SciELO) and the *Biblioteca Virtual em Saúde* (Virtual Health Library) Bireme. The search, screening, selection, study evaluation and data extraction steps were performed by 4 reviewers, independently, using controlled keywords from the Medical Subject Headings - MeSH Database ("COVID-19"; "Child"; "Oral Manifestations"; "Skin Manifestations"; "Ageusia"; "Dysgeusia") and corresponding descriptors from Bireme. In addition, additional search in the references of the included articles was also considered in the research.

Inclusion criteria: randomized clinical trials, observational studies and literature reviews published as of December 2019; without language restriction; studies that respected the acronym PECO (P=patients under 18 years old; E=exposure to the Sars-Cov-2 coronavirus; C= not applicable; O=oral manifestations, dysgeusia, ageusia and skin manifestations). Exclusion criteria: letters to the editor, abstracts, articles whose full access was not possible, absence of researched outcomes. Four independent reviewers performed the steps of searching, screening, selecting articles, evaluating the complete texts included and extracting the data.

RESULTS

Identification and selection of studies

After the searches were completed, 29 publications were identified in the databases, as described in table 1.

On PubMed, three articles [9-11] were retrieved for the combination of MeSH terms "COVID-19", "Child",

Table 1. Sources of information and search strategy.

Data base	Search strategies	Number of articles
PubMed	((COVID-19 [All Fields]) AND (Child [All Fields]) AND (Skin Manifestations [All Fields]))	3
	((COVID-19 [All Fields]) AND (Child [All Fields]) AND (Skin Manifestations [All Fields]))	11*
	((COVID-19 [All Fields]) AND (Child [All Fields]) AND (Dysgeusia [All Fields]))	3
	((COVID-19 [All Fields]) AND (Child [All Fields]) AND (Ageusia [All Fields]))	3
SciELO	((COVID-19) AND (Child) AND (Oral Manifestations))	1
	((COVID-19) AND (Child) AND (Skin Manifestations))	0
	((COVID-19) AND (Child) AND (Dysgeusia))	0
	((COVID-19) AND (Child) AND (Ageusia))	0
Bireme	(tw:(COVID-19)) AND (tw:(Child)) AND (tw:(Oral Manifestations))	2
	tw:(COVID-19)) AND (tw:(Child)) AND (tw:(Skin Manifestations))	6
	(tw:(COVID-19)) AND (tw:(Child)) AND (tw:(Dysgeusia))	0
	(tw:(COVID-19)) AND (tw:(Child)) AND (tw:(Ageusia))	0
	Total of articles identified:	29
	Manual search	05
	Excluded	25
	Total of articles included	09

Note: *1 duplicate.

“Oral Manifestations”; eleven articles for the combination “COVID-19”, “Child”, “Skin Manifestations” [12-21], among which [14] was a duplicate; three articles for the combination “COVID-19”, “Child”, “Dysgeusia”, [22-24] and three articles for the combination “COVID-19”, “Child”, “Ageusia” [25-27].

From the Bireme data platform, using the combination of Health Descriptors “COVID-19”, “Child”, “Oral Manifestations”, two articles were retrieved [9,10]; with the terms “COVID-19”, “Child”, “Skin Manifestations”, six articles [12,15-18,28]. Regarding the terms “COVID-19”, “Dysgeusia”, “Child” and “COVID-19” “Child”, “Ageusia” no articles were found.

On SciELO the combination “COVID-19”, “Child”, “Oral Manifestations” retrieved one article [9]. With the other keyword combinations, no articles were found. In the additional manual search, five articles were found [29-33].

After identification, the following were excluded: nine duplicate studies, one of which, twice [9,10,12,14-18]; thirteen publications that did not answer the question PECO [9-12,14,17-20,23,24,26,27] and three letters to the editor [16,21,28], totaling the exclusion of twenty-five publications.

Among the studies analyzed, nine met the eligibility criteria. For the synthesis of the articles, data

extraction was performed considering the following category variables: author/year, study design, population (sample/age), objectives/methods, oral manifestations, skin manifestations, conclusions (table 2).

DISCUSSION

The Sars-CoV-2 virus has infected more and more people around the world. Knowledge of the signs and symptoms of COVID-19 is important for the early diagnosis of the disease since the virus can be transmitted even without significant symptoms [32]. In children, the virus manifests more mildly, and extra-respiratory signs suggestive of association with manifestations of the virus can be observed [13,15,22,25,29-32]. For this association to be proven, factors such as drug use reactions, blood disorders and manifestations of other viral diseases, for example, dengue, rubella and measles must be ruled out [29].

In this review, cutaneous manifestations and taste disorders were found, whose authors associated to COVID-19. Among the articles researched, most of them are case reports [15,22,25], [30-32], with this, the CARE checklist was applied (available at: care-statement.org/checklist) to assess the methodological quality of the reports, where it was possible to identify the lack of

Table 2. Descriptive summary of the included studies and evaluated characteristics: most common oral and skin manifestations associated with pediatric patients with Covid-19.

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Author	Study design	Sample	Age (years)	Objectives / Methods	Oral manifestations	Skin manifestations	Conclusions
Tang et al. [29]	Literature review.	88 patients (Does not separate children and adults)	8-84	They reviewed 16 studies (case reports, case series, prospective and retrospective observational studies). A total of 256 confirmed cases of COVID-19	Not reported	Erythematous lesions Vesicular lesions Urticarias Livedo Petechiae - Location: Non-synthesized	Highly variable and heterogeneous manifestations.
Qiu et al. [22]	Case Series	161 patients (10 adolescents)	15-17	Multicenter study evaluated characteristics and prevalence of olfactory and gustatory symptoms in adult and pediatric patients related to COVID-19. Three hospitals in China, 1 in France, 1 in Germany participated	Gustatory dysfunction, hypogeusia	Not reported	Olfactory and / or taste disorders may represent early or isolated symptoms of COVID-19. They can serve as a useful additional screening criterion, primarily for identifying patients in the early stages of infection.
Mak et al. [25]	Case report	3 patients	14 15 17	Report 3 cases of pediatric patients with COVID-19 who had anosmia and / or ageusia	Gustatory dysfunction, ageusia	Not reported	Children and adolescents with COVID-19 infection may present only anosmia or ageusia in the absence of other respiratory symptoms
Klimach et al. [15]	Case report	1 patient	13	Report 1 case of a patient (13 years old) with COVID-19 who presented cutaneous lesions located in the armpits, lower limbs and soles	Not reported	Multiple erythematous papular eruptions Erythematous macules associated with petechiae - Location: Foot soles and legs	The morphology was predominantly maculopapular, but also included petechiae and annular lesions. This suggests that the professional should consider the possibility of diagnosing COVID-19 in the presence of these lesions
Kaya et al. [13]	Literature review.	57 studies (9 studies with	7,5 - 17	To present a review of the clinical and histopathological characteristics and the	Not reported	Erythematous, multiform rash Purpuric lesions	The minority of patients included in the studies

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Kaya et al. [13]		children and adolescents, n = 48 patients)	7,5 - 17	potential pathological mechanisms of skin lesions in patients with COVID-19 - from 57 studies (case reports or case series)	Not reported	Urticarias - Location: Torso, feet Hands, elbows scalp	were children with acral lesions, papular vesicular rashes or pediatric multisystem inflammatory syndrome similar to Kawasaki disease
Ortiz et al. [30]	Case report	1 patient	9	To report a clinical case of skin lesions (pruritic rash) associated with COVID-19 in a 9-year-old girl	Not reported	Erythematous micropapular rash Edematous lesions - Location: The entire surface of the body, most visible at the lower extremities, toes	Micropapular rashes spread throughout the body
Papa et al. [31]	Case report	1 patient	11	Report a clinical case of a child (11 years old) with foot lesions, after having observed it in 10 more patients who tested positive Sars-CoV-2, from a sample of 44,000 patients	Not reported	Erythematous cutaneous lesions similar to chilblains on the toes and various ulcerative lesions with nail dyschromia - Location: Feet and nails	The child had painful vasculitic skin lesions on his/her feet
Genovese et al. [32]	Case report	1 patient	8	Report a clinical case of a child (8 years old) with mild systemic symptoms of chickenpox associated with COVID-19	Not reported	Erythematous papules and vesicles - Location: Torso (bilaterally and symmetrically)	Although the data does not prove that this rash is caused or is definitely associated with COVID-19, the authors suggest that papulovesicular rashes are included in the spectrum of rashes possibly associated with COVID-19
Marzano et al. [33]	Literature review.	33 patients (3 children)	6 8 2 months	Provide an overview of the cutaneous manifestations associated with COVID-19.	Not reported	Erythema, non-purulent maculopapular rash, urticaria, asymptomatic papulovesicular lesions, skin lesion similar to chickenpox - Location: Torso Upper and lower limbs	Skin manifestations associated with COVID-19 can be prognostic markers that need to be studied in-depth, due to the heterogeneity of the lesions and other systemic factors involved

conformity with some criteria that characterize a case report, thus highlighting limitations in the studies and a possible increase in the risk of methodological bias. In many cases, for example, there are reports of patients who have not been tested, or with a negative result for Covid-19, different tests and at different times of presenting symptoms, make it more difficult and/ or impossible to make more assertive conclusions about the manifestations. Even so, these studies point out the importance of the theme.

By considering the cutaneous clinical aspects manifested with COVID-19, the heterogeneity of the characteristics is perceived. However, the pathogenic mechanisms are still unknown, although it is believed that hyperactivity of the immune response and microvascular lesion are involved [33]. The main symptoms described in the studies were: erythematous lesions and urticaria [13,15,29-31,33], and the main locations of these lesions were on the limb ends and torso [13,15,30-32], and [33]. However, it is necessary to observe other signs and symptoms, even less frequently, in order to promote early diagnosis and avoid complications during the course of the disease. One cannot forget the need for diagnosis that differs from other systemic infections and their manifestations.

With regard to oral manifestations, gustatory dysfunction was found in two reports, both with adolescents aged 15 to 17 years old [22,25]. The mechanism is still poorly understood, there are indications that it is related to the inflammation of the chemoreceptors, and that there is interference from phenotypic factors, but there are still few studies on the subject. It is worth mentioning that patients may have gustatory dysfunction as the first symptom of COVID-19 [25]. In Brazil [34], this manifestation associated with influenza syndrome is a criterion for performing the COVID-19 test. This is important information for the observation and management of cases in which loss of taste (ageusia) or decreased taste (dysgeusia) is reported, making it necessary to carry out a careful evaluation by the health professional regarding the extra respiratory manifestations that may occur, especially in children and adolescents, in order to early identify the presence of infection with the new coronavirus.

Multisystem inflammatory syndrome has been observed in children, with similar symptoms and which overlap with Kawasaki disease (KD). A systematic review of the manifestations of COVID-19 with children identified

that among 17 patients (out of 114), 12 (70.6%) had symptoms of KD [35], which is a systemic vasculitis, common in children under 5 years old, but rare after the age of eight, with unknown etiology. Its cutaneous manifestation is the polymorphic rash, and it presents, in addition to other symptoms, oral manifestations, such as erythema and edema on the tongue, lips, oral mucosa, lingual papillae, and cleft lip. KD has been identified simultaneously or shortly after confirmation of Covid-19 [36-38].

Despite the paucity of consistent and more easily comparable data, and due to such a diagnostic challenge, existing publications can serve as an alert for health professionals, until new studies can effectively demonstrate or not the cause and effect relationship.

The importance of the oral health professional is emphasized, especially the pediatric dentists involved in the screening process, so that they contribute by guiding patients in case they identify any changes.

CONCLUSION

This review addressed studies available in the literature regarding oral and skin manifestations of COVID-19 in pediatric patients, with erythematous rashes on the limb ends and torso being the most common. Regarding the manifestation in the oral cavity, the gustatory dysfunction reported by adolescents stands out. However, the scarcity of studies is still present, with several issues to be clarified. More careful studies must be carried out, as it is still a recent topic in the literature, whose cause and effect relationship is not well established. In addition, the information presented may change due to the dynamics of the disease course caused by the new coronavirus and the performance of new studies.

Collaborators

MF MORAES, YR NATALINO, AF HOLANDA, HF and SOUZA SOBRINHO bibliographical research, data extraction, writing and approval of the final version. LC SARMENTO, review of the manuscript and final approval. APM GOMES, participation in the writing of the methodology, review of the manuscript and final approval. LF SANGIARD, study design, data analysis, interpretation of results, writing, review of the manuscript and final approval.

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