STUDY ON THE EVALUATION OF PERIODONTAL CLINICAL PARAMETERS IN PEDIATRIC PATIENTS POST-SARS-COV-2 INFECTION

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Abstract
At the beginning of the COVID-19 outbreak, children appeared to be less susceptible to SARS-CoV-2 infection than adults or more prone to develop asymptomatic and mild forms of the disease, which could have led to an underestimation of epidemiological data in young patients. Age-related differences in viral receptor expression, immune system competence, and comorbidity rates partially explained the lower prevalence of COVID-19 infection in pediatric patients. However, especially after the spread of the Omicron virus variant and due to the relaxation of social and health measures, the number of young people infected with SARS-CoV-2 has increased. The **aim** of the conducted study was to investigate periodontal clinical parameters, represented by plaque index, probing bleeding index and clinical periodontal attachment loss in pediatric patients, along with a series of demographic parameters, in the post-SARS-CoV-2 infection period. **Conclusions**: Our study provided evidence of widespread declines in periodontal health status and access to oral health care among children post-SARS-CoV-2 infection. Subjects with a lower amount of plaque showed a high intensity of periodontal inflammation, negatively correlated with time since diagnosis, a fact that supports the influence of the cytokine storm released post-SARS-CoV-2 infection and at the periodontal level.

Keywords: *pediatric dentistry, pandemic, clinical parameters, SARS-CoV-2*

1 Introduction

In advanced disease, SARS-CoV-2 induces exaggerated inflammation and systemic immune activation, which can give rise to a cytokine storm in its most severe form. [1]

In the cytokine storm, infected cells expressing ACE2 release numerous proinflammatory chemokines/chemoattractants that recruit leukocytes, which in turn produce TNF-α, IFN-c, and various interleukins that trigger a proinflammatory cascade with massive cytokine expression. [2,3]

The oral cavity as a portal of entry for SARS-CoV-2

Expression of major SARS-CoV-2 entry factors, i.e., ACE2 and TMPRSS (among others), has been identified in the oral mucosa, tongue, and salivary glands [4] The mucosa of the oral cavity is lined by stratified squamous epithelium, divided into keratinized (gum and hard palate) and non-keratinized (vestibular, oral, ventral, and oropharyngeal) mucosa.

Saliva from individuals infected with SARS-CoV-2, in both acellular and cellular salivary fractions, harbors SARS-CoV-2 virus particles, and their detection allows saliva to be considered as a valuable diagnostic specimen. [5] Compared to nasopharyngeal exudate (a diagnostic standard for SARS-CoV-2), detection of SARS-CoV-2 by RT-PCR in saliva demonstrated a 96.1% concordance with nasopharyngeal exudate, with a detection

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sensitivity of 95.7% and a specificity of 97.62% [6].

SARS-CoV-2 infection in pediatric subjects

At the beginning of the COVID-19 outbreak, children appeared to be less susceptible to SARS-CoV-2 infection than adults or more prone to develop asymptomatic and mild forms of the disease, which could have led to an underestimation of epidemiological data in young patients [7]. Age-related differences in viral receptor expression, immune system competence, and comorbidity rates partially explained the lower prevalence of COVID-19 infection in pediatric patients [8].

However, especially after the spread of the Omicron virus variant and due to the relaxation of social and health measures, the number of young people infected with SARS-CoV-2 increased and a hyperinflammatory syndrome probably related to SARS-CoV-2 was observed, namely the infection called "Multisystem inflammatory syndrome in children" (MIS-C) or "Pediatric inflammatory multisystem syndrome temporarily associated with COVID-19" (PIMS-TS). This syndrome affects the oral cavity like other known diseases such as Kawasaki disease (KD), macrophage activation syndrome (MAS), toxic shock syndrome (TSS) and secondary hemophagocytic lymphohistiocytosis (SHLH) [9].

According to UNICEF data, covering 105 countries from the start of the COVID-19 pandemic to January 1, 2023, 8.4% of children aged 0-4, 4.6% of children aged 5-9 years, 5.8% of children aged 10–14 years and 6–14 years and 7% of people aged 15–19 years were infected with SARS-CoV-2 [10].

Among SARS-CoV-2-positive pediatric subjects, the risk of severe COVID-19 disease with possible hospitalization and death was expected to increase when comorbidities occurred, although pediatric patients hospitalized for COVID-19 typically did not have multiple diseases [8].

However, [11], evaluating 3,111,714 pediatric cases worldwide, showed that men and women had the same risk of infection, but men had a higher risk of hospitalization and death.

In the specialized literature, very heterogeneous terms were found for primary oral lesions, probably due to the fact that oral lesions were reported mostly in the context of systemic syndromes and thus encountered and described by medical service providers not specialized in oral medicine, with the additional risk of underestimation, as well as overestimation, of some primary oral lesions, as well as misdiagnosis [12].

Oral lesions were frequently described in association with skin lesions, and their overall prevalence was similarly estimated to vary between 2% and 20% of SARS-CoV-2 positive pediatric subjects [13]. A systematic review by [14] found that 60% of subjects with oral lesions also had skin involvement, and the association between oral mucosa and skin manifestations was greater in the group with oral lesions attributable to KD, which is more common in the pediatric population.

In addition, pediatric cases with severe COVID-19 have been described as having a higher incidence of oral lesions. Consequently, similar to SARS-CoV-2 positive adult subjects (M:F = 1.78:1), oral lesions were more frequently described in young men compared to women (M:F = 1.33:1), who were also more frequently hospitalized [15].

It is very likely that the higher hospitalization rate of male pediatric patients leads to earlier diagnosis of oral lesions, as it may be more difficult to detect oral lesions in home care patients.

However, based on the retrieved data, the oral lesions observed in pediatric subjects with COVID-19 are likely to be found in boys with severe forms of the disease, as previously proposed by [16] for adult men with severe COVID-19, although no studies were conducted in young patients. From this perspective, oral lesions may represent a sign of disease exacerbation resulting from systemic involvement and thus indirectly suggest the adjustment of the therapeutic approach by physicians [12].

However, it should be noted that oral lesions have also been proposed as prodromal signs in pre-/asymptomatic SARS-CoV-2 infections, similar to smell and taste. Indeed, [17] suggested that both oral and dermatologic manifestations may be early signs of SARS-CoV-2 infection to watch for, as infected individuals may not show respiratory symptoms until 14 days after infection. Recognition of

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these lesions is particularly important in the pediatric population, who typically present with mild to moderate disease forms.

The second systematic literature review examined 624 pediatric cases diagnosed with MIS-C or KD associated with SARS-CoV-2 infection. Oral manifestations were one of the most common signs of MIS-C and were not different from oral lesions reported in KD cases [18]. In both diseases, changes in the oral cavity have been observed as one of the earliest symptoms, and erythema of the oral mucosa and tongue has been reported, accompanied by aphthous/ulcerative lesions in some cases. The lips were affected by erythema, edema, dryness or superficial scaling. Burning or pain that prevented or limited normal food intake was rarely reported.

The finding of a very low prevalence of oral lesions after COVID-19 vaccination may have been biased, as outpatient epidemiologic data on oral adverse reactions in the pediatric population provided little information on frequency, presentation, and causative drugs [19].

Moreover, oral lesions in children who have received at least one dose of the COVID-19 vaccine may be undiagnosed before their spontaneous recovery or misdiagnosed with other common clinical manifestations, such as those related to Candida albicans or herpes virus infections simplex type 1, which does not require special diagnostic tests in routine clinical practice [20, 21-23]

Instead, more attention has been paid to severe adverse effects with systemic involvement in pediatric patients after COVID-19 vaccinations.

The primary oral lesions identified were erosions and ulcerations (40%) with herpetiform and nonspecific patterns and macules and petechiae (20%); other lesions (40%) were uniformly described as crusts and pseudomembranous lesions [20]. The higher prevalence of erosive-ulcerative lesions observed can be explained by the fact that parents of young patients can only rarely detect oral manifestations, especially if they are asymptomatic. However, oral erosions and ulcers, which are usually symptomatic, are considered the most common oral adverse reactions caused by COVID-19 vaccines, and pseudo-membranes and crusts, representing their natural progression, have been reported in 40% of cases.

2. The aim of the study

The aim of the conducted study was to investigate periodontal clinical parameters, represented by plaque index, probing bleeding index and periodontal clinical attachment loss in pediatric patients, along with a series of demographic parameters, in the post-SARS-CoV-2 infection period.

3. Material and method

Study design. Study population. Inclusion and exclusion criteria

This observational study was carried out on a group of 26 pediatric patients (under 18 years of age), female and male, who presented a diagnosis of SARS-CoV-2 infection in the last 3 months preceding the investigation.

The exclusion criteria from the study were represented by:

- the use of anti-inflammatory and immunosuppressive drugs and antibiotics in the last 3 months
- use of mouthwashes with antimicrobials in the last 3 months
- periodontal therapy in the last 6 months
- the presence of infectious diseases, systemic immunological and / or inflammatory conditions that could influence the periodontal status.

The research was conducted in accordance with the principles set out in the 2008 Declaration of Helsinki and subsequent amendments. Given that the sample was composed mainly of minor patients, at the time of admission to the dental emergency department, the signed consent of the parents or legal guardians was requested so that the data obtained could be used anonymously

Evaluation of demographic parameters

The investigated demographic parameters were represented by:

- Age of subjects - Gender (male/female)
- Environment of origin (urban/rural)
- Family environment (single or two-parent families)
- Average monthly net income per family member

Clinical evaluation

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We established the periodontal diagnosis after a detailed anamnesis, a careful analysis of the patient's systemic and local data and the evaluation of clinical signs and symptoms, as well as the results of various paraclinical tests (for example, radiographs, GCF tests, microbiological tests or blood tests). Diagnostic steps were performed in a systematized and organized manner, including methods of inspection, palpation, percussion.

From these data, an analysis parameter was represented by the Time since the diagnosis of SARS-CoV-2 infection, diagnosis confirmed by the family doctor.

The data obtained from the periodontal clinical examination, together with the parameter measurements, were entered in the patient's periodontogram.

Bacterial plaque and tartar were evaluated by inspection for the qualitative evaluation and for the quantitative evaluation we used the periodontal probe.

The investigated periodontal indices were represented by:

- BOP (bleeding on probing); bleeding that is induced by gentle manipulation of the tissue deep in the gingival sulcus or the interface between the gum and the tooth.
- PI (plaque index) (ie, measurement of oral hygiene status based on recording both soft debris and mineralized deposits on teeth)
- CAL (clinical periodontal attachment loss) was measured in six sites of a tooth (mesio-vestibular, centro-vestibular, disto-vestibular, mesio-oral, centro-oral and disto-oral). Measurements were made using a UNC-15 periodontal probe (University of North Carolina No. 15).

5. Statistical analysis

Normality tests (Shapiro-Wilk) were performed so that the appropriate test could be chosen. Correlation between demographic parameters and clinical parameters was calculated using the Pearson parametric correlation test. A significance level of 5% ($p < 0.05$) was used in all statistical analyses.

6. Results

Demographic results

8 female subjects (30.8%) and 18 male subjects (69.2%) were included in the study (Fig 1).

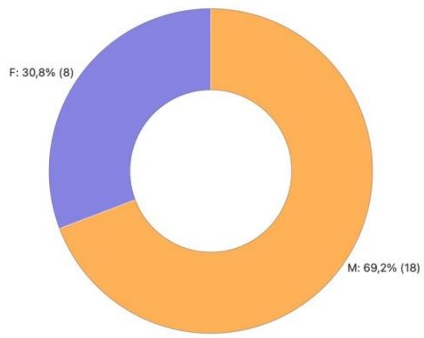

Figure 1 Gender distribution in the study group

The age of the subjects included in the study showed a normal distribution (Shapiro-Wilk coefficient 0.191) (Figure 2), with a mean ± SD of 11.57 ± 2.11 years.

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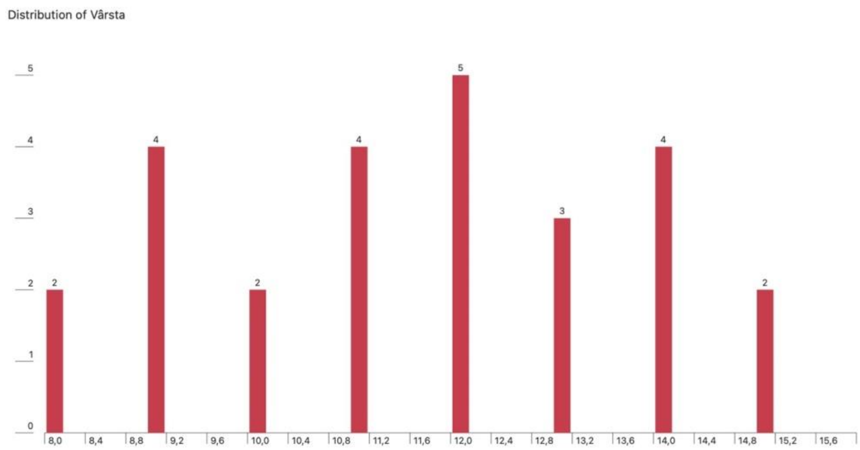

Figure 2 Age distribution of subjects

Seven subjects came from an urban environment (26.9%) and 19 from a rural environment (73.1%) (Figure 3).

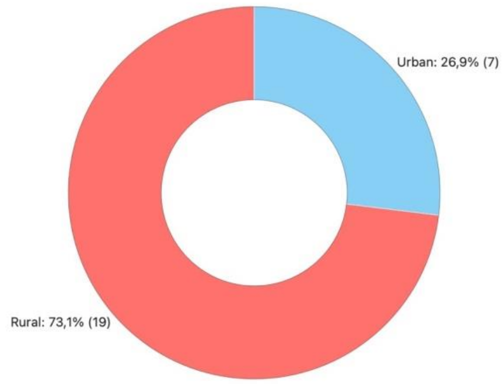

Figure 3 Distribution of the environment of origin

Five subjects (19.2%) came from a single-parent family (Figure 4).

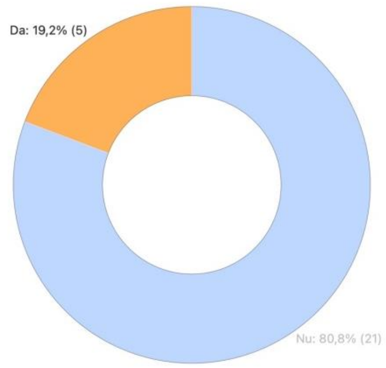

Figure 4 The percentage of single-parent families

The values of the net monthly income per family member showed a normal distribution (Shapiro-Wilk coefficient 0.249) (Figure 5), with a mean ± SD of 1238.76 ± 370.10 RON.

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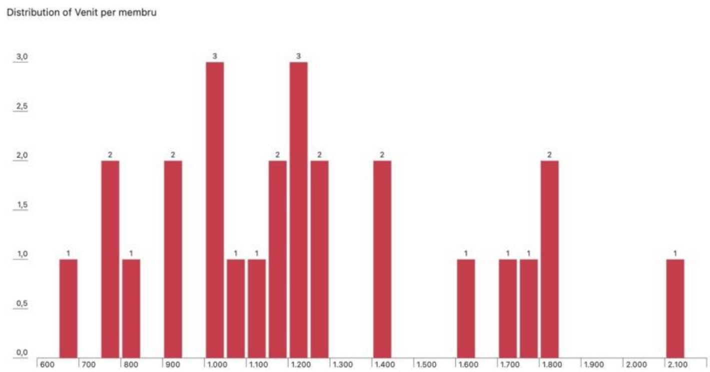

Figure 5 Distribution of monthly net income per family member

Time since diagnosis of SARS-CoV-2 infection also showed a normal distribution, (Shapiro-Wilk coefficient 0.754) (Figure 6), with a mean value of 30 ± 4.82 days.

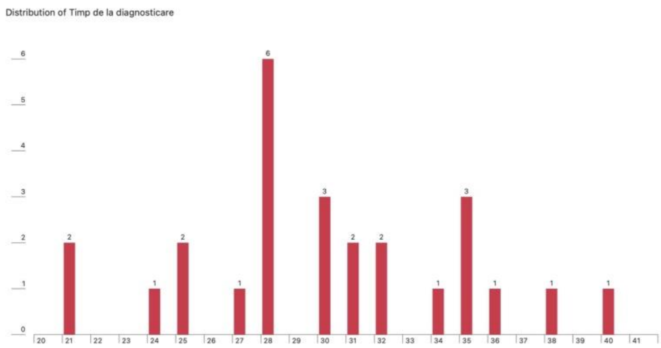

Figure 6 Time since diagnosis of SARS-CoV-2 infection

Clinical results

The plaque index (PI) showed a abnormal distribution (Shapiro-Wilk coefficient 0.016), with a median (minimum, maximum) of 53.5 (24, 76) (Figure 7).

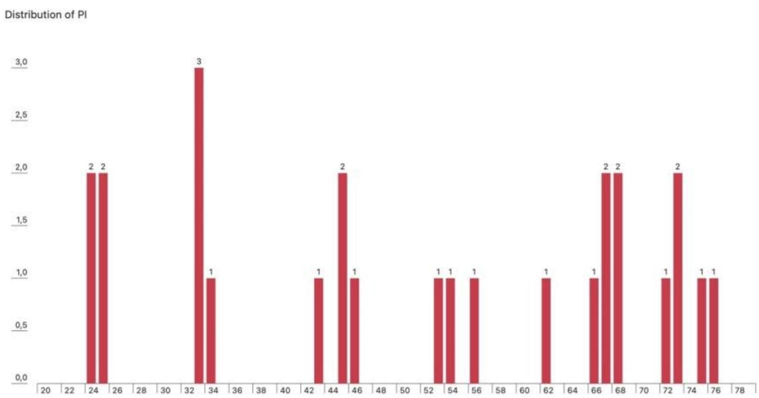

Figure 7 Plaque Index (PI) Distribution

The bleeding on probing (BOP) index showed a normal distribution (Shapiro-Wilk coefficient 0.067) (Figure 8), with a mean of 57.23 ± 16.03.

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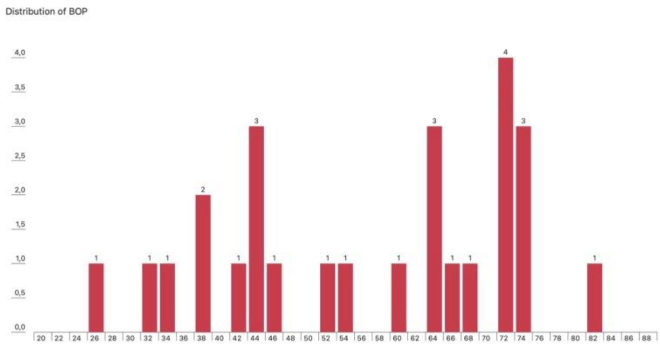

Figure 8 Distribution of bleeding on probing (BOP) index

Clinical periodontal attachment loss (CAL) showed a skewed distribution (Shapiro-Wilk coefficient <0.001), with a median (minimum, maximum) of 0 (0; 3.5) (Figure 9).

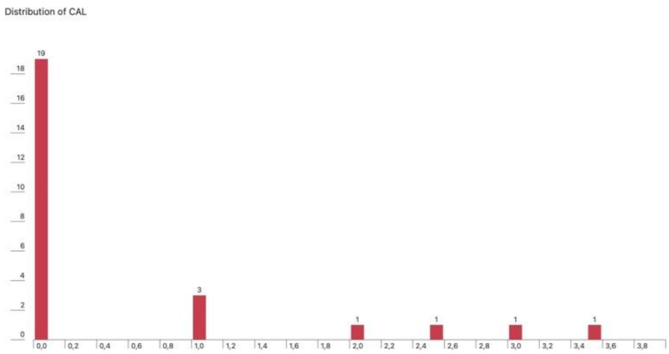

Figure 9 Distribution of clinical periodontal attachment loss

Analysis of correlations in the whole study group revealed positive correlations of PI with Time since diagnosis (r=0.467; p=0.014) and CAL (r=0.499; p=0.010).

7. Discussions

The aim of the present investigation was to analyze periodontal clinical parameters, represented by plaque index, probing bleeding index and clinical periodontal attachment loss in pediatric patients, in the post-infection period with SARS-CoV-2, as well as potential correlations between these parameters.

The face of epidemics and pandemics has changed over the years. Humanity has overcome these pandemics in the past, and the evolving immune system has helped it survive. Because SARS-CoV-2 is a new zoonotic pathogen, there is no pre-existing immunity and all of humanity is susceptible to infection and the development of COVID-19 disease [24-26]

Children can also be infected with SARS-CoV-2, but most pediatric cases of laboratory-confirmed SARS-CoV-2 infection are mild; severe COVID-19 disease in children is rare [24,27]. Immune preparation of children to any new pathogens, including SARS-CoV-2, can be based on several factors:

- Children have a more active innate immune response.
- Exposure to cigarette smoke and air pollution is lower in children compared to adults. Thus, they have healthier airways and fewer underlying disorders [28].
- Another suggested explanation is that viral interference in the respiratory tract of young children leads to a lower viral load in children.
- The ACE2 receptor for SARS-CoV-2 virus may be expressed differently in fetal lung compared to adult lung tissue [29].
- Children are exposed to other respiratory viruses, such as respiratory syncytial virus, influenza A virus, and influenza B virus, which increase serum antibody levels and could provide cross-protection [27,29].

Diagnosis can play a critical role in containing and spreading COVID-19[30]. An

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adequate history of contact, systemic symptoms, and radiographic changes of pneumonia can help establish the provisional diagnosis, but for the final diagnosis laboratory investigations are more reliable. [1,2,31]

For early infection assessment or diagnosis, WHO suggests rapid collection and nucleic acid amplification testing (NAAT) of respiratory specimens, including nasopharyngeal and oropharyngeal swabs.

In the present study, the patients' diagnosis was made by the family doctor and the periodontal evaluation was made 30 ± 4.82 days after the diagnosis.

The infection is acquired either by inhaling droplets or by touching contaminated surfaces and then touching the nose, mouth and eyes. While data on the incubation period for COVID-19 in the pediatric population are limited, it is believed to extend to 14 days, similar to adult patients with COVID-19 [32].

In the present investigation we noted a median of the plaque index of 53.5, accompanied by probing bleeding of 57.23 ± 16.03 and a clinical periodontal attachment loss between 0 and 3.5 mm.

To try and find an etiopathogenic difference that is less influenced by the amount of bacterial plaque, the analysis of correlations between parameters was performed on two subgroups of subjects: patients with PI less than 50% and patients with PI greater than 50%.

In the group with PI greater than 50%, PI correlated positively with patients' age, bleeding index, and clinical periodontal attachment loss.

Of course, this influence is known that a bacterial plaque with quantitative and qualitative risk parameters can generate both on the inflammatory status, quantified by BOP, but also on the loss of periodontal attachment.

Interestingly, in the group with PI less than 50%, PI correlated positively with time since diagnosis. Good oral hygiene is the practice of keeping the oral cavity, teeth and gums clean and healthy to prevent disease, and is important to a person's quality of life and physical and psychological health.

With all the progress made in researching the risk factors associated with poor oral health, preventive measures are the key factor essential to good oral hygiene, i.e. by removing dental biofilm (plaque), with tooth brushing as the most common means of effective dental care at home.[1-3,33,34]

For parents, brushing teeth at home is usually tied to other routine morning or evening events, such as before breakfast and going to bed.

The impact of quarantine on oral hygiene and sleep patterns is still in the early stages of investigation. Although stress, confusion, anger and other negative psychological disturbances have been reported during quarantine, exploring how this context can be reflected in the child's routine is fundamental [35].

Parental perception plays an essential role in identifying and solving children's problems. Every family faces difficult times with the necessary adjustments, making it difficult to maintain the child's sleep and hygiene routines [36].

Also, due to increased responsibilities and activities, including work, childcare and household tasks, parents/caregivers may not be able to pay close attention and supervise the child's oral hygiene. Several anatomical consequences of chronic mouth breathing are risk factors for sleep-disordered breathing. [27]. One study found that adolescents who breathe through their mouths have a greater increase in plaque index compared to adolescents who breathe through their noses [38]. This could indicate that sleep-disordered breathing could also influence the child's poor oral hygiene status.

Future studies evaluating the association between sleep-disordered breathing, mouth breathing, and oral hygiene are encouraged. Oral health care remains one of the largest unmet health care needs among children, with multiple barriers to access including unaffordable financial costs, lack of dental insurance, difficulty finding a dental provider with available funds, and costs of transport [39].

The pandemic has likely amplified one or more of these barriers to oral health care for most families, especially with the widespread closure of dental practices early on, social distancing measures, and loss of jobs and income for some families. [40]

Decline in oral health and use of oral care can lead to more untreated oral health problems among children, which can negatively

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affect their overall health and development in several ways.

In the same group with PI lower than 50% we noticed negative correlations of BOP with the time since diagnosis, a fact that supports the strong influence that the cytokine storm triggered by the SARS-CoV-2 infection generates at the periodontal level.

The findings in the present study highlight the importance of addressing oral health care needs and periodontal status among children, including their growth during the pandemic, through effective policy interventions that address barriers, including provider availability and reducing direct and indirect patient costs.[30]

The continuation of the monitoring of children's oral health and access to dental services should also be a public health and policy priority.

Real-time data collection and analysis, including through surveys and administrative data analysis are optimal for prompt monitoring and targeting of needs. However, these data resources lag over time, as do most national health surveys, indicating the need for new family surveys to monitor these population-level trends. [26]

These surveys can identify household-level factors that promote or worsen oral health and access to care during the pandemic. As such, they may inform the need for household and community-level interventions to mitigate the effects of the pandemic on children's oral health, including promoting low-sugar diets, water fluoridation, and educating parents and children about dental hygiene practices. [33,41,42]

8. Conclusions

Our study provided evidence of widespread declines in periodontal health status and access to oral health care among children post-SARS-CoV-2 infection.

Subjects with a lower amount of plaque showed a high intensity of periodontal inflammation, negatively correlated with time since diagnosis, a fact that supports the influence of the cytokine storm released post-SARS-CoV-2 infection and at the periodontal level.

These findings highlight the need to monitor these trends through timely data collection and counter the effects of the pandemic through prompt policies and oral health campaigns that increase awareness of household prevention activities and timely access to dental services.

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