Gingival inflammation in children and adolescents with cerebral palsy: a systematic review and meta-analysis

Manoel Pereira de Lima,¹ Brunna Rodrigues Grisi,¹ Clarissa Araújo Campos Camelo,² Renata Oliveira Guaré,³ Sérgio d'Avila Lins Bezerra Cavalcanti⁴ and Ítalo de Macedo Bernardino⁴

¹Department of Dentistry, Universidade Estadual da Paraíba (UEPB), Araruna, PB, Brazil; ²Department of Dentistry, Centro Universitário UNIFACISA, Campina Grande, PB, Brazil; ³Department of Dentistry, Universidade Cruzeiro do Sul (UNICSUL), São Paulo, SP, Brazil; ⁴Department of Dentistry, Universidade Estadual da Paraíba (UEPB), Campina Grande, PB, Brazil.

Abstract

Aims: This systematic review aimed to compare the gingival status of children and adolescents with cerebral palsy (CP) to those without CP.

Materials and methods: Nine databases were searched up to May 2020 for observational studies that evaluated the periodontal status of patients with and without CP. Risk of bias between studies was assessed using Joanna Briggs Institute Critical Appraisal tools. Random effects meta-analysis was performed.

Results: The search provided 425 results, from which only five met the eligibility criteria and were ultimately included in the qualitative assessment of the review. All studies presented low risk of bias. The total number of patients in case / control groups was 454/532. The standardized mean difference of the gingival index between cases and controls was 0.42 (95% CI = 0.21- 0.64; p < 0.001), whereas for the plaque index, it was 0.66 (95% CI = 0.49-0.84; p < 0.001), indicating worse periodontal status for individuals with CP. In general, heterogeneity was low (I2 <25.0%).

Conclusion: Children and adolescents with CP are more likely to have bacterial plaque accumulation, gingival inflammation, and gingival hyperplasia compared to individuals without CP.

Keywords: Periodontal Diseases; child; adolescent; cerebral palsy

Introduction

Cerebral palsy (CP) is a multifactorial encephalopathy that occurs in about 2 to 3 individuals per 1,000 live births (Jonsson *et al.*, 2019; Stavsky *et al.*, 2017). This condition is defined as a group of non-progressive movement and posture disorders caused by an injury that occurred during fetal or infant brain development, causing partial or total dependence on caregivers to perform daily activities, including oral hygiene (Bax *et al.*, 2005; Cardoso *et al.*, 2014; Cardoso *et al.*, 2018). CP is topographically classified into (1) monoplegia, a form that affects only one limb; (2) hemiplegia, characterized by the involvement of the lateral half of the body; (3) diplegia, which affects symmetrical parts of the body; (4) triplegia, a form of paralysis involving three limbs, that is, paralysis on one side of the body and an arm or leg on the other side and (5) quadriplegia, the most severe form of the condition that affects the upper and lower limbs of both sides (Sankar and Mundkur, 2005). CP is divided into subtypes according to the dominant neurological signs into spastic, dyskinetic or ataxic (Rana *et al.*, 2017).

Epilepsy, secondary musculoskeletal problems, behavioral, sensitivity, perception, cognition and communication disorders are frequent findings in CP patients

Correspondence to: Ítalo de Macedo Bernardino, Department of Dentistry, Rua Baraúnas, 351 - Bairro Universitário - Campina Grande-PB, Brazil. 58429-500. E-mail: italo.macedo50@gmail.com

(Santos *et al.*, 2016). These patients are at increased risk for oral problems, as acquired or genetic neuromuscular disorders can cause changes in skeletal and facial structures, number and morphology of teeth, irregular eruption pattern and malocclusion (El Ashiry *et al.*, 2016). In addition, CP patients have swallowing disorders, which makes oral feeding difficult and requires the use of external feeding devices (Cardona-Soria *et al.*, 2020).

Studies have shown that children with CP are more susceptible to the accumulation of dental biofilm and, consequently, to the development of caries and gingival inflammation (Guerreiro and Garcias, 2009; Cardoso *et al.*, 2017; Rodríguez *et al.*, 2018). The following are among the contributing factors for this condition: inability to control muscle function, which makes daily oral hygiene difficult, intraoral sensitivity and orofacial motor dysfunction, in addition to the use of antiepileptic drugs, such as phenytoin, which can increase the probability of occurrence of gingival hyperplasia (Wyne *et al.*, 1996; Jan and Jan, 2016; Rodríguez *et al.*, 2018).

Other factors that can influence the increase in the prevalence of periodontal problems in children and adolescents with CP are low unstimulated salivary flow, changes in pH and buffering capacity (Santos *et al.*, 2016). Taking into account the association between these factors, it is important to understand the oral health status and treatment needs of this population in order to expand scientific knowledge on the subject and outline special care strategies with emphasis on prevention and promotion of general and oral health.

Scientific evidence has shown that the periodontal status of children and adolescents with CP is worse compared to those without CP (Pope & Curzon, 1991; Guare & Ciampioni, 2004; Du *et al.*, 2010; El Ashiry *et al.*, 2016). However, there is no systematic review on this topic. Therefore, this systematic review aimed to compare the gingival status of children and adolescents with cerebral palsy (CP) to those without CP.

Materials and methods

Protocol and Registration

This systematic review was carried out following the PRISMA statement (Moher *et al.*, 2009) and Cochrane guidelines (Higgins and Green, 2011). The systematic review protocol was registered in the PROSPERO database (CRD42019120219).

Eligibility criteria

Eligibility criteria were designed to respond to the research question in the PECO format (i.e., P = population, E = exposure, C = comparison, and O = outcomes), as follows: Children and adolescents (P) diagnosed with cerebral palsy (E), have worse periodontal status (O) compared to those without cerebral palsy (C)?

Inclusion criteria were observational studies that assessed the periodontal status of children and adolescents with cerebral palsy compared to individuals without the disease. Restrictions regarding publication year, language, or status (Epub a head of print) were not applied. Exclusion criteria were studies not related to the topic, literature reviews, case reports, letters to the editor or editorials, conference abstracts, personal opinions, books and / or book chapters.

Information and Research Sources

Two eligibility reviewers independently conducted the search (MPL and BRG). As a primary study source, electronic databases PubMed / MEDLINE, Web of Science, Scopus, Cochrane Library, SciELO, LILACS and LIVIVO were used. The OpenThesis and OpenGrey databases were also searched (Table 1). Descriptors were searched in the Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH) databases. With the help of Boolean operators "AND" and "OR", the research strategy was developed (Table 1). Publications until May 3, 2020 were included. Studies retrieved after the search were imported into the MendeleyTM Desktop 1.19.2 software (MendeleyTM Ltd, London, UK) for the detection and removal of duplicates.

Selection of studies

As a calibration exercise, reviewers discussed the eligibility criteria and applied them to a sample of 20% of retrieved studies to determine inter-examiner agreement. With good level of agreement (Kappa \geq 0.80), reviewers read all studies, independently. This process was structured in three phases. In phase 1, titles were read by two reviewers (MPL and BRG). Studies with titles compatible with the research theme of this systematic review were selected for phase 2, which consisted of reading the abstracts. Reading of the full text was carried out in phase 3. The reference lists of included studies were analyzed to identify relevant research. A third reviewer (IMB) was consulted to provide a final decision in case of disagreement between the two reviewers.

Data collection and extraction process

Two evaluators performed data extraction independently (MPL and BRG). Both used spreadsheet especially created to extract the necessary information considering the following items: study identification (author, year, country and type of publication); sample characteristics (sample size, average sample age, distribution by sex, and origin of individuals); method to obtain results (for example, visible plaque index, gingival bleeding index) and main conclusions.

Table 1. Strategies for database search.

Database	Search Strategy (May 3, 2020)	Results
PubMed (http://www.ncbi.nlm.nih.gov/pubmed)	("Cerebral Palsy" [MeSH Terms] OR "Cerebral Palsy" [All Fields] OR "Disable child*") AND ("Periodontal Diseases" [MeSH Terms] OR "Periodontal Diseases" [All Fields] OR "Periodontitis" [All Fields] OR "Periodontal Attachment Loss" [All Fields] OR "Periodontal Pocket" [All Fields] OR "Alveolar Bone Loss" [All Fields] OR "Gingivitis" [All Fields] OR "Gingival Recession" [All Fields] OR "Tooth Mobility" [All Fields] OR "Periodontal Abscess" [All Fields] OR "Periodont*" [All Fields])	74
Web of Science (http://apps.webofknowledge.com/)	TS=(("Cerebral Palsy" OR "Disable child*") AND ("Periodontal Diseases" OR "Periodontitis" OR "Periodontal Attachment Loss" OR "Periodontal Pocket" OR "Alveolar Bone Loss" OR "Gingivitis" OR "Gingival Recession" OR "Tooth Mobility" OR "Periodontal Abscess" OR "Periodont*"))	38
Scopus (http://www.scopus.com/)	TITLE-ABS-KEY("Cerebral Palsy") OR TITLE-ABS-KEY("Disable child*") AND TITLE-ABS-KEY("Periodontal Diseases") OR TITLE-ABS-KEY("Periodontitis") OR TITLE-ABS-KEY("Periodontal Attachment Loss") OR TITLE-ABS-KEY("Periodontal Pocket") OR TITLE-ABS-KEY("Alveolar Bone Loss") OR TITLE-ABS- KEY("Gingivitis") OR TITLE-ABS-KEY("Gingival Recession") OR TITLE-ABS-KEY("Tooth Mobility") OR TITLE-ABS- KEY("Periodontal Abscess") OR TITLE-ABS-KEY("Periodont*")	107
Cochrane Library (http://www.cochranelibrary.com/)	("Cerebral Palsy" OR "Disable child*") AND ("Periodontal Diseases" OR "Periodontitis" OR "Periodontal Attachment Loss" OR "Periodontal Pocket" OR "Alveolar Bone Loss" OR "Gingivitis" OR "Gingival Recession" OR "Tooth Mobility" OR "Periodontal Abscess" OR "Periodont*")	15
SciELO (http://www.scielo.org/)	Cerebral Palsy AND Periodontal Diseases	4
	Cerebral Palsy AND Periodontitis	2
	Cerebral Palsy AND Gingivitis	6
LILACS (http://lilacs.bvsalud.org/)	tw:("Cerebral Palsy" AND "Periodontal Diseases") AND (instance:"regional") AND (db:("LILACS"))	5
	tw:("Cerebral Palsy" AND "Periodontitis") AND (instance:"regional") AND (db:("LILACS"))	0
	tw:("Cerebral Palsy" AND "Gingivitis") AND (instance:"regional") AND (db:("LILACS"))	8
LIVIVO (https://www.livivo.de)	("Cerebral Palsy" OR "Disable child*") AND ("Periodontal Diseases" OR "Periodontitis" OR "Periodontal Attachment Loss" OR "Periodontal Pocket" OR "Alveolar Bone Loss" OR "Gingivitis" OR "Gingival Recession" OR "Tooth Mobility" OR "Periodontal Abscess" OR "Periodont*")	166
OpenGrey (http://www.opengrey.eu/)	("Cerebral Palsy" AND "Periodontal Diseases")	0
ClinicalTrials (https://clinicaltrials.gov/)	("Cerebral Palsy" AND "Periodontal Diseases")	0
TOTAL		425

Risk of individual bias of studies

The risk of bias in eligible studies was assessed using the Joanna Briggs Institute's Critical Assessment tools for use in systematic reviews (Aromataris and Munn, 2017). For case-control studies, the checklist has 10 questions.

High risk of bias was considered when the study reached $\leq 49\%$ of "yes" responses. For moderate risk of bias, the percentage of "yes" responses varied between 50% and 69%, while for low risk of bias, responses reached $\geq 70\%$.

Outcome measurement and data analysis

Meta-analysis was performed to estimate the magnitude of difference in periodontal status in the case group compared to the control group. Outcome differences were reported through forest plots, considering the random effects model to determine standardized mean differences, 95% confidence intervals and p-values (Higgins and Green, 2011; DerSimonian and Laird, 2015). Heterogeneity among studies was assessed using the I² statistics and classified as follows: low (I² \leq 25%), moderate ($I^2 = 50\%$) and high ($I^2 > 75\%$) (Higgins and Thompson, 2002). Even in the absence of significant statistical heterogeneity (I2), the random effects model was used to control the possible influence of clinical heterogeneity found in the study samples. Publication bias was not assessed, as there were no more than 10 studies to be grouped in a funnel plot (Egger et al., 1997). Review Manager software version 5.3 (RevMan, Cochrane Collaboration) was used to perform all statistical analyses.

Results

Selection of studies

This review was carried out in nine electronic databases in May 2020. In the first phase, 425 records were identified and, after removing duplicates, 254 studies were submitted to analysis of titles and abstracts. Subsequently, only 13 studies were eligible for full-text analysis. Finally, five articles were submitted to analysis of results. Figure 1 exemplifies the process of searching, identifying, including and excluding studies.

Characteristics of studies

Table 2 presents a summary of the main characteristics of included investigations. Selected studies were conducted in Saudi Arabia (El Ashiry *et al.*, 2016), China (Du *et al.*, 2010), Brazil (Guare and Ciampioni, 2004), Nigeria (Oredugba, 2011) and England (Pope and Curzon, 1991). The total number of patients in case / control groups was 454/532. All patients came from schools or rehabilitation centers. The most prevalent motor deficiency and topographic classification of cerebral palsy were spastic and quadriplegia, respectively (Pope and Curzon, 1991; Guare and Ciampioni, 2004; Du *et al.*, 2010). The other studies did not report this occurrence (Oredugba, 2011; El Ashiry *et al.*, 2016).

To evaluate periodontal status (Table 3), the methods of Partial Score Modification described by Ramfjord (1967), the Löe method (1967), the Simplified Oral Hygiene Index (Greene and Vermillion, 1994), the Gingival Hyperplasia Index (Angelopoulos and Goaz, 1972), the Gingival Index (Löe and Silness, 1963) and the Visual Periodontal Index (Cappelli and Brown, 2002) were used. In descriptive terms, the results of individual studies have shown that the gingival index (Pope, 1991; Guare, 2004; Du, 2010), the visual periodontal index (El Ashiry, 2016), the plaque index (Pope, 1991; Guare, 2004; Du, 2010; Oredugba, 2011), the oral hygiene index (Guare, 2004; Oredugba, 2011; El Ashiry, 2016), the calculus index (Guare, 2004), as well as the frequency of gingival hyperplasia (Guare, 2004; Du, 2010) and gingivitis (Oredugba, 2011; El Ashiry, 2016) were higher among patients with CP compared to those without CP.

Meta-analysis and risk of bias

Figure 2 shows the magnitude of differences between individuals with CP and those without CP in relation to periodontal status. The standardized mean difference of the gingival index between cases and controls was 0.42 (95% CI = 0.21- 0.64; p < 0.001), whereas for the plaque index, it was 0.66 (95% CI = 0.49-0.84; p < 0.001), indicating worse gingival status for individuals with CP. In general, heterogeneity was low for the evaluated outcomes (I² <25.0%). The risk of bias was low for all studies analyzed, as shown in Table 4.

Discussion

Considering the need for dental practice based on scientific evidence, a systematic review of gingival and periodontal diseases and cerebral palsy becomes very important to clarify and evaluate the quality of available evidence and gather the main information on the subject. In this sense, this review sought to systematically analyze in literature case-control studies with results about gingival status of children and adolescents with and without CP.

The high prevalence of gingival inflammation can be associated with different factors, such as severity of CP and level of intellectual disability, which requires considerable changes in food consistency due to limitations of gnathic bones during the chewing process (Santos *et al.*, 2002). The findings of this research demonstrate that young individuals with CP have higher frequency of gingival inflammation, which is explained by the statistically significant association observed in most studies (Pope and Curzon, 1991; Guare and Ciampioni, 2004; Du *et al.*, 2010; Oredugba, 2011).

CP patients have motor alterations, according to the type of neurological damage, influencing muscle tone, spasticity, biofilm accumulation, absence of self-cleaning by the tongue, added to the ingestion of pasty foods. Currently, attempts have been made to characterize the immune and inflammatory profile of these individuals and the findings point to higher levels of interleukin and greater susceptibility to gingival inflammation in CP patients (Yoshida *et al.*, 2019). They generally drink less water, have thicker (viscous) saliva and consequently biofilm will be in the oral cavity for longer time, if it is not disorganized (Santos *et al.*, 2017).

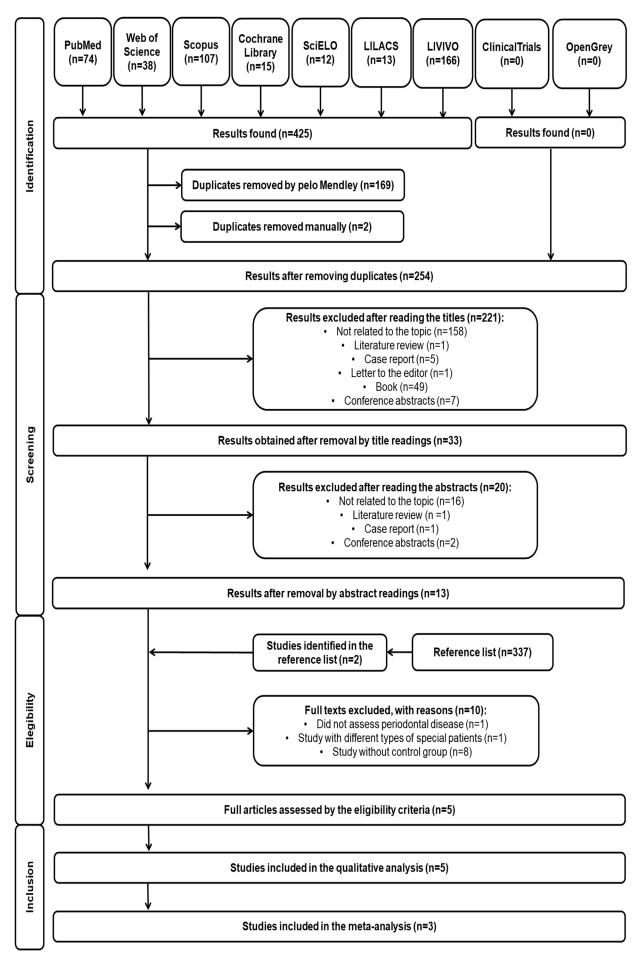


Figure 1. Flowchart of the process of literature search and selection adapted from the PRISMA statement.

First author and year of publication	Country	Sample (n)	Mean sample age	Origin of individuals	Characteristics of cerebral palsy	Method to obtain results
Pope, 1991	England	Case group (150): 82 ♂ 68 ♀ Control group (191): 104 ♂ 87 ♀	Case group: 10.25 years (range: 3.08 to 18.16) Control group: 10.39 years (range: 3.17 to 16.25)	Special Schools in Leeds	Most prevalent type of motor disability: Spastic Most prevalent topographic classification: Quadriplegia	Plaque Index Gingival Index
Guare, 2004	Brazil	Case group (100): – Control group (100): –	Case group: (range: 2.5 to 6.1 years) Control group: (range: 2.5 to 5.9 years)	Lar Escola São Francisco, Central of Rehabilitation in São Paulo	Most prevalent type of motor disability: Spastic Most prevalent topographic classification: Quadriplegia	Plaque Index Calculus Index OHI-S Gingival Index Gingival Hyperplasia
Du, 2010	China	Case group (72): 39 ♂ 33 ♀ Control group (72): 39 ♂ 33 ♀	Case group: 4.7 ± 1 year (range: 2.5 to 6.4 years) Control group: paired sample of preschoolers (age ± 0.3 years)	23 Special Child Care Centers in Hong Kong	Most prevalent type of motor disability: Spastic Most prevalent topographic classification: Quadriplegia	Plaque Index Gingival Index Gingival Hyperplasia
Oredugba, 2011	Nigeria	Case group (69): 45 $\stackrel{\circ}{\circ}$ 24 \bigcirc Control group (70): 42 $\stackrel{\circ}{\circ}$ 28 \bigcirc	Case group: 11.42 ± 4.56 years Control group: 11.35 ± 4.19 years	3 Centers for Individuals with Disabilities	*	OHI-S Bleeding on probing
El Ashiry, 2016	Saudi Arabia	Case group (63): – Control group (99): –	Case group: 8.05 ± 2.10 years Control group: 9.19 ± 2.11 years	8 Disability Centers in Jeddah	*	Visual Periodontal Index OHI-S Bleeding on probing

Table 2. Summar	y of the mair	characteristics	of the studies	eligible fo	or qualitative analysis.

Note. – There was no division according to sex; OHI-S = Oral Hygiene and plaque Index – Surface; * Not reported by the authors; \mathcal{Q} = female; \mathcal{J} = male.

Assessment of periodontal status	Periodontal status				
Partial scoring modification described by Ramfjord (1967) of the method of Löe (1967)	Plaque Index (mean \pm SD): Case group: 1.35 \pm 0.84 Control group: 0.87 \pm 0.80 Gingival Index (mean \pm SD): Case group: 1.54 \pm^*				
Simplified Oral Hygiene Index (Greene & Vermillion, 1964) e Gingival Hyperplasia Index (Angelopoulos & Goaz, 1972)	Control group: $0.46 \pm^*$ Plaque Index (mean \pm SD): Case group: 1.26 ± 0.72 Control group: 0.68 ± 0.63 Calculus Index (mean \pm SD): Case group: 0.02 ± 0.11 Control group: 0.01 ± 0.06 OHI-S (mean \pm SD) Case group: 1.28 ± 0.75 Control group: 0.69 ± 0.63 Gingival Index (mean \pm SD) Case group: 1.04 ± 0.59 Control group: 0.79 ± 0.52 Gingival Hyperplasia: Case group: $6/100$				
Simplified Debris Index (Greene & Vermillion, 1964), Gingival Index (Löe & Silness, 1963) e Gingival Hyperplasia Index (Angelopoulos & Goaz, 1972)	Control group: $0/100$ Plaque Index (mean \pm SD): Case group: 0.89 ± 0.28 Control group: 0.71 ± 0.35 Gingival Index (mean \pm SD): Case group: 0.81 ± 0.19 Control group: 0.73 ± 0.22 Gingival Hyperplasia: Case group: $14/72$ Control group: $0/72$				
Simplified Oral Hygiene Index (Greene & Vermillion, 1964)	OHI-S (mean ± SD): Case group: 1.35 ± 0.84 Control group: 0.87 ± 0.80 Gingivitis: Case group: 27/69 Control group: 17/70				
Visual Periodontal Index (Cappelli & Brown, 2002) e Simplified Oral Hygiene Index (Greene & Vermillion, 1964)	Visual Periodontal Index (mean ± SD): Case group: 0.86 ± 0.35 Control group: 0.82 ± 0.39 OHI-S (mean ± SD): Case group: 1.13 ± 0.60 Control group: 1.14 ± 0.66 Gingivitis: Case group: 54/63 Control group: 81/99				

Table 3. Summary of the evaluated periodontal variables and results of each study.

Note. * Not reported by the authors; SD = standard deviation.

META-ANALYSIS

GINGIVAL INDEX

	C	ases		Co	ntrols			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Du, 2010	0.81	0.19	72	0.73	0.22	72	42.0%	0.39 [0.06, 0.72]	
Guare , 2004	1.04	0.59	100	0.79	0.52	100	58.0%	0.45 [0.17, 0.73]	
Total (95% CI)			172			172	100.0%	0.42 [0.21, 0.64]	•
Heterogeneity: Tau² = Test for overall effect:			-0.5 -0.25 0 0.25 0.5 Favours [cases] Favours [controls]						

PLAQUE INDEX

	Cases			Со	ntrols			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Du, 2010	0.89	0.28	72	0.71	0.35	72	23.7%	0.56 [0.23, 0.90]	+
Guare, 2004	1.26	0.72	100	0.68	0.63	100	29.9%	0.85 [0.56, 1.14]	
Pope, 1991	1.35	0.84	150	0.87	0.8	191	46.4%	0.59 (0.37, 0.80)	+
Total (95% CI)			322			363	100.0%	0.66 [0.49, 0.84]	•
Heterogeneity: Tau² = Test for overall effect:			-2 -1 0 1 2 Favours [cases] Favours [controls]						

Figure 2. Forest plot showing the magnitude of differences between individuals with CP and those without CP in relation to gingival inflammation and plaque index.

	/	,									
First author, and year of publication	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	% Yes / risk
Роре, 1991						_	_		\checkmark		80.0% / Low
Guare, 2004						_	_		\checkmark	\checkmark	80.0% / Low
Du, 2010						_	_		\checkmark	\checkmark	80.0% / Low
Oredugba, 2011						_	_		\checkmark	\checkmark	80.0% / Low
El Ashiry, 2016						_	_		\checkmark	\checkmark	80.0% / Low

Table 4. Risk of bias assessed by the JBI Critical Appraisal Checklist for Case Control Studies.

Note. $\sqrt{:}$ Yes; —: No; NA: Not applicable. U: Unclear. Q1. Were the groups comparable other than the presence of disease in cases or the absence of disease in controls? Q2. Were cases and controls matched appropriately? Q3. Were the same criteria used for identification of cases and controls? Q4. Was exposure measured in a standard, valid and reliable way? Q5. Was exposure measured in the same way for cases and controls? Q6. Were confounding factors identified? Q7. Were strategies to deal with confounding factors stated? Q8. Were outcomes assessed in a standard, valid and reliable way for cases and controls? Q9. Was the exposure period of interest long enough to be meaningful? Q10. Was appropriate statistical analysis used?

The practice of oral health at home and regular dental treatment are significant factors for maintaining the quality of the periodontal status of these patients. A recent clinical study has shown that periodontal treatment influences the levels of inflammatory markers in individuals with CP, which can significantly reduce the levels of TNF- α , IL-1 β , IL-6 and IL-8 (Yoshida *et al.*, 2019). This shows the importance of periodontal evaluation, treatment and dental follow-up for this population, and caregivers must be trained to perform correct oral hygiene for these patients.

The removal of plaque is the main factor related to oral problems in people with disabilities and results from the lack of neuromuscular coordination (Subramaniam *et al.*, 2014). According to the meta-analysis, statistically significant differences were observed in the plaque index between individuals with CP and those without the disorder. These results suggest that children and adolescents with CP are unable to properly clean their own teeth and that they probably need modifications in their brushes or more assistance during tooth brushing.

Deviations in the correct way of brushing teeth and not using dental floss promote the deposition of biofilm on dental surfaces, favoring the appearance of carious lesions and as well as gingivitis and periodontitis (Kumar *et al.*, 2009). Risk factors for gingival inflammation in individuals with CP may include: salivary osmolarity (Santos *et al.*, 2016), degree of motor impairment and levels of inflammatory biomarkers (Santos *et al.*, 2017). Other factors such as amount of drugs used, degree of dependence on caregivers and socioeconomic conditions can also influence (Cardoso *et al.*, 2015; Barros *et al.*, 2019). Often the caregiver is the mother herself, with limitations and low quality of life, who cannot even perform her own oral hygiene adequately.

Periodontal changes are mainly associated with athetoid CP type, characterized by continuous and uncontrolled movements of muscles, especially neck, resulting from excessive head movements, which makes oral hygiene difficult and increases the frequency of gingival inflammation (Cardoso *et al.*, 2015). In eligible studies, little has been discussed regarding the occurrence of periodontitis in CP patients. This can probably be explained by the average age of participants.

The meta-analysis showed that significantly higher gingival index levels were observed in the group of individuals with CP. Evidence has shown that children and adolescents aged 7-18 years are those who most frequently have gingival calculus and bleeding (Cardoso *et al.*, 2015), which corroborates the average age of individuals investigated in this study. Another striking factor in this population is the presence of gingival hyperplasia, frequently associated with the use of antiepileptic drugs, such as phenytoin (Guerreiro and Garcias, 2009).

Phenytoin is associated with increased level of protein synthesis by fibroblasts, leading to a decrease in collagen degradation and, consequently, to an increase in gingival tissue (Guimarães Junior, 2007). In this study, it was observed that individuals in the control group did not present any level of gingival hyperplasia, differently from some patients in the group with paralysis. Therefore, it must be considered that individuals with CP who use drugs such as phenytoin need even greater attention, given the greater likelihood of periodontal changes.

Although the vast majority of studies have not evaluated the possible confounding effect resulting from the socioeconomic status of individuals from cases and control groups in the assessment of findings, this is a point that deserves to be further discussed. Greater purchasing power favors better conditions for the prevention and treatment of these conditions, which may not be possible for individuals from lower socioeconomic classes (Santos *et al.*, 2002; De Camargo and Antunes, 2008). Therefore, future studies should take into account the influence of variables such as family income and education level of parents and / or caregivers in the periodontal condition.

The findings of observational studies should be viewed with caution, since they do not allow establishing cause-and-effect relationships. As a way of minimizing the bias of comparative results, most studies attempted to organize control groups with a similar sample size to the exposure group, generally matching by age and sex. Control group individuals were usually recruited from schools in the same geographic area.

Studies varied especially in relation to the sample size and method used in the diagnosis of the periodontal condition. Another limitation is due to the fact that the eligible articles evaluated only gingival parameters (such as gingivitis, gingival hyperplasia and plaque index), more studies are necessary to evaluate the periodontal condition in detail. Multicenter studies, with representative samples using standardized diagnostic methods and evaluation of periodontal status (including probing depth, clinical attachment level, and bone loss), are needed.

This review is original and contributed to the advancement of scientific knowledge in two points. First, this is the first systematic review with meta-analysis that investigated the association between gingival condition and CP. Second, an extensive search strategy was applied without any restrictions on language or date of publication and including "grey literature", seeking to avoid selection and publication biases.

Conclusion

The results of the present review show that children and adolescents with CP are more likely of having bacterial plaque accumulation, gingival inflammation, and gingival hyperplasia compared to individuals without CP. These findings highlight the clinical relevance of offering special care to patients with CP aiming to control gingival inflammation and prevent its complications.

Funding information

None

Conflict of interest

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

References

- Angelopoulos AP and Goaz PW. Incidence of diphenylhydantoin gingival hyperplasia. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology 1972; 34:898-906.
- Aromataris E and Munn Z. Joanna Briggs Institute Reviewer's Manual. (2017). The Joanna Briggs Institute. Available from: https://reviewersmanual. joannabriggs.org/. Accessed August 10, 2019.
- Barros ALO, de Gutierrez GM, Barros AO and Santos MTBR. Quality of life and burden of caregivers of children and adolescents with disabilities. *Special Care in Dentistry* 2019; **39**:380-388.
- Bax M, Goldstein M, Rosenbaum P, et al. (2005). Executive Committee for the Definition of Cerebral Palsy.
 Proposed definition and classification of cerebral palsy. Developmental Medicine & Child Neurology 2005: 47:571-576.
- Cappelli D and Brown JP. Validation of school nurses to identify severe gingivitis in adolescents. *American Journal of Public Health* 2002; **92:**946-948.
- Cardona-Soria S, Cahuana-Cárdenas A, Rivera-Baró A, Miranda-Rius J, Martín de Carpi J and Brunet-Llobet L. Oral health status in pediatric patients with cerebral palsy fed by oral versus enteral route. *Special Care in Dentistry* 2020; **40**:35-40.
- Cardoso AM, Gomes LN, Silva CR, et al. Dental caries and periodontal disease in Brazilian children and adolescents with cerebral palsy. International Journal of Environmental Research and Public Health 2014; 12:335-353.
- Cardoso AMR, Medeiros MMD, Martins ML, Padilha WWN and Cavalcanti AL. Oral condition of institutionalized Brazilian children and adolescents with cerebral palsy. *Revista Portuguesa de Estomatologia, Medicina Dentária e Cirurgia Maxilofacial* 2017; **58**:105-110.
- Cardoso AMR, Medeiros MMD, Gomes LN, Martins ML, Padilha WWN and Cavalcanti AL. Factors associated with health and oral health-related quality of life of children and adolescents with cerebral palsy. *Special Care in Dentistry* 2018; **38**:216-226.
- DerSimonian R and Laird N. Meta-analysis in clinical trials revisited. *Contemporary Clinical Trials* 2015; 45:139-145.
- De Camargo MA and Antunes JL. Untreated dental caries in children with cerebral palsy in the Brazilian context. *International Journal of Paediatric Dentistry* 2008; **18**:131-138.

- Du RY, McGrath C, Yiu CK and King NM. Oral health in preschool children with cerebral palsy: a casecontrol community-based study. *International Journal of Paediatric Dentistry* 2010; **20**:330-335.
- Egger M, Smith GD, Schneider M and Minder C. Bias in meta-analysis detected by a simple, graphical test. *British Medical Journal* 1997; **315**:629-634.
- El Ashiry EA, Alaki SM and Nouri SM. Oral Health Quality of Life in Children with Cerebral Palsy: Parental Perceptions. *Journal of Clinical Pediatric Dentistry* 2016; 40:375-387.
- Greene JC and Vermillion JR. The Simplified Oral Hygiene Index. *The Journal of the American Dental Association* 1964; **68**:7-13.
- Guare RO and Ciampioni AL. Prevalence of periodontal disease in the primary dentition of children with cerebral palsy. *Journal of Dentistry for Children* 2004; **71**:27-32.
- Guerreiro PO and Garcias GL. Oral health conditions diagnostic in cerebral palsy individuals of Pelotas, Rio Grande do Sul State, Brazil. *Ciência & Saúde Coletiva* 2009; 14:1939-1946.
- Guimarães Junior J. Drug induced gingival hyperplasia – Part I. *Journal of Epilepsy and Clinical Neurophysiology* 2007; **13:**33-36.
- Jonsson U, Eek MN, Sunnerhagen KS and Himmelmann K. Cerebral palsy prevalence, subtypes, and associated impairments: a population-based comparison study of adults and children. *Developmental Medicine and Child Neurology* 2019; **61:**1162-1167.
- Higgins JP and Green S. Cochrane Handbook for Systematic Reviews of Interventions version 5.1.0. The Cochrane Collaboration 2011. Available from: http:// handbook.cochrane.org/. Accessed August 10, 2019.
- Higgins JP and Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine* 2002; 21:1539–1558.
- Jan BM and Jan MM. Dental health of children with cerebral palsy. *Neurosciences (Riyadh)* 2016; **21:**314-318.
- Kumar S, Sharma J, Duraiswamy P and Kulkarni S. Determinants for oral hygiene and periodontal status among mentally disabled children and adolescents. *Journal of Indian Society of Pedodontics and Preventive Dentistry* 2009; 27:151-157.
- Löe H. The gingival index, the plaque index and the retention index systems. *Journal of Periodontology* 1967; 38:610-616.
- Löe H and Silness J. Periodontal Disease in Pregnancy. I. Prevalence and Severity. *Acta Odontologica Scandinavica* 1963; **21:**533-551.
- Moher D, Liberati A, Tetzlaff J and Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLOS Medicine* 2009; **6**:1-6.

- Oredugba FA. Comparative oral health of children and adolescents with cerebral palsy and controls. *Journal* of *Disability and Oral Health* 2011; **12**:81-87.
- Pope JE and Curzon ME. The dental status of cerebral palsied children. *Pediatric Dentistry Journal* 1991: 13:156-162.
- Ramfjord SP. The Periodontal Disease Index (PDI). Journal of Periodontology 1967; **38**:602-610.
- Rana M, Upadhyay M, Rana A, Durgapal S and Jantwal A. A Systematic review on etiology, epidemiology, and treatment of cerebral palsy. *International Journal* of Nutrition, Pharmacology, Neurological Diseases 2017; 7:76-83.
- Rodríguez JPL, Ayala-Herrera JL, Muñoz-Gomez N, et al. Dental decay and oral findings in children and adolescents affected by different types of cerebral palsy: a comparative study. *Journal of Clinical Pediatric Dentistry* 2018; 42:62-66.
- Sankar C and Mundkur N. Cerebral palsy-definition, classification, etiology and early diagnosis. *Indian The Indian Journal of Pediatrics* 2005; **72**:865-868.
- Santos MT, Masiero D and Simionato MR. Risk factors for dental caries in children with cerebral palsy. *Special Care in Dentistry* 2002; **22**:103-107.

- Santos MT, Ferreira MC, Guaré RO *et al.* Gingivitis and salivary osmolality in children with cerebral palsy. *International Journal of Paediatric Dentistry* 2016; **26:**463-470.
- Santos MTBR, Diniz MB, Guaré RO, Ferreira MCD, Gutierrez GM and Gorjão R. Inflammatory markers in saliva as indicators of gingival inflammation in cerebral palsy children with and without cervical motor control. *International Journal of Paediatric Dentistry* 2017; **27**:364-371.
- Stavsky M, Mor O, Mastrolia SA, Greenbaum S and Than NG. Cerebral Palsy—Trends in Epidemiology and Recent Development in Prenatal Mechanisms of Disease, Treatment, and Prevention. *Frontiers in Pediatrics* 2017; 5:1-10.
- Subramaniam P, Mohan Das L and Babu KL. Assessment of salivary total antioxidant levels and oral health status in children with cerebral palsy. *Journal* of *Clinical Pediatric Dentistry* 2014; **38**:235–239.
- Wyne A, Saleem F and Kham N. Plaque, gingivitis, enamel defects and tooth wear among cerebral palsy children of Riyadh region. *Saudi Medical Journal* 1996; 17:466-470.