

Comparative assessment of periodontal conditions between bilateral cleft lip and palate (BCLP) and unilateral cleft lip and palate (UCLP): A systematic review and meta-analysis

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

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Abstract

The existing literature on the periodontal condition in different cleft types is inconclusive and has yielded conflicting results. Therefore, the aim of this systematic review and meta-analysis is to assess and compare the oral health needs of children with bilateral cleft lip and palate (BCLP) with those of children with unilateral cleft lip and palate (UCLP).

Six electronic databases were thoroughly searched for articles published up to June 2022 that directly compared the periodontal condition of BCLP patients with that of UCLP patients. A meta-analysis was conducted using the random-effects model with inverse variance weighting. The literature search yielded 858 articles, out of which 58 studies were selected for a full-text review. Finally, 5 articles, which compared 86 BCLP individuals with 132 UCLP patients across 3 continents, were evaluated. The selected papers compared gingival and periodontal parameters, including the plaque index (PI), the gingival index (GI), periodontal probing depth (PPD), and clinical attachment loss (CAL).

The meta-analysis revealed a significant difference in CAL on the facial side in BCLP individuals (mean difference: -0.44 , 95% confidence interval (CI): $0.27-0.61$, $Z = 5.07$, $p < 0.0001$). The remaining parameters did not reveal any significant differences between the 2 groups.

In light of the established correlation between cleft lip and palate morbidity and surgical interventions on gingival and periodontal health, these factors must be incorporated into treatment planning.

Keywords: cleft palate, plaque index, periodontal diseases, gingival index, cleft lip

Cite as

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Highlights

- Anatomical cleft characteristics, malaligned teeth and skeletal discrepancies contribute to periodontal attachment loss in cleft patients.
- The systematic review revealed higher attachment loss on mesial, facial and palatal surfaces of maxillary canines.
- Treatment planning for cleft lip and palate patients should consider periodontal conditions to ensure optimal oral health outcomes.

Introduction

Cleft lip and palate is one of most prevalent congenital malformations within the head and neck region,^{1–4} with incidence rates of 1:700 live births. Epidemiological studies have demonstrated that the prevalence of cleft anomalies may vary depending on geographical location, socioeconomic status and racial background.⁵ The American Indian population exhibited the highest prevalence rates of 2.62 per 1,000 live births, followed by the Japanese, Chinese, and White populations with 1.73, 1.56, and 1.55 per 1,000 live births, respectively. The Black population exhibited the lowest rate of 0.58 per 1,000 live births.⁶ Furthermore, data spanning a 5-year period revealed that the overall congenital anomaly rate increased in the United States and decreased internationally.⁷

Orofacial clefts represent a heterogeneous group of congenital malformations with different morphologic presentations, ranging from cleft lip alone to complete unilateral cleft lip and palate (UCLP), bilateral cleft lip and palate (BCLP), and isolated clefts of soft palate, resulting from the lack or incomplete fusion of the medial nasal process with the maxillary process during the first stage of embryonic development.

Cleft lip and palate is also associated with a number of syndromes, such as Treacher Collins syndrome, Pierre Robin syndrome and DiGeorge syndrome, which have been linked to a variety of factors, including increased maternal age, tobacco smoking and alcohol consumption. Although the precise etiology remains unclear, mutations in the *PAX9*, *TGF- β* , *IRF*, and *MSX1* genes play a pivotal role in fetal development. Unilateral clefts account for 75% of all cases, while 25% are bilateral. In unilateral clefts, the left side is more frequently affected. The majority of dental anomalies in CLP patients occur in the anterior region of the maxilla. This observation may be related to the surgical procedures performed in this region during the process of tooth bud formation.⁸

Individuals with cleft lip and palate often experience impaired orofacial functions, including speech, deglutition and oral health. Consultations with patients who present with cleft anomalies commence immediately after birth, and the initial treatment begins during the first month after childbirth. Cleft palate associations worldwide, including the American Cleft Palate Craniofacial Association (ACPA),

concur that the management of these patients is best provided by a multidisciplinary team of specialists, including oral and maxillofacial surgeons, pediatricians, orthodontists, speech therapists, prosthodontists, pedodontists, as well as medical professionals such as pediatricians, speech therapists, phoniatricians, and laryngologists.^{9,10}

The development of carious lesions and periodontitis is increased in individuals with cleft lip and palate.^{11,12} Even before the complete closure, the soft tissue folds complicate access to target areas with conventional cleaning techniques and may serve as a habitat for putative pathogens. This, in turn, increases the risk of intraoral translocation of pathogens, leading to periodontal infection.¹³ Authors have reported an increased prevalence of caries and periodontal breakdown rates among UCLP and BCLP patients, respectively.^{3,14,15} Dental and arch segment irregularities, orthodontic appliances and the presence of Simonart's band, a soft tissue band that connects the cleft gap of the base of the nostril or the margin of the alveolus after cleft closure,¹⁶ collectively contribute to the progression of periodontal disease.^{3,14,15,17}

A substantial body of epidemiological research has demonstrated that control subjects exhibited optimal oral health status when compared to subjects with cleft palate. There is a paucity of research regarding oral health status among different cleft types. To date, no systematic review has explored the periodontal status of individuals with different cleft types. Therefore, the present systematic review aimed to assess the periodontal status of patients with BCLP compared to those with UCLP.

Material and methods

This systematic review was performed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (Fig. 1) and the PICOS framework, as follows: Patients: children, adolescents and adults with cleft lip and palate; Intervention/exposure: presence of BCLP; Control: UCLP group; Outcome: periodontal status; Study design: observational and cross-sectional studies (Table 1). Two authors (JW and AG) independently performed the data extraction after selecting the articles relevant to the review. Any disagreements between the authors were resolved by the third reviewer (PB).

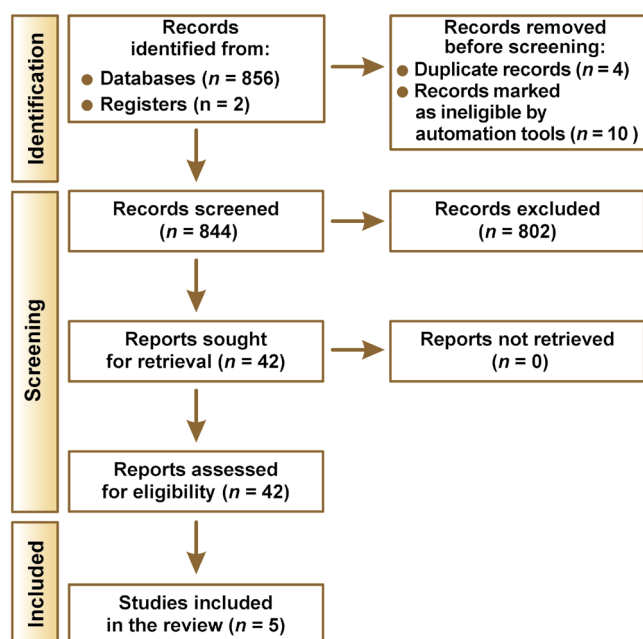


Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of the study

The collected data was organized in a tabular form consisting of study design, sample size, participants' age and gender, dentition type, cleft type, group matching, study outcomes, and utilized periodontal indices (Table 2). The study has been registered in Open Science Framework (doi:10.17605/OSF.IO/KNJZE).

Search strategy

A structured literature search of PubMed®, Scopus, Cochrane, Web Of Science, Cochrane Central Register of Controlled Trials (CENTRAL), and OpenGrey databases was conducted. Additionally, unpublished literature was retrieved from Clinical Trials Registry – India. The search was limited to articles published up to February, 2023. Reference lists of the selected articles were also screened using cross-referencing. The search utilized the following Medical Subject Headings (MeSH): “cleft lip”; “cleft palate”; “periodontal status”; “attachment loss”; “oral hygiene”. These terms were combined with Boolean

operators (AND and OR) to formulate a search strategy that was pertinent to the review question. The selection of MeSH terms from the top of the MeSH tree hierarchy was deliberate, ensuring the inclusion of subheadings within the search.

Screening and selection

The results obtained after the implementation of the search strategy were transferred into the online tool Rayyan (<https://www.rayyan.ai>), which enabled the authors to screen the titles and abstracts of the articles. The selection criteria encompassed observational and cross-sectional studies that compared 2 groups and presented the data quantitatively. The analysis included original research that compared the periodontal evaluation of BCLP with that of UCLP, with UCLP serving as the control. Studies involving bone grafts, dental anomalies, clefts in syndromic patients, as well as case reports, case series, and letters to the editor were excluded from the analysis. Reference lists of pertinent articles and gray literature (OpenGrey) were searched to identify potentially relevant papers that might have been missed during the previous steps. Studies reflecting indirect data, qualitative data, and studies without the control group were excluded, but the references of the articles were reviewed to identify any potential studies.

Objectives

This paper provides a comprehensive insight into the periodontal conditions that are prevalent among individuals with BCLP around the world. The infrastructure demands and treatment needs of these patients differ significantly from those with UCLP. This knowledge can assist healthcare centers and governing bodies in the formulation of policies for the care of cleft individuals across different age groups.

Results of the search

The literature search yielded 858 articles (Fig. 1). The selected article list was transferred to the online tool

Table 1. PICOS format and research question

PICOS	Description
Patients	children, adolescents and adults with cleft lip and palate who have or have not undergone surgical intervention and who have not been diagnosed with any syndrome
Intervention/exposure	presence of BCLP
Control	UCLP group
Outcome	assessment of the periodontal condition using established indices and protocols
Study design	observational and cross-sectional studies
Research question	Are there any differences in the periodontal condition of BCLP individuals compared to that of UCLP individuals?

BCLP – bilateral cleft lip and palate; UCLP – unilateral cleft lip and palate.

Rayyan for the purpose of sorting and selecting the relevant articles based their titles and abstracts. Following the removal of ineligible records and duplicates ($n = 14$), a total of 802 studies were excluded. After a full-text review, a total

of 42 studies were included. The final review included 5 articles that met the inclusion criteria and were selected for meta-analysis. The detailed characteristics of studies that met the inclusion criteria are outlined in Table 2.

Table 2. Characteristics of the studies included in the review

Study	Country	Design	Sample size	Control group	Cleft surgery	Mean age [years]	Dentition examined	Method of outcome assessment	Parameters assessed	Results
Sudhakar et al. 2007 ¹⁹	India	case-control	20 BCLP patients	20 UCLP patients	not reported	15	not reported	clinical examination	PI, SBI, PPD, CAL	With the exception of SBI, all parameters exhibited significantly higher levels in BCLP patients.
Eldeeb et al. 1986 ²⁰	USA	cross-sectional	26 cleft patients (17 M, 9 F, 8 BCLP, 18 UCLP)	29 non-cleft patients (11 M, 18 F)	patients have undergone alveolar bone grafting using an autogenous iliac crest graft which was covered with either a mucogingival or a mucobuccal flap using a surgical technique described by Broude and Waite	BCLP: 16.8 UCLP: 16.2	permanent (maxillary canine and 6 Ramfjord teeth)	clinical examination	PI, GI, PPD, CAL, width of attached gingiva in the canine region	Patients with cleft palate demonstrated higher PI values. No significant differences were observed in GI, PPD and CAL.
Gaggl et al. 1999 ²¹	Austria	cross-sectional	50 cleft patients (30 UCLP, 20 BCLP)	30 UCLP patients	not reported	BCLP: 21.4 UCLP: 18.9	permanent	clinical examination	CAL, API, SBI, pathologic mobility	Patients with cleft palate had elevated SBI scores. The BCLP group exhibited a higher prevalence of periodontal damage, particularly in teeth adjacent to the cleft area.
Hazza'a et al. 2011 ²²	Jordan	cross-sectional	98 cleft patients (52 UCLP, 46 BCLP)	98 non-cleft patients	not reported	12 $\pm$ 6.3	primary and permanent	clinical examination	PI, GI, DMFT, DMFS	The prevalence of plaque and gingivitis was higher in the cleft group. The BCLP group exhibited a higher incidence of gingivitis.
Pisek et al. 2014 ²³	Thailand	cross-sectional	68 cleft patients (34 M, 34 F, 20 BCLP, 36 UCLP)	118 non-cleft patients (48 M, 70 F)	not reported	BCLP: 11.9 UCLP: 11.9	primary and permanent	interview and oral examination	PI, GI, DMFT, DMFS, quality of life	The examined patients demonstrated high DMFT, PI and GI scores, which had an impact on their ability to speak and smile. No significant differences in caries were observed in the primary dentition.

M – male; F – female; PI – plaque index; GI – gingival index; DMFT – number of decayed, missing and filled permanent teeth; DMFS – number of decayed, missing and filled surfaces; PPD – periodontal probing depth; CAL – clinical attachment loss; API – approximal plaque index; SBI – sulcus bleeding index.

The majority of the analyzed studies were of a cross-sectional nature, while 1 study was of a case–control design. The studies reflected the data in the form of subset parameters of periodontal assessment of individuals with BCLP and UCLP. The articles assessed the periodontal condition of 86 BCLP individuals, with a mean age of 15 years. The studies were conducted in Jordan, Austria, the United States, Thailand, and India. None of the selected studies incorporated syndromic patients, a factor that could potentially introduce confounding variables. The studies have divided the sample according to the cleft type. The male-to-female ratio ranged from 30:70 to 62:38 in the experimental group, and it was 40:60 in the control group of UCLP patients. With regard to the cleft surgery, the presence or absence of surgery, and the time elapsed since surgery were reported in only 1 study.

Characteristics of the selected studies

The selected studies have evaluated the periodontal condition using various parameters. A study by Ali and Mazin selected teeth representative of the overall periodontal status for the individual patient, according to Ramfjord, namely maxillary right first molar, maxillary right canine, maxillary left central incisor, maxillary left canine, maxillary left first premolar, mandibular right central incisor, and mandibular right first premolar.¹⁸ Out of the 5 studies, 4 evaluated hygiene by means of the plaque index (PI),^{19,20,22,23} 1 study utilized the approximal plaque index (API),²¹ 3 evaluated gingival health by means of the gingival index (GI),^{20,22,23} 2 evaluated periodontal condition using the sulcus bleeding index (SBI),^{19,21} and 2 by means of periodontal probing depth (PPD).^{19,20} Additionally,

3 papers evaluated clinical attachment loss (CAL),^{19–21} 1 study measured pathologic mobility,²¹ and 1 study assessed patients' quality of life.²³ A study by Gaggl et al. evaluated the periodontium after orthodontic treatment.²¹ However, this evaluation may not accurately reflect the true state of the periodontium due to the potential adverse effects of orthodontic brackets and dentoalveolar expansion on oral hygiene, particularly in the cleft area that has undergone multiple surgical procedures throughout its lifetime.

Quality assessment

A set of 4 quality assessment criteria was established based on the Newcastle–Ottawa Scale (NOS) adapted for the evaluation of the quality of cross-sectional studies for the systematic review.²⁴ Table 3 presents a modified version of the NOS scale that was used to assess study quality. The criteria encompassed a series of assessments, including the extent to which the study has outlined the selection criteria for participants, control, ascertainment of exposure (disease), the comparability with respect to study design or analysis, and the control of confounding factors. Lastly, the outcome, whether structured or self-reported, was assessed. The study and control groups were matched in all studies.

Results

The oral hygiene of the participants was evaluated using PI, API²⁵ and GI. Gingival condition was assessed using the gingival index tool, which is based on the criteria outlined by Silness and Loe.²⁶ The results were based on the assessment of the mean difference in PI and GI scores between cleft groups (mean difference: 0.14 (0.01–0.27)). However, the comparison of the studies did not reveal any statistically significant differences ($Z = 2.09$, $p = 0.04$). As illustrated in Fig. 2 and Fig. 3, the BCLP group exhibits a favorable positioning within the forest plots.^{20,23} The heterogeneity between the studies was found to be low ($I^2 = 40\%$) when studies evaluating gingival indices were compared (Fig. 2). However, a considerable heterogeneity was identified in studies assessing plaque condition ($I^2 = 83\%$) (Fig. 3).

Table 3. Newcastle–Ottawa Scale (NOS) adapted to assess the quality of cross-sectional studies for the systematic review

Study	Selection	Comparability	Outcome	Quality score
Sudhakar et al. ¹⁹	**	**	*	5
Eldeeb et al. ²⁰	****	0	**	6
Gaggl et al. ²¹	****	*	***	8
Hazza'a et al. ²²	****	**	**	8
Pisek et al. ²³	****	**	**	8

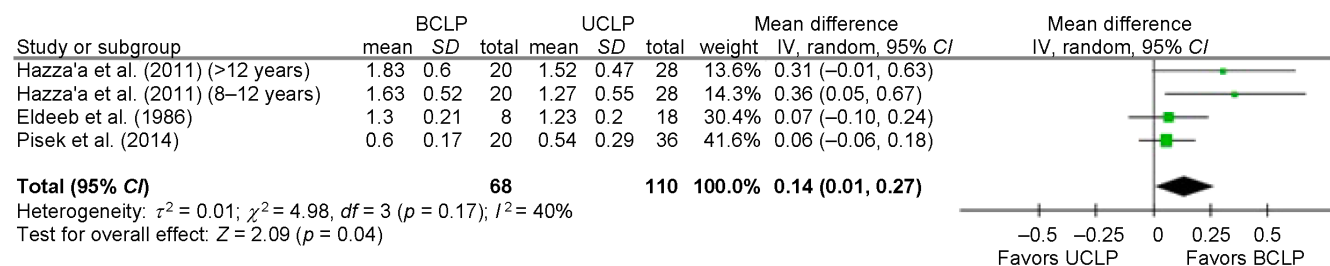


Fig. 2. Forest plot comparing the gingival index (GI) between bilateral cleft lip and palate (BCLP) and unilateral cleft lip and palate (UCLP) patients

SD – standard deviation; CI – confidence interval; df – degrees of freedom.

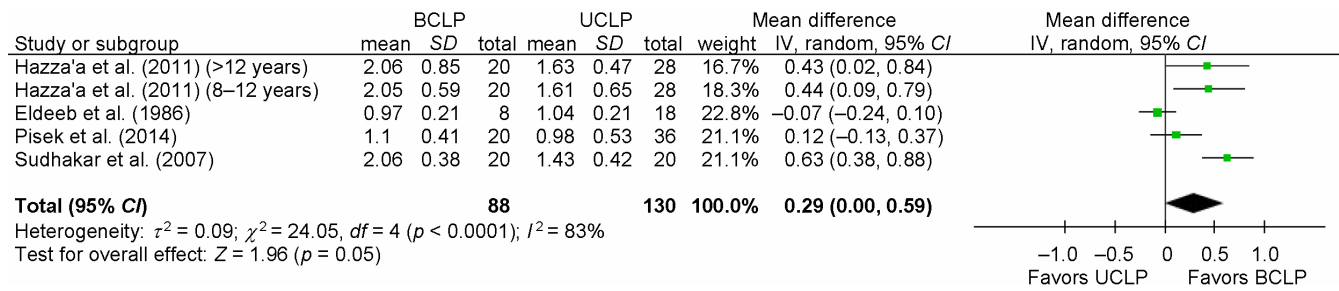


Fig. 3. Forest plot comparing the plaque index (PI) between BCLP and UCLP patients

Periodontal evaluation – CAL, SBI, PPD

The periodontal index developed by Silness and Loe²⁶ and CAL²⁷ were used to assess the periodontium. The selected studies evaluated the periodontal status of the maxillary arch in the anterior region, posterior region, and teeth adjacent to the cleft. However, these factors were not considered in the meta-analysis because the data could not be compared. Therefore, the present study considered CAL on all surfaces of the maxillary canine at the cleft side, namely the mesial, facial, palatal, and distal surfaces. A statistically significant difference was identified in CAL on the facial surface of BCLP (mean difference: -0.44, 95% confidence interval (CI): -0.61–-0.27,

$Z = 5.07$, $p < 0.00001$), and a low level of heterogeneity was identified ($I^2 = 0\%$) (Fig. 4). The assessment of publication bias was not feasible due to the limited number of studies available. On the 3 remaining surfaces, the periodontal condition in the BCLP group did not differ from that in the UCLP group, as depicted by their forest plots (Fig. 5–7).

Discussion

The current review focuses on the periodontal assessment among different cleft types. Previous studies have attempted to reflect the prevalence of caries, skeletal

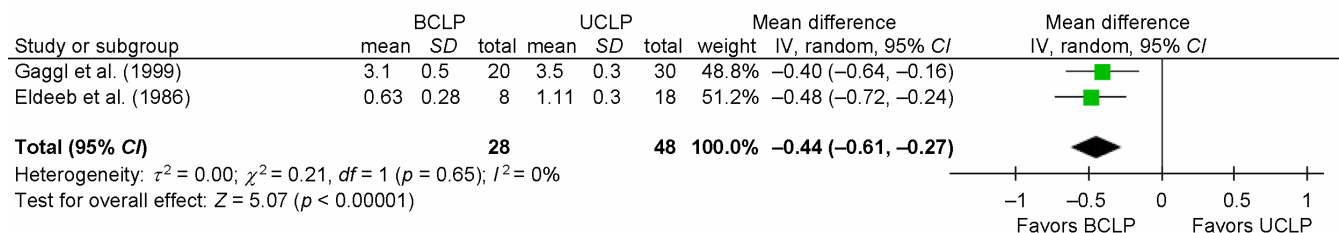


Fig. 4. Forest plot comparing clinical attachment loss (CAL) between BCLP and UCLP patients on the facial surface of maxillary canines

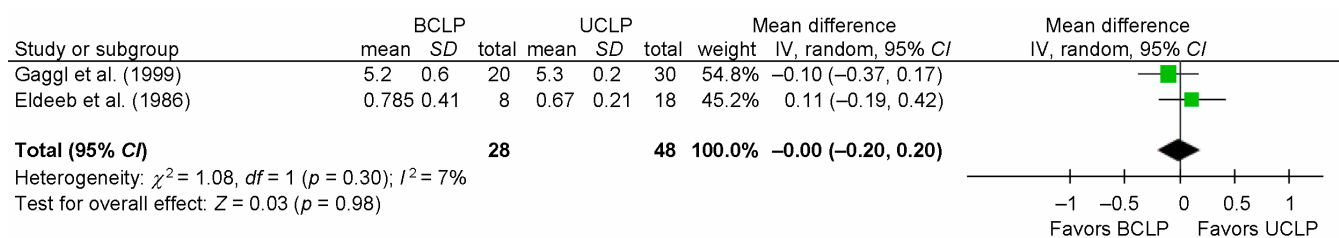


Fig. 5. Forest plot comparing CAL between BCLP and UCLP patients on the distal surface of maxillary canines

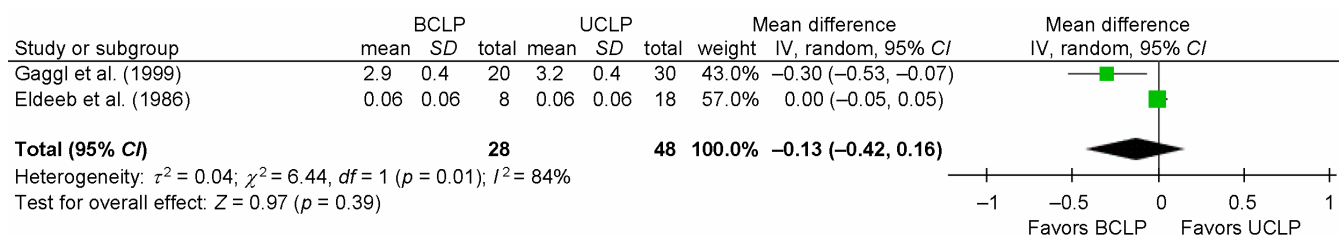


Fig. 6. Forest plot comparing CAL between BCLP and UCLP patients on the palatal surface of maxillary canines

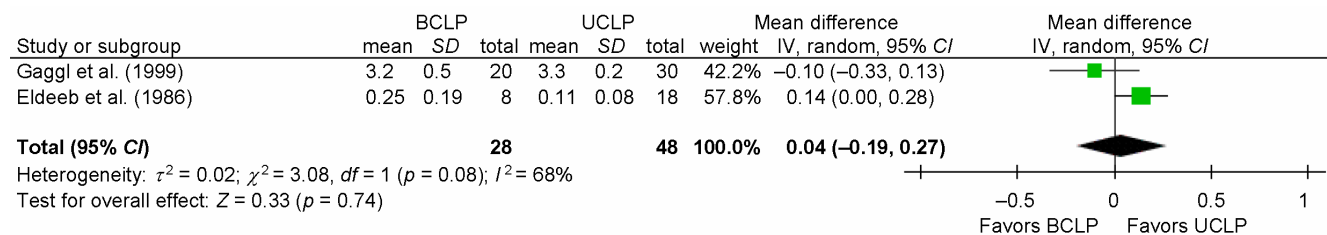


Fig. 7. Forest plot comparing CAL between BCLP and UCLP patients on the mesial surface of maxillary canines

morphology,²⁸ periodontal status, and quality of life^{12,29,30–35} in cleft individuals. However, none of the studies have analyzed the findings according to the type of cleft. A comparison of caries prevalence and periodontal condition between cleft and non-cleft groups is not feasible due to the non-comparability of the groups, as they have undergone different surgical interventions with varying levels of morbidity at different stages of development. Additionally, the treatment approach differs between cleft types, underscoring the need to identify existing periodontal problems in BCLP to facilitate the development of customized treatment planning.³⁶

Marzouk et al. conducted a systematic review to determine whether individuals with non-syndromic orofacial clefts (OCs) had more dental abnormalities (DAs) than those without OCs.³⁷ The outcomes proved that individuals with OCs are more likely to present with a range of DAs than their unaffected peers. Statistically significant associations were observed between OCs and supernumerary teeth, developmental enamel defects, malposition and/or transposition, rotation, and impaction.³⁷

In the present systematic review, 5 studies were identified, and data from these studies was assembled for the comparison of CAL, gingival indices and periodontal indices across different surfaces of canine teeth. The review encompassed a total of 86 individuals with BCLP and compared them to 132 UCLP patients. The data from the selected studies reflected that the 2 groups have comparable gingival and periodontal indices. However, significantly higher CAL values were reported in the BCLP groups. The meta-analysis revealed a significantly higher mean CAL on the facial aspect of canine teeth.

The observed discrepancy in CAL may be statistically significant, but not clinically significant, due to the potential role of scar tissue. A study by Lucas et al. reported no significant difference in PI between cleft and non-cleft individuals, as compared to studies performed by other authors.¹² This difference could be attributed to a small sample size. Additionally, participants with different cleft types received multidisciplinary care starting at an early age.¹²

A study by Paul and Brandt reported better dental health in participants in which cleft or palate was not involved.³⁸ Secondly, the surgical technique employed for uncovering the canines contributed to attachment loss. However, the absence of documentation regarding the exact technique used made this difficult to verify.

Limitations

The results of the review should be interpreted with caution due to the limited number of studies that reflect the data. Studies in languages other than English were not considered, and the articles were not searched manually. These factors could introduce a significant confounding factor into the study. Additionally, the data was not organized based on sex, as the number of studies was limited and the sample size was small, thus dividing the sample was not feasible. Consequently, the funnel plots were not created.

The included articles have followed the methodological criteria laid down by GI, PI and CAL indices. The studies have not elaborated on intraoperative errors, which could have affected the results of the present study.

Within the limitations of this review, the available evidence suggests that, due to the increased morbidity observed in the BCLP group, these individuals may exhibit slightly poorer PPD and CAL compared to the UCLP group. The clinical significance of this increase remains uncertain.

Conclusions

The primary factors contributing to attachment loss include the anatomical characteristics of the cleft area, maligned teeth, and discrepancies in the skeletal base relationship. In addition, developmental aspects related to surgical repair, surgical bone grafting procedures, hypoplastic defects, and scarring, in conjunction with various phases of orthodontic treatment, may restrict access to adequate oral hygiene and predispose patients to plaque accumulation. The present study systematically reviewed the extant literature, encompassing 5 studies that compared the periodontal parameters among individuals with cleft palates. The analysis revealed a significantly higher prevalence of attachment loss on the mesial, facial and palatal surfaces of canines, with grafted gingiva resulting in surgical uncovering rather than orthodontic intervention.

Ethics approval and consent to participate

Not applicable.

Data availability

The datasets supporting the findings of the current study are openly available in Open Science Framework at <https://osf.io/knjze> (doi:10.17605/OSF.IO/KNJZE).

Consent for publication

Not applicable.

Use of AI and AI-assisted technologies

Not applicable.

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