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Are People with an Orofacial Cleft at a Higher Risk of Dental Caries: A Systematic Review and Meta-Analysis.

Abstract

Objective: To establish whether children born with an orofacial cleft have a higher risk of dental caries than individuals without cleft: **Design:** A systematic review and meta-analysis
Methods: The search strategy was based on the key words “cleft lip palate,” and “oral hygiene caries decay”. Ten databases were searched from their inception to April 2016 to identify all relevant studies. All data were extracted by two independent reviewers. The primary outcome measure was caries measured by the decayed, missing, filled surfaces/teeth index (dmfs/dmft or DMFS/DMFT). **Results:** Twenty-four studies met the selection criteria. All of the studies were observational. Twenty-two studies were suitable for inclusion in the meta-analysis. The overall pooled mean difference in dmft was 0.63 (95% CI: 0.47 to 0.79) and in DMFT was 0.28 (95% CI: 0.22 to 0.34). **Conclusion:** Individuals with cleft lip and/or palate have higher caries prevalence, both in the deciduous and the permanent dentitions.

Key words: cleft lip and palate, oral health, systematic review, meta-analysis,

Introduction

Cleft lip and palate (CL/P) is a common birth anomaly occurring in approximately 1 in 700 live births.¹ It can occur in isolation (non-syndromic) or be part of a wider series of birth anomalies or syndromes (syndromic). CL/P impacts on the individual, their families, the healthcare system and society throughout life.

Risk factors for oral diseases include unhealthy diet, tobacco use, harmful alcohol use, and poor oral hygiene.¹ Good oral health (OH) is a mouth free of disease or decay. Dental caries experience can be described using the decayed, missing, filled teeth/surfaces index. This numerically expresses caries prevalence and is calculated by adding the number of Decayed (D), Missing (M), Filled (F), Teeth (T) or Surfaces (S). Upper case letters represent permanent teeth, *i.e.* DMFT or DMFS, lower case letters signify the deciduous dentition *i.e.* dmft or dmfs.

Those with CL/P may have a higher prevalence of dental caries linked to poorer oral hygiene as a result of a reluctance to brush around the cleft site, poorly aligned maxillary dentition and limited access following surgical repair of the upper lip and possible scarring. There may also be longer oral clearance times following eating. Some studies have concluded that individuals with CL/P have greater caries experience than non-cleft children.^{2,3} However other studies have concluded the inverse.⁴

Two previous systematic reviews that assessed the association between CL/P and caries

prevalence had limitations.^{5,6} Hasslof and Twetman⁵ used strict inclusion criteria; the control group had to be matched, at least by age and gender, which limited the number of studies included. Antonarakis *et al.*,⁶ used a checklist of items (recommended by Agbaje *et al.*,⁷) to be included to assess caries experience. However, there were several inaccuracies in their reporting specifically concerning; the use of radiographs; probe type/usage and lesion detection and examiner recruitment, training, calibration and the number of examiners involved. In addition, it is three years since this last review. An updated review will reflect recent research in this area as well as thoroughly re-appraising existing literature.

The aim of this systematic review was to identify published studies that have assessed caries in individuals with cleft and compare their findings to a defined non-cleft comparison group, to establish whether there is any reported difference in caries experience between the two.

Methods

Ten electronic databases were searched from their inception to April 2016 by two NHS librarians (EJ and BJ). These comprised MEDLINE, Embase, AMED via Ovid, Cochrane Library, Proquest, Cinahl, British Nursing Index, HMIC, PsychINFO, Health Business Elite (see appendix A for electronic search strategy). Google Scholar was also searched up to page 20.

All titles and abstracts retrieved from the search were assessed for eligibility against predetermined inclusion criteria by one reviewer (VW) and retrieved as a full document. The full-text articles were read in their entirety by two reviewers (VW/RP) and decisions on inclusion and exclusion recorded. Excluded studies are listed in Table 1. Any disagreements that arose were resolved through discussion. Reference lists of all full text articles and all relevant systematic reviews were hand-searched for additional studies. The Cleft Palate Craniofacial Journal; The American Cleft Palate-Craniofacial Journal and The Journal of Cleft Lip and Palate and Craniofacial Anomalies were also hand searched for additional studies from 1964 onwards.

No restrictions regarding language of the article were imposed. This review was conducted following a predetermined written protocol registered on the PROSPERO database; registration number: CRD42015020403.

In addition, this review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA).

Inclusion criteria for the studies were used:

- *Types of participants:* People (any age, gender, socio-economic status or geographical location) with non-syndromic CL/P (Syndromic CL/P only included if they comprised less than 20% of the study group)

- *Type of Outcome:* Decayed, missing, filled surfaces/teeth indices (dmft/DMFT and dmfs/DMFS) in the primary, mixed or secondary dentition were used as outcome measures
- *Type of Comparator:* A comparison of outcomes between a cleft and non-cleft group.

Comparison groups of any size were acceptable including any National Data.

The primary outcomes were dmft/dmfs and/or DMFT/DMFS.

Data were independently extracted by two reviewers (VW, RP) using a standardised form.

The methodological quality of studies was evaluated independently by the same two researchers (Table 2) using a standardised checklist from a previous systematic review of the methods for assessing caries experience in epidemiological surveys.⁷ Standard Risk of Bias tools were not applicable for this study type. Disagreements were resolved through discussion with a third reviewer (AI).

Results

Searches

The search strategy yielded 790 potentially relevant papers for inclusion. After duplicate titles were removed, 384 remained. Once screened, 64 full text copies were retrieved and scrutinised by two reviewers (VW and RP). Reasons for excluding articles are presented in Table S1. Four articles were accessed through hand-searching. In total, 24 were included in

this review (see Figure 1). Key information from each study is summarised in Tables 1 and 2. The 24 studies were published between 1964 and 2014 from 17 countries across four continents.

Description of participants

Eleven studies were conducted in European populations, nine from Asia, three from South America and one from North America. The total number of individuals with cleft was 4,768 (median:79; IQR:51 to 217), and the total number of controls was 3,672 (median:65; IQR: 49 to 125) (excluding studies that used national data). Two studies used national data as a comparison group with one having an unknown sample size and one with a sample size of 47,646.^{10,11} For one further study, complete translation was unavailable, but the control group comprised 28,000 participants, most likely based on national data.¹² There was partial reporting of gender in two of the studies.^{10,11} The age range spanned 18 months to 25 years. We were unable to calculate the mean age of the cleft and control groups across studies because it was not reported in seven studies.^{2, 8-13}

Whilst the majority of studies excluded children with multiple abnormalities, recognised syndromes, systemic disease or congenital malformations; two included children with syndromes.^{12, 14} Five studies also excluded people receiving any additional care e.g. under active care for caries, unable to provide an oral rinse, were under treatment using antimicrobials or immunosuppressants, or had clinical signs of oral candidiasis.

Source of comparison groups

Fifteen studies with a total of 2,111 controls selected the comparison sample from dental clinics, hospitals or schools in the same geographical area as the study. ^{2, 8, 10, 12, 13, 15-24}

AlDajani *et al.*, ²⁵ used 53 siblings of cleft as a comparison group (with a maximum difference in age of three years) and six studies matched control participants for sex and age. ^{14, 18-20, 23, 26}

Quality of outcome assessment and reporting

Examiner training and clinical examination procedures varied considerably (Table 3). Ten studies used just one examiner. ^{8, 10-12, 15, 19, 21, 22, 24, 26} Three studies reported that all participants were examined by trained and calibrated dentists. ^{16, 17, 20} A further three studies used two examiners. ^{9, 18, 23} All reported inter-rater reliability kappa scores are recorded in Table 3. Several of the studies failed to report details of any examiner training. ^{13, 14, 18, 19, 22, 23}

Fourteen studies documented the procedure used during the clinical examination, specifically mentioning the equipment used. ^{8-13, 17-22, 24, 26} Conditions of the clinical examination were not always reported. ^{2, 15, 16, 25}

The 1987 World Health organisation (WHO) recommendations for diagnosing dental caries were adhered to by seven studies. ^{2, 11, 15, 19, 22, 23, 26} The modified WHO criteria (1997) were

applied by three studies.^{10, 18, 21} One paper recorded caries according to the British Association for the Study of Community Dentistry (BASCD) criteria.⁹ Two studies took radiographs and two supplemented the clinical exam with radiographs.^{2, 20, 24}

Meta-Analysis

A random effects meta-analysis using the DerSimonian and Laird estimator was performed in order to obtain an overall summary estimate of the difference in caries experience between CL/P and non CL/P groups. Random effects meta-analysis was used because the studies came from several population sources around the World and one might expect variation in OH outcomes. However, fixed effect results were also reported as a check of robustness of the findings to the choice of model. The results were similar regardless of type of model and therefore only the results from the random effects model are described.

To be included in the meta-analysis, papers must have reported; the sample size and mean dmft/DMFT in each group, and either the standard deviation (SD), standard error (SE), standard error of difference, or p-value.

Where data were reported by age group, the age-specific estimates were used if sufficient information allowed. If not, the pooled estimate was included. This was the case for two papers.^{8, 9}

The data were also stratified by the source of the comparison groups (hospital/dental clinic, trauma clinics, general population, sibling matched) and type of dentition (primary,

mixed, secondary) to explore whether these explained for any between study heterogeneity. The year of study was also considered but the majority of studies were recent (post-2000), also stratifying by gender was considered, but in most studies the sample was mixed.

dmft

Out of 24 studies, 22 (91.7%) were suitable for inclusion in the meta-analysis. One study was excluded because it only reported dmfs/DMFS and the other because it did not provide sufficient detail to allow comparison.¹⁴

Figure 2 shows a forest plot of the mean difference in dmft (cleft minus comparison group) for each study, stratified by dentition (see Figure S1 supplementary material for the unstratified presentation ordered by year of study and age). The evidence for a difference between CL/P and non-CL/P individuals was equivocal in two studies^{10, 23} and in the 2-4yr age group of one study.²⁷ One study of 5 to 19 year olds showed evidence that dmft was worse among those without CL/P¹⁸ whereas a further study¹⁵ showed the cleft group had lower dmft scores than the control group. The other 12 estimates all suggested dmft was worse among individuals with cleft. The overall pooled mean difference in dmft was 0.63 (95% CI: 0.47 to 0.79) suggesting that individuals with CL/P have a greater dmft experience compared to individuals without cleft. However, there was substantial heterogeneity between studies, 86.6% of the variability between studies could be attributed to between study differences rather than sampling error. There was still substantial between study

heterogeneity when studies were stratified by dentition (Figure 2) and by the source of controls (Figure S2 in supplementary material) - the I^2 statistic ranged from 67.9% to 93.4%

DMFT

Figure 3 shows a forest plot of the mean difference in DMFT (cleft minus comparison group) for each study, also stratified by dentition (see Figure S3 in supplementary material for the unstratified presentation ordered by year of study and age). There was no evidence for a difference in DMFT between CL/P and non-CL/P individuals in three studies^{8, 12, 23} and weak evidence for a greater caries experience in CL/P individuals in one study.¹⁸ There was stronger evidence that CL/P individuals have worse DMFT in the eight other independent studies.^{2, 10, 11, 15, 19, 22, 25, 26} The overall pooled mean difference in DMFT was 0.28 (95% CI: 0.22 to 0.34) suggesting that individuals with CL/P have a greater DMFT experience compared to individuals without cleft. Again, there was substantial heterogeneity between studies (I^2 statistic was 80.9%). Figure 3 also shows that heterogeneity was reduced but still present when restricted to populations with the secondary dentition ($I^2=70.1%$). The mean difference in DMFT between cleft and non-cleft children was lower in those studies that included a mixed dentition (mean difference 0.26) compared to studies that included only the secondary dentition (mean difference 1.72). The source of controls explained little of the between study heterogeneity in DMFT outcomes (Figure S4 in supplementary material), although the solitary family-based study

that matched with siblings showed the largest association of DMFT with CL/P (mean difference: 3.02, 95% CI: 1.83, 4.21).

Sensitivity analysis and publication bias

When a sensitivity analysis was performed using a conservative estimate of SD in studies where this value was not available, the results were very similar (see figure S5 and S6 in supplementary material). There was a strong suggestion of publication bias in both directions for dmft and DMFT outcomes, in particular for studies showing that DMFT is higher among CL/P individuals (Figure S7 and S8 in supplementary material).

Discussion

From 22 of the 24 studies included in the meta-analyses, the overall pooled mean difference in dmft was 0.63 (95% CI: 0.47 to 0.79) and in DMFT was 0.28 (95% CI: 0.22 to 0.34). The evidence suggests that cleft affected individuals have a higher caries prevalence than noncleft affected individuals.

Strengths and Limitations of the Review

The selection process was rigorous and extensive to try and avoid bias. Most relevant studies were included, although there were limited funds so not all articles could be

translated. As only published studies were included, publication bias is possible and the funnel plots (Figures S7 and S8) suggest evidence that publication bias exists, particularly for DMFT.

Previous Systematic Reviews

The findings of this review agree with a previous Canadian review.⁶ However, this previous review had a number of limitations. The authors used a checklist whilst assessing caries experience that was described previously in a systematic review of the methods for assessing caries experience in epidemiological surveys.⁷ Employing the same checklist for the current review identified a number of disagreements. For example, the most obvious disagreement concerned the use of radiographs to assist in the diagnosis of caries. In every case where the same papers were investigated by our review and the Canadian review,^{8,21,22,23,25,27} Antonarakis *et al.*, reported a positive result for radiographs, where actually the opposite was found to be true. A further limitation of the Canadian review was the exclusion of a paper if the control group was larger than the cleft group. No reason is stated for this condition and lifting this restriction would have yielded an extra five papers for inclusion.

An earlier systematic review by Hasslof and Twetman (2007) reported that although the data investigated seemed to show a higher caries prevalence in children with CL/P, no definitive conclusion could be made, largely due to the poor quality of papers selected for inclusion. This Danish review included six papers, all of which were included in the current

review.^{12, 13, 14, 22, 23, 24} However, this Danish systematic review had a number of limitations. The key inclusion criteria was for the control group to be matched, at least by age and gender. Not having this stipulation would have meant a further 12 studies would have been available for inclusion. This point was partially addressed in the discussion, in which the authors state they were aware of issues with matching, but it was not made clear what these were. Our review was more inclusive and did not restrict by control group. We included studies that used National data as the control. Our review process was thorough and assessment of quality of the dental examination procedure was completed by two reviewers to ensure accuracy.

Limitations in study design

However, there are some limitations with our review. Selection of comparison group can theoretically lead to bias. Those recruited from a dental trauma clinic may not be regular dental attenders, whereas those recruited from dental practices are more likely to have attended regularly (healthy-user bias). However, the fact that the effect sizes were similar for different comparison groups is reassuring.

Thirteen studies reported that a single examiner was responsible for all clinical examinations which may have introduced bias. The quality of recording of dental caries may have introduced random error, which can limit direct comparisons of absolute risk difference between studies. Ideally caries experience would be assessed radiographically, but not purely for research purposes.

DMFT as a skewed variable

DMFT/dmft is widely reported as a mean value. This may not be appropriate as distributions are often skewed.²⁸ This review relied on reported means that may not accurately describe differences in caries experiences between groups. There was an issue with the quality of caries assessment and reporting in several of the studies such as; recording probe type and usage, light conditions, the use of radiographs, any cleaning of the tooth prior to assessment and the level of caries detection.

Factors that could confound or modify risk

Several factors could confound or modify the risk of CL/P. These include socioeconomic Status (SES), geographical location, age and dentition, gender, cleft type and syndromes, orthodontic treatment and fluoride. All these potential confounders are discussed below.

Studies from all continents except Africa and Australia were included in the current review and reported consistent associations. In developing countries, caries prevalence has typically been lower thought to be due to less frequent consumption of refined sugars. However, this is now increasing.²⁹ Although this review has included a broad range of studies from developing and developed countries, the individual SES of the participants could have had an effect on the level of caries experience and would warrant further investigation. No studies explored whether confounding by socioeconomic status explained these associations.

This review included studies which looked at the primary, mixed and the secondary dentitions. The dmft/DMFT scoring system is cumulative, which could lead to an increased score through childhood, which then declines as the deciduous teeth are exfoliated and replaced by the permanent dentition. The observation that the association is similar for the primary, mixed and permanent dentitions suggests the increased risk persists.

Though gender may influence risk caries risk, few studies reported the results by gender thus association was not possible.³⁰ Type of cleft may influence association with oral health and some evidence from India showed that children with less severe cleft types, such as isolated CL or CL/A had a lower caries experience than those with more severe types of cleft such as CP.³¹ These findings are supported by other studies.³²⁻³⁴ Just over half of studies in this review reported on cleft type and this potential variable could not be explored further. Only three studies included syndromic children.^{9, 12, 14} They all show an association with caries experience, but it is impossible to draw firm conclusions about the risk associated with syndromic clefting.

Orthodontic appliances have been linked to a higher caries experience. These appliances can facilitate the accumulation of caries inducing plaque due to the patient's difficulty in tooth brushing around them and the introduction of a primarily soft diet to attempt to avoid appliance breakages. As previously discussed, an infant with CL/P may require several episodes of orthodontic intervention starting soon after birth until the late teens. It has been shown that orthodontic appliances facilitate early colonisation

of *Streptococcus mutans* and *Lactobacilli* which can lead to dental caries in the already susceptible mouths of individuals with CL/P. ³⁵

In this review, few studies mentioned orthodontic treatment. Eleven studies included children of 10 years or older and it could be assumed the cleft group would more than likely have had, or were about to receive orthodontic treatment. ^{10-12, 15, 18, 22, 25, 26, 36-38}

Fluoridation of water and use of fluoride toothpaste can reduce caries risk. Ihezor-Ejiofor *et al.*, ³⁹ investigated the effects of water fluoridation on caries and found a 35% reduction in dmft and a 26% reduction in DMFT. In this review, all of the studies in non-fluoridated areas reported that individuals with CL/P have a greater caries experience than non-cleft controls. The results from the fluoridated areas were mixed, with the three studies reporting no such difference in caries experience. It may be that fluoridation has a greater impact on the cleft affected individual and reduces the caries risk to match that of unaffected individuals.

Future research

Despite the centralisation of cleft services in the UK following the recommendations made by Clinical Standards Advisory Group in 1998, the more recent Cleft Care UK (CCUK) study has shown there has been little improvement in caries experience post-centralisation. ⁴⁰

Future research is required to identify effective treatments and models of care for children with cleft lip and palate so that their oral health can be improved.

Conclusion

This comprehensive systematic review included 24 papers. The quality of the assessment of OH was poor in 13 of the papers. Despite these shortcomings, the systematic review and meta-analysis suggest that individuals with CL/P experience more decayed, missing or filled teeth when compared to non-affected individuals. Preventing and treating dental caries in children born with a cleft is therefore important. Further research is needed to describe and evaluate different integrated models of care for individuals with cleft lip and palate.

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