Oral manifestations in premature infants. A systematic review

CURRENT STATUS: UNDER REVIEW

Lara Vivero Couto
Universidad Complutense de Madrid Facultad de Odontologia
lvivero@ucm.com Corresponding Author

Elena Planells del Pozo
Instituto de Nutrición y Tecnología de los Alimentos. Centro de Investigaciones Biomédicas.
Universidad de Granada.

José Ignacio Salmerón Escobar
Universidad Complutense de Madrid

Jorge Molina López
Instituto de Nutrición y Tecnología de los Alimentos. Centro de Investigaciones Biomédicas.
Universidad de Granada.

Ángela Ruiz-Extremera
Universidad de Granada

Paloma Planells del Pozo
Universidad Complutense de Madrid Facultad de Odontologia

DOI:
10.21203/rs.2.20435/v1

SUBJECT AREAS
Pediatrics Dentistry

KEYWORDS
Enamel Defects, Oral sequels, Premature Children
Abstract
Background Preterm delivery, defined as delivery occurring before a gestational age of 37 weeks, represents 6-10% of all births in developed countries. Preterm infants are characterized by a short prenatal development period and are at an increased risk of systemic disorders as a result of their immaturity. Few studies have analyzed oral alterations among preterm infants. This systematic review examines the orofacial characteristics most commonly found among preterm infants versus infants born at term and evaluates their repercussions upon oral health and quality of life.

Methods The search was limited to articles published in English or Spanish that compared orofacial characteristics of preterm infants versus infants born at term. Their methodological quality was assessed based on the guidelines of the Joanna Briggs Institute (JBI).

Results Most of the studies found the prevalence of structural enamel defects of the primary dentition to be greater among preterm infants. Other disorders such as structural enamel defects of the permanent dentition, caries, malocclusions or alterations in dental composition, size and development also appeared to be more frequent among preterm infants, though the supporting evidence was weak.

Conclusions Further studies are needed, analyzing the association between preterm delivery and certain orofacial disorders such as caries, malocclusions and dental anomalies.

Background
The World Health Organization (WHO) defines preterm delivery as delivery occurring before a gestational age of 37 weeks. Approximately one-quarter of all premature deliveries are induced because of medical conditions that pose a health risk for the fetus, mother, or both. The rest of preterm deliveries are spontaneous (1–6).

Preterm delivery is associated with a number of genetic, socioeconomic and ethnic factors, as well as with stress and smoking and alcohol abuse during pregnancy, maternal age, weight and height, multiple pregnancies, a history of maternal periodontal disease, arterial hypertension or preeclampsia, and a history of premature deliveries (7–15). Causes of preterm delivery related to the fetus include congenital malformations, restricted intrauterine growth, or intrauterine infections (16,
Improvements in medical care have resulted in a decrease in mortality among preterm infants. This evidences the importance of developing studies and care programs targeted to this population (18-21). Many preterm infants survive with physical and/or psychological sequelae, including respiratory distress syndrome, cardiac and renal disorders, increased susceptibility to infections, necrotizing enterocolitis, and metabolic, nutritional and neurological disorders, among other problems (22–32). These complications often require invasive interventions and treatments such as orotracheal intubation or parenteral nutrition (33).

In addition to the systemic sequelae of prematurity, these patients can suffer a range of oral disorders. In this regard, pediatric dentists should be included in the multidisciplinary team in charge of caring for these children (18, 22, 34). However, few recent studies can be found on this subject, and the existing literature generally focuses on a single concrete oral manifestation, without addressing the global oral health of the preterm infant. The objectives of the present systematic review were to: (1) analyze the scientific evidence on the oral characteristics associated to preterm delivery; (2) describe the prevalences of these oral characteristics in the preterm population and compare them with those found in infants born at term; and (3) identify areas referred to the integral oral health of premature infants requiring further research, and propose possible new fields for future studies.

The objectives of the present study were based on the PICO format: “Patients” (studies involving preterm infants), “Interventions” (evaluation of orofacial characteristics), “Comparisons” (infants born at term, regarded as controls), and “Outcomes” (findings of the evaluation of orofacial characteristics), with the purpose of framing the following PICO question: “What characteristics are more frequent in preterm infants compared with infants born at term, and what are their consequences for oral health and quality of life?”.

Material And Methods
Search strategy
The present systematic review was carried out based on the PRISMA (Preferred Reporting Items for
Systematic Reviews and Meta-Analyses) guidelines (35). The literature search was carried out during August 2017, using the PubMed, Medline, Web of Knowledge, Scielo and Google Scholar databases with the keywords: “Preterm birth”, “Premature children”, “oral complications” and “dent*”. These keywords were inter-related using the boolean operator AND, yielding four search possibilities in each database: preterm birth” AND “oral complications; preterm birth” AND “dent*; premature children” AND “oral complications; premature children AND “dent*. After obtaining the search results, we eliminated duplicate publications and proceeded with article selection.

**Selection of articles**

Based on the publications identified by the literature search, we selected those involving a cross-sectional or longitudinal design and addressing oral manifestations associated to premature delivery, independently of the concrete sub-topic involved. The selected studies defined preterm delivery as delivery occurring before a gestational age of 37 weeks. In the case of the control group, we considered publications defining delivery at term as delivery occurring after a gestational age of 37 weeks. Only publications in English or Spanish were included. The selection of articles was made in duplicate by two independent reviewers. In the event of discrepancies, the decision to either include or exclude a publication was established by consensus following debate. Finally, the data corresponding to each study were extracted by two independent operators and entered in a table. In the same way as in selecting the publications, discrepancies were debated until consensus was reached.

**Evaluation of study quality**

The methodological quality of each individual study included in the review was evaluated based on the checklist of the Joanna Briggs Institute (JBI) (36) for case-control studies. This checklist scored each article from 0 to 20 (positive response = 2 points; negative response = 0 points; “Unclear” or “Not applicable” = 1 point). Based on this score, the studies were classified as being of “Very poor quality” (0–5 points), “Poor quality” (6–10 points), “Sufficient quality” (11–15 points) or “High quality” (16–20 points).

**Data availability**

The authors declare that the data supporting the results of this systematic review are available as
complementary files. The data may also be accessed upon request to the corresponding author.

Results
The literature search of the databases (Fig. 1) yielded 2005 publications, and the complementary manual search yielded an additional 20 articles. After eliminating duplicate publications, evaluation of the titles and abstracts yielded a total of 201 studies for initial analysis. Of these, 109 were excluded mainly because the study subject was unrelated to the objectives of our review. A total of 45 publications were selected for full-text evaluation, based on the study design involved (cross-sectional and longitudinal trials).

Of the publications included in the present review (Fig. 2), 27% corresponded to studies conducted in Brazil (the most numerous representation), while 22% were carried out in Sweden. Most of the studies had a cross-sectional design (63%), while 27% were retrospective longitudinal studies and 10% were prospective longitudinal studies. The most widely investigated topic was structural defects in premature infants referred to both the primary and the permanent dentition (33% of all the included studies). Less frequent topics were dental development and composition (each representing 6% of the studies).

Evaluation of the methodological quality of the studies
None of the 45 studies finally included in the systematic review were considered to be of “very poor quality”, while 8 were rated as “poor quality” (17.78%), 19 as “sufficient quality” (42.22%), and 18 as “high quality” (40%). The quality scores of these articles were between 6–18 points, and the mean score of all the selected articles was 13.85.

Discussion
Craniofacial alterations associated to intubation
Many premature infants require endotracheal intubation in the immediate postnatal period. This intervention is indicated when surfactant needs to be administered, aspirated foreign bodies must be removed, or mechanical ventilation is provided. An adverse effect of intubation is that it causes alterations in correct maxillofacial growth of the patient. Depending on the hospital center involved, intubation is via the oral or the nasal route, and this in turn determines the type of deformity produced (37).

The oral route is considered to be easier and less traumatic, though the tubes used in nasal intubation are easier to affix to the intubation site, thereby reducing the risk of accidental extubation (37). While oral intubation has been associated with an increased incidence of dental malocclusions, according to some authors nasal intubation could give rise to nasal deformities, particularly in very low weight premature infants and in cases of prolonged intubation (38, 39). Oral intubation can also give rise to a
palatine sulcus or groove extending from the incisor foramen to the soft palate. This sulcus can be observed in approximately one-quarter of all premature infants and generally disappears with bone remodeling associated with the growth of the child (40, 41).

In conclusion, while not without adverse effects, nasal intubation appears to be safer than oral intubation, and moreover causes fewer sequelae.

**Dental malocclusions**

Premature infants have been found to be at an increased risk of suffering dental malocclusions. As has been commented above, this risk is related to oral intubation, and to a greater susceptibility to develop mouth breathing and respiratory infections (1).

Premature infants have been shown to be 3.32-fold more likely to develop non-feeding sucking habits. This fundamentally may be due to difficulty in securing adequate breast-feeding and the use of a dummy to stimulate sucking action and thus oral feeding (42-45). No clear association can be postulated, however, since the studies on this subject are few and of low methodological quality.

The difficulty in achieving oral feeding may cause the patient to need parenteral nutrition for longer periods of time than infants born at term (46). In some cases, this type of nutrition must be maintained for several months, reducing physiological attrition of the primary dentition and increasing the risk of malocclusions (47).

As a consequence of the mentioned risk factors, some authors consider that preterm children may have a higher prevalence of maxillary compression, associated to a high-arched palate, posterior crossbite and an elongated facial shape (48, 49). Other authors have reported no differences in terms of the prevalence of malocclusion, but have found differences in the prevalence of alterations in head diameter (50).

Paulsson et al. (51) suggested that there is not enough scientific evidence to affirm a relationship between prematurity and malocclusion problems. In their opinion, this is because of the multifactorial etiology of malocclusion.

Germa et al. (49) analyzed the differences in the prevalence of posterior crossbite and anterior open bite between a group of 399 patients born at term and a group of 23 premature patients. The prevalence of posterior crossbite was significantly greater in the study group (35%) than in the control group (p=0.03). Anterior open bite was likewise more prevalent in the premature infants (30%) than among the infants born at term (28%), though in this case statistical significance was not reached (p=0.54).

In the year 2008, Paulsson et al (18) conducted a comparative study on the need for orthodontic treatment in a sample of premature children versus a control group. The prevalence of overbite and of diastemas was significantly greater in the 73 preterm patients than in the 41 patients born at term. Primozic et al. (52), on comparing the prevalence of malocclusions in a group of 80 premature infants with a birth weight of less than 2500 g versus a control group of 113 patients born at term and with normal birth weight, recorded no statistically significant differences between the two groups. However, this study was of poor methodological quality, with limited orthodontic exploration and perinatal information compiled from parent surveys.

Although research in this field is still limited, an association could be suggested between premature delivery and an increased need for orthodontic treatment. Such patients require periodic pediatric dental and orthodontic monitoring from an early age.

**Structural defects of the primary dentition**

The circumstances of premature delivery can result in structural anomalies of the enamel of the primary dentition, as evidenced by a number of publications (22, 44, 53-61). The results of these studies are summarized in Table 1.

In the event of damage during odontogenesis, the tooth does not experience a subsequent
remodeling process. The structural alterations are therefore permanent (62, 63). Structural defects of both the primary and the permanent dentition imply an increased risk of caries and aesthetic problems. Furthermore, the associated increase in dental sensitivity has a negative impact upon the quality of life of the patient, which in turn can result in worsened oral hygiene (53, 64).

Table 1. Prevalence of primary dentition enamel defects in the reviewed studies.

| Author             | Country | Control group (at term) | Study group (preterm) | Prevalence of enamel defects (at term) | Prevalence of enamel defects (preterm) | p-value |
|--------------------|---------|-------------------------|-----------------------|---------------------------------------|----------------------------------------|---------|
| Cruvinel, 2011     | Brazil  | n=40 5-10 years         | n=40 5-10 years       | 62.5%                                 | 65%                                    | 0.8161  |
|                    |         |                         |                       | 7.5%                                  | 37.5%                                  |         |
| Delimited          |         |                         |                       |                                       |                                       |         |
| opacities          |         |                         |                       |                                       |                                       |         |
| p=0.0013           |         |                         |                       |                                       |                                       |         |
| Hypoplasias        |         |                         |                       |                                       |                                       |         |
| Pinho, 2011        | Brazil  | n=171 1-5 years         | n=34 1-5 years        | 16%                                   | 36%                                    | 0.001   |
| Gravina, 2013      | Brazil  | n=96                    | n=96                  | 28.1%                                 | 18.8%                                  | 0.173   |
|                    |         |                         |                       | 8.3%                                  | 37.5%                                  |         |
| Correa-Faria, 2013 | Brazil  | n=338 3-5 years         | n=33 3-5 years        | 28.70%                                | 33.30%                                 | 0.576   |
| Pimlott, 1985      | Canada  | n=106 1-8 years         | n=106                 | 38%                                   | No statistical analysis               |         |
| Aine, 2000         | Finland | n=64 1-2 years          | n=32 1-2 years        | 20%                                   | 67%                                    | 0.001   |
|                    |         |                         |                       | 2%                                    | 66%                                    |         |
|                    |         |                         |                       | 19%                                   | 13%                                    |         |
| Franco, 2007       | Brazil  | n=61 1-3 years          | n=61 1-3 years        | 24.60%                                | 57.40%                                 | 0.001   |
|                    |         |                         |                       | 3.3%                                  | 21.3%                                  |         |
|                    |         |                         |                       | 24.6%                                 | 52.5%                                  |         |
| D'Oliveira-Ferrini, 2008 | Brazil | n=52 2-4 years         | n=52 2-4 years        | 8%                                    | 50%                                    | 0.001   |
|                    |         |                         |                       | 4%                                    | 23%                                    |         |
|                   |         |                         |                       |                                       |                                       |         |

A systematic review conducted by Jacobsen et al. (67) concluded that there is a relationship between premature delivery and structural enamel defects of the primary dentition - with hypoplasia being the most common alteration. This relationship has been confirmed by the great majority of the studies included in our review, with the observation of a significantly higher prevalence of primary dentition enamel defects in premature infants. These anomalies may be attributed to both local and systemic factors. Among the latter, mention can be made of hypoxia, respiratory distress syndrome, infections and nutritional disorders, among others. With regard to the local factors, both intubation and laryngoscopic maneuvering to place the tube have been associated to primary dentition enamel defects (48).
Seow et al. (68, 69) reported a higher prevalence of structural defects of the primary dentition in premature infants that have been intubated, and these defects were moreover seen to show a predilection for the teeth of the left hemiarch. This supports the role of local etiological factors in the structural anomalies (68-70). In concordance with this possible etiology, Takaoka et al (22) found the prevalence of enamel defects in premature patients to be significantly greater (p<0.05) in the upper central incisors and upper left lateral incisor. Thus, the defects were located on the midline and in the upper left hemiarch, as a result of positioning of the neonatologist in maneuvering the laryngoscope with the right hand.

The abovementioned dental structural sequelae are associated with an increased risk of caries; as a result, preventive measures should be adopted in these patients, and their parents and caregivers should be instructed on correct buccodental health.

**Structural defects of the permanent dentition**

In the same way that premature delivery has been associated with an increased prevalence of primary dentition enamel defects, it has also been postulated to have a similar impact upon the permanent dentition.

As can be seen in Table 2, most of the authors describe the prevalence of enamel defects of the permanent dentition to be significantly higher in premature infants than in infants born at term. Jacobsen et al. (67) suggested that there is no association between preterm delivery and structural enamel defects of the permanent dentition. However, research in this field is limited, and further high quality studies are needed to confirm these observations.

On the other hand, some authors suggest a possible relationship between premature delivery and Molar-Incisor Hypomineralization (MIH), though the results of the reviewed studies have been contradictory (56, 64, 71-75). Here again, further high quality studies are needed to clarify the association between MIH and premature delivery. The results of the studies on this subject are summarized in Table 2.

**Table 2.** Prevalence of permanent dentition enamel defects in the reviewed studies.
### Table 3

| Author                  | Country      | Control group (at term) | Study group (preterm) | Prevalence of enamel defects (at term) | Prevalence of enamel defects (preterm) | p-value |
|-------------------------|--------------|-------------------------|-----------------------|---------------------------------------|---------------------------------------|---------|
| Aine, 2000              | Finland      | n=64 9-10 years         | n=32 9-10 years       | 36%                                   | 84%                                   | p<0.001 |
|                         |              |                         |                       | 11%                                   | 38%                                   | p=0.002 |
|                         |              |                         |                       | 25%                                   | 47%                                   | p=0.031 |
| Arrow, 2009             | Australia    | n=506 6-9 years         | n=30 6-9 years        | 47%                                   | 63%                                   | p=0.023 |
|                         |              |                         |                       | 22%                                   | 20%                                   | p=0.023 |
| Brogårdh-Roth, 2011     | Sweden       | n=82 10-12 years        | n=82 10-12 years      | 16%                                   | 38%                                   | p=0.002 |
| Cruvinel, 2011          | Brazil       | n=40 5-10 years         | n=40 5-10 years       | 62.5%                                 | 65%                                   | p=0.816 |
|                         |              |                         |                       | 7.5%                                  | 37.5%                                 | p=0.001 |
| De Lima, 2015           | Brazil       | n=511 11-14 years       | n=83 11-14 years      | 18%                                   | 18.4%                                 | No stat |
| Lai, 1997               | Australia    | n=25 8-11 years         | n=25 8-11 years       | 4%                                    | 68%                                   | p<0.001 |
|                         |              |                         |                       | 40%                                   | 88%                                   | p<0.001 |

**Dental composition and structure**

In a study carried out by Rythen et al. (76), the enamel of the primary dentition of premature patients was seen to contain lesser concentrations of calcium and a larger carbon content than among the children of the control group. On the other hand, previously published studies recorded increased enamel porosity of the primary dentition in preterm infants, as well as an increase in the number of Retzius striae (incremental growth lines) of the enamel (77, 78). Zanolli et al. (79), in turn, observed thicker neonatal lines in the deciduous dentition of premature infants, evidencing a greater extent of hypomineralized enamel in these patients. It has been suggested that this lesser mineralization of the teeth in preterm infants may be due to a diminished incorporation of minerals from the mother after delivery, which in these patients occurs in an earlier stage of dental formation (68).

Although the dental composition of preterm infants has not been widely investigated to date, it is an interesting field for future research, since it could be related to other variables that are more difficult to study, such as the mineral status of other tissues – including bone – and the nutritional status of the child.

**Risk of caries**

Some authors point to an increased risk of caries in preterm infants, due mainly to the aforementioned structural anomalies of the dental enamel (33, 80). The results of the studies on this subject are summarized in Table 3.

**Table 3.** Prevalence of caries in the reviewed studies.
| Author, year | Country | Control group (at term) | Study group (preterm) | Prevalence of caries (at term) | Prevalence of caries (preterm) |
|-------------|---------|-------------------------|-----------------------|-------------------------------|-------------------------------|
| Saraiva, 2007 | Brazil | n=2914 2-5 years | n=275 2-5 years | 14.70% | 26.3% |
| Tanaka, 2014 | Japan | n=1962 3 years | n=93 3 years | 21.10% | 12.90% |
| Rajshekar, 2011 | India | n=250 6 years | n=250 6 years | 38.80% | 48% |
| Campus, 2009 | Italy | n=5005 4 years | n=533 4 years | 20.80% | 25.50% |
| Dos Santos Junior, 2014 | Brazil | n=291 3-4 years | n=29 3-4 years | 13.70% | 82.80% |

Although most of the published findings support the association between premature delivery and an increased risk of caries, some studies have failed to record statistically significant differences (56, 84, 85).

With regard to other risk factors for dental caries, Merglova et al. (86) investigated the oral microbiota of a group of 24 premature 12-month-old infants versus a control group of 45 patients of the same age but born at term. The presence of *Streptococcus mutans* was identified in all the samples of the control group, but in only 4.2% of the samples of the preterm group – the difference being statistically significant (p<0.05). Nevertheless, further studies are needed to confirm this possible association.

Another study recorded greater bacterial plaque and gingivitis scores, a lesser unstimulated salivary flow, and an increased bacterial burden in preterm adolescents, resulting in an increased risk of caries in this population (87).

All the above underscores the importance of parent and caregiver education, as well as of the incorporation of a pediatric dentist to the multidisciplinary team in charge of preterm infant care.

**Dental development and eruption**

The alterations in general development observed in preterm infants suggest that there also may be a delay in dental development in these patients. Backström et al. (88) studied a group of 30 preterm infants at 1-2 years of age and again at 9-11 years of age, using the method of Demirjian to quantify dental development versus a control group. In the primary dentition, the age at eruption of the first tooth was greater in the study group (9 months of chronological age and 7 months of corrected age) than in the control group (6 months). In contrast, in the permanent dentition, no statistically significant differences in dental development were observed between the two groups (p=0.14).

Another similar study likewise found age at eruption of the first deciduous tooth to be significantly greater in premature patients (8.44 months) than in patients born at term (7.05 months) (p<0.001). However, in the same sample, these differences were no longer significant on considering corrected infant age instead of chronological age (89).

The last of the analyzed studies, published by Ramos et al. (90), recorded no statistically significant differences in age at eruption of the first deciduous tooth between the control group (30.1 weeks) and the group of premature patients (34.6 weeks). This study was considered to be of poor methodological quality, however, and the information referred to both gestational age and age at eruption of the first deciduous tooth was obtained from the parents, not through exploration.

The scientific literature suggests that the difference between chronological age and corrected age exerts some influence in determining a possible delay in eruption of the primary dentition. However,
other authors speak of delayed eruption in premature infants as being attributable to systemic factors (62).

There are few studies of good methodological quality in this field. Further research is therefore needed on dental development and eruption among premature infants.

**Tooth size**

In the same way as has been observed in relation to dental growth and development, some authors have described lesser overall growth among premature infants, evidenced by lower percentiles referred to both body weight and height. Such findings again may suggest an impact upon the final size of both the deciduous and the permanent teeth in premature infants.

Some studies (91) have reported comparatively smaller permanent teeth in premature infants. However, it is not yet clear whether this smaller size reflects a decrease in global size of the tooth or a decrease in the thickness of the enamel layer. In support of the latter hypothesis, Seow et al. (92) reported lesser enamel thickness in the primary dentition of preterm infants compared with infants born at term. In contrast, other authors have reported no statistically significant differences between premature patients and the controls in terms of the size of the deciduous teeth (93, 94).

Crown size of the permanent dentition is reportedly smaller in preterm infants, though further studies are needed to confirm this. Moreover, one of the reviewed studies only measured the permanent incisors and first molars (93, 95). Therefore, with regard to tooth size, the available data are limited, and the studies are generally of insufficient quality. The evaluation of differences in deciduous and permanent tooth size between premature infants and patients born at term could be an interesting field for future research.

**Behavioral management**

In pediatric dentistry, the behavior of the patient is very important, and may prove decisive for defining a prevention or treatment plan.

Preterm infants are at an increased risk of developing cognitive and behavioral disorders, including learning deficits. However, no statistically significant differences in terms of dental anxiety have been found in comparison with patients born at term (96). On the other hand, parents report more behavioral problems in premature offspring than in offspring born at term (97).

Other studies (98) have described an association between preterm delivery and behavioral and attention disorders reported by the parents of Japanese children. There have also been descriptions of altered pain response in patients who have experienced recurrent pain during the neonatal period, associated to systemic diseases or medical and surgical interventions (99).

There have been few studies to date on behavior and dental anxiety in preterm children. Further studies are therefore needed in order to draw conclusions with potential applications in clinical practice.

**Other oral manifestations**

Other oral problems inherent to premature infants include lacerations caused during intubation (33, 48), as well as the accumulation of bilirubin in the developing dental tissues associated to the neonatal cholestasis seen in some premature children – giving rise to a greenish color of the primary dentition (100). There have also been reports of an increased prevalence of anomalies in dental shape, affecting particularly the permanent upper lateral incisors (16).

Lastly, it has been postulated that premature infants may be at an increased risk of dental and maxillofacial traumatisms due to their delayed motor coordination. A cross-sectional study has found no evidence of such an increased risk (101), though another publication found statistically significant
differences in the frequency of dental trauma between premature infants (21%) and patients born at term (6%) \( (p=0.02) \) (44). In any case, further studies on dental and maxillofacial trauma in preterm children are required before it can be concluded that premature delivery is a risk factor for traumatisms of this kind.

**Limitations of the study**

One of the main limitations of our study has been the need to resort to articles with a cross-sectional or longitudinal design, which are associated with the lowest levels of scientific evidence. This proved necessary because of the study subject involved, and we attempted to limit the problem by evaluating the methodological quality of each selected publication individually.

In the same context, the protocols guiding most systematic reviews focus on clinical trials, and in this regard we had to adapt our own approach to observational studies or resort to less solid protocols.

**Conclusions**

Cross-sectional studies were the most frequent publications in the present systematic review, followed by retrospective observational studies. The most widely investigated oral manifestations in premature infants were structural enamel defects, followed by caries and malocclusions.

Structural enamel defects of the primary dentition were the most common alterations according to the consulted literature. Both caries and malocclusions were more frequent in premature patients, though the results of the different studies were heterogeneous in this regard.

Other less widely studied orofacial disorders were enamel defects of the permanent dentition, as well as alterations in dental composition and size, and in tooth development and eruption. Such anomalies should be addressed by future studies.

The existence of oral sequels in children born at term accentuates the need for the pediatric dentist to be a part of the multidisciplinary team in charge of the preterm infant health care, with the purpose of defining prevention and care strategies for premature patients, and thus ensuring improved future quality of life.

**List Of Abbreviations**

World Health Organization (WHO).
Patient, Intervention, Comparison, Outcome (PICO).
Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).
Joanna Briggs Institute (JBI).
Molar-Incisor Hypomineralization (MIH).

**Declarations**

Ethics approval and consent to participate.

Not applicable.
Consent for publication

Not applicable.

Availability of data and material

The authors declare that the data supporting the findings of this study are available within the article and its supplementary information files.

Competing interests

The authors declare that they have no conflicts of interest in relation to the present study.

Funding

The present project was financed by the Fondo de Investigaciones Sanitarias (FIS) of the Instituto de Salud Carlos III (Spanish Ministry of Economics, Industry and Competitivity).

Authors’ contributions

Literature search, article selection, extraction of data and evaluation of study quality were carried out by two authors (LVC and EPP). LVC also redacted the manuscript. EPP, JISE, JML, ARE and PPP supervised the process and corrected and approved the final manuscript.

Acknowledgements

Not applicable

References

1. Harila V, Heikkinen T, Gron M, Alvesalo L. Open bite in prematurely born children. J Dent Child. 2007;74:165-170.
2. Frey HA, Klebanoff MA. The epidemiology, etiology, and costs of preterm birth. Semin Fetal Neonatal Med. 2016; 21;68-73.
3. Koullali B, Oudijk MA, Nijman TA, Mol BW, Pajkrt E. Risk assessment and management to prevent preterm birth. Semin Fetal Neonatal Med. 2016;21:80-88.
4. Platt MJ. Outcomes in preterm infants. Public Health. 2014;128:399-403.
5. Ray JG, Park AL, Fell DB. Mortality in Infants Affected by Preterm Birth and Severe Small-for-Gestational Age Birth Weight. Pediatrics. 2017;140.
6. Walsh MC. Neonatal outcomes of moderately preterm infants compared to extremely preterm infants. Pediatr Res. 2017;82:297-304.

7. O'Connell S, O'Connell A, O'Mullane E, Hoey H. Medical, nutritional, and dental considerations in children with low birth weight. Pediatr Dent. 2009;31:504-512.

8. Armson BA. Physical activity and preterm birth: risk factor or benefit? BJOG. 2017;124.

9. Hackbarth BB. et al. Preterm birth susceptibility: investigation of behavioral, genetic, medical and sociodemographic factors. Rev Bras Ginecol Obstet. 2015;37:353-358.

10. Fuchs F, Senat MV. Multiple gestations and preterm birth. Semin Fetal Neonatal Med. 2016;21:113-120.

11. Ion R, Bernal AL. Smoking and Preterm Birth. Reprod Sci. 2015;22:918-926.

12. Reza Karimi M, Hamissi JH, Naeini SR, Karimi M. The Relationship Between Maternal Periodontal Status of and Preterm and Low Birth Weight Infants in Iran: A Case Control Study. Glob J Health Sci. 2015;8:184-188.

13. Lima SAM. et al. Is the risk of low birth weight or preterm labor greater when maternal stress is experienced during pregnancy? A systematic review and meta-analysis of cohort studies. PLoS One 2018;13:e0200594.

14. Phillips C, Velji Z, Hanly C, Metcalfe A. Risk of recurrent spontaneous preterm birth: a systematic review and meta-analysis. BMJ Open 2017;7: e015402-2016.

15. Mannem S, Chava VK. The relationship between maternal periodontitis and preterm low birth weight: A case-control study. Contemp Clin Dent. 2011;2:88-93.

16. Gandhi RP, Lacy M, DeWitt P. The Association Between Gestational Age and Shape Anomalies of the Permanent Dentition. Pediatr Dent. 2016;38: 239-245.

17. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet 2008;371: 75-84.
18. Paulsson L, Soderfeldt B, Bondemark L. Malocclusion traits and orthodontic treatment needs in prematurely born children. Angle Orthod. 2008;78:786-792.

19. Johnson S, Marlow N. Early and long-term outcome of infants born extremely preterm. Arch Dis Child. 2017;102:97-102.

20. Manuck TA. Racial and ethnic differences in preterm birth: A complex, multifactorial problem. Semin Perinatol. 2017;41:511-518.

21. Nuyt AM, Lavoie JC, Mohamed I, Paquette K, Luu TM. Adult Consequences of Extremely Preterm Birth: Cardiovascular and Metabolic Diseases Risk Factors, Mechanisms, and Prevention Avenues. Clin Perinatol. 2017;44:315-332.

22. Takaoka LA, Goulart AL, Kopelman BI, Weiler RM. Enamel defects in the complete primary dentition of children born at term and preterm. Pediatr Dent. 2011;33: 171-176.

23. Brogardh-Roth S et al. Five years' follow-up of dental fear and anxiety, experience of dental care and oral health behaviour in Swedish preterm and full-term adolescents. BMC Oral Health. 2017;17:145-017.

24. Chehade H, Simeoni U, Guignard JP, Boubred F. Preterm Birth: Long Term Cardiovascular and Renal Consequences. Curr Pediatr Rev. 2018;14:219-226.

25. Di Fiore JM, Poets CF, Gauda E, Martin RJ, MacFarlane P. Cardiorespiratory events in preterm infants: etiology and monitoring technologies. J Perinatol. 2016;36:165-171.

26. Goedicke-Fritz S et al. Preterm Birth Affects the Risk of Developing Immune-Mediated Diseases. Front Immunol. 2017;8:1266.

27. Kotecha SJ, Gallacher DJ, Kotecha S. The respiratory consequences of early-term birth and delivery by caesarean sections. Paediatr Respir Rev. 2016;19: 49-55.

28. Luyckx VA. Preterm Birth and its Impact on Renal Health. Semin Nephrol. 2017;37:311-319.
29. Melville JM, Moss TJ. The immune consequences of preterm birth. Front Neurosci. 2013;7: 79.

30. O'Reilly M, Sozo F, Harding R. Impact of preterm birth and bronchopulmonary dysplasia on the developing lung: long-term consequences for respiratory health. Clin Exp Pharmacol Physiol. 2013;40:765-773.

31. Pike KC, Lucas JS. Respiratory consequences of late preterm birth. Paediatr Respir Rev. 2015;16:182-188.

32. Warner BB, Tarr PI. Necrotizing enterocolitis and preterm infant gut bacteria. Semin Fetal Neonatal Med. 2016;21:394-399.

33. Seow WK. Effects of preterm birth on oral growth and development. Aust Dent J. 1997;42:85-91.

34. Tsang AK. The Special Needs of Preterm Children - An Oral Health Perspective. Dent Clin North Am. 2016;60:737-756.

35. Moher D, LA. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2015;6(7):e1000097.

36. Moola S, M. Z. Chapter 7: Systematic reviews of etiology and risk. In: Aromataris E, Munn Z, editors. Joanna Briggs Institute Reviewer's Manual. The Joanna Briggs Institute, 2017. Available from https://reviewersmanual.joannabriggs.org/.

37. de Vries M, Sival DA, van Doormaal-Stremmelaar E, Ter Horst H. Traumatic perforation of the lamina cribrosa during nasal intubation of a preterm infant. Pediatrics 2014;133: e762-e765.

38. Loftus BC, Ahn J, Haddad J. Neonatal nasal deformities secondary to nasal continuous positive airway pressure. Laryngoscope 1994;104:1019-1022.

39. Kryvenko LS. Orthodontic aspects of dental status in prematurely born children. Текст научной статьи по специальности Медицина и здравоохранение 2014.
40. Cortines AAO, Costa LR. Associated factors and persistence of palatal groove in preterm infants: a cohort study. BMC Pediatr. 2016;16:143.

41. Angelos GM, Smith DR, Jorgenson R, Sweeney EA. Oral complications associated with neonatal oral tracheal intubation: a critical review. Pediatr Dent. 1989;11:133-140.

42. Fernandes IB. et al. Non-nutritive sucking habits after three years of age: a case-control study. J Indian Soc Pedod Prev Dent. 2015;33:19-24.

43. Khalessi N, Nazi S, Shariat M, Saboteh M, Farahani Z. The Effects of Pre-feeding Oral Stimulations and Non-nutritive Sucking on Physical Growth and Independent Oral Feeding of Preterm Infants. Iranian Journal of Neonatology. 2015;6:25-29.

44. Ferrini FR, Marba ST, Gaviao MB. Oral conditions in very low and extremely low birth weight children. J Dent Child. 2008;75:235-242.

45. Kaya V, Aytekin A. Effects of pacifier use on transition to full breastfeeding and sucking skills in preterm infants: a randomised controlled trial. J Clin Nurs. 2017;26:2055-2063.

46. Hwang YS, Ma MC, Tseng YM, Tsai WH. Associations among perinatal factors and age of achievement of full oral feeding in very preterm infants. Pediatr Neonatol. 2013;54:309-314.

47. Olczak-Kowalczyk D. et al. Does long term parenteral nutrition in children have an impact on malocclusion? Preliminary report. Dev Period Med. 2014;18:241-246.

48. Bodh MJ. M. Preterm Birth Complications On Oro-Dental Structures: An Updated Review. J Oral Health Comm Dent. 2015;9:85-89.

49. Germa A. et al. Early risk factors for posterior crossbite and anterior open bite in the primary dentition. Angle Orthod. 2016;86:832-838.

50. Guedes KM. et al. Stomatognathic evaluation at five years of age in children born premature and at term. BMC Pediatr. 2015;15:27-015.
51. Paulsson L, Bondemark L, Söderfeldt B. A systematic review of the consequences of premature birth on palatal morphology, dental occlusion, tooth-crown dimensions, and tooth maturity and eruption. Angle Orthod. 2004;74:269-279.

52. Primozic J, Farcnik F, Ovsenik M, Primozic JA controlled study of the functional and morphological characteristics of malocclusion in prematurely born subjects with low birth weight. Eur J Orthod. 2014;36:114-120.

53. Gravina DB, Cruvinel VR, Azevedo TD, Toledo OA, Bezerra AC. Enamel defects in the primary dentition of preterm and full-term children. J Clin Pediatr Dent. 2013;37:391-395.

54. Pinho JRO et al. Are low birth weight, intrauterine growth restriction, and preterm birth associated with enamel developmental defects? Pediatr Dent. 2012;34:244-248.

55. Prokocimer T, Amir E, Blumer S, Peretz B. Birth-Weight, Pregnancy Term, Pre-Natal and Natal Complications Related to Child’s Dental Anomalies. J Clin Pediatr Dent. 2012;39:371-376.

56. Tanaka K, Miyake Y. Low birth weight, preterm birth or small-for-gestational-age are not associated with dental caries in young Japanese children. BMC Oral Health. 2014;14:38-6831.

57. Velló MA et al. Prenatal and neonatal risk factors for the development of enamel defects in low birth weight children. Oral Dis. 2012;16:257-262.

58. Pimlott JF, Howley TP, Nikiforuk G, Fitzhardinge PM. Enamel defects in prematurely born, low birth-weight infants. Pediatr Dent. 1985;7:218-223.

59. Mellander M, Norén JG, Fredén H, Kjellmer I. Mineralization defects in deciduous teeth of low birthweight infants. Acta Paediatr Scand. 1082;71:727-733.

60. Lai PY, Seow WK, Tudehope DI, Rogers Y. Enamel hypoplasia and dental caries in very-low birthweight children: a case-controlled, longitudinal study. Pediatr Dent.
1997;19:42-49.

61. Correa-Faria P et al. Developmental defects of enamel in primary teeth: prevalence and associated factors. Int J Paediatr Dent. 2012;23:173-179.

62. Zaidi I, Thayath MN, Singh S, Sinha A. Preterm Birth: A Primary Etiological Factor for Delayed Oral Growth and Development. Int J Clin Pediatr Dent. 2015;8:215-219.

63. Franco KM, Line SR, de Moura-Ribeiro MV. Prenatal and neonatal variables associated with enamel hypoplasia in deciduous teeth in low birth weight preterm infants. J Appl Oral Sci. 2007;15:518-523.

64. Brogårdh-Roth S, Matsson L, Klingberg G. Molar-incisor hypomineralization and oral hygiene in 10- to 12-yr-old Swedish children born preterm. Eur J Oral Sci. 2011;119:33-39.

65. Cruvinel VR et al. Prevalence of enamel defects and associated risk factors in both dentitions in preterm and full term born children. J Appl Oral Sci. 2012;20:310-317.

66. Aine L et al. Enamel defects in primary and permanent teeth of children born prematurely. J Oral Pathol Med. 2000;29:403-409.

67. Jacobsen PE, Haubek D, Henriksen TB, Ostergaard JR, Poulsen S. Developmental enamel defects in children born preterm: a systematic review. Eur J Oral Sci. 2012;122: 7-14.

68. Seow WK, Brown JP, Tudehope DI, O'Callaghan M. Developmental defects in the primary dentition of low birth-weight infants: adverse effects of laryngoscopy and prolonged endotracheal intubation. Pediatr Dent. 1984;6:28-31.

69. Seow WK. Oral complications of premature birth. Aust Dent J. 1986;31:23-29.

70. Falcao de Oliveira Melo NS, Vieira Cavalcante da Silva RPG, Soares de Lima AA. The neonatal intubation causes defects in primary teeth of premature infants. Biomedical Papers-Olomouc 2012;158:605-612.
71. Arrow P. Risk factors in the occurrence of enamel defects of the first permanent molars among schoolchildren in Western Australia. Community Dent Oral Epidemiol. 2009;37:405-415.

72. de Lima MD et al. Epidemiologic Study of Molar-incisor Hypomineralization in Schoolchildren in North-eastern Brazil. Pediatr Dent. 2012;37:513-519.

73. Ghanim A, Manton D, Bailey D, Marino R, Morgan M. Risk factors in the occurrence of molar-incisor hypomineralization amongst a group of Iraqi children. Int J Paediatr Dent. 2013;23:197-206.

74. Lygidakis NA, Dimou G, Marinou D. Molar-incisor-hypomineralisation (MIH). A retrospective clinical study in Greek children. II. Possible medical aetiologica factors. Eur Arch Paediatr Dent. 2008;9:207-217.

75. Garot E, Manton D, Rouas P. Peripartum events and molar-incisor hypomineralisation (MIH) amongst young patients in southwest France. Eur Arch Paediatr Dent 2016;17:245-250.

76. Rythén M, Sabel N, Dietz W, Robertson A, Norén J. Chemical aspects on dental hard tissues in primary teeth from preterm infants. Eur J Oral Sci. 2010;118:389-395.

77. Rythén M et al. Morphological aspects of dental hard tissues in primary teeth from preterm infants. Int J Paediatr Dent. 2008;18:397-406.

78. Norén JG. Enamel structure in deciduous teeth from low-birth-weight infants. Acta Odontol Scand. 1983;41:355-362.

79. Zanolli C, Bondioli L, Manni F, Rossi P, Macchiarelli R. Gestation length, mode of delivery, and neonatal line-thickness variation. Hum Biol. 2011;83:695-713.

80. Saraiva MC, Bettiol H, Barbieri MA, Silva AA. Are intrauterine growth restriction and preterm birth associated with dental caries? Community Dent Oral Epidemiol. 2007;35:364-376.
81. Rajshekar SA, Laxminarayan N. Comparison of primary dentition caries experience in pre-term low birth-weight and full-term normal birth-weight children aged one to six years. J Indian Soc Pedod Prev Dent. 2011;29:128-134.

82. Campus G et al. National pathfinder survey on children's oral health in Italy: pattern and severity of caries disease in 4-year-olds. Caries Res. 2009;43:155-162.

83. dos Santos Junior VE, de Sousa RM, Oliveira MC, de Caldas Junior AF, Rosenblatt A. Early childhood caries and its relationship with perinatal, socioeconomic and nutritional risks: a cross-sectional study. BMC Oral Health. 2012;14:47-68.

84. Nirunsittirat A et al. Adverse birth outcomes and childhood caries: a cohort study. Community Dent. Oral Epidemiol. 2016;44:239-247.

85. Nelson S et al. Increased enamel hypoplasia and very low birthweight infants. J Dent Res 2014;92:788-794.

86. Merglova V, Koberova-Ivancakova R, Broukal Z, Dort J. The presence of cariogenic and periodontal pathogens in the oral cavity of one-year-old infants delivered pre-term with very low birthweights: a case control study. BMC Oral Health. 2014;14:109.

87. Rythen M, Niklasson A, Hellstrom A, Hakeberg M, Robertson A. Risk indicators for poor oral health in adolescents born extremely preterm. Swed Dent J. 2012;36:115-124.

88. Backström MC. Maduration of primary and permanent teeth in preterm infants. Arch Dis Fetal Neonatal Ed 2000;83:104-108.

89. Pavicin IS, Dumancic J, Badel T, Vodanovic M. Timing of emergence of the first primary tooth in preterm and full-term infants. Ann Anat 2016;203:19-23.

90. Ramos SRP, Gugisch RC, Fraiz FC. The influence of gestational age and birth weight of the newborn on tooth eruption. J Appl Oral Sci 2006;14:228-232.

91. Rythen M, Thilander B, Robertson A. Dento-alveolar characteristics in adolescents
born extremely preterm. Eur J Orthod. 2013;35:475-482.

92. Seow WK, Young WG, Tsang AKL, Daley TA. Study of primary dental enamel from preterm and full-term children using light and scanning electron microscopy. Pediatr Dent. 2005;27:374-379.

93. Harila-Kaera V, Heikkinen T, Alvesalo L, Osborne RH. Permanent tooth crown dimensions in prematurely born children. Early Hum Dev. 2001;62:131-147.

94. Harila V, Heikkinen T, Alvesalo L. Deciduous tooth crown size in prematurely born children. Early Hum Dev. 2003;75:9-20.

95. Ebrahim EPL. The impact of premature birth on the permanent tooth size of incisor and first molars. Eur J Orthod 2017;39:622-627.

96. Brogardh-Roth S, Stjernqvist K, Matsson L, Klingberg G. Dental fear and anxiety and oral health behaviour in 12- to 14-year-olds born preterm. Int J Paediatr Dent. 2010;20:391-399.

97. Brogardh-Roth S, Stjernqvist K, Matsson L, Klingberg G. Parental perspectives on preterm children's oral health behaviour and experience of dental care during preschool and early school years. Int J Paediatr Dent. 2009;19:243-250.

98. Higa Diez M, Yorifuji T, Kado Y, Sanada S, Doi H. Preterm birth and behavioural outcomes at 8 years of age: a nationwide survey in Japan. Arch Dis Child. 2015;101:338-343.

99. Carbajal R et al. Sedation and analgesia practices in neonatal intensive care units (EUROPAIN): results from a prospective cohort study. Lancet Respir Med. 2015;3:796-812.

100. Battineni S, Clarke P. Green teeth are a late complication of prolonged conjugated hyperbilirubinemia in extremely low birth weight infants. Pediatr Dent. 2012;34:103-106.
101. Brogårdh-Roth S, Matsson L. Preterm birth does not increase the risk of traumatic dental injuries or unintentional injuries. Acta Paediatr. 2014;103:331-336.

Figures
Figure 1

PRISMA flowchart of the literature search.

From: Moher D, Liberati A, Tetzlaff J, Altman DG. The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed.1000097

For more information, visit www.prisma-statement.org.
Figure 2

Principal study topics of the publications included in the review.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

Additional file 1.doc
Additional file 3.doc
Additional file 2.docx