

# General and oral health status of preterm one-year-old very low and extremely low birthweight infants (a cross – sectional study)

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**Aims.** The aim of the present study was to evaluate the general and oral health status of a group of preterm one-year-old very low (VLBW) and extremely low birthweight (ELBW) infants and make a comparison with full-term one-year-old normal birthweight infants (NBW).

**Methods.** A cross-sectional study was conducted in 102 one-year-old preterm VLBW and ELBW infants, and the data obtained were compared to 87 one-year-old full-term NBW infants. The infants' medical histories were obtained from hospital records and interviews with the mothers. The oral cavities of all infants were examined under the same conditions. The chi-square test, Pearson's chi-square test of independence and Mann-Whitney test were used for the statistical evaluation, with  $P < 0.05$  considered statistically significant. Relative risk (RR) and 95% confidence interval (CI) estimates for variables significantly associated with oral findings were calculated.

**Results.** Both perinatal variables (gestational age, mode of delivery, birthweight, Apgar score, resuscitation, orotracheal intubation and presence of intraoral pathology) and neonatal variables (antibiotic treatment and infections) had a significant association with prematurity, VLBW and ELBW. The one-year-old preterm VLBW and ELBW infants frequently suffered from general diseases, frequently received regular medication and had fewer erupted primary teeth; they also had a higher prevalence of developmental defects of the enamel and deformations of the hard palate.

**Conclusion.** This study confirmed anamnestic, medical and oral differences between one-year-old preterm VLBW and ELBW and full-term NBW infants.

**Key words:** preterm infant, very low birthweight, extremely low birthweight, primary teeth, developmental enamel defect, deformation of the hard palate

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## INTRODUCTION

Preterm birth and low birthweight are the main factors of early morbidity and mortality in neonates and late morbidity in infants across the world. According to the definition of the World Health Organization<sup>1</sup>, a preterm infant is defined as one born before completing gestational week 37. Low birthweight (LBW) is defined as weighing less than 2500 g, regardless of gestational age. LBW includes both appropriately grown preterm infants and term and preterm growth-restricted neonates. Blencowe et al.<sup>2</sup> estimated an LBW prevalence of 6.8–7.2 per 100 livebirths for 2000–2015 in developed countries (North America, Europe, Australia and New Zealand). Low birthweight neonates are additionally subdivided into very low birthweight infants (VLBW), with birthweight < 1500 g, and extremely low birthweight infants (ELBW), with birthweight < 1000 g. Preterm birth is frequently associated with LBW, VLBW or ELBW. Premature infants, especially those with VLBW and ELBW, have a shorter prenatal

period and are predisposed to various perinatal and neonatal complications and developmental problems that can affect their general growth and progress during infancy and throughout childhood. Premature VLBW and ELBW infants are prone to suffer from many serious conditions, such as breathing problems, patent ductus arteriosus, anemia, immunodeficiency, hypocalcemia, osteopenia, visual and hearing disorders and other alterations that affect development and growth<sup>3</sup>. These complications may be associated with poor feeding, lack of optimal nutrition, and vitamin and mineral deficiencies<sup>4</sup>. Some treatments and techniques to sustain life in preterm VLBW and ELBW infants have a negative impact on oral development. The developmental enamel defects (DDE) of the primary incisors, dilacerations of the primary incisors and anomalies of the hard palate may be connected with laryngoscopies and orotracheal intubations<sup>5-7</sup>. Preterm VLBW and ELBW infants are also at increased risk of delayed tooth eruption, DDE in permanent dentition, tooth discoloration and tooth crown dimension changes<sup>8-12</sup>.

The aim of the study was to evaluate anamnestic and medical data and oral conditions in one-year-old VLBW and ELBW preterm infants and compare these findings with one-year-old full-term normal birthweight NBW infants.

## MATERIALS AND METHODS

This cross-sectional study is part of a long-term research project supported by the Ministry of Health, Czech Republic, being conducted at the Departments of Dentistry and Neonatology, Faculty Hospitals in Pilsen and Hradec Kralove, Czech Republic. All infants were enrolled in the current study at birth by the Departments of Neonatology, Faculty Hospitals in Pilsen and Hradec Kralove, Czech Republic. Preterm VLBW and ELBW Caucasian neonates of both sexes were selected according to inclusion and exclusion criteria, and the same therapeutic principles were used during their perinatal and neonatal hospital care. A convenience sample, including full-term neonates with NBW, was used, and these neonates were recruited at the Neonatological Departments in Pilsen and Hradec Kralove. After birth, the oral cavities of the preterm VLBW and ELBW neonates and full-term NBW neonates were examined, and oral pathological conditions were recorded. The first dental examination of all the neonates was recommended at the corrected age of one year.

Gestational age < 37 weeks and birthweight < 1500 g were the inclusion criteria for the preterm VLBW and ELBW group, and gestational age > 37 weeks and birth weight > 2500 g were the inclusion criteria for full-term NBW neonates. The gestational age was estimated from the result of ultrasound examinations during pregnancy. A further inclusion criterion for both groups of neonates was self-perceived socioeconomic class of the parents. The exclusion criteria were the presence of systemic disease or immunological deficiency in the full-term group and genetic syndromes and malformations diagnosed during the neonatal period in the preterm VLBW and ELBW group.

The total number of preterm VLBW and ELBW neonates born during the evaluation period (2015–2016) was 242. Fewer infants were included in the final study sample for various reasons (newborn death, serious health complications, parental disapproval of participation in the study, remote residence, native language other than Czech, and abandonment of outpatient follow-up during the period of data collection). Preterm VLBW and ELBW infants were referred from the Developmental Centers of Neonatology Departments in Pilsen and Hradec Kralove, Czech Republic, for their first dental examination at the corrected age of one year. As prematurely born infants are not fully mature at the time of birth, their chronological ages do not correspond to their true biological ages. Hence, a comparison with full-term infants can only be made if the age of the preterm infants is corrected. The corrected age was calculated by subtracting the number of weeks born before 40 weeks of gestation from the chronological age. Full-term NBW infants were invited for their

first dental examination at the chronological age of one year.

The total number of preterm VLBW and ELBW infants and full-term NBW infants that passed the examination during the neonatal period and completed follow-up at the corrected or chronological age of one year was 200. Out of the 200 examined infants, 11 were excluded (parental lack of interest to continue in the study). The final research cohort was composed of 189 one-year-old infants of both sexes, 102 of whom were born prematurely with VLBW or ELBW and 87 of whom were delivered at full-term with NBW.

The infants' medical histories were obtained from the hospital records and interviews with the mothers. All infants included in the study were residents of communities with low natural fluoride content (< 0.3 ppm). Two previously trained and calibrated examiners at the Pediatric Dentistry Departments in Pilsen and Hradec Kralove, Czech Republic, performed the dental examination on all infants. The dental examiners were blinded to the infants' groups. The oral cavity of the infants was examined under ideal conditions using a sterile dental mirror, dental probe and artificial light, while the infants were held in their parents' lap. All erupted teeth were recorded in the dental chart. A tooth was considered erupted if any part of its crown had penetrated the oral mucous. The teeth were dried with gauze, and then dental mirrors and probes were used for the detection of DDE. DDE were recorded on the labial surface of each tooth. Defects measuring less than one millimeter were excluded, and when any doubt existed concerning the presence of DDE, the tooth was scored as being without enamel defects<sup>13</sup>. The alteration of primary teeth enamel was classified according to the Modified Developmental Defects of Enamel Index, suggested by the Commission on Oral Health, Research and Epidemiology<sup>14</sup>. Clinically, DDE can be classified into three types: demarcated opacity, diffuse opacity and hypoplasia. Opacities (hypomineralizations) are qualitative changes in enamel translucency without loss of enamel surface. Demarcated opacities are defects of enamel mineralization that are distinct from the adjacent healthy enamel and may present a white, creamy, yellow or brown color. Diffuse opacities comprise alterations in enamel translucency of variable degree and are white in color. There is no clear demarcation between normal enamel and opacity. Hypoplasia is a quantitative defect affecting the enamel surface; it is associated with reduced enamel thickness and can manifest as pits, grooves or other surface loss. Color photographs showing typical examples of different types of DDE were used as a guide in scoring the teeth for DDE<sup>15</sup>. The opacities were differentiated from white spot carious lesions based on color, texture, demarcation and relationship to the gingival margin<sup>15</sup>. Deformations of the hard palate (palatal grooving, high arch palate, palatal asymmetry) were diagnosed visually using the description of Ehrenberg and Nowak<sup>16</sup>.

The following variables were recorded for each infant: birthweight, mode of delivery, gestational age, Apgar score, resuscitation, laryngoscopy, antibiotic treatment, infections, general diseases, and regular medication. The

Apgar scoring system is a commonly used comprehensive screening tool to evaluate a newborn's condition at birth. The Apgar score is recorded at one, five and 10 min of life. Newborns are evaluated based on five variables: heart rate, respiratory effort, muscle tone, reflex irritability and skin color<sup>17,18</sup>. For this study, the presence of oral pathology was evaluated in all neonates. Variables involving oral conditions in the one-year-old infants were the number of erupted primary teeth, presence of DDE and deformation of the hard palate.

### Statistical analysis

The data were statistically analyzed using Statgraphics software distributed by Stat Point Technologies, Inc. of Warrenton, Virginia, USA. The comparison between the two groups was conducted using the chi-squared test for evaluation of the mode of delivery, need for resuscitation and laryngoscopy, antibiotic treatment, presence of infections, general diseases, regular medication, developmental enamel defects and oral pathology. The t-test was used for comparisons of gestational age, birthweight and Apgar scores. For comparison of the number of erupted teeth in preterm VLBW and ELBW and full-term NBW infants, the Mann-Whitney test was applied; in cases of hard palate deformation, Pearson's chi-squared test of

independence was used. A statistical significance level of  $P < 0.05$  was established. Relative risk (RR) and 95% confidence interval (CI) estimates for the variables significantly associated with oral findings were calculated using the online Med Calc tool ([http://www.medcalc-org/calc/relative\\_risk.php](http://www.medcalc-org/calc/relative_risk.php)).

### Ethical considerations

Ethical approval for the investigation was obtained from the Research Ethics Committee Faculty of Medicine in Pilsen and Hradec Kralove, Charles University in Prague, Czech Republic. The study was conducted in accordance with the Helsinki Declaration of 1975, as revised in 1983. All infants were recruited from the Department of Neonatology of the Faculty Hospitals in Pilsen and Hradec Kralove, Czech Republic. Prior to the study, the legal guardians of all infants provided informed consent for their children to participate in the research.

## RESULTS

### Characteristics of the subjects

The characteristics of the preterm VLBW and ELBW and full-term NBW infants are summarized in Table 1.

**Table 1.** Perinatal and neonatal variables.

Variables	Preterm VLBW and ELBW	Full - term NBW	<i>P</i>
N (%)			
Birthweight (g): Mean $\pm$ SD**	1148.9 $\pm$ 285.3	3418.6 $\pm$ 285.3	< 0.0001
Mode of delivery*			
Vaginal	12 (11.8)	71 (81.6)	< 0.0001
Sectio caesarea	90 (88.2)	16 (18.4)	
Gestational age (wks): Mean $\pm$ SD**	29.38 $\pm$ 2.73	39.36 $\pm$ 1.07	
Apgar score**			
1	6.78 $\pm$ 1.9	9.66 $\pm$ 0.34	< 0.0001
5	8.00 $\pm$ 0.99	9.84 $\pm$ 0.16	< 0.0001
10	8.53 $\pm$ 0.85	9.95 $\pm$ 0.05	< 0.0001
Resuscitation*			
No	69 (67.6)	84 (96.6)	0.0002
Yes	33 (32.4)	3 (3.4)	
Laryngoscopy*			
No	43 (42.2)	87 (100.0)	< 0.0001
Yes	59 (57.8)	0	
Atb treatment*			
No	0	87 (100.0)	< 0.0001
Yes	102 (100.0)	0	
Infections*			
No	52 (51.0)	87 (100.0)	< 0.0001
Yes	50 (49.0)	0	
General diseases*			
No	78 (76.5)	84 (96.6)	< 0.0001
Yes	24 (23.5)	3 (3.4)	
Medication*			
No	94 (92.2)	87 (100.0)	0.0196
Yes	8 (7.8)	0	

\* $\chi^2$  test, \*\*t-test





Fig. 1. Neonatal lower incisor in preterm neonate.



Fig. 2. Congenital epulis in preterm neonate.



Fig. 3. Epstein's pearls in preterm neonate.

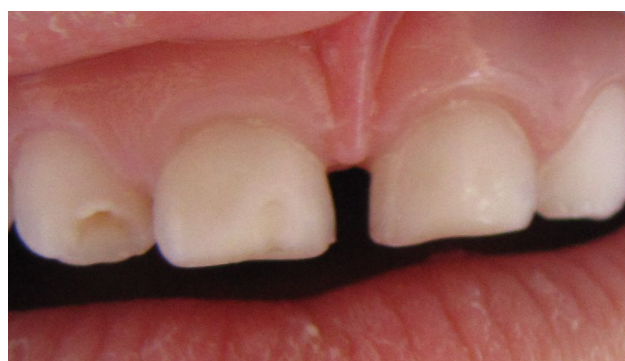


Fig. 4. DDE in one-year old infant.

In the preterm group, 102 infants were available for analysis. Their mean gestational age was 29.38 weeks, and their mean birthweight was 1148.9 g. Altogether, ninety (88.2%) of the preterm infants were delivered by cesarean section. In the full-term group, there were 87 infants with a mean gestational age of 39.36 weeks and a mean birthweight of 3418.6 g. The majority of the full-term infants were delivered vaginally (81.6%).

#### Perinatal and neonatal variables

Both perinatal variables (gestational age ( $P<0.0001$ ), mode of delivery ( $P<0.0001$ ), birthweight ( $P<0.0001$ ), Apgar score ( $P<0.0001$ ), resuscitation ( $P<0.0001$ ), laryngoscopy [ $(P<0.0001)$ ] (Table 1) and neonatal variables (antibiotic treatment ( $P<0.0001$ ), early and late infection ( $P<0.0001$ )) showed a significant association with prematurity and VLBW and ELBW (Table 1). Three preterm neonates and five full-term neonates were diagnosed with additional pathological conditions in their oral cavity. In preterm neonates, neonatal teeth (Fig. 1), congenital epulis (Fig. 2) and Epstein's pearls (Fig. 3) were established. Five full-term neonates had a sublingual frenum anomaly (frenulum linguae breve).

#### General health status

The one-year-old preterm VLBW and ELBW infants suffered more frequently from general diseases ( $P=0.001$ ) and received more regular medication ( $P=0.0196$ ) than the full-term NBW group of infants (Table 1). In total, 24 one-year-old preterm VLBW and ELBW infants were diagnosed with neurological disorders, congenital heart defects, renal and respiratory conditions, and vision impairments. Regular medication (corticosteroids, antihistamine and antiepileptic drugs) was prescribed in eight VLBW and ELBW preterm one-year-old infants.

#### Oral conditions

One-year-old preterm VLBW and ELBW infants had a significantly fewer erupted primary teeth (mean=6.01) compared to full-term NBW infants (mean=6.62) ( $P=0.0333$ ). The presence of DDE (Fig. 4) had a significant association with prematurity and VLBW and ELBW. The prevalence of enamel hypoplasia was 20.6%, and the prevalence of opacities was 10.8% in one-year-old preterm VLBW and ELBW infants. The RR for enamel hypoplasia for preterm VLBW and ELBW infants was 5.9%. The hard palate deformations diagnosed visually during examination were more often present in preterm VLBW and

**Table 2.** Oral conditions in one-year old infants.

Variables n (%)	Preterm	Full-term	<i>P</i>	RR	95 % CI
Enamel hypoplasia*					
No	81 (79.4)	85 (97.7)	0.0006	5.8676	1.4272 – 24.1238
Yes	21 (20.6)	2 (2.3)			
Enamel hypomineralization*					
No	91 (89.2)	84 (96.6)	NS		
Yes	11 (10.8)	3 (3.4)			
N of erupted teeth: Mean ± SD***	6.01 ± 2.21	6.62 ± 2.59	0.0333		
Deformation of hard palate****					
No	90 (88.2)	87 (100.00)	0.0008	21.3592	1.2829 – 355.6263
Yes	12 (11.8)	0			
Oral pathology*					
No	99 (97.1)	82 (94.3)	NS		
Yes	3 (2.9)	5 (5.7)			

\* $\chi^2$  test, \*\*\*Mann-Whitney test, \*\*\*\*Pearson test  
n number, RR relative risk, SD standard deviation

ELBW infants ( $P=0.0008$ ), and the RR was calculated at 21.4 (Table 2).

## DISCUSSION

Enamel hypomineralization and hypoplasia, tooth crown dimension changes, notching of the alveolar ridge, palatal grooving, high arched palate, cross bite, palatal asymmetry and a delay in dental development and eruption are the most frequent pathological oral conditions in preterm children<sup>19,20</sup>.

Oral pathological lesions in neonates represent a wide range of findings, the majority of which are asymptomatic and benign and can resolve themselves without treatment<sup>21</sup>. In preterm VLBW and ELBW neonates, Epstein's pearls, congenital epulis and the presence of neonatal teeth were diagnosed. Epstein's pearls are nonodontogenic cysts; they are clinically asymptomatic and appear as nodules in the middle of the hard palate<sup>22</sup>. The presence of teeth in neonates is a rare condition in full-term infants and extremely rare in prematurely delivered infants<sup>23,24</sup>. In the present study, one preterm infant delivered with ELBW had an erupted lower incisor with hypermobility and inflammation of the surrounding gingiva. The tooth was extracted due to extreme mobility. Congenital epulis appears as a mass protruding through the oral cavity of a newborn child<sup>25,26</sup>. It arises from the alveolar mucosa and occurs more frequently in the maxilla, mainly in its frontal region, in the site of unerupted deciduous canines. Congenital epulis is usually a single lesion and consists of a smooth or tuberous ovoid mass connected by broad or narrow pediculum to the alveolar mucosa. The lesion has a pink or reddish color and varies in size from several millimeters to a few centimeters in diameter. An extremely large congenital epulis can cause complications even before birth. Obstruction of the infant's mouth might cause ineffective swallowing of amniotic fluid, resulting in poly-

hydramnios. The preterm neonate with congenital epulis was treated surgically, and the lesion was completely removed.

DDE in primary and permanent dentition are well-studied complications of prematurity. The exact etiology of DDE is not yet fully understood. The basic mechanism of DDE is the disturbed function of ameloblasts during different stages of amelogenesis. DDE are defined as alteration of dental enamel resulting from several disturbances during amelogenesis<sup>14</sup>. Enamel hypoplasia is a quantitative defect caused by incomplete deposition of immature enamel produced by ameloblasts during the secretory stage. Opacities or hypomineralization occur because of incomplete mineralization or maturation of the enamel<sup>27</sup>. Enamel defects could be genetic or environmentally caused by either local factors or systemic factors in the mother or child. DDE related to systemic factors have been thought to be associated with systemic diseases of VLBW and ELBW infants, such as nutritional problems, hypocalcemia<sup>28,29</sup>, neonatal infections and sepsis<sup>30</sup>, metabolic disorders, neonatal asphyxia<sup>28</sup> or respiratory distress syndrome<sup>31</sup>. Aminabadi NA et al.<sup>32</sup> found that decreased Apgar values were connected with the presence of DDE in primary dentition and concluded that the Apgar value can be used for the risk assessment of DDE in primary dentition. Many chemicals and drugs have the potential to damage ameloblasts and cause DDE (ref.<sup>33</sup>). Levels of fluorides greater than 1 ppm in the water, tetracycline and, more recently, amoxicillin have been implicated as a cause of DDE (ref.<sup>34</sup>). All preterm VLBW and ELBW infants in the present study received ampicillin during the neonatal period. In the case of antibiotics, it is difficult to distinguish the effect of fever and infection and the influence of amoxicillin on ameloblasts during enamel development. Local traumatic factors, such as laryngoscopy and endotracheal intubation, applied during the neonatal period may contribute to the occurrence of DDE in primary anterior teeth. In newborns, access to the

trachea may be more difficult than in adults because of anatomic variations of the tongue, larynx and epiglottis. Orotracheal intubation trauma to oral tissue occurs during elevation of the laryngoscope blade to move back the tongue and expose the pharyngeal region. The pressure on the alveolar ridge can affect the primary teeth that are in the developmental phase of crown<sup>35</sup>. DDE arising from local causes tend to affect only single teeth or groups of teeth. The distribution of enamel defects within the dentition is usually localized to the anterior region of the maxillary teeth. Reports of DDE in preterm infants described in the literature were frequently connected with orotracheal intubation; however, Seow et al.<sup>6</sup> suggested that laryngoscopy, rather than the endotracheal tube itself, may be a more significant cause of DDE. In a study conducted by Seow et al.<sup>6</sup> 85% of intubated infants had DDE of maxillary anterior teeth compared to 21.7% of nonintubated infants. Previous studies have indicated a high prevalence of DDE in preterm infants ranging from 20% to 96%. In the current study, the prevalence of enamel hypoplasia was 20.6%, and enamel hypomineralization was 10.8%. Enamel hypoplasia with porous and rough surfaces, combined with feeding problems, frequent intake of sugars, behavioral disorders and other risk factors, can predispose preterm children to dental caries<sup>36</sup>.

The timing of primary tooth eruption in premature infants has not been well established. Some authors<sup>37,38</sup> have suggested that eruption of the first teeth is delayed in preterm infants. Viscardi et al.<sup>39</sup> noted that primary tooth eruption occurred significantly later in infants with birth-weight < 1000 g and gestational age ≤ 30 weeks. These authors have suggested that factors related to the severity of neonatal illness and postnatal nutrition as well as the degree of prematurity affect the timing of primary teeth eruption. Seow et al.<sup>40</sup> demonstrated that preterm VLBW infants have fewer teeth erupted compared to full-term NBW infants who were examined at the chronological age of 6 to 17 months. However, after 17 months of age, this difference was no longer evident, probably as a result of catch-up growth of the orofacial region. Seow et al.<sup>40</sup> recommended using corrected age for the comparison of primary teeth eruption in preterm and full-term infants because preterm infants are not fully mature at the time of birth; therefore, the chronological age of preterm infants does not correspond to their actual biological age. In the present study, the corrected age was used to achieve a meaningful comparison with full-term infants. A significantly lower number of erupted primary incisors was established in preterm VLBW and ELBW infants with the corrected age of one year than in full-term NBW infants of chronological age one year in the current study.

Multiple factors can influence abnormal hard palate formation<sup>5</sup>. The narrow elongated head of preterm infants may cause a narrow high vaulted palate. The endotracheal tube may press on the midline palate and alveolar ridge, disturbing its growth. Pressure applied to the endotracheal tube to keep it properly positioned may further affect the developing palate. Infants suckling their endotracheal tubes may also result in some molding of the tissues.

According to Cortines and Costa<sup>41</sup>, the palatal groove occurs transiently in approximately one quarter of pre-term infants. The palatal groove especially affects infants who have undergone a long stay in a neonatal intensive care unit, been intubated or used an orogastric tube. The incidence of palatal deformation increased with a longer use of tubes; the incidence was 87.5% in those neonates and infants requiring tubes for more than two weeks<sup>16</sup>. In the present study, the shape of the hard palate was visually evaluated during clinical examination, revealing a significant difference between the premature VLBW and ELBW groups and the full-term NBW group.

The authors of the present study are aware of certain limitations. A convenience sample of infants was used, in which significant differences may be due to the lack of statistical power of the sample, and only descriptive statistical analysis was used. Finally, it is worth noting that hereditary and individual factors associated with external factors, such as nutrition, pregnancy outcomes and maternal illnesses, can cause differences in the oral condition of infants.

## CONCLUSION

This study confirmed anamnestic and medical differences between one-year-old preterm VLBW and ELBW infants and full-term NBW infants. Preterm birth of neonates with VLBW and ELBW is the risk factor of enamel hypoplasia, delayed primary teeth eruption and abnormal hard palate formation.

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**Author contributions:** VM, RKI: contributed to the design of the study, oral examinations of all infants and interpretation of results; JD: performed the clinical examination of both groups of infants; VM, RKI, LH, ZB: analyzed the obtained data. All authors contributed to the preparation of the manuscript and approval of the final version.

**Conflict of interest statement:** The authors state that there is no conflict of interest regarding the publication of this article.

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