Radiographic Study of the Prevalence and Distribution of Hypodontia Associated with Unilateral and Bilateral Clef Lip and Palate in a Hungarian Population

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Background:
Cleft defects are one of the most frequent birth-deformities of the orofacial region and they are commonly associated with anomalies of the tooth structure, size, shape, formation, eruption, and tooth number. The aim of our study was to evaluate the prevalence, distribution, and potential association of combined hypodontia in cleft-affected patients with regard to all types of teeth in both jaws in the permanent dentition.

Material/Methods:
This retrospective radiographic analysis included patients with various types of clefts treated orthodontically in the Department of Orofacial Orthopedics and Orthodontics at Heim Pál Children's Hospital, Budapest. There were 150 patients (84 males, 66 females) with non-syndromic unilateral (UCLP; n=120 patients) or bilateral (BCLP; n=30 patients) cleft formation (lip, alveolus and palate) who met the inclusion criteria. Statistical analysis was performed using the chi-square test and Fisher's exact test (significance level p<0.05).

Results:
Hypodontia was significantly more frequent in patients with cleft-sided lateral incisor (104 patients, 69%), with a total of 235 missing teeth, followed by the second premolars of the upper and lower jaw. A significant correlation of congenital missing teeth was observed in left-sided clefts between the upper and lower second premolar in the cleft area.

Conclusions:
Hypodontia inside and outside the cleft area was frequently observed. This should affect the therapy plans, especially if the cleft-sided premolar is also absent. Further comprehensive research including numerous random samples is necessary for better estimating other possible associations.

MeSH Keywords: Anodontia • Cleft Lip • Cleft Palate • Orthodontics

Full-text PDF: http://www.medscimonit.com/abstract/index/idArt/897957
Background

Orofacial clefts are among the most frequent of all human congenital deformities [1–10] and in many cases are of non-syndromic appearance [10]. They are considered to have a multifactorial etiology, including genetic and environmental factors interacting with each other [3,7,10–12] and determining the probability of developing such an anomaly [13].


The highest incidence was reported in American Indians [25,26], with 3.6:1000 births [19], followed by Asians, Syrians, and blacks. With the lowest incidence [4,27,28] (0.3:1000 births) [19]. In central Europe and for white populations, the incidence is reported to be approximately 1:500 births [4].

Orofacial clefts are caused by disturbed embryonic development [5] in the area of the secondary definitive oral cavity and, according to the type of cleft, can be caused by an insufficient mesenchyme proliferation between the medial-nasal and maxillary prominences and/or a failure or insufficient fusion of the palatal shelves [1,12], so that the oral and nasal cavities are not separated from each other. Isolated cleft lips, as well as cleft lips and alveolus, have their origin during the 5th to 9th weeks of gestation [14] and can appear totally or partially on one or both sides (unilateral or bilateral) [12,29,30], whereas the development of the secondary palate takes place during the 8th to 12th weeks of gestation [8], and a missing fusion of the palatal processes [12] is always found to be median. A combination of both these deformities is called cleft lip and palate. According to this, 2 big embryogenetically and morphologically distinct groups can be distinguished: the cleft lip and alveolus with and without cleft palates, as well as isolated cleft palates. Independent of the cleft type, there is a high intra-individual variation in severity and extent of cleft formation, depending on the anatomical structures involved [3].

Hypodontia, which is defined as the congenital absence of 1 or more primary or permanent teeth [31,32], is the most frequently reported dental anomaly in cleft patients [33–42], and is associated with all types of clefts [36,43–45]. Although in the general population hypodontia is highly prevalent [46,47] and is the most common developmental dental anomaly reported in humans [1,31,32,48–55], it affects approximately 20% of the population worldwide [31]. Several studies have reported an increased incidence of hypodontia in patients with clefts [36,41,56–64], being up to 7 times more frequent [62].

In the general population the prevalence of congenitally missing teeth (except third molars) varies from 0.027% [65] to 11.3% [48], with most study results ranging between 2% and 7% [47,49,66–68]. A recent review about tooth agenesis in the normal population reported a prevalence of 0.15–16.2% missing teeth in the permanent dentition, third molars excluded [46]. Studies about cleft patients have shown that the prevalence was much higher, reaching totals from 29.5% to 77% [40,42].

Hypodontia can be found in the primary as well as the permanent dentition and is observed outside the cleft region as well as within it [45]. Usually, the frequency of missing teeth is considerably higher in the permanent dentition [36,41], whereas the values are reported to be highest in the cleft region [41]. Due to the cleft defect, in various types of clefts, the permanent upper lateral incisor on the cleft side is the tooth most commonly missing [33,36,37,39–42,56,60,61,69–80]. The frequency of missing upper lateral incisors in cleft patients ranges between 39% and 60% [33,70,80], but higher values are also reported (56.1–81.3%) [34,42,56,81,82]. For example, in a Japanese group of patients with clefts, 56.9% absence of upper lateral incisors was reported [82], in contrast with 74% in a group in the USA [42]. For UCLP and BCLP patients, frequencies of 27.9–61.2% [70,83,84] and 45–60% [39,41,70,82,83,85] can be found in the literature. In healthy populations, the lateral maxillary incisor is missing at considerably lower frequencies of 0.6–5.2% [32,86–94].

An increase in hypodontia outside the cleft region was also observed, and the most prevalent missing tooth was the second premolar, absent in 22.2–50.8% of such patients [36,60,76,81,95,96]. In contrast, the mandibular second premolar was missing in 0.4–18.7% [60,76,93–95].

In the permanent dentition, both jaws can be affected [60], 35 but missing teeth are generally more frequent in the upper arch [36,60,63,64,97] as well as in the cleft area (3-fold higher) [36,42,63] compared to the non-cleft side [33]. This phenomenon can be found for the lateral incisor [81,85] and the second premolar [56,83,85]. However, some studies could not find any [98] or only irrelevant differences between the frequencies of hypodontia in the 2 arches [58]. Further, in the lower jaw, no clear differences between the cleft and non-cleft side could be found [80]. By contrast, Shapira et al. found a cleft side predominance for missing lateral incisors and second premolars in the maxillary and mandibular arch [42]. However, there is a positive correlation between hypodontia and severity of the cleft, with an increasing frequency of missing teeth as the severity of the cleft increases, resulting in more missing teeth in UCLP and BCLP patients with more teeth missing both in side and outside the cleft area [1,2,33,36,56,60,85,99–101]. For example, in UCLP patients the second upper premolar was...
missing in 11.8–52.6% [2,33,60,81,85,86,95,97], and in BCLP patients values of 21.6–68.4% [2,60,97,102] have been reported. Hypodontia has direct clinical implications, with increasing importance as the number of missing teeth increases, particularly if several teeth of different dental groups are absent in the same quadrant [68], and at the same time in the contralateral jaw on the same side the tooth bud is present (Figures 1–3).

According to patterns of missing teeth in cleft patients, it was suggested that the absence of several teeth was interdependent, but it is not known how many affected patients lack these teeth simultaneously [99] and possible associations of missing teeth in cleft patients have rarely been reported in the literature [36,57,64]. So far, only a few studies [33,42,63,99] have focussed on the correlation of missing teeth in and outside the cleft area, regarding associations of specific tooth types, sidedness, and laterality in the upper and lower jaw.

To allow farsighted treatment planning, the number and distribution of missing teeth is of particular importance in estimating the need for orthodontic treatment [89], which is usual considerably higher in patients with dental agenesis [103,104] and in cleft-affected patients.

The aim of our study was to evaluate the prevalence and distribution of hypodontia inside and outside the cleft area (wisdom teeth excluded) associated with non-syndromic unilateral and bilateral cleft lip and palate patients in an orthodontically-treated Hungarian population, with the help of a radiographic analysis, as well as the evaluation of a potential associations in congenital missing tooth patterns in terms of tooth type, cleft type, sidedness, and laterality in the upper and lower jaw.

Material and Methods

Data for the present study were obtained from records of the pool of cleft patients, which had been treated in the Department of Orofacial Orthopedics and Orthodontics, Heim Pál Children’s Hospital, Budapest, Hungary. The study was approved by the Ethics Review Committee, TU Dresden, Germany (no. EK 442122014).

The evaluated patients were racially and ethnically similar, consisting of 183 white cleft subjects. Male and female cleft patients with unilateral or bilateral cleft formation (lip, alveolus, and palate) without additional diseases, with a minimum of 1 existing panoramic x-ray of a good quality, as well as a sufficient documentation, were included in the study. Subjects with other known syndromes, unique or atypical types of cleft, isolated cleft lip, isolated cleft palate, no or fuzzy panoramic x-ray, patients with previous extractions of permanent teeth, and those with insufficient documentation where excluded from the study.
Data of cleft location and type, sex, and age at the time the x-ray had been performed and other general information were evaluated from the medical and dental history. Due to the completion of crown calcification and in order to make sure calcification has reached a detectable minimum [46], according to studies of Beak et al. [80], Moorrees et al. [105], Kim et al. [84], and Bozga et al. [47], patients younger than 6 years of age at the time of the radiograph were also excluded from the study. Detailed information about the inclusion and exclusion criteria of the study is shown in Table 1. From 183 files initially analyzed, after first inspection of the documentation, 155 subjects met the inclusion criteria. Panoramic radiographs

Figure 2. Same patient as in Figure 1 at the age of 9 years 2 months.

Figure 3. Same patient as in Figure 1 and 2 at the age of 12 years 6 months during orthodontic treatment (problematic situation of the space distribution due to multiple tooth agenesis). Development of the wisdom teeth is not to be expected.
were analyzed for hypodontia of permanent teeth in and outside the cleft area, in the upper and lower jaw, and the type of teeth affected. Due to high variation in the age of the patients, unclear prognosis of the bud development in case of early examination [99,106], and possible late dental development among cleft patients [38,58,60,67], third molars were not considered in this study. Only 1 panoramic radiograph of each patient was finally used for evaluation.

All records were evaluated by a single experienced and trained observer in order to eliminate inter-examiner differences due to personal interpretations. A second observer was consulted only in cases of unclear outcomes. Potential divergences between the observers were discussed. Because this was a retrospective evaluation, if no agreement could be reached and doubts persisted, the subject was excluded from the study.

All analysis was performed on a digital screen in a dark room with the ability to enlarge relevant details for better examination. The diagnosis of hypodontia at the cleft region was performed according to Tereza et al. [34] and da Silva et al. [73]. Hypodontia was considered when the tooth bud was not radiographically detectable and any differentially calcified tissue in the area of the corresponding tooth was missing [33]. The development of the permanent dentition, and, if it was possible, the development of the tooth bud of the ipsilateral or contralateral side, served as orientation [107]. For the upper lateral incisor, any radiographic sign of mineralization of the tooth bud on the mesial or distal side of the cleft occurred without regard to tooth morphology, provided the lateral incisor was present. Hypodontia was noted if no permanent teeth were found between the central incisor and the canine in the vicinity of the cleft, either on the mesial or distal side. Even if a distal location of the permanent lateral incisor is more frequent, these criteria were chosen because the tooth bud can develop either at the mesial or distal side of the cleft [13,41,82,85,107]. Missing teeth were recorded using the FDI index of tooth numbering and were directly plotted into Excel worksheets.

Five records had to be excluded later due to the low quality of the radiograph, an overlap with orthodontic appliances, or inclusion criteria

Exclusion criteria

- Unilateral or bilateral cleft lip and palate
- Isolated cleft lip, isolated cleft palate, isolated cleft lip and alveolus
- Unique, atypical type of cleft
- No additional inherent diseases (syndroms)
- Syndromic cleft
- At least one panoramic x-ray in a good quality
- No or fuzzy panoramic x-ray
- Sufficient documentation
- Insufficient documentation
- Age older than 6 years at the time the radiograph was given
- Age below 6 years at the time the radiograph was given

Table 1. Overview of the inclusion and exclusion criteria of the study sample.

- Total number of cleft patients: 183
- Cleft patients meeting the inclusion criteria: 155
- Excluded due to CP (cleft palate and CL (cleft lip) only: 5
- Excluded due to age below 6 years at the time the radiograph was given: 8
- Excluded due to unclear, atypical type of cleft or syndromic cleft: 15
- Cleft patients evaluated: 150
- Excluded due to lack of potential interpretation (low quality, unclear status): 5

Figure 4. Flow-chart of the evaluation process of the study sample.
unclear status, in which hypodontia could not be adequately recognized. Finally, a sample of 150 subjects with complete UCLP and BCLP aged 6 years 4 months to 22 years 8 months were selected for inclusion in the study. Figure 4 gives an overview of the evaluation process.

Statistical analysis

A descriptive analysis using counts and percentages was performed to characterize prevalence of cleft formation, distribution, and tooth hypodontia. The rates of occurrence of hypodontia were calculated as a percentage of the total sample and of each cleft type.

Statistical analysis to verify differences in the incidence rate of cleft type, distribution, and associations between the presence and type of hypodontia and cleft type was performed using the chi-square test or Fisher’s exact test (R version 3.2.2, The R Foundation for Statistical Computing, Vienna, Austria, www.R-project.org). A p-value below 0.05 was deemed statistically significant, but only in a descriptive sense, because we did not correct for multiple testing.

Results

Distribution of study sample

The study sample consisted of n=150 white non-syndromic cleft patients, mean age 13 years 1 month, with the youngest patient 6 years 4 months and the oldest patient 22 years 8 months of age at the date of the radiological record; there were 84 males and 66 females. Thirty patients (20%) had bilateral cleft lip and palate (BCLP) and 120 (80%) had unilateral cleft lip and palate (UCLP), of which 46 (30.67%) had a cleft on the right side and 74 (49.33%) had a left-sided cleft (Table 2). In our sample the distribution of cleft types was significantly different for the 3 types (p<0.001), with bilateral clefts occurring least frequently and left-sided UCLP most frequently. A significant difference between sexes was not observed, but a general tendency of increased cleft incidence in males was found (p=0.14). Left-sided clefts occurred more frequently in males than right-sided ones, causing most of the inhomogeneity.

Incidence of hypodontia in the different cleft types

Out of the 150 patients studied, 104 patients (69%) presented with hypodontia of at least 1 missing permanent tooth, indicating an overall high susceptibility for missing teeth in cleft patients (p=0.0000022). Thirty-six patients presented with 1

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<th>Table 2. Distribution of UCLP and BCLP subjects by cleft type and gender (counts and percentages).</th>
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<tr>
<td>Male</td>
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<th>Table 3. Distribution of number and percentage of congenitally missing teeth according to cleft type and gender.</th>
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<td>Total Male</td>
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Number of teeth missing

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<th>UCLP (left)</th>
<th>BCLP</th>
<th>Total</th>
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<tr>
<td>Male</td>
<td>25 (54.35%)</td>
<td>43 (58.11%)</td>
<td>16 (53.33%)</td>
<td>84 (56.0%)</td>
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<tr>
<td>Female</td>
<td>21 (45.65%)</td>
<td>31 (41.89%)</td>
<td>14 (46.67%)</td>
<td>66 (44.0%)</td>
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missing tooth (34.62%), 35 with 2 missing teeth (33.65%), 17 with 3 missing teeth (16.35%), 6 with 4 or 5 teeth missing (5.77%), and 4 with no hypodontia detected (31%).

**Severity of hypodontia in the different cleft types**

Hypodontia was significantly (p=0.007) more frequent in BCLP patients (90%) than in UCLP patients (64.2%), but there was no significant difference between left-sided (66.2%) and right-sided clefts (60.87%) (p=0.098) (Table 3).

In a descriptive analysis of the data, concerning severity of hypodontia, the most frequently affected group was the left-sided UCLP group with most teeth missing (112; 47.66%), followed by BCLP patients (70 teeth missing; 29.79%), and right-sided clefts (60.87%) (p=0.098) (Table 3).

30 missing tooth (34.62%), 35 with 2 missing teeth (33.65%), 17 with 3 missing teeth (16.35%), 6 with 4 or 5 teeth missing (5.77%), and 4 with no hypodontia detected (31%).

**Distribution of hypodontia in the upper and lower jaw**

Tooth agenesis more occurred frequently in the maxilla (172 missing teeth) compared to the mandible (63 missing teeth), and lateral incisors and second premolars constituted most of the missing teeth. Absence of individual teeth differed significantly (p<0.001) for maxilla and mandible, with lateral incisors most frequently absent in the upper jaw and second premolars in the lower jaw (Figure 6).

**Correlation of hypodontia in the upper and lower jaw to sex**

We found no correlation of tooth agenesis with sex in the upper (p=0.9772) or lower jaw (p=0.7604).

**Correlation of hypodontia in the upper and lower jaw with different cleft types**

In the upper jaw, the occurrence of agenesis of individual teeth was significantly associated with cleft type (p=0.005645). In the upper jaw, the lateral incisors were most commonly missing. The side on which they were missing was highly correlated with the cleft side (p<0.001) with agenesis and cleft on the
same side. In contrast, the most frequently missing teeth in the lower jaw were the second premolars, but no correlation with cleft laterality was found (Figure 5). Differences were noticeable between left-sided (UCLP) and bilateral clefts (BCLP) (p=0.0221), but there were no clear differences between left-sided and right-sided clefts (p=0.368). Most missing upper lateral incisors were in the cleft area of left-sided UCLP patients (Figure 5).

Correlation of hypodontia of the lateral incisor and second premolar of the same quadrant

No significant correlation of the absence of the most common congenitally missing teeth, being the lateral incisor and second premolar, was observed for the whole group or for the single quadrants (whole group: p=0.4076; Q1: p=0.4043; Q2, Q3, Q4: p=1). No correlation of combined hypodontia of the lateral incisor and second premolar was found in the upper (p=0.4708) or the lower jaw (p=1).

Correlation of hypodontia of the lateral incisor and second premolar of the same side

A combined congenital absence of the upper lateral incisor and the upper second premolar in the same quadrant in correlation with the different single-cleft groups (right-sided UCLP, left-sided UCLP, and BCLP) could not be found for the first quadrant (12–15 congenitally missing in combination) or for the second quadrant (22–25 congenitally missing in combination). In the lower jaw, we also found no such correlation in the third and fourth quadrant (Table 4).

Correlation of hypodontia of the lateral incisor and second premolar in the counterjaw

Concerning sidedness and laterality, a correlation of the occurrence of a congenitally missing maxillary lateral incisor and second premolar in the counter jaw was not detected for the left or right side in all single-cleft groups or for the whole study sample (Table 4).

Correlation of hypodontia of the second premolars on the same side

We found a positive correlation for missing second premolars in the upper and lower jaw on the left side in left-sided UCLP patients (p=0.03613), as well as for right-sided UCLP patients (p=0.1275) and the whole study sample (p=0.05124) for the left side, but not for BCLP patients (p=0.5476) (Table 4). However, we found no correlation of congenitally missing second premolars in the upper and lower jaw on the right side (Table 4).
Discussion

Knowledge of tooth agenesis is fundamental for treatment planning, because such anomalies may lead to edentulous spaces that must be closed by orthodontic tooth movement, prostheses, or implants [71]. Knowledge of hypodontia can already provide valuable and important information to professionals working in the rehabilitation of patients with cleft malformations at an early age, in order to provide parents with information about inherent characteristics of these conditions [70].

Until recently, few studies have considered tooth agenesis in and outside the cleft region under inclusion of the complete dental description concerning laterality, sidedness, and possible associations of congenitally missing teeth in the relevant quadrants of the mouth.

In our study, we evaluated the prevalence of hypodontia in UCLP and BCLP patients regarding the complete dentition and any associations of these teeth missing in combination.

**Study sample and methods used**

Regarding the study sample, we only chose non-syndromic cleft patients with complete unilateral and bilateral cleft formation of lip alveolus and palate, because tooth agenesis increases with the severity of the cleft [36,43,56,60,99–101,108] and these patients were proved to be more affected by this divergence than any other group with cleft formation [34,56,58,97]. Furthermore, among cleft malformations, the cleft lip and palate had the highest susceptibility [109,110] and tooth agenesis was also increased outside the cleft area [59]. Syndromic clefts were excluded from our study due to the high likelihood of associations with other birth defects [110], often making a radiographic diagnosis and orthodontic treatment impossible.

Because our study was a retrospective analysis of panoramic radiographs of a pool of cleft patients at the Department of Orofacial Orthopedics and Orthodontics, Heim Pál Children’s Hospital, Budapest, Hungary, a large range of ages and different stages of dental development was present. Dental radiographs were routinely performed on all children predicted for orthodontic treatment for diagnostic purpose. On the basis of divergences in the development of the dentition, which is highly prevalent in cleft patients [1,70,71,97,111], in some cases radiographs had already been performed at an early age [80]. Since tooth formation is dependent on age [99], and because uncalkified tooth germs could not be visualized in patients [48], agenesis of specific teeth could not be radiographically diagnosed before the patient has reached a certain age [99] and a certain level of calcification was evident [112]. Therefore, inclusion of individuals who are too young might enter insufficient calcified tooth buds into the study sample, which could lead to misinterpretation [89,112].

Crown calcification of the laterals starts at the mean age of 10–12 months after birth [84], for the first premolars 1.8 year, of the second premolar on average 3–3.5 years after birth [105] and is generally completed at the age of 4–5 years [84], 5.2 years, and 6.2 years, respectively [105]. The mineralization of the second premolars can take place even later [113,114], and starts mostly later in the mandibular compared to the maxillary arch [48], so divergences may be a greater concern for these teeth [54,89,115]. Calcification of the third molar begins at an average age of 9.5 years and is initiated at 7.5 years in very few people [106,116]. To confidently exclude third-molar agenesis, according to Hermus et al. [99], an OPT by the age of 14.9 years is required. This could not be guaranteed for the whole random sample; therefore, wisdom teeth were excluded from our study.
Delay in tooth formation and a slower rate of mineralization is a common clinical condition reported in individuals with all types of clefts [58,60]. A delay of 0.3 years and 0.5 years \([67,117-119]\) up to 0.7 \([118]\), 0.9 \([58]\) and 1.1 years \([118]\) was reported in the literature and it similarly affected all permanent teeth, not merely specific tooth types or a specific jaw \([58,60,67]\). It tended to be more evident with the increase of the severity of the cleft and might be still more severe in children with hypodontia \([60,67,118,120]\). Threefold higher risk of asymmetric development of permanent teeth in both jaws, with a significant delay on the cleft side, was more common in these children \([60,69,121]\). The permanent lateral incisor was most commonly affected and for the premolars, a delayed development of contralateral teeth has been reported more frequently in the maxilla than in the mandible \([120]\).

Mooreess et al. provided a standard for the formation of 10 permanent teeth. They determined that when the crown was halfway to completeness, it could definitely be detected on the OPT \([105]\). Complete tooth crown calcification is not necessary for tooth bud detection and according to Beak et al. \([80]\) and Bozga et al. \([47]\) it could be assumed that at the age of 6 years it is possible to determine the presence or absence of all permanent teeth (third molars excluded), even when the delay of tooth development was added to the standards for the sample \([99]\). Therefore, we included only those patients in our study who were older than 6 years of age. Additionally, a right-left comparison, particularly for the second premolar, should help indicate possible hypodontia.

**Distribution of cleft patients**

From the 150 cleft patients included in our study, 84 were males and 66 females. UCLP presented with a higher frequency \((80\%)\) compared to BCLP \((30\%)\) and was more frequent on the left side. Boys were more commonly affected, but a statistically significant difference in sex distribution was not found. In the literature, boys are also reported to be predominantly affected by cleft lip and palate \([5,7,12,17,122-125]\) with a male: female ratio of 2:1 \([19]\) occurring twice as frequently on the left side \([5,11]\). Although the ratio that we could found was not as high as that in the literature, a comparable distribution was also found in our study sample. The composition of the cleft sample with UCLP being more prevalent, and being more frequent on the left side, is in accordance with most reports \([2,35,70,97,126]\).

**Tooth agenesis frequency and pattern and number of missing teeth**

The highest incidence of missing teeth is usually found in CLP patients \([34,58]\) and is generally much higher compared to the healthy population \([2]\). It largely depends on the methodology used and the cleft sample studied, so a large range of values for missing teeth in cleft patients can be found. Jamilian et al., for instance, evaluated the prevalence of hypodontia in 201 children with various types of clefts in an Iranian population and found 129 subjects \((64.1\%)\) presenting with hypodontia \([1]\). Al Jamal et al. investigated the prevalence of dental anomalies in a group of 78 Jordanian CLP subjects by a retrospective review of panoramic radiographs and found a 66.7\% prevalence of missing teeth \([71]\). Aizenbud et al. evaluated the prevalence of congenital missing teeth in and outside the cleft area in Israeli children \((n=179\) patients) with various types of clefts (CL, CLA, CP, and CLP) and reported a hypodontia frequency of 67.6\% with a total of 246 missing teeth \([56]\). Tereza et al. radiographically analyzed the prevalence of tooth anomalies by number and position in the permanent dentition of 205 BCLP individuals aged 7 to 18 years, and found 140 patients \((70.2\%)\) with hypodontia, most frequently the maxillary lateral incisor \([34]\). Lower values of 29.5\%, 31.6\%, 43.4\%, and 42.3\% in UCLP subjects have also been reported \([36,40,73,97]\). A few studies have demonstrated an even higher prevalence of missing tooth buds – 75\% \([45]\) and 77\% \([42]\) – in mixed cleft samples.

In our study, 69\% of patients presented with hypodontia of at least 1 missing tooth, which is in line with most of the above-mentioned studies and in nearly perfectly agreement with the study of Halperrn et al., who evaluated the location and presence of permanent teeth in 38 non-syndromic BCLP patients in and outside the cleft area, and also reported that 68.4\% of patients presented with hypodontia of at least 1 missing tooth \([107]\). Furthermore, 9 patients \((23.7\%)\) were missing only 1 tooth, 10 patients \((26.3\%)\) were missing 2 teeth, 3 patients \((7.9\%)\) were missing 3 teeth, and 4 patients \((10.5\%)\) were missing 4 teeth \([107]\), whereas 1–8 absent teeth were found in a mixed study sample consisting of CL, CP, and CLP subjects \([99]\).

The total number of missing teeth in our study was 235 and ranged between 1 and 6 teeth missing simultaneously. Out of the 104 patients with hypodontia, 6 patients had 4 and 5 missing teeth, respectively \((5.77\%)\), 17 patients had 3 missing teeth \((16.35\%)\), and only 4 patients had 6 missing teeth \((3.85\%)\). The most frequently found divergence, presented by 34.62\% \((36\) patients) and 33.65\% \((35\) patients), was for 1 or 2 missing teeth, respectively. We found few patients with severe hypodontia. Bartzel et al. examined serial panoramic radiographs of non-syndromic BCLP patients from 3 CLP centers in Norway, The Netherlands, and Sweden to measure tooth agenesis, reporting 59.8\% of subjects with at least 1 missing tooth and a range of 1–11 missing teeth \([57]\). They found that 3.8\% of subjects \((9\) persons) had 6 and more missing teeth \([57]\), which was in agreement with our finding of 650 missing teeth. However, we did not find any individuals with more than 6 missing teeth.
1 Severity of hypodontia in the different cleft types

The most frequently affected group with at least 1 missing tooth were the BCLP patients. UCLP patients with left-sided cleft had a higher incidence of missing teeth than UCLP patients with right-sided cleft. In contrast, more teeth were missing in UCLP patients with left-sided cleft, followed by BCLP patients and UCLP patients with right-sided cleft.

The higher incidence for hypodontia in BCLP patients can be explained by the cleft defect, since it is well known that the prevalence of hypodontia strongly increases in proportion to the severity of the cleft [36,56,60,85,99,101]. Aizenbud et al. evaluated the prevalence of congenitally missing teeth in Israeli children with various types of clefts, including CL, CLA, CP, and CLP, and found that CLP was the most frequently affected group. Hypodontia (wisdom teeth excluded) was most frequently found in bilateral total clefts (52.6%) compared to unilateral total clefts (49.1%) [56,97], indicating the above-mentioned association and our results described above.

A higher incidence of hypodontia in left-sided UCLP was also reported by Bartzela et al., who investigated tooth agenesis prevalence and pattern in UCLP subjects in the upper and lower jaw [33]. Right-sided clefts were far less likely to have missing teeth, whereas the prevalence of tooth agenesis was considerably higher on the cleft side [33]. This might possibly be because left-sided UCLP are more frequent [2,35,70,97,126], but there are not any explanations for this in the literature.

We found that left-sided UCLP patients had more missing teeth compared to BCLP patients. In UCLP subjects, 46 teeth (30.67%) were missing on the right side and 74 teeth (49.33%) on the left side, compared to BCLP with a total of 35 missing teeth (20%).

This is in contrast with most other reports, indicating that not only the prevalence, but also the number of missing teeth, is strongly correlated with the severity of the cleft defect, with a greater number of teeth missing as the severity of the cleft increases [37,43,44,62,64,81,99,102,108,118,127–130]. If one considers the cleft region of the upper arch exclusively, this might possibly be true, as a higher frequency of missing teeth is usually found in the upper arch [36,42,60,63,97,107,120].

Stahl et al. found a higher rate of missing teeth in left-sided UCLP, with 41 teeth missing on the cleft and 10 teeth missing on the non-cleft side, compared to right-sided clefts with 14 teeth missing in the cleft region and 8 outside the cleft area. The incidence of missing teeth in BCLP outside the cleft region was even higher (62.2%) compared to UCLP subjects (46.6%) [97], but only the upper arch was considered.

To the best of our knowledge, there has been no previous direct comparative study of the prevalence of hypodontia in UCLP and BCLP patients in and outside the cleft area for both arches, with differentiation between right and left side and number of teeth missing in the respective cleft samples. Most of the available studies considered only the upper arch, mixed cleft sample, only 1 cleft type (UCLP versus BCLP), or missing teeth exclusively in or outside the cleft area; therefore, no clear comparison with our results is possible. However, incidences for the single-cleft groups in the different investigations indicate a different distribution of missing teeth in UCLP and BCLP patients.

In our study, the teeth most commonly missing were the upper lateral incisors and both upper and lower second premolars, and these were usually the teeth most commonly affected in all CLP subtypes, with the highest prevalence in the upper lateral incisor in the cleft region [2,37,70,85,97,131]. In UCLP subjects, frequencies of missing upper lateral incisors of 27.9–61.2% [70,83,84] and in BCLP subjects frequencies of 45–60% [39,41,70,82,83,85] were reported and were more frequently absent on both sides in bilateral clefts [82]. Similar findings were confirmed in our study. Outside the cleft region, the second premolars were also highly prevalent and are known to be frequently congenital absent in both the upper and lower jaws [2]. In cleft patients, the second upper premolars are more commonly affected, with a lack of 22.2–50.8% [36,60,76,81,95,96]. In UCLP patients the second premolars are also frequently missing in the lower arch [33].

Mikulewicz et al. evaluated the prevalence of tooth agenesis outside the cleft area in special second premolars in patients with cleft lip and/or palate [2]; 19.3% of all patients examined had hypodontia in the premolar region. A gradual increase in the frequency of hypodontia was found, and the severity of the cleft with hypodontia in the premolar region was highest in the BCLP group (21.6%) compared to 15.8% of UCLP and 11.7% of CLA affected. The number of congenital missing second premolars was higher in the maxillary (8.7%) compared to the mandibular arch (5.7%). The frequency of missing premolars between UCLP and BCLP was the similar (6.9% and 6.8%, respectively), but in BCLP more teeth were absent in the upper jaw (10.8%) compared to the lower jaw (2.7%) and compared to the UCLP sample, in which the lower jaw was as frequently affected as the upper jaw (6.2% and 7.5% of premolars missing, respectively).
1. Lai et al. reported a comparable incidence for missing upper lateral incisors in the cleft region in UCLP and BCLP subjects (19.2% and 20.5%, respectively) [69]; however, they did not compare left vs. right side in UCLP patients.

5. The differences between the cleft types that we found might be explained by hypodontia outside the cleft region. Considering the complete dentition, this might to explain the higher values for missing teeth in left-sided UCLP in our study, which were consequently higher than those for BCLP patients. In contrast, we found more missing teeth in patients with left-sided UCLP, and this could be correlated with missing teeth in the lower jaw, especially the second premolars.

10. Distribution of hypodontia in the upper and lower jaw

In the permanent dentition of cleft patients, both jaws are generally affected [60], and in contrast to the healthy population in which tooth agenesis in the maxilla is comparable to that of the mandible [89], more teeth are congenitally missing in the upper than in the lower jaw [36,42,60,63,97,99,107], where tooth agenesis is very rare [99].

As mentioned above, the upper lateral incisor in the cleft region is usually most frequently affected [37,56,69–74]. Outside the cleft region, the incidence of congenially absent teeth was also much higher in the maxilla compared to the mandible [36,41,80,83,85]. Halpern et al. reported a prevalence of missing teeth outside the cleft region (with the great majority of missing teeth in the maxilla) of 11.9% for the second premolars and 10.5% for the central incisors, compared to 4% and 2.6% in the lower jaw, respectively [107].

Our investigation also found a higher frequency of missing teeth in the maxilla (172 teeth) compared to the mandible (63 teeth), and these data are in line with other studies [36,45,67,95,108,132]. When comparing agenesis in the maxilla and mandible, a difference was seen only for second premolars and lateral incisors, with agenesis for these teeth more common in the maxilla, which is in agreement with Bartze et al. [57]. However, some studies found a small difference in the frequency of hypodontia in both arches [58,98], particularly if the cleft region was not considered [76,97].

45. Correlation of hypodontia

In the healthy population, few studies have shown significant differences between the sexes [53,133], with a slight but non-significant increased prevalence of hypodontia in females [52,90,133–137]. Some studies have even reported that females were much more affected [46,66,89,138], with a prevalence 1.37 times higher than in males [2,89,139] and an inferential male-female ratio of 2.3 [61,89,134,139–143].

In both male and female subjects, no statistically significant differences were found between those who had hypodontia and those who did not [1,42,73] and this is evident for the cleft region [60] as well as outside it [13,60]. Da Silva et al. evaluated inter alia the prevalence of hypodontia in UCLP and BCLP patients to find a possible association between sex and cleft for hypodontia, but could not find any association [73]. Our results are in agreement with these findings. No correlation between tooth agenesis and sex was observed for the upper or for the lower jaw.

Correlation of hypodontia in the upper and lower jaw to the different cleft types

In our study, a correlation of hypodontia with the different cleft types between left-sided UCLP and BCLP patients was only observed in the upper arch, but we found no differences between the sexes between left-sided and right-sided UCLP patients. These results were obvious for the lateral incisor, most commonly missing on the cleft side, which was unilaterally missing in many UCLP patients and was more frequently bilaterally missing in BCLP patients.

These results correspond to most other reports, indicating the upper lateral incisor on the cleft side, is the most frequently congenitally absent tooth in cleft patients [33,36,37,39–42,56,60,61,69–76,78,80]. Furthermore, it was also reported that in BCLP subjects a bilateral absence of teeth and in UCLP patients a unilateral absence of teeth was more likely [1], which was also confirmed by our findings and was expected because differences in the upper arch can be explained by the cleft defect and hence by the cleft type. In BCLP subjects, Bartze et al. could not find a difference in the number of missing teeth between left and right side of the same jaw [57], indicating more frequent bilateral missing teeth in these patients.

In contrast, for the second premolars in the upper jaw, a left-right difference between UCLP and BCLP patients was not found in our study, but such a trend was recognizable. Some authors reported a cleft-sided predominance, not only for the lateral incisor, but also for the second premolar [36,42,63,67,83], but there are also some investigations which could not find any association between hypodontia and cleft type [35,73].

This might be lead back to a mixed cleft sample investigated in those studies or the fact that the whole dentition was considered, because in the lower jaw usually no association of missing teeth to the cleft side can be found and teeth are more commonly missing symmetrically [33,80,85,99], which corresponds to the distribution in the normal population [89] and also to our findings. In our investigation, no differences between hypodontia and cleft type in the lower arch could be detected.
1 Laterality, sidedness, and associations of hypodontia

Due to the growth deficiency in the maxillary arch [14,144] and divergences in the occlusion [13], which hinder the treatment, it is of great concern if more teeth are missing in the upper respectively the lower jaw and if a combination of missing teeth is to be expected symmetrically or asymmetrically or even simultaneously in the same quadrant.

10 Because of the frequent occurrence of hypodontia of the lateral incisors [56,70] and second premolars [109], it was of particular interest whether a correlation of these 2 differences was expected with a higher probability in the same quadrant.

15 Based on the reports of Pegelow et al. [13], it can be assumed that a combination of missing upper lateral incisors in the cleft region might be associated with teeth outside the cleft, mainly those which are already reported to be more frequently missing in cleft patients.

20 Pegelow et al. evaluated hypodontia in 129 white children with unilateral CL, CLA, and CLP and found a lack of permanent lateral incisors combined with hypodontia outside the cleft area in 37% of the patients. Inversely, 20 of 129 patients with hypodontia outside the cleft also had a lateral incisor missing in the cleft area [13]. Shapira et al. evaluated the prevalence of hypodontia of permanent teeth, excluding third molars, in and outside the cleft region of CL, CP, and CLP for a possible association between the side of the cleft and the side of the missing teeth. Hypodontia of both the maxillary lateral incisors and the second premolars was found more frequently on the left side [42]. Bartzela et al. evaluated the relationship between missing teeth in a relatively large sample size of 240 non-syndromic BCLP patients. Tooth agenesis pattern for the entire dentition were evaluated, included maxillary lateral incisors and second premolars, maxillary and mandibular central incisors, first premolars, and second molars. Varying combinations of upper lateral incisors with upper and lower second premolars (e.g., a simultaneous agenesis of the teeth 12, 22, 15, 25, 35, 45) was the most frequent pattern seen. Out of this, a combination of maxillary lateral incisors and second premolars in the same quadrant was the most common pattern of tooth agenesis per quadrant seen in this study [57].

45 However, our results could not confirm such a correlation for the whole group, nor for the different single-cleft groups or for the upper and lower jaw. No concurrent ipsilateral absence of the lateral incisor and second premolar in the counter jaw was confirmed for the whole sample or for the single-cleft groups.

50 In contrast, a positive correlation of second premolar agenesis in the upper jaw associated with the ipsilateral missing left side in left-sided UCLP patients and such a trend was also present for right-sided UCLP patients for the left side. In BCLP patients such a correlation could not be shown.

There are few studies which deal with the combination of distribution pattern of aplasia in cleft patients [33,42,57,63,99,107]. Most of the studies deal with the differences in the occurrence of hypoplasia within the different tooth types and its associations to the cleft and non-cleft side versus upper and lower jaw preferences.

In order to better identify specific distribution patterns, Hermus et al. evaluated tooth agenesis patterns in cleft-affected patients with CL, CP, and CLP and they found 3 different patterns. In the upper jaw, in the first and second quadrant, 90% had an absent maxillary lateral incisor and/or maxillary second premolar [99]. In the lower jaw, in the third and fourth quadrant, 74% had absence of the mandibular second premolar [99]. In the entire dentition, a large variety of tooth agenesis patterns were identified [99]. 89.5% had agenesis of the second premolar, central incisor, or lateral incisor on the left, right, or both sides [99]. Bartzela et al. analyzed symmetry and combinations of tooth agenesis patterns and overall prevalence of missing teeth for the whole dentition (third molars excluded) in white UCLP patients. There was an equal distribution of patients with tooth agenesis only outside the cleft quadrant and patients with agenesis of the maxillary lateral incisor in the cleft quadrant in combination with any of the 3 other quadrants outside the cleft [33]. Looking at the sides, the jaw, and the tooth types, there were 13 agenesis patterns identified, and the first and second premolars of the upper and lower jaw were involved in all patterns [33]. In almost 50% of the observed patterns, agenesis was found only outside the cleft quadrant of the maxilla or in the mandible [33]. In 7 patterns the lateral incisor on the cleft side was involved [33]. The maxillary central incisor and first maxillary premolar were part of only 2 patterns [33]. Halpern et al. evaluated the location and presence of permanent teeth outside the cleft area in 38 BCLP patients and found 13 (34.2%) patients with at least 1 missing tooth. Upper second premolars had the highest frequency, followed by the lower second premolars. Pairs of dental agenesis outside the cleft region were noted in 5 (13.2%) patients, including only bilateral missing upper second premolars or in combination with bilateral missing lower lateral incisors, bilateral missing lower second premolars in combination with unilateral missing of second upper premolar, and bilateral missing of central lower incisors or second lower molars [107].

These results show which patterns of tooth agenesis can be expected to occur in most orofacial cleft patients [99], but it would be better to search for certain distribution patterns in certain dental groups, mainly these which are missing in a high frequency in cleft patients.
Hypodontia in a unilateral and bilateral cleft Hungarian population
© Med Sci Monit, 2016; 22:

Berniczei-Roykó Á. et al.: The most common missing teeth in UCLP and BCLP patients are the cleft-sided lateral incisors and the maxillary and mandibular second premolars [57], which was also found in our study.

The association of hypodontia to the cleft side [1,33,35,56,63,81,95] and its more frequent appearance in the upper jaw is already very extensively investigated and has been previously well described [1,36,45,63,67,95,108,132]. This is evident for the cleft-sided lateral incisor [33,42,56,83,84,99] and in some studies is also described for the second premolar, more frequently missing on the cleft side of the upper arch [36,42,63,67,83]. Haataja et al. found 40% missing upper second premolars on the cleft side and only 14.3% missing on the non-cleft side [127]. In the lower jaw, second premolars were also frequently affected and were usually missing symmetrically [33,80,85,99].

In the normal population, unilateral tooth agenesis is more common than bilateral missing agenesis [47,89,115], but in more severe cases with patients having more than just a pair of missing teeth, bilateral absences were twice as frequent than unilateral absence [145]. There are several studies reporting a more frequent occurrence of bilateral absence for specific tooth types, mainly those which are most frequently missing normally. In the healthy population the most frequently missing teeth are the mandibular second premolars [134] and a bilateral absence is described in 43.5–47.7% [89].

Hellquist et al. evaluated the frequency of dental abnormalities in the permanent dentition of UCLP and UCLA patients at the age of 8 years; they found that the frequency of missing second premolars appeared to be similar to that reported for non-cleft individuals [95], suggesting that missing second premolars in cleft patients show the same distribution as in the normal population. In contrast, the upper and lower second premolars were more frequently missing on the cleft side [95]. Tortora et al. evaluated panoramic radiographs of 87 UCLP and 29 BCLP patients for quantification of missing teeth on the cleft and non-cleft side in the maxilla and mandible, reporting that a significant difference between the prevalence of hypodontia on the cleft side and non-cleft side, not only for the lateral incisors (48.8%), but also for the second maxillary premolars (4.9%) and second mandibular premolars (7.3%), missing in a higher frequency on the cleft compared to the non-cleft side (6.1%, 1.3%, and 1.2%, respectively) [83]. Shapiro et al. evaluated the frequency of missing second premolars and the possible association between the cleft side and the side from which the premolar was absent, both in the maxilla and the mandible of CL, CP, and CLP patients aged 5–18 years. The prevalence of missing premolars was 18% [63]. Among all CLP patients, the maxillary second premolar was the most frequently absent tooth [36,38,67,146]. A considerable higher incidence (3 times more common) of missing second premolars was found in the maxilla compared to the mandible, both for unilateral and bilateral missing teeth [63]. Unilateral clefts were more frequently found, and unilateral absence of second premolars was also more frequently found than bilateral [63]. In unilateral clefts, the left side of the upper jaw was primarily involved and missing second premolars were observed more frequently on that side [63]. A very interesting finding was that left-sided absence of second premolars was much more frequent in both jaws [63]. Comparable results for the non-cleft side of the maxilla and mandible could not be found [63].

In another study, Shapiro et al. evaluated the prevalence of hypodontia of permanent teeth inside and outside the cleft region of the maxilla and mandible of CL, CP, and CLP patients (excluding third molars) for a possible association between the side of the cleft and the side of the missing teeth, and they reported the above-mentioned findings for the whole dentition. Hypodontia was found more frequently in the clefted maxilla, but it was found considerably more often on the left side in both the maxilla and the mandible [42]. Mandibular second premolars were absent approximately 3 times more often on the left side than on the right side [42]. However, in both studies, Shapiro et al. evaluated a sample including cleft patients with CP, CLA, and CLP [42,63], which is in contrast to our study sample. We investigated UCLP and BCLP patients, but we found comparable results with a left-sided predominance for missing second premolars on the left side. Compared to our study, a differentiation between left and right-sided UCLP patients was not made and a possible combination for ipsilateral missing of second premolars in both arches on the left side was also not performed.

Due to the more frequent occurrence of cleft formation and hypodontia on the left side, a predominance for these both anomalies was also suggested to exist on the left side [42,63]. Aizenbud et al. also assumed that this phenomenon follows the higher prevalence of clefts on the left side [56], but this does not explain the simultaneously missing tooth on this side in the lower jaw.

The cause of the higher prevalence of left-sided clefts and missing second premolars is not known at the present time [63]. So far, no studies have found any significant right–left differences for the occurrence of congenitally missing teeth in the normal population [147]. Even a study of 100 000 dental patients showed that the number of missing teeth on the left and right side was almost identical, so that the explanation of the differences in the associations due to the cleft defect in the upper arch seems to be logical. However, an explanation of the higher frequency of missing second premolars in the lower arch on the left side of the mouth is still pending.
Many authors suggested that the frequent occurrence of hypodontia in cleft patients might be directly attributed to the cleft defect itself [40,71,80,84] and due to a severe deficiency of mesenchymal mass usually leading to hypodontia of the lateral incisor [34,36,37,41,60,73,85].

Disturbance of nutrition, inadequate blood and nerve supply [37,148] congenital or secondary to surgery [37], local loss [73], or initial lack of bone structure around the tooth germs [36], which would probably impair dental development, is another assumption.

Another explanation could be iatrogenic interference due to the surgical correction [109] of the cleft defect in early childhood [71,109] which might influence the physiological process of tooth formation [33,109], resulting in hypodontia not only inside the cleft but also outside it [109]. In contrast, other authors have found no correlation between the surgical correction of the cleft defect and hypodontia [83,95] and suggested that surgery seems to be of little importance as an etiologic factor for dental abnormalities in the cleft area [60,95], while others suggested that the etiology of the congenital absence of the lateral incisor and the second premolar might be different [38,80]. The surgical interventions in the initial phase of tooth formation could be responsible for tooth agenesis in the cleft area, whereas agenesis outside the cleft area is most likely related to genetic factors or gene regulation [33].

Cleft genes affect several tissues including the dental lamina [149] suspecting a common genetic background of both the cleft and hypodontia [34,59,82]. Several candidate genes for both tooth agenesis and clefting have already been identified. One of the key genes [59] is MSX1, a transcription factor expressed in several embryogenic structures [150], including the dental mesenchyme [151]. Mutation in MSX1 manifests both cleft palate and failure of tooth development [152,153]. PAX9 plays an important role in palatal development [59] and has been shown to be associated with specific patterns of hypodontia [59,154]. Interaction between MSX1 and PAX9 seem to play a role in tooth agenesis in humans [80] and may act in combination in the occurrence of clefting and hypodontia [34,152,155]. A positive correlation between MSX1 and TGFβ3 and hypodontia outside the cleft region and orofacial clefting has also been suggested by some authors [59,153], but the role of TGFβ3 in hypodontia is still poorly understood [59]. The possible candidate genes previously related to oral clefts are MSX1, TGFα, PAX9, FGFR1, and IRF6 genes associated with isolated tooth agenesis [153,156,157] and in many cases are associated with premolar agenesis [156]. The number of genes identified as having a role in tooth development exceeds 100 and all those genes are potential candidates for tooth agenesis in humans [154]; the true genetic disease model has not yet been identified [33,60,63].

Regardless of the genetic background, knowledge about the occurrence and distribution patterns of dental agenesis is clinically relevant because rehabilitation of patients can be planned much better if the variations are known, not only with regard to possibly spaces in the jaw, but also in terms of the occlusion to be expected.

The following findings can be summarized

Hypodontia of at least 1 missing tooth were observed in 69% of the study population.

BCLP patients were more likely to have missing teeth compared with UCLP patients, whereas the rate of missing teeth was the highest in left-sided UCLP patients and was the lowest in right-sided UCLP patients.

The most frequently missing teeth were the upper lateral incisors in the cleft area and in BCLP patients were most frequently bilateral absent.

The second most commonly missing teeth were the upper and lower second premolars.

More teeth were missing in the upper jaw compared to the lower jaw.

No differences between hypodontia in the upper and lower arch were observed.

Associations of missing teeth could be found for left-sided UCLP patients for ipsilaterally missing second premolars of the upper and lower jaw for the left side, and the same trend was observed for right-sided UCLP patients.

Conclusions

To the best of our knowledge, no other study exists in the literature which evaluated a correlation a left-sided ipsilateral missing second premolars in the upper and lower jaw. Our results are interesting in view of a therapy planning. Nevertheless, they have to be interpreted with caution due to the relatively small sample size of patients evaluated in our study. Special distribution patterns in the different cleft groups, including second premolars, should be investigated more precisely on the basis of larger random samples to draw more precise conclusions.

Conflicts of interest

The authors claim that there are no conflicts of interest.


64. Ringqvist M, Thilander B: The frequency of hypodontia in an orthodontic material. Svens Tandlak Tidskr, 1969; 62(9): 535–41


87. Ringqvist M, Thilander B: The frequency of hypodontia in an orthodontic material. Sven Tandlak Tidskr, 1969; 62(9): 535–41
129. Lekkas et al: Meta-analysis and systematic review of factors biasing the observed prevalence of congenitally missing teeth in permanent dentition excluding third molars. Prog Orthod, 2013; 14: 33