Dental Anomalies in Chinese Children with Cleft Lip and Palate

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Abstract

Background: The prevalence of dental anomalies in children with cleft lip and palate (CLP) has been said to be higher than in the normal children; however, such findings have not been expressed for different racial groups.

Aim: To determine the prevalence of anomalies in children with CLP and to ascertain if there were any differences between the prevalence figures for CLP and non-CLP children.

Design: This is a retrospective study looking at previously collected clinical records. The sample consisted of 231 pairs of age and gender matched CLP and non-CLP southern Chinese aged between 12 and 16 years. The dental records of the subjects were examined to gather data on anomalies of tooth number, size, and shape.

Results: It was found that 57.6% of the CLP children had hypodontia, 10.0% hyperdontia, 8.7% taurodontism, 0.8% a double tooth, 1.30% dens evaginatus, and 42.4% had microdontia in the permanent dentition. The CLP subjects had a statistically higher prevalence of hypodontia (p<0.001), supernumerary (p<0.01) and microdontia (p<0.001) than the non-CLP subjects. More CLP children were found to have one to three types of anomalies, than the non-CLP children (p<0.001).

Conclusion: This group of Chinese CLP children demonstrated a higher prevalence of dental anomalies than the non-CLP children.

Introduction

It has been reported that patients with cleft lip and palate (CLP) exhibit a higher frequency of dental anomalies than non-cleft subjects [1-7]. These dental anomalies can be numerical [8,9] or morphological [10]. However, any association between dental anomalies and the presence of clefts is poorly understood. Nevertheless, a direct relationship between the cleft formation and formation of the teeth, irrespective of the genetic predisposition and severity of the cleft type (i.e. uni- or bi-lateral) has been identified [11]. The frequency of dental anomalies among CLP subjects has been found to be higher than in their siblings, and non-cleft subjects, which were similar [12]. While familial and sporadic cleft cases show no difference in frequency [13]. However, it is unclear if there is any variation based on the ethnicity.

Hypodontia is commonly found in CLP patients and the prevalence ranges from 31.5% to 45.9% [14-19]. The lateral incisor is more often missing in CLP than in non-CLP subjects [20]. No gender difference for the prevalence of hypodontia has been found in CLP subjects [21]. As expected more maxillary teeth than mandibular teeth have been reported missing and the cleft side is most frequently affected; whilst both sides are similarly affected in the mandible [16].

In the non-cleft region, the prevalence of hypodontia is reportedly higher in CLP than non-CLP subjects [3,8,14,16,17,22,23,24]. Although these results are from different populations, the common findings are that the permanent maxillary lateral incisors and the premolars on the non-cleft side, are the teeth that are predominately involved.

The incidence of supernumerary teeth is highest in subjects with isolated cleft lip and appears to decrease with the severity of the cleft [14]. The prevalence of supernumerary teeth ranges from 6.7% to 22.2% [16,17,19] which is higher than in non-cleft subjects [20]. There is a tendency for a supernumerary primary incisor to be succeeded by a supernumerary permanent incisor [25]. However, the supernumerary primary lateral incisor can be followed by agenesis of the permanent lateral, or a permanent lateral on either side of the cleft, or a supernumerary tooth [16].

Morphological anomalies are found more often in cleft than non-cleft subjects [2,8,10,14,15,26,27]. The frequency of abnormally sized and shaped teeth in CLP subjects, ranges from 35.0% to 49.5% [14,17]. They may be incisal, conical or of an intermediate type [18]. These malformations of the teeth have been considered by many authors to be a microform of CLP presentation [28-30]. The reason for the diminutive teeth is unknown; however, surgery cannot be excluded as a possible aetiological factor.

Taurodontism was defined by Holt and Brook [31] as an increase in the pulp chamber at the expense of the root. It is usually more evident in the mandibular molars and the prevalence has been reported to be 28.9% [32]. The prevalence of taurodontism in Chinese subjects is reportedly 65% in females and 36% in males [33]. Taurodontism has seldom been investigated in CLP subjects. Akcam and colleagues [34] reported that 1.9% of the unilateral cleft lip and palate children had taurodontic molars.

Double tooth is the anomaly of conjoined teeth, which includes both fusion and germination [35]. The location is commonly unilateral in the mandibular lateral incisor region [35-41]. Fusion is said to be more common than germination [36,37,39,40,42-44]. The prevalence of this anomaly in CLP children has been reported by Pöyry and Ranta [45], who found it to be lower than in the non-CLP subjects.

Dens evaginatus is a rare developmental anomaly that is reported to be more common in mongolid races with a prevalence of 0.1% to 6.3% [46-48]. The corresponding figure for CLP subjects has been reported to be lower than other dental anomalies [34]. Interestingly

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Received December 19, 2011; Accepted March 26, 2012; Published March 28, 2012


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Materials and Methods

The investigation was based on a sample of southern Chinese CLP children living in Hong Kong. The sample was drawn from children registered at the only dental hospital in Hong Kong, the Prince Philip Dental Hospital in which the first Cleft Lip and Palate Centre in Hong Kong was established. The CLP patients of the centre came from a variety of sources including "walk-in" patients and referrals from Government Hospitals, private medical and dental practitioners. Approval to conduct this study was received from the Ethics Committee of the Faculty of Dentistry, the University of Hong Kong.

The host computer of the dental hospital was used to establish a sample of 548 CLP subjects of which 531 were of southern Chinese origin. The subjects with poor quality radiographic records or study casts, associated syndromes, or relevant medical diseases were excluded from the study. Thus, the final CLP group consisted of 231 children with ages that ranged from 12 to 16 years (mean age = 13.8 years).

A control group of non-CLP subjects was then randomly selected, using the same hospital host computer, so as to be gender matched to the CLP subjects. The exclusion criteria were the same as those of the CLP subjects except that children receiving orthodontic treatment were excluded. In addition, the non-CLP subjects were selected so that their ages and the date of panoramic radiographs matched, within 30 days, to those of the CLP subjects. This resulted in a total of 231 children without CLP who were age and gender matched with the 231 children with CLP.

In addition to studying the study casts, and medical and dental records of each CLP and non-CLP subjects, the panoramic, upper and lower anterior views and periapical radiographs taken during the entire period of treatment were thoroughly examined in a darkened room with an illuminated x-ray viewing box. Study casts (12 years) and panoramic radiographs exhibiting the early (6 - 7 years) and late mixed dentitions (11 - 12 years) were available for every subject.

A pilot study was conducted prior to the main study to test the feasibility of the computer program to be used for data entry, and to calibrate and train the investigator with the indexes and criteria for reproducibility of the diagnosis was highly accurate. The most common cleft type was L-UCLP which occurred in 103 (44.6%) children. Of the 231 CLP children, 123 (53.2%) were males and 108 (46.8%) females. The most common cleft type was L-UCLP (53.2%) and 108 (46.8%) females. The most common cleft type was L-UCLP which occurred in 103 (44.6%) children.

Statistical analysis

The data were analyzed using the SAS statistical software package. The results included descriptive statistics of each dental anomaly and test statistics (Chi-square) were calculated if necessary. The records of 10% of the CLP subjects were randomly selected for re-examination in order to test the reproducibility of the results. The Kappa coefficient (κ) was used to measure the intra-examiner reproducibility as recommended by Landis and Koch [59].

Results

The gender distribution for each cleft type in the CLP group is shown in Table 1. Of the 231 CLP children, 123 (53.2%) were males and 108 (46.8%) females. The most common cleft type was L-UCLP which occurred in 103 (44.6%) children.

Various types of anomalies

The Kappa coefficients for the diagnoses of dental anomalies of each tooth ranged from 0.93 to 1.00. The level of agreement was therefore either “almost perfect” or “total agreement”, indicating that the reproducibility of the diagnosis was highly accurate. The most common dental anomalies in the permanent dentitions of CLP children were

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hypodontia (57.6%) and microdontia (42.4%), see Table 2. The CLP subjects had a statistically higher prevalence of hypodontia (p < 0.001), supernumerary teeth (p < 0.001) and microodontia (p < 0.001) than the non-CLP subjects. Although taurodontism and dens evaginatus were more prevalent in the CLP children than the non-CLP children, the differences were not statistically significant. For the various types of CLP, hypodontia was the dominant dental anomaly in the BCLP children at 71.8% (Table 3).

Number of types of dental anomalies per individual

Of the 231 non-CLP children, 200 (86.6%) had no dental anomalies while this occurred in only 28 (12.1%) of the CLP children (p < 0.001), see Table 4. More CLP children were found to have one to three different types of anomalies than the non-CLP children (p < 0.001). Most of the CLP children had only one type of dental anomaly (41.6%).

The highest number of dental anomalies any one individual had was four for the CLP and two for the non-CLP children. The frequency of anomalies per individual for the different types of CLP are displayed in Table 5. Since there was no statistical difference in the prevalence figures in L-UCLP and R-UCLP groups, the data were pooled. The cleft types with four associated dental anomalies per individual were BCLP (n = 3) and UCLP (n = 1). All CL and BCLP children exhibited at least one type of anomaly.

Number of teeth affected per individual

Most of the CLP children had one tooth affected by an anomaly such as hypodontia, supernumerary, and microdontia; while in the case of taurodontism, two or four teeth were affected per person (Table 6).

Hypodontia

The cleft type associated with the highest percentage of missing teeth was BCLP (71.8%), see Table 3. The frequency of hypodontia in the permanent dentition of the different types of CLP children is displayed in Table 7. There was no statistical difference in the prevalence figures for hypodontia in L-UCLP (59.2%) and R-UCLP (58.5%), see Table 3, so the data were pooled for analysis. The most frequently missing tooth in the CLP children was the maxillary lateral incisor (Figure 1). It was most often missing in the children with UCLP (62.8%) and BCLP (59.0%). The most frequently missing tooth in the mandible was the second premolar and it was more often missing in the children with CP (46.4%) and BCLP (23.1%).

Supernumerary teeth

The cleft type associated with the highest percentage of supernumerary teeth was CL (25.0%), see Table 3. By contrast no supernumerary teeth were found in the CP group. Of the 30 supernumerary teeth that were identified in the CLP group, 27 (90%) were located in the anterior region of the maxilla with sixteen (64%) being in the cleft region. The predominant shape of supernumerary teeth

Table 4: The frequency of anomalies per individual in 231 CLP and 231 non-CLP southern Chinese children.

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>CLP (N=231)</th>
<th>non-CLP (N=231)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypodontia</td>
<td>133 (57.6%)</td>
<td>57 (24.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Supernumerary</td>
<td>23 (10.4%)</td>
<td>6 (2.6%)</td>
<td>0.007</td>
</tr>
<tr>
<td>Taurodontism</td>
<td>20 (8.7%)</td>
<td>10 (4.3%)</td>
<td>0.087</td>
</tr>
<tr>
<td>Double tooth</td>
<td>1 (0.4%)</td>
<td>1 (0.4%)</td>
<td>NS</td>
</tr>
<tr>
<td>Dens evaginatus</td>
<td>3 (1.3%)</td>
<td>0 (0.0%)</td>
<td>0.248</td>
</tr>
<tr>
<td>Microodontia</td>
<td>98 (42.4%)</td>
<td>2 (0.9%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 5: The frequency of anomalies per individual in 231 CLP southern Chinese children.

<table>
<thead>
<tr>
<th>Dental anomaly</th>
<th>CLP (N=231)</th>
<th>non-CLP (N=231)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypodontia</td>
<td>3 (13.7%)</td>
<td>28 (12.1%)</td>
<td>NS</td>
</tr>
<tr>
<td>Supernumerary</td>
<td>2 (8.7%)</td>
<td>15 (6.5%)</td>
<td>NS</td>
</tr>
<tr>
<td>Taurodontism</td>
<td>0 (0.0%)</td>
<td>10 (4.3%)</td>
<td>NS</td>
</tr>
<tr>
<td>Double tooth</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>NS</td>
</tr>
<tr>
<td>Dens evaginatus</td>
<td>0 (0.0%)</td>
<td>1 (0.4%)</td>
<td>NS</td>
</tr>
<tr>
<td>Microodontia</td>
<td>2 (8.7%)</td>
<td>14 (6.1%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Table 6: The number and percentage of dental anomalies in 231 CLP and 231 non-CLP southern Chinese children.
was conical in 90% of the CLP (Figure 2) and 85.8% of the non-CLP children. Supernumerary teeth of supplemental type were found in two children (6.7%) of the CLP group and one (14.2%) of the non-CLP group. One subject (3.3%) in the CLP group had supernumerary tooth of tuberculate shape. No molariform supernumeraries were found in this study.

**Taurodontism**

Approximately 10% of BCLP, UCLP and CP children were found to have taurodontism (Table 3). Forty nine out of 924 (5.3%) of the first molars in the CLP children exhibited taurodontism while the corresponding figure for the non-CLP children was lower at 2.7% (25/924). For the CLP children, 65% (32/49) of the teeth that exhibited taurodontism were the maxillary first molars (Figure 3).

**Double tooth**

Double tooth was found in only one child with BCLP (Table 3) and it was located in the mandibular left incisor region (Figure 4). In this case the canine in the same quadrant was present.

**Dens evaginatus**

Only three (1.3%) of the CLP children had dens evaginatus on their premolars (Figure 5). None of the non-CLP children had this anomaly (Table 2).

**Microdontia**

Microdontia was found in 42.4% of the CLP group and most of them were children with L-UCLP (Tables 2 and 3). Microdontic teeth in the CLP subjects, as demonstrated by the presence of peg-shaped lateral incisors in the cleft region, had a prevalence of 78.3% (90/115). In the non-cleft region of the CLP children, 8 lateral incisors, 12 premolars (Figure 6) and 5 central incisors were found to be microdontic. Only two microdontic teeth were found in the non-CLP children ($p<0.001$).

**Discussion**

As this retrospective study was based on the southern Chinese children registered in a dental hospital the sample data can be considered to be biased to a certain extent though children receiving orthodontic treatment were excluded from the non-CLP group. The collected data will still be useful for future meta-analysis studies. The male to female ratio for CLP in this study was in accordance with most

<table>
<thead>
<tr>
<th>Type of tooth</th>
<th>CL (N = 8)</th>
<th>BCLP (N = 39)</th>
<th>UCLP (N = 156)</th>
<th>CP (N = 28)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Maxillary</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central incisor</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>12.8</td>
</tr>
<tr>
<td>Lateral incisor</td>
<td>2</td>
<td>25.0</td>
<td>23</td>
<td>59.0</td>
</tr>
<tr>
<td>Canine</td>
<td>1</td>
<td>12.5</td>
<td>2</td>
<td>5.1</td>
</tr>
<tr>
<td>First premolar</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>7.7</td>
</tr>
<tr>
<td>Second premolar</td>
<td>0</td>
<td>0</td>
<td>14</td>
<td>35.9</td>
</tr>
<tr>
<td>First molar</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Second molar</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mandibular</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central incisor</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>5.1</td>
</tr>
<tr>
<td>Lateral incisor</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>5.1</td>
</tr>
<tr>
<td>Canine</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>First premolar</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>12.8</td>
</tr>
<tr>
<td>Second premolar</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>23.1</td>
</tr>
<tr>
<td>First molar</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Second molar</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

CLP = cleft lip and palate
CL = isolated cleft lip only
BCLP = complete bilateral cleft lip, alveolus, and palate
UCLP = complete unilateral cleft lip, alveolus, and palate
CP = isolated cleft palate only.

Table 7: The frequency of hypodontia in the permanent teeth of 231 CLP southern Chinese children.
While most studies have found CP to occur most frequently in females an equal gender ratio was found in the present study, which is similar to that found by Menezes and Vieira [24] who studied 17 Caucasians with CP. Other ethnic groups have been found to have higher prevalences of dental anomalies in CLP children than non-CLP children [1-4,8,10,12,23]. However, the overall prevalence values obtained from this study can not be directly compared to the results of other studies as the prevalence figures reported in those studies refer to different types of dental anomalies found in the CLP subjects. Some of these studies reported on the general prevalence of anomalies in cleft subjects [2,10] whereas others concentrated on only one or two specific types of dental anomalies such as tooth number, size, shape, time of formation or eruption [3,8,9,12]. Moreover, some authors reported only dental anomalies that occurred in the anterior maxilla [19,45] or on specific teeth [9,18,28,45,61-65]. Therefore, the figures from the present study are best compared with the published results for individual anomaly. Various factors such as the different characteristics of the samples in terms of size, age range, source of the sample, and the methodology may also influence the comparability of the results between this and other studies.

The prevalence figures of the various dental anomalies and their implications will be discussed independently.

### Hypodontia

The 57.6% occurrence of hypodontia in the CLP children was lower than the 79% reported by Carretero Quezada et al. [11]. However, in the children with only CL, the 37.5% prevalence of hypodontia was much higher than the 5.5% found by Olin [8] and the 21% by Jiroutova and Müllerova [66]. The discrepancy may be attributable at least partially to the small number of CL subjects in the present study. When the data for BCLP and UCLP were pooled together, the prevalence of hypodontia (61.5%) was higher at 29.5% than reported by Jiroutova and Müllerova [66], and the 26.6% by Olin [8]. The prevalence of hypodontia (32.1%) for the CP group in this study was remarkably similar to the 32.3% reported by Böhn [14] for 31 Danish and Norwegian children and with the 31.5% quoted by Ranta [9] for a group of 251 Finnish children.

The present study confirms that the maxillary lateral incisors are the most frequently missing teeth in CLP subjects [8,14,16,21,67]. The prevalence of missing permanent lateral incisors on the cleft side of children with UCLP (48.3%), was similar to that (42.6%) reported by Hellquist et al. [17].

In the present study, the prevalence of missing teeth on the non-cleft side of CLP children (51.3%) was approximately seven times greater than for the non-CLP children (7.4%). In CL children the prevalence published report [21,34]. While most studies have found CP to occur most frequently in females an equal gender ratio was found in the present study, which is similar to that found by Menezes and Vieira [24] who studied 17 Caucasians with CP.

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of missing teeth (37.5%) was higher than the 4.5% for Danish and Norwegian children [14], the 5.2% for Swedish subjects [17], and 10.1% for Finnish children [68]. The prevalence of hypodontia in the non-cleft region of UCLP children was 33.3% which is in the range of 28% to 48.8% reported by Böhn [14], Hellequist et al. [17], and Ranta [68]. Similarly, the prevalence (41%) of hypodontia in BCLP was within the 17.9% to 68.4% range quoted by Böhn [14] and Ranta [68]. When children with CP alone are considered, the finding from this study (32.1%) is similar to that of Böhn [14], but much higher than the 22.7% reported by Olin [8].

In the non-cleft region of the maxilla, the lateral incisors were the most frequently missing teeth (19.9%), followed by the maxillary (7.8%) and mandibular (7.6%) second premolars. Similar findings have been obtained in other studies [8,14,17,68]. The prevalence of hypodontia in the non-cleft region is said to increase with the severity of cleft [14,16,24,68,69] this tendency occurred in this study.

**Supernumerary teeth**

In the present study, the prevalence of supernumerary teeth (10%) in the permanent dentition was much lower than for hypodontia (57.6%) in the CLP children, which implies that the permanent tooth germs are more susceptible to irreversible damage than to splitting. In CL children where the alveolus was apparently intact, the tooth germs of supernumeraries and lateral incisors could be expected to be less affected by the clefting. This may account for the higher frequency of supernumeraries in the CL group than any other cleft type. In other words, there is a tendency for the frequency of supernumeraries to decrease with the severity of cleft, a finding that has been previously reported [14].

The number of supernumerary teeth per individual in the non-cleft region was higher for the CLP than the non-CLP children although the difference was not statistically significant. This result implies that a factor, other than that of the cleft influences the formation of supernumeraries in CLP children. As no published literature exists on this topic, it is difficult to verify or compare this observation.

While most authors have considered the cleft as being the aetiological factor responsible for supernumerary teeth in CLP subjects [25], the hypotheses for the aetiology of hyperdontia in normal subjects may also be applicable to CLP subjects. The most popular hypothesis is localised hyperactivity of the dental lamina [57,70-72]. Other postulates include the expression of an atavistic trait, polygenetic reversion [72-74], activation of the remaining clumps of epithelium following the break down of the primary epithelial band leading to tooth formation [73,74]; hyperactivity of the ectomesenchyme or neuroectoderm [74] and the formation of extra tooth buds or splitting of existing ones [72,73].

**Tauodontism**

The reported rates of taurodontism in normal populations vary from 0.6% to 11.3% [31,75-78] while the prevalence of this trait is higher in association with hypodontia [32,79]. The occurrence rates in the CLP (8.7%) and non-CLP (4.3%) children in this study were within the range for normal non-Chinese subjects, but much lower than the 46.3% found by MacDonald et al. [33] in a non-random sample of non-CLP southern Chinese people, and 70.5% in CLP Jordanians [21]. The use of different diagnostic criteria for taurodontism probably also contribute to this variation.

**Double tooth**

Double tooth occurred in 0.4% of the CLP children which was within the range (0.1% - 0.8%) for normal Chinese children [48]. Yuen et al. [40] believed that the double tooth in normal children arose from unseparated, rather than fused tooth masses. While Sawyer [80] thought that germination could result from either the splitting of a tooth germ during development or from fusion of a normal tooth bud with a developing supernumerary tooth. The occurrence of double teeth in CLP subjects can be explained by the incomplete splitting of tooth buds within the cleft region by the cleft inducing factor. The tooth buds could be those of a lateral incisor or a supernumerary tooth. Alternatively, it has been suggested that the dental lamina on each side of the fissure between the premaxilla and maxillary process may independently have the potential to form a lateral incisor tooth [81]. Under normal circumstances, the two adjacent tooth germs unite and proliferate as one tooth unit. However, an incomplete union would result in a double tooth. Therefore, a double tooth in the cleft region could be the result of an abortive union of normal lateral incisors. Another possibility for double tooth formation may be the fusion of a normal lateral incisor with a supernumerary tooth in the cleft region.

**Dens evaginatus**

Dens evaginatus has been reported to occur in 4.7% of non-CLP southern Chinese children [48], which is more than the 1.3% (CLP) and 0% (non-CLP) found in this study. The sample size in this study may not have been big enough to indicate the prevalence of this relatively rare anomaly.

**Microdontia**

The higher prevalence of microdontia in the CLP children (42.4%) than in the non-CLP children (0.9%) in this study was not only due to the high percentage of peg-shaped laterals in the cleft region, but also due to the higher number of microdontic teeth in the non-cleft region, as found in other studies [2,10,15,26,82]. In this regard it has been suggested that genetic factors and corrective surgery of the cleft are related to the diminution of tooth size in CLP subjects [60,83,84]. A generalised decrease in tooth size for the whole dentition was not observed generalized in this study, therefore, it can be speculated that the genetic impact on tooth size may only be partial.
Conclusions

This group of Chinese CLP children exhibited the various types of dental anomalies. Statistically higher prevalences of hypodontia, supernumerary teeth and microodontia were demonstrated in the CLP children than in the non-CLP children. Further studies of dental anomalies and traits in CLP children of various ethnic origins are required to facilitate future comparisons and ultimately a better understanding of their aetiology and relationship to the cleft defect.

References