Original Article - Retrospective Study

Tooth Agenesis in Patients with Complete Bilateral Cleft Lip and Palate

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Abstract

Aim: The aim of this study was to compare the number of teeth in the premaxilla (cleft area) and to assess the presence of tooth agenesis with the ultimate goal of finding whether differences existed in the two suggested subtypes of nonsyndromic bilateral cleft lip and palate (BCLP) patients. **Settings and Design:** A retrospective comparative study was conducted, where cone- beam computed tomography (CBCT) images of 22 BCLP patients (10 males and 12 females, with age range 8 to 14, mean age 9.6 years) obtained from archive of Cleft Clinic, affiliated to the Oral and Maxillofacial Surgery department, Ain-Shams University, Cairo, Egypt were assessed. **Subjects and Methods:** CBCT images were divided into two subtypes: Group (P) – this represents BCLP characterized by well-developed (P) prominent premaxilla and SNA >80 ± 2 and Group (R) – this represents BCLP characterized by ill-developed (R) rudimentary premaxilla and SNA <80 ± 2. The number of teeth in the premaxilla was evaluated, and the presence of agenesis in the premaxilla and posterior segments was documented. **Statistical Analysis Used:** Unpaired-Student's *t*-test was used to compare the number of teeth among the two groups and to test significance at $P < 0.05$. Intraobserver agreement was assessed using alpha (Cronbach) reliability analysis. A descriptive analysis using percentages was performed to characterize tooth agenesis. **Results:** A significant difference was found in the number of teeth in the premaxilla among Group R and Group P. Maxillary lateral incisor showed the highest percentage of agenesis in the two groups followed by the maxillary second premolar. **Conclusions:** The number of teeth might be useful in differentiating different subtypes of nonsyndromic BCLP.

Keywords: 3D zoom, agenesis, bilateral cleft lip and palate, cone-beam computed tomography, premaxilla

Introduction

Cleft lip and palate (CLP) is considered one of the most common congenital anomalies that show significant medical, psychological, social, and financial implications on the affected individuals and their families.[1] Orofacial clefts arise from failure of normal craniofacial developmental processes. Development of the craniofacial structures is a complex process that requires coordination of a complex series of events that include cell growth, migration, differentiation, and apoptosis.[2]

Individuals with CLP often suffer from multiple problems such as feeding difficulties, nutritional issues, abnormal speech and resonance, abnormal maxillofacial morphology, dental anomalies, and psychosocial issues.[3] The most common dental anomalies found in CLP patients are multiple missing teeth, ectopic eruption, impaction, supernumerary teeth, microdontia, enamel dysplasia, crown and root malformation, and multiple decayed teeth.[4] Among these anomalies is agenesis of the maxillary lateral incisors, which has the highest prevalence followed by the presence of supernumerary teeth.[5]

Several studies have demonstrated that dental anomalies are more frequent in children affected by cleft lip, cleft palate, or both than in the general population.[6] Moreover, it was found that patients with bilateral CLP (BCLP) were frequently more affected by dental anomalies than those with unilateral CLP (UCLP).[7]

Because there is a close embryological relationship between the development of tooth germs and the occurrence of CL/P

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in terms of timing and anatomical position, some studies use dental anomalies to identify the possible subtypes of nonsyndromic CLP.[8]

Therefore, the present study aimed to compare the number of teeth in the premaxilla (cleft area) and to assess tooth agenesis present in a suggested clinically oriented classification, dividing BCLP into two subtypes based on the premaxillary characteristics: Group P – characterized by well-developed (P) prominent premaxilla and Group R – characterized by ill-developed (R) rudimentary premaxilla.[9]

Subjects and Methods

This retrospective study involved 22 cone-beam computed tomography (CBCT) scans of BCLP cases obtained from the archives of the Cleft Care Center, affiliated to the Oral and Maxillofacial Surgery Department, at our university.

The current study was exempted from the Review Ethics Committee, as all included CBCT scans were made anonymous and were exposed for reasons other than the purpose of this study.

Each CBCT scan was given a number, and the identity of the patient was masked. Images were loaded into Ondemand 3D™ application software, CYBER MED, USA version 1.0.10.4304, where examination of the cases was carried out utilizing a slice thickness of 0.5 mm.

The selection of the cases was based on certain inclusion criteria including nonsyndromic BCLP, patients who had undergone lip repair surgery between 3 and 6 months of age, and palate was repaired between 9 and 18 months of age. None of them were subjected to surgical or orthodontic interference for repositioning of the premaxilla; moreover, CBCT scans that showed any artifacts that interfere with an identification of the required landmarks were excluded from the study.

CBCT scans were classified according to variation in the premaxillary characteristics and measurement of SNA into two groups:

- Group P where the premaxilla was prominent and protruding and SNA >80 ± 2 (12 cases)
- Group R where the premaxilla was hypoplastic and rudimentary and SNA <80 ± 2 (10 cases).

Measurement of SNA

The angle was measured on a sagittal slice, which was adjusted from the coronal view as follows: sequential slices were examined till the reference sagittal plane is passing through the middle of the crista galli posteriorly and between the lower central incisors anteriorly [Figure 1]. After identification of the required anatomical landmarks such as Point S, nasion, and Point A [Table 1], the angle tool was selected and the required angle was drawn [Figure 2].

The number of teeth in the premaxilla (cleft area) was counted for each case, and the presence of agenesis in the premaxilla and posterior segments was detected using 3D Zoom function.

In case of the premaxilla, a cube size was adjusted to include the whole premaxillary segment [Figure 3]. The right and left posterior segments were assessed separately, where a cube size was adjusted to extend from the first permanent premolar to the last molar for each side [Figure 4].

All measurements were repeated three times with 1-month interval by the same investigator and their average value was used in further analysis.

Statistical analysis

The statistical analysis was performed using GraphPad Prism 7.05 for Windows, GraphPad Software, La Jolla, California, USA, and Microsoft Excel. The data were expressed as mean and standard deviation. Unpaired Student's *t*-test was used to compare the number of teeth among the two groups and to test significance at $P < 0.05$. Intraobserver agreement was assessed using alpha (Cronbach) reliability analysis. A descriptive analysis using percentages was performed to characterize tooth agenesis. Tooth agenesis was calculated as a percentage of the total group number.

Results

A significant difference was found in the number of teeth in the premaxilla between Group P and Group R, where Group P showed a higher number of teeth and $P = 0.0043$ [Table 2].

The maxillary lateral incisors showed the highest percentage of agenesis. It reached 100% in Group R and 66.6% in Group P. In posterior segments, the maxillary second premolar showed the highest percentage of agenesis in both the groups. In Group P, the percentage of agenesis of the right and left maxillary second premolar was 16.6% and 10%, respectively, whereas in Group R was 30% and 10%, respectively. Maxillary first and second molars were present in all cases on both the sides. Cronbach's alpha to test intraobserver reliability ranged from good to excellent for all measurements.

Discussion

Cleft formation affects different parts of the craniofacial and dentofacial structure as it can occur at different times during

Table 1: Anatomical land marks

Landmark	Definition
A point (sub spinal)	Is the most concave point of anterior maxilla
Nasion (N)	Is the most anterior point on frontonasal suture
Sella (S)	Is the mid-point of sella turcica

Table 2: Means, standard deviations and two-tailed *t*-test results for number of teeth in premaxilla among Group P and Group R

Variable	Groups	Mean±SD	*P*
Number of teeth in premaxilla	P	2.08±0.5	0.0043*
	R	0.9±0.9	

SD=Standard deviation. *Indicates statistical significant: $P \leq 0.05$

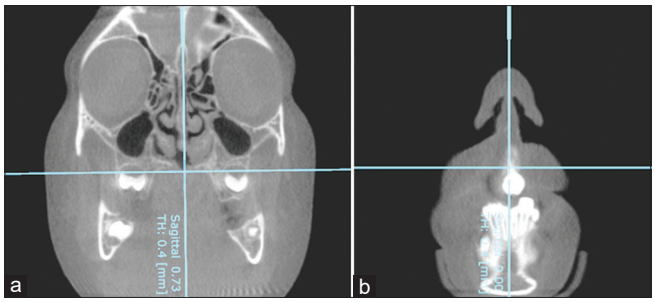

Figure 1: Adjusting sagittal plane in coronal image so that it passed through the middle of the crista galli posteriorly (a) and through lower central incisors anteriorly (b)

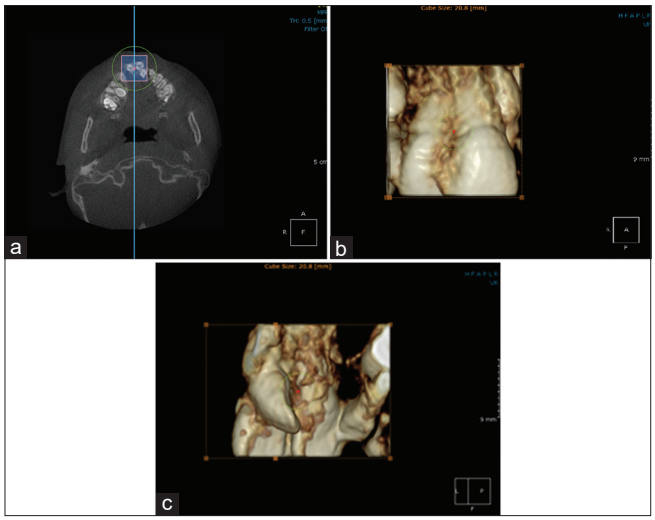

Figure 3: (a) Axial image showing cube size adjusted to include the whole premaxilla, (b) teeth in the premaxilla as viewed from labial aspect, (c) teeth in the premaxilla as viewed from palatal aspect

gestation. Dental abnormalities vary directly with severity of the cleft.[4-7]

Complete BCLP is a severe cleft subtype that represents a substantial challenge both clinically and surgically as not all bilateral cases show the same premaxillary characteristics. The difference in the premaxillary position could be attributed to the mobility of the premaxilla in BCLP since birth, where it is fixed to the vomer bone apically, leading to abnormalities in the position. Its position is also influenced by pressure from the tongue and lip together with forward growth of the midline structures and the lateral processes.[10]

Different handling protocols are needed, where surgical maxillary advancement via orthodontic functional devices, orthognathic surgery, or distraction osteogenesis are required in case of rudimentary hypoplastic premaxilla,[11] whereas in case of protruding premaxilla, presurgical orthopedics is usually required.[9]

In a study conducted by El-Kassaby *et al*.,[9] to test the response of BCLP patients to presurgical orthopedics and primary lip repair based on the premaxillary characteristics, a significant morphological difference was found between

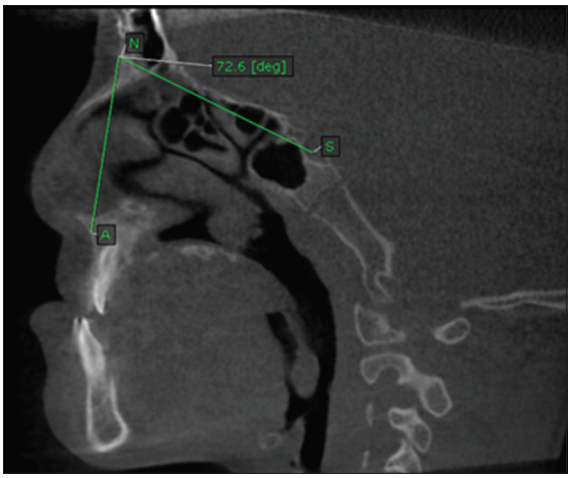

Figure 2: Sagittal image showing SNA angle; S = Sella, N = Nasion, A = Point A

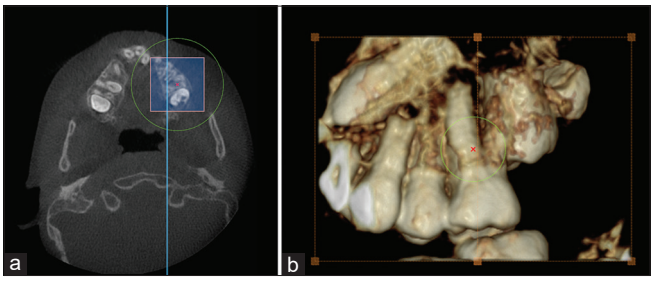

Figure 4: (a) Axial image showing cube size adjusted to include posterior segment on the left side and (b) corresponding zoomed cube

the two subtypes of BCLP. They found a reduction of the premaxillary anterior projection consequent to lip repair in Group P and Group R. Group R was more severely affected, and the authors contributed this finding to the more flexible attachment between the premaxilla and vomer in Group R compared to the firm attachment between the premaxilla and the vomer in Group P. Difference in the number of teeth among the two groups was also observed in the study, which was more in Group P. However, the study included only infants before and after primary lip repair.

No attempts in dental literature could be found to differentiate different subtypes of BCLP using CBCT. Since different presentations of the defect affect the response of cases to presurgical orthopedics and primary surgical repair of lip and not all associated anatomical irregularities can be detected clinically. It is important to detect them radiographically.

Therefore, our study was conducted to validate the differences among the two subtypes of BCLP by comparing the number of teeth in the premaxilla and detecting tooth agenesis in the premaxilla and posterior segments using CBCT images. Patients in mixed dentition stage were included in the current study because this stage is considered one of the advanced stages of growth and development during which variations and anomalies can be detected.[12]

In our study, certain exclusion criteria were chosen including cases with history of surgical or orthodontic interference for repositioning of the premaxilla, as in case of early manipulation of protrusive premaxilla (at the time of lip closure or after), the anteroposterior growth of the premaxilla and consequently SNA angle is unfavorably affected due to drastic effects on maxillary growth.[13]

The assessment of teeth in the premaxilla and posterior segment was done using 3D zoom function. Zoom reconstruction is an option provided by the software to highlight the details in part of the image. This facility allows reconstruction at a small region of interest in the image in a smaller voxel size, thus increasing the sharpness.[14]

Concerning the number of teeth in the premaxilla, our results showed a highly significant difference between Group P and Group R, where Group P, cases with a prominent well-developed premaxilla showed a higher number of teeth. Consequently, decreasing extraction in Group R should be considered in treatment planning.

This outcome is in accordance with Berkowitz,[15] who performed a review of literature and assumed that, in BCLP, the number of tooth buds and their distribution affect the shape and size of the premaxilla and that the size of the premaxilla is directly proportional to the number of teeth it carries.

Our results also found that the maxillary lateral incisors showed the highest percentage of agenesis. It reached 100% in Group R whereas in Group P it was 66.6%. This could be explained by the proximity of the lateral incisor to the cleft area or deficiency in blood supply, either congenital or secondary to the postnatal surgery or deficiency in the mesenchymal support.[16]

Our study agrees with a study by Camporesi *et al*.,[6] in which 156 Caucasian patients affected by nonsyndromic UCLP or BCLP were investigated. The study reported that the permanent lateral incisors showed the highest prevalence of agenesis (60%), followed by the maxillary second premolar.

Lesser attention was always drawn to anomalies outside cleft region, inspite the fact that not only the number but also the size of teeth is affected by the presence of the cleft. In a study conducted by Barghouth,[17] 110 CBCT scans of different cleft types and control patients were investigated to study the differences between actual and predicted combined mesiodistal width of the permanent canines and premolars. The results showed a statistically significant difference in case of UCLP and BCLP.

Detection of these malformations and comprehensive diagnosis is crucial for the planning of a multidisciplinary dental treatment and aids in understanding the etiology of cleft and overcoming drawbacks of surgical treatment.[18]

In our study, in posterior segments, the maxillary second premolar showed the highest percentage of agenesis in both the groups. This outcome agrees with a study performed by Mangione *et al*.,[18] in which the prevalence and location of the dental anomalies were assessed in CL/P patients inside and outside the cleft area, and the results showed that the lateral incisor had the highest prevalence of agenesis followed by maxillary and mandibular premolars.

The exact explanation of co-occurrence of tooth agenesis and orofacial cleft is still debatable; however, genes whose mutations were shown to cause tooth agenesis are often considered as genetic risk factors for orofacial clefts.[19]

Conclusions

The number of teeth is different among the two investigated subtypes of BCLP and may contribute to the different presentations of the premaxilla. Management should be modified according to each case as not all BCLP cases should be treated using the same protocol. Decreasing extraction in Group R should be considered as it showed less number of teeth compared to Group P. Different etiological background may be the cause of these variations; however, further investigation is required.

Recommendation

Different characteristics of BCLP should be taken into consideration during treatment planning and further genetic investigations with larger sample group at various stages are required to further validate differences between the two suggested subtypes.

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Conflicts of interest

There are no conflicts of interest.

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