The Prevalence of Cleft Lip and Palate and Their Effect on Growth and Development: A Narrative Review

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ABSTRACT

Cleft lip and/or cleft palate (CL±P) in addition to the cleft palate (CP) are a category of anomalies known as orofacial clefts (OC). These anomalies are accompanied by several aesthetic and functional problems. Information on the prevalence of OC showed different values between studies worldwide. In addition, the presence of cleft lip and/or cleft palate is determined by several changes during the embryonic stage. Besides, cleft repair may lead to a significant impact on the overall aesthetic and function and could negatively affect maxillary growth on certain occasions. Therefore, having the background and knowledge on this phenomenon is essential in designing the overall treatment and obtaining outcomes that are as close to normal as possible. This article reviews the maxillary development, occurrence of cleft lip and/or palate and their prevalence, facial growth in the presence of clefts, effect of cleft repair, an overview of alveolar cleft treatment, as well as the essential information related the prevention of cleft lip and palate.

Keywords: Alveolar bone grafting; cleft lip; cleft palate; maxilla; orofacial cleft (Siriraj Med J 2022; 74: 819-827)

INTRODUCTION

Cleft lip and/or cleft palate (CL±P) in addition to the cleft palate (CP) are a category of anomalies known as orofacial clefts (OC).[1] These anomalies are stated as significant congenital deformities in the oral and maxillofacial region and have a notable morbidity throughout the individual's lifespan, as well as complex etiology.[2] Several patients with OC do not present with other manifestations (non-syndromic OC), however, a good portion (30% to 50%) have other abnormalities that can be involved or presented as a syndrome (syndromic OC).[3]

Factors related to the etiology for the greatest number of incidences include genetic and environmental effects, in addition to the phenotypic differences that take action in early development.[4] Around 70% of the cases are listed as (non-syndromic) with complexity in their etiology, including environmental and genetic factors, in relation to a multifactorial threshold pumped by hereditary.[5] Mendelian/heterogeneous anomalies and teratogenic causes are the following possible etiologies.[6]

Clefts are normally accompanied by several aesthetic and functional problems, including the discontinuity of the lip, abnormal muscle attachments, phonetic issues,

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infections, tooth eruption within the clefts, oronasal fistula, and the deviation of alveolar segments. This will lead to speech problems in the case of large defects.[7,8] Certainly, patients with any type of cleft require critical care from birth until the adult stage.[9] This necessitates an understanding of the etiology, manifestations, associated issues, and possible complications that accompany this malformation, in order to provide acceptable treatment that will help restore the optimal function and aesthetics for these patients.

This article reviews the maxillary development, occurrence of cleft lip and/or palate and their prevalence, facial growth in the presence of clefts, effect of cleft repair, as well as an overview of alveolar cleft treatment.

Prevalence of cleft lip and/or palate

Information on the prevalence of OC showed different values between studies worldwide. The basic accepted estimation of OC prevalence is one in 700 infants. Moreover, the prevalence of cleft lip and palate is 9.9 per 10,000. Similar numbers were reported in the United States, with 10.2 per 10,000. In Japan, however, the prevalence of CL/P was twice that of the United States.[10] In a systematic review published in 2015, the prevalence of OFC birth was 1.57, 1.56, 1.55, 1.33, 0.99, and 0.57 in Asia, North America, Europe, Oceania, South America, and Africa, respectively. The highest prevalence rate was 2.62 per 1000 live-births among American Indians, followed by 1.73, 1.56, and 1.55 per 1,000 live-births among Japanese, Chinese, and whites, respectively.[9]

With regards to gender, males were found to have a higher chance of having CL/P and CL than females, while females were found to have CP at a higher rate than males. Females were more severely affected.[10,11] The most common cleft type was CLP, followed by CL and CP.[11]

According to European and American studies on non-syndromic cleft prevalence, unilateral cleft lip and palate (UCLP) is the most prevalent type, occupying 30-35% of the cases. Isolated CL and CP account for 20-25% of all cases, while bilateral cleft lip and palate (BCLP) is the most uncommon (about 10%), with submucosa and other clefts accounting for the rest.[12] As for the cleft palate, 30.2% had bilateral cleft and 69.8% had a unilateral cleft. The defect ratio on the right side was 41.1%, while on the left side it was 58.9%. CL is predominantly unilateral (around 90%), with approximately 2/3 (63.1%) of cases occurring on the left side.[13,14]

As can be noticed, CL and CLP tend to occur more frequently on the left side.[15] A possible reason for this higher incidence could be that development of the facial artery is slower on the left side compared to the right side. Moreover, the proximity of the blood vessels that supply the fetal head on the right side leaves the aortic arch closer to the heart, making this side possibly better perfused by blood than the left side.[11,13] This, however, has not been confirmed.

The incidence or birth prevalence of CLP in Thailand is known to vary by region. Oral clefts affect about 1.1-2.4 out of every 1000 live births. CLP was noted to occur more frequently than CL or CP alone, showing a percentage of 59.8, while CP had 21.9%, and CL had 18.3%.[15] Female patients showed relatively higher incidences of cleft lip or cleft palate alone, with CP 53.5% and CL 53.2%. On the other hand, male patients were more affected with cleft lip and palate (CL/P 58.3%).[16]

According to a study conducted in Thailand, more than half of CL/P patients were from the Northeastern region. In 2015, the average birth prevalence at Tawanchai Cleft Center was 1.51 per 1000 live births. Regarding cleft palate, Phisanulok had the highest CLP birth rate of 2.01 per 1000 live births, while Songkhla had the lowest rate of 1.06 CLP per 1000 live births. The CLP birth prevalence was 1.31, 2.01, 1.69, and 1.06 per 1000 live births in the Northeast, North, Center, and South, respectively,[17] as shown in Fig 1.

Embryology of cleft lip and palate

Cleft lip and palate are a defect resulting from the insufficient integration of facial prominences through the embryonic phase.

Maxillary bone growth

Changes in maxillary size have been well stated in the literature. The increase in the maxillary height occurs towards the frontal and zygomatic bones, as well as the lower aspect of the alveolar process. This takes place concurrently with the eruption of teeth in the maxilla. Growth in the length of the maxilla appears suturally directed to the palatine bones, accompanied by the maxillary tuberosities.[18]

Transverse palatine suture and tuberosity play an important role in elongating the maxilla in the anterior-posterior direction.[19] At the age of 13-15 years old, the hard palate had grown to its full length. The apposition appears to last for several years after this period. The posterior part of the palate was lower in the vertical direction than the anterior part of the palate.[20] Using the implant method, Bjork discovered that transverse growth is greater in the posterior than in the anterior. The median palatine suture grew at a rate comparable

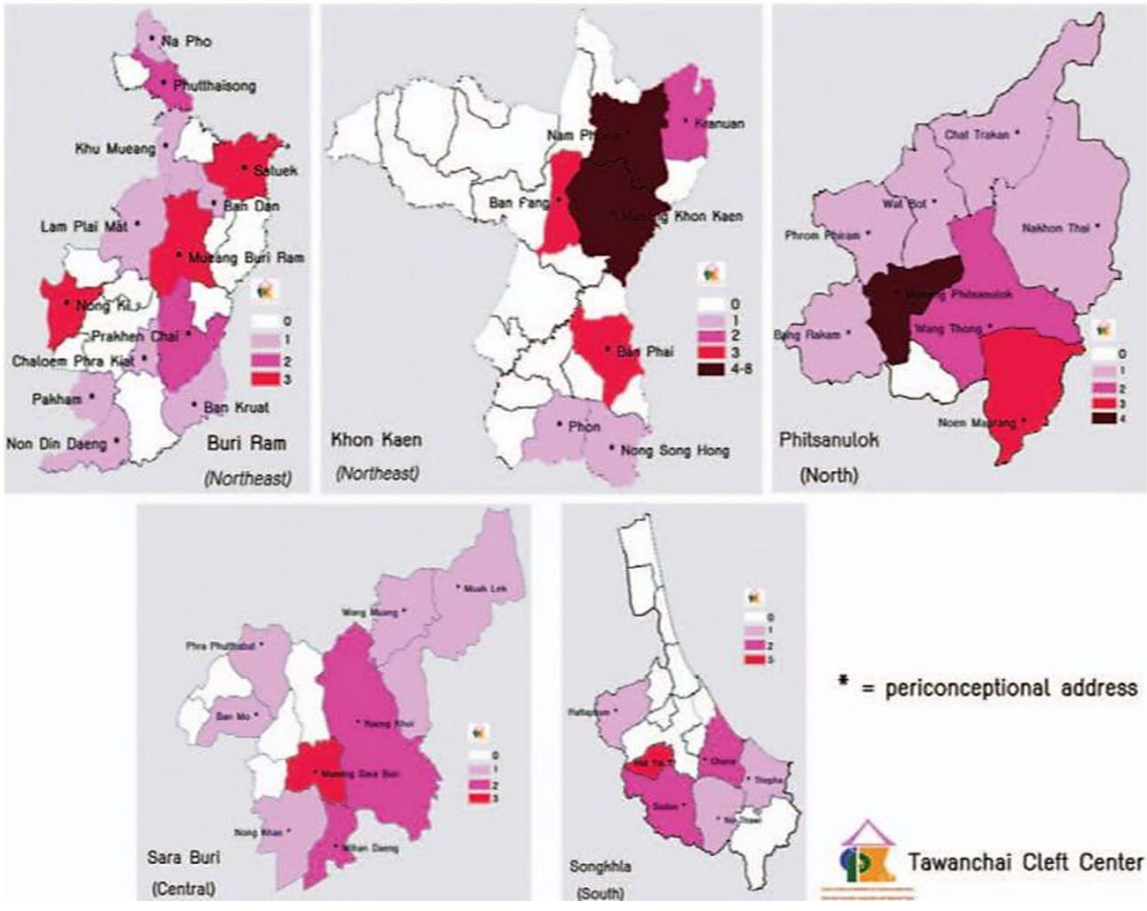

Fig 1. The number of newborns with CLP in 5 provinces by Tawanchai cleft center (Adapted from Chowcheun, 2015).

to that of the body height. The median suture grew two years faster than the rest of the body.[20,21] Sutural growth takes 18 years to complete, while body height growth takes 20 years. Sutural growth accounts for only about a quarter of the total width increase.[21]

The failure of the lateral palatine processes to meet and fuse results in a cleft palate. It takes place as a response to divergence from normal formation during frontonasal prominence development and fusion. This can be due to the lack of palatal shelf growth or the failure of these palatal shelves failure to rise above the tongue. Other factors such as the absence of any contact between the shelves, or any disturbance during or after fusion of the shelves will also result in cleft palate.[21] (Fig 2) The presence of cleft palate will cause a malformed maxillary process and distress the process of tooth eruption.[22] The most common cleft is situated in the area between the canine and the lateral incisor.[23]

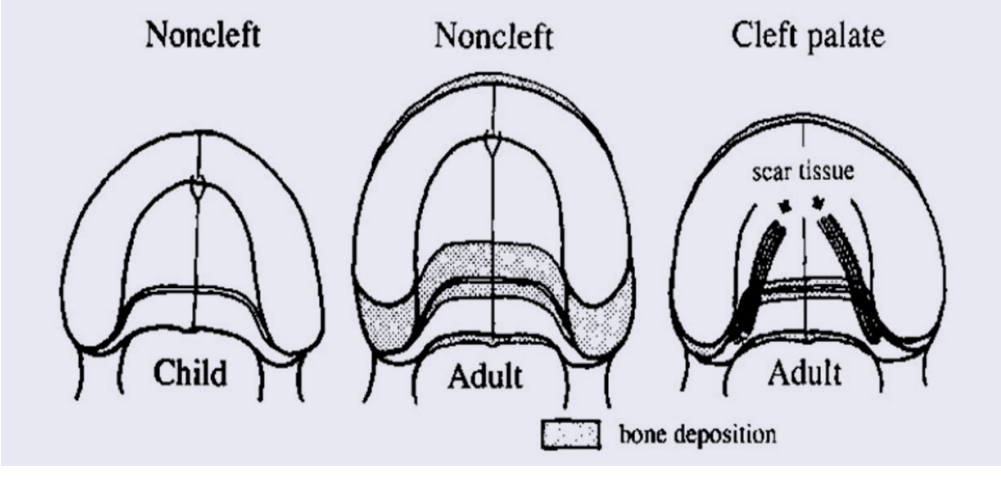

Fig 2. Growth of maxilla in non-cleft and cleft patients (adapted from Friede, 1998).

Surrounding soft tissue growth

The muscle systems that affect maxillary growth are composed of two different groups. The upper part of the orbicularis oris muscle and the nasolabial muscle ring represent the anterior facial muscle chain, while the posterior facial muscle chain consists of the deep facial and cervical muscle chains. The soft palate and tongue are supported by the upper part of the later ring, which provides momentum for the growth of the upper jaw, particularly the posterior and lateral aspects of the maxilla.[24,25] However, when clefts are present, the ossification takes place 2 weeks following the presence of muscle precursors. Consequently, bone formation occurs under the effect of asymmetrical muscular pull.[26] In addition, anatomical malformations that participate in the occurrence of cleft lip nasal defect involve a short columella, malpositioning of the lesser maxillary segment, as well as the displacement of the lower lateral cartilage.[27] (Fig 3)

Effect of cleft lip/palate on growth and development

Growth in cleft lip and palate

CL/P has an impact on craniofacial development due to a variety of factors, including inherent developmental deficiencies, functional distortions, and iatrogenic factors resulting from surgical treatment.[19] In patients with CL/P, the growth and form of the maxillary arch are affected in three planes: vertical, anteroposterior, and transverse. Skeletal class III in anteroposterior direction due to maxillary hypoplasia as a result of scar tissue. Occlusal canting, excessive freeway space, and altered mandibular posture were all found to be signs of vertical deficiency. In the transverse plane, a narrow maxilla with a lack of bony development, as well as scar tissue from previous palatal repair, can restrict maxilla growth.[28]

Patients with CL/P have trouble in the palatal suture system. The median palatine suture has an abnormal position lateral to the midline in complete unilateral clefts, and the segment on the cleft side has no sutural connection with the maxilla on the noncleft side in the untreated condition. The midpalatal suture is completely absent in the bilateral case, and the maxillary complex is divided into three parts.[21,28]

Considering the general growth of individuals with clefts, it has been documented that such patients have lower weight and are smaller in size, compared to children with no clefts. Becker et al[29] compared infants with isolated cleft palate, as well as cleft lip and palate, with the control group. Their results showed that these infants were lighter and shorter than the control subjects. Similarly, Jones[30] noticed that weight gain per week was lower in neonates with clefts, as opposed to normal individuals. In addition, Lee et al.[31] found that growth was disturbed during early infancy in patients with clefts. However, children reached their anticipated weight by the age of two. On the other hand, a study on a group of boys with clefts, that are aged between 6 to 20, indicated delayed skeletal maturity in these patients over the entire evaluation period, compared to the control group (subjects with no clefts).[32] All these data from previous studies suggest that clefts will have a potential impact on growth and development.

Effect of cleft lip/palate on food intake

As mentioned earlier, newborns with CL/P will have developmental delays. Aside from the genetic alterations that may lead to such incidences, food intake in cleft patients plays a role as a contributing factor. The main point is that a cleft lip, for instance, can result in issues in making a seal around the nipple when the infant is being breastfed, nevertheless, this may still be achieved in general.[33] In contrast, a cleft palate causes extreme difficulty for newborns, preventing them from generating the negative pressure that is essential for milk intake.[34] Moreover, having a cleft palate can also lead to problems in breathing while feeding. This will considerably prolong

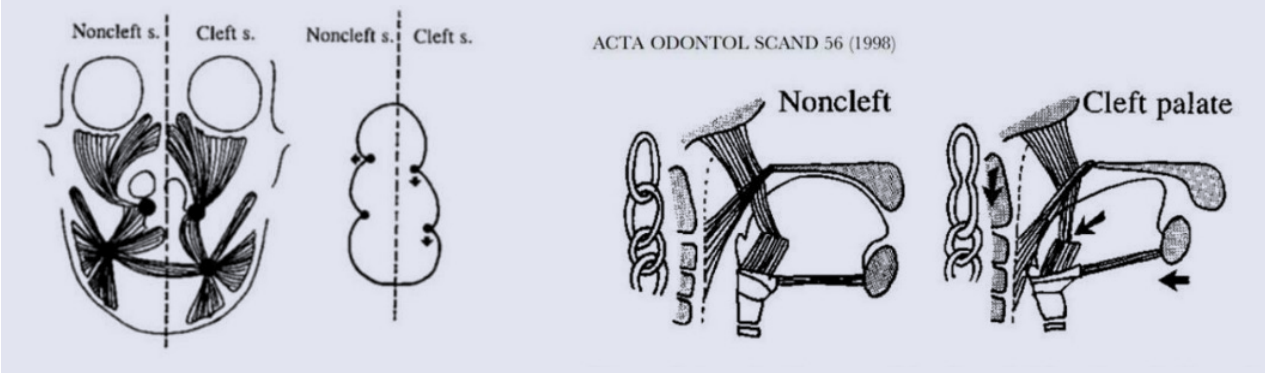

Fig 3. surrounding soft tissue affects growth (adapted from Friede, 1998).

the feeding time, keeping in mind that clefts of the hard palate also diminish the ability to utilize the tongue to compress the nipple and feed.

Based on all the mentioned problems with food intake that accompany children with CL/P, feeding is one of the main reasons why the surgical repair of clefts should be carried out and completed. Vries et al.[35] showed that the surgical repair of the palate led to a significant improvement in feeding, as reported by 79% of parents of children with cleft palate included in their study.

Effect of cleft lip/palate on speech and expression

Several investigations in the literature stated that patients with cleft lip and palate manifest problems with expressive language, as indicated by acquiring words and sounds at a slower rate, compared with individuals with no clefts.[36,37] Abnormalities in word production are seen in children with clefts due to the several factors; altered orofacial growth, anomalies in oronasal function and composition, affected neuromotor patterns during early development of infants, not to mention the disturbed psychosocial development for most of these individuals.[38] Children with cleft palate produce atypical consonants, have abnormal nasal resonance and airflow, and the laryngeal voice quality will also be impaired.[39] All these features will lead to what is termed "cleft palate speech". In addition, the major concern is that even with the early surgical intervention and the treatment of cleft palate, children still demonstrated delays in speech development and it was noted that they still had "cleft palate speech".[40] On the other hand, treating cleft lips resulted in better outcomes, as patients obtained age-suitable communication skills.[37]

Previous studies also showed that these early obstacles in language acquisition may continue throughout the childhood stage in some patients,[41] which reveals the importance of the early assessment of language acquisition and speech therapy for individuals with cleft lip and palate.

Growth in un-operated cleft patients

The growth of the maxilla in unoperated CL/P is similar to that of those without a cleft.[42] The cephalometric analysis revealed that the craniofacial growth pattern was normal, resulting in normal facial morphology.

Normal facial projection was seen in unoperated CL, with only dental arch malalignment in the cleft region. On the non-cleft side, the dental arch was normal, but there was medial collapse on the cleft side and lateral rotation of the premaxillary segment on the non-cleft side.[42,43] The nasal septum and columella were found to be shifted to the non- cleft side of the facial midline, while the incisor teeth shifted to the cleft side. Unoperated CLP, on the other hand, had a smaller and more protrusive maxilla, and the arch form was more V-shaped,[44] while unoperated cleft lip and alveolus showed greater premaxilla projection, increased maxillary length, prominence of the anterior teeth (labial tipping), a wider ANB angle, which represents the relative position of the maxilla to the mandible (Fig 4), as well as increased maxillary projection.[42]

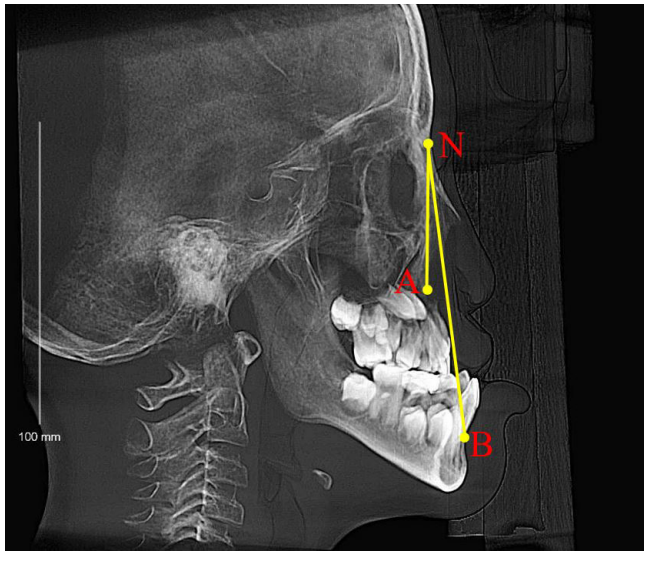

Fig 4. ANB angle of cleft lip and cleft palate patient.

Growth in operated cleft patients

Patients with CL/P can be treated by a multidisciplinary team of experts. From center to center, the surgical and orthodontic treatment schedules differ slightly. It usually includes the following components: infant orthopedics, surgical lip closure, surgical soft/hard palate closure, alveolar cleft bone grafting, orthodontic treatment, secondary lip and nose corrections, and maxillofacial skeleton osteotomies.

Early surgical closure of the lip and palate allows patients to return to normal in terms of both appearance and function. Early surgical treatment disrupted skeletal and dentoalveolar development. Negative consequences appear gradually during facial development, peaking when the patient reaches adulthood. On a skeletal level, the maxilla is frequently underdeveloped in three planes.

A transverse maxillary arch collapse often occurs on the dental level, resulting in a unilateral or bilateral crossbite, crowding, and retroclination of the upper incisors. The longitudinal study found that the growth curve for maxillary width in operated clefts differed significantly from that of normal clefts. The average increase in maxilla width from 10-11 years to adulthood

was 0.3 mm, which is significantly less than the growth in width observed for other transverse dimensions.[45]

The transverse maxillary width growth curve did not resemble the growth curve for body height. In these patients, the curve's shape was inhibited. The outcome is largely determined by the cleft type and the implemented method of surgery. Surgical procedures that may lead to osseous closure of the cleft should be postponed until the sutural growth of the upper part of the face has ceased, to reduce the adverse effects that cause reduction of total maxillary width and decrease the frequency of crossbite in cleft lip and palate patients.[25]

Surgical repair of a cleft is still thought to be the most important secondary factor in the development of specific transverse malocclusion. Bony ankylosis is formed, and scar tissue acts as fibrous ankylosis.

Effect from lip repair

During the months following birth, cleft lip procedure is normally performed, and the lip is closed. The impact of lip closure on the final development of the facial and skeleton, as well as tooth position, is disputable. Lip closure is regarded to have a minor influence by some authors.[45] Others, on the other hand, believe it has a significant impact on the final development of the face.[46] The effect of lip closure is limited to the anterior portion of the maxilla.

Effect from palatal surgery

The importance of palatal surgery for optimal speech development cannot be overstated. The operation to close the hard and soft palates is widely regarded as the most important factor in the development of dentoalveolar and facial growth problems. Palatal surgery may have a minor short-term effect on palatal growth, but because the posterior region continues to grow until maturity, it has no effect on palatal growth. Palatal surgery may have a significant limiting effect on the three-dimensional growth of the maxilla. It affects the upper face by shortening the maxilla and lowering the posterior maxillary height. With signs of an altered maxillary position in relation to the cranial base, the maxilla was retrognathic.[45]

Some authors believe that hard palate surgery is the most important factor in maxillary segment collapse, while others believe that lip closure is the most important factor. Most authors agree that palatal surgery appears to have a significant sagittal, vertical, and transversal impeding influence on the maxilla's development.

Alveolar cleft repair

An alveolar cleft is a well-explained inborn deformity that occupies 0.18–2.50 per 1000 births.[47] When cleft lip is present, alveolar clefts accompany this incidence in 75% of the cases.[48] when the fusion of the nasal process and oropalatal shelves does not fully manifest, this will result in alveolar clefts.[49] This malformation essentially involves the alveolar bone in the site of the canines and lateral incisors, with a possibility to include the central incisors as well.[50]

The guidelines of the surgical repair for clefts rely on obtaining sufficient closure of the mucosa of the nasal floor, aiming to terminate any contact between the nasal and oral cavities, augmenting this anomaly with bone grafts and reaching a proper seal of the oral mucosa on the palatal and labial aspects to attain a complete coverage over the grafted bone.[51]

Knowledge of etiology and risk factors is critical to set how prevention and treatment are planned and applied in the best way, in addition, to measuring the effectiveness of this specific intervention.[5] Bone grafting is a procedure that augments a defect or malformation in shape and size using biological materials,[52] based on the concept of bone regeneration, which is one of the major research fields and aims for craniofacial and orthopedic clinicians.[53]

This method in general has been implemented to treat patients with alveolar clefts as one of the important steps of the intricate treatment plan for cleft lip and palate repair.[54] Augmentation of defects associated with alveolar clefts is an essential part in the construction of bony flow of the dental arch,[22] thus, reestablishing the continuity of jaw segments and avoiding alveolar arch collapse. Bone grafts may also provide a suitable site for the eruption of the canines and can establish proper support for the periodontal tissues of maxillary incisors.[7] In addition, the grafted site offers support for the lip and takes part of the base for nasal floor elevation.[55]

Primary bone grafting (PBG) to repair the alveolar cleft using the rib bone during infancy was the dominant surgical procedure that was performed until the 1970s.[56] However, negative outcomes after PBG were noticed upon accurate examination and during the long-term follow-up, including anterior crossbite and midface retrusion. Conversely, positive results after secondary bone grafting (SBG) have been found.[57] Secondary alveolar bone grafting (SBG) is basically done during the mixed dentition stage of the patient, since the procedure during this stage will cause a minimal effect on maxillary growth.[47]

Moreover, optimal thickness of the bone graft is also a crucial aspect, as the prosthetic restoration might be inserted into the grafted portion in the absence of the desired eruption.[57] Nevertheless, a study was conducted

to evaluate the factors that may affect success when conducting alveolar bone grafting.[58] It was stated that older patients still ended the final follow-up with success. These patients attained bone continuity and healing (Bergland scale I or II), as well as the stabilization of the maxillary arch, without any complications or failure due to graft rejection, and no fistula formation up to one-year post-surgery. In addition, it is important to emphasize that the main idea of treating the alveolar clefts during the mixed dentition stage is to allow for canine eruption in the defect area, which took place inconsistently in the previous reports.[59,60] Therefore, the age of the patient is not likely a drawback that sets the surgical procedure far from success, as acceptable outcomes after bone grafting can still be achieved.

The iliac crest bone graft (ICBG) has been the most applicable grafting material for the secondary alveolar bone grafting procedure, since it provides a large volume of bone, is fairly easy to harvest, and the procedure can be done concurrently with the alveolar cleft preparation.[61] It is considered the gold standard for alveolar cleft repair, keeping in mind that the autogenous bone holds the three features of ideal bone formation; osteoconduction, osteoinduction, and osteogenicity.[62,63] The survival of ICBG is 84%, as stated by Oberoi et al.[64] A retrospective study reviewed cleft cases of 468 patient.[65] Cleft repair was performed at an age between 7 and 11 years.

It was concluded that the autogenous bone graft is a good option because it provides instant revascularization, can be placed easily in the cleft site, gives the possibility for the eruption of canine teeth in a suitable environment, and can be the graft for placing dental implants. The spongious bone allows faster healing of the defect than the cortical bone. Nevertheless, other sources of bone grafts are showing promising results that are comparable to the autogenous bone, with the valuable benefit of eliminating the second surgery and the donor site morbidity.[52] Therefore, future studies on the use of these grafts are of high importance, to confirm the outcomes provided by these alternatives to autogenous bone.

Prevention of cleft lip and palate

Prevention can be divided into 3 main categories. Primary prevention refers to blocking a disease process from starting. With respect to clefts, this could be achieved by eliminating any identified etiologic and risk factors. Secondary prevention entails the early diagnosis and treatment of this condition. In other words, prenatal diagnosis, as well as the earliest possible check-up at the hospital to obtain a thorough consultation, promptly manage this incidence and carry out the necessary treatment on time. When the possibility of primary prevention becomes inapplicable, and following secondary prevention, tertiary prevention is necessary. This focuses on psychosocial care and proper management of the condition, aiming to improve the patient's quality of life. Speech therapy to improve the patient's social life, in addition to later orthodontic treatment and orthognathic surgery to enhance function and aesthetics are essential steps in tertiary prevention. The most effective strategy to decrease the occurrence of cleft lip and palate is primary prevention.[66]

Environmental risk factors are also of importance in cleft lip and palate. These include maternal exposure to tobacco smoke, alcohol, poor nutrition, viral infection, medicinal drugs, and teratogens in early pregnancy. Moreover, advanced maternal and paternal age is known to result in gene mutation and chromosomal abnormalities. On the other hand, maternal use of multivitamin supplements in early pregnancy has been linked to decreased risk of orofacial clefts.[67] A previous meta-analysis concluded that the use of multivitamins resulted in a 25% reduction in birth prevalence of CL/Ps.[68]

Therefore, it becomes clear that best method for achieving an effective prevention of cleft lip and palate is likely to be the awareness of potential etiology and risk factors and proper counseling of physicians, which has been confirmed in previous reports.[67,69,70] Health care professionals must be fully informed about the various prevention strategies available, in order to deliver the necessary information and knowledge to parents, aiming to reduce the prevalence of cleft lip and palate in future generations.

CONCLUSION

Cleft lip and/or palate is a condition that necessitates critical and concise treatment planning and execution, keeping in mind all the factors that are involved in this phenomenon and all the possible manifestations and complications. This will ensure that each case will be handled with care, aiming to reach a result that is the closest to normal when possible.

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