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Review Article

Cleft Lip and Palate: A Review Article

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ABSTRACT:

Cleft Lip and Palate is severe birth defect occurring one in 700-1000 new-born infants. Cleft lip and palate together account for 50% of all cases whereas isolated cleft lip and palate occur in about 25% of cases. Management of Cleft Lip and Palate is carried out by multi-disciplinary team approach. Whenever a child is born with cleft lip and palate or one of them, it interferes with feeding and speech and hampers aesthetic severely. Consequently, it is psychologically traumatic to both patients as well as for their family members. Patients with cleft lip and palate are also are at high risk for dental diseases. So, in such situation proper education, guidance, motivation, and encouragement are required. Pre and post surgically paediatric dentist and orthodontics helps the patient by providing functionally and aesthetically acceptable occlusion, good oral hygiene, and preventive dental care. This paper describes the historical perspective, epidemiology, incidence, treatment protocol age specific intervention, multi center protocol and recent advancements.

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INTRODUCTION

As already been described regarding the orofacial defect in classical era, cleft lip and palate remains one of the main concerns in craniofacial surgery. Despite many diagnostic and technical aspect, it remains ambiguous, much progress has been achieved in understanding and treating this deformity.[1] The burden of disease and access to comprehensive care is disproportionate in low- and middle-income nations. Strengthening surgical and dental treatment, infrastructure is necessary to care for these patients throughout their initial development (Mars et al. 2008; Kling et al. 2014). Cleft lip and palate treatment is complicated due to the complex aetiologies. The formation of the complex craniofacial skeleton requires a complex genetic system with over 25,000 protein codes and over 17,000 genes. With variations seen in the types of cleft palate and lip, the clinical presentation of cleft lip and palate is further complicated by being associated with over 300 recognized syndromes.[2] However, greater understanding of the genetic mechanisms underlying embryologic facial development is encouraging for prevention efforts.

HISTORICAL PERSPECTIVE

Throughout history, many theories about the causes of cleft lip and palate have been proposed, including numerous folklore explanations. The Aztecs believed eclipses happened because a bite was taken out of the moon, and exposure to an eclipse during pregnancy could result in a bite out of the baby's mouth and they believe that pregnant women should cover their abdomens with obsidian knives before going out at night to avoid developing clefts. This belief was later extended to modern-day Mexico, where a metal key or safety pin is placed over the abdomen for protection during eclipses. An early Chinese belief was that eating rabbit during pregnancy could result in a "hare lip,"[3]and others believed that bad karma or wrongdoings were to blame. **Daack-Hirsh**[4] and colleagues surveyed among modern Filipinos is that clefts are caused by force to the foetal face. Clefts were thought to be familial or in the blood in many other cultures.

EPIDEMIOLOGY

Cleft lip and palate (CL/P) has a birth prevalence of 1:700 (Czeizel and Hirshberg(1997), Tolarona and Cervenka (1998), mosey and Little (2002)), ranging

from 1:500 to 1:2000 depending on race. Native Americans have the highest occurrence (3.6:1000), followed by Asians (2.1:1000 Japanese births and 1.7:1000 Chinese births), Caucasians (1:1000), and those of African descent have the lowest (0.3:1000). Cleft palate only (CP), which is genetically distinct from cleft lip and palate (CL/P), has a birth prevalence rate of 1:2,000 and is more prevalent in all populations. About half of all oral clefts (46%) involve both the lip and the palate, a third involve only the palate (33%) and 21% involve only the lip.[5] Among the cleft lip and palate population, the most common diagnosis is [6]: -

1. Cleft lip and palate at 46%, followed by isolated cleft palate at 33%, then isolated cleft lip at 21%.
2. Most bilateral cleft lips (86%) and unilateral cleft lips (68%) are associated with a cleft palate.
3. Unilateral clefts are nine times as common as bilateral clefts and occur twice as frequently on the left side than on the right.
4. Cleft lip and palate affect males predominantly, whereas isolated cleft palate occurs more commonly in females.
5. This racial heterogeneity is not observed for isolated cleft palate, which has an overall incidence of 0.5 per 1,000 live births.

INCIDENCE OF CLEFT

In India, the incidence of cleft lip and palate in the regional population was reported as 1:639 in a survey conducted by Christian Medical College in Vellore, Tamil Nadu, India. As a result, the overall incidence in live human births is 1:700. The overall incidence ranges between 0.3 and 6.5 per 1000 live births. With increasing parental age, the incidence rises. Patients with a family history of clefts and consanguine marriages are more likely to have clefts. Although there are more than 400 syndromes reported in association with cleft lip or cleft palate the three syndromes should receive special consideration.[7]

- Incidence varies from 0.3 to 6.5 per 1000 live births
- Mongoloid have the maximum incidence while Negroid race have minimum.
- Incidence of cleft lip is more common in males whereas cleft palate is more common in females
- Unilateral clefts are more common as compared to bilateral
- The left side has more predisposition for clefts
- Incidence is increased with an increase in parental age
- More chances of a cleft in patients with a family history of the same and in consanguine marriages.

ETIOLOGY

Cleft lip and palate development is thought to be influenced by both hereditary and environmental factors. Facial clefts can develop alone or as a result of a condition. The factors that can influence the formation cleft are as following: genetic factors, environmental influence, and syndromic clefts. Genetic linkage study findings on cleft lip and palate have suggested that several loci/genes, including those on chromosomes 1, 2, 4, 6, 14, 17, and 19 (MTHFR, TGFA, D4S175, F13A1, TGFB3, D17S250, and APOC2) may play a causal role in cleft lip and palate. Potential loci have also been suggested at 2q32-q35 and 9q21-q33. Some of the gene products include growth factors (such as TGFA, TGF-3), transcription factors (such as MSX1, IRF6, and TBX22), or factors that are involved in xenobiotic metabolism (such as CYP1A1, GSTM1 [glutathione S-transferase 1], NAT2 [N-acetyltransferase 2], nutrient metabolism (such as M (e.g., PVRL1, IRF6). The TGFA and MTHFR gene variations have received the greatest attention. It has long been known that there is a link between certain environmental factors (such as smoking, drinking, anticonvulsants, steroids, radiation, viral infections, and mechanical problems) during pregnancy and thus the likelihood of delivering a child with an orofacial cleft.[8] According to research, there is a 1:29 risk for CLP and a 1:32 risk for CP when a mother smokes[9]. Higher levels of alcohol consumption raise the incidence of both syndromic and nonsyndromic cleft [10]. The role of steroids as a risk factor has been clearly established. The risk of cleft does rise by 3.4 times with therapeutic doses of prednisone[11]. Cleft lip and palate are also predisposed to by exposure to radiation during pregnancy and viral illnesses. Mechanical elements resemble an effort to induce childbirth through uterine manipulation and hormone therapy. Study by **Puho *et al.*,**[12] suggested that phenytoin, carbamazepine, oxytetracycline, thiethylperazine has a possible association between oxprenolol and amoxicillin in inducing orofacial clefting. According to **Darab *et al.*** and **Powell and Ekert**, maternal use of Methotrexate (MTX) has also been associated with cleft lip and palate.[13] Study by **Diaz H**[14] suggested that the use of folic acid antagonist in early pregnancymay increase the risk of oral clefts particularly among the infants of women who do not use multivitamin containing folic acid.

CLASSIFICATION

Cleft lip &/ Palate will be classified as: Morphological and Embryological.

MORPHOLOGICAL

VEAU CLASSIFICATION[15]

Veau proposed the following classification in 1931.

Group I (A) - Defects of the soft palate only.

Group II (B) - Defects involving the hard palate and soft palate extending no further than the incisive foramen, thus involving the secondary palate alone.

Group III (C) – Complete unilateral cleft, extending from the soft palate to the alveolus, usually involving the lip.

Group IV (D) - Complete bilateral clefts, resembles Group III but is bilateral. When cleft is bilateral, pre-maxilla is suspended from the nasal septum.

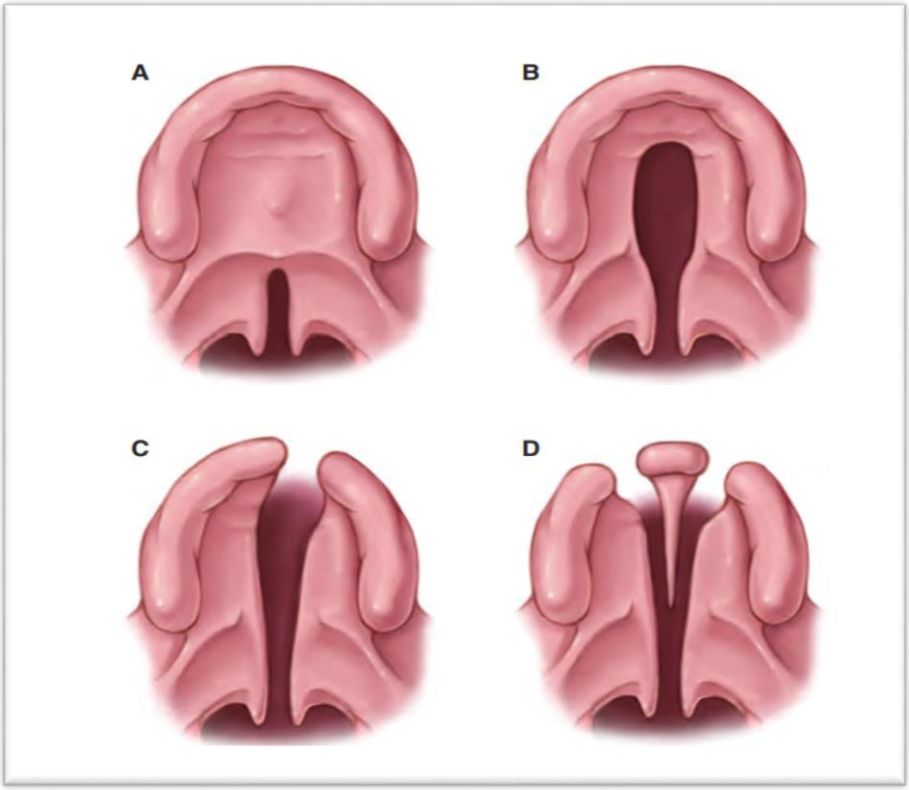

Figure 1: Veau classification. **A:Type 1, B:Type 2, C:Type 3, D:Type 4**.

LAHSAL Classification:

Kreins O (**Hodgkinson *et al***)[16] proposed the LAHSHAL system for classification of cleft lip and palate patients which was modified on the recommendation of Royal College of Surgeons Britain in 2005 by omitting one "H" from the acronym "LAHSHAL". LAHSAL system is a diagrammatic classification of cleft lip and palate as shown in Figure 2.

According to this classification, Mouth is divided into six parts.

- Right lip
- Right alveolus
- Hard palate
- Soft palate
- Left alveolus
- Left lip

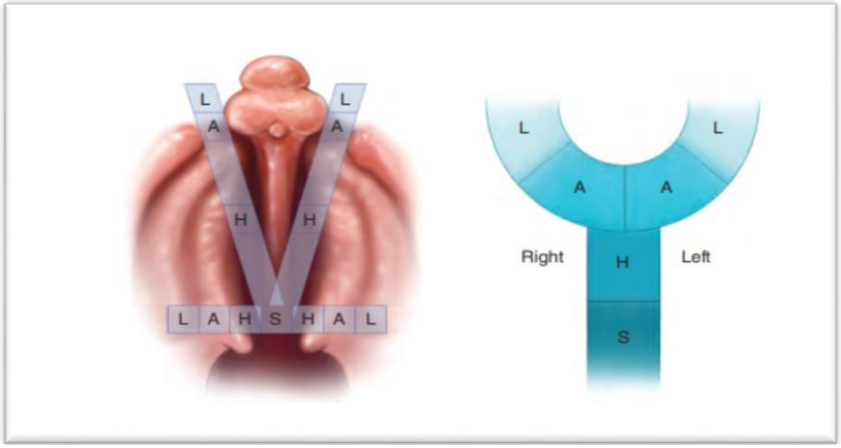

Figure 2: LAHSHAL (Lip, Alveolus, Hard palate, Soft palate, Hard palate, Alveolus, Lip) classification in which a letter is assigned to each portion of the orofacial anatomy to denote the location of the cleft. The use of uppercase and lowercase letters indicates whether the cleft is complete or incomplete, respectively.

❖ **EMOBROYOLOGICAL**

Kernahan striped Y Classification: Kernahan[17] proposed this classification in 1971. This system provides a graphic classification scheme using Y-configuration as shown in the figure 3.

- Areas 1 and 4 - Lip (It represents the fusion line between the maxillary prominence and medial nasal prominence at lip level).

- Areas 2 and 5 – Alveolus (It represents the fusion line between the maxillary prominence and intermaxillary segment).
- Areas 3 and 6 – Primary Palate (It represents the fusion line between the primary and secondary palate and lies anterior to the incisive foramen).
- Areas 7 and 8 - Hard palate (It represents the fusion line between palatine shelves of the hard palate posterior to the incisive foramen).
- Area 9 - Soft palate The small circle represents incisive papilla. In order to show the cleft, stippling of the appropriate areas is done on the below diagram.

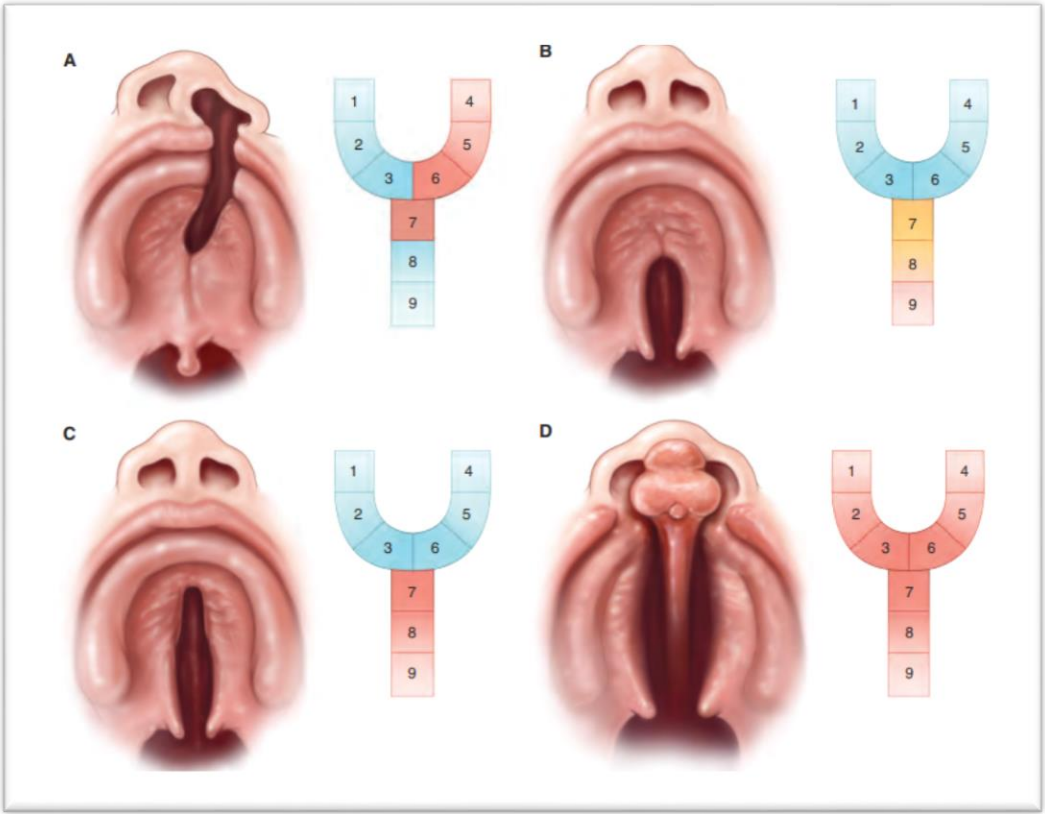

Figure 3: Kernahan and Stark "striped Y" classification and examples of scores based on affected areas. Areas 1 and 4, lip; areas 2 and 5, alveolus; areas 3 and 6, palate between the alveolus and the incisive foramen; areas 7 and 8, hard palate; area 9, soft palate. Red indicates complete cleft. Yellow indicates incomplete cleft. A, 4, 5, 6, 7: A left complete cleft of the lip, alveolus, and anterior palate. B, 8, 9: Incomplete (submucous) cleft of the hard palate and complete cleft of the soft palate. C, 7, 8, 9: Complete cleft of the hard and soft palate. D, 1-9 complete bilateral cleft lip, hard palate, and soft palate. L, patient's left side; R, patient's right side.

❖ INDIAN CLASSIFICATION

Indian classification as presented by Prof. Balakrishnan (1975)[18]:

Cleft type	Original abbreviation
Cleft lip	Gp1
Cleft palate	Gp2
Cleft lip, alveolus and palate Right Left Midline Alveolus	Gp3 R L M A
Additional abbreviation: Partial	 p
Submucosal	S
Simonart's band	Sb
Microform	Micro

DIAGNOSIS

Orofacial clefts can be detected intrauterinally using ultrasonography. Complete clefts may usually be observed after 17 weeks of pregnancy, although incomplete clefts are easier to see after 27 weeks. Palatal clefts are difficult to find with prenatal ultrasound. Both routine screening and high-resolution ultrasonography can be employed for prenatal diagnosis. More and more often, MRI is used to examine foetal defects that are difficult to detect with just sonography. Foetal MRI is less reliant on the optimal amniotic fluid volume, the location of the foetus, and the maternal body habitus than is sonography. Furthermore, bone shadowing does not stop an MRI from imaging small structures. Other physical anomalies are sometimes associated with CL/P such as velopharyngeal insufficiency (VPI), when VPI is suspected two simple investigations are undertaken: multiview videofluoroscopy (moving X-rays while speaking) and nasopharyngoscopy, this technique allows (most appropriate for children at the age of 3-4 years old), using a flexible fiberoptic endoscope with a camera to have a superior view of the velopharyngeal valve.[19]

PARENTAL COUNSELLING

Parents must adhere to a protocol for future dental care. In collaboration with other experts, we as a Paediatric Dental Surgeon established this procedure to offer comprehensive care for patients with cleft lip and palate.

1) **At Birth**- Parents should receive advice regarding predental care that aids in proper child feeding using a feeding bottle or acrylic plate so that the child can have the adequate nutrition along with it Presurgical orthopaedics, which aids the surgeon in repair by promoting palatal bone growth and preventing the collapse of dental arches, should be discussed with parents.
2) **3 to 5 months**- Parents will receive advice on how to fix the lip, as well as a referral to an ENT surgeon or audiologist for the child's audiological evaluation.
3) **9-12 months**- Pedodontic examination for any anomalies in eruption. At this age, palate repair should be performed, then speech therapy. Due of velopharyngeal incompetence at this age, parents should give their child special attention.
4) **2 to 6 years**- Special attention should be given to the youngster at this age to promote facial growth and development. Also offering carriers restorative care. Due to voice development, velo-pharyngeal incompetence can be treated at this age.
5) **6 to 7 years**- Early or preventive orthodontic treatment that addresses issues like crossbites and the removal of supernumerary teeth.
6) **6 to 9 years**- The surgeon will provide parents with advice regarding secondary bone grafting, fistula closure (if any), and secondary palate repair. For proper speech and hearing ability, the patient will be referred to an ENT surgeon and a speech therapist.
7) **14 to 16 years**- The orthodontist will correct your teeth, and a speech therapist will examine your voice pitch changes. Parents should receive advice regarding orthognathic surgery for face differences, if necessary.
8) **16 to 20 years**- Patients or their parents are advised to undergo corrective rhinoplasty or secondary scar revision because they are increasingly concerned with their child face appearance (if required).

PSYCHOSOCIAL AND PSYCHOLOGICAL PROBLEMS

Although there is a significant amount of research on the psychosocial outcomes in cleft lip and palate patients, there is relatively little on the psychological profile of unoperated cleft lip and palate. The severity of these issues is apparent in such people, though. Due to facial abnormalities and communication issues, most of these individuals are school dropouts or have never attended school. They are frequently mistreated by teachers as well as with their peers. These people experience more behavioural issues, depressive episodes, and low self-esteem. They endure constant tormenting and are dissatisfied with their morphological traits and verbal abilities. They coexist with their family members and are socially reclusive due to all these complicated psycho-social repercussions of untreated cleft lip and palate.[20]

TREATMENT PLAN

AGE SPECIFIC INTERVENTION[5,16]

AGE RANGE	INTERVENTION
Prenatal	• Refer to cleft lip palate team • Medical diagnosis and genetic counselling • Address psychosocial issues • Provide feeding instructions • Make feeding plan
Birth-1 month	• Refer to cleft lip palate team • Medical diagnosis and genetic counselling • Address psychosocial issues

	• Provide feeding instructions and monitor growth • Begin presurgical orthopaedics if indicated
1–5 months	• Monitor feeding and growth • Repair cleft lip • Monitor ears and hearing Begin, continue presurgical orthopaedics if indicated
5–15 months	• Monitor feeding, growth development Monitor ears and healing; consider ear tubes if indicated • Repair cleft palate • Instruct parents in oral hygiene
16–24 months	• Assess ears and hearing • Assess speech-language • Monitor development
2–5 years	• Assess speech-language; manage VPI • Monitor ears and hearing • Consider lip nose revision before school • Assess development and psychosocial adjustment.
6–11 years	• Assess speech-language; manage VPI • Orthodontic interventions • Alveolar bone graft • Assess school psychosocial adjustment
12–21 years	• Jaw surgery, rhinoplasty (as needed) • Orthodontics: bridges, implants as needed • Genetic counselling • Assess school psychosocial adjustment

INTERNATIONAL MULTICENTRE PROTOCOL [21]

The protocol provides parameters for the care of children with cleft lip and palate, in an interdisciplinary range of expertise including anaesthesiology, dentistry, genetics, nursing, plastic surgery, oral and maxillofacial surgery, orthodontics, otolaryngology, pediatrics, psychology, public health, radiology, and speech-language pathology (Bennun & Manassero, 1988; Lee, 1999; Shaw et al., 2001).[21]

Prenatal diagnosis	▪ Parent's consultation with the team coordinator. ▪ Family handling and understanding of diagnosis and treatment needs. ▪ Indication of main interventions
Supporting delivery:	Avoid baby separation from parents, oral tube utilization, and prolonged hospital stay.
Orofacial dysmorphology:	▪ Participate in the diagnosis and collection of pertinent records. ▪ Distinguish between syndromic and nonsyndromic.
Oral health:	▪ Oral examination. ▪ Dentist should collect an impression to build the oral plate. ▪ Early presurgical treatment.
Psychosocial support:	▪ Address barriers to medical and healthcare with family. ▪ Monitor parent–child issues. ▪ Referral to parent support groups.
Suction:	▪ Assess feeding and swallowing with interdisciplinary team
Speech and language support:	▪ Counsel parents on early stimulation development. ▪ Assessment of early vocal output and communicative behavior.
General pediatric health:	▪ Paediatric care provider screening and presurgical evaluation.
ENT health:	▪ Physical assessment of oral and pharyngeal structures. ▪ Middle ear status diagnosis.
Surgical reconstruction:	▪ Lip and nose primary reconstruction from 2 to 6 months.
Anaesthesiology:	▪ The airway skills of an experienced paediatric anaesthesiologist are required to provide clinical care during operative procedures in order to maximize success and minimize risk. The use of local and regional anesthesia with epinephrine as a complement is useful in reducing bleeding, pain, and general anesthesia dose, and to

	allow ambulatory care surgeries.
Oral health:	▪ Nasal component removing and oral plate adaptation. ▪ Caries prevention anticipatory guidance.
ENT health:	Follow-up for patients with recurrent infections, hearing loss, Eustachian tube dysfunction, myringotomy tube indication.
General Paediatric health:	▪ Paediatric care provider screening and presurgical evaluation.
Surgical reconstruction:	▪ Complete cleft palate closure from 8 to 14 months. ▪ Myringotomy tube insertion.
Complete diagnostic assessment (2 years):	▪ Address barriers to medicine and healthcare within family. ▪ Speech and language development. ▪ Facial growth and development. ▪ Scars and aesthetic evaluation.
Complete sequels detection (4–6 years):	▪ Annual Paediatric care provider screening. ▪ Monitor dental development and malocclusion. Assess Eustachian tube dysfunction, recurrent infections, sleep apnoea, airway issues. Monitor school achievement, screen for precursors of learning disability, and assess emotional and behavioural functioning. Evaluation of language comprehension and competence, and phonologic and phonetic development.
Complete sequels treatment (6–12 years):	▪ After permanent teeth eruption orthodontics treatment must be implemented. ▪ The interdisciplinary team must be ready to solve any dysfunctional condition.

RECENT ADVANCEMENT

❖ **ROBOTIC-ASSISTED TRANSORAL CLEFT PALATE SURGERY (TORCS)**[22,23,24]

A successful surgical outcome following cleft palate surgery depends critically on a proper palatal muscle repair. This result is deemed to be ideal when both velopharyngeal competence and Eustachian tube performance are enhanced. Several researchers proposed that preserving the palatal muscles' vascularization and innervation during their dissection, repositioning, and suturing would improve the function of the Eustachian tube. The 3D endoscopic vision offered by surgical robots offers the surgeon a true sense of depth. The micro endoscopic tools can move more freely thanks to this vision, which simulates their flexion, extension, pronation, and supination. The aforementioned benefits enable better surgical precision and more gentle manipulation of sensitive tissues (Haus et al., 2003; Hockstein et al., 2005). Additionally, robotic technology features scaling of movement, which reduces tremor by converting large hand movements into few instrument movements. The uncomfortable and painful body postures that arise during traditional palatal surgery are eliminated by an ergonomic position on the surgeon's console, which may have an impact on the procedure's success. The robotic surgical system's lack of "natural" tactile feedback could be a drawback. Although the robotic system's high-resolution 3D imaging compatibility effectively makes up for the absence of touch by maximising the value of visual cues. TORCS has the potential to help patients with cleft palate rebuild their palatal muscles, but more research and instrument development are necessary. To make sure that this strategy is safe, further extensive research will be needed in the future.

❖ **TISSUE ENGINEERING AND REGENERATIVE MEDICINE: EVOLVING APPLICATIONS TOWARDS CLEFT LIP AND PALATE SURGERY**[25]

Tissue engineering is a recent therapeutic approach for bone healing. Immune rejection, pathogen cross-contamination, and donor site morbidity would all be concerns that this method would solve. The idea behind bone tissue engineering is to remove cells from the patient's tissues and place them temporarily on a scaffold before re-implanting them. The cell sources for hard tissue engineering should integrate with the environment and have the ability to differentiate into osteoblasts. The alveolar cleft defect in a 9-year-old patient was filled using tissue engineering techniques, as demonstrated by Hibi et al., 2006, who used a gel matrix, platelet-rich plasma (PRP), and autologous MSCs from bone marrow taken from the patient's iliac crest. 9 months post-surgery, the bone volume increased to 79.1% of the preoperative level. The maxillary lateral incisor and canine teeth, which were next to the defect, also emerged out two years after the procedure, according to the authors. It was concluded that tissue engineering holds promise for treating cleft palates, although cell sources and tissue engineering materials still need to be improved. To promote matrix production and tissue regeneration, PRP—which

contains fibrinogen and chemical agents such vascular endothelial growth factor (VEGF)—was added. The therapeutic outcomes of tissue engineering repair vary based on each patient, taking into consideration factors including gender, age, habitual behaviours like sucking, underlying diseases, and architecture. The vascularization and functional stresses will vary amongst the distinct sites of the maxillofacial bone. The difficulties in tissue engineering therefore lie in regulating these settings and in vitro cell differentiation prior to implantation. This plan will help accelerate further healing.

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