Review Article

Cleft of lip and palate: A review

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Abstract

Cleft of lip and palate are most common serial congenital anomalies to affect the orofacial region . It can occur isolated or together in various combination and/or along with other congenital deformities particularly congenital heart diseases. .Patient with oro-facial cleft deformity needs to be treated at right time and at right age to achieve functional and esthetic well being. Successful management of the child born with a cleft lip and palate requires coordinated care provided by a number of different specialties including oral/maxillofacial surgery, otolaryngology, genetics/dysmorphology, speech/language pathology, orthodontics, prosthodontics, and other. This article aims to the review the point primary care physicians in literature knowledge about cleft lip and palate. A review of literature have made to discuss introduction, epidemiology, clinical feature, etiology factor and management of cleft lip and palate.

Keywords: Cleft lip, cleft palate, congentiel anomelies, genetic and environmental factor

Introduction

These are the most severe of congenital anomalies which affect the mouth and related structures. The roof is shaped from the palate and flooring from the constructions at the floor of the mouth. Laterally, it's bounded from the cheeks.[1] A cleft is a congenital abnormal space or gap in the upper lip, alveolus, or palate. The colloquial term for this condition is harelip. The use of this term should be discouraged due to its demeaning connotation of inferiority. The more appropriate terms are cleft lip, cleft palate or cleft lip and palate.[2] So cleft lip and cleft palate can be defined as:

Cleft lip: The failure of fusion of the frontonasal and maxillary processes, resulting in a cleft of varying extent through the lip, alveolus, and nasal floor (an incomplete cleft does not extend through the nasal floor, while a complete cleft implies lack of connection between the alar base and the medial labial element).[3]

Cleft palate: The failure of fusion of the palatal shelves of the maxillary processes, resulting in a cleft of the hard and/or soft palates.[3] Clefts arises during the fourth developmental stage. Exactly where they appears is determined by locations at which fusion of various facial processes failed to occur, this in turn is influenced by the time in embryologic life when some interference with development occurred.[4]

Clefts of lip and palate can occur isolated or together in various combination and/or along with other congenital deformities particularly congenital heart diseases. They are also associated features in over 300 recognized syndromes.[5] In the developed world, most scientists believe that clefts occur due to a combination of genetic and environmental factors (e.g., maternal illness, drugs, malnutrition). In developed countries, CL/P is typically identified before birth by ultrasonography. Early detection allows time for parental education about the potential

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causes of the CL/P and procedures that the child may need after birth. Consequently, due to the widespread access to medical care in developed countries, although beliefs unsupported by science (e.g., superstitious beliefs) do exist, scientific causal beliefs are the most commonly endorsed (Nelson *et al.*, 2009).[6]

In contrast, in developing countries where prenatal care is less advanced or less available, a CL/P is usually unexpected and families rely less on medical explanations for the cleft from doctors and rely more on religion and folklore to explain the deformity. For example, individuals in India who practice Hinduism believe that a CL/P is the result of sins from a past life (Weatherley-White *et al.*, 2005). Other religious and cultural beliefs regarding causation of clefts include witchcraft, God's will, and engaging in a behaviour associated with causal power (e.g., looking at a child with a facial deformity when pregnant).[6]

Overall incidence of cleft lip and palate is approximately 1 in 600 to 800 live births (1.42 in 1000) and isolated cleft palate occurs approximately in 1 in 2000 live births. Thus, the typical distribution of cleft types are[5]:

1. Cleft lip alone – 15%
2. Cleft lip and palate – 45%
3. Isolated cleft palate – 40%.

The potential problems of the condition include social handicaps such as impaired suckling and resultant failure to thrive, speech impediment, deafness, malocclusion, gross facial deformity and severe psychological problems. The clefting of lip and/or palate occurs at such a strategic place in the orofacial region, at such a crucial time (before birth) that it becomes a complex congenital deformity.[5]

Patient with oro-facial cleft deformity needs to be treated at right time and at right age to achieve functional and aesthetic well-being. The treatment process is complex, multidisciplinary and interdisciplinary approach.[7] Successful management of the child born with a cleft lip and palate requires coordinated care provided by a number of different specialties including oral/maxillofacial surgery, otolaryngology, genetics/dysmorphology, speech/language pathology, orthodontics, prosthodontics, and other. This successful reconstruction routinely requires multiple phase of surgical intervention.[8,9]

Ethical approval

This research did not need any informed consent because we did library research. References and quotations were written based on the journal guidelines.

Epidemiology

Overall incidence of orofacial clefting is around 1.5 per 1000 live birth (about 220,000 new cases per year) with wide variation across geographic areas, ethnic group and nature of cleft itself.[10]

The incidence appears high among Asians (0.82 – 4.04 per live births) intermediate in Caucasian (0.9 – 2.69 per 1000 live birth) and low in Africans (0.18 – 1.67 per 1000 live births). Chinese showed 1.76 per 1000 live birth, while Japanese reported 0.85 to 2.68 per 1000 live birth of orofacial clefting.[11]

Isolated CL comprises about 25% of all clefts, while combined CL/P accounts for about 45%. CL/P occurs more frequent and more severe in boys than in girls. Unilateral clefts are more common than bilateral clefts with a ratio of 4:1, and for unilateral clefts, about 70% occur on the left side of the face. Cleft palate is seen more frequently in females than in males. CL/P is frequently associated with other developmental abnormalities and majority of cases are presented as part of a syndrome. Syndromic clefts account for about 50% of the total cases in some reports with about 300 syndromes described. Although the percentage of cases directly linked to genetic factors is estimated to be about 40%, all clefts appear to show a familial tendency.[10]

Various epidemiological studies show that, if one parent affected with a cleft has a 3.2% chance of having a child with cleft lip and palate and a 6.8% chance of having a child with isolated cleft palate (Grosen *et al.*, 2010). Presence of a cleft in one parent and in one sibling is associated with a 15.8% chance that the next child will have a cleft lip or palate, and a 14.9% chance that the next child will have a cleft palate (Christensen *et al.*, 1996). In case where parents with one is child affected with a cleft have a 4.4% chance of having another child with a cleft lip and palate and a 2.5% chance of having a child with isolated cleft palate.[7]

Embryology

Throughout this time, the fundamental morphology of the face is shaped using the combination of the five fundamental facial prominences. CLP happen as a result of incomplete mix and integration of rectal protrusions, which generates the delicate and strong tissues that form the roof of their mouth. Cleft lip happens because of the failed mix between 4th and 6th months of pregnancy, whereas the cleft palate occurs between the 6th and 12th months of pregnancy.[12] To understand the reason behind oral cleft a review of lip, nose, and palate embryology is essential. The whole procedure occurs between the 5th to 14th days of life.[1]

It is that the "critical period" of embryonic confront. It's that time period through which the human craniofacial morphogenesis usually is vulnerable to known or suspected birth defect generating brokers, or teratogens.[12]

Etiology

The etiology of cleft lip and palate is complex and thought to involve genetic influences with variable interactions from environmental factors. The etiological factors of cleft lip and palate can be grouped as under:

A. **Non-genetic**: this includes various environmental (teratogenic) risk factors which may cause CL/P.

B. **Genetic**: Genetic cause includes:

(1) Syndromic: Here cleft is associated with other malformation. Usually it is due to a single gene (monogenic or Mendelian) disorder.

(2) Non-syndromic: Here the cleft is mostly an isolated feature and occurs in the vast majority of individuals having a cleft lip or palate (up to 70% cases). In this form, a cleft is neither a recognized pattern of malformation nor a known cause for the disorder can be identified.[13]

Non-genetic factors: Besides genetic factor environmental factors also play a very important role in etiology of CL/P.[14] Various environmental factors includes:

a) Smoking: The relationship between maternal smoking and CLP is not strong, but it is significant. Several studies have consistently yielded a relative risk of about 1.3–1.5. When maternal smoking was considered together with a positive genetic background, the combined effect was more significant. Furthermore, Beaty *et al.*(2002) reported that maternal smoking and infant *MSX1* genotypes acted together to increase the risk for CLP by 7.16 times.[14]

b) Alcohol use: Heavy maternal drinking, apart from causing fetal alcohol syndrome, also increases the risk of CLP. Munger *et al.* (1996) showed that maternal drinking increased the risk for CLP by 1.5–4.7 times in a dose-dependent manner Low-level alcohol consumption, however, did not seem to increase the risk of orofacial clefts. The link between alcohol consumption and genotypes on the risk of CLP has yet to be demonstrated.[14]

c) Others: Environmental factor includes maternal diseases, stress during pregnancy chemical exposure.[13] Decreased blood supply in nasomaxillary region.[15] increased maternal and parental age are also said to increase risk of cleft lip with and without palate while higher parental age has been associated with cleft palate only.[16] Fetal exposure to retinoid drugs can results in severe craniofacial anomalies.[17]

Genetic factor: Various epidemiological observation have laid the foundation of role of genetics in etiology of cleft lip and palate. Many studies have shown that monozygotic twins (60%) have considerable higher concordance rate than dizygotic twins and siblings (5-10%).[13,16,18]

Syndromic form of cleft lip and palate: It accounts for more than 400 known syndromes and many of them follows classic Mendelian inheritance pattern.[13,16,18] In some of the syndromes with cleft lip and palate genes have been identified and are listed as under [Table 1].

Non-syndromic form of cleft lip and palate: It accounts for 70% of CL/P cases and 50% of all CPO cases. These associated studies have identified many genes for clefting whose mutation may lead to non-syndromic cleft lip and palate [Table 2].[13,16,18]

Clinical Features

To date, few studies have evaluated the knowledge and experience of primary care physicians regarding the physical, dental, and behavioural/emotional needs of a child with an oral cleft.[19,20]

The various clinical findings in patient with cleft lip and palate can be categorized under two headings:

Dental problems in cleft lip and palate

Various abnormal dental conditions includes:

1. Natal and neonatal teeth:

Presence of neonatal teeth does not appear to influence primary or secondary dentition in clefts. Most natal teeth among clefts are located in the lateral margin of the premaxillary and maxillary segments unlike in non-cleft neonates.[21,22]

2. Microdontia

Small teeth (microdonts) frequently are found with CL/P. This is usually more common in cases where lateral incisors are not missing (van der Wal, 1993; Stahl *et al.*, 2006;Rawashdeh and Bakir, 2007). Generally peg shaped upper lateral incisors are seen.[21]

3. Taurodontism

Taurodontism has been reported to be associated with certain syndromes and dental developmental disorders (Cichon and Pack, 1985).[22]

4. Ectopic eruption

Clefts also contribute to the ectopic eruption of primary lateral incisors which may erupt palatally adjacent to or within the cleft side while permanent canine on side of alveolar clefts may erupt palatally. Delayed eruption of permanent incisors may be seen.[22,23]

5. Enamel hypoplasia

Enamel hypoplasia was found to occur more frequently in CL/P subjects compared with non-cleft populations, especially involving the maxillary central incisors (Vichi and Franchi, 1995).[22]

6. Delayed tooth maturation

Several growth factors are of major importance during craniofacial development, and these factors may be overexpressed or underexpressed when a cleft defect occurs. This aberrant expression can modify odontogenesis and cause abnormalities of the dental lamina.[24]

Other associated conditions

1. **Speech difficulties**

Due to the dysfunction of m. levator veli palatini muscle phonation are affected. Retardation of consonant sound (p, b, t, d, k, g) is most common findings. Abnormal nasal resonance

Table 1: Syndromic form of cleft lip and palate

Syndromes	Gene name (symbol)	Location on chromosome	Inheritance
Waardenburg syndrome, type II A	Microphtalmia associated transcription(MLTF)	3p14,1-12,3	AD
Di George syndrome	Di George syndrome chromosome region (CATCH 22)	22g11	AD
Treacher - Collins mandibulofacialdysostosis	Treacle (TCOF1)	5q32-q33,1	AD
Van der woude syndrome	Interferor regulatory factor - 6 (IRF 6)	1q32-q41	AD
CLP-Ectodermal dysplasia syndrome	Poliovirus receptor related-1(PVRL-1)	11q23,3	AD
Ectrodactyly, ectodermal dysplasia orofacial cleft syndrome	P 63	3q27	AD
Zollinger syndrome-3	Peroxisomalmembrame protein-3 (PXMP3)	8q21,1	AD
Diastrophic dysplasia	Diastrophic dysplasia sulphate transporter(DTDST)	5q32-q33,1	AD
Gorlin syndrome (Basal cell nevus syndrome)	Patched (PTCH)	9q22,3	AD

Table 2: Possible genes whose mutation may result in non syndromic clefting

Name of gene	Symbol	Chromosome location
Transforming growth factor - alpha	TGFA	2p13
Transforming growth factor - 133	TGF 133	14q24
Methylene tetra - hydrofolateReductase	MTHF3	1p36,3
Blood clotting factor XIII gene	ET1	6p24
Endothelin - 1 gene	ET1	6p24
Proto-oncogene BCL3	BCL3	19q13,2
Retinoic acid receptor alpha gene	RARA	17(t15/17)
MSX-1	MSX-1	4q25

and difficulty in articulation are another characteristic feature in most individuals with cleft lip and palate.[20,25]

2. **Ear infection**:

Due to improper function of m. tensor veli palatini muscle, which opens the Eustachian tube, otitis media is observed in these patients. In a case where infections frequently occur, results that can lead to hearing loss may occur. The incidence, however, increases sharply when there is associated submucous cleft palate.[20,26]

3. **Feeding problems:**

A child with a cleft palate can have difficulty sucking through a regular nipple due to the gap in the roof of the mouth. An infant's ability to suck is related to two factors: the ability of the external lips to perform the necessary sucking movements and the ability of the palate to allow the necessary build-up of pressure inside the mouth so that foodstuff can be propelled into the mouth. Most babies require a personalized or special nipple to properly feed. It may take a couple of days for the baby and parents to adjust to using the nipple before going home. Most babies learn to feed normally with a cleft palate nipple.[20]

Treatment of Cleft Lip And Palate

This correction involves surgically producing a face that does not attract attention, a vocal apparatus that permits intelligible speech and a dentition that allows optimal function and aesthetics. The cleft palate team concept has evolved from that need. Because optimal care is best achieved by multiple types of clinical expertise, the team may be composed of individual in: (1) the dental specialties (orthodontics, oral surgery, pediatric dentistry, and prosthodontics), (2) the medical specialties (genetics, otolaryngology, pediatrics, plastic surgery, and psychiatry), and (3) allied health care fields (audiology, nursing, psychology, social work, and speech pathology).[27]

Surgery Treatment

Unlike the artistic nature of the cleft lip repair, the cleft palate repair is very functional in nature. A team approach has decreased the morbidity and secondary deformities caused by the cleft and mostly focuses quality of speech.[28] Soft palate repair techniques may be used in isolation or combined with hard palate procedures, as necessary. Most surgeons today perform either some modification of an intravelar veloplasty, vs. a two flap palatoplasty with double opposing z-plasty to achieve levator muscular repositioning.[29] Maxillary distraction is increasingly used for the correction of severe maxillary retrusion in patients with cleft lip and palate.[30] Cleft lip and palate children benefit from team approach special treatment requirements. such a team lead by the plastic surgeon should include a speech therapist and orthodontist having ready access to pediatric, ENT and dental treatment facilities.[31] Esenlik *et al.* reviewed the literature on nasoalveolar molding (NAM) with an eye to both benefits and limitations. A review of the literature suggests that NAM Cleft lip and palate children benefit from team approach special treatment requirements. such a team lead by the plastic surgeon should include a speech therapist and orthodontist having ready access to pediatric, ENT and dental treatment facilities does not alter skeletal facial growth when compared with the samples that did not receive PSIO (Presurgical infant orthopedics). Nevertheless, the published studies on NAM show evidence of benefits to the patient, caregivers, the surgeon, and society. These benefits include documented reduction in severity of the cleft deformity prior to surgery and as a consequence improved surgical outcomes, reduced burden of care on the caregivers, reduction in the need for revision surgery and consequent reduced overall cost of care to the patient and society.[32] Robotic cleft surgery is a new and exciting field that holds numerous advantages to both patients and surgeons. Previous research in allied health specialities has paved the way to the feasibility studies of robotic cleft surgery. Finally, the use of surgical robots at present

introduces economic challenges to implementation because of increased operative time and high capital and operating costs and it is hoped that over time, costs will reduce and performance will increase as more systems are developed in the future.[33]

Summary and Conclusion

The perfect thing to do for CLP is certainly to prevent its occurrence in the first place. The primary aim in CLP is to educate parents and future mothers and fathers. Cleft lip and palate are both birth defects that affect different structure and function such as speech difficulty, aesthetic, eating, nutrition etc. Patients with oro-facial cleft deformity needs to be treated at right time and at right age to achieve functional and aesthetic well-being. The mental status of patients with CLP should be considered and supported by psychological rehabilitation and their morale should always be bolstered. Extensive dental treatment may be requires but it should not be made more extensive or complex than is necessary to achieve a reasonable standard of dental perfection. The multidisciplinary approach towards this problem led to a steady improvement in its end results.

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Conflicts of interest

There are no conflicts of interest.

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