Epidemiological Aspects of Cleft Lip and Cleft Palate

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ABSTRACT

BACKGROUND

A new-born baby having a cleft lip alone or a cleft lip with cleft palate is definitely painful to the parents. Such cases must be referred to a multi-disciplinary medical team having expertise in craniofacial defects. The role of a family doctor is significant in these cases as he / she is the one who can minimize the sufferings of the parents and their family members by ensuring antenatal diagnosis and extending support for the whole family post-diagnosis, during initial days of breastfeeding as well as bonding issues and also throughout an extended period of months and years of surgical interventions and speech therapies. These cleft lip and palate deformities are the most typical facial defects in children at birth. This leads to not only the altered appearance, defective speech, improper hearing, retarded growth of the baby but also deranged psychosocial well-being and disrupted social integration of the parents and family members. This article presents an overall epidemiological aspect of the said anomalies in the immense interest & benefit of all the concerned professionals. Patients with cleft lip or palate have significant problems in communication, and face difficulties with deglutition. The understanding of the anatomy and associated pathophysiology play a vital role in the management of these patients. The surgical correction remains the mainstay of treatment to date. This article describes common problems related to kids having cleft lip and palate anomalies and provides the latest surgical options available in such congenital cleft care. The genetic basis of the disease and recent advances in the developmental defects of this congenital abnormality is also discussed. In addition to physical corrections, psychological effects on the family need to be addressed at priority. The treating physician must consider the mental health of the parents. The current concepts of treatment will continue to evolve because of continuous developments in the fields of foetal surgery, genetic and tissue engineering.

KEY WORDS

Cleft, Lip, Palate, Aperture, Folic Acid, Congenital, Abnormality, Orofacial, Correction, Surgery

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DOI: 10.14260/jemds/2021/645

How to Cite This Article:
Muzammil K, Nasir N, Hassan A, et al. Epidemiological aspects of cleft lip and cleft palate. J Evolution Med Dent Sci 2021;10(36):3178-3183, DOI: 10.14260/jemds/2021/645

Submission 30-08-2020,
Peer Review 04-08-2021,
Acceptance 10-08-2021,
Published 06-09-2021.

BACKGROUND

Orofacial clefts that are all together, either cleft lip alone or cleft lip along with cleft palate, are considered to be the most typical congenital anomalies of the head and neck at birth. Basically, cleft lip occurs due to the complete or partial failure of maxillary prominence fusion with that of the medial nasal eminence on either or both sides. However, the loss of fusion of palatine shelves gives rise to cleft palate. The causes of these congenital anomalies are not very clear, but environmental and genetic factors seem to be responsible. 8 - 10. Intake of folic acid during the first trimester and even before conception is related to a 25 – 50 % decrease in the cleft lip palate incidence.[1,2] The prevalence fluctuates between 1 / 600 and 1 / 700; this fluctuation depends mainly on ethnic and geographical distribution.[3]

The disparities in the prevalence among blacks & whites at various geographical areas hint towards the variations in the genetic components. Genetic predisposition and certain environmental factors are mainly considered the causative factors for orofacial clefts. Cleft lip or palate is the resultant failure of union between the structures involved in formation of the upper lip or palate before birth.

The exact causes of these anomalies are not known till today. However, some of the cleft lip and palate cases are said to be associated with:

1. Genetics
2. Smoking / alcohol status of parents
3. Obesity condition of parents
4. Lack of maternal folic acid
5. Medications, especially anti-epileptics or steroids

In few instances, it's a part of a more comprehensive range of congenital disabilities, viz 22q11 deletion syndrome often known as DiGeorge & Pierre Robin sequence.

The orofacial cleft prevalence of 0.41 per thousand births, as revealed in Indian hospital-based research, is consistent with that of a similar survey conducted in Africa, both being developing nations.[4] One should be cautious enough when comparing the results of similar studies conducted in different regions or continents as the sample size, analytical procedure, and other ascertainments are quite different from each other.

In a Japanese study among 39696 babies as study subjects, the incidence of orofacial cleft abnormalities was reported to be 0.163 %. Among these affected babies, 41.3 % had cleft lip only, 46.0 % had cleft lip along with cleft palate, and 12.7 % had cleft palate alone.

These findings reveal that the orofacial cleft incidence is more than other races in different regions.[5] The incidence of cleft palate and lip together in India is 0.128 %. Early identification and suitable programs are critical in addressing the hazardous effects on speech in such a disadvantaged population.[6]

These deformities are generally detected at the time of level – 2 USG anomaly scan, usually from 18 to 21 weeks of gestation. Only cleft lips are visible during USG anomaly scanning as cleft palate detection is challenging on USG scanning.

If the USG level – 2 anomaly scan is normal, then cleft palate may be diagnosed either immediately post-delivery or within 72 hours of delivery during the new-born's physical examination.

In 2003, World Health Organization emphasized the need for a surveillance system to estimate the data related to orofacial clefts.[3] Further initiatives should focus on diverse geographically defined populations and ultimately heading towards having national registries for birth and congenital disabilities.[7] Reliable data must start with the studies aiming at the aetiology & prevention of these orofacial clefts in India.[7]

Cleft lip and palate management is a life-long issue and is complex too. The shocking figure compelling for intervention is indicated by the findings of a study undertaken by the Tata Institute of Sciences.[8] The essential features of this study are as under -

- The estimated incidence of these anomalies, viz., cleft lip and / or cleft palate, in India is 1 in every 781 live births.
- Female incidence is half that of males.
- In India, about 35000 neonates are born with these cleft deformities almost every year.
- The major proportion of these anomalies is from low socioeconomic status.
- Approximately 46 % of the families with the affected child never put any effort to correct or undertake any intervention to remedy orofacial cleft abnormality. It is also referenced that the parents might have consultations, but no surgery was performed because of financial constraints, fear of surgical intervention, or ill-health reasons.

It can cause several issues, especially in the first few months of life. These problems may include: -

1. Feeding difficulty – a new-born with a cleft deformity / s often fails to suck the breast milk or even bottle.
2. Hearing problems – affected children are usually prone to ear infections and thereby have hearing issues.
3. Dental problems – improper teeth development may result in an increased risk of decaying tooth.
4. Speech problems – affected older children may have unclear or nasal - sounding speech.

The goals of treatment for all these cleft deformities are to enhance and restore the ability to properly eat, hear and speak, as well as have a better facial appearance.

Management of such anomalies requires a multi-disciplinary team of medical and paramedical professionals like:

- Specialized plastic surgeons
- Specialized otorhinolaryngologist
- Specialized oral surgeons
- Expert paediatricians
- Expert orthodontists
- Expert pedodontics
- Child psychologists
- Genetic counsellors
- Expert speech therapists
- Auditory or hearing experts
- Expert nurses
- Social workers

Surgical intervention and repair are the mainstays of management. Special therapies are also required to restore the associated defective conditions as far as possible. Surgical intervention is individual base; following the initial cleft repair, the surgeon may recommend follow-up surgeries to improve speech and facial appearance further. Surgical interventions are being done usually in the following sequence – the first repair of the cleft lip at 3 to 6 months of age, then repair of palate if present is being done by the period of one

year and lastly between two years of age and late teens follow-up surgeries to restore or improve the facial appearance.

Various surgical methods and procedural techniques are being used nowadays in this modern era of science to repair these cleft deformities, reconstruct the anatomical parts affected and prevent and manage complications. Usually, these modern surgical techniques include the following;

To close the cleft lip, usually, the surgeon makes an incision on each side of the cleft and thereby creates tissue flaps; after that, these flaps are stitched together along with the underlying muscles of the lips. This helps in better appearance structure and function of the affected lip. If nasal repair is also required, then in such a case, it is done first at the time of cleft repair. Depending on the case condition, various techniques are employed to proximate and ultimately close the separation and rebuild the mouth roof.

Surgical intervention for the ear tube requires inserting tiny bobbin - shaped tubes in the tympanic membrane to make an opening & thereby prevent fluid build-up. To improve the appearance of mouth - lip - nose complex, more advanced surgical interventions are usually required. Surgical interventions play a significant role in improving and restoring the facial appearance, QoL (quality of life), and ultimately the ability to perform eating, talking, and breathing functions to near normal. Associated complications due to surgical intervention may be bleeding, poor healing issues, infections, wide or elevated scarring, damage to vessels, nerves and nearby anatomical structures.

These findings revealed that early identification and early intervention are the best solutions and need of the hour. Surgical interventions in India have now become a reality due to the efforts done by some NGOs / non - profit organizations such as Smile Train, which is the world's largest cleft charity.[6, 8] The nasal emission could be ascertained like nasal fricative substitutions. In addition, the PSNE (Phoneme - specific nasal emission) pattern may be noticed, which is restricted to some particular sounds. In children, speech and language development with clefts depend on several factors, including hearing status, type and severity of the aperture, and a syndrome's presence.

Canonical babbling is delayed in affected children. They have less variety in the production of canonical forms. During babbling, children have a bit more limited consonant inventory. They also have fewer total consonant productions, and they also have glottal fricative and nasal glide preferences. They demonstrate an appreciation for words starting with sonorants. A child having a syndrome might have a severe language disorder like that of the one with only developmental delays related to the syndrome.

HISTORICAL LANDMARKS

Harelip is reported around a millennium before. Para, a French surgeon in 1561, used the obturator. Hippocrates and later on Galen described cleft lip anomaly in their scripts only. Perforations of the palate actually were considered for many decades to be associated with secondary to syphilis. Cleft palate was never thought to be of congenital origin. It was Fanco in the year 1556 who mentioned cleft palate as a genetic disability. For the first time, the successful closure of the soft palate defect was done by a French dentist LeMonnier in 1764; Dieffenbach did the early ever successful closure of the hard palate in the year 1834. It was Kilner and Wardill who independently developed the "pushback" procedure in the 1930s.[9]

EPIDEMIOLOGY

Cleft Lip and Palate

The cleft lip is also known as cheiloschisis and cleft palate, also known as palatoschisis, collectively known as harelip, is a common non-life-threatening abnormality having a profound impact on maternal bonding. These defects are considered to have a syndromic association in 30 % of cleft lip and palate cases together. Harelip is a split or an opening in the palate and the upper lip or both. It happens in the developmental stage of facial structures. It is among the most common congenital disabilities, mostly occurring as isolated congenital disability but linked to many genetic syndromes. It is stressful for the parents to have their new-borns having harelip due to its appearance and fear of non- correction. But now, it has been witnessed in most cases that planned surgical interventions can improve & restore routine activities and adhere to a regular facial look with the most negligible scarring.

Incidence & Prevalence

Orofacial clefts are among the most typical congenital disabilities having a global incidence of 1.4 per 1000. Its incidence is more among Asians at 1.7 / 1000; American Indians 3.6 / 1000 and seen less commonly in African Americans - 0.4 per 1000. The global incidence of cleft palate alone is found to be 0.5 in 1000.[10]

The cleft lip incidence among white people is nearly 1 in 1000 live births. The same among Asians is double as great, and among black people, it is < 50 % as excellent. The incidence of cleft lip is more among boys than girls. It has been noted that left - sided isolated unilateral clefts occur twice as compared to the right - sided isolated unilateral clefts. The occurrence of isolated unilateral cracks is nine times higher than the occurrence of bilateral clefts. More than 700 babies are affected by cleft lip alone or with cleft palate in the United States. In the USA, harelip is considered the 4th most familiar congenital disability. The babies of Asian native American or Latino are affected more than the other races. Boys are affected twice commonly as compared to girls with cleft lip only. Whereas, in comparison to males, females have twice more chance to have cleft palate only. Cases require several surgical procedures and multi-disciplinary treatment and care for correcting these defects; around $100,000, amounting to $750 million spent annually for these anomalies in the United States.[11] Serious psychological problems are seen among children and their families.

The most common orofacial cleft presentation is combined cleft & palate, i.e., 50 %, followed by isolated cleft palate only, i.e., 30 per cent, and small cleft lip or cleft lip & alveolus, i.e., 20 %. The bilateral clefts are < 10 %. There is a 4 % birth risk of the newborn with congenital disabilities for a child with orofacial cleft or parents with the same defect. It has been observed that such risks get increased by 9 % provided the previous two babies were born with the same congenital disabilities. It has also been noted that the risk of such defects

to the following siblings increases with its severity.[12] After the birth of a neonate having harelip in a family, parents are afraid to have a second child due to few deformities in further pregnancy. In that case, prevention becomes an essential tool in reducing the fear and chances of an abnormal cleft and palate. Genetic counselling plays an important role. Also, a prenatal genetic workup is quite fruitful. Lifestyle modifications such as smoking, tobacco and alcohol intake can be minimized. Education regarding some medications like anti - epileptic drugs also plays an essential role.

The prevalence of cleft deformities are found to be highest among the Asians & Native Americans (Japanese: 0.82 / 1000 - 3.36 / 1000, Americans: 3.74 / 1000, Chinese: 1.45 / 1000 to 4.04 / 1000), and the lowest prevalence rates of 0.18 / 1000 to 1.67 / 1000 in Africans.[13]

Risk Factors

There is an evidence of risk in consuming some drugs during pregnancy, viz., Sodium valproate, corticosteroids, phenytoin, and benzodiazepines. Maternal smoking may also be associated as a risk factor for the development of orofacial clefts. For those foetuses that lack enzymes involved in the detoxification of tobacco - derived chemicals, the risk of development of clefts in them gets increased.[14] Consumption of alcohol and mainly its type may also be considered as one of the risk factors in cleft development. [15] The debate on folic acid role & its dose - dependency in predisposing clefts has already been undertaken and discussed on various academic platforms.[16-18]

Genetic Factors

The chance of developing a similar cleft in the second child of normal parents with a first child affected by a cleft is 2 – 8 %. If either parent has a cleft, then the risk of cleft development with each pregnancy in their child is estimated to be 4 – 6 %. A gene is associated with cleft development if is not linked with some syndrome. A gene variant called Interferon Regulatory Factor 6 seems to be responsible for cleft lip & palate occurrence, and the same can be determined in nearly 15 % of cases.[19] Recently conducted genetic studies on humans found that a non - syndromic cleft has a definite genetic makeup and may be revealed by environmental factors. Numerous loci (1-10) have already been identified as proof in the same connection.[20]

Aetiology

The definite cause for cleft development is not clear till now, but it is presumed by many that their occurrence is because of one or more of the following three critical factors: -

- The genetic composition (characteristics) is inherited from either of the parents or both.
- Environment factors like poor maternal health or exposure to toxins viz alcohol or cocaine.
- Genetically determined syndromes.

The evidence relates to isolated clefts due to phenytoin (a teratogenic drug) during pregnancy. The said use is said to have ten times more chance of developing cleft lip. Syndromic clefts are related to congenital disabilities in otherwise different developmental regions, with an incidence range extending from 5 to 14 %. The syndrome predominantly related to harelip is Van der Woude, an autosomal dominant disorder. It is associated with a harelip or both blind sinuses of the lower lip.

If a microform is found, then the family prognosis will be bad, especially if it is found in near relatives. In a family that does not have harelip, microform cases might increase the chances of developing cleft, but the probability is less. If cleft microforms are noticed in both consanguineous partners, then it should be considered as a warning sign. The number of microforms cases in a specific group of people must be considered appropriately in epidemiological researches for the prevention of incorrect interpretation of the findings.[21]

A significant development while classifying cleft lip is in identifying and describing sub-phenotypes of the cleft. Marazita reported that the sub-epithelial defects of the muscle - superior orbicularis oris represents the mild form of the lip portion of harelip.[22]

Pathophysiology

The fusion process of the maxillary prominences with lateral and medial nasal prominences starting during the fourth gestational week and ending by the seventh gestational week is responsible for developing of the upper lip. It is the failure of the mesenchymal migration, to fuse either or both of the maxillary prominences with that of the medial nasal prominences, respectively, held responsible for unilateral or bilateral cleft lip.

Classification

There are no classification criteria which is unified globally in the case of orofacial clefts. It was Veau who classified these defects into the following four categories - [12]

1. Soft palate cleft
2. Both hard and soft palate cleft
3. Complete unilateral cleft of the palate and lip
4. Complete bilateral clefts of the lip and palate

Embryology

By 5 - 6 weeks of gestation, the lip is formed, and the palate is formed by the 10th week of pregnancy. Ultrasonologically, cleft may be detected around 20th week of gestation; otherwise, diagnosis is confirmed only post-delivery.[23]

Presentation

It may be with the unilateral or bilateral declaration. The split extends from the margin of the philtrum to the edge of the respective nostril. It may be complete (covering the whole lip up to nose base) or incomplete. There is a clear gap in the lip of the affected new-born, with upper lip predominance. However, in the palate, the cleft is central.

Management

A cleft lip is best repaired during early infancy. Counselling and advice to the parents of the affected babies must be given so that the corrective procedure undertaken at around 2 to 3 months of age gives the best results. There is a rule of 10 that serves best as a safer guideline for cleft repair, i.e., the weight of the affected baby should be around 10 pounds, the

haemoglobin concentration should be nearly ten g / dl, and the age > 10 weeks. The affected baby should be handled by a team of experts from various disciplines, including plastic surgery, otorhinolaryngology, maxillofacial surgery, pedodontics, orthodontics, paediatrics, therapists for speech and language, specialist nurses, social workers, and child psychologists. This entire team is responsible for supporting and managing the affected child until the age of 18. Surgery is the mainstay of treatment for cleft lip repair, which is generally and primarily performed between 2 – 3 months of age of the affected baby to have noticeable results keeping 10 in mind. However, palate closure is undertaken best during 6 - 12 months of age of the affected baby. Multiple interventions may be required as per the need to improve the appearance of orofacial clefts of any type. In such cases, more recent techniques evolved for intra - uterine surgery using foetal endoscope results in scarless healing and without callus formation in case of bone healing.[24]

HISTORY OF THE SURGICAL PROCEDURE

The Chinese medical professionals first developed the cleft lip repairing technique. Initially, the methods involved extracting the cleft margins and then applying sutures on the opposed margin segments. Later on, in the mid - 17th century, this technique was replaced by local flaps of tissues to repair cleft lip and ultimately laid the foundation of todays' corrective surgical principles. The credit for introducing the triangular flap technique of unilateral cleft lip repair goes to Tennison. Randall described and popularized the geometry of the triangular flap and the method of lip repair, respectively. The technique described by Millard for rotating the medial segment & advancing the lateral flap thereby helps preserve the Cupid's bow with the philtrum; this has proved to have better outcomes in the repair of the cleft.[12]

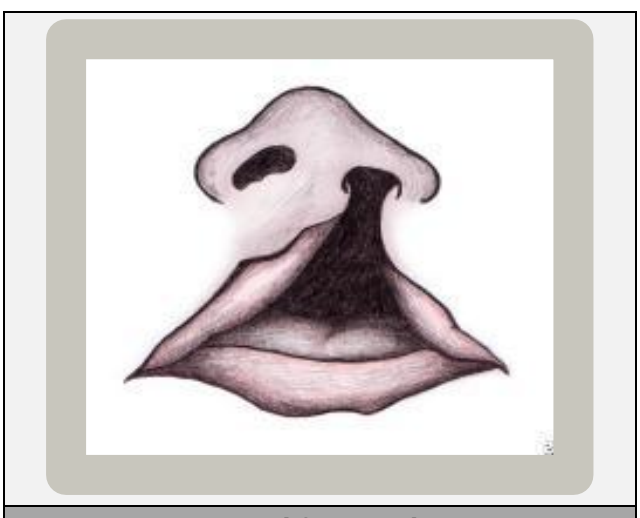

Figure 1. Cleft Lip in Newborn

Among the problems or complications of cleft-feeding & breathing issues, the problem of ear infections that lead to affected hearing, delay in talking, language development delays, and dental problems are the commonest ones. These problems may vary depending upon the extent and site of the aperture. These problems or difficulties happened either alone or in combination. More research is recommended to determine the factors responsible for developing clefts among the various groups exhibiting distinct epidemiological determinants for other races. [25]

The Smile Train

An American NGO popularly known as Smile Train runs a project globally named after the NGO itself is entrusted in helping millions of babies affected with a harelip. They provide corrective surgery for affected babies and training to doctors free of any charges. They are also promoting researches to find a much better cure further. For the past many years, this project has benefitted more than half million affected poor babies. It focuses mainly on treatment, education, and training programs at the international level. Their firm belief is that the local practitioners can be game twisters in helping and supporting the affected babies in their localities. It takes less than one hour only to accomplish the cleft surgery under Smile Train.

Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jemds.com.
Author Contributions: KM is responsible for the intellectual content & design of the article. NN is responsible for shaping & drafting the manuscript. AH is responsible for searching relevant literature. PP is responsible for the thorough review of the article. ZS is responsible for critical analysis and necessary corrections. RA is responsible for finalizing the manuscript before publication.

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