

REVIEW ARTICLE

VISTA OF CLEFT LIP AND PALATE IN INDIA

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ABSTRACT: Congenital craniofacial anomalies like orofacial clefts are of concern for the entire health organisation all over the world. World Health Organisation (WHO) has started its own surveys and is analysing the data available from various countries. WHO has standardised the process of collection of data and has provided a multidisciplinary approach for the treatment of such cases. Surveys, research and application of multidisciplinary treatment strategies are successful on the urban Indian population but a lot needs to be done in terms of rural areas of India (which constitutes 70% population of India) and is posing a serious challenge of overall objective of health for all.

KEYWORDS: Cleft lips & Palate + Craniofacial anomalies

INTRODUCTION: Cleft of lip, hard and soft palate are the most common congenital abnormalities of the craniofacial structure. Worldwide incidence of cleft lip and palate is 1 in 600. ⁽¹⁾ The overall worldwide prevalence of cleft lip with or without the cleft of palate is 9.92 per 10,000. The prevalence of cleft lip is 3.28 per 10,000, and that of the cleft lip and palate together is 6.64 per 10,000. ⁽²⁾ Lowest incidence occurs in Native American tribes of Montana, USA, which is 1:2076. ⁽³⁾

Indian sub-continent still remains one of the most populous areas of the world with an estimated population of 1.1 billion in India alone. The Approx birth rate is estimated to be 24.5 million births per year and prevalence of clefts cases are somewhere between 27,000 and 33,000 cases per year. Inequalities exist, both in access to and qualities of cleft care with distinct differences among urban versus rural areas. Due to this inequality along with lack of awareness had lead to the accumulation of untreated clefts of the lip and palate leading to a significant health care problem in India.

The term cleft lip and palate inadequately describes the potential complexities of the deformity which may involve nose, lips, alveolus or palate. As a consequence breathing, appearance, dentition, dental occlusion facial growth, speech and hearing can all be affected

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leading to psychosocial implications.⁽⁴⁾ It may not be the end of life but for children suffering from cleft problem, it goes beyond the obvious disfigurement of face to repeated infections, social stigma, and mental impairment that affects the speech, hearing, and dentition development or dentition as a whole. Such children are often misbehaved about their cleft-related problems such as speech, teeth and lip appearance etc which results in lower level of confidence among such children.⁽⁵⁾ Research has shown that normal children are considered to be brighter having more positive social behaviour, socially more accepted than those children suffering from cleft diseases. These children suffer with emotional "burn out" in adolescence. Therefore, it has been suggested that these patients should also be included in national policies for integration of handicapped people, in agreement with programs of human rights, establishing a collaborative action between state and society. This would assure their inclusion in the socioeconomic and cultural context and equal opportunities in society, without privileges or paternalism.⁽⁶⁾

Studies have shown association of clefts disease with haematological abnormalities such as anemia, eosinophilia and defects of the clotting mechanism. ⁽⁷⁾ A common clinical observation among children with cleft palate is high prevalence of recurrent upper and lower respiratory tract infection.⁽⁸⁾⁽⁹⁾

Indian sub continent being a geographically and economically different region than others, the demographic, prenatal and clinical profile of the clefts cases found in this region also differs. The condition in tropical countries like India becomes even worse due to poverty and illiteracy. India being economically a developing country is expanding the medical facilities available in the rural area. The various geographically difficult regions such as mountainous region of North and North-eastern India and plains of the Central Indian and the Southern region have diverse culture, religion and living standards. Due to insufficient, ineffective and disproportionate penetration of health care facilities the population at large have suffered a lot in terms of basic health care facilities. However certain NGOs and government agencies by means of various health projects have done excellent work but still lot of rural masses are deprived of quality and good health care. In addition, due to lack of awareness and illiteracy rate, the patients of cleft remain untreated or misguided by some quacks. ⁽¹⁰⁾

DOCUMENTATION OF CRANIOFACIAL ANOMALIES AND CLEFT LIP AND PALATE IN INDIA

India is one of the many countries of the world where documentation of birth anomalies is incomplete or not done. Efforts and hard work of certain NGOs and government health organisations has lead to an improvement in terms of health care needs, social and economical upliftment of Oro-facial Cleft (OFC) children but the problem is aggravated manifold due to unavailability of reliable and complete record of cleft cases statistics because of want of proper infrastructure and also due to poor association and non sharing of data recorded by various agencies dealing with craniofacial anomalies in India. It is well known fact that in many parts of India the parents of a child born with a cleft have no access to counselling on the care and treatment modalities of the disease affecting their children. Cleft lip and palate may be perceived to be a life threatening abnormality by such parents and also there is less awareness of the fact that clefts cases can be surgically repaired with considerable success both aesthetically and functionally. The lack of knowledge and resources results in unacceptable delay in seeking and receiving adequate medical care of such cases, due to which, many infants suffering from OFC die of malnutrition or infection. This grim situation is further compounded by failure of healthcare authorities to recognize craniofacial anomalies as a notifiable disease.⁽⁴⁾

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From the facts presented above it becomes important that the issue of registering of cases of birth deformity is taken seriously in India. Various studies on cleft cases should be performed along with collection of data from different centres covering the various geographical and economical section of India, presence of consanguinity and high and low incidence areas as noted in previous studies. The agency entrusted with the task of registering of cases should establish network and communication with various neonatal units present in the different cities which are routinely involved in the collection of statistics of the newborns. In each center, a medical doctor and a social worker should work together for diagnosing and collection of appropriate information and data regarding birth anomalies.⁽²⁾ They should also liaise and collaborate with other medical centres within their area of work for collection of data. Craniofacial anomalies including cleft lip and palate would be a sub-set of the data collected, and the protocols used should be governed by the guidelines as issued by the WHO.⁽²⁾

MULTIDISCIPLINARY APPROACH AND STATUS OF SURVEYS IN INDIA: It is widely recognized that the optimum approach to the treatment of children born with cleft defects, either of the lip or palate, is a multidisciplinary approach as the treatment requires combined efforts from a paediatrician, orthodontist, specialist nurse, cleft surgeon, speech therapist and ear, nose and throat specialist (ENT) and because of which there is a need to provide the best possible collective expertise so as to ensure that correct and proper treatment interventions are carried out at the appropriate time to result in best possible functional and aesthetic result.⁽²⁾

Multidisciplinary treatment approach is the need for treatment of OFC children but such a scenario is best available in urban area while its application in rural area is still debatable due to lack of facilities available. Due to increased awareness Indian researchers have also started carrying out study and research on OFC children collecting data from various regions of the country. Various studies have shown that due to improvement of economic condition, literacy rate and more importantly the improvement in health care infrastructure are resulting in better care of cases suffering from cleft disease. Situation has also shown marked improvement due to the involvement of the non-governmental organizations in providing quality health care to the general masses especially to the weaker sections of the society is rapidly changing the cleft care scenario in the country. But despite the general improvement of the environment there is lack of interdisciplinary treatment approach at majority of the centres, and hence there is a need for better and effective collaboration among the specialist for the health care needs of the cleft cases.⁽¹¹⁾ Consanguineous relationship and illiteracy rate among the rural masses has also resulted in a situation of increased developmental deformity as well as inefficiently handling of the cleft cases in India.⁽¹²⁾⁽¹³⁾

Many researches through their studies have revealed the genetic complexity in Indian children suffering from oral cleft lip and palate.^(14,15,16,17,18) India being one the fastest developing country is bubbling with young and enthusiastic researchers who are struggling hard to find the genetic reasons along with the environmental effects resulting in oral clefting in Indian population. Surveys of rural and urban Indian population and statistical analysis and evaluation of the data are the main areas of concern, as these are also in developing state but are progressing positively with the help of the government health organisations together with certain NGOs and many researchers.

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ENVIRONMENTAL FACTORS: Epidemiological and experimental evidences suggests that environmental risk factors such as maternal exposure to tobacco, tobacco smoke, alcohol, poor nutrition, viral infection, improper medications, and teratogens at the workplace and home in early pregnancy are some of the important etioloical factors. The role of maternal nutrition and, multivitamins in particular, in orofacial clefts cases remains unclear. Furthermore, assessments of dietary intake or biochemical measures of nutritional status of OFC cases are challenging and often not available among the many impoverished populations suffering from the highest rates of orofacial clefts disease. The main environmental factors which has been reported to possibly increasing the risk of orofacial clefts cases is tobacco smoking,⁽¹⁹⁾ alcohol consumption,⁽²⁰⁾ solvents⁽²¹⁾ and agricultural chemicals.⁽²²⁾ Certain types of anti-epileptic drugs have also been reported to increase the risk.⁽²³⁾ It is, however, an established fact that the magnitude of the risk of recurrence of orofacial clefts to siblings.⁽²⁴⁾ increases after two or more affected siblings and is greater than that predicted by the familial aggregation of environmental risk factors. If measure of genetic susceptibility are not taken into account in epidemiological studies, measures of the relative risk of a disease associated with an environmental factor can be diluted considerably.⁽²⁵⁾

GENETIC FACTORS: There are two types of CL-P: syndromic and nonsyndromic. Nonsyndromic CL-P represents almost half of facial malformations and could be familial. Nonsyndromic cleft lip with or without cleft palate (CL-P) is one of the most frequently occurring congenital malformations among live births. This prevalence varies widely, depending on the ethnicity and geographic location of the population, ranging from 1 in 300 to 1 in 2,500⁽²⁶⁾ In the United States, it affects 1 in 700–1,000 newborns each year and is the fourth most common birth defect. In India, cleft lip/palate occurs in nearly 1 in 500 live births and the majority of these defects are not corrected either surgically or asymptotically.⁽²⁷⁾ Although Asians have the highest rate of orofacial clefts (OFCs) at birth; majority of the genetic studies have been conducted on white population. OFC may be included as one of the manifestations in more than 400 recognised syndromes. Some of the common syndromes and/or anomalies associated with clefting include Apert,⁽²⁸⁾ Meckel,⁽²⁹⁾ Treacher Collins,⁽³⁰⁾ and van der Woude syndromes.⁽³¹⁾ Dental anomalies such as supernumerary, hypoplastic, or congenitally missing teeth and malocclusion are common in patients affected with CL-P.

Orofacial clefts present as part of the phenotype in over 600 specific genetic syndromes are more commonly in association with isolated CP.⁽³¹⁾ The proportion of CL/P associated with specific syndromes has been reported to be between 5% to 7% ⁽³²⁾ The concordance rates for CL/P is higher in monozygotic twin pairs.⁽³³⁾ there has been familial clustering and concordance in twins of CL/P and CP and are specific for each defect, and therefore the defects are considered to be etiologically heterogeneous. ⁽³⁴⁾ There exists a male preponderance in CL/P along with predominance of cleft affecting the left side ⁽³⁵⁾. $TGF\alpha$ ⁽³⁶⁾ and $MTHFR$ ⁽³⁷⁾ genes have been amongst the most intensively studied variants over the years. However, the results are characterized by their inconsistency, reflecting the fact that further investigation of gene-disease associations and related interactions is required to be done.⁽³⁸⁾

An interesting recent finding is that the gene, IRF6, the gene implicated in Van der Woude syndrome has been shown to play a strong role in the isolated form of clefting,⁽³⁹⁾ and a number of other independent studies in a range of different populations and ethnic groups have reported this finding.^(40,41) Other examples of gene variants involved in syndromic forms of CL/P with a Mendelian mode of inheritance producing phenocopies of non-syndromic CL/P include

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Kallmann syndrome (FGFR1),⁽⁴²⁾ ectrodactyly-ectodermal dysplasia/clefting (TP63),⁽⁴³⁾ X linked ankyloglossia/clefting (TBX22),⁽⁴⁴⁾ Gorlin Syndrome (PTCH),⁽⁴⁵⁾ and heterozygotes for the Margarita Island clefting syndrome (PVRL1),⁽⁴⁶⁾ The implication is that these genes might harbour a mutation that could cause or modify the expression of isolated cleft lip and /or cleft palate.

GENE-ENVIRONMENT INTERACTION: In the light of the foregoing discussion, it seems plausible that common genetic polymorphisms are modifiers of the relationship between environmental and lifestyle factors and orofacial clefts. Hence, there may be population subgroups which have a particularly high or particularly low risk of clefts due to a combination of genetic susceptibility and exposure. Genetic polymorphisms involving the metabolism of alcohol, agents in tobacco and smoke as well as those involved in nutritional metabolism may be relevant to orofacial clefts. Hypotheses can be tested if appropriate information on these factors is collected retrospectively from the affected families. One of the main reasons for the difficulty in determining the aetiology of non-syndromic clefts is that it is polygenic multifactorial, with genetic predisposition to environmental factors being important aetiology.⁽⁴⁷⁾ Because of the potential public health benefits, numerous studies have been carried out to examine possible interactions. These include those between: TGF α (with smoking⁽⁴⁸⁾ and vitamin supplements),⁽⁴⁹⁾ TGF β 3 (with smoking, alcohol), MSX1 (with smoking, alcohol),⁽⁵⁰⁻⁵¹⁾ polymorphisms influencing xenobiotic metabolism and smoking,⁽⁵²⁻⁵⁵⁾ occupational exposures,⁽⁵⁶⁾ maternal medication usage,⁽⁵⁴⁾ retinoic acid receptor alpha (RARA) polymorphisms, maternal intake of vitamin A,⁽⁵⁷⁾ polymorphisms influencing folate metabolism (MTHFR, RFC) and maternal folate intake.^(50,58-60)

At a WHO consensus meeting in December 2004, a collaborative research pooling initiative was established through the WHO International Collaborative on Craniofacial Anomalies Project (<http://www.who.int/genomics/anomalies/cfaproject/en/#mtg>) to undertake meta- and pooled analyses of studies. Collaborative efforts with different populations, ethnic groups, gene pools and environmental exposures across the world will assist in determining the multiple genes that modulate the effects of an exposure.⁽⁶¹⁾ The principles of genetic Mendelian randomisation can be employed to aid in the identification and understanding of environmental factors in disease⁽⁶²⁾

FUTURE OF CLEFT LIP AND PALATE IN INDIA: India, 1871 being one of the first documents to provide information on prevalence of a range of disabilities and diseases such as leprosy, blindness, deafness and insanity. (One of the first documents to provide information on prevalence of disability and disease in India such as leprosy, blindness, deafness and insanity was documented in 1871). Since then India has made significant progress in combating infectious disease through improvements in sanitation, childhood nutrition, vaccination and other public health initiatives; and as a result, genetic disorders have assumed greater importance.

Based on the National Family and Health Survey, 1992-1993 (NFHS),⁽⁶³⁾ consanguinous marriages are uncommon in the Northern, Eastern and North Eastern states and its influence on diseases has not been quantified, with recessive genetic disorders being one example of an influence of consanguinity in the spectrum of human disease. There are very few studies and research about the influence of consanguinity on craniofacial anomalies or cleft lip and palate.

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In Southern India, consanguineous unions between biological kinds have a long tradition. ⁽⁶⁴⁾ The highest rates are reported in the states of Andhra Pradesh, Karnataka and Tamil Nadu, with Kerala being an exception because of the strict avoidance of consanguineous marriage. In the pursuit of genetic research into cleft lip and palate and craniofacial anomalies, it would seem appropriate that an investigation/ research study is carried out on the influence of consanguineous marriage on non-syndromic cleft lip and palate.

Indian Doctors, Government health authorities along with the NGOs have expressed a keen desire to be involved with research studies of OFC and contribute towards multidisciplinary treatment approach as recommended by WHO. These included the establishment of high volume treatment centers, modern equipments, availability of specialist doctors of all departments, inter departmental co-ordination and sharing of inter-center research projects in relation to registration of OFC cases, treatment and the outcome of the treatment. The large volume of cleft cases in India is partly contributed, by the unmitigated debt of past generations wherein a proportion of the adult population with unrepaired clefts who were not treated for primary surgery and other rehabilitation care. To date, however, there has been little attempt by various health agencies to register and evaluate treatment outcome, carry out inter-centre comparisons of treatment protocols and to implement multi disciplinary treatment outcome as recommended by WHO.

CONCLUSION: Congenital facial defects are a pressing problem in India owing to the limited resources to treat such patients. Setting up an institute to treat children with cleft and craniofacial deformities in India presents problems with financing treatment for poor patients, procuring the right infrastructure, and employing well-trained human resources.

The logistics of setting up such a facility in a developing country like India and the future of funding for cleft treatment are important factors to consider while establishing a centre and upgrading of established health centre for patients with cleft and craniofacial anomalies. The aim of setting up such centres should be to provide quality comprehensive & multidisciplinary treatment for patients belonging to sections of society with cleft and craniofacial anomalies.

In India large number of NGOs, government health agencies and health policies, and institutes are trying to address the problem of treatment and quality care of OFC cases. There is wide acceptance among various health agencies that an improvement in birth defects research, surveillance, and registration and quality treatment is required. Surveys and research on OFC by the various organization providing medical services for cleft lip and palate patients, availability of care, effects of previous surveys and importance of specific management techniques in bringing about improvement in the quality health care for OFC cases in our country is the need of time.

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