OPEN ACCESS
Scholars International Journal of Anatomy and Physiology
Abbreviated Key Title: Sch Int J Anat Physiol
ISSN 2616-8618 (Print) |ISSN 2617-345X (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: http://saudijournals.com/sijap/

Original Research Article

# The Karyotype Analysis in Cases of Cleft Lip and Cleft Palate

Dr. Brijesh M. Patel, M.D [1], Dr. Bhavin B. Kodiyatar, M.D[1], Dr. Sejal Patel, M.D[2]
[1]Assistant Professor, Department of Anatomy, B. J. Medical College, Ahmedabad, Gujarat, India
[2]Tutor, Department of Anatomy, B. J. Medical College, Ahmedabad, Gujarat, India

***Corresponding author:** Dr. Bhavin B. Kodiyatar
| **Received:** 02.03.2019 | **Accepted:** 05.03.2019 | **Published:** 30.03.2019
**DOI**:10.21276/sijap.2019.2.3.8

## Abstract

Cleft lip and cleft palate are common congenital craniofacial anomalies ranging between 1:600 and 1:1000 live births respectively. It is a birth defect that occurs due to arrest of development or failure of fusion of components taking part in the formation of face and palate. Most clefts of the lip and palate result from multiple factors, which includes genetic and non-genetic causes. Studies of twins and familial incidence indicate the importance genetic factors. The aim of this chromosomal study is to determine the types of chromosomal abnormalities that play a major role in the causation of cleft lip and cleft palate and also in subsequent management and carrier detection. The early investigation to detect genetic abnormality gives better understanding about prognosis of the disease for timely intervention and management and also risks involved in transmission of abnormality to subsequent generations. For present study 25 clinically diagnosed cases of cleft lip and cleft palate were selected and their karyotypes were prepared and studied for chromosomal abnormalities.The numerical chromosomal abnormality was found in the form of Trisomy 21 of Down's syndrome in 1 (4%) case and 19 (76%) cases had normal karyotypes and in 5 (20%) cases metaphase were not detected. It was also found that 6 (24%) cases had associated congenital heart disease and 1 (4%) case was of Down's syndrome with Congenital Heart defects.The karyotype study in cases of cleft lip and cleft palate helps to confirm the diagnosis, to predict severity of the condition and to counsel the families for the recurrence risk with greater accuracy.

**Keywords:** Cleft lip, Cleft Palate, Karyotypes, Down's syndrome.



## INTRODUCTION

Clefts of the lip and palate are common congenital craniofacial anomalies. The incidence ranges between 1:600 and 1:1000 live births. The incidence of cleft lip and cleft palate varies according to geographical location, ethnicity and socio-economic status [1]. A cleft is a fissure occurring during embryonic development consequent to arrest and failure of fusion of components taking part in the formation of face and palate. The components include five processes, a fronto-nasal process, a pair of maxillary processes and a pair of mandibular processes [2]. A cleft lip is also referred to as harelip due to the presence of a median cleft normally in lip of hare. It may be incomplete when there is only a small notch in the lip or complete when cleft extends into the base of the nostril. A cleft palate is an opening in the palate in the roof of the mouth. The primitive palate is a wedge shaped area in front of the incisive fossa which carries the four incisor teeth fuses with permanent palate in a Y-shaped manner, from before backwards during 2nd month of intra-uterine life and failure of the fusion of these parts result in various types of cleft palate [3].

The cleft lip and palate results from minor developmental disturbance due to genetic and non-genetic causes [4]. Approximately 70 percent of cleft lip and cleft palate cases are non-syndromic occurring as an isolated condition unassociated with any other recognizable anomaly. While the remaining 30 percent are syndromic cases occurring in association with chromosomal abnormalities such as trisomy 13 (Patau syndrome), trisomy 18 (Edward syndrome), trisomy 21 (Down's syndrome), Deletion of 22q11.21, Di George syndrome deletion of 22q, Teacher Collins syndrome-autosomal dominant disorder involving chromosome 5q32-q33 [5]. A sibling of a child with a cleft palate has an elevated risk of having a cleft palate. Studies of twins indicate that genetic factors are of more importance in cleft lip with or without cleft palate. Non-genetic or environmental factors that increase the risk of cleft lip and palate include cigarette smoking in mothers, use of alcohol during pregnancy, maternal diabetes mellitus, hormone imbalance, and vitamin deficiency. Some drugs such as phenytoin, sodium valproate, and methotrexate also have been known to contribute to increase the incidence [6].

## MATERIAL & METHODS

For the present study 25 clinically diagnosed patients of Cleft lip and Cleft palate were selected. The cases were undergoing treatment in department of plastic surgery, at civil hospital, Ahmedabad. The approval was obtained from the institute Research council and Ethics committee of civil hospital, Ahmedabad prior to the commencement of the study. Patient's detailed clinical history with personal data including name, age, sex, registration number, father's age, mother's age at the time of birth, mother's detailed obstetric history, relevant past history and family history was noted. Complete physical and systemic examination was done to find out other associated anomalies. All routine and specific investigations, regarding the disease were also noted to rule out other associated disorders.

Karyotype study was done in all 25 cases of Cleft lip and Cleft palate. The procedure protocols were followed according to the guidelines from the book *Rooney* and Czepulkowski, Human Cytogenetics: A practical approach [7]. About 25 metaphase plates were observed in each case and finally a photograph was obtained from a good quality metaphase slide. The chromosomal findings were described according to the international system of Human Cytogenetic Nomenclature using Automatic Karyotyping software. Correlation of chromosomal finding was done with other parameters and with similar studies done in past.

## OBSERVATIONS & RESULT

The clinically diagnosed 25 cases of cleft lip and cleft palate that came for the treatment were selected. Following observations were noted after relevant history, laboratory investigations and cytogenetic study in 25 such cases.

Out of 25 cases of cleft lip and cleft palate studied, 8 (32%) cases had isolated cleft lip among which 6 (75%) were males & 2 (25%) were females, 12 (48%) cases had cleft lip with cleft palate among which 8 (67%) were males & 4 (33%) were females, 5 (20%) cases had isolated cleft palate among which 1(20%) was male & 4 (80%) were females.

**Table-1: Type of deformity with its Sex distribution in cases studied**

| Type of deformity | Gender of patients | | Total |
|---|---|---|---|
| | Male | Female | |
| Isolated Cleft lip only | 6 | 2 | 8 |
| Cleft lip with Cleft palate | 8 | 4 | 12 |
| Isolated cleft palate only | 1 | 4 | 5 |
| Number of cases | 15 | 10 | 25 |

Their family history and maternal history revealed 4 (16%) cases had a positive family history of the deformity and in in 2 (8%) cases the deformity was also found in his brother/ sister (Table-2).

**Table-2: Family history in cases studied**

| Family history for cleft lip & cleft palate | Positive history | Negative history | Total |
|---|---|---|---|
| Number of cases | 4 | 21 | 25 |

Maternal age distribution showed that in 11 (44%) cases the mother's age was less than 30 years and in 14 (56%) cases mother's age was more than 30 years (Table-3). In 3 (12%) cases the mother had history of smoking during pregnancy. No mother had history of alcohol consumption or exposure to any other risk factor during pregnancy.

**Table-3: Maternal age distribution in cases studied**

| Maternal age group (in Years) | <30 years | >30 years | Total |
|---|---|---|---|
| Number of cases | 11 | 14 | 25 |

Upon their examination for associated malformations it was revealed that out of 25 cases of cleft lip & cleft palate, 6 (24%) cases had only congenital heart disease (CHD) and 1(4%) case was of Down's syndrome with CHD (Table-4).

**Table-4: Associated malformations**

| Associated malformations with cleft lip & cleft palate | Congenital heart disease alone | Down's syndrome with CHD | Other malformations | Total |
|---|---|---|---|---|
| Number of cases | 6 | 1 | 0 | 07 |

Out of the 25 cases studied total only 1 (4%) case showed constitutional chromosomal abnormality in the form of numerical abnormality of Trisomy 21 (Down's syndrome). 19 (76%) cases had normal karyotypes (no structural abnormality) and in 5 (20%)

cases metaphase were not found (Table-5). The above abnormality was found in a male case.

**Table-5: Cytogenetic findings in cases studied**

| Metaphase findings | Males | Females | Total |
|---|---|---|---|
| Numerical abnormality | 1 | 0 | 1 |
| Structural abnormality | 0 | 0 | 0 |
| Normal | 12 | 7 | 19 |
| Metaphase not found | 2 | 3 | 5 |
| Total number of cases | 15 | 10 | 25 |

## DISCUSSION

An attempt was made to find out chromosomal abnormalities in 25 cases of cleft lip and cleft palate and to determine the types of chromosomal abnormalities that play a major role in the causation of such condition. The attempt was also made to find the other factors, which contributes in the formation of cleft lip ad cleft palate and associated abnormalities. In the present study 8 (32%) cases had isolated cleft lip among which 6 (75%) were males & 2 (25%) were females. According to the 100 cases studied by Ivan Subrt et al**,** 26 (26%) had an isolated cleft lip in with higher incidence in male (68%) compare to females (32%) [8]. Bellis TH et al reported the incidence of infants born with the cleft lip and palate anomaly in out of 502 cases the higher cases of 291 (58%) were males and 211(42%) were females. The positive family history in present study was revealed in 4 (16%) cases and the deformity was found in the siblings of 2 (8%) cases [9]. Study conducted by Michael Melnick et al in 1,895 cases of clefts of lip and palate reported that its incidence was 40 times greater in siblings than in the general population [10]. In present study the mother's age was less than 30 years in 11 (44%) and higher age of more then 30 years of maternal age was found in 14 (56%) cases. Bille C. et al. studied the impact of maternal and parental age on the occurrence of cleft lip and cleft palate. They concluded that both high maternal age (Mean 36 years) and high paternal age (Mean 42 years) were associated with the deformity in 126 cases they studied [11]. Balgir RS reported maternal and paternal age effects on 90 patients (61 males and 29 females) have cleft lip & cleft palate anomaly. The study reported that younger mothers are at higher risk of getting a child with congenital oral clefts than the older (above 30 years of age). Parental age gaps increase the incidence of congenital malformations [12]. In the present study the examination for associated malformations revealed that out of 25 cases, 6 (24%) cases had associated congenital heart disease (CHD). In the study of 123 cases of cleft lip and palate conducted by Shafi T and team revealed that 35 (29%) children were found to have associated malformations. The most common of these was congenital heart disease in 18 (51%) cases [13]. The associated malformations in 460 cases were studied by C. Stoll et al, they reported that 36.7% had associated malformations in the central nervous system and in the skeletal system were the most common other anomalies, followed by malformations in the urogenital and cardiovascular systems. In present study the malformation was found only in the form of cardiovascular system [14].

In the present study 1 case (4%) of Numerical chromosomal abnormality was found in the form of 47 XY, trisomy 21 (Down's syndrome). Jun-ichi Azumi and co-workers studied 110 cases of Cleft lip and/or cleft palate. Major chromosomal abnormalities were found in 4 (3%) cases. 3 cases had deletion in form of karyotype 46, XX, 4p- and 1 case was of trisomy 21 [15]. In the cytogenetic study in 200 cases of cleft lip and cleft palate done by Roberto Coco and co-workers found the chromosomal abnormality in 42 (21%) cases. Out of 200 cases, 16 (8%) had complete or mosaic aneuploidies and 26 (13%) had structural defects [16]. Karen Sohan and co-workers also found 1(3%) case was associated with trisomy 21 out of 39 cases they studied [17].

## CONCLUSION

The evidence is suggestive history of exposure of mother to risk factors during pregnancy and history of twin birth increases the risk of developing this anomaly. Cleft lip & cleft palate have lifelong implications requiring complex multidisciplinary treatment. The treatment includes reconstructive plastic surgery, orthodontic treatment and speech therapy. Cytogenetic or the study of chromosomal abnormalities has revealed a wide range of physical chromosomal alterations, including variation in both number and structure. Karyotyping is helpful for the correct documentation of chromosomal status, further management & also helpful for the counseling of the parents for the next baby. The cases with structural chromosomal abnormality and apparently normal karyotypes by conventional cytogenetic methods were counseled for genetic screening by sophisticated genetic investigation like FISH or CGH to find out micro-deletion in chromosome. All the cases of study group should be counseled for possible genetic diagnosis (PGD) and possibility of diseases in subsequent child.

**Conflict of Interest:** None

**Abbreviations:** CHD: Congenital Heart disease.

**Authors' Contributions**

BMP: Concept and design of study, Collection of data, Acquisition of data, analysis & interpretation of

data, literature search, BBK: Concept and design of study, analysis & interpretation of data, literature search, drafting the article and final version to be published.

**SMP:** Concept and design of study, Collection of data, Acquisition of data, analysis & interpretation

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