

Aetiology and Statistics in Cleft Lip and Palate

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Cleft of the face is a common congenital malformation which causes facial disfigurement and is a hinderance in the proper development of speech and hearing.

Up to the present, very little is known with certainty about the definite influences which cause and produce this congenital anomaly. The issue can be broadly divided into two groups i. e.

- i) Hereditary or Genetic
- ii) Environmental

These may effect the developing embryo directly or indirectly by interfering with normal foetal/maternal relationship. Still some congenital defects may be produced as a result of interplay of both environmental and genetic factors. On the other hand teratogenic agents administered to a group of animals of different genetic constitution, can cause congenitally malformed young ones in one group while normal offspring in the other.

The aetiological factors concerned in cleft lip and palate may be summarised as follows: Maternal infection and Toxicity,

Dietary imbalance, hormonal activity, genetic influences, foetal and paternal causes and familial influences.

Though many aetiological agents have been held responsible for the cleft causation yet exact pathogenesis is still to be determined. Divergent views are expressed regarding the actual nature of the malformation i. e. non union of the normal tissues or deficiency and non-union together.

Cleft of the lip and palate occur during 4-12 week of intrauterine life, before the definite bony system takes its shape. Hence, these are primarily soft tissue defects. Many theories have been put forwarded from time to time to explain the cleft. Some of which are mentioned below.

1. Classical Theory of His, (His, 1880).
2. Failure of Mesodermal Penetration.
(Stark, 1954).
3. Deficient Circulation Theory.
4. Inductor-organisator Theory.
5. Epithelial Cyst Theory.
(Steininger, 1941).

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Chromosomal abnormalities (Numerical and morphological) may be responsible for cleft formation. Abnormal chromosomal (13-15 group) is seen in Patau's syndrome (Patau, 1960) whereas abnormal autosome (18th number) is seen in Edward's syndrome. Cases with Turner syndrome (XO) and Klinefelter syndrome (XXY) may have facial cleft as an associated anomaly. Hypothesis concerning the influences of the X-Chromosome on palatal form and maxillo-mandibular relationship have been proposed by Gorlin and Redman (1964).

The studies of Fogh-Anderson (1942) revealed that cleft lip and palate is hereditary and therefore, genetic in origin. However, in clinical practice it is unusual to get a family history of a cleft from about 70 percent of the parents. Cleft palate appears to be of different genetic origin than cleft lip and combined cleft lip and palate. They are inherited in "pure" form and are more commonly associated with other malformations.

Observations :

Experiences of studying 1826 cases of cleft lip and palate in the department of Burns, Plastic and Maxillofacial Surgery, Safdarjung Hospital, New Delhi-16 during the past 10 years (1963-1973) have been documented to outline the magnitude of problems.

Detail maternal and family history was available in 968 cases out of 1326 cases.

(Fig. 1). Inheritance or genetic influences are seen to operate in 14 percent cases. Out of these only 4 percent of the parents were conscious of the genetic transmission whereas rest 10 percent were ignorant.

CLEFT LIP & PALATE AETIOLOGY I		
TOTAL NUMBER OF CASES	=	1326
DETAIL HISTORY AVAILABLE	=	968
POSITIVE FAMILY HISTORY	=	14 PERCENT (135 CASES)
S.NO.	CLEFT	PERCENT
1.	LIP	4 (39 CASES)
2.	PALATE	9 (87 CASES)
3.	LIP & PALATE	1 (9 CASES)

PARENTS CONCIOUS OF THE FACT = 4 %
PARENTS NOT CONCIOUS OF THE FACT = 10 %

Fig. 1--Shows the number of cases having positive genetic inheritance.

The incidence of the cleft formation in the relatives of the parents is approximately 0.9 percent in aunts, uncle, niece and nephews and 0.5 percent in the first cousins.

CLEFT LIP & PALATE AETIOLOGY II		
S.NO	ENVIRONMENTAL FACTORS	NUMBER OF PATIENTS
1	MENSTURATION DURING PREGNANCY	15
2	HORMONAL MEDICATION DURING PREG.	11
3	ABORTION ATTEMPTED	10
4	ABORTION THREATENED	6
5	CONFINEMENT AFTER 40YRS.	8
6	HISTORY OF FEVER	8
7	TWIN PREGNANCY ONE INVOLVED	2
8	POX - VACCINATION	5
9	DIABETES	6
10.	SYPHILIS (+VE VDRL)	2
11.	ROAD ACCIDENT DURING PREGNANCY BLUNT TRAUMA ABDOMEN	4
TOTAL		77
PERCENTAGE		8

Fig. 2--Various environmental factors responsible for cleft causation.

The pure form of the genetic influence was seen mainly in cleft palate cases

(9 percent) where as combined cleft cases showed mixed genetic outcome. In none of the cases, both the parents had cleft in our series.

Environmental factors like menses during pregnancy, hormonal medication, attempted abortions which may throw some light on the aetiology were found to operate in 8 percent cases (Fig. 2).

Other aetiological factors of minor importance e. g. paternal age, birth mark, seasonal incidence and sex had no significance to mention (Fig. 3)

CLEFT LIP & PALATE
AETIOLOGY III
AETIOLOGICAL FACTORS OF MINOR IMPORTANCE

1. PATERNAL AGE
2. BIRTH WEIGHT
3. BIRTH MARK
4. SEASONAL INCIDENCE
5. MATERNAL AGE
6. SEX

Fig. 3—Shows Aetiological factors of minor importance.

Importance of *maternal age* has been stressed by many authors i. e. "Older the mother, more the chances of the child getting the cleft". In our series majority of the mothers were in third decade because of early marriages in our country. (Fig. 4)

Maximum number of cleft children were found to be first child which suggest the importance of stress factors (Table I)

CLEFT LIP & PALATE
AETIOLOGY IV

<u>SNO.</u>	<u>MATERNAL AGE GROUP</u> <u>IN YEARS</u>	<u>PERCENT OF CASES, BORN</u>
1.	UNKNOWN	25
2.	15-20	7
3.	20-30	50
4.	30-40	17.2
5.	OVER 40	0.8

Fig. 4—Shows break up of the mothers age group.

Incidence and Morphology :

The incidence of the cleft vary from 1 : 500 to 1,000 in live births (Fig. 5). Fogh-Anderson (1942) reported an incidence of 1 : 665 whereas Theogaraj (1970) mentioned it as 1 : 639.

CLEFT LIP & PALATE
INCIDENCE II

<u>S.NO.</u>	<u>AUTHOR</u>	<u>YEAR</u>	<u>COUNTRY</u>	
1.	SANDER	1934	ENGLAND	1:954
2.	GROTH KOPP	1934	GERMANY	1:638
3.	EDBERG	1939	SWEDEN	1:960
4.	FOGH-ANDERSON	1942	DENMARK	1:665
5.	SEGIN & STARK	1961	AMERICA	1:500 TO 1:1694
6.	KNOX AND BRAITHWAITE	1963	ENGLAND	1:715
7.	THEOGARAJ	1970	INDIA	1:639
8.	PRESENT SERIES	1973	INDIA	1:897

Fig. 5—Shows incidence of cleft lip and palate from world literature.

Table 1

Order of "Child Birth" with a cleft

Number	Ist	2nd	3rd	4th	5th	6th & above	Not known	Total
of cases in each group	519	307	110	40	50	20	280	1326

Out of a total of 130740 new cases seen in our department during the last ten years, 1326 cases had cleft lip and palate. This gives an incidence of 1 : 835.

Again total number of births during the same period were 64970 in our hospital and out of them, 68 cases had cleft giving an incidence of 1 : 960. Thus an average incidence is 1 : 897 (Fig. 6).

Various systems of classification for cleft lip and palate have been used till now (Fig. 7) These classifications have got their own merits and demerits. We in our department use the following classification.

CLEFT LIP & PALATE CLASSIFICATION		
S.NO.	AUTHORS	YEARS
1.	DAVIS AND RICHIE	1922
2.	VEAU	1931
3.	FOGH-ANDERSON	1942
4.	KERNAHAN AND STARK	1958
5.	HARKIN et al	1962

CLASSIFICATION USED IN OUR DEPARTMENT OF BURNS, PLASTIC & MAXILLOFACIAL SURGERY	
GROUP I	CLEFT LIP ONLY
GROUP II	CLEFT PALATE ONLY
GROUP III	CLEFT LIP & PALATE BOTH
GROUP IA	CLEFT LIP EXTENDING INTO THE NOSTRIL FLOOR UPTO INCISIVE FORAMEN

Fig. 7—Various classifications.

Group I : Cleft of the lip element only.

Group IA : Cleft involving the lip and extending into the floor of the nostril up to the incisive foramen.

Group II : Cleft of the palate only.

Group III : Cleft of the lip and palate both.

There were 625 (47.1 percent) cleft cases which involved various degrees of the lip and anterior palate. Of the remaining, 309 (23.4 percent) cases had their palate (hard and soft) affected and 392 (29.5

CLEFT LIP & PALATE MORPHOLOGY I		
NUMBER OF CASES = 1326		
S.NO.	CLEFT	PERCENTAGE
1.	LIP	47.1
2.	PALATE	23.4
3.	LIP & PALATE	29.5

NUMBER OF CLEFT LIP CASES = 625		
S.NO.	CLEFT LIP	PERCENTAGE
1.	GROUP I (R)	21.1
2.	GROUP IA (R)	9.2
3.	GROUP I (L)	40.7
4.	GROUP IA (L)	20.3
5.	MEDIAN	1.0
6.	BILATERAL	7.7
7.	SUB-SURFACE	2.0

Fig. 8—Shows detailed distribution of cases in Group I and Group IA.

CLEFT LIP & PALATE INCIDENCE I		
A	TOTAL NUMBER OF NEW CASES = 130742	1 : 835
	1963-1973	
TOTAL NUMBER OF CLEFT CASES = 1326		
B	TOTAL NUMBER OF BIRTHS = 64970	1 : 960
	1963-1973	
TOTAL NUMBER WITH CLEFTS = 68		
AVERAGE		1 : 897

Fig. 6—Shows incidence of cleft lip and palate in our hospital.

percent) cases belong to group III. Therefore two-third cases had lip involvement (Fig. 8).

The cases having cleft lip (Group I, Group IA, Group III) (Fig. 9) are brought to us early for treatment than group II cases.

CLEFT LIP & PALATE										
AGE IN YEARS										
S.NO.	CLEFT	1YR.	1-2	2-3	3-4	4-5	5-9	9-16	16+	TOTAL
1.	LIP	235	116	68	87	35	20	28	36	625
2.	PALATE	123	56	40	26	30	14	9	11	309
3.	LIP & PALATE	236	68	32	22	15	8	7	4	392
TOTAL		594	240	140	135	80	42	44	51	1326

Fig. 9—Shows the age of "First presentation" to us for treatment in each group.

Left side cleft commanded a majority in all groups. The largest percentage (61 percent) is seen in group I cases. Bilateral Group I cases were 7.7 percent (Fig. 8). Whereas bilateral Group III cases amounted to 28.3 percent. (Fig. 10).

CLEFT LIP & PALATE MORPHOLOGY II		
NUMBER OF CLEFT PALATE CASES = 309		
S.NO.	CLEFT PALATE	PERCENTAGE
1.	COMPLETE	78.5
2.	SOFT PALATE	16.4
3.	SUB-SURFACE	4.1
NUMBER OF CLEFT LIP & PALATE CASES = 392		
S.NO.	CLEFT LIP & PALATE	PERCENTAGE
1.	Rt. SIDE	20.4
2.	Lt. SIDE	51.3
3.	BILATERAL	28.3

Fig. 10—Shows detail break up of cases in Group II and Group III.

Sex incidence revealed that 359 cases (55.5 percent) were male in group I. Sex incidence were equal in group II while male predominance was again seen in group III

cases (68.8 percent). (Fig. 11)

The presence of associated anomalies is important for prognosis i.e. more the associated deformities, higher the rate of mortality. Major anomalies often render operation for cleft repair impossible.

CLEFT LIP & PALATE INCIDENCE III-SEX RATIO					
FIGURE WITHIN BRAKET IN PERCENTAGE					
S.NO.	FEMALE	MALE	CLEFT	MALE	FEMALE
1.	1	1.50	OVER ALL	787 (59.2)	539 (40.8)
2.	1	1.33	LIP	359 (55.5)	266 (44.5)
3.	1	1.00	PALATE	158 (51.1)	151 (46.9)
4.	1	1.225	LIP & PALATE	270 (68.8)	122 (31.2)

Fig. 11—Shows sex incidence.

These malformations were noticed in 80 cases (6 percent.) 1st and 2nd arch syndrome ranked first (16 cases) followed by congenital telipes equino varus 14 cases. Syndactly and congenital heart diseases followed them whereas sternomastoid tumour trailed behind last. (Fig. 12).

CLEFT LIP & PALATE			
NUMBER OF CASES = 1326			
S.NO.	ASSOCIATED CONGENITAL ANNOMALIES	NUMBER OF CASES	PERCENTAGE
1.	I & II ARCH SYNDROMES	16	
2.	CONGENITAL TELIPES EQUINUS VARUS	14	
3.	CONGENITAL HEART DISEASE	12	
4.	SYNDACTLY	12	
5.	EAR MALFORMATIONS	10	
6.	HYPERTOLERISM	6	
7.	PIERE-ROBINSON SYNDROME	4	
8.	NERVOUS SYSTEM ANNOMALIES	3	
9.	STERNOMASTOID TUMOUR	1	
10.	HYPOSPADIUS	2	
TOTAL		80	

Fig. 12—Shows various associated congenital anomalies.

Genetic Counselling :

This study of hereditary pattern provides

some pathways in counselling the parents in regard to cleft formation.

The following points were obtained after studying the hereditary pattern of the affected families.

(i) If a male or female with cleft marries a normal partner the chances of the child getting cleft are 1.5 percent. This risk increases to 12 percent, if, there is already a relation with cleft lip.

(ii) Normal parents (who have a child with cleft), carry a chance of 3 percent cleft lip and five percent for cleft palate for the next child.

(iii) Parents with cleft palate or with an issue having cleft palate do not carry any serious risk of left lip for the subsequent issues.

(iv) The risk of transmission of congenital defect to the off-spring is more, if affected parent is female.

(v) There is no increased risk of cleft if two normal individuals marry with history of cleft in their family.

Discussion :

The analysis of the present series revealed that the incidence of the cleft in relatives, other siblings, parents and children are more in group II cases.

Data from this study of the large number of families of the cleft lip with or without palate from various countries, reveal that the incidence of cleft formation in the

relations of the parents is approximately as follows : 3 percent children, 4 percent siblings, 0.7 percent in first cousins. It is assumed that the genetic influence is due to the action of many genes working in unison.

For many years hereditary and has been known to be an important factor in the causation of facial cleft. Most geneticians believe that the cleft lip and palate are as a result of hereditary transmission. Wide variation is encountered in literature about the incidence of hereditary influences. (Table II).

In the present study, hereditary influence is observed in 14 percent cases. Ignorance or unwillingness to reveal the positive family history on the part of the parents may be the major factor for the low incidence of definite genetic inheritance as compared to other figures in literature (Table II). Thirty percent and 31 percent has been quoted by Fogh-Anderson (1942) and Metrakos et al (1958) respectively. Whereas low incidence of 10.9 percent and 12.3 percent has been reported by Theogaraj (1970) and Oldfield (1959), respectively. (Table II).

Table II

Incidence of Hereditary Transmission

S. No.	Authors	Percent
1.	Gilmore & Hofman (1966)	6.9-40
2.	Old field (1959)	12.3
3.	Theogaraj (1970)	10.9
4.	Holdsworth (1967)	33-42
5.	Fogh-Anderson (1942)	30
6.	Present series (1973)	14

Current belief is that many birth deformities result due to the adverse intrauterine environment in addition to hereditary. Stress as a result solitary or multiple factors e.g. viral infections, nutritional diseases, hypoxia, drugs, radiation and psychic factors are considered to be important during the 8th to 12th week of intrauterine life.

In our series, no case had positive history of using drugs and exposure to radiation. 11 cases had positive history of progesterone medication. These were all cases of habitual abortion. Twin pregnancy was involved in two cases.

One of the important factor in knowing the family background is to get the nutritional status especially of the mother in the early period of pregnancy. An attempt has been made to devise the working classification (Table III). 48 percent of the parents

Table III

Socio-economic status of parents

S. No.	Status	Percent
1.	Government employee	48
2.	Labour class	30
3.	High Social class	12
4.	Not known	10

were Government Employees whose income may be considered just sufficient to make both ends meet. 30 percent were of labour class whose socio-economic status could not afford reasonable nutrition. Further, lack of education leads to unhygienic living.

Twelve percent belong to high socio-economic class who could afford good nutrition. Regarding the nutrition value of the food, it was difficult as most of the families came from middle class and had very less opportunity for a balanced diet.

Therefore, in our series, aetiological factors can be associated in 22 percent cases only. Perhaps, psychic trauma, physical stress, psychological stress and emotional upsets may have some role to perform in the causation of clefts in remaining 78 percent of cases. (Fig. 13)

CLEFT LIP & PALATE	
AETIOLOGY	
PROBABLE AETIOLOGICAL FACTORS	
1.	PHYSICAL STRESS
2.	PSYCHIC TRAUMA
3.	PSYCHOLOGICAL STRESS
4.	EMOTIONAL UPSETS
5.	INDIVIDUAL FACTORS

Fig. 13—Shows probable aetiological factors in cleft causation.

The maximum number of cases are of group I type (47.1 percent) followed by group II (29.5 percent) and group III (23.4 percent), in present series. Fogh-Anderson (1966) gave an incidence of group I, 33.4 percent, group II, 25.3 percent and group III, 41.3 percent. This shows difference when both series are compared. In our series cleft lip forms by far the largest group. The ratio being 2 : 1 : 1.25.

Overall incidence is more in boys than in girls. (3 : 2). The percent of females in group I, group II, group III, in present series is 44.5 percent, 48.9 percent and 31.2

percent, respectively. These are little different when compared with Fogh Anderson series (1966). Group I, 34.8 percent; group II, 66.2 percent, and group III, 24.6 percent.

Summary and Conclusion :

1. 1326 cases have been seen during the last ten years (1963-1973) in the department of Burns, Plastic and Maxillofacial Surgery, Safdarjung Hospital, New Delhi-16.

2. The numerous operative factors in the causation of cleft have been studied.

3. Male preponderance has been seen in group I and group III, cases.

4. Incidence of cleft is worked out as 1 : 897.

5. Genetic counselling has been worked out.

6. Socio-economic status could not offer any satisfactory clue towards the etiology.

7. Ignorance or unwillingness to reveal the positive family history on the part of the parents may be the major factor for the low incidence of definite genetic inheritance.

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