# Analysis of Lip Prints in Patients with Nonsyndromic Cleft Lip with or without Cleft Palate and their Parents

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**Abstract**

**Background** Non syndromic cleft lip with or without cleft palate (NSCLP) is one of the most common birth defects. If genetic predisposition of individuals towards cleft lip can be detected, it can improve its prediction rate. Hence, this study was conducted to assess the specific pattern of lip prints in patients and parents of NSCLP. The study was also investigated to know whether any specific pattern of lip print exists in patients and in their accompanying parents, which can aid in predicting the risk of incidence of cleft lip and palate. **Methodology** 100 patients with NSCLP, and their accompanying parents attending Mahaveer Jain Hospital, M.S.Ramaiah Dental College and Hospital, Bangalore and Smile Train Centre at Jubilee mission hospital, Kerala were selected for the study. Lip print analyses were done and the data was statistically analysed using Chi-square test. **Results** 17 % of NSCLP patients and 32 % of parents showed whorl type lip prints. There was no statistically significant difference in the incidence of whorl type pattern among patients from different states ($p = 0.721$). Statistically significant difference was not observed in the incidence of whorl type pattern among parents from different states ($p = 0.377$). Parents showed significantly higher incidence of whorl type pattern as compared to NSCLP patients ($p = 0.0213$). **Interpretation & Conclusion** The whorl type lip print pattern varied between patients and parents of NSCLP without any state-wise differences. Parents showed significantly higher incidence of whorl type pattern. As majority of parents of NSCLP patients had whorl type pattern, it may be considered as an extended phenotype of NSCLP.

**Keywords:** Lip Prints, Non Syndromic Cleft Lip With or Without Cleft Palate, Whorl Type Pattern

## Introduction

Cleft lip and palate is one of the most common craniofacial deformities. The first evidence of clefting was in an Egyptian mummy that dated back from 2400 to 1300 BC.[1]The prevalence of cleft lip with or without cleft palate shows ethnic variation. Prevalence range is 1.2 in 1000 live births in Asians, approximately 1 in 1000 live births in Caucasians, and 0.3 in 1000 live births in African derived populations. Reasons for this variation in cleft lip with or without cleft palate remain unsolved, despite genetic variation in different racial groups being considered as an etiological factor.[2]

Clefts are divided into nonsyndromic and syndromic forms. Syndromic cases of clefts are those that have added birth defects or malformations, whereas nonsyndromic clefts are those wherein the affected individuals have no other developmental defects. At present, most studies suggest that about 70 % of cases of cleft lip with or without cleft palate and 50 % of isolated cleft palate are nonsyndromic. Clefting syndromes are rare and possibly make up only 5 % of all cases. The mode of transmission of clefts can be polygenic inheritance or monogenic/syndromic.[1]

NSCLP is a common orofacial defect that originates from both genetic and environmental factors. Affected individuals may have either cleft lip or cleft lip with cleft palate. In NSCLP, the cleft is not in the midline. Midline cleft lip is indicative of another underlying disorder, such as one of the oral-facial-digital syndromes or the

holoprosencephaly sequence. In NSCLP, unilateral clefts are more common than bilateral involvement.

Recurrence risk for nonsyndromic cleft lip depends on several factors, including severity of the clefting, number of affected relatives, and degree of genetic relationship to the affected individual (e.g. first-degree relatives have higher risk than second- and third-degree relatives).[3]

Lips are soft, highly sensitive movable folds and composed of skin, muscle, glands and mucous membrane. The wrinkles and grooves present on labial mucosa, represented as sulci labiorum that form a characteristic pattern are called 'lip prints'. The study of lip prints is called as cheiloscopy. Lip print pattern is an anatomical character of human lips and unique for an individual.[4]

Lip prints are used in forensic odontology for personal identification, criminal investigations and sex determination according to particular pattern of grooves and lines on lips. In recent years, lipsticks have been developed that do not leave any visible trace after contact with surfaces such as clothing, glass or cigarette butts. These lip prints are identified by their permanence and are therefore, named as persistent lip prints. The corners of the lips have sebaceous glands, with sweat glands present in between. Hence, secretions of oil and moisture from these enable development of 'latent lip prints', comparable to latent finger prints and considered to be most important forms of transfer evidences.[5,6]

It will be useful if any type of cleft microforms manifested in lip prints of parents of cleft patients that can be detected by cheiloscopy. Soft tissue cleft microforms are minimal manifestations or subclinical signs that are detected in non-cleft subjects, indicating a greater propensity to clefting in their offspring.[7]

If any special lip print pattern is universally seen in cleft lip patients and in their parents, this may help to predict occurrence of clefts in offspring and also useful for parents to prepare themselves to accept the child with cleft. This will reduce the social impact on this matter. If genetic predisposition of individuals or families towards cleft lip can be detected, that can improve their prediction rate. Hence this study was conducted to assess the specific pattern of lip prints in patients and parents of NSCLP in three Indian states.

## Methodology

The study group included 100 patients with NSCLP and their accompanying parents attending Mahaveer Jain Hospital, M.S.Ramaiah Dental College and Hospital, Bangalore and Smile Train Centre at Jubilee Mission Hospital, Kerala. Patients were informed about the procedure and written informed consent was obtained. Duration of the study was 24 months. Patients with NSCLP and parents who accompanied them were included in the study. Known forms of syndromic cleft lip, lesions on lip such as lymphangioma, lip cheilitis, Melkersson- Rosenthal Syndrome and hypersensitivity reactions to lip stick were excluded from the study.

Dark coloured lipstick was applied evenly on the vermilion border with a single stroke. Then, the person was asked to rub both the lips to spread the applied lipstick. After about two minutes, lip impressions were taken on a strip of cellophane tape on glued portion and stuck to a white paper. The impressions were subsequently visualized with the help of a magnifying lens. Upper lip whorls were not included in the phenotype definition as the lip patterns of individuals with cleft lip were often obscured as a result of surgery. So the left and right sides of the lower lip was taken into consideration. The results obtained for each clinical parameter were tabulated and analyzed using Chi-square test of significance.

## Results

### Non syndromic cleft lip Patients with or without cleft palate

Cleft lip patients with or without cleft palate (n = 100) consisted of 47 male patients and 53 female patients. Out of 100 patients, 42 patients were from Karnataka, 49 patients were from Kerala

and 9 from Andhra Pradesh. 15 % of patients had positive family history of cleft lip and only 5 % cases of cleft lips were diagnosed prenatally.29 % of cleft lip patients were low birth weight babies. 25 % of patients had cleft lip without cleft palate, 75% of patients had cleft lip with cleft palate (Table 1).

20% of patients had incomplete cleft lip and 80 % patients had complete cleft lip. Out of 100 patients, 84 % patients had unilateral cleft lip (32% of patients had cleft lip on right side, 52 % patients had cleft lip on left side). 16% of patients had bilateral cleft lip.

Among 100 patients,8 % of patients showed asymmetric /laterally positioned whorls, 9% patients showed faint /incomplete or unclear whorls. 83 % patients had no whorl type pattern (Table 1.). There was no statistically significant difference in the incidence of whorl type pattern among patients from different states as 'p' value was 0.721(Fig. 1).

**Table 1. Showing clinical details of non syndromic cleft lip Patients with or without cleft palate**

| Clinical Parameter | Number of Patients |
|---|---|
| Gender | |
| Male | 53 |
| Female | 47 |
| State | |
| Karnataka | 42 |
| Kerala | 49 |
| Andhra Pradesh | 09 |
| Family history | |
| Negative | 85 |
| Positive | 15 |
| Prenatal diagnosis | |
| Cleft lip not detected in USG or USG not done | 90 |
| Cleft detected before birth | 05 |
| Don't know | 05 |
| Birth weight | |
| Low birth weight | 29 |
| Normal birth weight | 57 |
| Don't know | 14 |
| Occurrence of cleft | |
| Cleft lip without cleft palate | 25 |
| Cleft lip with cleft palate | 75 |
| Type of cleft | |
| Incomplete | 20 |
| Complete | 80 |
| Side of cleft | |
| Right | 32 |
| Left | 52 |
| Bilateral | 16 |
| Type of whorl in lip prints | |
| Asymmetric /laterally positioned whorl | 08 |
| Faint/incomplete/unclear | 09 |
| Definite whorl | 00 |
| Absent | 83 |

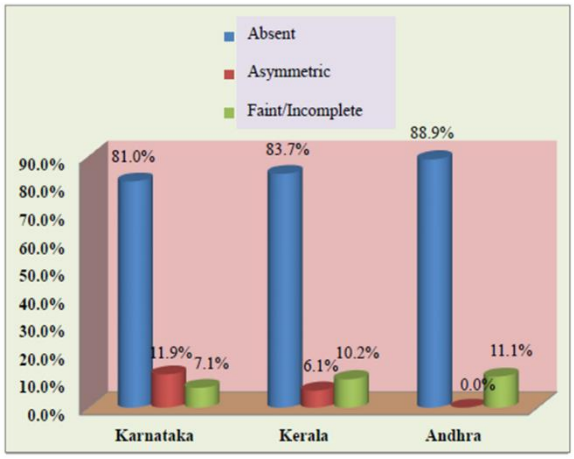


**Fig. 1 Showing state - wise distribution of whorl type of lip prints in Non Syndromic cleft lip Patients with or without cleft palate**

**Parents of Non Syndromic Cleft Lip Patients with or without Cleft Palate**

Parents who accompanied NSCLP patients were also examined and comprised of 5 males and 95 females (n = 100).Among them, 26% of parents had history of consanguineous marriages and 4% of mothers had various medical problems during pregnancy. Two of them were reported with fever. Two of them were reported with jaundice and diabetes mellitus respectively.8% showed asymmetric /laterally positioned whorls, 24 % were faint/ incomplete/ unclear whorls and 68 % parents had no whorl type pattern (Table 2.). There was no statistically significant difference in the incidence of whorl type pattern among parents from different states as 'p' value was 0.377(Fig. 2).

When the incidence of whorl type of lip pattern was compared between patients and parents, there was a statistically significant difference between patients and parents with 'p' value of 0.0213. Parents had significantly higher incidence of whorl type pattern (Fig. 3).

**Table 2. Showing clinical details of the parents of Non syndromic cleft lip patients with or without cleft palate**

| Clinical Parameter | Number of Patients |
|---|---|
| **Gender1** | |
| Father | 05 |
| Mother | 95 |
| **Consanguinity of parents** | |
| Not Present | 74 |
| Present | 26 |
| **Medical problem of mother during pregnancy** | |
| Not present | 92 |
| Present | 04 |
| Don't know | 04 |
| **Type of whorl in lip prints** | |
| Asymmetric /laterally positioned whorl | 08 |
| Faint/incomplete/unclear | 24 |
| Definite whorl | 00 |
| Absent | 68 |

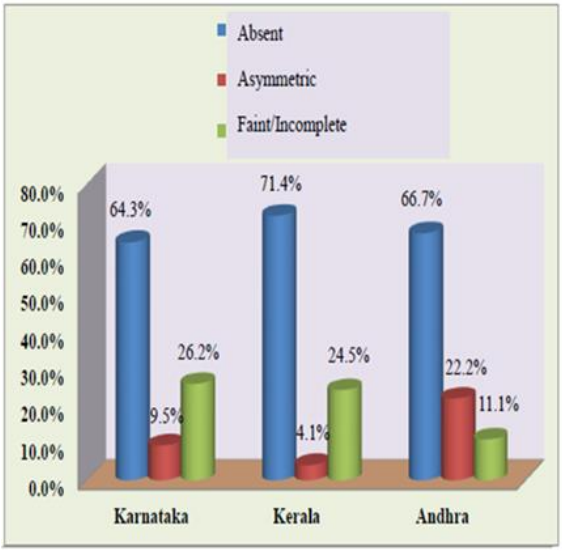


**Fig. 2 Showing state - wise distribution of whorl type of lip prints in parents of Non syndromic cleft lip patients with or without cleft palate**

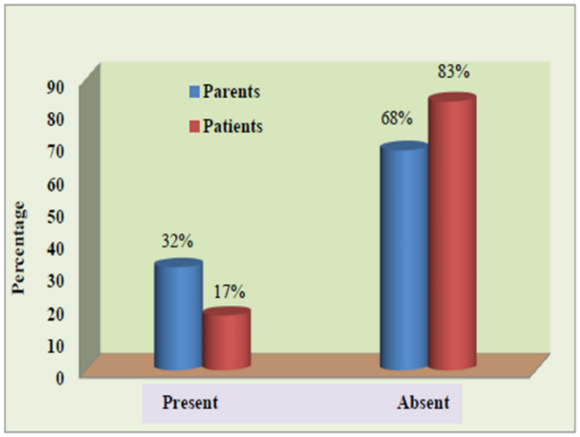


**Fig. 3 Showing comparison of whorl type pattern between parents and patients of Non Syndromic cleft lip with or without cleft palate**

**Discussion**

NSCLP is the most common craniofacial birth defect and its pervasiveness may vary according to socioeconomic status, ethnic factors and geographic origin.

In the present study, 100 NSCLP patients and parents who accompanied them were examined. It was noted that 15% of patients had positive

cleft lip family history. According to study conducted by Kot M et al. (2007),17% of children with cleft lip and/or palate had positive family history.[8] Martelli et al. (2010), in their study noted that 35.13% patients presented a positive history of cleft in their families. Cleft lip is multifactorial in origin, any positive family history of genetic mutation may cause cleft lip. Segregation analysis has demonstrated that NSCLP is a complex, multifactorial trait, with no obvious mode of inheritance.[9]

26% of parents had history of consanguineous marriages in the current study. Isabel Cristina Gonçalves Leite et al. (2009) reported that parental consanguinity was significantly associated with cleft lip and palate.[10] The study conducted on incidence of cleft lip and palate in Tehran, Jamilian A et al. (2007) reported that 31.8% of parents of cleft lip and palate children had positive parental consanguinity.[11]

In the present study, 4% of mothers of cleft lip patients had various medical problems during pregnancy. Two of them were reported with fever. Two of them were reported with jaundice and diabetes mellitus respectively. According to Spilson SV et al. (2001),diabetic mothers were found to be 1.352 times more likely to have a newborn with cleft lip or palate compared tonon-diabetic mothers.[12]The time of greatest risk of structural defect is before the 9th week of gestation.[13]Poor metabolic control, hyperglycaemia and viral infection also increases the risk for clefts and activation of interferon regulatory transcription factors 6 (IRFs 6) may act as an etiological factor. IRFs belong to a family of transcription factors that code for a novel helix-turn-helix DNA-binding motif and can act as an obvious candidate for lip whorls. Zucchero et al. (2004) identified an association between *IRF6* and nonsyndromic cleft lip in different populations. In general, variation at *IRF6* was responsible for 12% of the genetic contribution to cleft lip or palate.[2,14,15]

The prenatal detection rate of cleft lip and palate in low-risk patients is especially low.[16]In the present study only 5 % cases of cleft lips were diagnosed prenatally. According to Jones MC (2002), 14% to 25% of cleft lip with or without cleft palate was detected antenatally.[17]Clementi et al. (2000) reported the detection rate of 27% for cleft lip and 7% for cleft palate.[18] Many factors like sophistication of instrument, number of weeks into pregnancy, position of foetus in womb, maternal body structure (overweight of mother causes difficulty for diagnosis), amount of amniotic fluid (reduced amniotic fluid limit visualization) will affect detection rate of cleft lip by ultrasonogram (USG).

In the present study, 29 % of cleft lip patients were low birth weight babies. Jamilian A et al. (2007) reported that in their study about 50 % of cleft infants had birth weight of less than 2.5kg.[11] According to Triin Jagomagi et al. (2010), the birth weight of children with clefts is similar to the birth weight of children without clefts.[19]Becker M et al. (1998) had suggested an association between the severity of intrauterine growth deficiency and the width of the cleft. Infants with cleft lip and palate presented greater risk for low birth weight for gestational age.[20]

25 % of patients had cleft lip without cleft palate in the present study whereas 75% had association of cleft lip with cleft palate. According to Fogh – Andersen (1942), theratio of incidence of cleft lip to that of cleft lip with palate was 1:2. In our study 80.9 % of male patients and 69.8% of female patients had cleft lip with palate. 19.1% of male patients and 30.2% of female patients had cleft lip without cleft palate. This is in accordance with Fogh – Andersen (1942), who noted that male preponderance was more marked in severe cleft lip with palate defects.[21,22]

In the present study, 84 % patients had unilateral cleft lip (52 % patients had cleft lip on left side, 32% of patients had cleft lip on right side) and 16% of patients had bilateral cleft lip with a ratio of 3.2:2:1. Both male and female patients showed more incidence of left sided clefting. (54.7 % of female and 48.9 % male patients had left sided cleft lip while 34 % of female and 29.8 % of male patients had right sided clefting, 11.3% of female and 21.3% of male patient had bilateral clefting). According to Wilson et al.(1972), bilateral clefting, unilateral right sided clefting and

unilateral left sided clefting occur in 1:3:6 relationship.[22]There is no specific explanation in the literature for increased left sided clefting. However, Johnston and Brown have suggested that blood vessels supplying the right side of the foetal head leave the aortic arch very closer to the heart and may be perfused better by blood than those on the left side.

17 % of patients showed whorl type lip print pattern in the current study whereas 83 % patients had no such pattern. There was no statistically significant difference among patients from different states (Karnataka, Kerala and Andhra Pradesh) with respect to incidence of whorl type pattern as 'p' value was 0.721. According to Neiswanger K et al. (2009),14 out of 55 patients of cleft lip (25.4%) in U.S, 4 out of 19 patients (21.1%) in Hungary and 25 out of 34 patients (73.5%) in Argentina showed whorled type lip print pattern in lower lip. A study conducted by Pruszewicz et al. found lower lip whorl in 5% of cleft lip with or without cleft palate patients.[2]

In the present study, 32% of parents showed whorled type lip print pattern whereas 68% of them revealed no pattern. The parents of different states did not show statistically significant difference with respect to incidence of whorl type pattern with a 'p' value of 0.377. According to Neiswanger K et al. (2009),34 out of 116 family members of cleft lip patients (29.3%) in U.S, 23 out of 46 (50%) in Argentina and 1 out of 34 (2.9%) in Hungary had whorl type lip prints in lower lip.[2]

There was statistically significant difference in the incidence of whorl type pattern between parents and patients (p =0.0213) in the current study. Parents had significantly higher incidence of whorl type pattern compared to patients. The results obtained in the present study were correlated with Neiswanger K et al. (2009).Thus, regardless of methodological and racial differences, whorl type pattern is seen in association with clefting. Comparison of results from various studies from different countries showed that whorl frequencies varied depending on the population. So whorl type pattern may be part of an extended phenotype of NSCLP.[2]

The current study was unable to analyze more number of family members including males because in many instances children would be accompanied by mothers to hospital wards. Probably, with a larger sample size including more family members, more significant relationship can be established between whorl type pattern and cleft lip. Because of limitation of time and resources, analysis of patients from more geographical areas to test universal occurrence of whorl type phenotypic expression was not done. Further studies are necessary to find out the association between whorl type lip print pattern and NSCLP with larger population.

## Conclusion

Whorl type was the predominant lip print pattern observed in patients and parents of NSCLP. However, there was no difference in the lip print pattern between the states assessed. Parents showed significantly higher incidence of whorl type pattern in comparison to NSCLP patients. As a substantial percentage of parents of NSCLP patients had whorl type pattern, it may be considered as an extended phenotype of NSCLP to predict the risk of developingcleft lip and palate.

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