J Orofac Orthop
https://doi.org/10.1007/s00056-022-00435-1

ORIGINAL ARTICLE

Cephalometric analysis of parents of patients with cleft lip and/or palate

H. Hari Kishore Bhat[1] · Venkatesh Anehosur[2] · Varsha Haridas Upadya[3] · Niranjan Kumar[4] · Vijayanand Madhur[5]

Received: 18 September 2021 / Accepted: 11 October 2022

Abstract

Background Cleft lip and/or palate (CL ± P) or isolated cleft palate (CP) are the most common congenital malformations of the face. Although there have been advances in prenatal diagnosis and the discovery of genetic markers, there has been no breakthrough in the identification of parents at risk of giving birth to a child with a cleft.

Aims To determine a possible phenotypic difference in the craniofacial morphology of parents of children with CL ± P and to investigate whether cephalometric analysis can help identify parents at risk of giving birth to a child with a cleft.

Methods Cephalometric data of 25 sets of parents having children with CL ± P were compared with that of 25 sets of parents of children without CL ± P. The study population was indigenous to North Karnataka. In all, 10 linear, 2 angular, and 5 triangular measurements were made on lateral cephalograms and compared using an unpaired t-test.

Results The length of the posterior cranial base (S-Ba) in mothers was smaller in the study compared to the control group. Total facial height (N-Me) both in fathers and in the group with both parents, upper facial height in the group with both parents, and lower facial height (ANS-Me) in fathers was smaller in the study than in the control group. The area of the nasopharyngeal triangle (S-PNS-Ba) in mothers and that of the anterior maxillary triangle (S-N-A) in fathers was smaller in the study group than in the control group.

Conclusion Parents of children with CL ± P showed variations in craniofacial morphology. Future research correlating cephalometric findings with genetic studies may indicate whether cephalometric analysis can be an adjunct to genetic tests for risk prediction among susceptible parents.

Keywords Cleft palate · Parents · Susceptibility · Anthropometry · Congenital malformation

Kephalometrische Analyse von Eltern von Patienten mit Lippen- und/oder Gaumenspalte

Zusammenfassung

Hintergrund Lippen- und/oder Gaumenspalten (CL ± P) oder isolierte Gaumenspalten (CP) sind die häufigsten angeborenen Fehlbildungen des Gesichts. Trotz Fortschritten in der Pränataldiagnostik und der Entdeckung genetischer Marker konnte bisher kein Durchbruch bei der Identifizierung von Eltern erzielt werden, die ein erhöhtes Risiko für ein Kind mit einer Spaltbildung haben.

✉ Dr. H. Hari Kishore Bhat, MDS
harikishore@yenepoya.edu.in, hariyenepoya@gmail.com

[1] Centre for Craniofacial Anomalies, Department of Oral and Maxillofacial Surgery, Yenepoya Dental College and Hospital, Yenepoya (Deemed to be University), Deralakatte, 575018 Mangalore, Karnataka, India

[2] Department of Oral and Maxillofacial Surgery, SDM College of Dental Sciences and Hospital, Sattur, Dharwad, Karnataka, India

[3] Department of Oral and Maxillofacial Surgery, Yenepoya Dental College and Hospital, Yenepoya (Deemed to be University), Deralakatte, 575018 Mangalore, Karnataka, India

[4] Department of Plastic and Reconstructive Surgery, SDM College of Medical Sciences, Dharwad, Karnataka, India

[5] Department of Orthodontics and Dentofacial Orthopedics, Coorg Institute of Dental Sciences, Virajpet, Karnataka, India

Published online: 07 December 2022

Ziele Es sollte ein möglicher phänotypischer Unterschied in der kraniofazialen Morphologie von Eltern von Kindern mit CL ± P festgestellt werden und untersucht werden, ob eine kephalometrische Analyse dazu beitragen kann, Eltern zu identifizieren, die ein Risiko haben, ein Kind mit einer Spaltbildung zur Welt zu bringen.

Methodik Die kephalometrischen Daten von 25 Gruppen von Eltern mit Kindern mit CL ± P wurden mit denen von 25 Gruppen von Eltern von Kindern ohne CL ± P verglichen. Die Studienpopulation stammte aus Nord-Karnataka. Insgesamt wurden 10 lineare, 2 anguläre und 5 trianguläre Messungen an den seitlichen Kephalogrammen vorgenommen und mittels eines ungepaarten t-Tests verglichen.

Ergebnisse Die Länge der hinteren Schädelbasis (S-Ba) war bei den Müttern in der Studiengruppe kleiner als in der Kontrollgruppe. Die gesamte Gesichtshöhe (N-Me) sowohl bei den Vätern als auch der Mittelwert-Elterngruppe, die obere Gesichtshöhe in der Mittelwert-Elterngruppe und die untere Gesichtshöhe (ANS-Me) bei den Vätern war in der Untersuchungsgruppe kleiner als in der Kontrollgruppe. Die Fläche des nasopharyngealen Dreiecks (S-PNS-Ba) bei den Müttern und die des vorderen Oberkieferdreiecks (S-N-A) bei den Vätern war in der Studiengruppe kleiner als in der Kontrollgruppe.

Schlussfolgerung Die Eltern von Kindern mit CL ± P zeigten Abweichungen in der kraniofazialen Morphologie. Künftige Untersuchungen, die kephalometrische Befunde mit genetischen Studien korrelieren, könnten zeigen, ob die kephalometrische Analyse eine Ergänzung zu genetischen Tests für die Risikovorhersage bei besonders disponierten Eltern sein kann.

Schlüsselwörter Gaumenspalte · Eltern · Suszeptibilität · Anthropometrie · Angeborene Fehlbildung

Introduction

Cleft lip and/or palate (CL ± P) or isolated clefts of the palate (CP) are among the most common congenital malformations, requiring complex long-term treatment and having lifelong implications [26]. They reflect a breakdown in the normal mechanisms involved during the early embryological development of the face [6, 30].

Various modes of inheritance of craniofacial morphology have been postulated based on epidemiological evidence [17, 18]. If the shape of the face is genetically determined and relates to the predisposition to cleft lip, we may assume that the faces of parents of children with congenital cleft lip differ from the faces of parents with healthy children [8, 21]. Studies have shown that siblings frequently show the defect too, in an attenuated condition, or the parents may be carriers, exhibiting morphological or biological peculiarities [26]. Distinctive differences exist in the craniofacial morphology of parents of children with orofacial clefting when compared to controls. Increased mandibular length and a larger posterior maxillary triangle as well as an altered palatal shape have been noted in mothers, whereas a shorter posterior cranial base, significantly smaller mandibular, maxillary and symphyseal areas, and a reduced palatal length (ANS-PNS) have been noted in fathers of cleft children [7, 17, 22, 30].

Many studies have shown that identification of the individuals at risk of giving birth to a child with a cleft anomaly using only a genetic approach is very difficult at present.

This study was conducted to test the hypothesis that the craniofacial morphology of parents of cleft children, as determined by cephalometry differs from parents of normal children and whether the genetic assessment of parents at risk, can be supplemented with an adjunct like craniofacial data analysis.

Materials and methods

Ethical clearance for the study was obtained from the institutional ethics committee of SDM College of Dental Sciences and Hospital, Dharwad (IRB No. 2014/P/OS/4).

The Cohen's d effect size of magnitude 0.5 (referring to the medium effect) is assumed for important cephalometric measurements in the study. In order to detect the moderate effect of cephalometric measurements of mid-parents (mean value obtained for both parents) of the study and control group with 80% power and 5% level of significance, a minimum of 50 subjects must be included in each group. The sample size is calculated using G*Power software.

The subjects of this study were 25 sets of parents (25 fathers and 25 mothers) of children with nonsyndromic CL ± P representing the study group ($n = 50$) and a control group ($n = 50$) of 25 sets of parents (25 fathers and 25 mothers) of children without CL ± P or familial history of orofacial clefts (OFC). Subjects were selected in the age range of 22 to 36 years, as previous studies [5] have shown that the amount of craniofacial growth/change in subjects in that age range is negligible. All subjects were indigenous to the population of North Karnataka, India, and had a full complement of teeth from the central incisor to the second molar in all four quadrants of the jaws. Subjects who had previous orthodontic treatment and/or maxillofacial surgery, history of injury to the craniofacial

Table 1 Comparison of study and control groups with respect to different lateral cephalometric measurements by unpaired t-test (fathers)
Tab. 1 Vergleich von Studien- und Kontrollgruppe hinsichtlich verschiedener lateraler kephalometrischer Messungen anhand des ungepaarten t-Tests (Väter)

Cephalometric measurements	Study group		Control group		t-value	*P*-value	95% CI for difference
	Mean	SD	Mean	SD			
S-N-A angle	83.4800	3.8310	82.5200	3.0567	0.9794	0.3323	[–2.931 1.011]
N-S-Ba angle	127.8000	4.7346	130.0400	5.5188	–1.5403	0.1301	[–0.684 5.164]
ANS-PNS	52.9600	2.3889	53.6800	2.5612	–1.0279	0.3092	[–0.688 2.128]
Co-Gn	114.0400	4.7739	115.9200	4.7427	–1.3969	0.1689	[–0.826 4.586]
S-Ba	47.2800	3.2980	48.2000	4.1533	–0.8674	0.3901	[–1.213 3.053]
N-ANS	49.3600	3.6842	51.2400	3.8109	–1.7734	0.0825	[–0.252 4.012]
S-PNS	46.7200	3.2853	46.8400	3.5903	–0.1233	0.9024	[–1.837 2.077]
Go-Gn	76.1200	5.8546	75.7600	5.7175	0.2200	0.8268	[–3.651 2.931]
N-Ba	106.0000	3.5119	107.6000	4.3970	–1.4216	0.1616	[–0.663 3.863]
S-N	70.8000	2.6458	71.8400	2.0551	–1.5522	0.1272	[–0.307 2.387]
N-Me	113.8400	6.0186	119.5600	6.6900	–3.1782	0.0026*	[2.101 9.339]
ANS-Me	66.0400	4.9454	69.8800	5.5477	–2.5835	0.0129*	[0.851 6.829]
SNA triangle	1908.7200	150.9796	2014.724	174.1771	–2.2994	0.0259*	[13.3118 198.6962]
S-N-PNS triangle	1554.1000	119.1012	1595.400	137.1737	–1.1367	0.2613	[–31.7519 114.3519]
Co-Gn-Go triangle	2189.0600	304.1688	2251.180	361.4148	–0.6575	0.5140	[–127.8352 252.0752]
S-N-Ba triangle	1292.1800	144.1872	1278.3200	156.6459	0.3255	0.7462	[–99.4742 71.7542]
S-PNS-Ba triangle	925.3600	102.7173	930.8800	96.3943	–0.1959	0.8455	[–51.1253 62.1653]

SD standard deviation, *95% CI* 95% confidence interval

region, history of endocrine disorders, or gross skeletal defects were excluded from the study.

Patients who had visited the hospital for dental treatment during the study period and who fulfilled the inclusion criteria were recruited to the control group along with their spouses. Parents of children with nonsyndromic CL ± P enrolled in the hospital database were recruited to the study group after satisfying the inclusion criteria. Pre-existing lateral cephalometric radiographs of the participants were used when available. When unavailable, the participants were informed of the need for radiographs for the study. Written informed consent was obtained from all the participants in accordance with the guidelines of the Institutional Ethics Committee.

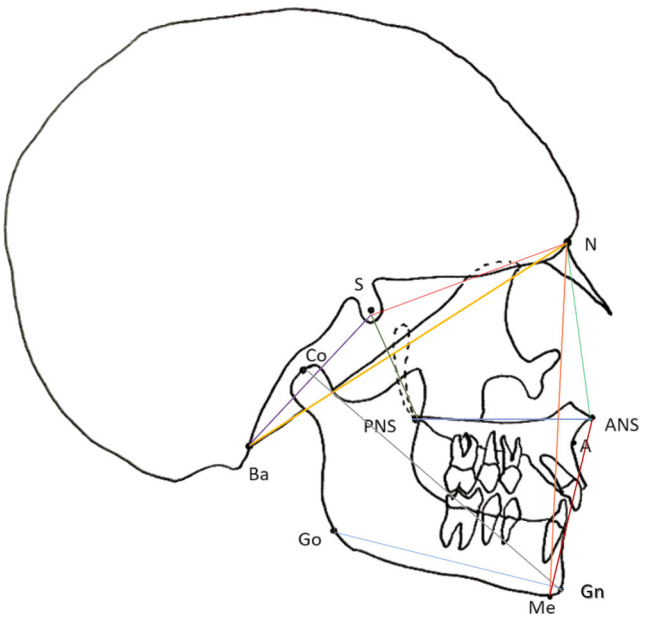

Fig. 1 Linear measurements
Abb. 1 Lineare Messungen

Ten craniofacial landmarks were identified and cephalometric tracings were made using Dolphin Imaging software 9.0. Each cephalogram was traced twice by the same orthodontist with a 2-week interval to assure reliability. The intra-observer error was insignificant for statistical analysis. Seventeen parameters were obtained from the lateral cephalometric radiographs which included ten linear, two angular, and five triangular area measurements.

Linear measurements are illustrated in Fig. 1: ANS-PNS length, S-Ba length (clivus length), N-Ba length, S-PNS length, Co-Gn length, Go-Gn length, S-N length (anterior cranial base length), N-Me length (total anterior facial height), N-ANS length (mid-face height), ANS-Me length (lower anterior facial height).

Angular measurements included the S-N-A angle and N-S-Ba angle (Fig. 2).

The following triangles were constructed (Fig. 3):

- Anterior maxillary triangle (S-N-A),
- Posterior maxillary triangle (S-N-PNS),
- Mandibular triangle (Co-Gn-Go),

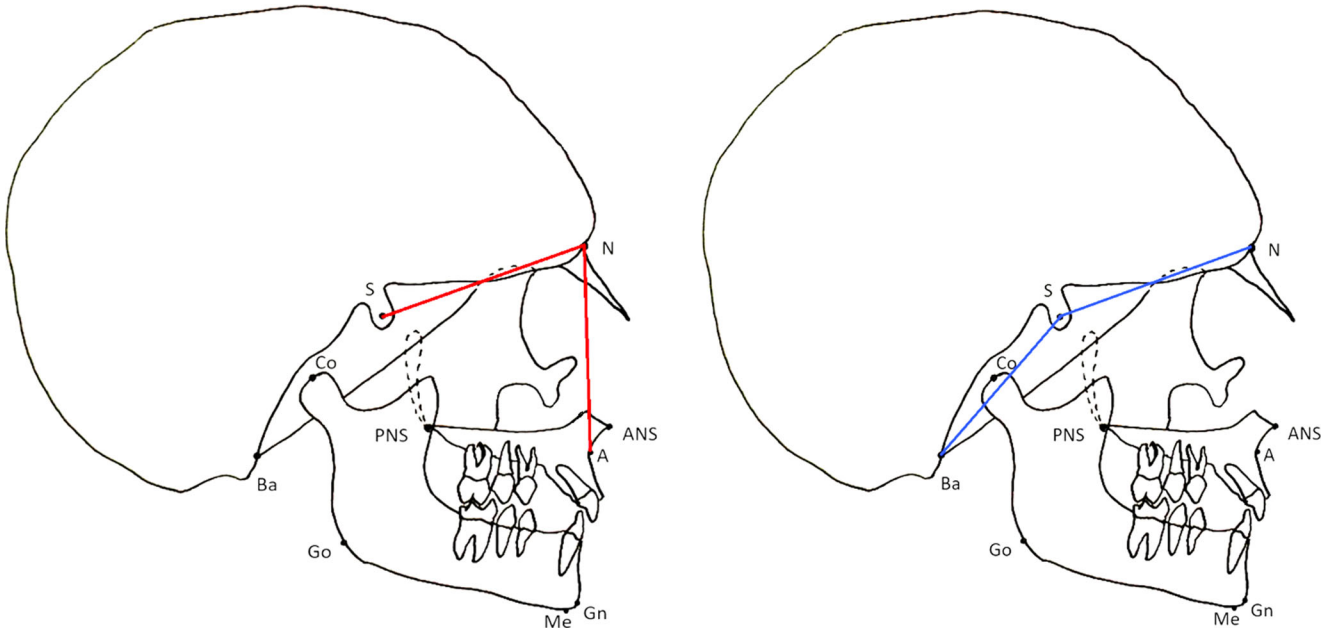

Fig. 2 Angular measurements – S-N-A angle (*red*) and N-S-BA angle (*blue*)
Abb. 2 Anguläre Messungen – S-N-A-Winkel (*rot*) und N-S-BA-Winkel (*blau*)

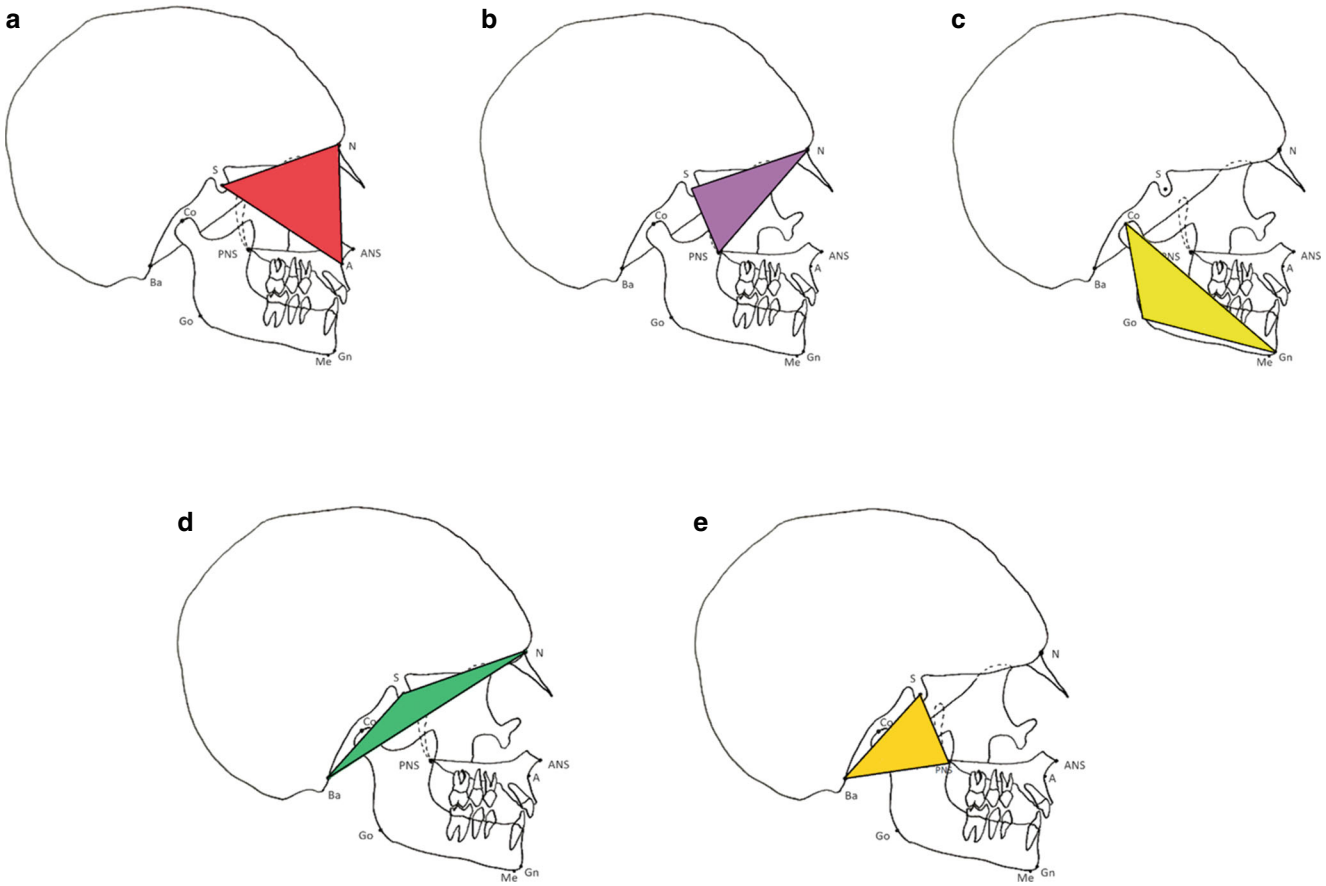

Fig. 3 Triangular measurements. **a** Anterior maxillary triangle (S-N-A), **b** Posterior maxillary triangle (S-N-PNS), **c** Mandibular triangle (Co-Gn-Go), **d** Cranial base triangle (S-N-Ba), and **e** Nasopharyngeal triangle (S-PNS-Ba)
Abb. 3 Trianguläre Messungen – **a** anteriores Oberkieferdreieck (S-N-A), **b** posteriores Oberkieferdreieck (S-N-PNS), **c** Unterkieferdreieck (Co-Gn-Go), **d** Schädelbasisdreieck (S-N-Ba), **e** nasopharyngeales Dreieck (S-PNS-Ba)

- Cranial base triangle (S-N-Ba), and
- Nasopharyngeal triangle (S-PNS-Ba).

The linear, angular, and area measurements were chosen to comprehensively describe the relevant anatomic regions of the head and face, with particular attention to areas of interest in the context of heredity of cleft lip and palate. We used parameters defined by landmarks that were easily identified and reliably produced.

The means and standard deviations of the cephalometric variables of the study and control groups for the father group, mother group, and a mid-parent group (mean value obtained for both parents) were calculated and subjected to an unpaired t test. The t value was calculated. A 5% level of significance was calculated and $p < 0.05$ was considered significant.

SPSS (Statistical Package for the Social Sciences, version 21, IBM, Armonk, NY, USA) software was used for statistical analyses.

Results

The mean age of the overall parental sample was 31 years. The mean age of the fathers was 32.1 ± 8 years and 32.4 ± 7 years in the control group and in the study group, respectively, and the mean age of the mothers in the control group and study group was 30.79 ± 10 years and 30.46 ± 9 years, respectively. The difference between the groups in terms of mean age was statistically insignificant ($p < 0.05$). The parents of the study group had a single affected child with CL ± P.

Cephalometric evaluation of fathers

A significant difference was observed between the groups concerning (a) ANS-menton length (ANS-Me), (b) nasion-menton length (N-Me), and (c) S-N-A triangle. A negative t value implied that the control group had higher values than the study group for all three parameters (Table 1). The other measurements showed no significant difference between fathers of affected and healthy children.

Cephalometric evaluation of mothers

Significant differences in craniofacial morphology between the mothers of affected and healthy children were mainly expressed in S-Ba length and S-PNS-Ba triangle. The negative t value implied that the control group had higher values than the study group in both parameters. All the other measurements were almost similar in the mothers of the study and control groups (Table 2).

Mid-parent values

Table 3 represents a comparison of the study and the control group concerning different lateral cephalometric measurements using mid-parent values. A significant difference

Table 2 Comparison of study and control groups with respect to different lateral cephalometric measurements by unpaired t-test (mothers)
Tab. 2 Vergleich von Studien- und Kontrollgruppe hinsichtlich verschiedener lateraler kephalometrischer Messungen anhand des ungepaarten t-Tests (Mütter)

Cephalometric measurements	Study group		Control group		t-value	*P*-value	95% CI for difference
	Mean	SD	Mean	SD			
S-N-A angle	81.8800	3.5393	82.6400	3.9674	–0.7147	0.4782	[–1.378 2.898]
N-S-Ba angle	131.0400	5.8771	131.6400	4.7861	–0.3958	0.6940	[–2.448 3.648]
ANS-PNS	50.4800	2.1432	50.8000	2.4152	–0.4955	0.6225	[–0.978 1.618]
Co-Gn	105.8000	4.3012	107.5200	6.0147	–1.1630	0.2506	[–1.253 4.693]
S-Ba	42.6400	2.5475	44.8800	2.7737	–2.9739	0.0046*	[0.726 3.754]
N-ANS	47.8800	2.9343	49.0000	2.5495	–1.4406	0.1562	[–0.443 2.683]
S-PNS	43.1600	2.7031	44.3200	3.0100	–1.4337	0.1582	[–0.467 2.787]
Go-Gn	71.7200	4.1081	73.3200	3.3630	–1.5068	0.1384	[–0.535 3.735]
N-Ba	100.2800	5.2402	100.5600	3.6410	–0.2194	0.8273	[–2.286 2.846]
S-N	66.9200	3.0265	66.4400	2.8443	0.5779	0.5661	[–2.150 1.190]
N-Me	109.5200	6.6841	109.7200	6.2418	–0.1093	0.9134	[–3.478 3.878]
ANS-Me	63.5200	5.1891	63.0800	4.3677	0.3244	0.7471	[–3.167 2.287]
SNA triangle	1762.6000	137.4041	1753.3200	164.8720	0.2162	0.8298	[–95.5853 77.0253]
S-N-PNS triangle	1359.8600	124.7850	1389.4800	127.5036	–0.8301	0.4106	[–42.1216 101.3616]
Co-Gn-Go triangle	1713.5200	312.7658	1836.3200	273.6047	–1.4776	0.1461	[–44.3039 289.9039]
S-N-Ba triangle	1064.1600	125.1555	1080.8000	141.6515	–0.4402	0.6618	[–59.3705 92.6505]
S-PNS-Ba triangle	764.1800	68.5723	877.6200	265.4409	–2.0689	0.0440*	[3.1948 223.6852]

SD standard deviation, *95% CI* 95% confidence interval

Table 3 Comparison of study and control groups with respect to different lateral cephalometric measurements by unpaired t-test (mid-parent values)

Tab. 3 Vergleich von Studien- und Kontrollgruppe hinsichtlich verschiedener lateraler kephalometrischer Messungen anhand des ungepaarten t-Tests (Mittelelternwerte)

Cephalometric measurements	Study group		Control group		t-value	*P*-value	95% CI for difference
	Mean	SD	Mean	SD			
SNA angle	82.6000	2.9651	82.5800	2.8088	0.0245	0.9806	[–1.5567 1.6782]
N.S.Ba angle	129.4400	3.6295	130.8400	4.2835	–1.2468	0.2185	[–0.9426 3.5072]
ANS-PNS	51.6200	1.5961	52.2400	1.5147	–1.4088	0.1653	[–0.2620 1.4727]
Co-Gn	109.9400	3.5949	111.7200	3.7779	–1.7066	0.0944	[–0.1463 4.0093]
S-Ba	45.0000	2.1890	46.5400	2.9823	–2.0814	0.0428*	[0.1510 3.0828]
N-ANS	48.8000	2.4109	50.1200	2.2093	–2.0183	0.0492*	[0.0932 2.6853]
S-PNS	45.1000	2.0616	45.5800	2.8346	–0.6847	0.4968	[–0.7804 2.0558]
Go-Gn	73.7000	3.2178	74.5400	3.5879	–0.8715	0.3878	[–1.1791 2.6437]
N-Ba	103.2000	3.0788	104.0800	2.6484	–1.0834	0.2840	[–0.7316 2.4685]
S-N	68.8400	2.3793	69.1400	1.6363	–0.5195	0.6058	[–0.9333 1.3672]
N-Me	111.8200	4.5481	114.6400	4.5860	–2.1831	0.0340*	[0.4583 5.6294]
ANS-Me	64.7400	3.7973	66.4800	3.1639	–1.7602	0.0847	[–0.0725 3.8787]
SNA-triangle	1840.7400	114.4159	1884.0220	123.3030	–1.2865	0.2044	[–21.88185 110.73354]
SN-PNS triangle	1463.6600	90.5446	1492.4400	111.0321	–1.0044	0.3202	[–23.94497 90.40189]
Co-Gn-Go triangle	1946.5800	204.0672	2043.7500	261.1851	–1.4658	0.1492	[–33.69235 227.46158]
S-N-Ba triangle	1175.7800	95.0945	1179.5600	115.5683	–0.1263	0.9000	[–54.63188 63.30957]
S-PNS-Ba triangle	850.5300	59.6104	904.2500	149.5658	–1.6682	0.1018	[–5.36467 123.30697]

*$p < 0.05$

SD standard deviation, *95% CI* 95% confidence interval

between the parents of affected and healthy children was noted in the S-Ba length, N-ANS length, and N-Me length.

The negative t values indicated that the control group had higher values than the study group in all three parameters. None of the other measurements showed any significant difference between the parents of affected and healthy children.

Discussion

Orofacial clefting arises as a complex multifactorial trait, being a myriad of Mendelian patterns exhibiting varying levels of penetrance, sex differences, and environmental overlays. Even in those individuals whose genetic backgrounds verify familial tendencies for orofacial clefting, the mode of inheritance is complex and not completely understood [6, 29]. About 40 genes/loci have been recognized through mutation screening, linkage, candidate gene, genome-wide association studies (GWAS), and recently, studies on whole exome sequencing (WES); however, it has been possible to identify only 20% of the underlying genetic variation in nonsyndromic cleft lip and palate [16]. As a result, identification of the individuals at risk for having a child with a cleft using only a genetic approach is difficult at present.

Based on the results of many other studies [2, 13, 14, 20, 27, 28], we employed a supplementary approach of craniofacial data analysis using Dolphin Imaging Software to identify at-risk individuals in a North Karnataka population. This is in contrast to other studies which used manual cephalometric tracings.

The main significant differences between the two groups in our study were

- N-Me length, ANS-Me length, and S-N-A triangle values in the father group as shown in Table 1,
- S-Ba length and S-PNS-Ba triangle area values in the mother group as shown in Table 2, and
- S-Ba length, N-Me length, and N-ANS length values in the mid-parent group as shown in Table 3.

The S-Ba (posterior cranial base length) difference was significant for the mothers and for the mid-parent groups with the control group having higher values than the study group. Zandi et al. [30] found that the posterior cranial base length in Iranian fathers was shorter than that in their control group ($p < 0.01$). This finding is in contrast to the findings of Mossey et al. [18] who found a larger posterior cranial base in their study group.

In our study, among the fathers and mid-parents (mid-parent value), the N-Me length was larger in the control group than in the study group. The upper anterior facial height (N-ANS) was larger in the control group than in the

study group in the mid-parents (mid-parent value). ANS-Me length in the father group was significantly larger in the control group than in the study group, pointing out a tendency for a smaller lower facial height in the study group. Similar results of a reduced anterior facial height were reported by Coccaro et al. [5] and by Suzuki et al. [28] which is in contrast to the increased lower facial height in parents of children with OFC reported in other studies [23, 25, 27].

Nakasima et al. [20] found that the parents of children with a cleft had a greater interorbital width, greater bizygomaticofrontal suture dimension, and wider nasal width, despite a narrower head width and shorter facial height. They concluded that larger horizontal dimensions and shorter vertical dimensions of the upper face in these parents seem to indicate a genetically determined predisposion to the development of CL ± P. Maxillary height was reported to be shorter in subjects with cleft lip or palate (CL/P) and also in parents of children with CL/P [28].

Raghavan et al. [25] observed a significantly larger cranial base angle (more obtuse) in parents of children with CL/P in contrast to the findings of Coccaro et al. [5] who found a decrease in this angle. However, our study did not show any significant difference for this parameter between the two study groups. Raghavan et al. [25] also observed an increase in the S-N-ANS and the S-N-A angle together with a significant increase in palatal length measured as ANS-PNS. Our study did not show significant findings for both palatal length and S-N-A angle.

One of the often-mentioned findings concerning the craniofacial morphology of parents of children with a cleft was an increase in mandibular body length (Go–Gn) among mothers [18, 30] and fathers [19]. In the present study, the mandibular body length did not differ significantly between the groups, similar to the results of Raghavan et al. [25].

The difference in S-N length was not statistically significant in our study contrary to Suzuki et al. [28], Prochazkova J and Tolarova M [23], and Mossey et al. [19] who reported a significantly larger S-N dimension in parents of children with CL/P compared to parents of children without CL/P.

The anterior maxillary triangle (S-N-A) area was significantly larger among fathers of the healthy children compared to fathers of affected children in our study, which was contrary to the findings of Zandi et al. [30]. It could be concluded from our observations that it is not the position of the nasomaxillary complex in relation to the cranial base (S-N-A angle) but an actual decrease of the nasomaxillary complex (S-N-A triangle) along with the total facial height in the experimental group that may be related to the development of OFCs.

The nasopharyngeal triangle (S-PNS-Ba) in the mothers was significantly larger in the control group than in the study group. However, Zandi et al. [30] found that the area of the posterior maxillary triangle (S-N-PNS) in their study group mothers was larger than that of the control group.

The segregation of subjects into father, mother, and mid-parent groups in cephalometric studies is substantiated by evidence suggesting that the morphological factors are unevenly distributed among the parental pairs and may be heavily weighted to one parent [15, 18]. From the results of the cephalometric analysis, it appears that both sexes (mother and father) of our study group demonstrated significant findings.

Studies have demonstrated that there is ethnic and geographic variability in craniofacial morphology, and the norms and standards of one racial group cannot be used without modification for another racial group [1, 3]. India is a large country, its inhabitants being multiracial and multiethnic. Indian population is largely divided into seven ethnic groups based on anthropometric measurements and skin color. These are Indo-Aryans, Sytho-Dravidians, Mongolo-Dravidians, Monogoloids, Dravidians, Aryo-Dravidians, and Turko-Iranians, of which the Dravidians inhabit southern India [12]. An anthropometric study was conducted among 200 subjects native to Dharwad, India, aiming to establish norms in the craniofacial region. The authors found that males and females of the study population showed relatively smaller facial frameworks, especially in the lower half of the face, and a larger transverse dimension of the nasal region when compared to the Caucasian population. The majority of the females had a dolichocephalic head shape with a leptoproscopic face type, whereas the majority of males showed a brachycephalic head shape with an euryproscopic face type [4].

Hughes and Moore [10] concluded that craniofacial growth is under strong hereditary control and subscribed to a multiple-gene concept of inheritance. Horowitz et al. [9] demonstrated the significance of heredity in craniofacial form using cephalometric measurements. In 2005, Johannsdottir et al. estimated the heritability of different cephalometric parameters between parents and their children, using lateral cephalograms at ages 6 and 16. They found that daughters showed similar heritability to both parents at both ages; however, more variables were highly significant in the daughter–father group. At both ages, sons demonstrated stronger heritability to their mothers. The position of the mandible, the anterior and posterior facial heights, and the cranial base dimensions showed the greatest heritability. They concluded that cephalometric data can support predictions, and analyzing parental data can be of predictive value for offspring [11].

Studies investigating the influence of heredity in orofacial clefting have shown that noncleft relatives of affected individuals display variations in facial features [5, 8, 13, 20, 21, 24]. Central to most of these studies is the premise that

such features reflect the expression of genetic susceptibility to clefting.

Fraser and Pashayan [8] studied the facial morphology of parents of children with clefts of the lip and palate and found that compared to controls they had underdeveloped maxillae, wide bizygomatic diameters, and thinner upper lips. Coccaro et al. [5] found that the parents of children with a cleft had shorter vertical and horizontal measurements of the upper face and shorter nose length when compared to a control group and that the mandible tends to be relatively prognathic giving a reduced profile convexity.

Our results support the hypothesis that the parents of children with cleft lip, with or without cleft palate, tend to differ from the general population in certain variables of lateral cephalometry. However, apparent differences in parental cephalometric variables in conjunction with an offspring affected by a cleft may also be found occasionally and may not necessarily mean that the cephalometric findings are a risk factor or marker for clefting. Both features may be independent consequences of underlying multifactorial sequelae which are a combined genetic predisposition and environmental factors such as in utero nutritional factors, vitamin deficiency, maternal health, amongst others.

Limitations

This study sought to identify cephalometric criteria in adults and proposes that these persons have an increased risk of giving birth to a child affected by a cleft, although the level of this assumed risk is not quantified. We analyzed just 25 pairs of parents in each group, which may not be adequate to guarantee identical variations of the morphology in the study and control groups. Also, the study group did not include any children with cleft palate alone.

Conclusion

The N-Me length, ANS-Me length, and S-N-A triangle values among fathers, the S-Ba length and S-PNS-Ba triangle values among mothers, and the S-Ba length, N-Me length, and N-ANS length values among both parents (mid-parent value) were significantly lower in the study group compared to the control group. This indicates that there is indeed a decrease in the size and length of the nasomaxillary complex and cranial base in parents of children with orofacial clefts.

We conclude that there is an association between cephalometric findings of the parents and the occurrence of clefting in the offspring. Correlation studies combining cephalometric and genetic analysis of parents may be more conclusive. Larger multicentric studies including various ethnic groups may indicate whether these variations could be skeletal markers for parents who are genetically predisposed to give birth to a child with an orofacial cleft. The cephalometric analysis may be an adjunct to a genetic evaluation, which includes an increasing array of recognized chromosomal and gene anomalies.

Declarations

Conflict of interest H.H. Kishore Bhat, V. Anehosur, V.H. Upadya, N. Kumar and V. Madhur declare that they have no competing interests.

Ethical standards Ethical clearance for the study was obtained from the institutional ethics committee of SDM College of Dental Sciences and Hospital, Dharwad (IRB No. 2014/P/OS/4). Written informed consent was obtained from all the study participants in accordance with the guidelines of the Institutional Ethics Committee of SDM College of Dental Sciences and Hospital, Dharwad.

References

1. Alcalde RE, Jinno T, Pogrel MA, Matsumura T (1998) Cephalometric norms in Japanese adults. J Oral Maxillofac Surg 56:129–134
2. Al Emran SE, Fatani E (1999) Craniofacial variability in parents of children with cleft and palate. J Clin Pediatr Dent 23(4):337–341
3. Altemus LA (1960) A comparison of cephalofacial relationships. Angle Orthod 30:223–240
4. Anitha E, Ganeshkar SV, Jayade VP (Mar 2005). Establishment of anthropometric norms in craniofacial region for Dharwad population. [Unpublished Master's thesis]. Rajiv Gandhi University of Health Sciences, Bangalore.
5. Coccaro PJ, D'amico R, Chavoor A (1972) Craniofacial morphology of parents with and without cleft lip and palate children. Cleft Palate J 9:28–38
6. Cobourne MT (2004) The complex genetics of cleft lip and palate. Eur J Orthod 26:7–16
7. El Sergani AM, Brandebura S, Padilla C, Butali A, Adeyemo WL, Valencia-Ramírez et al (2021) Parents of children with nonsyndromic orofacial clefting show altered palate shape. Cleft Palate Craniofac J 58(7):847–853. https://doi.org/10.1177/10556656209 67235
8. Fraser FC, Pashayan H (1970) Relation of face shape to lip susceptibility to congenital cleft. A preliminary report. J Med Genet 7:112–117
9. Horowitz SL, Osborne RH, Degeorge FV (1960) A cephalometric study of craniofacial variation in adult twins. Angle Orthod 30:1–5
10. Hughes BO, Moore GR (1941) Heredity, growth and the dentofacial complex. Angle Orthod 11:127–122
11. Johannsdottir B, Thorarinsson F, Thordarson A, Magnusson TE (2005) Heritability of craniofacial characteristics between parents and offspring estimated from lateral cephalograms. Am J Orthod Dentofacial Orthop 127(2):200–207
12. Kharbanda OP (1999) What is the prevalence of malocclusion in India? Do we know Orthodontic Treatment Needs of our country? J Indian Orthod Soc 32:33–41
13. Kurisu K, Niswander LJD, Johnston MC, Mazaheri M (1974) Facial morphology as an indicator of genetic predisposition to cleft lip and palate. J Hum Genet 26:702–714
14. McIntyre GT, Mossey PA (2002) Asymmetry of the parental craniofacial skeleton in orofacial clefting. J Orthod 29(4):299–305
15. McIntyre GT, Mossey PA (2002) The craniofacial morphology of the parents of children with orofacial clefting: a systemic review of cephalometric studies. J Orthod 29(1):23–29

16. Morris VE, Hashmi SS, Zhu L, Maili L, Urbina C, Blackwell S, Greives MR, Buchanan EP, Mulliken JB, Blanton SH, Zheng WJ, Hecht JT, Letra A (2020) Evidence for craniofacial enhancer variation underlying nonsyndromic cleft lip and palate. Hum Genet 139(10):1261–1272. https://doi.org/10.1007/s00439-020-02169-9
17. Mossey PA, Arngrimsson R, Mccoll J, Vintiner GM, Connor JM (1998) Prediction of liability to orofacial clefting using genetic and craniofacial data from parents. J Med Genet 35:371–378
18. Mossey PA, Mccall J, O'Hara M (1998) Cephalometric features in the parents of children with orofacial clefting. Br J Oral Maxillofac Surg 36:202–212
19. Mossey PA, McColl JH, Stirrups DR (1997) Differentiation between cleft lip with or without cleft palate and isolated cleft palate using parental cephalometric parameters. Cleft Palate Craniofac J 34(1):27–35
20. Nakasima A, Ichinose M (1983) Characteristics of craniofacial structures in parents of children with cleft lip/or palate. Am J Orthod 84:140–146
21. Nakasima A, Ichinose M (1984) Size of the cranium in parents and their children with cleft lip. Cleft Palate J 21(3):193–203
22. Perkiomaki MR, Yoon YJ, Tallents RH, Barillas I, Herreraguido R, Moss ME et al (2003) Association of distinct craniofacial features in nonsyndromic cleft lip and palate family members. Cleft Palate Craniofac J 40(4):397–402
23. Prochazkova J, Tolarova M (1986) Craniofacial morphology features in parents of children with isolate cleft palate. Acta Chir Plast 28:194–204
24. Prochazkova J, Vinsova J (1995) Craniofacial morphology as a marker of predisposition to isolate claft palate. J Craniofacial Genet Dev Biol 15(3):162–168
25. Rhagavan R, Sidhu SS, Kharbanda OP (1994) Craniofacial pattern of parents of children having cleft lip and/or cleft palate anomaly. Angle Orthod 64(2):137–144
26. Setó-Salvia N, Stanier P (2014) Genetics of cleft lip and/or cleft palate: association with other common anomalies. Eur J Med Genet 57(8):381–393
27. Shibasaki Y, Ohtsuka S (1978) A cephalometric study on craniofacial morphology of parents and children with cleft lip and palate. J Stomatol Soc Jpn 3:31–43
28. Suzuki A, Takenoshita Y, Honda Y, Matsura C (1999) Dentocraniofacial morphology in parents of children with cleft lip and/or palate. Cleft Palate Craniofac J 36(2):131–138
29. Ward RE, Bixler D, Raywood E (1989) A study of cephalometric features in cleft lip – cleft palate families I: phenotypic heterogeneity and genetic predisposition in parents of sporadic cases. Cleft Palate J 26(4):318
30. Zandi M, Miresmaeili A (2007) Study of the cephalometric features of parents of children with cleft lip and/or palate anomaly. Int J Oral Maxillofac Surg 36:200–206