

Assessment of the Posteroanterior Cephalograms of the Parents of Children with Cleft Lip and/or Cleft Palate in Latvia

Ieva Maulina, Ilze Akota

SUMMARY

Objective. To compare the craniofacial morphology of parents of children with cleft lip with or without palate (CL±P), children with isolate cleft palate (CP) and individuals without family history of orofacial clefting in Latvia.

Materials and methods. Posteroanterior (PA) cephalograms were obtained from all participants: 37 couples of noncleft biological parents of children with nonsyndromic CL±P and 17 couples of noncleft biological parents of children with nonsyndromic CP (the parents groups were made dividing the parents after gender and children cleft type). The control groups consisted of 40 females and 42 males, who had no history of clefts in the family. A conventional cephalometric analysis was used to measure various measurements of facial widths.

Results. Statistically significant differences (decreased facial and biorbital width) were found between fathers of children with CP and males from the control group. Results showed asymmetry of zygomatic width (left side dominance) in all parents groups compared with the control groups. The asymmetry was detected in maxillary part (left side dominance) in CP children mothers and females and males control groups.

Conclusion. Some statistical significant differences in the PA cephalometric measurements among parents groups of children with CL±P and CP, and control groups were found. However the differences among study groups and the control groups were small, often not larger than variations in the population.

Key words: cleft lip with or without palate; parents; craniofacial morphology, posteroanterior cephalogram.

INTRODUCTION

Cleft lip with or without cleft palate (CL±P) and cleft palate (CP) is one of the most common malformations among newborns. They occur among all ethnic groups with an incidence that varies by race and nationality – Asians are at higher risk than Caucasians or Afro-Americans (1, 2). Orofacial clefts show considerable geographical variation in life birth prevalence from approximately 1/ 500 in Mongoloid populations to 1/ 2000 in Afro-American

populations (1, 2). The estimated prevalence in Latvia is 1/700 (3).

Epidemiological and family studies indicate that CL±P and CP are separate aetiological entities (4). Cleft lip with or without cleft palate and isolated cleft palate are caused by primary defects in the fusion of craniofacial processes that form the primary and secondary palate, but differ in respect to timing. Fusion of primary palate takes place at about the fifth week of embryonic life by a highly regulated process of mesenchymal proliferation and epithelial breakdown in three facial prominences: the medial nasal, lateral nasal and maxillary, whereas elevation and fusion of the secondary palate occurs at about eight weeks (4, 22).

Several craniofacial studies showed that not only subjects with cleft lip and or palate but also their parents were characterized by distinct cranio-

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facial features (2, 5-20). Initial study to test this hypothesis was based on the experimental investigation in mice, which demonstrated that the shape of the embryonic face could be a predisposing factor to clefting (21). After that followed the first study which investigated a number of craniofacial features that appeared to be predisposing to cleft lip in humans (22). Other studies followed and reported differences in the craniofacial morphology of the parents of children with CL±P, CP and general population and also differences between the parents of children with CL±P and parents of children with CP, but the results were inconsistent (2, 6, 7, 10, 12-18, 20). The variations of results could be explained by methodological differences and various populations studied. Summary of the investigated cephalometric features in the PA of parents of children with orofacial clefts and general information about these studies is described in the Table 1.

The identification of craniofacial differences in the parents who have children with CL±P or CP may assist in the identification of the genes involved in the aetiopathogenesis of orofacial clefting (OFC) and might be a help in genetic counselling.

The aim of our study was to compare the craniofacial morphology of parents of children with CL±P, parents of children with CP and individuals without family history of orofacial clefting in Latvia.

METHODS

The subjects in this study were the parents of children with nonsyndromic CL±P or CP born in Latvia. All families of the study were registered in the Riga Cleft Lip and Palate Centre of the Institute of Stomatology, Riga Stradins University, the only one referral unit for cleft children in Latvia. They visited the specialists of the Cleft Lip and Palate Centre between 2006 and 2008, and had voluntary agreed to take part in this study. Parental analysis was made to select biological parents. The data collection was performed in accordance with the regulations issued by the Central Medical Ethics Committee of Latvia. All participants in this study had acceptable occlusion, no serious anomalies of a skeletal, genetic and endocrinal systems, no history of maxillofacial traumas, previous orthodontic treatment, orthognathic surgery (due to the possible changes in the maxillofacial region). Participants in this study were:

1) 37 couples of noncleft biological parents of children with nonsyndromic CL±P. The cephalograms were taken of mothers at age of 21-45 years

(mean age 32 years), fathers at age of 22-45 years (mean age 32 years). When children were born mothers were 18 to 38 years old (mean age 26 years) while the fathers were 19 to 37 years old (mean age 27 years);

2) 17 couples of noncleft biological parents of children with nonsyndromic CP. The cephalograms was taken of mothers at age of 19-37 years (mean age 30 years), fathers at age of 23-37 years (mean age 31 years). When children were born mothers were 17 to 34 years old (mean age 26 years) while the fathers were 21 to 33 years old (mean age 27 years);

3) the control group was composed from volunteers of 40 females and 42 males, who had no history of clefts in the family. Females were at the age range between 21 and 35 years (mean age 24 years), males – between 21 and 33 years (mean age 25 years).

Posterioroanterior cephalometric measurements.

Cephalometric measurements of 190 subjects were obtained. The craniofacial landmarks and

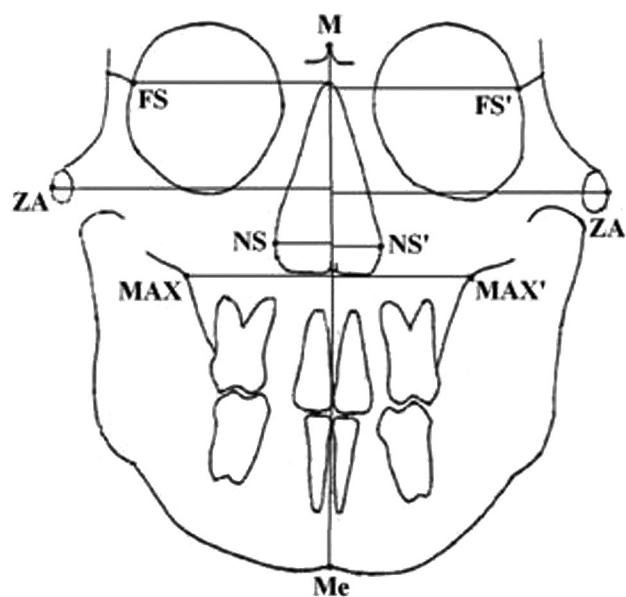


Fig. 1. Craniofacial landmarks and measurements

M – the most superior point of the outline of the nasal orifice;

FS; FS' – a point located on the lateral border of the orbital margin, at the inner aspect of the fronto-zygomatic suture;

N; N' – the most lateral point on the outline of the nasal orifice in the region of the pyriform aperture;

ZA; ZA' – the lateral aspect of the zygomatic arch;

Max; Max' – a point located at the depth of concavity of the maxillary contour, at the junction of the maxilla and the zygomatic buttress;

Me – the most inferior point on the border of the mandible at the symphysis;

M-Me – ML midline;

FS-FS' – biorbital width;

N-N' – nasal width;

ZA-ZA' – facial width;

Max-Max' – maxillary width.

measurements, as demonstrated by Saksena et al. are described in the Figure (23). Craniofacial measurements in the study and control groups were carried out by the same investigator. Digital cephalograms were taken by Kodak Trophy 6.0, analyzed using the Dolphin Imaging version 10.5 program. The magnification of x-rays was 5.6%, which was not corrected. Measurements were verified by double digitization of all the radiographs. Dahlberg's calculation formula used to calculate the method error between duplicate measurements (24).

$$ME = \sqrt{\Sigma(X - X_1)^2 / 2n}$$

Where X and X_1 – first and second measurement;
 n – sample size (number of measurements).

Mean intra-examiner error varied from 0.2-1.0 mm in different measurements.

ANOVA was used for statistical analysis. For the comparison of mean values among groups BONFERRONI analysis was used. Comparison of the right and left side symmetry was made by t-test. Significance level was considered $p < 0.05$.

RESULTS

Comparing the study groups and the control groups, significant differences were found in some measurements. The mean values, standard deviations and comparison of craniofacial measurements among all study groups and control groups are shown in the Tables 2 and 3.

Table 1. Summary of studies investigated cephalometric features in the posteroanterior cephalograms of parents of children with orofacial clefting

	Nakasima and Ichinose (6, 7) Japanese population	Raghaven et al. (2)* Indian population	Prochazkova and Vinsova (10)** Czech population	McInture and Mossey (14-16, 20) Scotch population	AlEmran et al. (12) Saudi Arabia population *	Suzuki et al. (13) Japanese population	Yoon et al. (17, 18) Costa Rican population (European origin)
Max head width	↓	↓	↑M	↓F	↓F		↓F
Interorbital width (O-O'')	↑		↑F intercanthal width ↓ biocular distance			↑	↑M
Bizygomatico-frontal sutures distance	↑	↓		↓			
Intercoronoid process distance				↓		↑	
Nasal width (NC-NC')	↑	↑		↑	↑M	↑	↑M
Maxillary width (MX-MX'')	↑	↓		↑	↓M		↑M
Bizygomatic width		↓	↓F	↓F	↓F		
Bigonial width O/O'' to Midline	↑	↓		↓F	↓F		
NC/NC'' to Midline				≠M	≠M		≠
MX/MX'' to Midline	≠			≠M	≠M		
Facial width in relation total face height	↓						↑

Keys:

* – the study examined the parents of children with cleft lip with or without palate;

** – the study examined only the parents of children with isolated cleft palate;

↑ – increased;

↓ – reduced;

≠ – asymmetry;

F – females only;

M – males only.

Between the fathers of children with CP and males from the control group significant differences were found in facial width (ZA-ZA'; $p < 0.05$), biorbital width (FS-FS'; $p < 0.01$), in measurement from midline to the right side zygomatic arch (ZA-ML; $p < 0.01$) and in measurements from midline to the right and left side orbital margin (FS-ML; $p < 0.05$; FS'-ML; $p < 0.01$). These values were smaller for fathers of children with CP compared to control males.

There were no statistically significant differences in measurements of facial widths among CL(P) mothers, CP mothers and control females.

Comparison of symmetry of right and left side of the CL±P mothers and fathers, CP mothers and fathers and control group are shown in the Tables 4 and 5. There was found asymmetry of zygomatic width in all study groups compared to controls (ZA-

ML, ML-ZA'; $p < 0.01$). Left side dominance was found in all these measurements. There was detected left side dominance in maxillary part in CP children mothers as well as in both control groups (MX-ML, ML-MX'; $p < 0.01$), but did not in the CL±P mothers and fathers, and CP fathers.

There was detected the asymmetry in the orbital region only in the female control group (FS-ML, ML-FS'; $p < 0.05$). Left side dominance was found in that measurement, too.

All other measurements were not significantly different.

DISCUSSIONS

The cephalometric contributions of characteristics of craniofacial morphology in parents, of children with orofacial clefts had been focus of re-

Table 2. Comparison of craniofacial measurements (mm) among CL(P) fathers, CP fathers and control group of males

	CL(P) fathers (n=37)		CP fathers (n=17)		Control group (n=42)		p value
	Mean	SD	Mean	SD	Mean	SD	
Max'-ML (left)	31.1	1.9	30.8	1.9	31.4	1.8	Ns
Max-ML (right)	30.6	1.7	30.6	2	30.3	1.8	Ns
ZA'-ML (left)	67.3	2.2	66.5	3	68.4	2	Ns
ZA-ML (right)	66	2.4	65"	3	66.2"	2.6	0.012**
FS'-ML (left)	46.5	2.1	45.4"	1.5	47.1"	1.8	0.006**
FS-ML (right)	46.4	2.6	45.1"	1.7	46.8"	2	0.028*
N-N' Nasal width	30.7	2.7	30.2	2.3	30.5	2.5	Ns
Max-Max' Maxillar width	61.7	3.2	61.6	3.5	61.8	2.7	Ns
ZA-ZA' (facial width)	133.3	3.9	131.4"	5.7	134.7"	4	0.031*
FS-FS' (biorbital width)	92.9	4.4	90.5"	2.6	93.9"	3.5	0.007**

ML – midline;

Ns – not significant difference;

" – the values with statistically significant difference;

* – $p < 0.05$; ** – $p < 0.01$.

Table 3. Comparison of craniofacial measurements (mm) among CL(P) mothers, CP mothers and control group of females

	CL(P) mothers (n=37)		CP mothers (n=17)		Control group (n=40)		p value
	Mean	SD	Mean	SD	Mean	SD	
Max'-ML (left)	29.7	2	30	2.5	29.5	1.6	ns
Max-ML (right)	29.3	2	29.2	1.8	28.7	1.6	ns
ZA'-ML (left)	63.2	2.1	62.3	2	63.2	2.2	ns
ZA-ML (right)	62.1	2.1	61.1	2.1	61.3	2.2	ns
FS'-ML (left)	44.8	1.9	44.8	2.1	44.8	2	ns
FS-ML (right)	44.9	1.8	44.6	2.1	44.3	1.6	ns
N-N' Nasal width	28.4	2.9	28.7	2.9	28.5	2.7	ns
Max-Max' Maxillar width	59	3.6	59.1	4.1	58.1	2.6	ns
ZA-ZA' (facial width)	125.4	3.2	123.3	3.7	124.5	4.1	ns
FS-FS' (biorbital width)	89.8	3.2	89.4	3.9	89.1	3.2	ns

ns – not significant difference.

search for years. However, no clear morphological differences had been delineated. The variations in study results could be explained by methodological differences and by variation of studied populations.

The choice of measurements was based on easily identified and reliably reproduced landmarks in an attempt to establish the main facial parameters of Latvia population. In Latvia no series of PA cephalograms that could be used as control group in our study were not available. Furthermore, involving ionizing radiation would be unethical to sample the population randomly. After the approval from the Central Medical Ethics Committee of Latvia, volunteers took part in this study.

The aetiology of orofacial clefts is considered to be polygenetic and multifactorial, with influence from genetic and environmental sources. The genetic influence in some cases could be minimal, in other cases – heavily weighted to one parent, or approximately equal where each parent happens to possess the same degree of predisposing factors (9). All of parents of cleft children in our study were without history of cleft in previous generations which could mean that the main role in the etiology of cleft in these families were interaction of genes and environmental factors.

One of the most investigated craniofacial parameter is width of the nasal cavity, but the results

are contradictory (2, 6, 7, 12-18). The increased nasal width of the parents of children with clefts has found several authors (2, 6, 12, 13, 17, 26). It has been suggested that increased width of midfacial structures may prevent palatal shelf contact (6, 13, 18, 22, 26). Some authors found a significant reduction in nasal width in the CL±P noncleft twin's group. Explanation was that smaller nasal cavity width could represent an inherited reduced size of the frontonasal processes due to a deficiency or failure of contact with the maxillary processes and thus a cleft of primary palate was developed (19, 27). We did not find differences in the nasal width between different groups in our study. Our results with respect to nasal width were similar with those observed in anthropometric study done in Latvian population (25) and Czech population (10).

The zygomatic width in the CL±P father and mother group, as well as CP mother group was the same as in the controls, and this corroborated the findings of other researchers (6, 13, 17). There were no significant differences in the zygomatic width of the cleft mother and control females in the anthropometric study in Latvia (25). Statistically significant smaller zygomatic width in our study was found of the fathers of children with CP comparing with the male's control group. The decreased zygomatic width in the cleft parents was found in

Table 4. Comparison of symmetry of right and left side of the CL±P fathers, CP fathers and control males (mm)

Measurements of the symmetry		CL(P) fathers		CP fathers		Control group	
Right	Left	Right (mm)	Left (mm)	Right (mm)	Left (mm)	Right (mm)	Left (mm)
FS – ML	ML – FS'	46.4	46.5	45.1	45.1	46.8	47.1
p value		ns		ns		ns	
ZA – ML	ML – ZA'	66	67.3	65	66.5	66.2	68.4
p value		0.0028**		0.0065**		ns	
Max – ML	ML – Max'	30.6	31.1	30.6	30.8	30.3	31.4
p value		ns		ns		0.0044**	

** – $p < 0.01$;

ns – not significant difference.

Table 5. Comparison of symmetry of right and left side of the CL±P mothers, CP mothers and control females (mm)

Measurements of the symmetry		CL(P) mothers		CP mothers		Control group	
Right	Left	Right (mm)	Left (mm)	Right (mm)	Left (mm)	Right (mm)	Left (mm)
FS – ML	ML – FS'	44.9	44.8	44.6	44.8	44.3	44.8
p value		ns		ns		0.02**	
ZA – ML	ML – ZA'	62.1	63.2	61.1	62.3	61.3	63.2
p value		0.0137**		0.0129**		ns	
Max – ML	ML – Max'	29.3	29.7	29.2	30	28.7	29.5
p value		ns		0.0132**		0.009**	

** – $p < 0.01$;

ns – not significant difference.

Indian population (2).

The biorbital width in the CL±P father and mother group, as well as CP mother group was the same as in the controls, and this is in agreement with the findings of other authors (2, 11-13, 17). Decreased biorbital width was found in fathers of CP children compare to control group in our study.

There was an established asymmetry of zygomatic width in all study groups compared with the control groups in our study. Left side dominance was found in all these measurements.

A detected asymmetry (left side dominance) in maxillary part in CP children mothers as well as both control groups was found, but not in the CL±P mothers and fathers, and CP fathers. Some other authors have reported the left side dominance in the maxillary part of the cleft fathers' groups (11, 26).

The asymmetry in the orbital region we detected only in the female control group.

Some authors reported craniofacial asymmetry in noncleft population with the left side being overall greater than the right (28), but others also suggested left side dominance in maxillary asymmetry (29). The controversially results were found in frontal cephalometric study on 18 to 25

year old noncleft subjects. It was reported that the craniofacial skeleton is asymmetric in the general population with the right side being greater than the left (30).

We found statistically significant differences between CP fathers group and males control group in facial and biorbital widths as well as the statistically significant differences among study groups and the control groups in symmetry measurements in our study, but the clinical relevance of these findings could be questionable. This determine the necessity for the further investigations for specific traits.

These results might be of value in the prediction of liability to clefting and have to be taken into account in the pathogenesis of both CP and CL(P).

CONCLUSION

Some differences in the PA cephalometric measurements among parents groups of children with CL±P and CP, and control groups were found. However the differences among study groups and the control groups were small, often not larger than variations in the population.

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