ORIGINAL ARTICLE

CRANIOFACIAL CHARACTERISTICS IN PARENTS OF CHILDREN WITH NON-SYNDROMIC CLEFT LIP AND/OR CLEFT PALATE

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كان الغرض من الدراسة هو تحديد فيما إذا كانت الاختلافات في الشكل الوجهي القحفي بين والدي الأطفال المصابين بشق الشفة والحنك وبين مجموعة المقارنة الطبيعية والذين لا يوجد لديهم تاريخ إصابة بالشق في عوائلهم ، وذلك في المجتمع السعودي ، لهدف المساعدة في إيجاد طريقة مسح ممكن أن تساعد في تعيين الأشخاص المعرضين لإنجاب أطفال مصابين بشق الشفة والحنك .
تم الحصول على أشعة السيفالوميتريك الجانبية من مجموعة التجربة التي اشتملت على ٤٠ ذكراً و٤٠ أنثى لديهم أطفال مصابين بالشق . ومن مجموعة المقارنة الطبيعية أيضاً التي اشتملت على ٣٢ ذكراً و٣٥ أنثى ، ذوي العوائل السليمة غير المصابة بالشقوق . وقد تم إعداد برنامج كمبيوتر خاص وتحديد ١٩ علامة رقمية (لمسية) لكل شخص .
طبق اختبار – T والتحليل الترددي المنطقي لفحص الحقائق . وقد بدت النتائج متميزة لكل من الذكور والإناث ضمن مجموعة التجربة ؛ إذ أبدى الذكور فك سفلي وقبة حنك أقصر ، وزيادة في كل من زاوية قاعدة القحف ، وزاوية غونيال gonial ، وزاوية المحور– Y ، وزاوية مستوى الفك السفلي ، أما الإناث فقد أبدين زيادة في انخفاض الارتفاع الوجهي ، وقصر في الفك السفلي وتراجع في الجزء الأوسط من الوجه مع انخفاض زاوية S NA . وأيضاً زيادة في كل من المحور – Y وزاوية غونيال gonial وزاوية مستوى الحنك .

The purpose of this study was to determine whether there are differences in craniofacial morphology between parents of children with non-syndromic cleft lip and palate and normal controls with no family history of cleft in their families in a Saudi sample, that might possibly assist in devising a screening method that could identify an individual as "at-risk" in producing a child with a cleft.
Lateral cephalometric radiographs were obtained from a study group consisting of 40 males and 40 females who have children with cleft deformity, and a control group of 32 males and 35 females who have no family history of clefts. A total of 10 landmarks were digitized for each individual by a custom-made computer program.
T-test, logistic regression analysis were applied to the data. Significant findings were obtained for both males and females of the experimental group. The fathers exhibited a shorter mandible, a shorter palate, an increased cranial base angle, increased gonial angle, Y axis angle and mandibular plane angle. The mothers showed increased lower facial height, a shorter mandible and a retrusive mid-face with a reduced SNA angle. Also, an increased Y-axis, gonial angle and palatal plane angle were found.

Introduction

Cleft lip and palate (CL/P) is the most common oralfacial congenital deformity. This malformation has intrigued a wide range of professionals in trying to expand their understanding of its etiology. Over the years, numerous etiological possibilities have been considered.[1]

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Warkany et al[2] reported that as early as 1757, Trew recognized that heredity played a role in the production of CL/P. Insight into the etiology of non-syndromic CL/P, as well as identifying individuals at high risk, may perhaps pave the way for preventive programs.

Fraser and Pashayan[3] have advanced the hypothesis that if facial shape is genetically determined and also related to predisposition to

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the cleft lip and palate anomaly, then the parents of children with CL/P should have facial dimensions different from those of the normal population. Based on this hypothesis, the present study investigated and analyzed cranio-facial structures in a group of Saudi parents who have CL/P children and compared them to a control group with no history of clefts in the family.

Materials and Methods

The material for this study consisted of a study group and control group. The study group included 80 parents of 49 cleft children (probands) with non-syndromic cleft lip and/or cleft palate, referred from the University Hospital and the College of Dentistry, King Saud University. The control group consisted of 32 adult males and 35 adult females, with no family history of oro-facial cleft. All participants in this study are Saudi nationals. Age range, mean and standard distribution for experimental and control groups are shown in Table 1.

Table 1. Age range, means and standard deviation for study and control subjects.

Group		Number	Age Range	Mean Age	SD
Study	Male	**40**	16-42	**25**	**6.2**
	Female	**40**	19-51	31.6	**7.6**
Control	Male	**32**	18-37	**24**	3.69
	Female	**35**	18-38	**30**	4.49

Lateral cephalograms were taken for each subject in both the experimental and control group using standard cephalometric machine with the following setting: MA 10, 10 seconds, KV 85, film size 8x10. The subject was asked to sit upright and the head was stabilized by the cephalostat and oriented with the Frankfurt horizontal plane, parallel to the floor. Nineteen landmarks were selected from each cephalogram (Table 2). These landmarks were modified after Nakasima and Ichinose[4] and

Table 2. Landmarks and their definitions on lateral view cephalograms.

Glabella (Gl)	The most prominent point midway between the two supraorbital ridges just above the frontonasal suture.
Opistocranion (Op)	The point in the midline that projects further backwards and marks the posterior end of the maximum cranial length.
Nasion (N)	The most anterior point of the naso frontal suture.
Sella turcica point (S)	The mid point of the hypophysial fossa.
U point (U)	Lower point on the outline of hypohyseal fossa.
R Point (R)	Intersection of U-N line and cranium outline.
Porion (Po)	The most superior point on the external auditory meatus.
Orbital (Or)	The lowest point on the infra orbital margin.
Pterygomaxillary Fissure (Ptm)	The most superior point on the outline of the pterygo-maxillary fissure.
Condylon (Cd)	The most superior aspect of the condylar head.
Basion (Ba)	Lowest point on the anterior margin of the foramen magnum. Also the most caudal point of the clivus.
Anterior nasal spine (Ans)	A median point on the spinous process of the maxilia.
Posterior nasal spine (Pns)	A median point on the spinous process formed by the most posterior midline projection of the juncture of the palatine bones.
Subspinale (A)	A median point on the innermost curvature on the anterior nasal spine to the crest of the maxillary alveolar process.
Supra mentale (B)	A median point on the mandibular profile from the crest of the alveolar process to progonion.
Pogonion (Pg)	The most anterior point on the contour of the bony chin.
Gnathion (Gn)	The most anterior - inferior point on the contour of the bony chin symphysis.
Menton (Mn)	The most inferior point on the symphyseal outline.
Gonion (Go)	A constructed point, the intersection of the lines tangent to the posterior margin of the ramus and the mandibular base.
Articulare (Ar)	The point of intersection of the posterior margin of the ascending ramus and the outer margin of the cranial base.

Rakosi[5](Fig. 1). In case of two shadows of a landmark, the mid-point was selected. The landmarks were digitized using a numonic digitizer with 0.010 level of accuracy. Linear and angular measurements were then calculated by "PCDIC" program Version 5, being the program

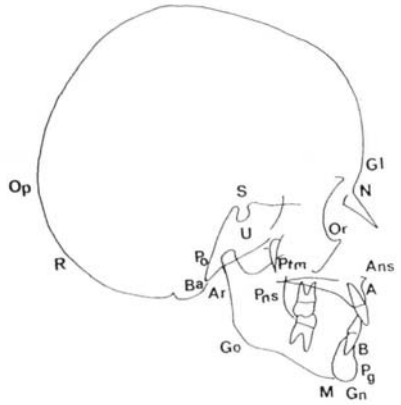

Fig. 1. The cephalometric landmarks used. Lateral view.

Gl, glabella; Op opistocranion; N, nasion; R, intersection of UN line and cranium outline; Po, porion; Or, orbitale; Ptm, pterygomaxillary fissure; Ba, basion; Ans, anterior nasal spine; Pns, posterior nasal spine; A, subspinale, B, supramentale; Pg, pogonion; Gn, gnathion; M, menton; Go, gonion; Ar, articulare

used for digitizing two-dimensional images and licensed by Dental Technology and Biomaterial Karolinska Institute, Sweden. In addition, method error due to landmark location was evaluated using Dahlbergs Equation[6] on the data of 15 radiographs randomly selected and re-digitized. This program requests the user to register each image twice when the difference during the second registration is greater than the tolerance level of 0.5. Under such condition, an additional registration of the landmark is required. Descriptive statistical analysis which consisted of minimum, maximum, mean and standard deviation was carried out. The differences between study and control group were tested using unpaired student "t" test. Stepwise logistic regression[7] was then used to select a set of variables that discriminated between the study and control parents. These analyses were performed using the Statistical Package for Social Sciences Version 6.

Results

Mean, standard deviation, mean difference of linear and angular cephalometric variables for the study and the control males are presented in Table 3. Fathers with cleft children showed a significantly shorter mandible corpus length ($p < 0.01$) and a shorter palate ($p < 0.05$) compared to the control group. The findings also revealed that the cranial base angle was more obtuse in fathers of cleft lip and palate children ($p < 0.05$). The Y-axis was greater ($p < 0.05$), the gonial angle and the mandibular plane angle were also significantly increased ($p < 0.001$, $p < 0.01$ respectively) in the same group of fathers (Fig. 2).

Table 3. Comparison between experimental and control group measurements obtained from lateral cephalograms in males:
(n =32 in control group, n=40 in experimental group).

Variables Linear (mm)	Control		Experimental		Mean Difference	P
	Mean	SD	Mean	SD		
Gl-Op	178.7	8.4	178.2	7.6	0.5	0.7972
N-R	162.7	7.7	161.2	7.8	1.5	0.4291
N-U	67.8	3.2	66.4	3.1	1.4	0.0761
U-Ba	42.6	4.2	42.4	3.9	0.2	0.8737
N-GN	114.1	6.1	116.1	7.4	-2	0.2137
N -Ans	51.2	3.1	50.4	3.3	0.8	0.3182
U - Pns	40.8	2.9	39.9	3.1	0.9	0.2310
Ans - M	66.7	4.9	68.9	6	-2.2	0.1068
Ar - Go	47.5	5.1	49.9	5.1	-2.4	0.0856
Go-Pg	76.9	4.7	73.9	4.2	3	O.Or*
Cd -Go	59	4.7	58.8	5.1	0.2	0.8503
Cd-Gn	114.4	4.8	113.1	5.1	1.3	0.3089
Cd -A	83.1	4.4	81.4	3.6	1.7	0.0741
Ans - Pns	53.1	3.6	50.3	3.8	2.8	0.05*
U-Go	74.1	4.5	72.8	6.1	1.3	0.3231
Angular (Degree)						
N - S/Ba	129.3	5.3	132.5	6.7	-3.2	0.05*
SNA	81.8	4.7	81.7	5.3	0.1	0.8985
SNB	80.1	3.8	79.2	4.7	0.9	0.3761
N - S/Gn	66.6	3.7	69	4.5	-2.4	0.05*
S-N/ Ans-Pns	12.9	4.2	12.7	4.7	0.2	0.8423
Ar-Go/ Go-Gn	118.5	6.2	123.9	7.8	-5.4	0.001***
S-N/ Go-Gn	28.2	5.9	32.1	7.2	-3.9	O.Or*
NPg/ Or-Po	86.2	3.1	87.5	4.1	-1.3	0.1305

Asterisks indicate a significantly different value from the corresponding value in the control groups.
* $p < 0.05$ " $p < 0.01$ *** $p < 0.001$

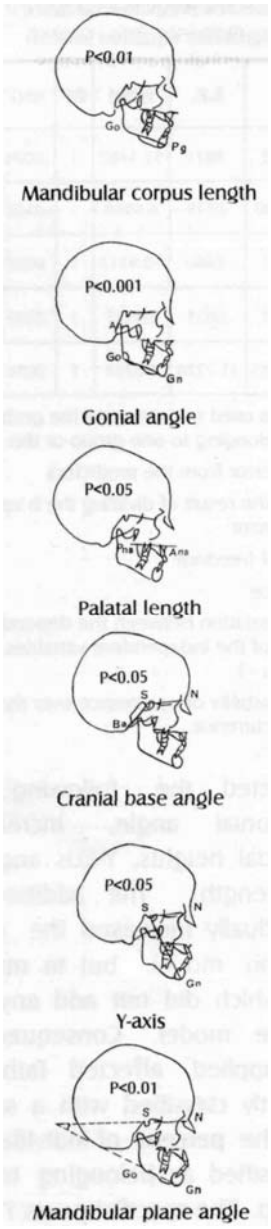

Fig. 2. Significant cephalometric findings for fathers.

For the mothers, the discrepancy analysis for both groups are shown in Table 4. The results revealed that the mothers of cleft lip and palate children differ from the control by having an increased total anterior facial height ($p < 0.05$) and lower anterior facial height ($p<0.01$).

Table 4. Comparison between experimental and control group measurements obtained from lateral cephalograms in females:
(n = 35 in control group, n = 40 in experimental group).

Variables Linear (mm)	Control		Experimental		Mean Difference	P
	Mean	SD	Mean	SD		
Gl -Op	168.9	6.1	168.6	7.3	0.3	0.8671
N-R	151.6	9.4	151	7.7	0.6	0.7807
N-U	63.5	3	64.3	3.2	-0.8	0.2528
U-Ba	39.1	2.7	38.5	3.3	0.6	0.3549
N -GN	105.3	7.9	109	6	-3.7	0.05*
N-Ans	47.8	3.6	47.9	3.1	-0.1	0.8554
U- Pns	38.2	3.5	37.1	2.7	1.1	0.1205
Ans - M	61.4	5.8	64.6	4.6	-3.2	0.01"
Ar - Go	43.5	4.7	42.8	5	0.7	0.5812
Go-Pg	73.3	4.6	70.8	3.9	2.5	0.05*
Cd-Go	54.4	4.1	52.5	4.5	1.9	0.0569
Cd-Gn	106	5.9	106.4	4.9	-0.4	0.7658
Cd-A	79.9	3.9	78.2	3.5	1.7	0.05*
Ans - Pns	50.1	3.2	49.9	2	0.2	0.8489
U -Go	66.9	5.4	64.9	5.5	2	0.1112
Angular (Degree)						
N - S/Ba	131.7	5.6	133.4	5.3	-1.7	0.1859
SNA	83.1	4	80.9	3.5	2.2	0.05*
SNB	79.5	4.2	78	2.9	1.5	0.0700
N - S/Gn	67.2	4.6	69.1	3.2	**-1.9**	0.05*
S-N/ Ans-Pns	12.6	4	13.9	3.2	-1.3	0.1342
Ar-Go/ Go-Gn	116.6	7.5	124.2	6.7	-7.6	o.oor**
S-N/ Go-Gn	28.9	6.9	34.1	5.6	-5.2	o.oor**
NPg/ Or-Po	87.1	3.9	87.2	3	-0.1	0.8802

Asterisks indicate a significantly different value from the corresponding value in the control groups.
* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

The mandible corpus length and the mid-facial length were significantly shorter ($p < 0.05$) compared to unaffected mothers. The SNA angle was smaller ($p < 0.05$) and Y-axis was greater ($p < 0.05$) in mothers with cleft lip and palate children. The gonial angle and mandibular plane angle were greater ($p < 0.001$) in the

same group of mothers (Fig. 3). All other differences in the measurements were not statistically significant for both fathers' or mothers' cleft lip and palate children compared to the control subjects.

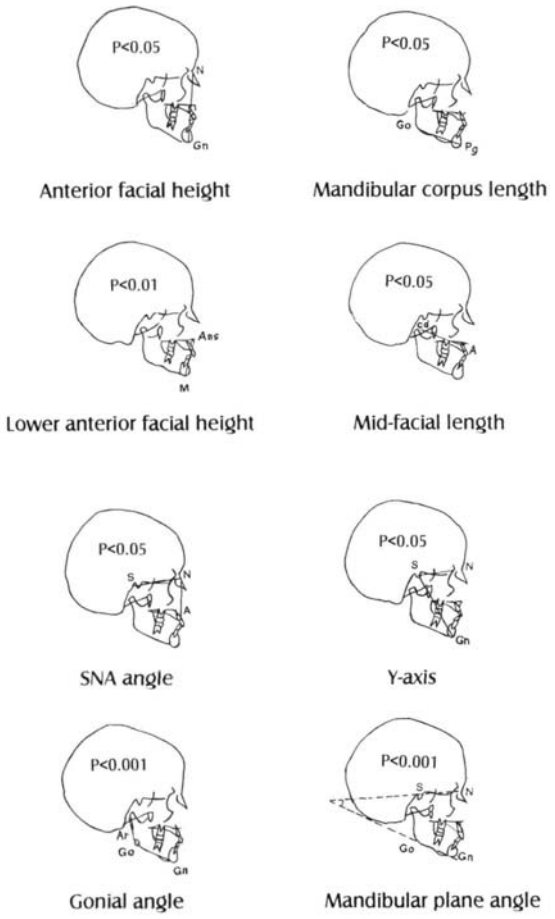

Fig. 3. Significant cephalometric findings for mothers.

Logistic Regression Analysis

A step-wise regression analysis was performed on 22 variables (Table 5) of the lateral skull radiographs for 72 cases, representing both the study and the control groups of the fathers. This was to determine which of the variables could best explain the difference between the two groups in the craniofacial characteristics. Among the twenty-two variables, the regression model selected the following variables: increased gonial angle, increased lower posterior facial heights, Y-axis angle and the mandibular length. The addition of more variables gradually increased the efficiency of the regression model, but in much smaller increment, which did not add any significant effect to the model. Consequently, as the model was applied, affected fathers (82.5%) were correctly classified with a sensitivity of 71.8%, i.e., the percent of individuals who are correctly classified as belonging to the experimental group. The specificity was 75%, i.e., the percent of individuals correctly classified as belonging to the control group. The same analysis was applied on data obtained from the mothers. An overall correct classification regarding affected mothers reached up to 75% with a sensitivity of 70% and a specificity of 77.14%. The model indicated that an increased gonial angle and a reduced SNA were the only variables to differentiate the two groups (Table 6).

Table 5. The selected predictive variables in the logistic regression equation (males).

Variable	B	S.E.	wald	DF	SIG	R	Odd Ratio
Ar-Go	.2892	.0823	12.3432	1	.0004	.3234	1.3354
Cd-Gn	-0.1890	.0736	6.5950	1	.0102	-.2155	.8278
Ar-Go/Go-Gn	.2246	.0680	10.9117	1	.0010	.3001	1.2519
N-S/S-Gn	.2472	.0851	8.4357	1	.0037	.2551	1.2519
Constant	-36.3755	11.7228	9.6284	1	.0019		

B - b-weight is used to determine the probability of a subject belonging to one group or the other

S.E. - standard error from the predictors

wald - square of the result of dividing the b value by its standard error

DF - degrees of freedom

SIG - significance

R - partial correlation between the dependent variable and each of the independent variables. R ranges from -1 to +1

Odds Ratio - probability of occurrence over the probability of non-occurrence.

Table 6. The selected predictive variables in the logistic equation (females).

Variable	B	S.E.	Wald	DF	SIG	R	Odd Ratio
Ar-Go	.1646	.0457	12.9837	1	.0003	.3255	1.1789
SNA	-.1767	.0770	5.2624	1	.0278	-.1774	.8380
Constant	-5.1938	7.7236	.4522	1	.5013		

B - b-weight is used to determine the probability of a Subject belonging to one group or the other

S.E. - standard error from the predictors

wald - square of the result of dividing the b value by its standard error

DF - degrees of freedom

SIG - significance

R - partial correlation between the dependent variable and each of the independent variables. R ranges from -1 to +1

Odds Ratio - probability of occurrence over the probability of non-occurrence

Discussion

For many years, researchers have been developing methods to identify individuals at high risk to various diseases. Identified individuals are then subjected to special programs such as prevention or early detection.[8]

From the literature review, there appears to be several studies which have investigated the craniofacial characteristics of parents with a child born with cleft lip or palate.[3913] These studies suggest that the parents of children with cleft lip and palate might have some morphological features different from the rest of the population. Therefore, this study was carried out to test the hypothesis that Saudi parents with cleft lip and/or palate children have different features from the normal Saudi parents, and to compare the findings of other investigators.

The overall results of the present study appear to support the tested hypothesis. From the lateral cephalometric measurements, it appears that both sexes of the experimental group demonstrated significant findings compared to the control group. Findings common to both fathers and mothers of children with cleft lip and palate revealed an increased gonial angle, an increased mandibular plane angle and a shorter mandibular corpus length. This was associated with a backward and downward inclination of the mandible, thus increasing the lower facial height and increasing the Y-axis angle. An increase in lower facial height was also found in the studies carried out by some authors,[34] whereas others[910]reported a decrease in lower facial height. Whereas, in the present study, the increased lower facial height was found to be statistically highly significant for mothers only ($p > 0.01$).

The increased gonial angle and short mandible observed in the present study was reported also by Raghavan et al,[13] whereas Nakasima and Ichinose[4] did not observe a significant difference in the gonial angle. The decreased mandibular length was also in contrast to the findings reached by Coccaro et al.[9]

The mothers of the cleft lip and palate showed a significant retrusion in the linear measurement of point "A." This was indicated by a significantly smaller SNA angle compared to the control group. The fathers of cleft lip and palate children, despite having a significantly smaller palatal length ($p < 0.05$), did not show a significant decrease of the SNA angle when compared to the control group. This finding may be attributed to the fact that SN line and palatal plane were in a relatively retruded position. Another possible explanation could be that in the male, the shorter anterior cranial base (N-S) probably resulted in a deficient downward and forward growth of the maxilla.

The logistic regression analysis provided the authors with a model that identified certain facial characters that may help differentiate and explain the variations between the two groups. Still, a major practical difficulty is the requirement of large sample sizes in order to achieve definitive results.

Conclusion

The parents of children having cleft lip and/or palate anomaly differed from the control group in the following aspects:

1. Both parents showed shorter mandibular body with increased gonial, Y-axis and mandibular plane angle.
2. The fathers showed an increased cranial base angle and a shorter palate, and an increased lower posterior facial height.
3. The mothers on the other hand, demonstrated an increased total and lower facial height and a deficient mid-face with a reduced SNA angle.

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