http:// ijp.mums.ac.ir
Original Article (Pages: 13691-13702)

Comparative Three-Dimensional Evaluation of Spheno-Occipital Synchondrosis and Zygomatico-Maxillary Suture in Cleft Lip and Palate Children versus the Normal Population

Arezoo Jahanbin[1], *Alireza Chamani[2], Seyed Hosein Hoseinizarch[3], Saeedeh Hajebi Khaniki[4]

[1]Department of Orthodontics, School of Dentistry, Mashhad University of Medical Sciences, Mashhad, Iran. [2]Resident of Orthodontics, School of Dentistry, Mashhad University of Medical Sciences, Mashhad, Iran. [3]Department of Oral and Maxillofacial Radiology, School of Dentistry, Mashhad University of Medical Sciences, Mashhad, Iran. [4]Student research committee, Department of Biostatistics, School of Health, Mashhad University of Medical Sciences, Mashhad, Iran.

Abstract

Background: The purpose of the present study was a three-dimensional evaluation of the spheno-occipital synchondrosis (SOS) and zygomatico-maxillary suture (ZMS) in cleft lip and palate patients versus the normal population.

Materials and Methods: In the case-control study, cone beam computed tomography scans of 153 unilateral or bilateral cleft lip and palate patients and 153 scans of healthy non-cleft individuals with skeletal Class I occlusion from 6 to 18 years were selected. Then the ZMS and SOS maturation stages were determined. Mann-whitney test, spearman correlation, repeated measurement, and bayesian transition analysis were used for statistical analysis. P-value < 0.05 was considered as significant.

Results: The result of this study showed ZMS maturation in cleft lip and palate patients was significantly earlier than control group; although, there were no statistically significant differences between case and control groups in SOS maturational stages. This study showed that in the normal population, the mean age of stage B, which is the ultimate level of favorable response to growth modification in ZMS development, is 11.50 ± 1.50 years for females and 10.79± 1.89 years for males and in cleft lip and palate patients, the mean age of stage B is 9.53 ± 1.46 years for females and 9.71 ± 1.36 years for males. There was no significant difference in mean age at any of maturational stages of ZMS and SOS between unilateral and bilateral cleft lip and palate patients (P>0.05).

Conclusion
Maturation of zygomatico-maxillary suture in cleft lip and palate was earlier than non-cleft children, however sphenooccipital synchondrosis did not show any significant differences in maturational stages between cleft lip and palate patients and healthy controls.

Key Words: Cleft lip and palate, Spheno-occipital syncondrosis, Zygomatico-maxillary suture.

*Please cite this article as: Jahanbin A, Chamani A, Hoseinizarch SH, Hajebi Khaniki S. Comparative Three-Dimensional Evaluation of Spheno-Occipital Synchondrosis and Zygomatico-Maxillary Suture in Cleft Lip and Palate Children Versus the Normal Population. Int J Pediatr 2021; 9(6): 13691-702. DOI: **10.22038/IJP.2020.50056.3991**

Corresponding Author:

Dr. Alireza Chamani, Address of Correspondence: Department of Orthodontics, School of Dentistry, Park Square, Mashhad, Iran, Fax: +985118829500.

Email: Alireza.chamani72@yahoo.com

Received date: Sept. 22, 2020; Accepted date: Jan.22, 2021

1- INTRODUCTION

The most common craniofacial malformation found at birth is unilateral (UCLP), and bilateral cleft lip and palate (BCLP). Nearly one out of every 700 live births has a kind of cleft that may be a result of genetic and environmental factors (1-3). Class III malocclusion is a common anomaly in cleft lip and palate children, mainly due to maxillary deficiency. Conventionally, growing patients with maxillary deficiency are treated with a facemask with a heavy anterior traction applied to the maxilla to stimulate its forward and downward movement and to redirect mandibular growth. There is some evidence showing more favorable results with facemask therapy in younger patients. However, the best treatment timing based on the best responses to facemask therapy remains controversial and long-term results and stability of this treatment modality remain debatable (4-7).

The maturation of the circum-maxillary sutures, including the transverse palatine suture, the fronto-maxillary sutures, and the zygomatico-maxillary sutures (ZMSs), determine the amount of maxillary protraction (8-10). Among the maxillary sutures, ZMS is more important because of the greater complexity in its interdigitation than other circumaxillary sutures (11). The ZMSs are the tallest and coarsest circum-maxillary sutures. So, analysis of the maturation of ZMSs may be an indicator of the response to orthopedic maxillary protraction (12).

In orthodontics, the cranial base is also important because the growth changes of the maxillo-mandibular complex are affected by the cranial base. In some studies it has been recommended that a guard rail for growth of the maxilla, mid-face, and even lower facial complex be placed at the cranial base (13, 14). As in cleft lip and palate patients the development of the maxillofacial and dental arch are different from normal growth, one of the questions could be whether there is a difference in cranial base as well as maxillary sutures maturation in these patients versus normal children (15, 16). Therefore, in this study, we aimed to investigate development of the spheno-occipital synchondrosis and the zygomatico-maxillary suture in cleft lip and palate patients versus the normal population from 6 to 18 years of age to find the best time for maxillary growth modification.

2- MATERIALS AND METHODS

2-1. Study design and population

In this case-control study, cone beam computed tomography (CBCT) scans of 153 cleft lip and palate (CLP) patients (94 unilateral and 59 bilateral) as case group and 153 scans of healthy skeletal Class I individuals as control group from 6 to 18 years were selected. Both groups were matched in terms of age. All CBCTs were selected from a radiology clinic archive. The reason for taking CBCTs from control group, was to diagnose sinusitis or bone fracture; however, we excluded all cases with theses diagnoses from the control group and only CBCTs of healthy non-cleft persons were selected for this investigation.

Exclusion criteria were CBCTs that showed head trauma or bone fracture or sinusitis. ZMSs maturation was identified in the sagittal view, at the infra orbital (superior), and infra zygomatic (inferior) sections of the suture. Since the sagittal cross-sectional slice allows the long axis of the ZMS to be observed, radiographic interpretation was performed in the sagittal cross-sectional slice. The contrast or brightness of the images was not changed. An expert examiner categorized the ZMS maturation stage of samples in a dark room based on the visual analysis method mentioned by Angelieri et al. (11). Similar maturational stages are commonly found in the two sides of the ZMSs. Therefore, in the staging phase, only the higher maturational stage of the ZMSs for each patient was identified.

Angelieri et al. (11) determined and described the five stages of ZMS maturation (**Figure. 1**):

Stage A: Even high-density sutural line, without or slight interdigitation.

Stage B: Scalloped appearance of the high-density sutural line.

Stage C: Dual parallel, scalloped, high-density lines, detached in a few minor low-density spaces.

Stage D: Union in the inferior section of the suture.

Stage E: Complete union.

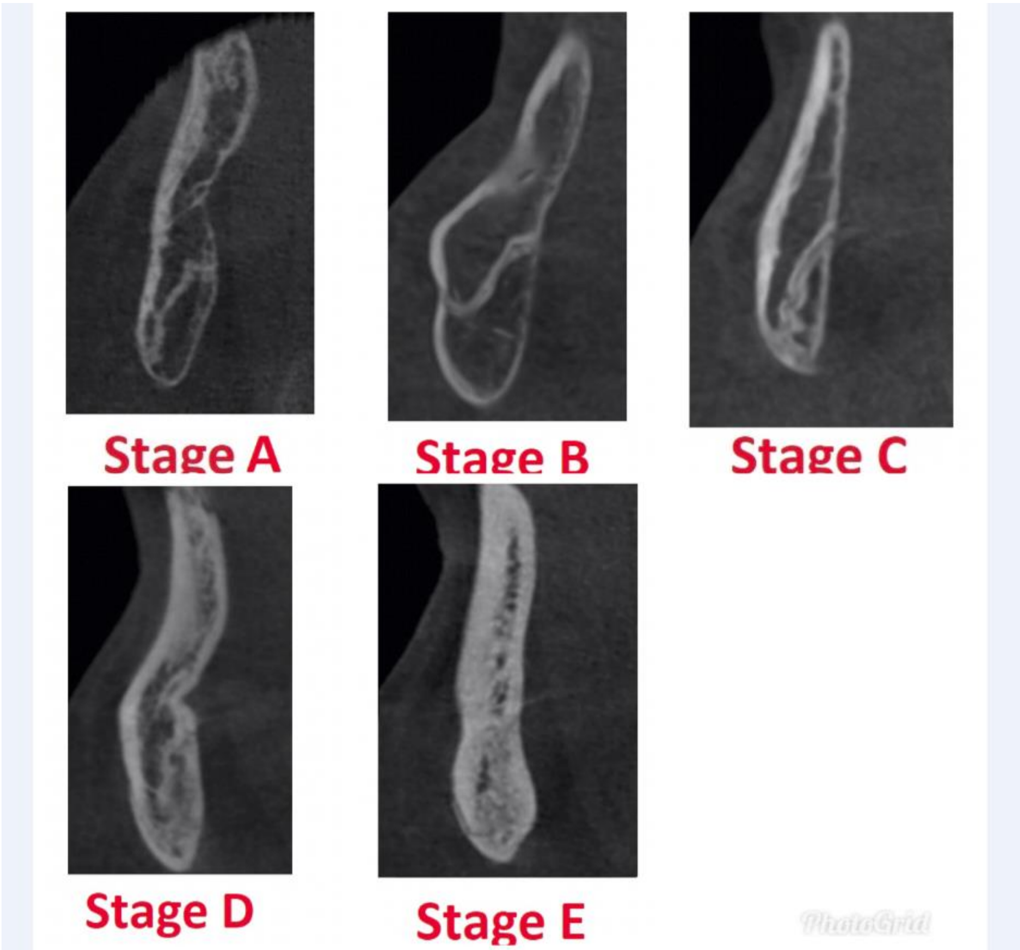

Fig.1: Stages of zygomatico-maxillary suture maturation.

The ossification status of the spheno-occipital synchondrosis was examined using an altered four-stage system (**Figure.2**) (17).

0: (Unfused) – Fully open and showing no indication of union between the basilar section of the occipital and the sphenoid, and bone was not observed in the gap.

1: (Fusing endocranially) – Half or less of the length of the synchondrosis has merged.

2: (Fusing ectocranially) – More than half the length of the synchondrosis has merged.

3: (Complete fusion) – Total union that shows normal bone all over.

All images were scored by one observer, and 52 scans were reevaluated after four weeks by a second observer to calculate inter and intra-examiner agreement. Observer agreement was accordingly calculated using the Fleiss's Kappa coefficient (18, 19). The Kappa measure of agreement for the inter-examiner was 0.88 (P <0.001) for both SOS and ZMS; the strength of agreement between repeated observations is thus rated as "almost perfect" (17). The Kappa measure of agreement for the intra-examiner was 0.77 (P <0.001) for SOS. The Kappa measure of agreement for the intra-examiner was 0.81 (P <0.001) for ZMS. Mann-Whitney test, Spearman correlation, Bayesian Transition analysis, and repeated measurement were used for data analysis. SPSS software version 18.0 was used for data analysis. P-value <0.05 was considered as significant.

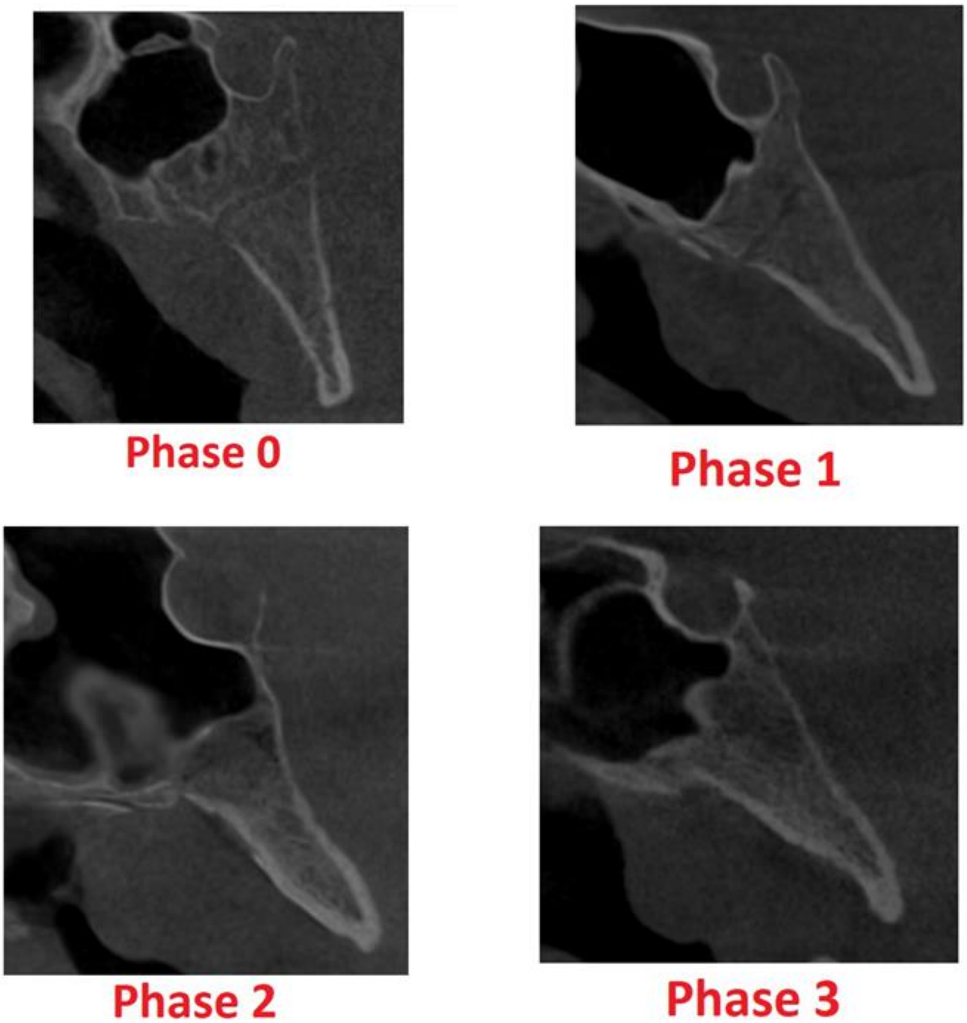

Fig.2: Stages of spheno-occipital synchondrosis fusion in the mid-sagittal plane.

2-2. Bayesian Transition analysis

The Bayesian transitional analysis is a distinguished approach for modeling an ordinal variable in which its categories can be considered as stages defined by a skeletal trait while the morphological changes are progressive (means unidirectional) (20). Recently, the fundamentals of the Bayes theory and its application in age estimation have been studied substantially (20-22), and was evaluated and compared to other traditional methods (23). This analysis is based on a cumulative probit model in which age can be considered as an independent variable and would be estimated for an individual who moved from one stage to the other. Estimates of the regression slope for age and intercepts corresponding to each transition (for example stage 1 to 2 of spheno-occipital synchondrosis) of the cumulative regression model with the probit link were obtained for normal populations and CLP patients. Then, by assuming uniform prior probabilities that allocate the same probability to each age categories and combine this information with parameter estimates, the posterior mean and standard deviation were calculated. The obtained parameters corresponded to means and standard deviation of lognormal distributions for each transitional path.

The standard error of means (SEM) were computed by bootstrap method a nonparametric resampling Monte Carlo method. For this purpose, 1000 samples of length 153 (number of observations in each group) with replacement were generated for normal populations and CLP patients separately. For each sample, the Bayesian transitional model was executed and parameter estimates were obtained, and the bootstrap SEM of each group and transition was computed based on the estimated parameters. All analyses were done for normal populations and CLP patients. Finally, two independent sample t-test was used to assess the hypothesis of any statistical difference in estimated mean age between the two populations in each transition using estimated mean and SEM. The applied Bayesian cumulative probit model was implemented by means of "arm" package in R 3.5.3. P-values less than 0.05 considered statistically different.

3- RESULT

The current study consisted of 306 samples (154 males and 152 females) between the ages of 6 to 18 years. 153 CBCTs of cleft lip and palate (CLP) patients (94 unilateral and 59 bilateral) and 153 scans of healthy non-cleft individuals were entered in this study. The mean age of both groups was 13.27 ± 3.49 year. The study showed spheno-occipital synchondrosis and zygomatico-maxillary suture fusion degree increases in correlation with age. In regard to complete fusion of SOS (stage 3) in cleft lip and palate patients and control groups, this study showed that in the normal population the mean age is 16.96 ± 0.91 years for females, and 17.00 ± 0.85 years for males and in cleft patients, the mean age at stage 3 is 17.36 ± 0.64 years for females and 17.08 ± 0.7 years for males (**Table.1**). According to **Table.1**, there were no significant differences between males and females regarding SOS maturation stages not only in CLP patients but also in the normal population (P>0.05).

According to **Table.2**, in cleft patients, there were no significant differences between males and females regarding ZMS maturational stages (P>0.05). In comparing the mean age of both sexes in the normal population, there was no significant statistical difference in any of the maturation stages of ZMS except in stage D (P = 0.006). This study showed in the normal population, the mean age of stage B, which is the ultimate level of favorable response to growth modification, is 11.50 ± 1.50 years for females and 10.79± 1.89 years for males and in CLP patients, the mean age of stage B is 9.53 ± 1.46 years for females and 9.71 ± 1.36 years for males. According to **Table.3**, ZMS maturation in the cleft patients was significantly earlier than in the normal population in stage B, C, and D (P < 0.001, P=0.001, P = 0.008, respectively), whereas there were no statistically significant differences between the case and control groups for SOS maturation stages (P > 0.05).

Table-1: Descriptive means of age in different groups by closure state of the spheno-occipital suture (SOS).

Group	Stage	Gender	Number	Mean ± SD	Range (Min-max)	Median	P-value
Normal population	0	Female	22	9.23±2.02	6 - 12	9.0	0.716*
		Male	25	9.44±1.96	6 - 13	10.0	
	1	Female	13	12.23±1.69	9 - 14	13.0	0.591**
		Male	17	11.88±1.93	7 - 14	12.0	
	2	Female	16	16.00±1.67	14 - 18	16.5	0.059**
		Male	21	14.90±1.18	13 - 17	15.0	
	3	Female	24	16.96±0.91	15 - 18	17.0	0.939**
		Male	15	17.00±0.85	16 - 18	17.0	
CLP patients	0	Female	16	8.56±1.79	6 - 12	9.0	0.855*
		Male	17	8.47±1.84	6 - 13	8.0	
	1	Female	18	12.11±2.05	8 - 15	12.0	0.263**
		Male	39	12.82±1.89	10 - 16	13.0	
	2	Female	18	15.06±1.76	12 - 18	15.5	0.941*
		Male	7	15.00±1.41	13 - 17	15.0	
	3	Female	25	17.36±0.64	16 - 18	17.0	0.258**
		Male	13	17.08±0.76	16 - 18	17.0	

*:t-test, **: Mann Whitney U, CLP: Cleft lip and palate.

Table-2: Descriptive means of age in different groups by closure state of the zygomatico-maxillary suture (ZMS).

Group	Stage	Gender	Number	Mean ± SD	Range (Min-Max)	Median	P value
Normal population	A	Female	10	7.50±1.27	6 - 9	7.5	0.834*
		Male	8	7.38±1.19	6 - 9	7.0	
	B	Female	20	11.50±1.50	9 - 14	12.0	0.182*
		Male	24	10.79±1.89	7 - 14	10.5	
	C	Female	15	13.80±2.40	9 - 17	14.0	0.412**
		Male	21	13.43±1.91	10 - 17	14.0	
	D	Female	16	16.81±0.83	15 - 18	17.0	0.006**
		Male	15	15.60±1.18	14 - 17	15.0	
	E	Female	14	17.43±0.85	16 - 18	18.0	0.508**
		Male	10	17.20±0.92	16 - 18	17.5	
CLP patients	A	Female	5	6.80±1.30	6 - 9	6.0	0.623**
		Male	6	6.83±0.75	6 - 8	7.0	
	B	Female	15	9.53±1.46	7 - 12	9.0	0.731**
		Male	17	9.71±1.36	7 - 12	10.0	
	C	Female	12	12.00±1.28	10 - 14	12.0	0.553*
		Male	20	12.30±1.42	10 - 15	13.0	
	D	Female	24	15.71±1.57	13 - 18	16.0	0.126**
		Male	21	15.00±1.14	13 - 18	15.0	
	E	Female	21	17.24±0.83	16 - 18	17.0	0.435**
		Male	12	17.00±0.85	15 - 18	17.0	

***: t**-test, **: Mann Whitney U, CLP: Cleft lip and palate.

Table-3: Comparison between the mean age of normal populations and CLP patients in each stages of ZMS and SOS.

Group	Stage	Type	Number	Mean ± SD	Range (Min-Max)	Median	P-value
ZMS	A	Normal	18	7.44±1.20	6 – 9	7.0	0.167
		CLP	11	6.82±0.98	6 – 9	7.0	
	B	Normal	44	11.11±1.74	7 – 14	11.0	<0.001
		CLP	32	9.63±1.39	7 – 12	9.5	
	C	Normal	36	13.58±2.10	9 – 17	14.0	0.001
		CLP	32	12.19±1.35	10 – 15	12.5	
	D	Normal	31	16.23±1.18	14 – 18	17.0	0.008
		CLP	45	15.38±1.42	13 – 18	15.0	
	E	Normal	24	17.33±0.87	16 – 18	18.0	0.355
		CLP	33	17.15±0.83	15 – 18	17.0	
SOS	0	Normal	47	9.34±1.97	6 – 13	9.0	0.059
		CLP	33	8.52±1.79	6 – 13	9.0	
	1	Normal	30	12.03±1.81	7 – 14	13.0	0.208
		CLP	57	12.60±1.95	8 – 16	13.0	
	2	Normal	37	15.38±1.50	13 – 18	15.0	0.442
		CLP	25	15.04±1.65	12 – 18	15.0	
	3	Normal	39	16.97±0.87	15 – 18	17.0	0.149
		CLP	38	17.26±0.69	16 – 18	17.0	

ZMS: Zygomatico-maxillary suture, SOS: Spheno-occipita suture, CLP: Cleft lip and palate, SD: Standard deviation.

Table.4 compares ZMS and SOS maturity between unilateral and bilateral CLP patients. Accordingly there was no significant difference between unilateral and bilateral cases at any of the maturation stages of ZMS and SOS (P>0.05). Linear regression parameters for the prediction of age in both sexes for the SOS and ZMS fusion stages was done. For a unit stage increase in SOS maturity, the mean age increases 2.76 years for females and 2.65 years for males. Moreover, a unit increase in ZMS maturity increases the mean age to 2.43 year for males and 2.48 year for females. Parameter estimates of the Bayesian transition analysis based on the cumulative logit models are presented in **Table.5**. The most probable age of an individual at which a transition will occur in SOS and ZMS maturation individual were reported as estimates and the standard deviation for each transition are dispersion parameters, which were, illustrate graphically in terms of probability distribution in **Figure.3**. Based on Bayesian transition analysis (**Table.5**), there were statistically significant differences between CLP patients and normal population in ZMS and SOS in all transitional stages (P<0.05) except stages 2 to 3 of SOS maturation, where in no significant differences were shown between the two groups (P>0.99). Furthermore, transition age demonstrated earlier maturation of ZMS in CLP patients for all phases (p<0.001). The transition analysis was carried out in patients with unilateral and bilateral cleft lip and palate anomaly separately. There were no statistical differences between two types of cleft lip and palate in terms of transition age at stages of SOS and ZMS (p>0.05).

Table-4: comparison between the mean age of UCLP and BCLP patients in each stages of ZMS and SOS.

Group	Stage	Gender	Number	Mean ± SD	Range (Min-Max)	Median	P- value
ZMS	A	UCLP	6	6.83±0.75	6 - 8	7.0	0.623**
		BCLP	5	6.80±1.30	6 - 9	6.0	
	B	UCLP	21	9.67±1.28	7 - 12	10.0	0.819
		BCLP	11	9.55±1.63	7 - 12	9.0	
	C	UCLP	21	12.14±1.28	10 - 14	13.0	0.918**
		BCLP	11	12.27±1.56	10 - 15	12.0	
	D	UCLP	22	15.59±1.59	13 - 18	16.0	0.351**
		BCLP	23	15.17±1.23	14 - 18	15.0	
	E	UCLP	24	17.21±0.88	15 - 18	17.0	0.387**
		BCLP	9	17.00±0.71	16 - 18	17.0	
SOS	0	UCLP	20	8.50±1.57	6 - 12	9.0	0.953*
		BCLP	13	8.54±2.15	6 - 13	9.0	
	1	UCLP	35	12.40±1.79	10 - 16	13.0	0.229**
		BCLP	22	12.91±2.20	8 - 16	14.0	
	2	UCLP	11	15.00±1.67	13 - 18	16.0	0.917*
		BCLP	14	15.07±1.69	12 - 18	15.0	
	3	UCLP	28	17.36±0.68	16 - 18	17.0	0.146**
		BCLP	10	17.00±0.67	16 - 18	17.0	

ZMS: Zygomatico-maxillary suture, SOS: Spheno-occipita suture, UCLP: Unilateral cleft lip and palate, BCLP: Bilateral cleft lip and palate, SD: Standard deviation. *:t-test, **: Mann Whitney U.

Table-5: Bayesian estimates of age at transition from the cumulative logit on transition analysis for fusion stages of the spheno-occipital synchondrosis and Zygomaticomaxillary suture maturation in Normal and CLP patients.

Transition stage		Normal Population (n=153)		CLP patients (n=153)		t- statistic	P-value
		Estimate ± SEM	SD	Estimate ± SEM	SD		
SOS	0-1	11.16±0.31	0.84	9.95±0.29	0.82	2.85	0.005
	1-2	13.63±0.19		14.49±0.27		-2.60	0.01
	2-3	16.31±0.23		16.31±0.21		0.00	>0.99
ZMS	A-B	8.37±0.31	0.89	7.43±0.28	0.65	2.25	0.025
	B-C	12.45±0.31		10.88±0.26		3.88	<0.001
	C-D	15.15±0.23		13.55±0.17		5.60	<0.001
	D-E	17.33±0.26		16.65±0.22		1.99	0.046

ZMS: Zygomatico-maxillary suture, SOS: Spheno-occipita suture, CLP: Cleft lip and palate, SEM: Standard error of mean, SD: Standard deviation.

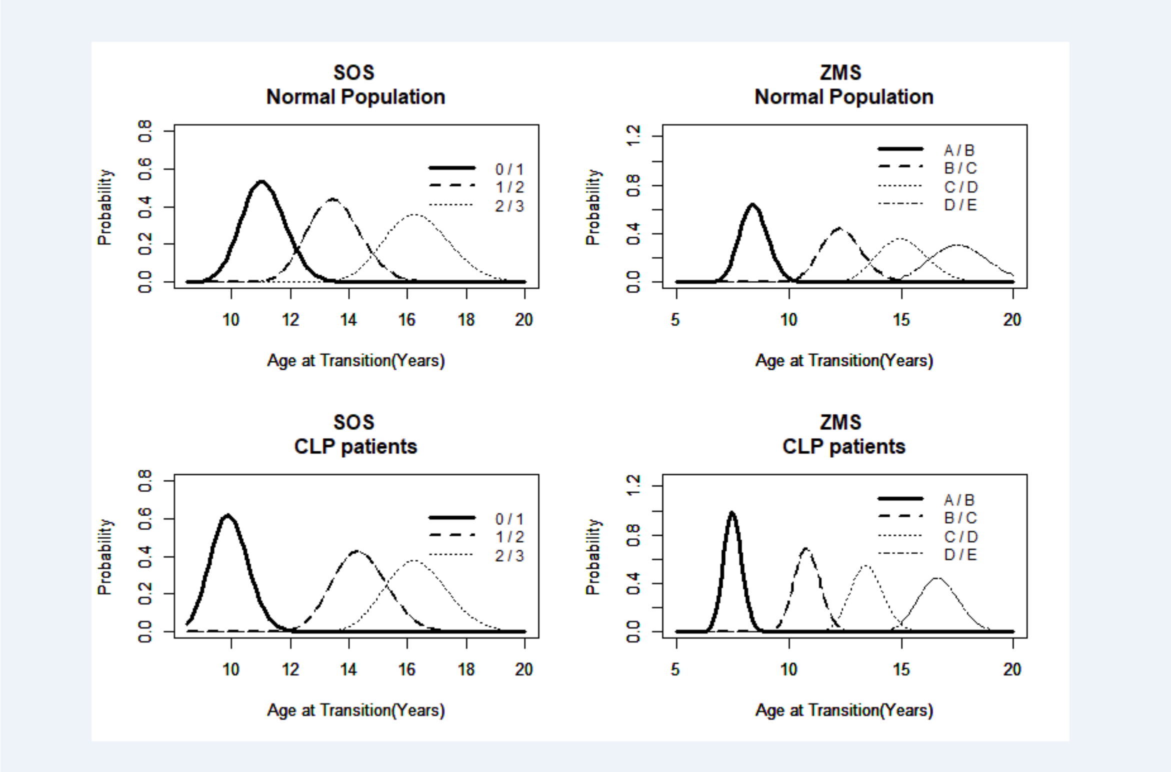

Fig.3: Probability density plot of age-at-transition in normal and cleft population for sphenooccipital synchondrosis maturation (left), and zygomaticomaxillary suture maturation (right).

4- DISCUSSION

The purpose of the present study was three-dimensional evaluation of the SOS, and ZMS in cleft lip and palate patients versus the normal population. The study showed spheno-occipital synchondrosis and zygomatico-maxillary suture fusion degree increases in correlation with age. This study also showed in the non-cleft children, the mean age of stage B, which is the ultimate level of favorable response to growth modification, is 11.50 ± 1.50 years for females and 10.79± 1.89 years for males and in CLP patients, the mean age of stage B is 9.53 ± 1.46 years for females and 9.71 ± 1.36 years for males. Maxillary hypoplasia is commonly found in cleft lip and palate patients. Contributions to restricted maxillary growth have been widely accepted to be caused by two main factors: surgical intervention for cleft lip and palate repair and intrinsic growth deficiency. Intrinsic factors of maxillary deficiency have been correlated to various clinical markers including severity of clefting, dimensions of the premaxilla, and palatal surface area. Combination of these factors leads to a class III malformation with maxillary deficiency in these patients. It has been proven that cleft patients show less dysmorphic characteristics in transverse dimensions of the face and basicranium; however, lateral cranial base is more affected by cleft compared with the middle basicranium (24). The ZMSs and SOS are the most impressive factors in maxillary growth and development. Hence, analysis of the maturation of ZMSs may indicate a response to orthopedic maxillary protraction (12). On the other hand, the cranial base is also considered important because the growth changes of the maxillo-mandibular complex is affected by the cranial base (13, 14). As there was considerable dissimilarity in the literature regarding closure time of SOS and ZMS in the normal population and cleft patients, further investigation is needed to compare their maturation between the two groups (12, 25). According to Angelieri et al.'s study, the suture with higher maturity should always be considered as the criterion for evaluation because if the maturational stage in one side is higher than stage B, the maxilla will not protract well (12). Therefore, in our study, we also considered the highest stage when there were differences between the sutures on both sides. According to Lottering et al., SOS maturity varies in different races and nationalities due to different environmental factors such as cultural and nutritional diversity, as well as genetic diversity of different nationalities due to mixing of genes (21). In a study by Akhlaghi et al., in the male Iranian population, the mean age at which the SOS was completely open was 12.78 years and the highest age at which the SOS was completely open was 19 years (26), while in our study the mean opening age was about 9.44 and the highest opening age was 13 years.

Although the age range studied in our study was 6 to 18 years, the reason for the differences between these two studies can be explained by the different climatic and cultural conditions of these two metropolises from one country. This study showed ZMS maturation in CLP patients was significantly earlier than in normal population, whereas SOS maturity occurred earlier in stage 0 and 2 in CLP patient; however, it was not statistically significant. The result of this study could answer an important clinical question existing about when to use facemasks for maxillary protraction in class III patients among cleft or non-cleft patients. The main goal in the early use of the facemask is to maximize anterior displacement of the maxilla due to the sutural growth. According to previous studies, before the age of 8, the sutures around the maxilla are smooth and broad, but they are more heavily interdigitated around puberty. Therefore, it is often recommended that maxillary protraction begins at the end of the primary dentition or at the beginning of the mixed dentition (27, 28). According to the study of Angelieri et al., at stages A and B of ZMS maturity, maxilla responds well to facemask therapy (12). In our study, the mean age of stage B in the Iranian population was 10.79 ± 1.89 in males and 11.50 ± 1.50 in females. In cleft patients, the mean age at stage B was 9.71 ± 1.36 and 9.53 ± 1.46, respectively in males and females. Therefore, according to our study, it seems that in the Iranian population, maxillary protraction through the facemask will have acceptable orthopedic effects when used in the normal population before age 11 and in cleft patients before age 10. Nonetheless, clinical studies are needed to prove this. On the other hand, in our study, the mean age of females with cleft lip and palate was significantly lower than the normal population at stage B, C and D of ZMS maturation. Therefore, the importance of early initiation of growth modification therapies in patients with cleft lip and palate compared to normal individuals, especially in girls, can be understood.

However, more studies are needed to prove this. Linear regression analysis of age prediction in relation to SOS and ZMS maturation stages revealed that for a unit stage increase in SOS maturity, the mean age increased as 2.76 units for females and 2.65 units for males. In addition, this study showed for a unit stage increase in ZMS maturation, the mean age increased 2.43 units for males and 2.48 units for females. While in the study of Can et al., for per unit increase in SOS maturation, the mean age increased to 2.75 in females and increased to 2.45 in males (29). No study was found for ZMS maturation regarding this issue. In the comparison between UCLP and BCLP patients, no significant statistical difference was found in the mean age at each stage of ZMS maturation as well as SOS. Due to the limited number of samples, it was not possible to compare the two groups by gender. Therefore, we recommend further studies with a larger sample size.

5- CONCLUSION

This study showed because of earlier maturation of ZMS in CLP patients compared to the normal population, growth modification of maxillary deficiency should be started sooner in such patients than non-cleft children. The study also revealed there is no difference between the maturation of SOS between CLP patients and the normal population. However, ZMS and SOS in UCLP and BCLP patients had similar maturational stages.

6- CONFLICT OF INTEREST: None.

7- REFERENCES

1. Dixon MJ, Marazita ML, Beaty TH, Murray JC. Cleft lip and palate: understanding genetic and environmental influences. Nat Rev Genet. 2011;12(3):167-78.

2. Murray JC. Face facts: genes, environment, and clefts. Am J Hum Genet. 1995;57(2):227.

3. Menezes C, de Arruda J-A, Silva L-V, Monteiro J-L, Caribé P, Álvares P, et al. Nonsyndromic cleft lip and/or palate: A multicenter study of the dental anomalies involved. J Clin Exp Dent. 2018;10(8):e746.

4. Woon SC, Thiruvenkatachari B. Early orthodontic treatment for Class III malocclusion: A systematic review and meta-analysis. Am J Orthod Dentofacial Orthop. 2017;151(1):28-52.

5. Mandall N, DiBiase A, Littlewood S, Nute S, Stivaros N, McDowall R, et al. Is early class III protraction facemask treatment effective? A multicentre, randomized, controlled trial: 15-month follow-up. J Orthod. 2010;37(3):149-61.

6. Wendl B, Stampfl M, Muchitsch A, Droschl H, Winsauer H, Walter A, et al. Long-term skeletal and dental effects of facemask versus chincup treatment in Class III patients. J Orofac Orthop. 2017;78(4):293-9.

7. Liou EJ-W, Tsai W-C. A new protocol for maxillary protraction in cleft patients: repetitive weekly protocol of alternate rapid maxillary expansions and constrictions. Cleft Palate Craniofac J. 2005;42(2):121-7.

8. Sun Z, Hueni S, Tee BC, Kim H. Mechanical strain at alveolar bone and circummaxillary sutures during acute rapid palatal expansion. Am J Orthod Dentofacial Orthop. 2011;139(3):e219-e28.

9. Christie KF, Boucher N, Chung C-H. Effects of bonded rapid palatal expansion on the transverse dimensions of the maxilla: a cone-beam computed tomography study. Am J Orthod Dentofacial Orthop. 2010;137(4):S79-S85.

10. Ballanti F, Lione R, Baccetti T, Franchi L, Cozza P. Treatment and posttreatment skeletal effects of rapid maxillary expansion investigated with low-dose computed tomography in growing subjects. Am J Orthod Dentofacial Orthop. 2010;138(3):311-7.

11. Angelieri F, Franchi L, Cevidanes LH, Hino CT, Nguyen T, McNamara Jr J. Zygomaticomaxillary suture maturation: A predictor of maxillary protraction? Part I-A classification method. Orthod Craniofac Res. 2017;20(2):85-94.

12. Angelieri F, Ruellas A, Yatabe M, Cevidanes L, Franchi L, Toyama-Hino C, et al. Zygomaticomaxillary suture maturation: part II—the influence of sutural maturation on the response to maxillary protraction. Orthod Craniofac Res. 2017;20(3):152-63.

13. Proff P, Will F, Bokan I, Fanghänel J, Gedrange T. Cranial base features in skeletal Class III patients. Angle Orthod. 2008;78(3):433-9.

14. Leonardi R, Cutrera A, Barbato E. Rapid maxillary expansion affects the spheno-occipital synchondrosis in youngsters: a study with low-dose computed tomography. Angle Orthod. 2010;80(1):106-10.

15. Awarun B, Blok J, Pauwels R, Politis C, Jacobs R. Three-dimensional imaging methods to quantify soft and hard tissues

change after cleft-related treatment during growth in patients with cleft lip and/or cleft palate: a systematic review. Dentomaxillofac Radiol. 2019;48(2):20180084.

16. Shi B, Losee JE. The impact of cleft lip and palate repair on maxillofacial growth. Int J Oral Sci. 2015;7(1):14-7.

17. Franklin D, Flavel A. Brief communication: timing of spheno-occipital closure in modern Western Australians. Am J Phys Anthropol. 2014;153(1):132-8.

18. Fleiss JL, Levin B, Paik MC. Statistical methods for rates and proportions: john wiley & sons; 2013.

19. Umie B, Mmed I, Mohamed M. Estimation of age from spheno-occipital synchondrosis closure using computed tomography in Yemen. Forensic Res Criminol Int J. 2015;1:00005.

20. Boldsen JL, Milner GR, Konigsberg LW, Wood JW, Hoppa RD, Vaupel JW. Transition analysis: a new method for estimating age from skeletons. Paleodemography: age distributions from skeletal samples: Camb Univ Press; 2002. p. 73-106.

21. Lottering N, MacGregor DM, Alston CL, Gregory LS. Ontogeny of the spheno-occipital synchondrosis in a modern Q ueensland, A ustralian population using computed tomography. Am J Phys Anthropol. 2015;157(1):42-57.

22. Tangmose S, Thevissen P, Lynnerup N, Willems G, Boldsen J. Age estimation in the living: transition analysis on developing third molars. Forensic Sci Int. 2015;257:512. e1-. e7.

23. Clark MA, Simon A, Hubbe M. Aging methods and age-at-death distributions: Does transition analysis call for a re-examination of bioarchaeological data? Int J Osteoarchaeol. 2020;30(2):206-17.

24. Jahanbin A, Eslami N, Kobravi S, Hoseinizarch H. Comparative evaluation of cranial base and facial morphology of cleft lip and palate patients with normal individuals in cone beam computed tomography.J Craniofac Surg. 2015;26(3):785-8.

25. Bassed RB, Briggs C, Drummer OH. Analysis of time of closure of the spheno-occipital synchondrosis using computed tomography. Forensic Sci Int. 2010;200(1-3):161-4.

26. Akhlaghi M, Valizadeh B, Gharadaghi J. Closure time of spheno-occipital suture in the male cadavers referred to legal medicine organization. Acta Medica Iranica. 2008;46(2):106-8.

27. Kim J-H, Viana MA, Graber TM, Omerza FF, BeGole EA. The effectiveness of protraction face mask therapy: a meta-analysis. Am J Orthod Dentofacial Orthop. 1999;115(6):675-85.

28. Lee D-Y, Kim E-S, Lim Y-K, Ahn S-J. Skeletal changes of maxillary protraction without rapid maxillary expansion: a comparison of the primary and mixed dentition. Angle Orthod. 2010;80(4):692-8.

29. Can IO, Ekizoglu O, Hocaoglu E, Inci E, Sayin I, Kaya KH. Forensic age estimation by spheno-occipital synchondrosis fusion degree: computed tomography analysis. J Craniofac Surg. 2014;25(4):1212-6.