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Incidence of Congenital Heart Diseases Anomalies in Newborns with Oral Clefts, Zahedan, Iran

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Abstract

Background

Oral cleft is the most common orofacial congenital anomaly among live births. This anomaly at birth is one of the main causes of children disability and mortality. Congenital heart disease (CHD) is one of the most common anomalies in oral clefts. This study aimed to assess the incidence of congenital heart diseases anomalies in newborns with oral clefts.

Materials and Methods

This study performed on 48,692 live born to estimate incidence of oral clefts from 1st December 2013 to 31th November 2015 from three general hospitals in Zahedan, The capital city of the Sistan & Baluchestan province, Iran. All oral cleft patients were under echocardiography to diagnosis the incidence of CHD as associated anomaly. The collected data were processed using SPSS-16.

Results

The results of the analysis showed that the incidence of cleft lip was higher in boys than girls, while the cleft palate was higher in girls. Lip/palate cleft was higher for boys. Oral clefts patients accounted of 102 (0.2%) with incidence rate of 2.095 per 1000 lives. Of 102 patients 19 (18.62%), 39(35.24%) and 44(43.14%) were oral lip, oral palate and both respectively. The incidence of CHD in patients with oral clefts was 26.5%, while the incidences for cleft lip, cleft palate and both were 15.79%, 20.51%, and 36.36% respectively.

Conclusion

From the study concluded that the rate of CHD among children with oral clefts was high compared with the healthy children. Strongly is suggested the echocardiography for these patients to have early diagnostic of CHD to manage any life-threatening.

Key Words: Children, Congenital heart diseases, Estimation, Oral clefts.

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1- INTRODUCTION

A cleft is a gap or split. This can be in the upper lip, the roof of the mouth (palate) or sometimes lip and palate which is the most common head and neck anomalies that is called oral cleft (1). Also, it has been introduced as an orofacial congenital anomaly among live births (2). Birth defects are the main causes of disability, morbidity and mortality in children (3). Cleft lip and Palate occur when the upper area of the central face do not quite join together properly and then is leaving a gap in the lip, palate or both (4). Oral cleft sometimes appeared with other types of anomalies such as heart defects (1). The sex ratio of the cleft lip is 2:1 while it is 1:2 for palate (5). Therefore, cleft palate is more common in girls (5). The oral cleft prevalence is 1.43/1000 live births across the world. The prevalence is the highest of 2/1000 in Asians, followed by Caucasians with 1/1000 and the lowest of 0.4/1000 for the African populations (6). The overall incidence rate of lip/palate is 0.9 in Sudan (5). Rajab reported that the prevalence of oral clefts is 1.5/1000 in in Oman (6), and for the Iranian population varies from 0.86 to 3.73/1000 at birth (7). In the Southern area of Iran this prevalence has been reported 0.80/1000 (8), while in Northern is 1.05/1000 (9). In Hamedan a city in Iran has been reported that the prevalence of oral cleft was 1.016/1000 (10). In the capital city of Iran (Tehran) this disease reported as 2.14/1000 (11) and 1.9 /1000 / in Mashhad, North East of Iran (12). The distributions of oral clefts are 25% to 35%, 25% and 50% in blip , palate and lip/palate(13-14).

In many studies considerable concentration focused on correlation between oral clefts at birth and other anomalies. Congenital heart disease (CHD) is the most common associated anomalies with oral clefts (15). But there were wide variations in the prevalence of CHDs in patients with oral clefts and importantly, it is reported as the principal cause of death among infants with OFCs (16). The prevalence of CHD in oral cleft patients is 51% of all malformations in Pakistan, 9.5% in Brazil and 5.4% in Taiwan and 56 % in China (17). The prevalence of 8/1000 live births has been reported for CHD as leading cause of death (18). The most common form of CHD is VSD that involved 35% of CHD patients; and the considerable type of cyanotic CHD is Tetralogy of Fallot (TF) with the prevalence of 0.26 to 0.80 in 1000 live birth (19). A wide variation has been reported in the incidence of CHD in oral clefts patients in different countries; the prevalence of CHD in children with oral cleft anomalies is about 23 times more than general population in Pakistan, while this chance of risk is 16 times in Swedish (20). Tannent reported that the most common congenital anomaly groups at livebirth were cardiovascular system anomalies, orofacial clefts, nervous system anomalies and showed that children with these types of congenital anomalies had lower survival than general population (21). Wehby focused on the importance of the association anomalies with oral cleft in affected children and their families and reported that in the case of health care use, cost and quality of life studying this subject is very important. This importance could be exacerbated by some specific associated anomalies such and CHD anomalies (22).

Fakhim performed a study on the Northwest of Iran in this subject and resulted that the most common associated anomaly among cleft patients is CHD (23). With the consideration of the importance of obtaining accurate estimates of the frequency and other epidemiological features of oral clefts and its relation with CHD and in spite of many studies about the prevalence of the oral cleft in various regions in Iran, but low number investigations on the association of oral clefts with congenital heart defects and

because of the province of Sistan and Baluchistan is the biggest province of Iran with very low demographic and economic situations and strong religious beliefs and costumes, so that, we aimed to present this study with the objective of incidence of congenital heart diseases anomalies in newborns with oral clefts.

2- MATERIALS AND METHODS

2-1. Study Design and Population

This prospective and epidemiologic based study carried out in concentration of incidence to measure exposures, confounders and outcomes. In this study target population was newborn babies with oral clefts who were born within two years period from 1st December 2013 to 31th November 2015. Our target population had Iranian nationality and those who had foreign nonutility excluded from the study. Another excluded criterion was having bifid uvula.

In this two years period, 48,692 babies were born in three general hospitals accordance with unpublished but, documented report of statistical and planning office, Health Deputy (HD) of Zahedan University of Medical Sciences (ZaUMS) of Zahedan, the capital of the largest province of Islamic republic of Iran, Sistan and Baluchestan.

The first step of the study was estimating the incidence of oral clefts with a classification of cleft lip, cleft palate and cleft lip/palate and the second step was estimating the incidence of CHD anomalies among patients with oral clefts.

2-2. Methods

By organizing the results according to the affiliated information from the hospitals, 102 subjects were referred to the Pediatric Heart Center. All mothers with Oral cleft babies were interviewed by the pediatric cardiologist in the pediatric heart center. Family history was reviewed with some easy and basic questions such as gender, family history of clefts, birth order and finally, patients were under echocardiography studies using Manual (M) Mode and two-dimensional with Doppler irrespective of whether they are symptomatic or not for the presence of congenital heart diseases.

2-3. Ethical considerations

The study was approved by Ethics Committee of Zahedan University of Medical Sciences as thesis for degree of doctor of dental surgery (DDS) numbered 6831. Written informed consent was obtained from each participant's parents.

2-4. Data analyses

The collected data were processed using the statistical package for social science, version 16.0 (SPSS Inc, Chicago, IL, USA). Descriptive statistics, Chi-square test and analysis of variance were used for data analysis. P-value less than 0.05 were considered statistically significant.

3- RESULTS

The present study performed on 48,692 [23,391 girls and 25,301 boys] live births within two years and observed 102 (0.2%) babies with oral cleft and the incidence oral cleft was 2.095/1000 live births. The sex distributions live births babies with oral cleft were 53 (51.96%) and 49 (48.04%) for boys and girls respectively. The incidence of oral cleft for boys and girls had equal rate with both sexes. Of 102 patients 19 (18.62%), 39(35.24%) and 44(43.14%) had oral lip, oral palate and lip/palate respectively. The results of the analysis showed that the prevalence of cleft lip and cleft lip/palate was higher for the boys than the girls. Also, the cleft palate was higher in the girls than the boys (**Table.1**).The analysis showed 27 (26.47%) out of 102 patients had CHD, so that, the distribution was 16(59.26%), 8(26.63%) and 3(11.11%) in cleft lip/palate, cleft palate and cleft lip. Amongst the oral cleft patients, we

observed a great range of congenital heart diseases. The prevalence of CHD in patients with cleft lip was 15.79% and in patients with cleft palate was 20.51%, and in patients with cleft lip/palate was 36.36%. This prevalence in total was 265 in 1000 live births with oral cleft (**Table.2**). Atrial septal defect observed in 8 oral cleft patients with the highest percent (29.63%) which is distributed of 12.5%, 37.5% and 50% in the cleft lip, cleft palate and cleft lip/palate respectively. In the second rank, 5 (18.52) of CHD patients involved with TF. Of five TF patients, 20%, 60% and 20% had cleft lip, cleft palate and cleft lip/palate respectively. Four patients had ventricular septal and observed all of them were patients with cleft lip/palate only (**Table.3**). Three (11.1%) of our 27 patients had siblings cleft history, one (3.7%) in cleft lip and two (7.4%) with cleft palate and one of patients was twins. Analysis of the present study showed that parents marriage between relatives not correlated with the type of oral cleft (P= 0.985). The analysis also, showed that the factor of consanguineous marriages didn't show any correlation with the attendant of CHD in oral cleft patients (**Table.4**).The analysis of the ANOVA showed that patients with lip/palate cleft had the highest mean of birth order (3.25 ± 2.02) in compared with cleft lip (2.84 ± 1.42) and cleft palate (2.97 ± 1.58), but these difference was not significant.

Table-1: Sex distribution of Patients with oral clefts based on type of cleft and presence of CHD

Variables	Category	Statistics	Gender		Total
			Male	Female	
Oral Cleft	Lip	n	10	9	19
		%	52.63	47.37	100
	Palate	n	18	21	39
		%	46.15	53.85	100
	Lip And Palate	n	25	19	44
		%	56.82	43.18	100
	Total	n	53	49	102
		%	51.96	48.04	100
CHD	No	n	37	38	75
		%	49.33	50.67	100
	Yes	n	16	11	27
		%	59.26	40.74	100

Table- 2: The presence of CHD in oral clefts patients

Cleft	Statistics	Without CHD	With CHD	Total
Lip	Number	16	3	19
	%	84.21	15.79	100
Palate	Number	31	8	39
	%	79.49	20.51	100
Lip and palate	Number	28	16	44
	%	63.64	36.36	100
Total	Number	75	27	102
	%	73.53	26.47	100

Table 3: Individual background distribution of oral clefts

Patients, No.	Gender	Birth Order	Family oral cleft history	Type of Oral Cleft	CHD	Consanguineous Marriages
2	Girl	2	No	Lip/Palate	HLHS	No
5	Girl	3	No	Lip	TAIB	No
6	Girl	3	No	Lip/Palate	VSD	No
14	Boy	4	No	Lip/Palate	TGA	No
17	Girl	1	No	Lip/Palate	ASD	Yes
18	Girl	2	No	Lip/Palate	ASD	Yes
19	Girl	1	No	Palate	ASD	No
23	Girl	2	No	Lip/Palate	AS,AI	Yes
24	Girl	2	No	Palate	TA	Yes
25	Boy	6	No	Palate	ASD	Yes
26	Boy	5	No	Palate	TF	Yes
36	Girl	4	No	Lip/Palate	TF	Yes
37	Boy	9	No	Lip/Palate	ASD, VSD	Yes
38	Boy	3	No	Lip/Palate	AVSD-PH	Yes
41	Girl	2	No	Palate	ASD	Yes
42	Boy	1	No	Lip/Palate	ASD	No
43	Boy	3	No	Palate	TF	No
45	Boy	2	No	Lip	ASD	Yes
50	Boy	4	No	Palate	PA-VSD	Yes
67	Boy	2	No	Lip	TF	No
69	Boy	1	No	Lip/Palate	VSD	Yes
71	Boy	8	No	Lip/Palate	VSD	Yes
73	Girl	1	No	Lip/Palate	AVSD	Yes
85	Boy	2	No	Lip/Palate	VSD	No
87	Boy	3	Yes	Lip/Palate	VSD-PDA	Yes
94	Boy	2	No	Lip/Palate	ASD	Yes
100	Boy	1	No	Palate	TF	No

Table-4: Results of Chi-square test of consanguineous marriages with types of Oral clefts and presence of CHD

Variable	Category	Statistics	Consanguineous Marriages		Total	P-value
			Yes	No		
Types of Oral Cleft	Lip	n	13	6	19	0.985
		%	68.42	31.58	100	
	Palate	n	27	12	39	
		%	69.23	30.77	100	
	Lip and Palate	n	31	13	44	
		%	70.45	29.55	100	
	Total	n	71	31	102	
		%	69.61	30.39	100	
CHD	No	n	54	21	75	0.261
		%	72	28	100	
	Yes	n	17	10	27	
		%	62.96	37.04	100	
	Total	n	71	31	102	
		%	69.61	30.39	100	

4- DISCUSSION

The referred patients with oral cleft were assessed for congenital heart diseases. Of patients with oral clefts, those who had cleft lip/palate were counted more than their counterparts. Cleft lip and cleft lip/palate were higher in the boys than the girls; cleft palate was higher in the girls than the boys. Patients with cleft lip/palate had the highest mean of birth order. Family's marriage was not correlated with the type of oral cleft. The prevalence of CHD in patients with cleft lip was lower than two other oral clefts. Amongst the oral cleft patients, observed a great range of congenital heart diseases. Atrial septal defect observed in 8 (7.84%) oral cleft patients with the highest percent. Three of our patients (11.1%) had sibling cleft history. Some investigators have reported different incidence rates of oral cleft from region to region (24) with different causes (25). Borno observed that the incidence of Cleft lip, with or without cleft palate had variably been 0.3 and 2.19/1000 live births in the Middle East; while our study received to the conclusion of 2.095 per 1000 live birth that was placed in the reported range by Borno (26.)

Oral cleft incidence for the Iranian population varies from 0.86 to 3.73/1000 births (27), while Conway reported that the incidence of oral cleft was 1.43 for over the world, Also, for the Asian population reported was 2 and 0.4 in 1000 live birth for the African population (6). The reported incidence of oral cleft for the various regions in Iran showed that this incidence was 1.03 in Shiraz, 1.9 in Masshad (14), 2.14 in Tehran (13), 0.97 in Gorgan with three different incidence for Sistani (1.47), Fars (0.86) and Turkmean (0.88) ethics (11), 0.86 in Yazd (28), 1.016 in Hamedan (12) and 0.557 in Rasht, 0.352 in Arak, 0.503 in Sanandaj and 0.559 in Tabriz per 1000 live birth (9). Accordance with the incidence resulted of the present study the incidence of oral cleft in Zahedan was much higher than the major cities such as Gorgan, Shiraz, Mashhad and was lower that the incidence reported in Tehran. In Gorgan city the reported incidence of oral cleft for the Sistani ethnics was higher than two other ethnics. The majority of people who live in Zahedan are Baluch and Sistani ethnics. Our results was similar with the Gorgan results for specific ethnic of Sistani that showed this ethnic is more at risk of oral clefts. In comparison of different studies evaluated that the prevalence of anomalies associated with oral clefts is difficult for a variety of reasons. Some of studies have been conducted based on the hospital data and some on data from the birth certificates. The present study was hospital based and the incidence rate of oral clefts reported cannot be generalized to the entire population. The incidence of CHD anomalies in oral clefts patients was 46.6% in Jordan (29), 36% in Turkey (30) and 20% in the Northern Nigeria (31) and 12.8% in Korea (32), 16. 7% in Hangarian (1), and 10 % in Colorado of USA (33). The prevalence of CHD anomalies in oral clefts patients was 26.5% (27 of 102) in this study, which was lower than Jordan and Turkey, higher than Nigeria, Korea, Hangarian and Colorado in USA.

Shafi from Pakistan performed a study and reported that of 123 patients with oral clefts 35 (29%) were associated with various malformations. The most common was CHD, which accounted for 51% of all associated malformations. Therefore 18% of 123 patients were associated with CHD (24) which was lower than our result. In Harry study the overall prevalence of CHD in oral cleft patients was 10% (33/329) compared with our prevalence of 26.5% (27/102) was very low. The prevalence of CHD malformation was 4% (4/102) in cleft lip, 15% (17/115) in cleft palate, and 11% (12/112) in cleft lip/palate; while in our results were 15.75% (3/19) for cleft lip, 20.51%(8/39) for cleft palate and

36.36%(16/44) for cleft lip/palate respectively (33). Sun reported that among all associated malformations with oral clefts, CHD was the most common one with 45.0% of all malformations. The incidence of CHD in cleft palate (20%) was higher than that in cleft lip (3.1%) and cleft lip/palate (16.3%). In compare with our results, the CHD prevalence in cleft lip and cleft lip/palate patients were much lower than our results and the incidence of cleft palate was approximately equal.

Sun also, observed that atrial septal defect (ASD) was the most common heart defects, which accounted for 39.7% of all associated heart malformations in which was similar to our results. Common defects such as ventricular septal defect (VSD) 31.8%, patent ductus arteriosus (PDA), 11.5% and pulmonary valve stenosis (PS) 7.8% were popular (20). In this regards we resulted dissimilar with Sun findings. We received to the conclusion that from all CHD malformations 29.63% (8 of 27) had ASD with the distribution of 1, 3, 4 patients in cleft lip, cleft palate and cleft lip/palate respectively. The percent of TOF was 18.52% (5 of 27) with 1, 3 and 1 in cleft lip, cleft palate and cleft lip/palate respectively. Observed that from all CHD malformations 14.81%(4/27) were VSD with the distribution of 0,0 and 4 patients in cleft lip, cleft palate and cleft lip/palate respectively and for AVSD the trend was 7.41%(2/27) that 2 patients had cleft lip/palate. Eight patients with CHD anomalies had AS & AI, ASD & VSD, HLHS, PA & VSD, Tricuspid atresia 1b, TGA, Truncus arteriosus, and in VSD & PDA one patient. Yang reported that the incidence of CHD was about 0.82% in general population in which was 24 times more in Cleft Palate (20%) , 20 times more in Cleft Lip / Palate (16.4%), 4 times (3.1%) in Cleft Lip and 16 times more in oral clefts(13.6%) (31). with regards to our results clearly could be observed that all these incidence rate are lower that our incidences.

4-1. Limitations of the study

Because we do not have the services of a clinical dysmorphology geneticist, therefore some children with syndromes may not be diagnosed was a limitation of the study.

5. CONCLUSION

In conclusion, this studies provided that high relatively rate of CHD among children with oral clefts and justified the need for echocardiography for these categories of children to diagnosis CHD early in life so as to manage any life-threatening CHD appropriately. We recommend that it would be appropriated for all oral cleft patients to receive a routine examination for associated anomalies by a pediatrician especially heart anomalies. With using of echocardiography, the early diagnosis and treatment of this anomaly is possible.

6- ABBREVIATION

Hypoplastic left heart syndrome (HLHS), Tricuspid atresia 1b (TAIB), Ventricular septal defect (VSD), Transposition of great arteries (TGA), Atrial septal defect (ASD), Aortic Stenosis and Aortic Insufficiency (AS,AI), Truncus arteriosus (TA), Tetralogy of Fallot (TF), Atrioventricular septal defect (AVSD), Pulmonary hypertension(PH), Pulmonary atresia with ventricular septal defect (PA-VSD), Patent ductus arteriosus (PDA).

7- CONFLICT OF INTEREST: None.

8- ACKNOWLEDGMENTS

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