Original Article

J Babol Univ Med Sci
23; 2021. P: 421-428

Prevalence of Orofacial Clefts and Associated Factors in Infants

S. Khosroshahian (DDS, MS)[1], A. Mehdipoor (DDS, MS)[2], M. Aghaali (MD, PhD)[3], F. Salehi (DDS)[4], H. Rahimi (DDS, MS)*[5]

1.Department of Orthodontics, School of Dentistry, Qom University of Medical Science, Qom, I.R.Iran

2.Department of Pediatrics Dentistry, School of Dentistry, Qom University of Medical Science, Qom, I.R.Iran

3.Department of Family and Community Medicine, School of Medicine, Qom University of Medical Sciences, Qom I.R.Iran

4.School of Dentistry, Qom University of Medical Science, Qom, I.R.Iran

5.Department of Periodontics, School of Dentistry, Qom University of Medical Science, Qom, I.R.Iran

J Babol Univ Med Sci; 23; 2021; PP: 421-428

Received: Nov 22nd 2020, Revised: Feb 8th 2021, Accepted: Mar 13rd 2021.

ABSTRACT

BACKGROUND AND OBJECTIVE: Orofacial clefts are the most common congenital facial defect. Genetic and environmental factors play a role in their development. The prevalence of orofacial clefts in Qom province has not been studied so far. The aim of this study was to evaluate the prevalence of orofacial clefts and associated factors in infants born in Qom province during 2010-2018.

METHODS: In this cross-sectional study, during nine years, the medical files of all infants with orofacial clefts and the files of their mothers in all hospitals of Qom province were examined. The files of 476 healthy infants were also evaluated to investigate the associated factors. Healthy infants were selected one number before and one after the case number of sick infants. Infant-related variables (weight, blood type, and other illnesses) and parent-related factors (age, smoking, alcohol, and medications, illness, consanguineous marriage, and number of children) were extracted through reviewing the files or telephone interview.

FINDINGS: Of the 171,270 infants, 238 were found with orofacial clefts (1.39 per 1,000 births). Isolated cleft palate with 39.5% was the most common type of anomaly. Among the studied factors, the percentage of smoking in fathers in the case group (34.5%) was higher than the control group (24.2%) (p=0.004). Moreover, the history of maternal high blood pressure in the case group (7.6%) was higher than the control group (3.4%) (p=0.013). The incidence of diabetes in mothers of the case group (18.9%) was higher than the control group (8.2%) (p=0.001).

CONCLUSION: The results of the study showed that the prevalence of orofacial cleft is 1.39 per 1000 births and smoking, diabetes and high blood pressure are the associated risk factors.

KEY WORDS: *Cleft Lip, Cleft Palate, Infant, Congenital Malformation*.

Please cite this article as follows:

Khosroshahian S, Mehdipoor A, Aghaali M, Salehi F, Rahimi H. Prevalence of Orofacial Clefts and Associated Factors in Infants. J Babol Univ Med Sci. 2021; 23: 421-8.

***Corresponding Author: H. Rahimi (DDS, MS)**
Address: Department of Periodontics, School of Dentistry, Qom University of Medical Science, Qom, I.R.Iran
Tel: +98 25 37700094
E-mail: hamedr2003@yahoo.com

[DOR: 20.1001.1.15614107.1400.23.1.59.8]
[DOI: 10.22088/jbums.23.1.421]

Introduction

Orofacial clefts affect all aspects of the patient's life throughout life and have many material and spiritual consequences for the patient and the health system (1). The term orofacial cleft often refers to a set of congenital anomalies that result from a disorder in the integrity and cohesion of the fetal facial clefts, including between the lateronasal and maxillary processes (oral-nasal-ocular cleft), between medionasal and maxillary processes (cleft lip) and between maxillary processes (cleft palate) and between maxillary and mandibular processes (macrostomy) (2). The most common congenital malformation in the craniofacial region is cleft lip or cleft palate (3, 4).

Among all congenital skeletal abnormalities of the body, the incidence of cleft lip and cleft palate is in the second place and based on statistics, the prevalence is reported to be 1 in every 500 to 2500 births according to socio-economic conditions, racial background and geographical location (5). Orofacial clefts are most common in Asians and least common in Caucasians and black people (6). The total prevalence of orofacial clefts in Asia is reported to be about 1.76 to 1.81 per 1000 people (7, 8). According to reports in Iran, its prevalence varies from 0.93 to 1.3 per 1000 births (9, 10).

Orofacial clefts have a multifactorial origin. Some of the causes mentioned for these abnormalities include consanguineous marriages, drug use, alcohol consumption, smoking, and maternal obesity, all of which are preventable (11). Despite the unknown genes involved in this disorder, the definitive effect of several specific genes including IRF6, PVRL1 and MSX1 has been documented (12). Children and people with cleft lip and cleft palate suffer from many problems including respiratory, speech and hearing problems, difficulty in eating and drinking, recurrent ear infections, poor development of teeth and skeletal and dental malocclusions, and beauty problems, which require multiple, costly and difficult treatments (13, 14).

In addition to physical problems, this anomaly has significant negative psychological and socio-economic effects such as psychosocial dysfunction, decreased quality of life and self-esteem, and inability to interact socially with relatives. Orofacial clefts may also occur with other systemic abnormalities or syndromes that can sometimes be life-threatening (15). Assessing the prevalence of an anomaly or disease is one of the most important routine assessments in epidemiological studies. Such studies are the first step in accurately describing a problem, needs assessment and a background for further research on prevention planning and the introduction of health factors and insurance policies (16). At present, there is no exact information about the extent of cleft lip and cleft palate in the Iranian population. Various statistics are available. Unfortunately, due to problems such as disagreements over the definition of the problem, evaluation of limited centers and outdated statistics, as well as the impact of geographical conditions and ethnicity, these statistics cannot be generalized (5). Obtaining accurate statistics on this problem can help in the planning of the Ministry of Health, both in terms of prevention and treatment of patients. Considering the importance of the subject and the undeniable effects of the disease on the mental and physical health of individuals and the lack of accurate statistics in this regard in Qom province, this study was conducted to determine the prevalence of orofacial clefts and associated factors over a 9-year period in Qom province.

Methods

This cross-sectional study was performed after approval by the ethics committee of Qom University of Medical Sciences with the code IR.MUQ.REC.1398.143. Samples were selected by census method. During the period of 2010-2018, all medical files of infants reported with orofacial clefts were reviewed. The files of 476 healthy infants were also examined to determine the factors associated with orofacial clefts. Healthy infants were selected one number before and one after the case number of sick infants. Inclusion criteria were all neonates with nasopharyngeal clefts. Files with incomplete and ambiguous information without the possibility of contacting were excluded. All hospitals with obstetrics and gynecology wards in Qom province (Forghani, Imam Reza, Shohada, Izadi, Vali-E-Asr and Golpayegani hospitals) were surveyed.

First, the total number of births and infants with cleft lip and cleft palate was extracted in a period of nine years and also based on each separate year to assess the prevalence. Then, information forms were completed for case and control groups through reviewing the files or telephone interview. Infant-related information included: year of birth, gender, presence of comorbidities (all information recorded in the file), baby weight (grams), time of birth (weeks of birth), and blood type. Parent-related information included: demographic information of father and mother, history of maternal illness and medication use (all drugs listed),

[DOR: 20.1001.1.15614107.1400.23.1.59.8]
[DOI: 10.22088/jbums.23.1.421]

history of miscarriage, nationality of parents, maternal BMI in the first trimester of pregnancy (based on weight and height recorded in maternal record and body mass index), smoking, alcohol and drug use by parents, number of children and the presence of first-degree relatives with anomalies, consanguineous marriage, education and occupation. Parents' occupations were also registered in the categories of self-employed, employed, unemployed (housewife). Body mass index was calculated based on height and weight in the first trimester (11). The nationality of the parents was extracted as Iranian and non-Iranian.

All steps of collecting and recording data in the control and case groups were performed by one person. Permission to access their files was obtained after going through the legal process. In the telephone interview, informed consent was obtained to use the information in accordance with the principles of patient confidentiality. Data were analyzed using independent t-test, chi-square, Mann-Whitney and logistic regression, and by SPSS 20. For logistic regression, the Backward Stepwise (Wald) method was used and $p<0.05$ was considered significant.

Results

The total number of deliveries in these 9 years was 171,270 deliveries and 238 infants with orofacial cleft anomalies were identified in Qom province during the study period. The prevalence of orofacial cleft was 1.39 per 1000 births. Among 238 patients with orofacial clefts, 123 were girls (51.7%) and 115 were boys (48.3%) and out of 476 patients in the control group, 231 were girls (48.5%) and 245 were boys (51.5%). Among the types of orofacial clefts, isolated cleft palate with 39.5% was the most common type, cleft lip and cleft palate with a prevalence of 34.4% and isolated cleft lip with a prevalence of 25.6% were in the next ranks. One case of oblique facial cleft was also observed. The distribution and prevalence of orofacial clefts were studied separately for each year and different types of clefts among those born during these nine years in Qom province (Figure 1).

Due to the small number of some cases, statistical analysis was not possible, so these cases were reported only descriptively. 7 mothers in the control group and 3 mothers in the case group reported smoking. 7 fathers in the case group and 2 fathers in the control group were drug users. 1 mother in the control group reported drug use and none of the parents reported alcohol use. The gender distribution of patients was slightly higher in girls (51.68%) relative to boys (48.32%) and no significant relationship was found between infant gender and the incidence of orofacial clefts. Cleft lip (52.5%) and cleft palate (54%) were more common in girls. However, the prevalence of cleft lip and palate was higher in boys (54.9%) (Figure 2).

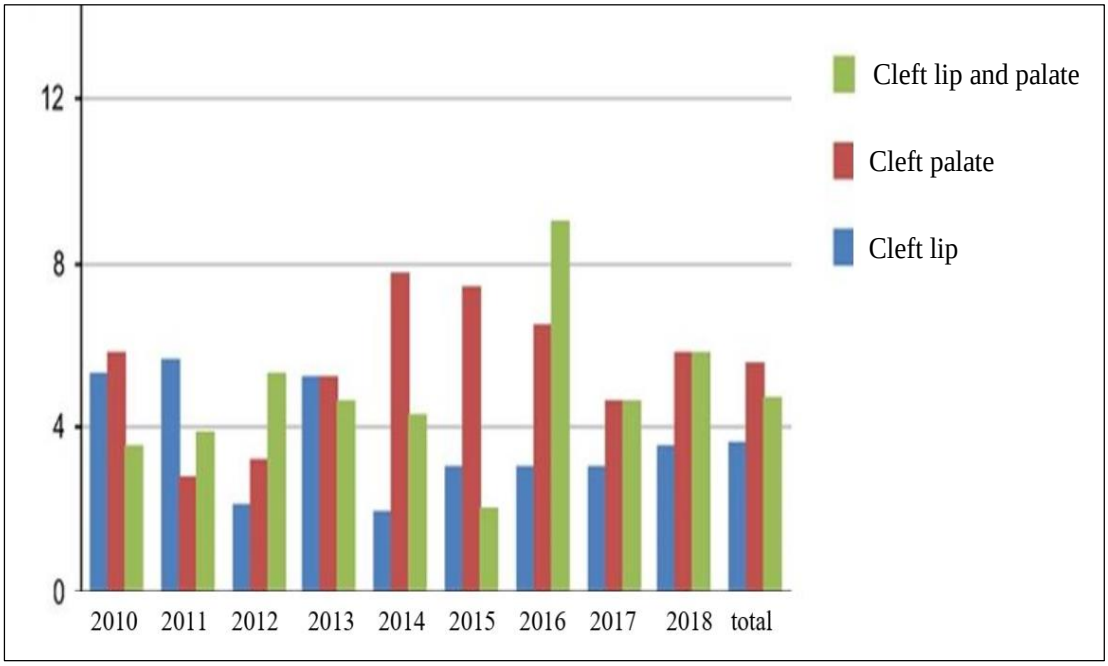

Figure 1. Prevalence of orofacial clefts per 10,000 births in Qom province during 2010-2018

[DOR: 20.1001.1.15614107.1400.23.1.59.8]
[DOI: 10.22088/jbums.23.1.421]

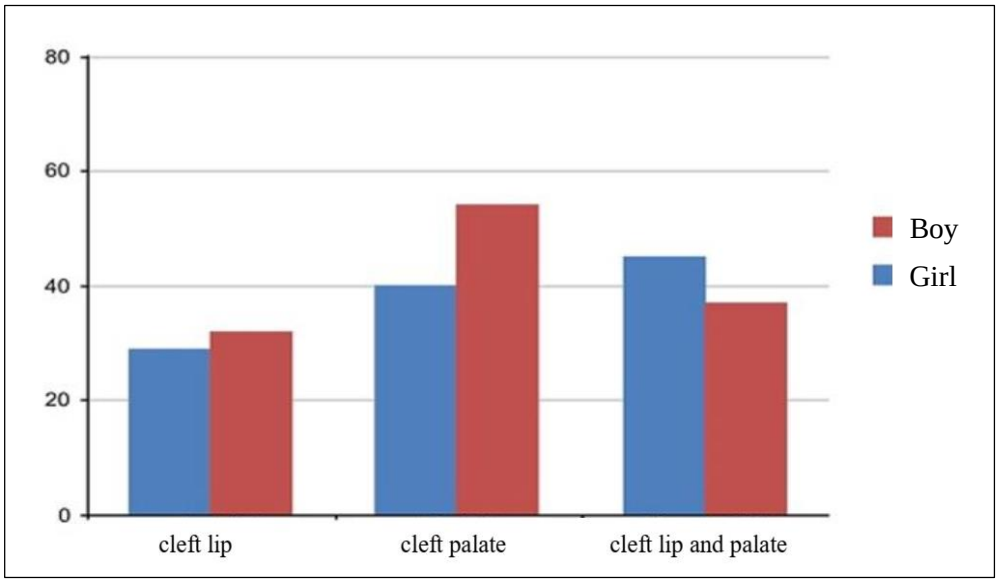

Figure 2. Gender distribution of patients with orofacial clefts by type of cleft

The number of children in the family in the case and control groups was almost equal and no significant relationship was observed in this regard. Among the studied variables, there was a significant difference between the two groups of patients and controls in terms of studied syndromes (Table 1).

Table 1. Comparison of risk factors in the case group and the control group

Variable	Case group (238) Number(%) or Mean±SD	Control group (476) Number(%) or Mean±SD	p-value
Premature baby	53(22.4)	94(18.1)	0.416
Blood type			
O	75(31.5)	164(34.5)	
A	70(29.4)	108(22.7)	0.109
B	68(28.6)	131(28.6)	
AB	25(10.5)	73(15.3)	
Suffering from syndrome	79(33.2)	26(5.5)	<0.001
History of abortion	51(21.4)	108(22.7)	0.703
Consanguineous marriage	98(41.2)	136(28.6)	0.003
Smoking in fathers	82(34.5)	115(24.2)	0.004
Mother with non-Iranian nationality	42(17.6)	86(18.1)	0.890
Father with non-Iranian nationality	43(18.1)	87(18.3)	0.945
Family history of cleft lip and palate	68(28.7)	0(0)	-
Mother's education			
Lower than high school diploma	86(36.1)	158(33.2)	
high school diploma	95(39.9)	202(42.4)	0.639
Higher than high school diploma	57(23.9)	116(24.4)	
Father's education			
Lower than high school diploma	68(28.6)	95(20)	
high school diploma	99(41.6)	220(46.2)	0.017
Higher than high school diploma	71(29.8)	161(33.8)	
Mother's job			
Housewife	194(81.5)	385(80.9)	
Employed	26(10.9)	51(10.7)	0.927
Self-employed	18(7.6)	40(8.4)	
Father's job			
Unemployed	4(1.7)	4(0.8)	
Employed	54(22.7)	112(23.5)	0.592
Self-employed	180(75.6)	360(75.6)	
Mean weight of infants	3010.90±614.47	3094.65±600.64	0.082
Mean age of mothers	28.28±4.93	27.92±5.53	0.388
Mean age of fathers	31.90±5.26	31.53±5.65	0.4
BMI of the first trimester of pregnancy	33.1±10.07	32.90±11.06	0.758

[DOR: 20.1001.1.15614107.1400.23.1.59.8]
[DOI: 10.22088/jbums.23.1.421]

In terms of type of disease or syndrome in the case group, 19 infants (8%) had Pierre Robin syndrome, 18 infants (7.1%) had other skeletal abnormalities, 8 infants (3.4%) had heart disease, 7 infants (2.9%) had eye abnormalities, 6 infants (2.5%) had hydrocephalus and 6 infants (2.5%) had urinary-genital abnormalities. Regarding the history of maternal disease, 78 (32.8%) of mothers in the case group and 138 (29%) of mothers in the control group had a history of underlying disease. None of the types of maternal diseases except anemia, diabetes and high blood pressure were significantly associated with the occurrence of cleft lip and cleft palate anomalies. 18 patients in the case group (7.6%) and 16 patients in the control group (3.4%) had high blood pressure (p=0.013). 40 patients (16.8%) in the case group and 32 patients (6.7%) in the control group had anemia (p=0.001). In the case group, 45 mothers (18.9%) and in the control group, 38 mothers (8.2%) had diabetes (p=0.001). Regarding the use of medications by the mother, 60 people (25.2%) in the case group and 97 people (20.4%) in the control group used medications. Statistical analysis of any medication used by the mother, except iron tablets, was not significantly associated with the occurrence of cleft lip and cleft palate anomalies. In the case group, 26 mothers (10.9%) and in the control group, 18 mothers (3.8%) took iron tablets (p<0.001). Logistic regression analysis showed that based on a 95% confidence interval, mothers with hypothyroidism, anemia and diabetes 1.8, 1.9 and 1.7 times, respectively, fathers who smoke, 1.5 times and parents of consanguineous marriage were 1.7 times more likely to have a child with cleft lip and palate. Moreover, infants with orofacial clefts were 7.5 times more likely to have a disease or syndrome compared to neonates in the control group (Table 2).

Table 2. Risk factors associated with orofacial clefts in those born in 2010-2018 in Qom province

	Raw coefficient	p-value	Adjusted coefficient	p-value	Odds ratio	95% confidence interval
Hypothyroidism	0.542	0.005	0.621	0.006	1.824	1.189-2.798
Anemia	1.031	<0.001	0.686	0.019	1.987	1.119-3.529
Father's smoking	0.498	0.004	0.464	0.017	1.590	1.088-2.322
Infant accompanying syndrome	2.15	<0.001	0.025	0.001	7.577	4.700-12.216
Diabetes	0.989	<0.001	0.542	0.049	1.720	1.002-2.954
Consanguineous marriage	0.56	0.001	0.579	0.002	1.758	1.240-2.568

Discussion

The results of this study showed that the prevalence of orofacial clefts in these nine years in Qom was 1.39 per 1000 people, which is close to the mean prevalence of orofacial clefts in Iran (1.03 per 1000 births) (17). It has been almost identical to existing global statistics (1 in 700 births) and Asia (1.3 per 1,000 births) (11). Among the types of orofacial clefts, isolated cleft palate with 39.5% was the most common type of cleft in Qom province and cleft lip and cleft palate with a prevalence of 34.4% and isolated cleft lip with a prevalence of 25.6% were in the next ranks. In the study of Rajabian et al. on an Iranian population, the highest prevalence belonged to cleft lip (39.9%) and the lowest prevalence was related to cleft lip and palate (17.4%) (17). According to the present study, the prevalence of cleft in girls (51.7%) was slightly higher than boys. However, in general, the prevalence of orofacial clefts in Iran is slightly higher in boys (53.6%) than girls (46.4%) (17). The reason for the lack of statistically significant differences in the gender distribution of cleft lip and palate can be the presence of abnormal genes on the autosomal chromosome and lack of dependence on gender (18). In the present study, cleft lip and cleft palate were more common in girls and cleft lip and palate was more common in boys. Most studies agree with these results. Such gender differences in clinical data have been explained by the assumption that the secondary palate closes faster in the female fetus than in the male fetus at the same age (19, 20). In this study, no relationship was observed between blood type and orofacial clefts. In the study of Deolia et al. (21), statistical analyses did not show an association between blood type and the occurrence of orofacial clefts. But contrary to our results, Jamilian et al. (22) concluded that there is a significant relationship between blood type A and the incidence of cleft lip and palate, and contradictory results have been reported in this regard. In this study, the most common syndrome was Pierre-

[DOR: 20.1001.1.15614107.1400.23.1.59.8]
[DOI: 10.22088/jbums.23.1.421]

Robin Syndrome. In the study of Genisca et al., a quarter of patients had Pierre-Robin Syndrome, followed by skeletal anomalies and heart disease as the most common diseases associated with orofacial clefts (23). In this study, no relationship was observed between advanced maternal age and the incidence of cleft palate. Also, several other studies in Iran, such as the present study, did not find a connection between the two (13-17, 24). On the other hand, Cooper et al. reported that the risk of developing anomalies in children, including cleft lip and palate, increases eightfold in older mother. In this study however, only other anomalies were examined (23). Nevertheless, some researchers have found a positive relationship between advanced maternal age and chromosomal and non-chromosomal abnormalities in the infant (24). In our study, the mean age of fathers of infants with cleft palate was 31.9 years and there was no relationship between the father's age and cleft lip and palate in the infant.

In a study in West Azerbaijan province, no association was found between advanced parents age and the incidence of orofacial clefts (25). But in the study of Savitz et al., advanced father's age played a positive role in the incidence of cleft palate. However, in that study, in addition to the father's age, other factors such as smoking and alcohol consumption of the fathers might have influenced the results (26). Due to the traditional context and culture of the people of Qom province, the age of marriage is often low and therefore, no significant difference was found between the age of the parents in the case and control groups. The results regarding the relationship between parents' age and the occurrence of cleft lip and palate are contradictory.

There was no association between birth weight and cleft lip and palate in evaluations. Studies on the weight of infants and cleft palate show diverse results. In some studies, the affected infants had lower weight, similar weight, and even heavier than the infants in the control group. The reason for these differences can be the number of different samples and racial differences (27 – 29). In this study, there was no relationship between the number of children and the presence of cleft lip and palate. In other studies (30), they found that in large families, cleft lip and palate are more likely to occur in children. The reason for this discrepancy may be the lower number of children in the families in Qom province.

In the present study, the most commonly used drugs by mothers in the case group were levothyroxine, insulin and iron tablets. According to our results, no association was found between the drugs used by the mother and cleft lip and palate (31). In the study of Krapels et al. (32), iron intake of mothers of control group was higher than that of mothers in the case group during pregnancy. However, this contradicted our results. In the case group, mothers with anemia may not have adhered to iron tablets, and therefore the effect of iron tablets in the prevention of orofacial clefts has not been established. Cigarette smoke is a complex combination of toxic and teratogenic chemicals, including carbon monoxide and nicotine, and has negative effects on the development of several vulnerable fetal structures (19). In this study, there was a positive relationship between fathers' smoking and children with cleft lip and palate, as in other studies, and fathers in the case group smoked more than the control group (17).

Interpretation of the results of such studies should be done while taking into account the complex interactions between genetic and environmental factors in creating cleft anomalies, ethnic and racial differences between populations evaluated in different studies and differences in assessment methods and number of samples in different studies. Among the limitations of this study, we can mention the problem of incompleteness of some files and inaccurate registration of information and collection of some data by self-declaration method and memory errors of samples. Unfortunately, due to the lack of such assessments in the past, it was not possible to compare the results with the past and assess the decreasing or increasing trend of this anomaly in Qom province. For future studies, it is suggested that the exact type of cleft be recorded by the relevant physicians in the files of infected infants and, if possible, a photograph be added to the files. Due to the participation of genetic and environmental factors in the occurrence of cleft lip and palate, public awareness of these factors and efforts to prevent the occurrence of this disorder are essential.

In this study, the prevalence of orofacial clefts in Qom province was 1.39 per 1000 births and the highest risk factors for this abnormality were smoking in fathers and diabetes and high blood pressure in mothers.

Conflict of interest: The authors of the article did not report any conflict of interest.

Acknowledgment

We would like to thank the Vice Chancellor for Research of Qazvin University of Medical Sciences for the financial support of the research.

[DOR: 20.1001.1.15614107.1400.23.1.59.8]
[DOI: 10.22088/jbums.23.1.421]

References

1.Wehby Gl, Cassell CH. The impact of orofacial clefts on quality of life and healthcare use and costs. Oral Dis. 2010;16(1) 3-10.

2.Burg ML, Chai Y, Yao CA, Magee W, Figueiredo JC. Epidemiology, Etiology, and Treatment of Isolated Cleft Palate. Front Physiol. 2016;7:67.

3.Perko M. The history of treatment of cleft lip and palate. Prog Pediatr Surg. 1986;20:238-51.

4.Pereira AV, Fradinho N, Carmo S, de Sousa JM, Rasteiro D, Duarte R, et al. Associated Malformations in Children with Orofacial Clefts in Portugal: A 31-Year Study. Plast Reconstr Surg Glob Open. 2018;6(2):e1635.

5.Noorollahian M, Nematy M, Dolatian A, Ghesmati H, Akhlaghi S, Khademi GR. Cleft lip and palate and related factors: A 10 years study in university hospitalised patients at Mashhad -- Iran. Afr J Paediatr Surg. 2015;12(4):286-90.

6.Boulet SL, Grosse SD, Honein MA, Correa-Villaseñnor A. Children with Orofacial Clefts: Health-Care Use and Costs Among a Privately Insured Population. Public Health Rep. 2009;124(3):447-53.

7.Kim S, Kim WJ, Oh C, Kim JC. Cleft lip and palate incidence among the live births in the Republic of Korea. J Korean Med Sci. 2002;17(1):49-52.

8.Wang W, Guan P, Xu W, Zhou B. Risk factors for oral clefts: a population-based case-control study in Shenyang, China. Paediatr Perinat Epidemiol. 2009;23(4):310-20.

9.Jahanbin A, Mokhber N, Sahhafian AA. Seasonal and yearly fluctuations in birth date of cleft lip and palate children in northern east of Iran, 1992-2007. Iran J Otorhinolaryngol. 2008;20(1):45-50. [In Persian]

10.Jamiliyan A, Nayeri F, Babayan A. Prevalence of cleft lip and palate in Imam Khomeini Hospital in Tehran during 1999-2004. J Res Dent Sci. 2009;5(4):48-54. [In Persian] Available from: https://www.sid.ir/fa/journal/ViewPaper.aspx?id=123783

11.Noorbakhsh N, Davari HA, Akochakian S, Davari M. Comparative evaluation of risk factors in children with cleft lip and palate and healthy children. J Isfahan Dent School. 2011;6(4):526-32. [In Persian]

12.Cox TC. Taking it to the max: the genetic and developmental mechanisms coordinating midfacial morphogenesis and dysmorphology. Clin Genet. 2004;65(3):163-76.

13.Tehranchi A, Kazemi B, Seyfi M, Mahjoub E. Association between TGFβ3 mutation and cleft lip/palate in Iranian Population. J Dent School. 2010;28(3):160-4. [In Persian]

14.Golali Pour MJ, Mohammadian S, Taziki MH, Mobasheri E, Borghei A. Epidemiology of cleft lip and cleft palate in Gorgan, 1998-2003. J Babol Univ Med Sci. 2005;7(2):41-7. [In Persian]

15.Duarte GA, Ramos RB, Cardoso MC. Feeding methods for children with cleft lip and/orpalate: a systematic review. Braz J Otorhinolaryngol. 2016;82(5):602-9.

16.Williams R, Wright J. Epidemiological issues in health needs assessment. BMJ. 1998;316(7141):1379-82.

17.Rajabian MH, Sherkat M. An epidemiologic study of oral clefts in Iran: analysis of 1669 cases. Cleft Palate Craniofac J. 2000;37(2):191-6.

18.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.

19.Saxén I. Epidemiology of cleft lip and palate. An attemp to rule out chance correlations. Br J Prev Soc Med. 1975;29(2):103-10.

20.Burdi AR, Silvey RG. Sexual differences in closure of the human palatal shelves. Cleft Palate J. 1969;6(1):1-7.

21.Deolia Sh, Gaikwad RN, Sen S, Jaiswal A, Suhang P, Singh B. Role of consanguineous marriages and blood groups in cleft lip and palate patient: A retrospective study. J Datta Meghe Inst Med Sci Univ. 2016,11(1):61-4.

22.Jamilian A, Sarkarat F, Jafari M, Neshandar M, Amini E, Khosravi S, et al. Family history and risk factors for cleft lip and palate patients and their associated anomalies. Stomatologija. 2017;19(3):78-83.

23.Genisca AE, Frías JL, Broussard CS, Honein MA, Lammer EJ, Moore CA, et al. Orofacial clefts in the national birth defects prevention study. Am J Med Genet A. 2009;149A(6):1149-58.

24.Zandi M, Heidari A. An epidemiologic study of orofacial clefts in Hamedan city, Iran: a 15-year study. Cleft Palate Craniofac J. 2011;48(4):483-9.

[DOR: 20.1001.1.15614107.1400.23.1.59.8]
[DOI: 10.22088/jbums.23.1.421]

25.Abdollahifakhim S, Mousaviagdas M, Sohrabpour M. Study of risk factors related to the orofacial clefts in Eastern Azerbaijan, Iran: Population-based from 2000 to 2015. Int J Epidemiol Res. 2016;3(4):336-44.
26.Savitz DA, Schwingl PJ, Keels MA. Influence of paternal age, smoking, and alcohol consumption on congenital anomalies. Teratology. 1991;44(4):429-40.
27.Duncan PA, Shapiro LR, Soley RL, Turet SE. Linear growth patterns in patients with cleft lip or palate or both. Am J Dis Child. 1983;137(2):159-63.
28.Johnston MC, Bronsky PT. Prenatal craniofacial development: new insights on normal and abnormal mechanisms. Crit Rev Oral Biol Med. 1995;6(1):25-79.
29.Ranalli DN, Mazaheri M. Height-weight growth of cleft children, birth to six years. Cleft Palate J. 1975;12:400-4.
30.Vrijheid M, Dolk H, Stone D, Abramsky L, Alberman E, Scott JE. Socioeconomic inequalities in risk of congenital anomaly. Arch Dis Child. 2000;82(5):349-52.
31.Yoon PW, Rasmussen SA, Lynberg MC, Moore CA, Anderka M, Carmichael SL, et al. The National Birth Defects Prevention Study. Public Heath Rep. 2001;116(Suppl 1):32-40.
32.Krapels IP, van Rooij IA, Ocke MC, West CE, van der Horst CM, Steegers-Theunissen RP. Maternal nutritional status and the risk for orofacial cleft offspring in humans. J Nutr. 2004;134(11):3106-13.

[DOR: 20.1001.1.15614107.1400.23.1.59.8]
[DOI: 10.22088/jbums.23.1.421]