



Cleft lip and palate and related factors: A 10 years study in university hospitalised patients at Mashhad – Iran

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ABSTRACT

Background: Oral-facial clefts including cleft lip and palate are the most common congenital malformations of the head and neck. Environmental factors such as maternal hormonal disorders, use of psychiatric medications, vitamin and folic acid deficiency, hypoxia, cigarette smoking and maternal obesity and overweight can affect the incidence of these disorders. In Iran, one of the associated problems is a lack of accurate statistics regarding the present status of the patients, which can cause a disturbance in the health programmes of Ministry of Health and Medical Education. The aim of this study was to report the status of 398 cases of cleft lip and palate in Sheikh and Imam Reza Hospitals of Mashhad over a 10-year period. **Materials and Methods:** This retrospective descriptive study was performed using data collection method and included the evaluation of the recorded files and completing the data forms. In this study, the file records of 398 patients referring to Mashhad Sheikh and Imam Reza (P.U.H) Hospitals were studied, from the beginning of 2002 to the end of 2011; the obtained data from the files were collected and classified.

Results: The highest frequency was related to cleft palate alone (40.7%); frequencies were lower regarding the cleft lip and palate and cleft lip alone (34.41% and 24.87%, respectively). Approximately, half of the patients were from rural areas of the city and had articulation disorders. Most of the patients were the first-born children of the family and their parents were consanguineously married; about one-third of the patients had a family history of the disease. **Conclusion:** According to the results of the present study, cleft lip is more frequent in males and cleft palate is more prevalent in females; the obtained results are consistent with the global statistics.

Key words: Cleft lip, cleft lip alone, cleft palate alone, palate

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INTRODUCTION

Oral-facial clefts including cleft lip and palate are the most common congenital malformations of the head and neck, which are observed on the lips, jaw bones and hard and soft palates. Various problems are observed in the patients such as dental disorders, poor occlusion, deformation of the face and nose and nutritional, respiratory, hearing and articulation problems.^[1]

The different environmental factors are suggested regarding the incidence of these disorders, which are as follows: Maternal hormonal disorders,^[2] use of psychiatric medications,^[3] vitamin and folic acid deficiency,^[4] hypoxia and cigarette smoking,^[5] maternal obesity and overweight,^[6] hereditary factors such as race, ethnicity and genetics^[7] and geographical situation.

Birth prevalence of cleft lip is 1 out of every 1000 live births in the United States while that of cleft palate is 1 in 2000 live births. The highest incidence of cleft lip is observed in Native Americans (3.6 per thousand), Asians (2.1 per thousand) and the white-skinned (one per thousand); the prevalence of this disorder is lower in black people (0.41 per thousand).^[10] In contrast, the incidence of cleft palate is not different among various ethnic groups and occurs in 1:2000 live births. Cleft lip is more observed in boys in comparison with girls (2 to 1) while cleft palate is less frequent in boys than

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girls (1 to 2); this might be due to the fact that palatine shelves close 1-week later in females than males.^[1]

According to the studies performed in Asia, the incidence of oral cleft in every 1000 live births is reported as follows: 1.91 in Pakistan,^[8] 1.39 in Jordan,^[9] 1.76 in North China,^[10] 1.81 in Korea,^[11] 1.34 in Japan^[12] and 1.5 in Oman.^[13] The differences observed in the incidence of oral cleft can be related to social influences and racial/ethnic factors in different parts of the world, which is more commonly defined as genetic disorders.^[14]

The incidence rate of oral clefts in different parts of Iran ranges from 0.8 to 2.4 per 1000 live births.^[14] However, according to a review study conducted on these abnormalities in Iran, the incidence of cleft lip and palate is estimated 1 in every 1000 live births, which is less than other Middle Eastern and Asian countries and also natives of North America.^[15]

Among congenital malformations and skeletal deformities, the incidence of cleft lip and palate ranks second in the world.^[16] However, one of the associated problems in Iran is a lack of accurate statistics regarding the status of the patients, which can cause a disturbance in the health programmes of Ministry of Health and Medical Education. The aim of this study was to report the status of 398 cases of cleft lip and palate in Mashhad Sheikh and Imam Reza Hospitals over a 10-year period.

MATERIALS AND METHODS

This retrospective descriptive study was performed using data collection method and included the evaluation of the files and completing the data forms. The study population consisted of all the patients who had undergone surgery due to cleft palate or cleft lip or both at the beginning of 2002 to the end of 2011 (a 10-year period) in Mashhad Sheikh and Imam Reza Hospitals.

The registered files of the patients were carefully evaluated, and the data related to the variables were extracted. The variables included gender, cleft type, the location of residency, medications during pregnancy, folic acid supplementation in the first trimester of pregnancy, family history and parental consanguinity. Afterwards, data were collected and analysed using SPSS software Version 16.0 for Windows (SPSS Inc., Chicago, IL, USA).

RESULTS

In this study, of the total of 398 patients referring to Mashhad Sheikh and Imam Reza Hospitals over 10 years, 188 were females and 210 were males. The frequencies of cleft palate alone, cleft lip alone and both cleft lip and palate are separately shown in Table 1, according to the patients' gender.

As it is observed, the incidence of cleft lip alone and cleft palate alone is higher in males and females, respectively. Cleft lip alone and both cleft palate and lip are significantly more common in males ($P = 0.02$); however, cleft palate alone is more common in females.

Residency location of these patients included the city (Mashhad), towns, city suburbs and rural areas. It was revealed that most patients (approximately 40%) are living in rural areas and it can be concluded that the prevalence of this congenital anomaly is more observed in the group, which has an economically lower status. In addition to the history of residency, other demographic characteristics such as family history, parental consanguinity and child's place in the family birth order are studied and summarised in Table 2.

As it is indicated in Table 2, most of the patients with malformations were first-born children (40.8%). Furthermore, in our study, we observed parental consanguineous marriage in 63.63% of the cases while only 28% of the patients had a family history of diseases similar to cleft lip and palate.

Since, the present study is retrospective, and the data were collected from the recorded files, there was a defect in the collected data and the gathered information was incomplete. However, as it is evident in Table 2, the patients were different regarding various factors and a higher risk is predicted for people living in the rural areas and towns ($P < 0.001$); the same applies to those who are the first child in the family ($P < 0.001$) or whose parents are consanguineously married ($P = 0.007$).

Table 1: The frequency of cleft lip and palate according to the patient's gender

Sex	Cleft palate	Cleft lip	Cleft lip and palate	Total	P-Value
Male	66 16.58%	59 14.82%	86 21.6%	211	$P < 0.001$
Female	96 24.12%	40 10.05%	51 12.82%	187	$P < 0.001$
Total	162 40.7%	99 24.87%	137 34.42%	398	
	0.2=P	1=P	0.02=P		$P < 0.001$

Evaluation of Articulation disorders in children shows that about half of our patients (47.68%) have this type of disorder. Furthermore, data indicate that 45% of mothers had taken medications and 125 mothers (31%) had not used folic acid in the first trimester of pregnancy [Table 3].

DISCUSSION

The present study showed that the highest prevalence of cleft anomalies in patients was related to cleft palate (40.7%); 34.41% and 24.87% of the patients presented with cleft lip and palate and cleft lip alone, respectively; cleft lip alone was more prevalent in males while cleft palate alone was more common amongst females.

In this study, the results show that the incidence of oral cleft was higher in males in comparison with females; the results are similar to those of the studies performed by Rittler, *et al.* in Argentina, Pakistan and Croatia, respectively.^[8,17,18]

Table 2: Demographic characteristics of the patients

Characteristics	Number (%)	Total Number (%)	P-Value
Residency location			
Mashhad	84 (21.21)	396	$P < 0.001$
Towns	99 (25)		
City suburbs	57 (14.39)		
Rural areas	156 (39.39)		
Family history			
Positive	54 (27.83)	194	$P < 0.001$
Negative	140 (72.16)		
Parental consanguinity			
Cases with parental consanguinity	126 (63.63)	198	$P < 0.007$
Cases without parental consanguinity	72 (36.36)		
Child's place in the family birth order			
First	91 (40.08)	227	$P < 0.001$
Second	64 (28.19)		
Third	34 (14.97)		
Fourth and higher	38 (16.74)		
Articulation disorders			
Positive	134 (48)	281	$P < 0.05$
Negative	147 (52.31)		

Table 3: The frequency of folic acid supplementation in first trimester of pregnancy

Folic acid supplementation	Number (%)
Yes	72 (19.56)
No	125 (33.96)

In terms of gender, the incidence rate of different types of the cleft was different between the two genders; in local studies, the overall prevalence of oral clefts was higher in males.^[19] In terms of the frequency of cleft types according to gender, the results of these studies are consistent with those of the present one.

In Taiwan, in a study by Lei *et al.* in 2013, the prevalence of facial clefts and the related factors were assessed and it was concluded that cleft lip and palate in combination are more prevalent than other types of clefts; it was also revealed that cleft lip and palate is more frequently observed in males, though cleft palate alone has been more prevalent in females. In our study, the highest prevalence was related to cleft palate, which is inconsistent with the aforementioned study; however, with regard to the cleft frequency in different genders, the findings are similar to the results of the present study.^[20]

In a study by Tafazzoli and Shahriari in 2001 in Qazvin, Iran, the highest incidence was observed in cleft lip and palate and then in cleft palate alone and cleft lip alone; however, in our study, cleft palate alone had the highest frequency. Tafazzoli and Shahriari study and the present research indicate that cleft lip and palate together and cleft lip alone are more observed in males and cleft palate alone is more frequent in females in comparison with males.^[21]

In the study of Rajabian and Sherkat, the incidence of different types of cleft was higher in males than females, as it is also shown in the present study; however, in our study, cleft palate was more common in females while in the study of Rajabian and Sherkat, cleft lip was mostly observed in females.^[19] In the study performed by Mclead, all three types of cleft (cleft palate alone, cleft lip alone and cleft palate and lip) were more observed in men than women.^[22]

In the study by Kim *et al.* in South of North Korea, the prevalence of cleft lip and cleft palate and lip together was more common in men than women and the incidence of cleft palate was higher in women in comparison with men; the results are in consistence with those of the present study.^[23]

Rajabian and Sherkat conducted a study on 1669 patients during 1976-1991. Consanguineous marriage was frequent in the parents of 45.8% of the case group and 43.1% of the control group.^[19] In 2008, Razmpa *et al.* performed a study on patients referring to Tehran genetics clinic, who had neonatal abnormalities of

head and neck as a result of parents' consanguineous marriage. They observed that among 220 cases of head and neck abnormalities, the third common disease after deafness and dumbness was cleft palate alone; among 10 studied cases, five cases were children of consanguineously married parents and among these five cases, four cases were girls and one was a boy. The fourth most common disease was cleft lip; among the six reported cases, parents of three cases were consanguineously married and among these three cases, two were boys and one was a girl; 14 cases presented with cleft lip and palate.^[24]

In the study of Khazaei *et al.* in 2010, on children with cleft palate and lip in Kermanshah; Iran, it was reported that the parents of 51.4% of these patients were consanguineously married.^[25] In the study of Jamilian A *et al.* in 2008 in Tehran, 31.8% of the neonates with a cleft palate had parents who were consanguineously married. Parental consanguinity in 8% of the infants with cleft lip and palate was at least 5 times higher than the group without cleft lip and palate.^[26] In our study, based on the collected data (recorded data of 200 cases regarding this variable), approximately, 25% had a family history of cleft lip and palate and the parents were consanguineously married in 63.63% of the cases.

In 2010, Messer *et al.* performed a study on the incidence of cleft lip and palate in urban and rural areas of Texas and they concluded that living in rural areas is associated with an increased risk of cleft lip and palate, though it is not related to the incidence of cleft palate alone. Behavioural factors such as maternal smoking or drug use leads to an increased incidence of cleft lip and palate (not the cleft palate); this may be due to the fact that women living in rural areas have less access to insurance, health services and medical care.^[27] Similarly in the present study, the highest prevalence was observed in the group who were living in rural areas.

Similar to the study of Khazaei *et al.* in Kermanshah, in the present study, the neonates with oral cleft were generally the first and then the second children of the family.^[25] The same results were reported in other Iranian studies, but some studies in other countries have reported that the prevalence of these disorders is higher in the mothers' next labours; in this regard, increased age is considered as the influential factor.^[28]

Carinci *et al.* in 2005 performed a study in Italy on the relationship between cleft types and the patterns associated with gender, smoking history, family history

of diabetes and receiving folic acid; they concluded that there was an association between environmental factors such as smoking and folic acid use and the type of cleft (left cleft lip). Furthermore, for the first time, a significant association was found between family history of diabetes and a higher incidence of clefts.^[29]

In the study of Golalipour *et al.* in Iran on 2005, they concluded that the incidence of these malformations is higher in the month of July due to the formation of cleft lip and palate during 4-6 weeks after impregnation; this may be due to the reduced amounts of folic acid in the mother's diet in some seasons of the year such as winter and early spring;^[30] in our study, 125 mothers did not use folic acid. From the Table 3, can be observed that 69% of mothers among pregnancy supplements folic acid were used. It can be observed that folic acid supplementation is another factor can be affected in the first trimester of pregnancy.

In a retrospective study by Jahanbin *et al.*, the birth dates of 358 children born in Khorasan Razavi Province from 1992 to 2007 with a diagnosis of cleft palate or cleft lip with/without cleft palate were collected and the corresponding findings demonstrated the peak incidence of cleft palate birth in autumn. However, cleft lip and the palate showed a different seasonal trend, with the peak of occurrence in the spring and then autumn for boys and in the winter for girls. In addition, this study demonstrated an annual decrease in cleft lip, isolated cleft palate and cleft lip and palate during the period of the study.^[31]

Kelly *et al.* conducted a study in 2012, in Ireland on folic acid supplementation and the risk of cleft lip and palate in children. The obtained results were in favour of the hypothesis of the role of folic acid in the prevention of cleft lip and palate.^[32]

A prerequisite for natural speech production is the regular structure and coordinated function of the speech organs. In cleft lip and palate, many articulation problems can be found due to the involvement of speech organs. In Delphi's study in Ahvaz (2013), the score of speech skills and lingual expression was lower in children (of all age ranges) with cleft lip and palate in comparison with normal children.^[33] Davari *et al.* in 2012, in Isfahan carried out a study on the prevalence of hypernasality after the first surgery of cleft palate in children; it was indicated that the prevalence of hypernasality was 70.9%.^[34] Furthermore, in the present study, almost half of the children (47.68%) had identified articulation disorders.

CONCLUSION

The present study shows the influence of various factors such as family history, ethnicity and parental consanguinity on the incidence of cleft lip and palate. It was also shown that in Iran, same as other countries, genetic and environmental factors play essential roles in the incidence of these congenital malformations.

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Conflicts of interest

There are no conflicts of interest.

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