

Incidence of Cleft Lip and Palate in Gorgan - Northern Iran: An Epidemiological Study

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Abstract

Objective: Cleft lip with or without cleft palate is the most common orofacial congenital anomaly among live births. This study was carried out to determine the incidence rate of oral clefting in Gorgan, Northern Iran during 2004-2009.

Methods: This descriptive hospital-based study was performed on 35,009 live newborns in Dezyani Hospital in Gorgan, Northern Iran during 2004-2009. All newborns were screened for oral clefts. Data including birth date, gender, type of oral clefts, parents' consanguinity, parental ethnicity and presence of other congenital anomalies were recorded for analysis.

Result: The overall incidence rate of oral clefts during this 6-year period was 1.05 per 1000, or 1 per 946 live births. The incidence of cleft lip and isolated cleft palate was 0.08 and 0.37 per 1,000 live births, respectively. The ratio for different cleft types was 1:7:4 (CL: CLP: CP). The incidence of oral clefting was 1.2 per 1,000 male births and 0.86 per 1,000 female births (RR=1.40; 95% CI: 0.73-2.71). According to parental ethnicity, the incidence of oral clefting was 0.7, 1.7 and 1.26 per 1,000 in Native Fars, Turkman and Sistani, respectively. The relative risk for oral clefting in Turkman to native Fars group was 2.56 ($p < 0.02$). In this study, 56.7% of clefts were CL+P, 8.1% were CL and 35.1% of cases were CP. CP was more common among girls (54%) than among boys (46%) but CL was more common among boys.

Conclusion: The results showed that the incidence of oral clefts in the study population as being 1.05 per 1,000 live births, which has increased from 0.97 per 1,000 live births reported in an earlier study in this area.

Keywords: Cleft lip; Cleft palate; Gender; Ethnicity; Iran.

Introduction

Cleft lip with or without cleft palate is the most common orofacial congenital anomaly among live births.¹ The oral clefting rates varies from 1:500 to 1:2000 births in different countries.² The incidence rate of oral clefts in various parts of Iran varies from 0.80 to 2.14 per 1,000 births. Oral clefting incidence in northern Iran was reported to be at 0.97 per 1,000 (1 in 1025) births during

1998-2003.³ The International Prenatal Database of Typical Orofacial Clefts has recently reported that the overall incidence of cleft lip with or without cleft palate was 0.99 per 1,000. The incidence of cleft lip was 0.328 per 1,000 and that of cleft lip and palate was 0.664 per 1,000.⁴

Oral clefting is affected by gender, geographic location, nationality, nutritional and periconceptional consumption of folic acid.⁵⁻⁷ In addition, several studies have reported that positive family history is associated with oral clefts.^{1,8,9} Indeed, maternal age, maternal alcohol consumption, psychological stress during pregnancy, diabetes mellitus type 1, anticonvulsant drugs, and maternal smoking have been shown to be risk factors for oral clefts.¹⁰⁻¹⁵ Racial and ethnic factors have also shown to have an effect on the incidence rate of oral clefts. A high rate of oral clefting is found in Asian and Native American populations and the lowest is reported among African populations.⁶ An intermediate rate of oral clefts is shown in Caucasians.^{5,16,17} The main objective of this study was to establish the incidence and explore effective variables on cleft lip and palate in Gorgan, Northern Iran during 2004-2009.

Methods

This hospital-based study identified all newborns with an oral cleft from among 35,009 live births between 2004 and 2009 in the Dezyani Hospital. This hospital is the largest hospital with labor facility in Gorgan, a capital city in the Golestan province in Northern Iran. It is a referral hospital with an annual rate of more than 6,000 deliveries, accounting for the largest portion of deliveries in the city. Patients are usually from moderate to low socioeconomic class families with various ethnic backgrounds.

Native Fars, Turkman and Sistani are the three main ethnic groups in the area. Native Fars are the predominant inhabitants and have the most members. Turkman is the ethnic group that emigrated from central Asia more than three centuries ago. The Sistani group emigrated from southeastern Iran since half a century ago. All live births delivered in this hospital during the investigation were examined and screened for oral clefts immediately after delivery by a gynecologist. The diagnosis was later confirmed by a pediatrician according to ICD-10. A questionnaire addressing relevant clinical and demographic factors was completed for each case by the pediatrician and completed by a nurse during an interview with the parents. The questionnaire included date of birth, gender, type of oral clefts, parents' consanguinity, parental ethnicity and the

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presence of other congenital anomalies. According to the clinical examination. Newborns with oral clefts were divided into three groups: cleft lip, isolated cleft palate, and cleft lip with cleft palate. The questionnaires were collected and the data were processed using SPSS Version 11.5 software for descriptive analysis. The results was expressed as OR with 95% confidence interval (CI). The significance level was adjusted at $p < 0.05$.

Results

The overall incidence rate of oral clefts during the 6-year period was 1.05 per 1,000 or 1 in 946 live births. Oral clefts were found to be more common in males than females (1.2 vs. 0.86 per 1,000). The male to female relative risk for oral clefts was 1.40 (95% CI: 0.73-2.71); however, the difference was not significant, (Table 1). CP was more common in girls (54%) than in boys (46%) but CL was more common among boys.

According to ethnicity, the incidence rate for oral clefting was 0.7, 1.7 and 1.26 per 1,000 in Native Fars, Turkman and Sistani, respectively, (Table 2). The relative risk for oral clefting in Turkman to native Fars group was 2.56 ($p < 0.02$). Also, the relative risk for oral clefting in Sistani to Fars ethnic group was 1.84; however, the difference was not significant.

The incidence of cleft lip and isolated cleft palate was 0.08 and 0.37 per 1,000 live births, respectively. In this study, 56.7% of clefts

were CL+P, 8.1% were CL and 35.1% of cases were CP, (Table 1). The ratio for different cleft types was 1:7:4 (CL: CLP: CP). According to ethnicity, the CL: CLP: CP ratios were 1:10:4, 1:4:4, 1:6:3 in native Fars, Turkman, and Sistani groups, respectively.

The parents of 13 babies were related, 7 couples were first cousins, and 6 were weakly related. In this study, 21.6% of cases with oral clefts had other accompanying congenital anomalies; three with hydrocephalus, two with polydactyly, one with microcephalus, one with hypospadias, and one with microphthalmia. The lowest and highest incidence rates for oral clefts was observed in 2006 and 2007, respectively.

Discussion

In this study, the overall incidence rate of oral clefts was 1.05 per 1,000 live births which is higher than the figure reported by a previous study in Gorgan with 0.97 per 1,000 live births.³ The increase in oral clefts may be due to the immigration phenomenon in the area because this area is a farm land and has good job opportunities. Some low-income families emigrated to the area from southeastern Iran. Another reason may be due to Dezyani Hospital being a referral hospital, i.e., high-risk patients and families of low-socioeconomic status being referred there from other areas of Golestan province.

Table 1: Incidence (per 1,000) of oral cleft, isolate cleft lip and isolate cleft palate according to years, and gender in live births in Northern Iran from 2004-2009.

| Total | Number of Births | All Oral Clefts | | Cleft Lip | | Cleft Palate | | Cleft Lip with Palate | |
|-------------|------------------|-----------------|-----------|-----------|-----------|--------------|-----------|-----------------------|-----------|
| | | Number | Incidence | Number | Incidence | Number | Incidence | Number | Incidence |
| Birth Years | | | | | | | | | |
| 2004-2006 | 17828 | 14 | 0.78 | 1 | 0.05 | 4 | 0.22 | 9 | 0.5 |
| 2007-2009 | 17181 | 23 | 1.34 | 2 | 0.11 | 9 | 0.52 | 12 | 0.69 |
| Gender | | | | | | | | | |
| Male | 17857 | 22 | 1.2 | 3 | 0.17 | 6 | 0.33 | 13 | 0.72 |
| Female | 17152 | 15 | 0.87 | 0 | 0 | 7 | 0.41 | 8 | 0.46 |

Table 2: Incidence (per 1000) of oral clefts, isolate cleft lip and isolate cleft palate according to ethnicity in live births, North of Iran from 2004-2009.

| Total | Number of births | All Oral clefts | | Cleft lip | | Cleft palate | | Cleft lip with palate | |
|-----------|------------------|-----------------|-----------|------------|-----------|--------------|-----------|-----------------------|-----------|
| | | Number | Incidence | Number (%) | Incidence | Number (%) | Incidence | Number (%) | incidence |
| Ethnicity | | | | | | | | | |
| Fars | 21935 | 15 | 0.7 | 1(6.7) | 0.04 | 4(26.7) | 0.18 | 10(66.6) | 0.46 |
| Turkman | 5143 | 9 | 1.7 | 1(11.2) | 0.19 | 4(44.4) | 0.77 | 4(44.4) | 0.77 |
| Sistani | 7931 | 10 | 1.26 | 1(10) | 0.12 | 3(30) | 0.37 | 6(60) | 0.76 |

Table 3: Incidence of Oral clefts in various areas in Iran.

| Author | Location | Time span of study | Incidence per 1000 birth |
|---------------------|----------------------|--------------------|--------------------------|
| Present study | Gorgan, North | 2004-2009 | 1.05 |
| Zandi et al(18) | Hamedan, North West | 1993-2008 | 1.016 |
| Rajabian et al(19) | Shiraz, South West | 1993-2003 | 0.80 |
| Yassaie et al(20) | Yazd, Central | 2003-2006 | 0.86 |
| Jamilian et al(21) | Tehran, Capital City | 1998-2005 | 2.14 |
| Golalipour et al(3) | Gorgan, North | 1998-2003 | 0.97 |

The rate of oral clefting in this area is higher than those reported in other studies from Hamedan 1.01, Shiraz 0.80, and Yazd 0.86.^{18,19,20} On the other hand, this rate is lower than the 2.14 per 1,000 births reported for Tehran, (Table 3).²¹ The incidence rate of oral clefts in this study is higher than the Khazaei study (a meta-analysis of 11 studies in Iran) with 1.0 per 1,000 live births.²² Also, it was reported that the high incidence of oral clefts in Tehran may be due to the use of mustard gas during the Iran-Iraq war,²³ but recently in a Jamalian study, consanguinity was reported to be the main risk factor.²¹ The incidence rate of oral clefts in the current study is lower than the rates reported by studies in Asia: 1.91 for Pakistan, 1.39 for Jordan, 1.76 for Northern China, 1.81 for Korea, 1.34 for Japan, and 1.5 per 1,000 births for Oman.^{9,24,25,26,27,28}

In this study, the incidence rate of oral clefts was lower than the rate reported by studies from Denmark (1.66),²⁹ Netherland (1.68),³⁰ Spain (1.44),³¹ Canterbury/New Zealand (1.69),³² Bolivia (1.23),³³ Argentina (1.7),³⁴ Canada (1.1 to 1.53 in 2002-2008),³⁵ Sweden (2.01),³⁶ USA (1.21),³⁷ and Ethiopia with 1.49 per 1,000 births,³⁸ but the rate was higher than the rate reported from Uganda with 0.73 per 1,000 births.³⁹

More details about the incidence rate of oral clefts in various parts of the world are mentioned in Wyszynski's text.⁴⁰ Various incidence rates of oral clefting could be related to the influence of social and ethnical/racial factors in different parts of the world, which are commonly explained as genetic disorders. Also, the differences among these findings could be related to the study population, type of classification, and various selection criteria such as live births and still births in the study or eliminating aborted fetus from the study.

The rate of isolated cleft palate was 0.37 per 1,000 live births. This finding is similar to our previous study in Northern Iran,³ but this rate is lower than a report in Tehran with 0.77 per 1,000 births,²¹ lower than Pakistan with 0.46,⁹ Canterbury/New Zealand with 0.84,³² and Argentina with 0.46 per 1000 births.³⁴ The rate of cleft lip was 0.08 per 1,000 live births and this rate is lower than that among Jordanian people.²⁴

Oral clefts are found to be more common in boys than girls (1.2 vs. 0.86 per 1000). The male to female relative risk for oral clefts was 1.40 (95% CI: 0.73-2.71). This finding is similar to several studies in Jordan,²⁴ Japan,⁸ Korea,⁴¹ Tanzania,⁴² Tehran,⁴³ South-Western Iran,¹⁹ and our previous study in Northern Iran.³ Also, oral clefting was significantly more common among boys in Japan and Estonia,^{8,11} and most commonly affected by cleft lip and cleft lip with cleft palate in Pakistan.⁹

Indeed, the International Perinatal Database of Typical Orofacial Clefts has recently reported that the overall incidence of cleft lip with or without cleft palate was 0.992 per 1,000; cleft lip was 0.328 per 1,000; and cleft lip and palate was 0.664 per 1,000.⁴

According to ethnicity, the incidence rate of oral clefting in this study was 0.7, 1.7 and 1.26 per 1,000 in Native Fars, Turkman and Sistani, respectively. The relative risk for oral clefting in Turkman to native Fars group was 2.56 ($p < 0.02$). Also, the relative risk for

oral clefting among Sistani to Fars ethnic group was 1.84, which was not significant.

Native Fars, Turkman and Sistani are the three main ethnic groups in Gorgan, Northern Iran. Previous researches have pointed to the effect of race/ethnicity on the incidence of oral clefts.^{5,44-45} Also, it was found that the incidence of oral clefts varies in different populations such as black, Caucasian, Asian, and Native Americans.⁶ This difference especially in a given population could be related to differences in nutritional habits, environmental exposure or genetic factors.¹⁶

In this study, 56.7% of clefts were CLP, 8.1% were CL and 35.1% of cases were CP. The ratio for different cleft types was CL: CLP: CP (ratio 1:7:4). The CL: CLP: CP ratio according to ethnicity groups were 1:10:4, 1:4:4, 1:6:3 in native Fars, Turkmens and Sistani groups, respectively. A previous study by Fogh-Andersen (1942) reported a CL: CLP: CP ratio (1:2:1), which is often described as the normal ratio for different cleft types in Caucasians.⁴⁶ Also, studies from Japan and Africa revealed a much lower incidence of CP.^{8,47} Furthermore, a study in Estonia found a high occurrence rate of CP among all clefts (CL: CLP: CP ratio 1:2:2), which was different from the normal Caucasians ratio.¹¹

Regarding the high occurrence rate of CP in all ethnic groups, the study results were similar to the ones observed in Estonia,¹¹ Finland,⁴⁸ and Sweden.⁴⁹

In this study, 21.6% of cases with oral clefts were associated with other anomalies including hydrocephalus, polydactyly, microcephalus, hypospadias and microphthalmia. But among Koreans, 8.4% of cases with oral clefting were associated with congenital heart disease, short frenulum, Pierre Robin syndrome, Down syndrome, Patau syndrome, and van der Woude syndrome.⁴¹ Recently, a study in USA showed that 15.9% of reported cases had malformations in other systems.⁴ Another study in Estonia reported that 30.3% of patients with clefts had accompanying developmental anomalies including syndactyly, heart defects, mental and physical retardation and inguinal hernia.¹¹

The absence of stillbirths, small number of cases, limited study period (6 years), as well as the lack of side of cleft proportions, and submucosal clefts were the main limitations of the current study. Also, the ethnicity of 3 cases was not recorded.

Conclusion

The present study shows that the incidence rate of oral clefts in the population as being 1.05 per 1,000 live births, which has increased from 0.97 per 1,000 live births in comparison to an earlier study in this area.

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