Influence of Ethnicity on the Incidence Rate of Oral Clefts in Northern Iran

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Abstract
Objective: Oral clefting including cleft lip with or without cleft palate (CL/P), are considered as common congenital anomalies, particularly in Asia population. The aim of this study was to evaluate the incidence rate of CL/P according to ethnicity in Northern Iran.

Materials and Methods: This cross-sectional, analytic study was carried out on 92,420 live newborns in Golestan province, the Northern Iran, from 2008-2011. The newborns were evaluated for the CL/P and recorded according to ICD10. Gender, ethnicity and parental consanguinity were filled out for each subject. The subjects grouped according to ethnicity into native Fars, Turkmen, and Sistani groups.

Results: The rate of oral clefts was determined 0.72 per 1000 live newborns. The incidence rate of CL/P was 0.69 per 1000 in males and 0.75 per 1000 in females. The incidence of CL/P among native Fars, Turkmen and Sistani was 0.96, 0.61, and 0.57 per 1000 live births, respectively.

Conclusion: The incidence rate of oral clefting was lower than in our previous study (1.05 per 1000), and it was higher in the native Fars population.

Keywords: Cleft lip, Cleft palate, Ethnicity, Gender, Iran

Introduction
Oral clefts including cleft palate (CP), cleft lip with or without cleft palate (CL/P) and cleft lip (CL) are considered as common congenital anomalies (1). Oral clefting has reported with an incidence rate of 0.5-2.5 per 1000 live births worldwide, although ethnic and different geographical area can be the significant affect on the incidence rate (2-4) and widely among different populations (5). Previous reports have shown that the incidence rates of CL/P are varied in different region worldwide (6-8). Several factors including sex, geographic area, country, maternal nutrition and usage of the folic acid pre-pregnancy period and during the first semester of pregnancy can affect on the incidence rate of CL/P. Also, studies have shown that the role of having a child with oral clefts in the family, age, usage of alcohol, smoking, stress and tension during pregnancy, diabetes mellitus, antiepileptic medicine by mothers on the rate of oral clefts (9).

Several complications are observed in the patients with oral clefting including poor occlusion, dental disorders, speech disorders, feeding difficulties and stigma, facial deformities and nutritional, respiratory, hearing and articulation problems (10,11).

Psychological and behavioral disorders may be observed in patients with oral clefts. (12). Several studies have reported that psychiatric disorders such as depression increase in children and adolescents with oral clefts (12,13).

A study has shown that male to female ratio is 2:1 and 1:2 for cleft lips and cleft palates, respectively, also unilateral and left side in cleft palates are common (14).

Geographic location, socioeconomic status and racial/ethnicity influence the incidence of oral clefts (8,13,15). Indeed, consanguineous marriages increase the incidence of congenital anomalies including CL/P (16,17).

The ethnicity of the population influences the incidence rate of CL/P. It is generally thought that highest, intermediate and lowest incidence rates belong to the Asian and Native North American, Caucasian and African populations (5,18-22). Also, a study has reported that the incidence rate of CL/P is 0.5 per 1000 in Nigeria (23).

According to a study in Denmark oral clefts are more in babies born to women which were originally from Denmark compared to those born to foreign women (24).

In Iranian population, the rate of oral clefts determined to be 0.86-3.73 per 1000 births (25). Also, the rate of CL/P is reported 0.97 per 1000 live births in northern Iran during 1998-2003 (26).

Objectives
Golestan province in the north of Iran has 1.6 million populations and an area of 20 380 km² with different
Ethnicity groups. There are few reports on the incidence rate of CL/P in Golestan province. Therefore, the aim of this study was to evaluate the rate of CL/P according to ethnicity in Golestan province, the Northern Iran since 2008-2011.

Materials and Methods
This analytic study was carried out on 92 420 live newborns in Golestan province in the northern Iran from 2008-2011.

1.6 million populations are live Golestan province in northern Iran with an area of 20 380 km² with different ethnic groups. The 3 ethnic population including Fars, Turkmen and Sistani are living in this area. Native Fars is the predominant ethnic group, according to the population. The Turkmen are originally from central Asia. The Sistani are originally from southeastern Iran. Subjects were chosen from among those newborns whose direct ancestors for the last three generations all had married interethnic marriages.

During the period of the study, pediatricians screened all live newborns that delivered in the 13 hospitals throughout the Golestan province for oral clefting. Consent forms were completed by parents of the newborns. Data including gender of the newborns, parental consanguinity, and parental ethnicity were collected and registered for each subject.

Babies with oral clefts without other malformation enrolled in our study. In order to determine the relationship between gender of the newborns, parents’ consanguineous marriage, parents’ ethnicity and the rate of CL/P, 239 control healthy newborns were randomly chosen.

Data was analyzed using SPSS software, chi-square test and confidence interval. A P value of 0.05 was used in this study.

Results
From 1 January 2008 to 20 March 2011, out of 67 newborns with oral clefts, cleft lip, cleft palate and cleft lip with cleft palate were observed in 23 (34%), 18 (27%) and 26 (39%) of newborns, respectively.

The rate of CL/P was 0.72 per 1000 live births, totally, 0.69 and 0.75 per 1000 in males and females, respectively (Table 1). This rate was 0.24, 0.19 and 0.28 per 1000 live births for cleft lip, cleft palate and for cleft lip with cleft palate.

The incidence of oral cleft among the native Fars, Turkmen, and Sistani was 0.96, 0.61 and 0.57 per 1000 live births, respectively (Table 1 and Figure 1). Between ethnicity and sex with CL/P, no significant relationship was seen.

Seventeen (25%) newborns with oral clefts were born to consanguineous parents in first cousin marriages and 9 (22%) newborns with oral clefts were born to consanguineous parents in second cousin marriages. Out of 67 newborns with orofacial clefts, 41 (61.1%) newborns did not have consanguineous parents.

Discussion
Oral clefting (CL/P) is a common birth defect which causes speaking, auditory, swallowing, feeding and respiratory disorders. With the growth of the world’s population, the number of CL/P cases per year is expected to increase.

Our study characterized the birth incidence of CL/P in Golestan province, the north of Iran over a 38-month period. Totally, the rate of CL/P was 0.72 per 1000 live births and the rate for cleft lip, cleft palate and for cleft lip with cleft palate was 0.24, 0.19 and 0.28 per 1000 live births, respectively. The rate of oral clefting in worldwide is depicted in Table 2.

A previous study in Gorgan (the capital of Golestan province) showed that the incidence rate of CL/P, cleft lip and isolated cleft palate was determined to be 1.05, 0.08 and 0.37 per 1000 live births, respectively (9).

A research in Hamadan, in the northwest of Iran, has shown that the rate of cleft lip and palate was higher than our study (0.83 vs. 0.72 per 1000 ) (27). According to Hamadan report, Cleft lip and palate in bi or unilateral form and isolated cleft palate were the high and low prevalence, respectively (27).

The rate of oral clefts is reported 1.9 per 1,000 live births in Kianifar et al study, in northeastern Iran (28). In Kianifar study, 50%, 35.2% and 14.8% of live newborns affected with oral clefts isolated cleft lip and isolated cleft palate, respectively (28).

Jalili et al study in the west and northwestern Iran reported that out of 2083 live birth, one baby born with CL/P (29).

The incidence rate of cleft deformities was seen 1 and 0.4 per 1000 birth for CL/P and CP, respectively in Taiwan (30).

Table 1. The Incidence Rate of Cleft Lip, Cleft Palate and Cleft Lip With Cleft Palate Per 1000 According to Gender and Ethnicity in North of Iran

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Oral Clefts</th>
<th>Cleft Lip</th>
<th>Cleft Palate</th>
<th>Cleft Lip With Palate</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Incidence</td>
<td>Number</td>
<td>Incidence</td>
<td>Number</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Native Fars</td>
<td>37</td>
<td>0.96</td>
<td>8</td>
<td>0.20</td>
<td>13</td>
</tr>
<tr>
<td>Turkmen</td>
<td>19</td>
<td>0.61</td>
<td>7</td>
<td>0.22</td>
<td>6</td>
</tr>
<tr>
<td>Sistani</td>
<td>8</td>
<td>0.57</td>
<td>1</td>
<td>0.07</td>
<td>4</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>34</td>
<td>0.69</td>
<td>12</td>
<td>0.24</td>
<td>7</td>
</tr>
<tr>
<td>Female</td>
<td>33</td>
<td>0.75</td>
<td>6</td>
<td>0.13</td>
<td>16</td>
</tr>
</tbody>
</table>
In another study, the oral cleft rate was 1.5 per 1000 and 0.80 per 1000 live births. However, our overall incidence rate of CL/P was lower than in these studies (31,32).

In the study of Conway of 33 African countries from 2001 to 2011, cleft lip with cleft palate was the most frequent with 58.87% followed by cleft lip with 34.44% and isolated cleft palate with 6.69% (14).

According to a review study in India, the incidence rate of oral clefts varies from 0.2 to 2.9 per 1000 births (33).

In Finland, the incidence rate of CL/P was 2.56 per 1000 live births and abortions followed by CP with 1.36 per 1000 (15).

In Canada, the incidence rate of CL/P and CP has reported 0.82 and 0.58 per 1000 live births, respectively (34).

A study in Uganda has shown that the incidence rate of the total oral clefts and CLP with 0.77 and 0.46 per 1000 live births, respectively (10).

The incidence rate of overall oral clefts, cleft lip, cleft lip and palate and isolated cleft palate was 1.17, 0.47, 0.42 and 0.28 per 1000 births, respectively in Riyadh, Saudi Arabia (16).

According to gender in our study, the incidence rate of oral clefts was 0.69 and 0.75 per 1000 live births in males and females, respectively.

In the study of Jalilevand et al, there was an incidence variation between males and females for various types of CL/P. Also, CLP was found most frequently in males (29).

In the study of Lin et al in China, being female has a risk factor for non-syndromic oral clefts (35).

In the study of Conway et al of 33 African countries (14), males have a high chance for oral clefts than females.

According to oral clefts in females was more than males. Our results are contrasted to Mashhad's study (28), and our previous study in Gorgan (9), which oral clefts was more common in males than females.

Indeed, in Kurdistan province, the incidence of cleft lip and cleft palate was lower in females than males (36).

In the study of Noorollahian et al, the rate of isolated cleft lip and cleft lip with palate was higher in males than females (11).

In the present study, 38.8% newborns with oral clefts were born to consanguineous parents. While in our previous study (17) this rate was low. In addition, in Saudi Arabia, parental consanguineous marriage specifically in the first cousin increased the chance of cleft palate(16).

Furthermore, in the study of Noorollahian et al, parental consanguineous marriage was observed in 63.63% of the cases (11).

According to ethnicity, the incidence rate of CL/P among native Fars, Turkmen and Sistani was 0.96, 0.61 and 0.57 per 1000 live births, respectively. According to our recent finding CL/P is the commonest in the native Fars population, but in our previous study, the incidence rate of CL/P was higher in the Turkmen group in compared to native Fars and Sistani population (9). In Amaratunga and Chandrasekera’s study on Sri Lanka’s 3 major ethnic groups, the incidence rate was significantly higher for the Moors than for the Sinhalese and Tamil populations (37).

Also, the patients were distributed according to their parent-reported race/color of the skin in Campos Neves et al study in Brazil, as well as White (46.02%), Black (19.47%), Brown (34.51%), and Native American (2.60%) (38).

Saad et al, in the state of California, reported that the incidence rates for CL/P and CP based on ethnicity varies in different ethnic groups (22), the highest and lowest
rate of oral clefting were reported in white (non-Hispanic) and Native American population, respectively (22).

Also, the rate of oral clefting is varied in Asians and whites populations, indeed a maternal country of origin can affect on the oral clefting in the Asians populations (39).

The study of Pedersen et al in Denmark on 1,319,426 live births during 1981 to 2002 reported that the rate of oral clefting is more in babies born to Danish women in compared to those born to foreign women (24). They concluded that maternal country of origin is a risk factor in the oral clefts in Denmark (24).

Nutrition, environmental and genetic factors can be caused the verity of oral clefts particularly within the population with different ethnical and geographical origin (20). Exposure to pesticides, alcohol, cigarettes and drugs, folic acid deficiency, and ethnicity are known factors influencing the incidence rate of oral clefts (9).

Limitation
The aborted fetus did not enroll in this study.

Conclusion
According to our findings, the rate of oral clefts was lower than in our previous study (1.05 per 1000), but it was higher in native Fars. Further researches are needed to understanding the risk factors of oral clefts in northern Iran.

Ethical Issues
The ethical committee of Golestan University of Medical Sciences approved this research with Ethical code: 191390080826. Consent forms were completed by the parents of the newborns.

Conflict of Interest
There is no conflict of interest.

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