EPIDEMIOLOGICAL STUDY OF OROFACIAL CLEFTS AMONG POPULATION OF EASTERN SLOVAKIA DURING THE PERIOD 1996–2013

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SUMMARY

Background and Aim: Over the past 18 years, according to data from the Clinic of Plastic and Reconstructive Surgery, L. Pasteur University Hospital, there have been 493 cases of orofacial clefts (OC) reported in the area of Eastern Slovakia. The aim of this study was to map the occurrence of orofacial clefts reported in the area of Eastern Slovakia during the years 1996–2013. Also, we compared the occurrence of different types of clefts between the groups in relation to gender and ethnicity.

Methods and Results: The statistical analysis shows relationship between variables of location and gender and gender differences in the occurrence of various types of clefts. Moreover, in comparison with another study which analyzed the years 1985–2000 (1.29/10^3 live births), there was an increase in the incidence (1.42/10^3 live births) of OC in Eastern Slovakia.

Conclusion: Our findings seem contradictive to similar studies which discuss ethnic differences in relation to OC. We recognize the relatively high occurrence of OC in Eastern Slovakia, and we link this phenomenon to several extrinsic factors, in particular socioeconomic status and embryotoxic factors.

Key words: cleft lip and/or palate, incidence, ethnic group, Eastern Slovakia regions

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INTRODUCTION

The most common orofacial anomaly, a cleft lip (CL) and/or cleft palate (CLP/CP) (1), occurs in approximately one of 600–660 births in Slovakia, which is slightly higher than the European average (1 out of 700–750 births). According to the epidemiological statistics, the frequency of occurrence of the cleft lip and/or palate in Slovakia ranks 9th among all congenital anomalies (2). Anomalies occurrence shows substantial variation among ethnic groups (3), gender and geographical areas (4). Cleft lip and/or palate represent a multifactorial malformation including genetic disorders, and multiple nutritional and toxicological factors. Failure in palatogenesis causes a cleft lip and/or palate. The palate is formed relatively late in organogenesis: at 8–12 intrauterine weeks in humans (3). Experimental study on the normal palate closure and experimental analysis of mechanisms using teratogens and genetic differences have contributed greatly towards understanding of palatogenesis process and clefting although the whole mechanism of cleft is not yet fully explored. CP and CL are not homogeneous in population. There are crucial variables that provide basis for the establishment of subgroups (5). To determine the incidence of CP and CL, a classification of orofacial clefts is needed.

The aim of this study was to map the occurrence of orofacial clefts reported in the area of Eastern Slovakia during the years 1996–2013. Also, we compared the occurrence of different types of clefts between the groups in relation to gender and ethnicity.

Classification of Orofacial Clefts

There are several classifications of orofacial clefts available. Some scholars consider the alveolar ridge as a significant landmark in the division of oral clefts. For instance, Kernahan and Stark's classification puts an emphasis on incisive foramen which marks the boundary between the primary palate (anterior to the incisive foramen) and the secondary palate (posterior to the incisive foramen). Clefting can therefore occur in the primary palate, the secondary palate or in both. Thus it may be complete, incomplete, unilateral or bilateral (4). In Kernahan and Stark's classification, deformity is linked to the letter Y. Also, this classification divides clefts into three groups: clefts of primary palate, clefts of secondary palate and clefts of both palates (primary and secondary) (6).

Different clefts represent different epidemiology and rates due to social and demographic variables (7). We use the classifica-

tion of orofacial clefts (OC) by Kernahan and Stark to determine the incidence of cleft lip and palate in the Eastern Slovakia (ES) population.

MATERIALS AND METHODS

Over the last 18 years, 493 new cases of cleft lip and/or palate have been reported by the Department of Plastic, Reconstructive and Aesthetic Surgery, L. Pasteur University Hospital, the catchment area of ES. Out of 493 children (gender ratio 1.38:1), 286 (58.01%) were male, 207 (41.99%) were female; 54.97% belonged to a non-Roma population, and 45.03% to a Roma population. The data for statistical analysis gathered from the medical records were divided into four groups based on the types of clefts by Kernahan and Stark – CLP, CL, CP, associated malformations (AM), including variations between gender and ethnic group. According to location, types of clefts were left-sided, right-sided and bilateral clefts. The data from the CLP, CL, CP groups included individuals whose clefts were nonsyndromic. The AM group included individuals with Pierre Robin syndrome. We applied the unpaired T-test for statistical analysis of data with statistical significance $p < 0.05$, to analyze differences in types of clefts between the two groups in relation to gender and ethnicity.

RESULTS

From 1996 to 2013, 493 diagnosis and treatment of cleft lip and/or palate had been performed in ES at the aforementioned Department of Plastic, Reconstructive and Aesthetic Surgery, L. Pasteur University Hospital (Table 1, Fig. 1). Total incidence of orofacial clefts was $1.42/10^3$ live births (LB). 45.23% of 493 cases affected the primary and secondary palate, 27.79% were cleft palate, 24.34% cleft lip, and 2.64% were associated malformations with variation between gender and ethnic group. Out of 120 diagnosis of CL, 65.83% were on left side, 30% right-sided and 4.17% were bilateral. There were 47.53% left-sided CLP cases, 19.73% right-sided CLP and 32.74% bilateral CLP of total incidence of CLP (n = 223) in the examined patients. Comparing between gender (females vs. males), out of 128 cases of CL and CLP in 57.81% of females left side was affected, in 24.22% right side and 17.97% were bilateral. Out of 215 cases of CL and CLP in males 51.63% were left-sided, 22.79% were right-sided and

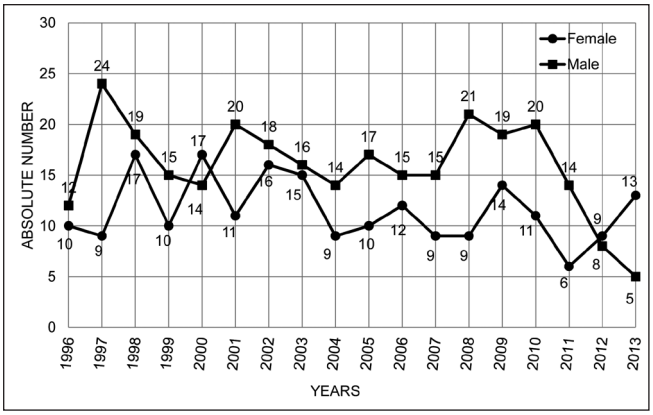

Fig. 1. *Absolute number of orofacial clefts/gender in the period 1996–2013.*

Table 1. *Number of orofacial clefts in the period 1996–2013, according to cleft types*

Year	Cleft types				Total
	CL	CLP	CP	AM	
1996	5 (22.73%)	12 (54.54%)	5 (22.73%)	0 (0%)	22
1997	10 (30.30%)	14 (42.43%)	9 (27.27%)	0 (0%)	33
1998	7 (19.44%)	18 (50%)	10 (27.78%)	1 (2.78%)	36
1999	4 (16%)	14 (56%)	7 (28%)	0 (0%)	25
2000	7 (22.58%)	12 (38.71%)	11 (35.48%)	1 (3.23%)	31
2001	6 (19.35%)	19 (61.30%)	6 (19.35%)	0 (0%)	31
2002	8 (23.53%)	11 (32.35%)	14 (41.18%)	1 (2.94%)	34
2003	11 (35.48%)	12 (38.71%)	6 (19.35%)	2 (6.46%)	31
2004	5 (21.74%)	15 (65.22%)	2 (8.69%)	1 (4.35%)	23
2005	7 (25.92%)	10 (37.04%)	10 (37.04%)	0 (0%)	27
2006	8 (29.63%)	6 (22.22%)	11 (40.74%)	2 (7.41%)	27
2007	5 (20.83%)	13 (54.17%)	4 (16.67%)	2 (8.33%)	24
2008	4 (13.34%)	13 (43.33%)	13 (43.33%)	0 (0%)	30
2009	12 (36.37%)	11 (33.33%)	10 (30.30%)	0 (0%)	33
2010	8 (25.81%)	18 (58.06%)	5 (16.13%)	0 (0%)	31
2011	3 (15%)	10 (50%)	6 (30%)	1 (5%)	20
2012	4 (23.53%)	9 (52.94%)	4 (23.53%)	0 (0%)	17
2013	6 (33.33%)	6 (33.33%)	4 (22.23%)	2 (11.11%)	18
Total	120 (24.34%)	223 (45.23%)	137 (27.79%)	13 (2.64%)	493

CL – cleft lip, CLP – cleft lip and palate, CP – cleft palate, AM – associated malformation

25.58% were bilateral. The following part of the article is devoted to the detailed results of the statistical data processing.

Cleft Lip and Palate

From 220 cases of patients with a cleft lip and palate, in 33.18% of non-Roma males and 30.04% of Roma males the primary and secondary palate was affected (Fig. 2). Roma females were less affected (17.04%) compared with Roma males and non-Roma males; non-Roma females represented 19.74% of cases. Statistical significance was found in the three compared groups: non-Roma females vs. non-Roma males ($p<0.0106$); Roma females vs. Roma males ($p<0.0184$); females vs. males ($p<0.0002$). This significance represents a very close correlation between females and males in the examined patients (Table 2).

Cleft Lip

The incidence of cleft lip ranged from 21.67% for non-Roma females to 30% for non-Roma males with the total incidence of CL (n=120) in the examined patients. The incidence of cleft lip was lower among Roma females compared with non-Roma females, and it represented 16.66%; for Roma males the rate was 31.67% of total incidence of cleft lip (n=120) in the examined patients (Fig. 3). Statistical significance was found in the two compared groups, including Roma males and Roma females ($p<0.0104$), the significance was also found between females and males ($p<0.0089$) (Table 2).

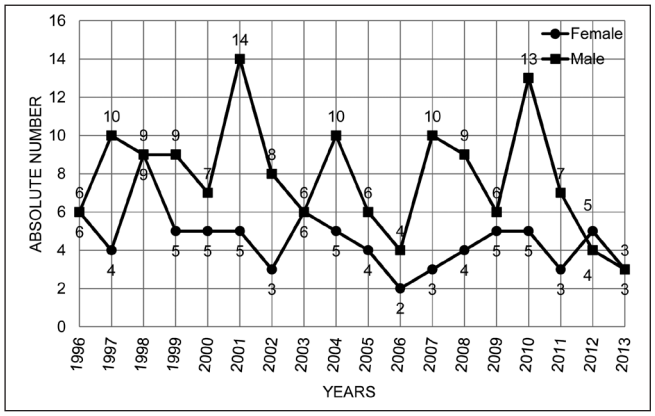

Fig. 2. *Absolute number of cleft lip and palate for males (square) and females (circle) in the period 1996–2013.*

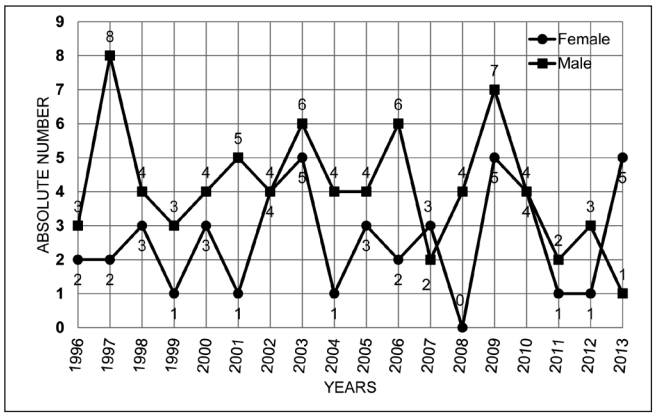

Fig. 3. *Absolute number of cleft lip for males (square) and females (circle) in the period 1996–2013.*

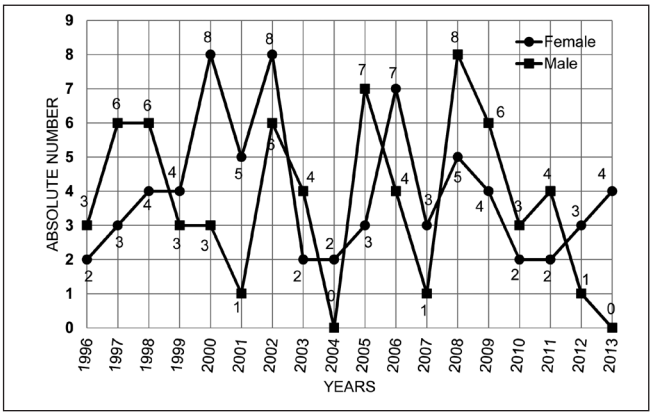

Fig. 4. *Absolute number of cleft palate for males (square) and females (circle) in the period 1996–2013.*

Cleft Palate

The highest incidence of cleft palate (n=137, 30.66%) occurred among non-Roma females and also males. The total incidence of cleft palate was 137 cases, 21.16% of cleft palate were observed in Roma females and 17.52% in Roma males (Fig. 4). There was no significant difference between the compared groups in this type of cleft (Table 2).

Associated Malformations

Out of 13 cases, the highest incidence of AM was observed in non-Roma females (38.46%). Also, 15.38% of non-Roma males

Table 2. *Statistical significance of each type of cleft/group in the period 1996–2013 (p values)*

	Cleft types			
	CLP	CL	CP	AM
Group1	ns	ns	ns	ns
Group 2	ns	ns	ns	ns
Group 3	0.0106*	ns	ns	ns
Group 4	0.0184*	0.0104*	ns	ns
Group 5	0.0002***	0.0089**	ns	ns

*p value < 0.05, **p value < 0.01, ***p value < 0.001, ns – not significant
Group 1 represents Roma male compared with non-Roma male. Group 2 represents Roma female compared with non-Roma female. Group 3 represents non-Roma female compared with non-Roma male. Group 4 represents Roma female compared with Roma male. Group 5 represents female compared with male.
CLP – cleft lip and palate, CL – cleft lip, CP – cleft palate, AM – associated malformation

were affected with AM, the proportion of Roma females and Roma males were the same (23.08%). There was no statistical significance in this type of cleft between the compared groups (Table 2).

DISCUSSION

OC are the most common congenital malformations which occur frequently all over the world (1, 8). In Europe, a higher incidence of OC was detected in Poland, Sweden and the Czech Republic (2.0/10^3 live births). Finland, for example, is a European country with the lowest incidence of clefts (0.79/10^3 live births); nevertheless, the incidence in this country is increasing. The Slovak Republic is considered to be a country with a relatively high incidence (1.60/10^3 live births) of clefts anomalies (8, 9).

The various differences in incidence of OC have been greatly discussed amongst scholars. The occurrence of OC varies in geographical distribution, race and ethnic differences. Generally, a higher risk of clefts has been found in the white race population than in the black population, although a high range of differences among countries exist (8, 10). The results of this study show no significance between chosen ethnic groups (non-Roma vs. Roma). Although, there is a significance between females and males in following types of clefts – CLP, CL (non-Roma females vs. non-Roma males, Roma females vs. Roma males, females vs. males in CLP; and Roma females vs. Roma males, females vs. males in CL). These results support findings of many researchers who discuss gender differences in health status (11–14). Gender distribution of particular OC showed a male predominance in the CL (61.67%) and CLP (63.23%) types of clefts, and female predominance in CP (51.82%) and AM (61.54%) types of clefts, which is in accordance with the data of the epidemiological study from Croatia and related studies (8, 10, 15, 16). Due to the predominance of left-sided OC as documented in similar studies (7, 10, 15, 17), our results confirm left-sided OC as the most common (65.83% for CL and 47.53% for CLP) in the examined patients. Mossey et al. suggest the importance of genetic susceptibility in the predominance of a left-sided clefting and the male excess of a cleft lip and palate (17). Others, for instance, analyze sexual dimorphism in the male predominance of CLP and CL, and female predominance of CP and their resistance to the development of CLP and CL (8).

Drawing on our data findings, the total incidence of 1.42/10^3 live births in ES in 1996–2013 (the overall number of live-born children in ES per 18 years was 347,715) marked an increase of prevalence compared to the previous study, analysing the data between 1985–2000, where the total incidence of OC in ES was defined as 1.29/10^3 LB (8). According to the study from 1985–2000, the lowest incidence was documented in the eastern part of Slovakia. This fact, however, is not consistent with our results.

More research needs to be done to examine the link between ethnic affiliation and socioeconomic status in regard to the occurrence of OC. In this respect, Roma are well-known for their low socioeconomic status and this may reduce the level of health among Roma (18).

Although there is some evidence supporting a positive relationship between ethnic groups and socioeconomic status in the literature (19–22), our study has found little or no significance between the ethnic groups. However, some associations between socioeconomic status and health in non-Roma populations have been found in many studies (23–25). Genetic, biological, medical, and anthropological analyses of Roma health status focus greatly on infectious diseases or hereditary defects (18, 26–28). However, due to the socioeconomic conditions, these factors seem to be potential risk factors of incidence of OC in ES.

To analyze the potential risk factors related to the occurrence of OC, the Department of Plastic, Reconstructive and Aesthetic Surgery, L. Pasteur University Hospital conducted the study. The questionnaires were used to investigate possible risk causes. The results showed that 45% of pregnant women overcame upper respiratory infections and flu, 28% of pregnant women used drugs during pregnancy, in 23.4% of cases the cleft occurred in the family and in 9% of cases the other congenital defects occurred in the family (29). Environmental and genetic factors play an important role in aethiopatogenesis of OC. Finding the embryotoxic factors, such as maternal smoking, infectious diseases, drugs, professional exposure to chemicals during pregnancy and lifestyle, allow prevention of OC during pregnancy, mainly during the critical period of prenatal development (27th–60th embryonic day) (30).

CONCLUSION

The occurrence of various types of clefts was studied in a population of ES in relation to gender and ethnic group. We recorded an increased incidence of OC in Eastern Slovakia (1.42/103 LB) from 1996 to 2013, and also gender differences in prevalence of OC, which show a male predominance in the CL (61.67%) and CLP (63.23%) types of clefts, and female predominance in the CP (51.82%) and AM (61.54%) types of clefts. Our study does not support findings of authors who discuss ethnic differences in the incidence of OC. Little or no significance has been found between selected ethnic groups (non-Roma vs. Roma). In case of the low socioeconomic status in ES and its relation to the potential embryotoxic factors affecting women during pregnancy, we acknowledge these factors as potential risk factors of incidence of OC.

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Conflict of Interests

None declared

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