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Epidemiologic factors causing cleft lip and palate and their regularities of occurrence in Estonia

Triin Jagomagi, Marianne Soots, Mare Saag

SUMMARY

Objectives. To study epidemiological factors causing development of cleft lip and palate and their occurrence regularities.

Materials and methods. This study included 583 cleft lip and palate patients and the information for statistical analyses was gathered from Tartu University Hospital.

Results. 19% of the patients had a cleft lip (CL), 39% of the patients had a cleft palate (CP), and 42 % of the patients had a cleft lip and palate (CLP). The ratio for different cleft types CL: CLP: CP was 1:2:2. In unilateral CLP and CL cases, the left side was affected 2.2 times more frequently than the right side. Boys had a CLP nearly 2.1 times more often than girls. CP was more common for girls (60%) than for boys (40%). 30% of children had multiple malformations. 2.6% of children with clefts were born premature, half of which had accompanying developmental anomalies. The average birth weight for cleft child was ~ 3400 grams. 6.8% of children with clefts had a birth weight below 2.5 kg.

In case of children with clefts, the mother's age exceeded 30 years in 1/4 of cases and father's age in 1/3 of cases. Both parents were older than 30 years in 66% of the cases. 1/5 of both parents were older than 30 years.

1/3 of mothers of children with clefts had suffered psychological stress, 1/5 of mothers had done hard physical work.

1/5 of mothers had an exposure to teratogenic toxic substances. 15% of them received medications during the first trimester of pregnancy.

15% of mothers had experienced hormonal disorders.

Conclusions. As a result of the study we found a high occurrence rate of CP (CL: CLP: CP – 1:2:2), which is similar to the studies conducted in Finland and Sweden. The reasons for this ratio need further research.

Key words: cleft lip and/or cleft palate, epidemiologic factors.

INTRODUCTION

Oral clefts – cleft lip with or without cleft palate (CL/P) and cleft palate (CP) – are among the most common congenital malformations worldwide. The overall incidence of cleft lip (CL), cleft palate (CP) and cleft lip and palate (CLP) in Caucasians ranges from 0.91 to 2.69 per 1,000 [1]. In Estonia the incidence of clefting is 1 per 777 live births during the period between 1970 and 1980 [2]. Since 1950 the birth of children with congenital deformities has doubled from 0.7% to 1.3%. Cases of CL and CP make 13.2% among all the malformations [2].

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The gender ratio among individuals with CLP is distorted in the general population, with males being affected 1.5 to 2.0 times more frequently than females [3]. The opposite situation, a significantly higher incidence of females compared to males is found in CP [3, 4]. The unilateral left side cleft is a common finding and seems to be a feature in all ethnic groups [4, 5]. The left side is affected twice as often as the right side [4].

Fogh - Andersen [6], reported a CL: CLP: CP ratio of 1:2:1, which is often regarded as the normal ratio for different types of cleft, especially for the Caucasian population.

There is earlier data suggesting a positive association between oral cleft malformation and an advanced maternal age [7, 8]. Many studies have found statistically significant associations with maternal smoking and clefting [9, 10].

Maternal alcohol consumption increases the risk for multiple CLP in infants [11]. Diabetes mellitus type I have been shown to be a risk factor for oral clefts [12]. Drugs are known to have a teratogenic effect on

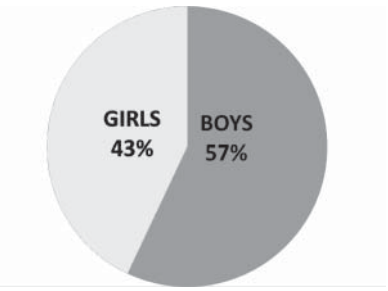

Fig. 1. Gender of the patients

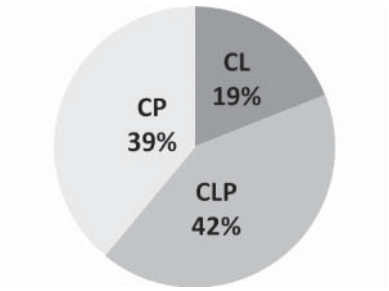

Fig. 2. Occurrence of different cleft types (CL – cleft lip; CP – cleft palate; CLP – cleft lip and palate)

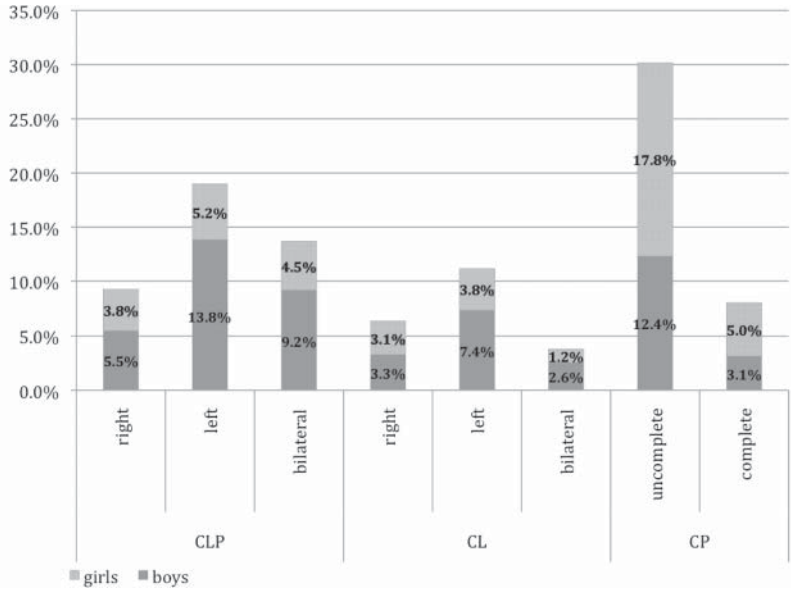

Fig. 3. The most common cleft types according to gender and face involvement (CL – cleft lip; CP – cleft palate; CLP – cleft lip and palate)

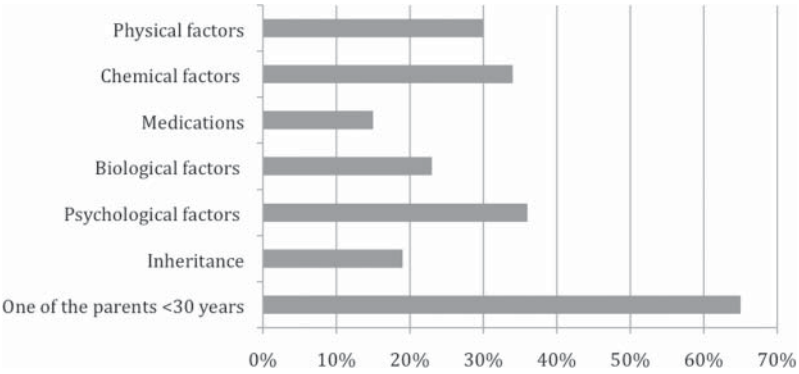

Fig. 4. Epidemiological factors which affected in the first trimester of pregnancy

facial development from exogenic factors and include valporate acid, an anticonvulsant, retinoic acid derivates, thalidomide and phenytoin [13-15]. Dietary factors such as deficiency of vitamins and folic acid, and intrauterine irritation have all been implicated. Folic acid is recommended as a supplement for women of childbearing age not only to prevent neural tube and abdominal wall defects, but also to help prevent CL/P [16].

Many studies have demonstrated that children with CL/P presented smaller body dimensions when compared with typical children [17], but some studies have shown that the birth weight of children with clefts is similar to the birth weight of children without clefts [18]. Reports indicate that growth problems are more severe in children with CP and CLP, than in children with isolated cleft lip [19]. Some authors have suggested an association between the severity of intrauterine growth deficiency and the width of the cleft, with infants with CLP presenting greater risk for low birth weight birth for gestational age [20].

Objective

To give a statistical overview about treated patients with clefts in 1910 – 2000 in the Department of Oral and Maxillofacial Surgery of the Tartu University Hospital, based on patient records. To determine the rate of occurrence between different cleft types on the basis of gender. To find out the average birth weight of newborn children with clefts and the number of premature children. To determine the number of accompanying developmental anomalies among the children with clefts. To determine the age of parents upon birth of the child with a cleft and mother's medical status.

MATERIAL AND METHODS

For the purpose of the present study, data has been collected from the preserved database in the Department of Oral and Maxillofacial Surgery at the Stomatology Clinic of Tartu University Hospital and processed on the basis of standard form of data collection and input data. The preserved patient records are available for the years 1910 to 2000. During this period of time 585 health files of patients with clefts had been preserved in total. In 583 cases, the patient's gender was known (it was missing in two files), there were 333 boys (57.1%) and 250 girls (42.9%) among the patients (Figure 1).

RESULTS

42% of clefts were CLP, 19% were CL and 39% of cases were CP (Figure 2).

The most common cleft type was incomplete cleft palate (30% of patients with clefts), the most infrequent was bilateral cleft lip (3.8%). Boys had most frequently left side CLP (13.8%) and the girls had CP (17.8%). Bilateral CL occurred least frequently in boys (2.6%) and girls (1.2%) (Figure 3).

The left side of the face was damaged 2.2 times more frequently than the right side.

30.3% of patients with clefts had accompanying developmental anomalies (syndactyly, heart defects, mental and physical retardation, hernia inguinalis, etc).

488 patients with clefts also had their birth weight marked on patient records.

2.6% of children with clefts were born premature, half of which had accompanying developmental anomalies. The average birth weight of children with clefts was 3416 grams (boys 3447 g, girls 3376 g). 6.8% had a birth weight of less than 2500g, half of them had developmental anomalies.

28.4% of mothers and 37.7% of fathers were older than 30 years. Both parents were older than 30 years in 21.9% of cases. 2.6% of mothers were older than 40 years and 53% of subjects were between the ages of 20-30.

Epidemiological factors which affected the mother in the first trimester of pregnancy (Figure 4):

- Physical factors – 5.8% had physical traumas, 12.9% did heavy physical labour and 45% underwent medical abortions before the pregnancy.
- Chemical factors – 6.7% had toxicosis during the first trimester; 5.2% had hormonal dysbalance, 5.2% had exposure to chemicals.
- Biological factors – 9.8% had common cold, 4% had gynaecological disorders.
- Psychological factors – stress, fright.

DISCUSSION

In Estonia, the patients with clefts are treated at the Tartu University Hospital and in the North Estonia Medical Centre. There is no exclusive database for patients with clefts and therefore it is not possible to include all of the cleft cases in the study. We can use the findings by Lõvi-Kalnin [2], conducted in 1970 – 1980. Based on the data of the study, the current rate of occurrence of clefts in Estonia is 1 case per 777 live births and it has increased from 0.7% in the 1950s to 1.3% [2]. Today the occurrence rate of cleft lip and/or cleft palate and cleft palate is under observation. Different ethnic groups have different occurrence rates of different cleft types. In Europe, the highest occurrence rate of cleft lip and/or cleft palate is in the Netherlands (1.46/1000 per newborn child) and the lowest in France (0.67/1000) and the highest occurrence rate of isolated cleft palates is in Finland (0.97/1000) and the lowest in Denmark (0.36/1000) [21].

In the present study, CL formed 19% of all clefts, CLP formed 42%. 39% of cases were CP. Fogh-Andersen [6] was first to emphasise the proportions of occurrence of different cleft types in the Caucasian race, CL: CLP: CP – 1:2:1. As a finding of the study we found high occurrence rate of CP (CL: CLP: CP – 1:2:2), which is similar to the studies conducted in Finland and Sweden [22,23] and the reasons of which need further research. Different ethnic groups have different occurrence proportions of different cleft types, and the proportion of isolated cleft palate in general is significantly smaller than the total number of clefts [24].

30.3% of patients with clefts in the study had accompanying developmental anomalies, which is significantly higher than in Finland – 5.7% [22] – and France – 4.3 % [25] – based on the studies conducted; however, in Scotland, accompanying developmental anomalies were detected in over the half of patients with clefts [7]. According to the data by Wyszynski [21], developmental anomalies occur less in patients born with CLP than in patients with CP. As different studies assess accompanying developmental anomalies differently, variance in results might be due to different interpretation and different methods of assessment.

All unilateral CLP and CL considered, the left side of the face was involved in 2/3 of cases [3, 15]. Therefore, according to the present study, the left side of the face was damaged 2.2 times more frequently than the right side. No definite explanation for the left and rights side differences are given in literature. Johnston and Brown [26] have suggested that blood vessels supplying the right side of the fetal head leave the aortic arch closer to the heart and may be perfused better by blood than those on the left side. Among the Caucasian race, men have CLP twice as frequently as women, while CP is more common among women than men [3, 15]. It also became evident in the present study that there are significantly more boys born with CLP (ratio with girls 2.1), the girls compared to the boys had more frequently (1.5 times) CP. Boys also have more severe diagnoses – there are more CLP patients than CL patients and there are also more bilateral than unilateral cases [15]. According to the study, boys have CLP 2.2 times more frequently than CL, but there are fewer bilateral cases than left side cases. There is no definite scientific explanation on differences in clefts between sexes. One reason is given that the development of clefts occurs at different stages of development in male and female foetuses in the critical stage [27], but there is no correct justification of this claim.

Several studies have shown that the birth weight of children with clefts is similar to the birth weight of children without clefts [18], which was also confirmed by the present study. But the majority of studies demonstrated that children with CLP presented smaller body dimensions when compared with controls [17].

In the case of children with clefts, the mother's age exceeded 30 years in 1/4 of cases and father's age exceeded 30 years in 1/3 of cases. Both parents were older than 30 years in 1/5 of cases. Half of mothers were between the age of 20 and 30. 2.6% were older than 40 years.

An association between advanced maternal age and the occurrence of any type of oral clefts has been found

in several studies [7, 8], but not in all studies [28, 29]. In this study no maternal age effect could be observed.

Based on the present data, over a third of mothers of children with clefts (37%) have experienced psychological stress during pregnancy, mainly problems in the family have been described. However, stress is an important factor in the occurrence of clefts [15]. A fifth of mothers did hard physical work during pregnancy (field work, stock raising) or experienced physical trauma (struck by an animal, domestic violence). 45% of mothers had previously undergone at least one and 23% more than one medical abortion. A third of mothers (34%) had an exposure with some chemical factor: A fifth (22%) had been exposed to teratogenic toxic substances (fertilizers, various chemicals, medications) – 15% had hormonal disorders during pregnancy (toxicosis during the first trimester or diseases – diabetes or thyreotoxicosis).

There is little information regarding the temporal sequence between exposure and the outcome of the environmental risk factors and a dose-response relationship can not be demonstrated. Not enough information is available to draw any conclusions on the role of these exposures and the risk of oral cleft formation.

CONCLUSIONS

As a result of the study we found a high occurrence rate of CP (CL: CLP: CP – 1:2:2), which is similar to the studies conducted in Finland and Sweden. The reasons for this ratio need further research.

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