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Cleft lip and Palate Incidence Among the Live Births in the Republic of Korea

We present an epidemiologic study of cleft lip and palate in the Republic of Korea from January 1, 1993 through December 31, 1993. In 1993, the number of total live births was 715,817. And from 1993 through 1995, a total of 1,293 new patients with cleft lip and palate who were born in 1993 were identified. The incidence of cleft lip and palate was 1.81 per 1000, that is, 1 per 554 live births. The cleft lip: cleft lip and palate: cleft palate alone ratio was 1.13:1:1.19. The male: female ratio was 2.1:1 in the cleft lip group, and 2.5:1 in the cleft lip and palate group. We could detect a male predominance in both groups. In contrast, the ratio was 0.95:1 in the cleft palate group. The left: right: bilateral ratio was 1.9:1:0.23 in cleft lip group, and the ratio was 2.2:1:1.1 in the cleft lip and palate group. This is the first nation-wide study to provide detailed data on the incidence of cleft lip and palate in the live births in the Republic of Korea.

Key Words : *Cleft Lip; Cleft Palate; Incidence; Korea; Epidemiology*

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INTRODUCTION

Cleft lip and palate are the most common congenital malformations in the head and neck throughout the world. Surgical techniques for the appropriate treatment of cleft lip and palate have developed very rapidly, but the epidemiologic study for prevention remains in its infancy. Both genetic and environmental influences are believed to cause cleft lip and palate (1-3). Many authors have investigated the epidemiology and etiologic factors of cleft lip and palate. Though several investigations have been performed in Korea, the epidemiologic studies of cleft lip and palate have been based on only one or a few hospitals (4-8). Hence, the previous data do not represent the nationwide epidemiologic status in Korea. Since 1989, National Federation of Medical Insurance (NFMI) system has been operative in Korea. A nationwide investigation of the prevalences of other congenital malformations was performed with using this medical insurance data (9). There has not been any birth defect monitoring project in Korea, so we investigated the incidence of cleft lip and palate among the live births in Korea using the medical insurance data. This is the first study that covered throughout the country.

MATERIALS AND METHODS

We could obtain the annual birth rates and the number of the babies with cleft lip and palate from the NFMI in Korea. Since 1989, the medical insurance has covered on nation-wide all the people in Korea. The current payment system for medical services is an indirect one. Direct contact with the insured is made by medical care institutions, which in turn submit medical care bills to NFMI. By the help of NFMI, we could collect data from the submitted claims from medical institutions for the patients who have been first diagnosed as cleft lip and/or palate.

Because the system of the early period was not fully set up, the data for 1991 and 1992 were not reliable. As shown in Table 1, most patients with cleft lip and palate were diagnosed with their diseases within the first three years of age. Also NFMI followed the International classification of disease (ICD) 10 as a reference of disease classification instead of the ICD 9 since 1996, the disease classification was not consistent with former years. So we estimated the incidence in the group of babies born in 1993, using the data of the newly diagnosed cases during the first 3 yr from 1993 to 1995.

According to Ryu et al., the accuracy of medical insurance claim data is about 76% in Korea (10), and Lee also has reported that the agreement rate between medical records and medical claim data was about 80% (11). Therefore assuming that the NFMI's data has about 80% accuracy, we used the following method to decide the sample size to study the validity, and to get precise information from medical records. We wanted to estimate validity with 95% confidence interval

Table 1. The chronological distribution of the cases of cleft lip and palate

Birth year	Year the diagnosis was first made					
	1991	1992	1993	1994	1995	Total
1991	244	217	290	118	68	937
1992	0	429	554	204	39	1,226
1993	0	0	841	543	142	1,526
1994	0	0	0	895	457	1,352
1995	0	0	0	0	710	710

Table 2. The distribution of the cleft types

Type	Frequency	Percent
Cleft lip	102	34.1
Cleft lip and palate	90	30.1
Cleft palate	107	35.8
Total	299	100

Table 3. Sexual distribution

	Male		Female	
	Frequency	Percent	Frequency	Percent
Cleft lip	69	67.7	33	32.3
Cleft lip and palate	64	71.1	26	28.9
Cleft palate	52	48.6	55	51.4

Table 4. Laterality pattern of the cleft deformities

	Left	Right	Bilateral	Uncertain	Total
Cleft lip	60 (58.8%)	31 (30.4%)	7 (6.9%)	4 (3.9%)	102
Cleft lip and palate	42 (46.7%)	19 (21.1%)	21 (23.3%)	8 (8.9%)	90

Table 5. The frequency of positive family history

	Case	Percent
Cleft lip	11/102	10.8
Cleft lip and palate	6/90	6.7
Cleft palate	4/107	3.7
Total	21/299	7

Table 6. Associated anomalies

Anomalies	Frequency	Percent
Congenital heart disease	16	5.4
Short frenulum	5	1.7
Hernia	1	0.3
Accessary ear lobe	1	0.3
Congenital megacolon	1	0.3
Extremity malformation	1	0.3
None	274	91.6

(alpha=0.05), allowing 5% measured error (d=0.05). We knew that estimated P* is about 0.8 based on the previous studies (Rue 2000, Lee 1994). Using following sample size equation $N>P^*(1-P^*)[Z_{\alpha/2}/d]^2$ (Z=cumulative normal distribution), we concluded that more than 256 cases were required to satisfy the condition. So we visited 9 hospitals from all over the country and reviewed 351 candidate cases of cleft lip and palate who were born in 1993 by cluster random sampling. We found that only 299 babies were compatible with the diagnosis of cleft lip and palate. Therefore the validity of the NFMI's cleft lip and palate data was estimated to be 85%. So we estimated that 1,293 babies (85% of the 1,526 babies who were born in 1993 and diagnosed with cleft lip and palate in their first 3 yr of age) had cleft lip and palate. Then the patients were subdivided as having cleft lip, cleft lip and palate, and cleft palate. The incidence, sexual ratio, laterality pattern, family history, and associated anomalies and syndromes were investigated.

RESULTS

According to the data from NFMI, the number of total live births in 1993 was 715,817. And we identified 1,293 new patients with cleft lip and palate who were born in 1993 during the period from 1993 to 1995. So the overall incidence of cleft lip and palate was 1.81 per 1,000, that is, 1 per 554 live births. In Korea, previous investigations reported that the incidence of cleft lip and palate was from 1.16 to 1.77 per 1000 (4-8). These studies were based on a few hospitals or limited area except Min's reports which was not based on all live births in one year but cumulative live births data from 1984 to 1994 (5).

Also we could get more detailed epidemiologic information through a supplementary inspection of the selected medical records (299 patients) among the newly identified 1,293 cases with cleft lip and palate.

Among the 299 cases, there were 102 cases of cleft lip, 90 cases of cleft lip and palate, and 107 cases of cleft palate (Table 2). The male: female ratio was 2.1:1 in the cleft lip group, and was 2.5:1 in the cleft lip and palate group. We could detect a male predominance in both groups. In contrast, the ratio was 0.95:1 in the cleft palate group (Table 3). We also observed that the unilateral cleft lip occurred more frequently on the left side than on the right side in both cleft lip only and cleft lip and palate group. Bilateral cleft cases were more frequent in the cleft lip and palate group than in the cleft lip only group (Table 4). The family history of cleft lip and palate was detected in 21 out of 299 cases. The frequency of positive family history was higher in the cleft lip group than in the other groups (Table 5).

In this study, we included the cases of cleft lip and palate in association with other anomalies and recognized syndromes. A total of 25 out of 299 (8.4%) cases of cleft lip and palate were associated with other anomalies. Congenital heart dis-

ease was the most frequently combined anomaly in 16 cases, followed by short frenulum in 5 cases (Table 6). Pierre-Robin syndrome was associated in 4 of 7 cases with combined syndroms. There were one each of Down syndrome, Patau syndrome, and Van der Woude syndrome. Syndromic diseases were more frequently combined with cleft palate: 4 out of 7 cases with syndromic diseases were combined with cleft palate.

DISCUSSION

In the majority of the isolated cleft lip and palate, the etiology has been considered to be multifactorial: combined genetic and environmental factors. According to Fogh-Andersen in Denmark, the incidence of cleft lip and palate doubled during the last 50 yr and tripled during the last 100 yr (12). A 30-yr follow-up study of Rintala et al. in Finland also showed a clear trend of rapid increase in cleft lip and palate (1). These investigations suggest an increasing effect of the environmental factors.

In our study, the proportion of cleft palate was higher than in other studies (2, 13) (Table 2). In fact, we included the cleft lip and palate associated with other anomalies and syndromes in our investigation, and this might have contributed to the high ratio of cleft palate. But even after an exclusion of such cases, the proportion of cleft palate (33%) is still higher than that in other investigations. So the high ratio of cleft palate in Korea might be the result of different genetic background.

Similar to Rintala's study in Finland (14), the Koreans are genetically fairly homogeneous population of 46 million people and have almost same culture and environment. The genetic inheritance may play a significant role in the cleft lip and palate in Korea. So Korea seems to be an ideal country for epidemiologic studies of cleft lip and palate.

This study included all the live births born in 1993. This is the first nationwide investigation in Korea. Until now in Korea, a nationwide registration system for congenital anomalies has not been fully set up. All the data used in our study were derived from the submitted claims from medical institutions to NFMI. But these data had several limitations. Because the data recording was not performed by plastic surgeon, the case ascertainment was relatively incomplete. So we investigated the validity of NFMI's data by chart review. But the validity test of these data was performed with cluster random sampling (9 hospitals). If the validity test was performed with random sampling, more precise result could be obtained. But it is expensive and time consuming because there are so many hospitals in Korea.

The primary surgery of cleft lip and/or palate was covered by the NFMI system, therefore all the cases of primary surgery of cleft lip and palate were claimed to NFMI. If cleft lip and palate patients did not visit hospital or did not recognize their deformities (in case of submucous cleft palate or microform cleft lip, etc.), the incidence might be underestimated. Nevertheless, the estimated incidence of cleft lip and palate in Korea is rather higher than in other Asian countries, especially the neighboring country, Japan. Natsume reported the incidence of cleft lip and palate among Japanese people as 1.65 per 1000, or 1 out of 607.6 newborns (15).

The review by Apostole suggests that the incidence of cleft lip and palate differs among races (16). The American Indians showed the highest values followed by the Japanese, the Maoris, and the Chinese. The Whites showed lower values and the Blacks the lowest values. The incidence of cleft lip and palate in Korea may be ranked between the American Indians and Japanese.

We could not get the respective incidences of cleft lip, cleft lip and palate, and cleft palate in this study. Until 1995, NFMI followed the ICD 9 as a reference of disease classification. In ICD 9, cleft deformities (cleft lip, cleft lip and palate, and cleft palate alone) are classified as a unicode. So we could get only the total incidence of cleft deformities and the ratio could be obtained from a sample study. ICD 10, which subdivided the cleft deformities, was introduced in Korea since 1996. We are planning to make a more meticulous epidemiologic study of the clefts, through a longer follow-up.

Many authors have used the Japanese and Chinese data as a reference incidence of cleft lip and palate in Asians. This study will provide another valid incidence of cleft lip and palate in Asians.

In conclusion, from the nationwide epidemiologic study in 1993, we could determine the incidence of cleft lip and palate in the Republic of Korea as 1.81 per 1000 or 1 out of 554 live births. Genetic influence was suggested as an etiology of the relatively high ratio of cleft palate in the Republic of Korea, and this needs to be verified by a further prospective epidemiologic study.

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