

## ORIGINAL ARTICLE

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## Prevalence of congenital malformations and genetic diseases in Korea

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**Abstract** A nationwide investigation of congenital malformations and genetic diseases in Korea was conducted by analyzing Medical Insurance data for infants aged under 1 year. Medical Insurance data were obtained for 1993 and 1994 and the ICD-9 (International Classification of Diseases, Ninth Revision) code was used to classify the diseases. The coverage rate of medical insurance was approximately 95% of the total population. Anomalies of the cardiovascular, musculoskeletal, and gastrointestinal systems, in descending order of frequency, were more frequent than anomalies in other systems. The average prevalence of cardiovascular anomalies for 1993 and 1994 was 15 per 1000 infants, and ventricular septal defect, with an average prevalence of about 3.50 per 1000 for 1993 and 1994, was the most frequent cardiovascular anomaly in infants. Polydactyly was the most frequent musculoskeletal anomaly, with an average prevalence, for 1993 and 1994, of about 1.20 per 1000 infants. Anencephaly had the highest frequency of nervous system anomalies. Congenital hypertrophic pyloric stenosis was the most common of the gastrointestinal anomalies. The prevalence of the congenital malformations and genetic diseases examined was similar to that reported in other countries. Total medical expenses for the care of patients with each disease entity were also estimated. The highest medical expenses were incurred for ventricular septal defect, congenital coagulation factor VIII disorders, atrial septal defect, tetralogy of Fallot, and spinal anomalies, in descending order of magnitude. This investigation could be helpful in planning social welfare systems, as well as for elucidating the current status of congenital malformations and genetic diseases in Korea, and in other Asian countries.

**Key words** Congenital malformations · Genetic diseases · Prevalence · Infant · Korea

### Introduction

In all countries, the priorities for medical approaches to genetic diseases depend upon the local frequencies of those diseases, the health care burden that they represent, the possibilities for prevention and treatment, available resources, and the health care infrastructure. Congenital malformations and genetic diseases can be of varying degrees of severity, may have, at onset, any degree of severity, and the onset may be at any stage in the patients lifetime. However, those diseases in which symptoms are presented at birth are particularly burdensome, because they may cause early death or lifelong disability. Investigation on the prevalence of genetic diseases is important not only as a matter of medical interest but also for the planning of social welfare systems. In developed countries, congenital and genetic disorders are the second most common cause of death in infancy and childhood (Forfar 1992), and in those countries the incidence of births of infants with congenital disorders, including disorders that are regarded as trivial or relatively easily corrected (such as Congenital hypertrophic pyloric stenosis and polydactyly), is about 25–60 per 1000 (WHO Scientific Group 1996). Approximately 20% of all conceptions result in fetuses that have a chromosomal disorder, but most of these fail to implant or are spontaneously aborted, so that the birth frequency of infants with chromosomal disorders is 0.6% (Connor and Ferguson-Smith 1997).

There have been reports of congenital malformations and genetic diseases in Korea, but, as most of them were based on data from single hospitals or limited areas, they could not represent the status of genetic diseases in the country as a whole. Therefore, we investigated nationwide medical insurance data and analyzed these data to elucidate the current status of congenital malformations and genetic diseases in Korea.

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## Subjects and methods

Medical insurance benefit data from the Korean Federation of Medical Insurance were examined for 1993 and 1994. The coverage rate of medical insurance was approximately 95% of the total population. The medical insurance benefit data originally included all medical activities for diagnosis and treatment. Information on the insurance society, type of medical care institution, episodes of hospital admission, national identification number, birthday, day of first visit, days of visits, major disease code, and total expenses was collected. We used the International Classification of Diseases, Ninth Revision (ICD-9) to classify genetic diseases and congenital malformations. For congenital anomalies, ICD-9 codes 740.0–759.9 were investigated, except for the chromosomal anomalies (ICD-9, 758.0–758.9). All candidate codes for single gene disorders and other congenital anomalies that were not included in ICD-9 codes 740.0–759.9 were also investigated. The disease data were analyzed according to the four-digit subcategory of ICD-9. To avoid double registration of a patient, spell-based data were converted to person-based by national identification number and disease code. Therefore patients with multiple anomalies could be counted separately with different disease codes. Data from pharmacies, dental clinics, and oriental medical clinics were excluded because of the unreliability of diagnosis. Prevalences were calculated using the number of infants below age 1 year among medical insurance dependants as the denominator. To estimate medical expenses for the care of patients with congenital malformations and genetic diseases, insurance benefits and patient-charged consultation fees were also investigated.

## Results

Medical insurance covered approximately 95% of the total Korean population in 1993 and 1994. Of the population of infants aged under 1 year, 601,376 were covered by medical insurance in 1993 and 601,459 in 1994. The overall prevalence of congenital malformations per 1000 infants aged less than 1 year was 39.3 in 1993 and 34.4 in 1994. Cardiovascular anomalies were the most common congenital malformations in infants. The second most common were musculoskeletal anomalies, with the third most common, gastrointestinal anomalies. The prevalence of cardiovascular anomalies was 15.6 per 1000 infants in 1993 and 14.0 in 1994 (Table 1).

Anencephaly was the most frequent congenital anomaly of the nervous system (Table 2), with a prevalence of 0.26 per 1000 infants in 1993 and 0.42 in 1994. The prevalence of spina bifida was also high (0.30 per 1000 infants in 1993 and 0.27 in 1994) among nervous system anomalies. The most frequent cardiovascular anomaly was ventricular septal defect, and its prevalence per 1000 infants was 3.59 in 1993 and 3.24 in 1994. Pulmonary valve anomalies were the second most common cardiovascular anomaly, followed by,

**Table 1** Prevalence of congenital anomalies by system in infants aged less than 1 year in Korea

System (ICD-9)	Number of patients		Prevalence (/1000)	
	1993	1994	1993	1994
Nervous system (740.0–742.9)	632	669	1.05	111.2
Eye, ear, face, and neck (743.0–744.9)	2,988	2,613	4.96	434.4
Circulatory system (745.0–747.8)	9,367	8,398	15.58	13.96
Respiratory system (748.0–748.9)	187	166	0.31	0.27
Digestive system (750.0–751.9)	4,432	3,839	7.37	6.38
Urogenital system (752.0–753.9)	602	581	1.00	0.96
Musculoskeletal system (754.0–756.9)	5,260	4,251	8.75	7.07
Skin and appendages (757.0–757.9, 759.0–759.9)	167	153	0.28	0.25
Total	23,635	20,670	39.30	34.37

ICD, International classification of diseases, 9th revision

**Table 2** Prevalence of congenital anomalies of nervous system in infants aged less than 1 year in Korea

Disease	Number of patients		Prevalence (/1000)	
	1993	1994	1993	1994
Anencephaly	156	255	0.26	0.42
Spina bifida	178	162	0.30	0.27
Encephalocele	65	48	0.11	0.08
Microcephalus	28	33	0.05	0.06
Congenital hydrocephalus	103	87	0.17	0.15

**Table 3** Prevalence of cardiovascular anomalies in infants aged less than 1 year in Korea

Disease	Number of patients		Prevalence (/1000)	
	1993	1994	1993	1994
Transposition of great vessels	180	166	0.30	0.28
Tetralogy of Fallot	421	458	0.70	0.76
Ventricular septal defect	2158	1946	3.59	3.24
Ostium secundum type atrial septal defect	591	574	0.98	0.95
Endocardial cushion defects	91	82	0.15	0.14
Pulmonary valve anomalies	1471	1305	2.45	2.17
Ebstein's anomaly	37	20	0.06	0.03
Patent ductus arteriosus	479	367	0.80	0.61

in descending order, atrial septal defect, patent ductus arteriosus, and tetralogy of Fallot (Table 3). Congenital hypertrophic pyloric stenosis was the most frequent gastrointestinal anomaly. Its prevalence was 1.81 per 1000 infants in 1993 and 1.53 in 1994. The prevalence of cleft lip with or without cleft palate was about 1.0 per 1000 infants in both 1993 and 1994. The prevalence of congenital

**Table 4** Prevalence of gastrointestinal anomalies in infants aged less than 1 year in Korea

Disease	Number of patients		Prevalence (/1000)	
	1993	1994	1993	1994
Cleft palate	448	368	0.75	0.61
Cleft lip	648	579	1.08	0.96
Cleft palate with cleft lip	254	285	0.42	0.47
Tongue tie (ankyloglossia)	359	271	0.60	0.45
Tracheo-esophageal fistula, esophageal atresia and stenosis	101	88	0.17	0.15
Congenital hypertrophic pyloric stenosis	1087	917	1.81	1.53
Atresia and stenosis of large intestine, rectum, and anal canal	337	295	0.56	0.49
Congenital megacolon (Hirschsprung's disease and other congenital functional disorders of colon)	479	411	0.80	0.68
Gallbladder, bile duct, and liver anomalies	189	161	0.31	0.27

**Table 5** Prevalence of urogenital anomalies in infants aged less than 1 year in Korea

Disease	Number of patients		Prevalence (/1000)	
	1993	1994	1993	1994
Ovarian anomalies	20	19	0.03	0.03
Undescended testis	162	151	0.27	0.25
Hypospadias and epispadias	45	33	0.08	0.06
Renal agenesis and dysgenesis	44	31	0.07	0.05
Cystic kidney disease	43	38	0.07	0.06

megacolon was about 0.80 per 1000 infants in 1993 and 0.68 in 1994 (Table 4). The frequency of urogenital anomalies was extremely low, with undescended testis being the most frequent, with a prevalence of about 0.25 per 1000 male infants in 1993 and 1994 (Table 5). Polydactyly was the most frequent of the musculoskeletal anomalies with a prevalence of about 1.41 per 1000 infants in 1993 and 1.22 in 1994. The prevalence of congenital dislocation of the hip was about 1.10 per 1000 infants in 1993 and 0.93 in 1994, with the prevalence of varus deformity of feet about 0.83 in 1993 and 0.55 in 1994 (Table 6). Of the single gene disorders investigated (Table 7), the prevalence of adrenogenital disorders was 0.28 per 1000 infants in 1993 and 0.30 in 1994. Phenylketonuria was rare, with a prevalence of 0.01 per 1000 infants in 1993 and 0.02 in 1994. Mucopolysaccharidosis was also rare (0.01 per 1000 infants in 1993 and 1994). The prevalence of congenital coagulation factor VIII disorders was 0.22 per 1000 infants in 1993 and 0.15 in 1994 (0.16 per 1000 male infants in 1993, 0.11 in 1994).

Total medical expenses for the care of patients with each congenital malformation and genetic disease entity were relatively high. The greatest expenses incurred were for ventricular septal defect, congenital coagulation factor VIII disorders, atrial septal defect, tetralogy of Fallot, and spinal anomalies, in descending order of magnitude. Total medical expenses for patients with ventricular septal defect were

**Table 6** Prevalence of musculoskeletal anomalies in infants aged less than 1 year in Korea

Disease	Number of patients		Prevalence (/1000)	
	1993	1994	1993	1994
Congenital dislocation of hip	663	560	1.10	0.93
Varus deformity of feet	499	331	0.83	0.55
Valgus deformity of feet	99	55	0.17	0.09
Polydactyly	845	734	1.41	1.22
Syndactyly	155	173	0.26	0.29
Spinal anomalies	87	95	0.15	0.16
Cervical rib	9	6	0.02	0.01
Chondrodystrophy	35	14	0.06	0.02
Diaphragmatic anomalies	72	47	0.12	0.08
Abdominal wall anomalies	79	42	0.13	0.07

**Table 7** Prevalence of some single gene disorders in infants aged less than 1 year in Korea

Disease	Number of patients		Prevalence (/1000)	
	1993	1994	1993	1994
Adrenogenital disorders	168	182	0.28	0.30
Phenylketonuria	2	5	0.01	0.02
Mucopolysaccharidosis	2	2	0.01	0.01
Hereditary spherocytosis	37	26	0.12	0.09
Thalassemias	2	1	0.01	0.01
Congenital coagulation factor VIII disorders	68	48	0.22	0.15
Congenital coagulation factor IX disorders	2	5	0.01	0.02

about 7 billion Korean won (US \$ 7,778,000), and for patients with congenital coagulation factor VIII disorders, about 5 billion Korean won (US \$ 5,556,000), in 1993. The order was similar in 1994, but the expenses were slightly lower (Table 8).

## Discussion

In evaluating the epidemiological study of congenital malformations, different methods of case ascertainment can give rise to considerable variability in estimating prevalence; this is a significant problem worldwide. The reported prevalence of congenital malformations ranges from 30 to 50 per 1000 births, depending on study methods and diagnostic criteria. Our study was not based on medical record review but on medical insurance benefit data. These data had several limitations. The case ascertainment was relatively incomplete, because some disease codes for these data were based on tentative diagnoses. The disease data were analyzed by four-digit subcategory of ICD-9, but a proportion of disease records had been reported with the wrong code, which was not included in the ICD-9 system; we assumed this was because of input or recording error. In these cases we regarded the record as being included in the corresponding three-digit category; therefore, the fre-

**Table 8** Total expenses for the care of infants, aged less than 1 year, with genetic diseases and congenital malformations in Korea

Year Rank	1993		1994	
	Disease	Total expenses <sup>a</sup>	Disease	Total expenses <sup>a</sup>
1	Ventricular septal defect	7062	Ventricular septal defect	5544
2	Congenital coagulation factor VIII disorders	4974	Congenital coagulation factor VIII disorders	4812
3	Ostium secundum type atrial septal defect	3423	Ostium secundum type atrial septal defect	2625
4	Tetralogy of Fallot	2221	Tetralogy of Fallot	1854
5	Spinal anomalies	1810	Spinal anomalies	1465
6	Other specified anomalies of circulatory system	1102	Undescended testis	895
7	Undescended testis	1072	Other specified anomalies of circulatory system	871
8	Patent ductus arteriosus	1005	Patent ductus arteriosus	793
9	Transposition of great vessels	833	Transposition of great vessels	766
10	Cleft palate	753	Cleft palate	741

<sup>a</sup>Total expenses, shown in million Korean won (exchange rate of US\$ to Korean won was about 1:900 in 1993 and 1994)

quency and prevalence of diseases in our report by the four-digit subcategory were somewhat underestimated.

The overall prevalence of congenital anomalies in our study was similar to that reported in other studies in Korea (Chi 1987, Park et al. 1993). The prevalence of anencephaly was lower than that reported in Los Angeles County, USA (Sever 1982) and Osaka city, Japan (Imaizumi et al. 1991). The estimated prevalence of neural tube defects, including anencephaly, spina bifida, and encephalocele, was 0.67–0.77 per 1000 infants, which was very much lower than that in other countries (Congenital Malformations Worldwide, International Clearinghouse 1991). The prevalence of ventricular septal defect was higher than that in the United States (Ferencz 1990, Gillum 1994, Grabitz et al. 1988), but the frequencies of other cardiovascular anomalies were similar to those in other countries (Connor and Ferguson-Smith 1997, Hanna et al. 1994). Congenital hydrocephalus was less common than in Utah, United States (Blackburn and Fineman 1994); however, our prevalence data may have been underestimated, as many cases of congenital hydrocephalus were counted as neural tube defects in our medical insurance data. The prevalence of cleft lip and cleft palate was similar to that in western countries (Farhud et al. 1986, Connor and Ferguson-Smith 1997). Among Asian countries, Japan (Natsume et al. 1987) also showed a similar prevalence (2.06 per 1000 births), but China (Xiao 1989) and Singapore (Thein et al. 1992) showed slightly lower figures (1.82 and 1.72 per 1000 births apiece). The prevalence of congenital hypertrophic pyloric stenosis was similar to that in New York, United States, and other countries (Applegate and Druschel 1995). Hirschprung's disease and diaphragmatic anomalies, including congenital diaphragmatic hernia, were less common than in the United States (Goldberg 1984, Cannon et al. 1996).

We also investigated the prevalences of single gene disorders. The prevalence of adrenogenital disorders was higher than that reported in Sweden (Thilen and Larsson 1990). The rate of congenital factor VIII disorders was similar to that in other countries (Mosher 1996).

We studied medical expenses for the care of patients with each disease category in order to investigate the health care load of congenital malformations and genetic diseases borne by Korean society. In 1993, the total medical expense

for congenital anomalies (ICD-9, 740.0–759.9) was 36 billion Korean won (US\$ 40 million). Although this figure ranked fourteenth among 18 disease categories in descending order of magnitude of expense, it ranked second in order of expenses per claim in 1993 (Korean National Federation of Medical Insurance 1993). These results indicate the burden of these diseases to society as a whole, as well as to the patient and the carer.

This study was the first nationwide investigation of genetic diseases in Korea, but to obtain clearly ascertained cases we are planning to establish a registry system for several congenital malformations and genetic disorders, via the Internet (<http://www.nih.go.kr>). We are also planning a validity study of medical insurance benefit data by retrieving medical records of sampled hospitals. These studies could be very helpful for elucidating the status of congenital malformations and genetic diseases in other Asian countries, as well as in Korea.

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