Time Trend and Geographic Distribution of Treated Patients with Congenital Hypothyroidism Relative to the Number of Available Endocrinologists in Japan

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Objective To investigate the time trend and geographic distribution of treated patients with congenital hypothyroidism (CH) and explore their possible relationship to the availability of endocrinologists in Japan.

Study design The 2-source capture-recapture method was used to estimate the total number of patients. The ratio of the total estimated number of patients with CH to the number of endocrinologists and Spearman correlation coefficients were calculated. Curve fitting for changes in incidence or prevalence was estimated.

Results The incidence and prevalence of CH exhibited upward trends, with linear slopes of increase during the period 1994-2002. A statistically significant positive correlation was observed between the prevalence of CH and the ratio of the number of patients with CH to the number of endocrinologists in the 10 regions studied. The prevalence of CH was significantly higher in the regions with a higher ratio of patients with CH to endocrinologists, and also in younger patients.

Conclusions A shortage of endocrinologists may be one reason for the upward trend in the incidence and prevalence of treated patients with CH. *(J Pediatr 2010;157:153-7)*.

A nationwide neonatal screening program for congenital hypothyroidism (CH) was implemented in Japan in 1979. Since 1984, nearly 100% of all neonates in Japan have been screened.[1] In 1989, a highly sensitive method for detecting CH was introduced, and by 1992, enzyme-linked immunosorbent assay had completely replaced older methods such as radioimmunoassay and enzyme immunoassay. Nationwide follow-up surveys to evaluate the status of neonatal screening were conducted every year during the periods 1979-1987 and 1994-2003.[1,2] The 1994-2003 follow-up survey was conducted by the Aiiku Maternal and Child Health Center, Tokyo (Aiiku), and had a response rate of 54.2%-91.5%.[1,2]

In Japan, treatment of patients with CH is supported by 3 categories of medical subsidies provided by the national and/or local government: medical expenses for infants, the Medical Aid Program for Chronic Pediatric Diseases of Specified Categories (MAPChD), and Medical Aid for Immature and Premature infants.[3] Only 1 of these 3 subsidies may be used. MAPChD was implemented in 1968. The number of diseases eligible under this program has expanded annually, and currently stands at 514. A national registry of MAPChD beneficiaries was started in 1998. In 2005, the MAPChD was legalized and was included under the Child Welfare Law in Japan.[3] Beneficiaries of the MAPChD should be registered every year, and beneficiaries who sign a document of informed consent may be enrolled as subjects for MAPChD study projects. The registered data used for the study projects do not include any personal data, such as names, home addresses or phone numbers. Thus, the list of patients with CH is incomplete in both the follow-up survey at the Aiiku center and the registered data in the MAPChD.

The 2-source capture-recapture method (CRM) is widely used to estimate the total number of patients with CH. With CRM, an estimated whole number of patients can be calculated using information from overlapping lists of patients from 2 distinct, independent, incomplete sources. This statistical method, originally developed to estimate the size of a closed animal population, is used increasingly in epidemiologic studies to assess the completeness of cancer registries, to evaluate the incidence of many diseases and health problems (including diabetes), and in governmental disease surveillance.[4-9]

Obtaining an accurate estimate of the number of treated patients with CH in Japan is important. The present study was performed to estimate the total number of patients treated for CH and further explore the time trend and geographic distribution of CH by CRM, using lists from the Aiiku follow-up survey and the registered data in the MAPChD.

Aiiku	Aiiku Maternal and Child Health Center, Tokyo
CH	Congenital hypothyroidism
CI	Confidence interval
CRM	Capture-recapture method
MAPChD	Medical Aid Program for Chronic Pediatric Diseases of Specified Categories

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Table I. Estimated total number of patients with CH, rate of registration with the MAPChD, the annual incidence from April 1994 to March 2003, and the prevalence of CH by age group as of October 1, 2002

Birth year (April–March)	CH registered with the MAPChD (source 1)		CH patients in Aiiku (source 2)							By age group as of October 1, 2002		
	Total number	Eligible number (N1), comparable rate in CRM (N12/N1 × 100%)	Total number	Eligible number (N2), comparable rate in CRM (N12/N2 × 100%)	Patients with CH from both sources (N12)	Estimated total number of patients with CH calculated by CRM, N (95% CI)	Registration rate of patients with CH with the MAPChD (N1/N, %)	Live births (April- March)	Incidence of CH in infants per 10 000 live births (95% CI)	Population (P) (January-December)	Prevalence of CH in each age group per 10 000 children, N/P (95% CI)	Age, years
1994	250	230, 30.0%	179	179, 38.5%	69	597 (504-689)	41.9	1 233 072	4.8 (4.5-5.2)	1 209 000	4.9 (4.5-5.3)	8
1995	250	237, 32.9%	203	203, 38.4%	78	617 (529-705)	40.5	1 187 067	5.2 (4.8-5.6)	1 205 000	5.1 (4.7-5.5)	7
1996	255	237, 25.7%	150	150, 40.7%	61	583 (486-680)	43.7	1 206 551	4.8 (4.4-5.2)	1 186 000	4.9 (4.5-5.3)	6
1997	297	273, 32.6%	211	211, 42.2%	89	647 (563-731)	45.9	1 194 510	5.4 (5.0-5.8)	1 192 000	5.4 (5.0-5.8)	5
1998	375	354, 20.9%	193	193, 38.3%	74	923 (776-1070)	40.6	1 199 183	7.7 (7.2-8.2)	1 198 000	7.7 (7.2-8.2)	4
1999	363	348, 24.1%	195	195, 43.1%	84	808 (694-921)	44.9	1 184 302	6.8 (6.4-7.3)	1 170 000	6.9 (6.4-7.4)	3
2000	395	373, 17.2%	171	171, 37.4%	64	997 (821-1172)	39.6	1 190 547	8.4 (7.9-8.9)	1 168 000	8.5 (8.0-9.1)	2
2001	461	438, 11.6%	124	124, 41.1%	51	1065 (854-1276)	41.1	1 170 662	9.1 (8.6-9.6)	1 171 000	9.1 (8.5-9.6)	1
2002	377	357, 14.8%	153	153, 34.6%	53	1031 (824-1238)	36.6	1 153 855	8.9 (8.4-9.5)	1 168 000	8.8 (8.3-9.4)	0
Total	3023	2847, 21.9%	1579	1579, 39.5%	623	7216 (6826-7605)	41.9	10 719 749	6.8 (6.6-6.9)	10 667 000	6.8 (6.6-6.9)	

Methods

Data Sources

Data source 1 included data from the electronic registry of MAPChD beneficiaries born between April 1994 and March 2003. This database comprised patients with both primary and central CH, either detected by neonatal screening or diagnosed later after false-negative results on neonatal screening.

Data source 2 was lists from the Aiiku nationwide follow-up survey for the neonatal screening. This database comprised 1579 patients with primary CH born between April 1994 and March 2003 who were started on treatment with L-thyroxine. They were first identified as having CH by neonatal screening and then referred for further examination to a hospital or clinic in any of the various study regions, except the Hokkaido region[1,2] (Tables I and II).

Data Matching

In accordance with the Japan Personal Information Protection Act,[10] personal information about patients, such as names, was not available from the MAPChD electronic registry. The identifying variables were date of birth, sex, location of hospital or clinic, date of diagnosis, prefecture of birth, and prefecture of current residence. A matching software for 2-source CRM developed by our department and Mitsubishi Electric Business Systems Co. Ltd., (Tokyo, Japan) was used.

Two-Source CRM Analysis

A 2-source CRM model (Lincoln method) was used to estimate the total number and 95% confidence interval (CI) of patients with primary and central CH.[8,9] There are 3 fundamental assumptions in 2-source CRM: a closed population, independent sources, and an equal probability of individual cases being captured within any source. The formulas are as follows:

Total number = (eligible number of patients in source 1 [N1]) × (eligible number of patients in source 2 [N2])/ number of patients in sources 1 and 2 [N12]); 95% CI of estimated total number of patients = N ± 1.96 {√var (N)}, var (N) = {(N1 - N12) × (N2 - N12) × N1 × N2} / {N12 × N12 × N12}.

The number of patients captured by both sources was determined by data matching. The number of patients missed by both sources was estimated based on the assumption of an equal probability of ascertainment from both sources.

Stratified analysis was performed by birth year, age as of October 2002, and location of hospital or clinic, excluding the Hokkaido region (Tables I-III).

Other Statistical Analyses

The number of nationwide live births and the mortality of children were obtained from Japan's Ministry of Health, Labor, and Welfare.[11] The nationwide number of children under age 9 years in each prefecture as of October 2002 was obtained from the Ministry of Internal Affairs and