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CONGENITAL HYPOTHYROIDISM IN TURKEY: A RETROSPECTIVE EVALUATION OF 1000 CASES*

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SUMMARY: Tarım ÖF, Yordam N. (Endocrinology Unit, Department of Pediatrics Hacettepe University Faculty of Medicine, Ankara, Turkey). Congenital hypothyrodism in Turkey: A retrospective evaluation of 1000 cases. Turk J Pediatr 34: 197-202, 1992.

In this retrospective investigation, 1000 cases of congenital hypothyroidism followed-up in the Pediatric Endocrinology Unit at Hacettepe University Children's Hospital between 1964-1989 were evaluated with respect to age at diagnosis, main complaints, symptoms and physical findings. The mean age at diagnosis was 49.22 months, with 55.4 percent of patients diagnosed after two years of age and only 3.1 percent during the neonatal period. The main complaints of the patients were growth failure (26.7%), inability to speak (21.4%), and inability to walk (18.1%). The physical signs and symptoms most commonly detected by the physician were hypotonia (72%), constipation (66.8%), cretinoid face (64.6%), and macroglossia (64.6%).

These results emphasize the necessity for routine neonatal screening programs to be established in Turkey, with the aim of detecting congenital hypothyroidism. *Key words: congenital hypothyroidism, neonatal screening.*

Among the causes of mental retardation, congenital hypothyroidism (CH) is the most easily treated. Its treatment is also economical. Since 1970, neonatal screening programs have succeeded for the most part in preventing or minimizing mental and motor retardation due to CH[1-6].

The purpose of this study was to enumerate the signs and symptoms of CH according to the age at diagnosis and to determine the relevance of neonatal screening in Turkey.

Material and Methods

The Pediatric Endocrinology Unit at the Hacettepe University Faculty of Medicine is one of the referral centers in Turkey for this particular disorder. Congenital hypothyrodism was diagnosed in 1000 patients who had been followed-up in our department between 1964-1989.

The diagnosis was confirmed in all patients by the measurement of serum protein-bound iodine and buthanol extractable iodine or serum thyroxine and thyroid-stimulating hormone levels in accordance with the facilities of the laboratory. There were 535 females (53.5%) and 465 males (46.5%).

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All patients were evaluated taking into account sex, age at diagnosis, main complaints, symptoms and physical findings related to CH elicited by history and physical examination (hypotonia, cretinoid face, macroglossia, dry skin, constipation, umbilical hernia, cold intolerance, neonatal jaundice and goiter).

Results

The mean (± SD) age at diagnosis was 49.22 ± 49.17 months (range: 18 days to 15 years), with 3.1 percent of patients diagnosed during the first month of life, 9.4 percent between 1-3 months of age, 8.6 percent between 4-6 months of age, 9.5 percent between 7-11 months of age, and 14 percent between 1-2 years of age.

The majority of patients (55.4%) were older than two years of age at the time of diagnosis.

The main complaints of the patients were directly related to hypothyroidism or at times completely unrelated to CH (fever, seizures, diarrhea, etc.). As seen from Table I, the most frequent complaints listed are growth failure and inability to speak and walk. Constipation, jaundice, and large tongue were the most common

Table I: Main Complaints of Patients With Congenital Hypothyroidism

	0-3 Months (125)		4-6 Months (86)		> 6 Months (789)		Total (1000)	
Complaint	n	%	n	%	n	%	n	%
1. Growth failure	–	–	19	22.1	248	31.4	267	26.7
2. Inability to speak	–	–	–	–	214	27.1	214	21.4
3. Inability to walk	–	–	–	–	181	22.9	181	18.1
4. Constipation	30	24.0	16	18.6	87	11.1	133	13.3
5. Large tongue	20	16.0	21	24.4	57	7.2	98	9.8
6. Hypoactivity	11	8.8	14	16.3	56	7.2	81	8.1
7. Abdominal swelling	12	9.6	10	11.6	31	3.9	63	6.3
8. Swelling in the neck	12	9.6	–	–	36	4.6	48	4.8
9. Mental retardation	–	–	–	–	44	5.6	44	4.4
10. Hoarse cry	17	13.6	9	10.5	8	1.0	34	3.4
11. Inability to sit	–	–	–	–	33	4.2	33	3.3
12. Jaundice	28	22.4	–	–	–	–	28	2.8
13. Delay in tooth eruption	–	–	–	–	28	3.6	28	2.8
14. Anorexia	1	0.8	–	–	18	2.3	19	1.9
15. Umbilical hernia	9	7.2	8	9.3	1	0.1	18	1.8
16. Others (edema, cough, vomiting, fever, diarrhea, etc.)	17	13.6	21	24.8	75	9.4	113	11.3

Table II: A Comparison Between the Signs and Symptoms in 1000 Patients With Congenital Hypothyroidism (CH) Followed up at the Hacettepe University Children's Hospital and those in 141 CH Patients Reported by Raiti and Newns[8]

		0-3 Monts		4-6 Months		> 6 Months		Total	
Symptoms		n	%	n	%	n	%	n	%
1. Hypotonia	a	77	61.6	67	77.9	576	73.0	720	72.0
	b	22	55.0	11	47.8	24	30.8	57	40.4
2. Constipation	a	81	64.8	71	82.6	472	66.8	624	62.4
	b	26	65.0	11	47.8	46	58.6	83	58.9
3. Cold intolerance	a	24	19.2	14	16.3	300	38.0	338	33.8
	b	x	x	x	x	x	x	x	x
4. Feeding problems	a	x	x	x	x	x	x	x	x
	b	24	60.0	14	60.9	27	34.6	65	46.1
5. Respiratory symptoms	a	x	x	x	x	x	x	x	x
	b	12	30.0	3	13.0	1	1.2	16	11.3
Signs									
1. Macroglossia	a	86	68.9	70	81.4	490	62.1	646	64.6
	b	26	65.0	21	91.3	78	100.0	125	88.7
2. Cretinoid face	a	79	63.2	66	76.7	501	63.5	646	64.6
	b	10	25.0	21	91.3	78	100.0	109	77.3
3. Dry skin	a	63	50.4	62	72.1	513	65.0	638	63.8
	b	x	x	x	x	x	x	x	x
4. Umbilical hernia	a	81	64.8	70	81.4	216	27.4	367	36.7
	b	27	67.5	15	65.2	34	43.6	76	53.9
5. Neonatal jaundice	a	71	56.8	47	54.7	204	25.9	322	32.2
	b	11	27.5	4	17.4	12	15.4	27	19.2
6. Goiter	a	18	14.4	1	1.2	92	11.7	111	11.1
	b	x	x	x	x	x	x	x	x
7. Hoarse cry	a	17	13.6	—	—	—	—	17	1.7
	b	9	22.5	7	30.4	16	20.5	32	22.7

a : Hacettepe study
b : Raiti & Newns study[8]
x : no data

complaints in the 0-3 month-old infants, while a large tongue, growth failure, and constipation were observed mostly in the 4-6 month old infants.

The signs and symptoms detected by the physician either by obtaining the history of the patient or by physical examination, and which supported the diagnosis of CH, are shown in Table II. The most common symptom was hypotonia and the most common sign was a cretinoid face. The most common symptom found in the 0-3 month and in the 4-6 month-old patients was constipation, while the most common physical signs were macroglossia and umbilical hernia.

Discussion

The most striking result of our study was that the mean age of diagnosis was 49.22 months. The fact that inability to speak and walk were the main complaints in 39.5 percent of our patients, was due to a delay in diagnosis.

The physical findings of CH are very rarely observed during the neonatal period. Cretinoid face and other findings appear after 4-6 weeks of age, even in cases where thyroid agenesis is present, while it takes 3-6 months for hypoplasia or ectopia of the thyroid gland to develop[7]. However, the mean age of diagnosis in our patients exceeded the time required for the symptoms and physical findings of hypothyroidism to appear. This time differential may be attributed to the socio-economic or cultural level of families and also the difficulties encountered in diagnosis by physicians.

Cretinoid face, macroglossia, hypotonia, constipation, and umbilical hernia were noted with increasing frequency among the complaints listed by parents and physicians, the older the patient was at diagnosis.

The symptoms and findings of congenital hypothyroidism with respect to age at diagnosis were investigated extensively by Raiti and Newns[8] in a series of 141 cases (Table II). When comparing the physical findings of our patients with this series, we found that during the first three months of life, umbilical hernia ranked first, followed by macroglossia and constipation. Although they are not synonymous, the "lethargy" noted in Raiti's patients was comparable to the "hypotonia" observed in our patients. During the first three months of life, these symptoms were observed in both series and occurred in percentages whose values were near each other. Raiti claims that neonatal jaundice in hypothyroid patients lasts about two months, and therefore, the percentages obtained after three months are likely to be elicited by medical histories, rather than by physical examination. A history of neonatal jaundice was considered to be a sign in diagnosing CH in our patients.

The ratio of females to males was found to be 1.15 (535/465) in our patients instead of the 2.5-3 ratio reported in the literature[9-11]. Although there is no

explanation for the predominance of the disease in girls, the lower female/male ratio in our patients may be due to the sociocultural preference of male infants and lower prevalence in seeking medical care for girls.

The difficulties encountered in early clinical diagnosis of CH have been reported in many studies. The screening of 1,046,362 newborns in Canada and North America between 1974 to 1978 revealed that out of 239 patients with CH, only eight were clinically suspected of having the disease at the time of biochemical screening. Regarding the cumulative results of different screening programs, only five percent of 452 primary CH cases detected by screening 1,998,845 children, could be clinically diagnosed[12].

In the United States, it is noted that 30 days after the diagnosis of CH by screening, treatment was initiated in 70 percent of patients, while by the end of 45 days, 90 percent of patients had already been treated.

The intelligence quotients (IQ) of these patients measured when they were 4 and 7-years-old were within normal limits[13]. The ages at onset of treatment in countries with neonatal screening programs were: 18-days-old in Holland, 32-days-old in England, 12-days-old in West Germany, four-weeks old in Sweden, and two-weeks old in Switzerland[14]. The mean age at diagnosis in our patients was over four years. This figure did not correspond to the age reported in other countries with neonatal screening programs.

In Europe, 6500 cases of CH were detected by screening 25 million children between 1975 to 1987, showing an incidence of 1/3800[15]. Although we do not know the actual incidence of CH in Turkey, the huge number of patients diagnosed in the absence of routine screening gives the impression of a high incidence.

The results of our investigation once again prove the necessity for neonatal screening programs for CH, a disease which causes mental retardation.

We hope we can overcome the limitations of our economic resources to establish a routine screening program in the future in Turkey.

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