Clinico-aetiological Profile of Congenital Hypothyroidism

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Abstract

Introduction: Thyroid hormone is critical for normal brain development in the early postnatal months. Biochemical diagnosis must be made soon after birth and effective treatment must be initiated promptly to prevent irreversible brain damage. Early diagnosis and adequate treatment from the first weeks of life result in normal linear growth and development. This study was conducted to find out the clinical features suggestive of congenital hypothyroidism and also its causation. **Materials and Methods:** This was a hospital based retrospective study of 40 congenital hypothyroid children conducted at endocrine unit of Kanti Children's hospital from 2067 to 2072. All congenital hypothyroid children were reviewed in detail and frequency of signs/symptoms was calculated and also the possible causes were established using ultrasonography and scintigraphy. **Results:** Out of 40 congenital hypothyroid children 55% were male and 45% were female with M: F ratio of 1.23:1.Common age of presentation of congenital hypothyroidism was 6 to 12 months. The most frequent symptoms were decreased activity/ lethargy (78.9%) followed by stunted height (68.4%) and hypotonia (65.8%).Technetium thyroid scan was performed in 19 cases among which thyroid agenesis was the most common cause of congenital hypothyroidism (42.1%) followed by dyshormonogenesis (31.6%) and ectopic thyroid (26.3%). **Conclusion:** Early diagnosis of congenital hypothyroidism is possible in some children based on clinical features followed by biomedical investigation soon after birth.

Key words: Congenital hypothyroidism, Thyroid hormone, Ectopic thyroid, Dyshormonogenesis, Thyroid agenesis

Introduction

Congenital hypothyroidism is the most common preventable cause of mental retardation in children. Most cases of congenital hypothyroidism (CH) are not hereditary and result from thyroid dysgenesis or a defect in thyroid hormonogenesis[1].

The clinical features of congenital hypothyroidism are so subtle that many newborns remain undiagnosed at birth and delayed diagnosis leads to the most severe outcome of CH, mental retardation, emphasizing the importance of neonatal screening of the worldwide birth population of 127 million. So far, only 25% of babies

are being screened for CH worldwide. For the remaining 75% infants particularly concentrated in developing countries, mere clinical suspicion of hypothyroidism leads to thyroid function evaluation[2].

Most infants with congenital hypothyroidism are asymptomatic at birth, even if there is complete agenesis of the thyroid gland. Despite the critical importance of thyroid hormone (TH) on multiple organ systems, especially the brain, most infants with CH appear normal at birth. The hypothyroid foetus appears to be protected at least in part by placental transfer of maternal TH[3].Before neonatal screening programs, congenital hypothyroidism was rarely recognized in the newborn because the signs and symptoms were usually not sufficiently developed. It can be suspected and the diagnosis established during the early weeks of life if the initial, but less characteristic, manifestations are recognized. Early diagnosis and adequate treatment from the first weeks of life result in normal linear growth and development[4].

New born screening and thyroid therapy started within 2 weeks of age can normalize cognitive development. Five or six month delay in treatment of CH could result in an IQ of 70 in a child who probably otherwise would have had normal intelligence[5].

TH deficiency will affect basically all tissues to a lower or greater extent. However, it is during intrauterine life that the lack of adequate TH production determines more damaging consequences, since these hormones have a fundamental role in normal foetal brain development[6].

In Nepal, till date the awareness of importance of congenital hypothyroidism is not much even among medical fraternity and, usually diagnosis is missed or diagnosed when they already develop neurological manifestations. Congenital hypothyroidism is suspected and diagnosed based on clinical features.

Therefore, this study was aimed to find out the clinical features of congenital hypothyroidism in our context and also its causation so that it can be detected and treated on time.

Material and Methods

This was a hospital based retrospective study of 40 children from newborn to age up to 14 years having congenital hypothyroid. It was conducted at endocrine unit of Kanti Children's hospital from 2067 to 2072 (five years). Ethical clearance of the study was taken from the institutional review committee (IRC).

The details of clinical symptoms were reviewed. The growth parameters weight for age and height for age were calculated and classified as underweight and stunted if weight for age and height for age were less than -2 Z score. The investigation reports of thyroid function test, ultrasonography of thyroid gland, thyroid scan, bone age, were also evaluated. Thyroid scan was done while on treatment but after stopping thyroxine for four weeks. After detail review of clinical and investigation findings the congenital hypothyroidism was confirmed with the presence of signs and symptoms and low T4 and high TSH level for age. Cause of hypothyroidism was confirmed by the findings of thyroid sonography and thyroid scan.

Data was analysed by SPSS version 17 and presented in the form of table, bar diagram and pie chart. Baseline characteristics, frequency of signs and symptoms were calculated.

Results

Out of 40 congenital hypothyroid children included in this study,ratio of male and female was 1.23:1. Maximum number of hypothyroid children were presented at the age group of 6 to 12 months (30%) followed by 12 to 36 months (25%). Less than 10% were presented at age of less than three months.

Table1: Distribution of sign and symptoms of congenital hypothyroidism

Signs/symptoms*	No	%
Decreased activity/lethargy	30	78.9%
Stunted height	28	68.4%
Hypotonia	25	65.8%
Underweight	23	65.5%
Dry skin	23	60.5%
Constipation	22	57.9%
Wide anterior fontanel	22	57.9%
Course faces	21	55.3%
Abdominal distension	18	47.4%
Persistent jaundice	15	39.5%
Umbilical hernia	14	36.8%
Macroglosia/Protruding tongue	14	36.8%
Pallor	12	31.6%
Difficult feeding	10	26.3%
Puffiness of face	9	23.7%
Hoarseness of voice	4	10.5%
Difficult breathing/ Nasal obstruction	4	10.5%
Open posterior fontanel	3	7.9%
Pedal oedema	2	5.3%
Pericardial effusion	2	5.3%

*Each case had more than one signs or symptoms

Table 2: Correlation of TSH levels with signs and symptoms of congenital hypothyroidism at the time of diagnosis

Parameters	TSH level in miu/l				
	10-50	50–100	>100	Total	*p*-value
Persistent Jaundice	2	7	6	15	0.148
Abdominal distension	1	6	11	18	0.258
Coarse face	1	4	16	21	0.009*
Dry skin	3	5	15	23	0.304
Hoarseness of voice	1	0	3	4	0.230
Wide anterior fontanels	3	3	16	22	0.024*
Protruding tongue	0	1	10	11	0.007*
Pallor	2	4	6	12	0.9
Umbilical hernia	2	5	7	14	0.784
Lethargy	3	9	15	27	0.57
Underweight	4	5	14	23	0.484
Stunted	4	5	17	26	0.125

Table 3: Imaging findings of cases with congenital hypothyroidism

Imaging findings	USG FINDINGS(N=34)		Thyroid Technetium scan findings(n=19)	
	No	%	No	%
NORMAL FINDINGS	20	58.8	NA*	-
ABSENT THYROID	10	29.4	NA	-
ECTOPIC THYROID	2	5.9	5	26.3
HYPO PLASTIC THYROID	2	5.9	NA	-
DYSHORMONOGENESIS	NA	-	6	31.6
THYROID AGENESIS	NA	-	8	42.1

*NA: not applicable

Discussions

Most of the hypothyroid children were presented at the age group of 6 to 12 months (30%) followed by 12 to 36 months (25%). Majority of children fell into the age group of less than one year (50 to 60%) and first 3 months of age made less than 10%. This might be because of the fact that parents notice problems in their children only when they do not achieve normal milestones like sitting, crawling, standing as other peers. Therefore, most parents seek medical care at the age between 6 months to 36 months when most striking gross motor milestones are developed. Most children with congenital hypothyroidism (>95%) have little or no clinical manifestation of the disease at birth due to the trans-placental passage of maternal T4. Moreover, most affected children have some functioning thyroid tissue. As thyroid hormone has a half-life of 7 days, the maternal hormone is metabolized and excreted approximately 3-4 weeks after birth[7, 8].This fact can explain our results which showed only less than 10% cases with clinical manifestation of congenital hypothyroidism presented within the first 3 months of life.

Though not very similar to our study, a Danish study found just 10% of affected children with clinical manifestation of congenital hypothyroidism presented during their first month of life, 35% by 3 months and 70% by the age of one year. The remaining affected children were not diagnosed until their third or fourth years of life[9]. A retrospective analysis of 1,000 cases of CH in Turkey found just 3.1% of cases were diagnosed during the neonatal period and 55.4% were diagnosed after 2 years of age[10]. About 40% of the hypothyroid patients were detected within the first 3 months and 70% within the first year of life, which is reported from the study in Netherlands and Sweden[11, 12].

An enlarged anterior fontanel combined with an open posterior fontanel can be an early sign of hypothyroidism in the new born. Wide anterior fontanels, stunted growth, abdominal distension and dry skin

are common findings for the diagnosis of congenital hypothyroidism. Presenting features of congenital hypothyroidism can vary depending upon the age of the child. Lethargy/decreased activity, dry skin, stunted growth, hypotonia, constipation, coarse face and wide anterior fontanels were found in more than 50% of the cases in the present study. Abdominal distension, persistent jaundice, umbilical hernia, protruding tongue/ macroglossia, pallor, and feeding difficulty were seen in less than 50% of the cases. Most prevalent clinical signs found by Isabela LP et al in Brazil were umbilical hernia (51%), enlarged anterior fontanel (50.3%) and open posterior fontanel (47.2%)[13]. A study carried out in 2004 in Mexico with the objective of describing the epidemiological characteristics of CH showed that the most commonly identified signs of hypothyroidism among the children screened were umbilical hernia (43.7%) and jaundice (41.5%)[14].

The patients with higher value of TSH especially >100 miu/l were found to be more symptomatic in the present study, however, statistical significance was seen only with the signs like coarse faces, wide anterior fontanels and protruding tongue. Hypotonia, macroglossia and feeding difficulties were the common clinical signs presented in children with the biochemical severity of the disease. Delayed bone age was present in 32.1% of the children at diagnosis.

Several imaging methods are suitable to describe the position and size of the thyroid. Most common cause of congenital hypothyroidism established by Technetium thyroid scan in 19 children in our study was thyroid agenesis (42.1%) followed by dyshormonogenesis (31.5%) and ectopic thyroid gland (26.3%). This is similar to the findings from other studies which found thyroid dysgenesis in 84% (agenetic 47%, ectopic lingual28%, hypoplastic 9%) an enlarged thyroid in 6% and a normal-sized ectopic gland, so-called “thyroid in situ”in 10% of children[15,16].Generally, the manifestations of the hypothyroidism appeared earlier in patients with aplasia than in those with ectopic thyroid glands which correspond to the reports by other authors[17,18,19,20]. Our data are also similar to those found by neonatal screening programmes in North America[21].

Conclusion

Early diagnosis of congenital hypothyroidism could be possible in some children based on clinical features followed by biomedical investigation soon after birth. Delayed diagnosis due to asymptomatic nature of the disease initially and other reasons lead to delayed treatment resulting in grave consequences including intellectual retardation.

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