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An Observational Study of the Clinical Profile of Congenital Hypothyroidism in Children.

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Abstract

Background: Thyroid hormones are important for the general growth and development of the infant and the child, particularly in the differentiation and function of the nervous system. They are essential in the maturational events involved in the transition of the neonate to the adult. **Subjects and Methods:** The prospective, observational study was conducted in Department of Pediatrics, Institute of Maternal and Child Health, Calicut Medical College for a period of two years. After getting informed consent from the parents, history was taken followed by physical and systemic examination of the baby. Physical and systemic examination was done. Anthropometric measurements were taken and laboratory investigations were done. Results are expressed in terms of frequencies and means. Data is analyzed using SPSS. **Results:** Congenital hypothyroidism is often diagnosed very late. Mean age at diagnosis was 1.32 year in the present study. Birth weight may not be a clinically useful indicator of congenital hypothyroidism. Absence of classical clinical features in the new born period is the major reason for the delay in diagnosis. With delay in diagnosis of congenital hypothyroidism the predominant clinical features are those of prolonged hypothyroid state like microcephaly, short stature, macroglossia, dry skin and delayed bone age. **Conclusion:** Any child with facial puffiness, recent onset poor scholastic performance or excessive sleepiness with or without goiter should be suspected to have juvenile hypothyroidism and evaluated.

Keywords: Congenital, Hypothyroidism, children, symptoms.

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Introduction

Thyroid hormones are important for the general growth and development of the infant and the child, particularly in the differentiation and function of the nervous system. They are essential in the maturational events involved in the transition of the neonate to the adult.[1]

Hypothyroidism is the commonest endocrinological problem in childhood and it is a preventable cause of mental retardation.[1] Early detection and careful and skillful follow up has been shown to prevent much of the morbidity associated with the hypothyroid state.[2]

Hypothyroidism in children can be due to congenital causes and acquired causes. Congenital hypothyroidism is usually seen and detected in infancy whereas acquired hypothyroidism though typically seen in adolescence can occur as early as in the first year of life.[3]

Being a preventable cause of mental retardation, several studies have been carried out in the world for early detection of congenital hypothyroidism. Most of these studies were based on newborn screening program for congenital hypothyroidism.[4]

At birth, the clinical signs and symptoms of congenital hypothyroidism are usually absent or so nonspecific or subtle that the majority of infants look completely normal. The development of features of hypothyroidism will depend upon the type of the defect, the age of onset and the duration and severity of the thyroid hormone deficiency. Since irreversible damage to the central nervous system may take place even before the clinical manifestations suggest the diagnosis, the early detection and treatment is critical to the mental development.[5,6]

Acquired hypothyroidism is usually seen in school aged children and the first and often unrecognized feature is deceleration of growth. Chronic lymphocytic thyroiditis is the most common cause of this disorder though iatrogenic, autoimmune and other diseases contribute to this state.[7]

With the introduction of highly sensitive radioimmunoassay for the detection of thyroid hormones and TSH, newborn screening has come to the forefront as a part of the general system of delivering health care in developed countries. However, in developing countries like India the economic and social problems involved in screening a vast population of neonates, most of whom are from rural areas, are formidable. Therefore, the awareness of the signs and symptoms of congenital hypothyroidism will help the clinician to diagnose the disease as early as possible so that we can prevent one of the most important preventable

causes of mental retardation.[8]

All premature infants have some degree of hypothyroxinemia.[9] This hypothyroxinemia is transient correcting spontaneously over 4-8 weeks. Postnatal growth and development is normal so that they do not require treatment and treatment does not increase growth rates.[10]

The clinical profile depends on the underlying etiology, the age of onset and the duration of thyroid deprivation before seeking medical attention. The classical clinical picture of well-established disease is unmistakable but the detection of the disorder in the newborn and young infants, where symptoms and signs are often vague and nonspecific poses problems. Less than 5% of the newborns detected on screening can be diagnosed clinically and in the best of the clinics, only 10% may be clinically diagnosed by 2 months and 30% by three months.[9] There is a tendency for prolonged gestation (20% greater than 42 weeks) among the mothers, the mean birth weight and length are near the 50th percentile, and the head circumference will be near the 70th percentile. In the newborn period, length and weight are normal.

Prolonged physiological jaundice may be the earliest sign.[11] Hyperbilirubinemia may persist for as long as 7weeks. The cause of hyperbilirubinemia in hypothyroidism include, delay in maturation of bilirubin conjugating enzymes. It is seen in 10% of newborn with congenital hypothyroidism.[12] Other features include large posterior fontanel, respiratory distress, and hypothermia, and peripheral cyanosis, hypo activity, feeding difficulty, constipation, abdominal distension, vomiting and edema.[13]

Respiratory distress may be associated with nasal congestion, hoarse cry and cyanosis and is caused by myxedema of the tongue, epiglottis, pharynx and larynx. Myxedema is the edema in skin, other tissues, and serous cavities secondary to hypothyroidism. It is due to increased extravasations of plasma proteins and leak of a compensatory increase in lymph flow and protein return rate. The skin can be pale, cool, dry and circulating mottling may be present. Heart murmurs are frequently present and if cyanosis is also present congenital heart disease may be suspected.[14]

Patients developing hypothyroidism in early childhood differ from cretins in their clinical manifestations. Symptoms may appear gradually over several years. Linear growth and eruption of teeth become retarded. Mental sluggishness may develop but mental retardation does not occur if the hypothyroidism develops after the 2nd year of life.[15] The present study was conducted to study the clinical profile of hypothyroidism in children up to 12 years of age.

Subjects and Methods

The prospective, observational study was conducted in Department of Pediatrics, Institute of Maternal and Child Health, Calicut Medical College for a period of two years.

Inclusion criteria

All children in the age group 0-12 years diagnosed to have hypothyroidism, who are outpatients or inpatients of the Department of Pediatrics, Calicut Medical College.

Exclusion criteria

Children with

- Major congenital anomalies
- Chromosomal anomalies
- Moderate to severe birth asphyxia

Definitions

Congenital hypothyroidism:

When the thyroid hormone deficiency features are present since birth.[2]

Acquired hypothyroidism (Juvenile hypothyroidism):

A previously normal child subsequently develops thyroid hormone deficiency.[2]

Goiter:

The enlargement of thyroid gland.[4]

Myxedema: The mucoprotein and fluid accumulation with the resultant edema seen in hypothyroidism.[3]

Methodology

After getting informed consent, history is taken in detail and a thorough physical examination is done as per the proforma with special emphasis on age at diagnosis and starting treatment, antenatal history of thyroid disease or drug intake, history of delayed passage of meconium, prolonged physiological jaundice, constipation, lethargy, poor feeding, umbilical hernia and developmental delay and in older children history of poor school performance, excessive sleep, facial puffiness, cold intolerance and neck swelling.

Presence of any associated illnesses like insulin dependent diabetes mellitus, adrenal insufficiency or vitiligo was assessed. Parents were asked for any history of consanguinity, thyroid diseases in family and use of iodised salt.

Physical examination included a general examination specifically looking for presence of wide fontanels, hypothyroid facies, jaundice, macroglossia, pseudohypertrophy of muscles, thyroid swelling or myxedema.

Anthropometric parameters were taken as per the Performa. Developmental assessment was done in detail. Systemic examination was done especially nervous system examination in detail for any tone abnormalities and delayed relaxation of ankle jerk.

Investigations included hemoglobin, mean cell volume (MCV), thyroid function test by using chemiluminescence immunoassay and serum cholesterol in all patients. Anti TPO antibody and anti thyroglobulin antibody titre was done in selected patients who were suspected to have acquired hypothyroidism. X-ray for bone age assessment and ultra sound scan of the neck for thyroid gland was done in almost all the patients. FNAC was done in three patients

who presented with a large goiter.
Results are expressed in terms of frequencies and means. Data is analyzed using SPSS.

Results

Out of the 80 children studied, 61 had congenital hypothyroidism and 19 had acquired hypothyroidism. female to male ratio was 1.44:1 [Figure 1]. Mean age at diagnosis was 1.32 year [Figure 2].

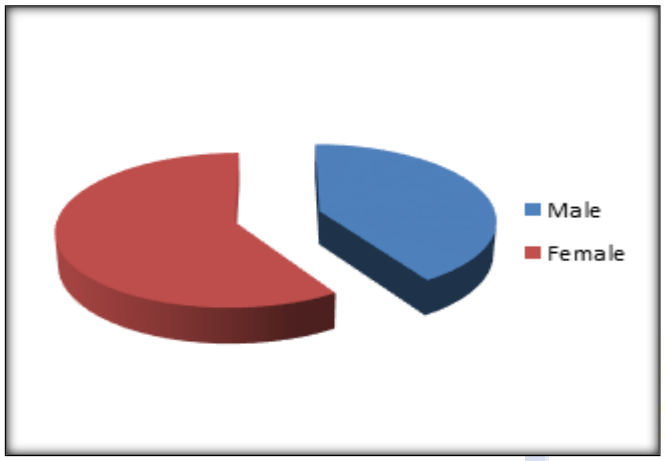

Figure 1: Gender distribution

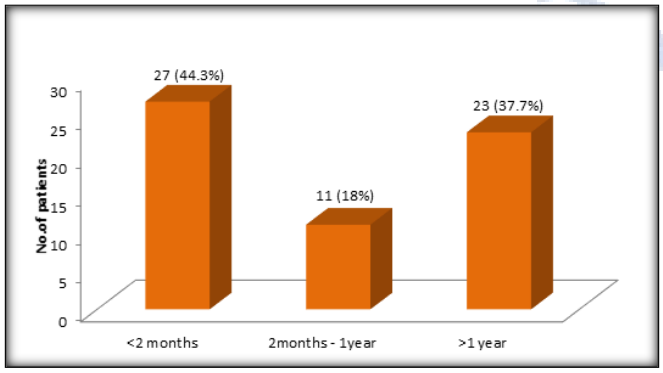

Figure 2: Age at diagnosis

Table 1: Birth weight (n=43)

Wt. (Kg)	Number	Percentage
<2.5	13	30.2
>2.5-3.5	26	60.5
>3.5	4	9.3

Out of the 61 patients birth weight was available in only 43 patients. 13 had low birth weight, 26 had a birth weight between 2.5-3.5kg and only 4 patients had a birth weight more than 3.5 kg [Table 1].

Table 2: Clinical Features (n=61)

Complaints	Number	Percentage
Developmental delay	29/34*	85.2
Constipation	51	83.6
Lethargy	42	68.9
Poor feeding	38	62.3
Abdominal distension	36	59
Prolonged jaundice	20	32.8
Delayed passage of meconium	19	31.1
Short stature	13	21.3
Family history	12	19.7
Consanguinity	7	11.5
Antenatal intake of antithyroid drugs	2	3.3
Thyroid enlargement	2	3.3

Out of 61 patients, 27 were diagnosed before 2 months of age whose development was difficult to assess at that point of time. Hence out of the remaining 34 patients, 29 had developmental delay [Table 2].

Table 3: Anthropometry (n=61)

Findings	Number	Percentage
Weight		
Over weight	0	0
Normal	60	98.4
Under weight	1	1.6
Length / Height		
Normal	43	70.4
Short stature	18	29.6
Head circumference		
Macrocephaly	0	0
Normal	55	90.2
Microcephaly	6	9.8

Table 4: Physical findings (n=61)

Findings	Number	Percentage
Hypothyroid facies*	53	86.9
Wide fontanels	49	80.3
Dry skin	31	52.5
Macroglossia	27	44.3
Umbilical hernia	21	34.4
Myxedema	3	4.9
Goiter	2	3.3

*Lid edema, hypertelorism, broad and flat nasal bridge, macroglossia etc.

Table 5: Investigations

Investigations	Number	Percentage
Abnormal thyroid function test	50	82
Low T4	61	100
↑TSH		
Delayed bone age (n=56)	42	75
USG thyroid (n=48)		
Normal	17	35.4
Small	27	56.3
Absent	4	8.3
Low Hb	12	19.7
Elevated serum cholesterol	7	11.5

Discussion

Out of the 80 patients in the study, 61 patients had congenital hypothyroidism, and 19 patients had acquired hypothyroidism.
Out of the 61 patients, 59% were females and 41% were males, with a female to male ratio of 1.44:1. This is in concordance with the other major studies which show a 2:1 incidence in females compared with males.[16]
The mean age at diagnosis was 1.32 year with 44% being diagnosed before 2 months, 18% between 2 months to 1 year and 37.7% after 1 year of age. A study by Desai MP et

al,[17] showed that nearly 25% of congenital hypothyroidism is diagnosed by 3 months of age and greater than 70% after that (without a neonatal screening program). The early diagnosis in this study may be because of the better awareness among the clinicians regarding the clinical features of congenital hypothyroidism now-a-days.

60% of our patients had a normal birth weight, 30% had low birth weight and only 9.3% had a birth weight greater than 3.5kg. Birth weight of greater than 3.5kg was 18% in a study by Desai MP et al.[17] Another study18 showed that 33% of their patients had birth weight of greater than 4kg68. The mean birth weight of normal Indian children is only 2.8kg and majority of our patients had normal birth weight. So this might indicate that birth weight may not be a major clinical indicator for the screening of congenital hypothyroidism in our setting.

Table 6: Comparison between Desai MP and present study.

Clinical Features	Percentage	
	Desai MP17	Present study
Birth weight >3.5Kg	18	9.3
Constipation	87	82.6
Lethargy	55	69
Poor feeding	57	62.3
Signs		
Hypothyroid facies	87	87
Macroglossia	87	44.3
Dry skin	66	52.5
Large fontanels	82	80.3

The results of the present study were comparable with the other Indian study by Desai MP et al except for parameters like birth weight greater than 3.5 Kg and macroglossia. It shows that all the above tabulated clinical symptoms and signs (except large birth weight and macroglossia which needs confirmation by larger population based studies) can be used as markers of congenital hypothyroidism in our population, as emphasized by various scoring systems (Quebec, Apgar and hypothyroid index) and as shown by other different studies.[6,11,14]

The incidence of large birth weight was not that high in the present study as compared to the study by Desai MP17. This may be due to true fact that most of the patients in our study belonged to a lower socioeconomic strata as opposed to a more affluent group in the other study. The incidence of macroglossia was also found to be less in the present study. Our data was obtained from the mother and the old records, which might not have been accurate, thus contributing to the above result.

Other clinical features:

Umbilical hernia was present in 34% of our patients, the North west regional screening program showed an incidence of 28%.3 But the another study8 showed that 58% of their patients had umbilical hernia. Umbilical hernia was given higher scores in various scoring systems like Quebec (score 1), Apgar (Score 2), hypothyroid index (score 3). The present study showed a lower incidence.

Short stature was a complaint in 21% of our patients and was observed in 30% of the study group. These were the children who were diagnosed after 1 year of age. This shows the effect of prolonged hypothyroid state on bone growth and physical development.

Abdominal distension was observed in 9% in the present study, 20% in the North west regional screening program and 40% in the study.[10] It was not included in the study by Desai MP et al,[17] and also in various scoring systems. This is in par with the literatures which denote abdominal distension as a nonspecific finding.

Delayed passage of meconium, though mentioned in the literature as an important finding in congenital hypothyroidism was observed in only 3% of patients in the present study.[14] This is in accordance with the various scoring systems mentioned. None of them included delayed passage of meconium as a criterion in their scoring system.

90% of the patients in the present study had normal head circumference and 10% had microcephaly (all of whom were children with late diagnosis). None of them had macrocephaly. This is comparable to the currently available literature.[7,14]

Even though two of the patients had history of thyroid enlargement ultrasound scan did not show any definite increase in the size of the gland in any.

Investigations

Thyroid function test was abnormal in all the patients. All of them had an elevated TSH. Low T4 was observed in 82%. T4 was normal in 18%. In 11.5% of the patients elevated Serum cholesterol was found. Anemia was found in only 20%. This observation was not seen in other studies in India. Literature shows that upto 65% of children with hypothyroidism may be anemic.[1,8]

Delayed bone age was observed in 75% of our patients. Literature,[10,13] review shows that bone age delay is seen in around 60% of patients at birth. This difference may be because of the fact that many of our patients were diagnosed late, emphasizing the importance of thyroid hormones for normal bone growth and physical development.

Conclusion

- Congenital hypothyroidism is often diagnosed very late. Mean age at diagnosis was 1.32 year in the present study.
- Birth weight may not be a clinically useful indicator of congenital hypothyroidism.
- Absence of classical clinical features in the new born period is the major reason for the delay in diagnosis.
- With delay in diagnosis of congenital hypothyroidism the predominant clinical features are those of prolonged hypothyroid state like microcephaly, short stature, macroglossia, dry skin and delayed bone age.
- Any child with facial puffiness, recent onset poor scholastic performance or excessive sleepiness with or without goiter should be suspected to have juvenile hypothyroidism and evaluated.

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