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A Study on the Clinical profile and the Outcome of Treatment of Congenital Hypothyroidism in Children– Early versus Late diagnosis.

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ABSTRACT

Background: Hypothyroidism is one of the most common diseases in pediatric endocrinology. Congenital hypothyroidism in this vital period will result in mental retardation and other neurological sequelae and is one of the commonest causes of preventable mental retardation and hence early diagnosis and treatment is mandatory. **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 on the Clinical profile and the outcome of treatment of Congenital hypothyroidism in children based on their age at diagnosis (below one year versus above one year) . After getting informed consent, history was taken. Physical and systemic examination was done. Anthropometric measurements were taken and laboratory investigations were done. Treatment was given and followed up to see the effect. Results are expressed in terms of frequencies and means. Data is analyzed using SPSS. **Results:** Delayed passage of meconium, constipation, prolonged physiological jaundice, wide fontanels and umbilical hernia were the clinical features present in a statistically significant proportion in the early treated group. Microcephaly, short stature, macroglossia, dry skin, and delayed bone age was high in the late diagnosis group. Treatment outcome was comparable in both groupsexcept for improvement in coarse facies and development quotient. **Conclusion:** Developmental delay at diagnosis is a significant problem even in the early diagnosis group, emphasizing the need of new born screening program. Irrespective of the age at diagnosis, thyroxine replacement helps to attain a comparable intellectual and physical development.

Keywords: Congenital, Hypothyroidism, children, symptoms.

INTRODUCTION

Hypothyroidism is one of the most common diseases in pediatric endocrinology. The thyroid hormones are essential in brain development, which takes place during fetal life and early postnatal life up to 2 year of age. Congenital hypothyroidism in this vital period will result in mental retardation and other neurological sequelae and is one of the commonest causes of preventable mental retardation and hence early diagnosis and treatment is mandatory. The main etiologic factors are anomalies of development, function and regulation of the thyroid gland. Clinical signs of thyroid hormone deficiency in infants are non-specific. Early diagnosis is based on newborn screening for congenital hypothyroidism, which was started in Quebec and Pittsburg in1974.[1] Treatment within first few days of life with appropriate dosage of thyroxin prevents mental retardation.[2]

The objective of treatment is to establish euthyroidism as rapidly as is safe for the patient. The thyroid hormone preparations available fall into two general categories; crude animal thyroid gland preparations and synthetic hormones. The former include desiccated thyroid and purified porcine thyroglobulin and these preparations should no longer be prescribed.[2]

Administration of L-T4 is the treatment of choice. Although T3 is the more biologically active thyroid hormone, most brain T3 is derived from local monodeiodination of T4, so T3 should not be used. The pill should be crushed and suspended in a few milliliters of formula, breast milk, or water. Care should be taken to avoid concomitant administration of soy, fiber, or iron. Breastfeeding can continue. Only T4 tablets should be used; currently there are no liquid formulations licensed by the US Food and Drug Administration. T4 suspensions that may be prepared by individual pharmacists may lead to unreliable dosage. T4 is expected to increase to more

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than 10 µg/dL, FT4 is expected to increase to more than 2 ng/dL by 2 weeks after initiating therapy, and TSH should normalize by 1month. FT4 measurement at 1 week of therapy can confirm whether the serum concentration is increasing appropriately. The L-T4 dose should be adjusted according to the infant's clinical response and serum FT4 and TSH concentrations.[3] The following study was done to know the outcome of treatment of hypothyroidism in children.

MATERIALS 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 Congenital 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 develop 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.

Anthropometric parameters were taken as per the Proforma. 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, 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.

Treatment history with eltroxin was taken in detail including the dosage, duration of treatment and any adverse effects. Necessary dose adjustments were done for all the patients at appropriate times.

These children were followed up at 6 monthly intervals for a period of 1year. On follow up, their height, weight and head circumference were recorded and looked for any coarse facies or constipation. Developmental assessment was done in detail. Thyroid function test including T4 and TSH was done and the thyroxine dose was adjusted accordingly. In children above three year of age intelligence quotient and in those below that development quotient was assessed (from the Institute of mental health and neuro sciences). Necessary rehabilitative measures were taken for those in need under their guidance.

Analysis was done to compare the clinical profile and outcome of treatment based on the age at diagnosis (below one year versus above one year).

Results are expressed in terms of frequencies and means. Data is analyzed using SPSS.

RESULTS

Out of the 61 patients with congenital hypothyroidism, 38 patients were diagnosed at or before 1 year of age and 23 after 1 year of age.

Table 1: Comparison of presenting complaints.

Symptoms	<1yr (n=38)		>1yr (n=23)		p value	Interpre-tation
	No.	%	No.	%		
Consanguinity	7	18.4	0	0	0.02	S
Delayed passage of meconium	17	44.7	2	8.7	0.003	S
Constipation	36	94.7	15	65.2	0.003	S
Prolonged jaundice	16	42.1	4	17.4	0.046	S
Umbilical hernia	17	44.7	4	17.4	0.029	S
Developmental delay	9/11	81.8	20	87	0.18	NS
Lethargy	29	76.3	13	56.5	0.108	NS
Abdominal distension	25	65.8	11	47.8	0.16	NS

S – Significant NS – Not significant

Table 2: Comparison of physical findings.

Finding	<1 yr (n=38)		>1 yr (n=23)		p value	Interpre-tation
	No.	%	No.	%		
Head circumference						
Normal	38	100	17	73.9		
Microcephaly	0	0	6	26.1	0.001	S
Short stature	4	11.1	14	60.9	0.000	S
Macroglossia	20	57.1	7	30.4	0.046	S
Wide fontanels	35	92.1	15	65.2	0.008	S
Dry skin	13	36.1	18	78.3	0.002	S
Hypothyroid facies	34	89.5	19	82.6	0.44	NS

Table 3: Comparison of laboratory findings.

Test	< 1 yr (n=38)		>1 yr (n=23)		p value	Interpre-tation
	No.	%	No.	%		
Abnormal TFT	38	100	23	100	0.29	NS
Elevated S.Cholesterol	4	14.3	3	16.7	0.82	NS
USG thyroid						
Normal	10	31.3	7	43.8		
Small	21	65.6	6	37.5	0.07	NS
Absent	1	3.1	3	18.8		
Delayed bone age	19	57.6	23	100	0.000	S

Follow up

Table 4: Change in height of children who were initially short statured (n=18)

Age group	After treatment				Before treatment <5th Percentile
	<5th percentile		>5th percentile		
	No.	%	No.	%	
<1 yr	2	50	2	50	4
>1 yr	8	57	6	43	14

p value 0.8

No statistically significant difference in gain in height was observed between the two groups.

Table 5: Coarse facies (n=53)

Age	After treatment coarse facies		Before treatment coarse facies
	No.	%	
<1 yr	2	5.8	34
>1 yr	8	42.1	19

p value 0.001

Early treatment has shown a statistically significant better outcome regarding the coarse facies.

Constipation: None of the children had constipation on follow up among either groups.

Table 6: Developmental quotient.

Age	Normal		Decreased		p value	Interpre-tation
	No.	%	No.	%		
<1 (n=30)	25	83.3	5	16.7	0.001	S
>1 (n=11)	3	27.3	8	72.7		

DQ was better in early diagnosed and treated group.

Table 7: Intelligence quotient.

Age	Normal		Decreased		p value	Interpre-tation
	No.	%	No.	%		
<1 yr (n=13)	11	84.6	2	15.4	0.506	NS
>1 yr (n=15)	13	86.7	2	13.3		

No statistically significant difference was noted in the IQ among the two groups on follow up.

DISCUSSION

Once the diagnosis is established, the need for lifelong therapy should adequately be stressed. It is essential for the attending physician to explain the nature of the disorder, the importance of thyroid hormones for physical and mental growth and maturation in children and adolescents and their role in all normal subjects for various body functions all throughout life.[1,3] We can expect a great deal of parental co-operation once the parents and guardians understand the nature of the problem and the need for continuous treatment and follow up.

Other indicators of adequate replacement therapy include normal growth and development and normal skeletal maturation. Skiagram should be done at least once in year. Patient with hypothyroidism treated in the first weeks of life and followed up to 9 years of age have shown their linear growth to be within normal range.[5]

Out of the 61 patients, 38 were diagnosed at or before 1 year of age and 23 after 1 year of age. Statistically significant clinical differences at presentation, observed between the two groups were, delayed passage of meconium, constipation, prolonged physiological jaundice, umbilical hernia, consanguinity, microcephaly, short stature, macroglossia, wide fontanels, dry skin, and bone age.

Statistically significant difference was not observed in the incidence of developmental delay, lethargy, abdominal distension, hypothyroid facies, thyroid function tests, serum cholesterol and USG thyroid results.

Delayed passage of meconium, constipation, prolonged physiological jaundice, wide fontanels

and umbilical hernia were the clinical features present in a statistically significant proportion in the early treated group. These are the classical and the early findings of congenital hypothyroidism and the presence of these features might have helped in the early diagnosis of the disease in them. It may be that these findings were not that evident in the late (after one year) diagnosis group thus causing a delay in the clinical diagnosis.

Consanguinity was noted only in the first group (18.4%) while none of those in the 2nd group were born to consanguineous parents. It may be that children with congenital hypothyroidism born out of consanguineous marriage had more severe hypothyroidism, and they presented early with major classical clinical features.

As opposed to what is said in the literature[6,7] the serum cholesterol level was comparable between the two groups. Even in younger children, a similar percentage had high serum cholesterol values.

The incidence of microcephaly, short stature, macroglossia, dry skin, and delayed bone age was high in the later diagnosed group. These are the late findings of congenital hypothyroidism due to the effect of prolonged hypothyroid state and puts a stress on the importance of early diagnosis and treatment.[1,8]

On follow up, a statistically significant difference was not observed in the pattern of gain in height, intelligence quotient, constipation, ADHD or scholastic performance.

Development quotient and improvement in coarse facies was found to be better in the early diagnosis group and the results were statistically significant.

Only a comparable percentage had low IQ among both the groups. The difference was not statistically significant. This shows the importance of treating and following up these children with congenital hypothyroidism meticulously even if they are detected after 1 year of age. Even in children with normal IQ, scholastic backwardness was a problem. They had specific learning disorders especially in mathematical skills. This observation is comparable to what is said in literature.[9]

It would have been better if we could follow up a larger cohort of children with congenital hypothyroidism for a longer period. This study shows the importance of early diagnosis and treatment of congenital hypothyroidism. Further studies incorporating more number of patients may be done to study the outcome of treatment of congenital hypothyroidism in various parameters especially the intellectual, scholastic and neuropsychological development.

CONCLUSION

- Developmental delay at diagnosis is a significant problem even in the early diagnosis group emphasizing the importance of new born screening program.
- Irrespective of the age at diagnosis, thyroxine replacement helps to attain a comparable intellectual and physical development.

REFERENCES

1. Desai MP. The thyroid gland. In: Desai MP, Vijalakshmi B, Menon PSN. Pediatric Endocrine Disorders, Orient Longman, Hyderabad, 2nd ed, 2007; 285-334.
2. Hung W. Thyroid Gland. In: Hung W. Clinical Pediatric endocrinology. Mosby Yearbook, 1992; 129-178.
3. AAP, Rose SR, Brown RS, Foley T et al. Update of newborn screening and therapy for congenital hypothyroidism. Pediatrics 2006; 117: 2290-2303.
4. LaFranchi S. Disorders of the thyroid gland. IN: Behrman RE, Kleigman RM, Jenson HB, Eds, Nelson Text book of Pediatrics, Harcourt Asia, WB Saunders, New Delhi, 18th edn. 2008; 2316-2332.
5. Fisher DA. Disorders of the thyroid in the newborn and infant. In: Sperling MA, ed. Clinical Pediatric and Adolescent Endocrinology. Philadelphia, PA: Saunders; 2002:164.
6. Wolff J. Congenital goiter with defective iodine transport. Endocr Rev 1983; 4: 240-54.
7. De Nayer P, Cornette C, Vander Shueren M et al. Serum thyroglobulin levels in preterm neonates. Clin Endocrinol 1984; 21: 149-153.
8. Ingbar SH. The thyroid gland. In: Wislon JD, Foster DW eds. Textbook of endocrinology. Philadelphia; WB Saunders, 1985; 682-815.
9. Morley JE. Neuroendocrine control of thyotropin secretion. Endocr Rev 1981; 2: 236.

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