

Physical growth and intellectual function of children with congenital hypothyroidism: An observational study

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Abstract

Introduction: Congenital hypothyroidism (CH) is an important preventable cause of mental retardation.

Objectives: To assess growth parameters and the developmental outcome of children with permanent CH on follow up.

Method: This was a hospital-based observational study done in the paediatric endocrinology clinic of a tertiary care hospital in South India. The study population included all children with permanent CH aged 5-18 years attending the clinic from March 2017 to March 2018. Weight, height and head circumference of children were measured and the body mass index (BMI) was calculated. Ultrasonography (USG) of the thyroid was done for all patients and structural abnormalities of the thyroid (aplasia, hypoplasia or ectopic gland) were taken as dysgenesis. If USG had normal thyroid it was taken as dysmorphogenesis. Intelligence quotient (IQ) assessment was done by a clinical psychologist.

Results: There were 35 children with CH enrolled in the study. Of this, 17 (49%) were diagnosed on or before 6 months of age and 18 (51%) after 6 months of age; 24 (69%) had thyroid dysgenesis and 11 (31%) had dysmorphogenesis; 4 had severe stunting and 5 were obese. Among the 17 children diagnosed on or before 6 months of age, 12 (70.6%) had normal intelligence and 5 (29.4%) had IQ <85 whereas among the 18 children diagnosed after 6 months of age 6 (33%) had normal intelligence and

12 (66%) had IQ <85, which was statistically significant ($p=0.028$). There were no significant differences between early and late diagnosis groups in other parameters like developmental delay, stunting and BMI. Among 24 children with dysgenesis of thyroid gland, 14 (58%) had IQ <85 whereas among 11 children with dysmorphogenesis, 3 (37.5%) had IQ <85. This was not statistically significant ($p=0.08$).

Conclusions: In this study, a statistically significantly larger proportion of children diagnosed on or before 6 months of age had normal intelligence compared to children diagnosed after 6 months of age. There were no significant differences between early and late diagnosis groups in other parameters like developmental delay, stunting and BMI.

(Key words: Congenital hypothyroidism, Growth assessment, Developmental outcome)

Introduction

Congenital hypothyroidism (CH), a preventable cause of mental retardation in children, has an incidence of 1 in 1000 in India^{1,2}. In most cases, the disorder is permanent and results from an abnormality in thyroid gland development (dysgenesis or agenesis) or hormone synthesis (dysmorphogenesis)³. The altered thyroid function can also be transient⁴. It may be due to transplacental passage of maternal medication, iodine deficiency or excess or maternal blocking antibodies⁴. Rarely, CH may result from hypothalamic or pituitary dysfunction (central hypothyroidism)⁴. Normal cognitive outcome is possible even in severe CH if the postnatal therapy with levothyroxine is early and adequate and maternal thyroid status is normal⁵. In contrast to the excellent outcome in infants treated early, prognosis for normal mental and neurologic performance is less certain for infants not detected early by newborn screening⁶.

Objectives

To assess growth parameters and the developmental outcome of children with permanent CH on follow up.

Method

This was a hospital based observational study in the Paediatric Endocrinology Clinic, Government Medical College, Thrissur, Kerala, India. The study

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population included all children with permanent CH aged 5-18 years attending the clinic from March 2017 –March 2018. Children with permanent CH diagnosed within the first year of life and requiring L-thyroxine supplementation beyond 3 years of life were enrolled in the study. Basic demography and developmental histories were taken. Anthropometric parameters like weight, height and head circumference of children were measured and body mass index (BMI) was calculated. The Indian Academy of Pediatrics (IAP) 2015 growth charts were used for assessing anthropometry. Intelligence quotient (IQ) assessment was done by a clinical psychologist. Development quotient <70% in two or more fields was taken as global developmental delay. Ultrasonography (USG) of thyroid was done for all patients and structural abnormalities of the thyroid (aplasia, hypoplasia or ectopic gland) were taken as dysgenesis. If USG scan showed a normal thyroid, it was taken as dyshormonogenesis.

Ethical issues: The study was approved by the Institutional Ethics Committee of Government Medical College, Thrissur, Kerala, India (Letter No: B6 -8772/2016/MCTCR dated 13/1/2017). Written informed consent was taken from the parents of the participants and assent from the older children.

Statistical analysis: All quantitative variables were treated as discrete or continuous type or categorised and it was summarised using percentage and appropriate measures of central tendency and dispersion. Quantitative data were analysed using mean and standard deviation (SD). Analysis was carried out by appropriate statistical methods like Chi square test. Statistical software used was SPSS version 16.0.

Results

There were 35 children with permanent CH enrolled in the study. Of them 18 (51.4%) were males and 17 (48.6%) were females. Mean age was 10.37 ± 4.11 years. Figure 1 gives the age group distribution.

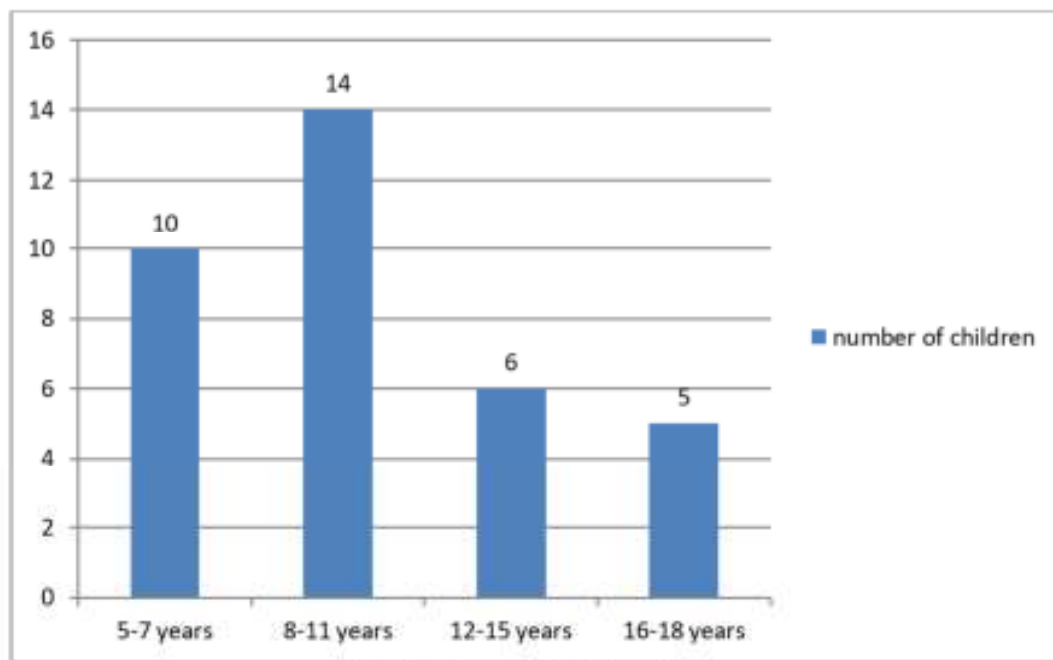


Figure 1: Age group distribution

Three babies were born preterm and the remaining 32 were term at birth. The mean birth weight was 2.71 kg; 9 (25.7%) children had low birth weight (LBW) and the remaining 26 (74.3%) were appropriate for gestational age (AGA) at birth. None of the babies were large for gestational age (LGA) at birth. Of the total, 17 (49%) children were diagnosed on or before 6 months of age and 18 (51%) children were diagnosed after 6 months of age; 24 (69%) children had thyroid dysgenesis and 11 (31%) had dyshormonogenesis; 74% children had regular follow-up i.e., never defaulted and came

for follow-up at least once in 6 months. Two children had associated congenital heart disease at birth. One had patent ductus arteriosus (PDA) with atrial septal defect (ASD) and the other had ASD. Both were surgically closed.

The most common symptom at the time diagnosis was delayed development (42.9%). The next common symptom was constipation (31.4%); 66.7% children were asymptomatic in the newborn period. Among the symptomatic children, neonatal jaundice

was present in 20%, delayed passage of meconium in 8.5% and feeding problems in 2.8%.

Twenty-nine (82.8%) children had normal weight according to IAP 2015 charts i.e., weights between -2 SD and +2 SD; 2 (5.7 %) were moderately undernourished (weight between -2 SD and -3 SD) and 4 (11.4 %) had severe undernutrition (weight < -3 SD). The mean SD for weight was -0.94.

Twenty-three (65.7%) children had height in the normal range i.e., between -2 SD and +2 SD; 12 (34.2%) children had short stature i.e., height < -2SD. Of these, 4 (11.4%) children had height < -3SD

indicating severe stunting and 8 (22.8%) children had moderate stunting with height between -2 SD and -3SD according to IAP 2015 charts. The mean height SD was -1.48. Of 35 children, none had microcephaly but one had macrocephaly.

Among the 35 children 18 (51.4%) had normal intelligence, 9 (25.7 %) had borderline intelligence (IQ between 71-84), 6 (17.1%) had mild mental retardation (IQ between 51-70) and 2 (5.7%) had moderate mental retardation with IQ between 36-50. None of the children had severe mental retardation (IQ <35) (Figure 2). The mean IQ of the study group was 85.8 ± 18.8 .

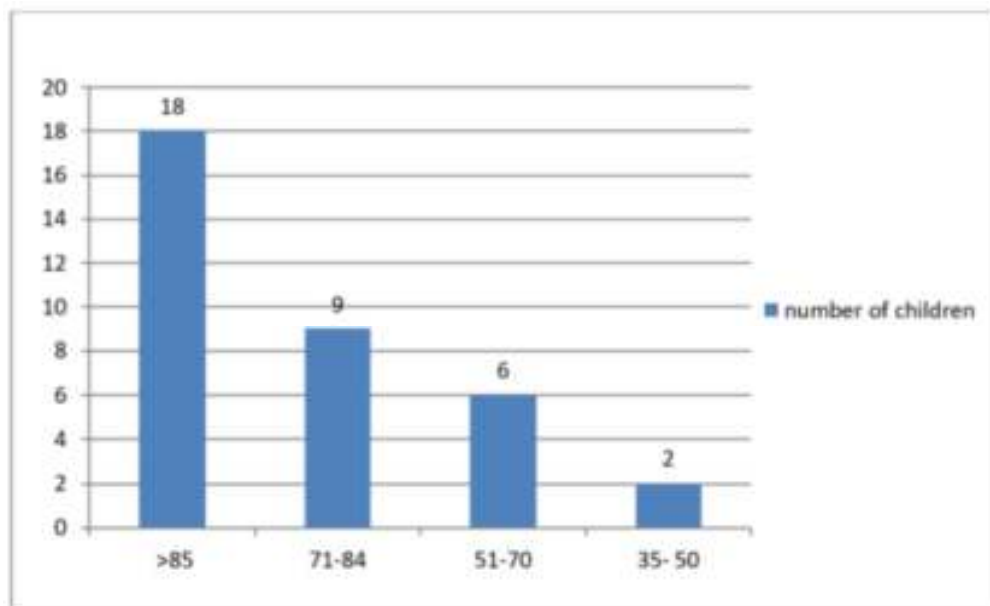


Figure 2: Intelligent quotients (IQs) in study group (X-axis: IQ score; Y-axis: Number of children)

Among the 17 children diagnosed on or before 6 months of age, 12 (70.6%) had normal intelligence and 5 (29.4%) had IQ<85, whereas among the 18

children diagnosed after 6 months of age, 6 (33%) had normal intelligence and 12 (66%) had IQ<85 (Figure 3).

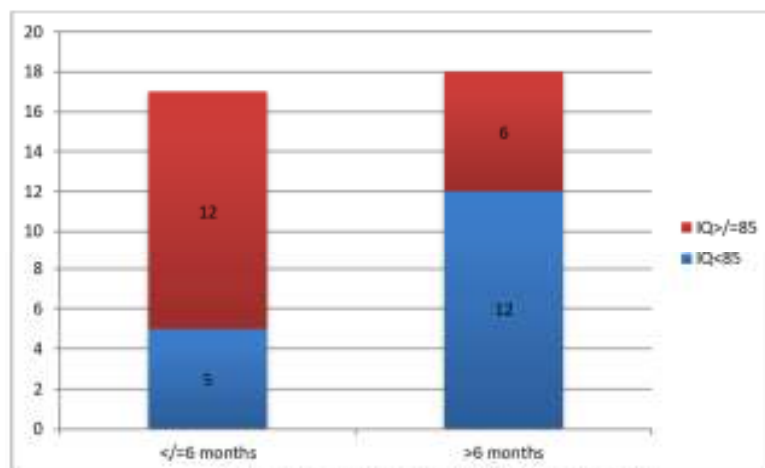


Figure 3: Age at diagnosis and intelligence quotient (IQ)

The IQ levels of the two groups i.e., diagnosis on or before 6 months and after 6 months, were compared using Chi square test and was found to be statistically significant ($p=0.028$). Other parameters like history of developmental delay, stunting and BMI did not show any significant difference between the groups.

Among 24 children with dysgenesis of the thyroid gland 14 (58%) had $IQ < 85$ whilst among 11 children

with dyshormonogenesis, 3 (37.5%) had $IQ < 85$ (Figure 4). This was not statistically significant ($p=0.08$). The mean IQ was 82.08 in the dysgenesis group and 91.9 in the dyshormonogenesis group. The association between aetiology of hypothyroidism and other parameters like developmental delay, stunting and BMI were not statistically significant.

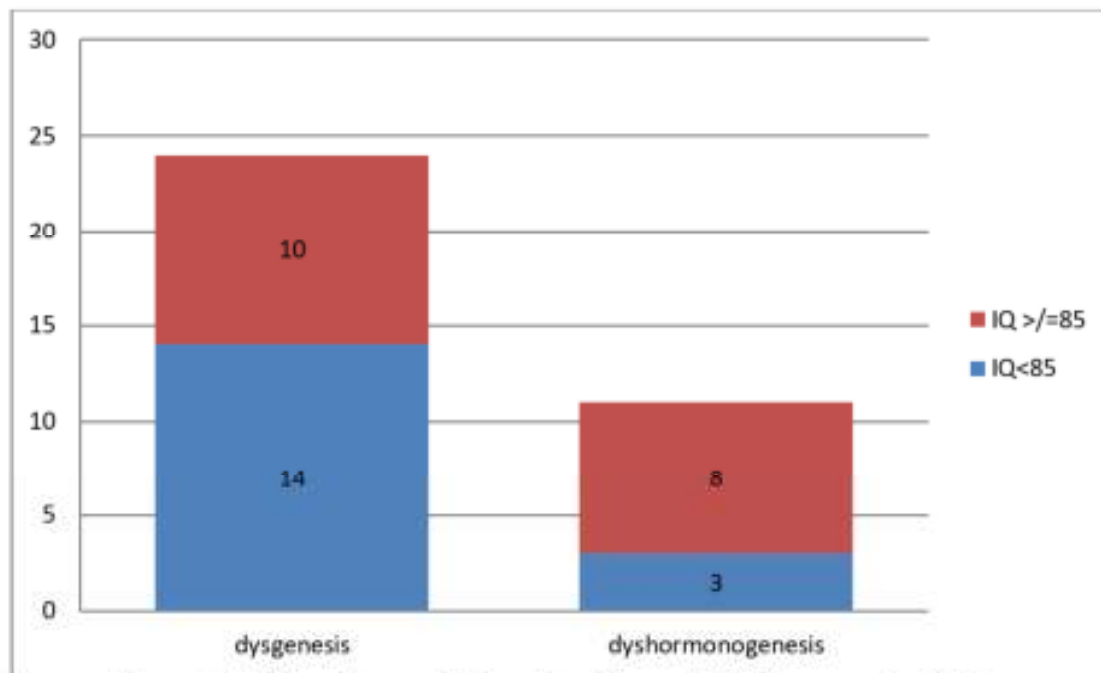


Figure 4: Aetiology of congenital hypothyroidism and intelligence quotient (IQ)

Discussion

In developing countries CH is still one the major preventable causes of mental retardation^{7,8}. The main factors which affect the growth and development of these children are the time of onset of treatment, treatment compliance, starting dose of thyroxine, level of thyroxine at birth and maintenance of the euthyroid state⁹. We conducted an observational study among children with permanent CH who were under follow-up in the paediatric endocrinology clinic of Government Medical College, Thrissur to assess the physical growth and developmental outcome of these children. The study also assessed whether the time of onset of thyroxine administration and aetiology of CH affected the physical and developmental outcome.

In our study, 35 children with permanent CH were enrolled. They were divided into 2 groups on the basis of time onset of thyroxine administration, those with treatment started on or before 6 months of life and those with treatment started after 6

months of age. The mean IQ of children diagnosed on or before 6 months of age was 91.53 and that of children diagnosed after 6 months of age was 80.39 which was statistically significant on analysis with the Chi squared test ($p=0.028$). These results were comparable with other studies where late diagnosis of CH was found to be associated with low IQ scores^{10,11,12}. In a study by Klien AH, *et al*¹¹, significant differences were found in IQ values for children who were put on treatment with thyroxine at less than 3 months of age. These children had higher mean IQ values compared to children diagnosed after 3 months. A study conducted by the French National Screening Programme reported the effect of age of onset of thyroxine administration, divided into four time periods, and IQ outcome¹³. In infants started on treatment after 30 days of life, mean IQ was 109.8; if started between 22 and 30 days of age, mean IQ was 107.7; between 5 and 21 days, mean IQ was 115.3 and before 15 days of age it was 119.2. This French study demonstrates the importance of early treatment in CH with respect to

the intellectual outcome which was also demonstrated in our study.

Another factor said to affect outcome of hypothyroidism at birth, was the aetiology of hypothyroidism. Studies have shown that children with thyroid agenesis had lower IQs, when compared to children with dysmorphogenesis¹⁴. In the present study, though the mean IQ of children with thyroid dysgenesis was less compared to the mean IQ of thyroid dysmorphogenesis, the difference was not statistically significant ($p=0.08$). Studies have shown that IQ scores of subjects with early treated CH diagnosed through a neonatal screening test were within the normal range, regardless of aetiology, thyroid function, initial dose of levothyroxine and age at start of treatment^{11,15}.

In our study, 82.8% of children had normal weight and 65.7% had normal height. Although children with CH were found to have lower mean SD scores in height compared to weight and there was a higher incidence of stunting in children started on treatment after 6 months, this was not statistically significant. In a study by Grant DB¹⁶, by the age of 3-4 years, the values for mean height in the children with either severe or less severe CH were equal to or greater than those for healthy children. Our study agrees that anthropometry on follow up is not affected if treatment has been adequate. A study by Bain P, *et al*¹⁷ found that the final adult height is not affected much if the compliance to treatment was good. In our study, there was no difference in short stature children with regard to aetiology; 33% were short in the dysgenesis group and 36% in the dysmorphogenesis group. Studies by Darendeliler F, *et al*¹⁸, Heyerdahl S, *et al*¹⁹, Chiesa A, *et al*²⁰ and Morin A, *et al*²¹ also support this observation that the final height of hypothyroid children on treatment is not affected by the time of onset of treatment. This study further supports other studies which have shown that effective screening and treatment completely assures normal neurodevelopment and linear growth in patients with CH²²⁻²⁴.

The study had some limitations. Many parameters assessed like height, weight and BMI and their relationship with aetiology of hypothyroidism and onset of treatment may not have reached statistical significance as the sample size was low. Also, some factors like compliance could not be accurately assessed which may be a confounding factor in the parameters. The initial thyroxine values were not available for many of the patients and hence their relationship to the intellectual outcomes could not be studied. This study underscores the importance of early diagnosis of CH by neonatal screening, appropriate treatment and good follow-up of these children to ensure good intellectual outcomes.

Conclusions

In this study, a statistically significantly larger proportion of children diagnosed on or before 6 months of age had normal intelligence compared to children diagnosed after 6 months of age. There were no significant differences between the early and late diagnosis groups in other parameters like developmental delay, stunting and BMI.

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