

Neuro-developmental status of children with congenital hypothyroidism: experience in a tertiary hospital of Bangladesh

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ABSTRACT

Background: Congenital hypothyroidism is one of the most common preventable causes of mental retardation. Early diagnosis and initiation of treatment is fundamental for optimal neuro-developmental outcome in children with congenital hypothyroidism. Thyroid hormones play crucial role in early neuro-development especially in the first 2-3 years of life. If left untreated or delayed initiation of treatment in congenital hypothyroidism results in neurological and psychological deficits. Aim of this study was to assess neuro-developmental status of children with congenital hypothyroidism who were on treatment (levo-thyroxine) started at different ages.

Methods: This cross-sectional study was done at paediatric endocrine outpatient department (OPD) and child development centre (CDC), BIRDEM General Hospital. Children with congenital hypothyroidism presenting at different ages who were followed up at pediatric endocrine OPD between January 2014 and January 2015 were included in the study. Their functional status in different domains were studied by rapid neuro-developmental assessment (RNDA) in CDC. Children with Down syndrome and perinatal asphyxia were excluded.

Results: Neuro-developmental assessment was done in 34 children (male 21, female 13). Mean age during assessment was 36 months (standard deviation 18.56). Eighteen patients (53%) were diagnosed in BIRDEM General Hospital and rest 16 (47%) were diagnosed outside BIRDEM General Hospital. Patients were grouped into 4 on the basis of age of diagnosis and start of treatment: group I (age 0-1 month), n=6 (18%); group II (age >1-3 months), n=7 (21%); group III (age >3-12 months), n=9 (26%); group IV (age >12 months), n=12 (35%). In group I, five (84%) had normal development and one had mild delay in cognition. In group II, three (43%) had normal development. Cognition and behavior was delayed in 3 patients (43% each), followed by delay in speech in 2 (29%). All patients (100%) in group III and IV had developmental delay, predominant domains affected were speech, cognition and behavior.

Conclusion: We have found developmental delay especially in the domain of speech, cognition and behavior in children with congenital hypothyroidism who have started levo-thyroxin late. Early diagnosis and initiation of treatment is fundamental for optimal neuro-developmental outcome in children with congenital hypothyroidism.

Key words: Congenital hypothyroidism, early initiation of treatment, neuro-developmental status.

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INTRODUCTION

Thyroid hormones play an essential role in brain development, both during pre-natal and post-natal life, especially in the first 2-3 years of life.¹ Untreated congenital hypothyroidism results in neurological and psychological deficits including intellectual disability, spasticity and disturbance of gait and co-ordination.²

Congenital hypothyroidism is one of the most common preventable causes of mental retardation.² Early detection and treatment of congenital hypothyroidism prevent neuro-developmental disability and optimize developmental outcome. To identify the babies in an early stage, screening of babies in first few days of life is the only choice. Estimates of the prevalence of congenital hypothyroidism vary according to the method of ascertainment: about 1 in 2000-3000 live births in countries with neonatal screening versus about 1 in 6700 live births before the screening era.³ Some of the highest incidence (1 in 1400 to 1 in 2000) has been reported from various locations in the Middle East.⁴ Incidence of congenital hypothyroidism in Bangladesh is not yet known. Preliminary study shows an incidence of 1:2200, which is also much higher than world incidence (1:4000).⁵

Most of the affected children gradually develop growth failure, irreversible mental retardation and a variety of neuro-psychological deficits without treatment. Studies on cognitive function in patients with congenital hypothyroidism treated soon after birth have shown that normal development can be achieved in most of the patients; although some may have subtle neuro-cognitive deficits.³ Choosing initial dose of levo-thyroxine at the higher end of the recommended range and achieving normal thyroid function at 1 or 2 weeks of therapy is important to achieve optimal neuro-developmental outcome.^{6,7}

This study was done to assess the neuro-developmental status of children with congenital hypothyroidism who were on treatment (levo-thyroxine) started at different ages.

METHODS

It was a cross-sectional study carried out between the period of January 2014 to January 2015 in Paediatric endocrine out-patient department and Child Development Centre (CDC), BIRDEM General Hospital. Children with congenital hypothyroidism

presenting at different ages were followed up at pediatric endocrine out-patient department. They were diagnosed either in BIRDEM General Hospital or outside during study period. They were followed up regularly at 3-6 months interval at CDC. Neuro-developmental assessment was done at least once in total forty-five children with congenital hypothyroidism who were on treatment with levo-thyroxine started at different ages. These children were included in this study and eleven children with congenital hypothyroidism with history of perinatal asphyxia, Down syndrome were excluded from the study.

Screening for congenital hypothyroidism is being done in our hospital for the past years and parents were informed about the screening protocol at the time of delivery. A written parental consent was obtained during the study.

All children were grouped into four on the basis of age of starting of treatment: Children upto 1 month of age were in group I, in group II children aged 1-3 month, in group III children of >3-12 month and children >12 month of age were in group IV. Neuro-developmental status was assessed by using Rapid Neuro-Developmental Assessment (RNDA) tools at CDC, BIRDEM. Rapid Neuro-Developmental Assessment (RNDA) is being widely used in developing countries in South Asia including Bangladesh. RNDA is a reliable and valid neuro-developmental assessment tool is being used with children <2 years which is particularly useful for early identification of children at high risk for neuro-developmental impairments.⁸ RNDA determine functional status in different domains like primitive reflexes in children less than 1 month; motor, vision, hearing, speech, cognition, behavior including self-care for children over five year of age.

Statistical analysis

Data were analyzed with the help of SPSS version 21.0. Descriptive statistics are presented as mean (SD) score for normally distributed data. Continuous data were compared using Chi-square test.

RESULTS

A total 34 patients were included; male were 21 and female 13. Mean age during diagnosis of children with congenital hypothyroidism and treatment started was 8.6 ± 8.3 months (ranges from 10 day to >12 months).

Mean age of their developmental assessment was 36± 18 months (range 18-54 months). Eighteen patients (53%) were diagnosed in BIRDEM and rest 16 (47%) were diagnosed outside BIRDEM. Patients were grouped into 4 on the basis of age of diagnosis and starting of treatment: group 1 (age 0-1month), n=6 (18%); group 2 (age >1-3 months), n=7 (21%); group 3 (age >3-12 months), n=9 (26%); group 4 (age >12 months), n=12 (35%) (Figure1).

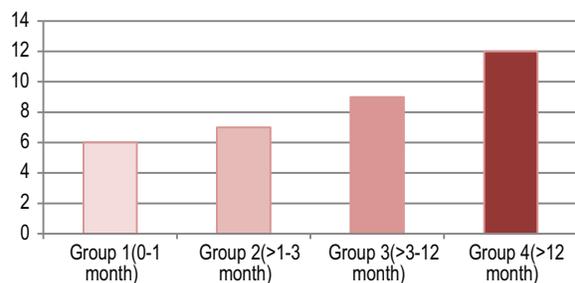


Figure 1 Group 1 (n=6), group 2 (n=7), group 3 (n=9), group 4 (n=12)

In group 1, five (84%) had normal development and one had mild delay in cognition Figure 2. cognition and behavior was delayed in 3 patients (43% each), followed by delay in speech in 2 (29%) (Figure 4, 5, 6).

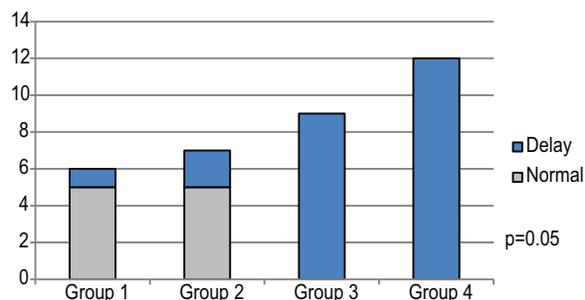


Figure 2 Comparison of developmental outcome in different groups

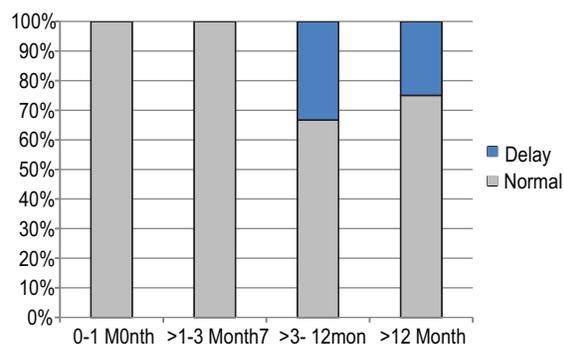


Figure 3 Comparison of motor function in different groups

We have found 100% developmental delay in children in group 3 and 4 who have started l-thyroxin late (Figure 2). Predominant domains affected were speech, cognition and behavior. (Figures 4, 5 and 6). Vision and hearing assessment in different groups were within normal limits. No impairment had been noticed in motor function in group 1 and 2 (figure 3).

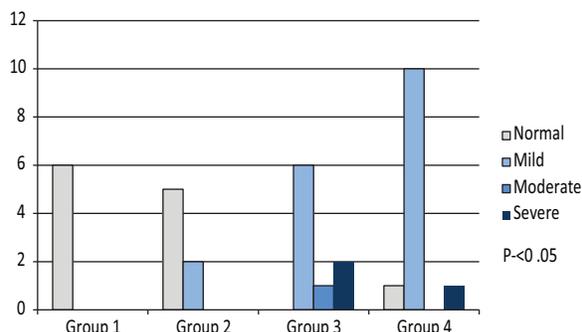


Figure 4 Comparison of speech problem in different groups

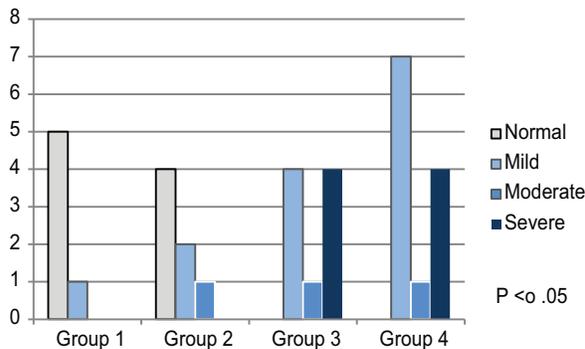


Figure 5 Comparison of cognitive function in different groups

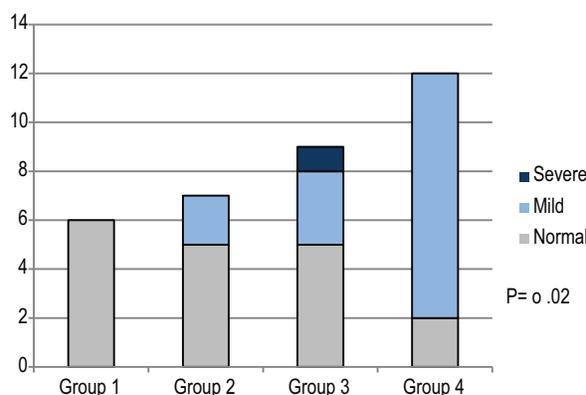


Figure 6 Comparison of behavioral problem in different groups

DISCUSSION

Congenital hypothyroidism is one of the most common preventable causes of mental retardation.⁹ Despite early and effective treatment in newborn with congenital hypothyroidism retardation in neurological development has been detected. Many newborns with congenital hypothyroidism have some residual thyroid hormone production and trans-placental passage of maternal thyroid hormone offers some protection for a time. The neonatal T4 level fall and disappear over the first 2-3 weeks of life. Thus there is a 'window of opportunity' to correct the hypothyroidism and minimize the time the brain is exposed to hypothyroxinemia.¹ Early detection through neonatal screening and immediate initiation of treatment of congenital hypothyroidism prevents neuro-developmental disability and optimizes developmental outcomes.² We have found that neuro-developmental status was almost normal in whom treatment was started before 1 month of age (84%). It was found in a previous study done in BIRDEM with congenital hypothyroidism that administering initial dose of within 2 weeks of life had a better intellectual outcome.⁷ Some delay was seen in different domains in whom, treatment was initiated after 1 month of age. Significant developmental delay was observed in speech, cognition and behavior in those who was diagnosed and treated after 3 month of age. In one study it was shown that neuro-developmental deficits exist in children whose median age of onset of treatment was more than 2 weeks.¹⁰ Vision and hearing were unaffected in all groups. One patient may have delay in more than single domain. This study was consistent with another study that showed children who had diagnostic delay beyond three month of age and had significant gross as well as fine motor delay. Speech delay was present among 12 (20%) early treated and 16 (76%) late-treated group of children.¹¹ Rovet JF. et al has shown similar findings in a study showed that poor developmental outcome in children with congenital hypothyroidism were due to delay in diagnosis and initiation of treatment.¹²

Recommendation

Early diagnosis and treatment of congenital hypothyroidism is fundamental for achievement of optimal neuro-developmental outcome and initiation of therapy by two weeks of life should be advocated.

Authors' contribution: NI conceived and designed the study, collected and analyzed data, and drafted the manuscript. SK collected data. FM designed and implemented the research. SM analyzed data. BJ contributed to the writing of the paper. AB and JN had other critical contribution. All authors read and approved the final manuscript for submission.

Conflicts of interest: Nothing to declare.

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