Original Article

Assessment of Thyroid Function in Children with Autism Spectrum Disorders

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Abstract:

Background: *Thyroid hormone plays a key role in the development and physiological functioning of central nervous system. They regulate the process of neurogenesis, myelination, dendritic proliferation and synapse formation. Different studies suggested an association between thyroid function and autism spectrum disorders.* ***Objective:*** *Our study was aimed to assess the thyroid function in children with autism spectrum disorders.* ***Methods:*** *This analytical type of cross-sectional study was conducted in the Dept. of Physiology, DMC, Dhaka during the period of July 2012 to June 2013.A total number of 120 subjects were selected with age ranging from 3 to 15 years. Among them 60 autistic children were included in the study group. They were selected from Autistic Foundation of Bangladesh, 114/3, Provatibagh, Tilpapara, Khilgaon, Dhaka. Age matched 60 apparently healthy children were included in the control group for comparison. Data were collected in pre-designed structured questionnaire by the researcher herself. For assessment of thyroid function serum FT_3 and FT_4 levels were estimated by RIA method and serum TSH level was estimated by IRMA method. The statistical analyses were done by unpaired students' 't' test.* ***Results:*** *In the present study, the mean serum FT_3 level was almost similar and within normal range in both the groups. The results showed no statistically significant difference among the groups. The mean serum FT_4 level was also within normal range but significantly ($p<0.001$) lower in the study group in comparison to that of the control group. Again, the mean serum TSH level was significantly ($p<0.001$) higher in the study group in comparison to that of the healthy group.* ***Conclusion:*** *Our study concludes that, increased serum TSH level with significantly decreased serum FT_4 level may be one of the non-genetic risk factors associated with autism spectrum disorders.*

Keyword: Autism spectrum disorders, FT_3, FT_4, Thyroid Stimulating Hormone (TSH)

Introduction:

Autism spectrum disorders (ASD) are cognitive and neurobehavioral disorders having three core features: Deficits in socialization, deficits in verbal & non-verbal communication and restricted & repetitive patterns of behaviors[1]. Worldwide prevalence of ASD is reported to be 3 to 6 per 1000 children with a familial incidence of 2% to 8% in siblings of affected children[2]. In Bangladesh the current estimates of prevalence is nearly 10.5 lakhs. The Centre for Child Development and Autism of BSMMU started its journey in 2001 and only 12 children with autism attended the center, but the number increased to 105 children in the year 2009[1].

The exact cause of autism is unknown but it is believed to be multifactorial. It usually appears within the first three years of life[3]. It is clear that genetics alone do not determine the entire ASD phenotype. The process is determined by genetic susceptibility but other non-genetic factors can modify it. So in most cases autism appear to be caused by a combination of autism risk genes and non-genetic factors that influence early brain development[4]. Studies indicate that non-genetic factors such as thyroid dysfunction due to endocrine disrupting toxins, teratogens, obstetric complications and prenatal infections such as rubella, cytomegalovirus are responsible for autistic cases[5].

The diagnosis of autism is based solely on behavioral characteristics, as currently there is no biochemical marker for autism. Research suggests that there are various types of neuroendocrinological abnormalities present in autistics and possibly TSH could serve as a biochemical parameter of the disease[6]. Several studies were undertaken in other countries to evaluate thyroid hormones as possible biochemical marker for ASD. A recent study showed that children born with very low levels of thyroxine had a higher risk of

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developing an autism spectrum disorder[7]. Thyroid hormones are essential for normal growth and development of brain during the early years of life[8]. They regulate neuronal proliferation, migration and differentiation in discrete regions of the brain during definitive time periods. Different patterns of cognitive effects results from prenatal and postnatal thyroid hormone insufficiency. It was noticed that nearly three-quarters of children with autism are found to have an underactive thyroid[9].

Insufficiency of thyroid hormone during brain development reduces cell number, synaptogenesis and dendritic arborization; alters cell migration patterns and decreases axonal myelination[8]. At present, researchers are beginning to appreciate the Thyroid-Autism connection and suggesting hypothyroidism as a major contributor to the development of autism[9]. Studies indicate that the general level of TSH was higher in young autistic patients and was most pronounced in those with complete impairment of verbal communication[6]. A different study showed that hypothyroidism is one of the non-genetic factors associated with autism[10].

Autism spectrum disorders are an increasingly important health concern in Bangladesh at present. The heightened awareness has been accompanied by a renewed interest to uncover the underlying pathophysiologic mechanisms and to find possible causes of the disorder at multiple levels. It has been hypothesized that disturbance in the thyroid hormone availability and metabolism during critical periods of neuronal development may lead to behavioral disturbances as noted in ASD[11]. Deficiency of thyroid hormones may have a significant contribution to the web of causes of ASD but their exact relationship remains debatable. Hence, the present study was designed to evaluate serum free triiodothyronine (FT_3), free thyroxine (FT_4) and thyroid-stimulating hormone (TSH) levels in children with autism to explore the role of thyroid hormone deficiency as one of the risk factors associated with autism.

Methods:
This analytical type of cross-sectional study was conducted in the Department of Physiology of Dhaka Medical College, Dhaka from July 2012 to June 2013. Ethical permission was taken from Ethical Review Committee of Dhaka Medical College. A total number of 120 children with age range 3-15 years participated in this study. Sixty autistic children diagnosed by psychiatrist according to Childhood Autism Rating Scale were included in the study group from Autistic Foundation of Bangladesh, 114/3, Provatibagh, Tilpapara, Khilgaon, Dhaka and sixty apparently healthy children selected from personal contact were included in the control group. After selection, proper counseling was done by explaining the aim, objectives, benefits, risks and procedure of the study to the parents of the subjects. They were encouraged for voluntary participation and written informed consent were taken in a prescribed form. Detailed family history and medical history were also taken. Physical and clinical examinations were done and all the information were recorded in a prefixed questionnaire.

Anthropometric measurement including height and weight were taken and BMI was calculated. Then under aseptic precaution, 5 ml venous blood was collected from antecubital vein of each subject of both groups for biochemical test. Serum FT_3 and FT_4 were measured by Radioimmunoassay (RIA) TSH level was measured by Immunoradiometricassay (IRMA) method using radio isotope I-125 as tracer. These tests were carried out in the Centre for Nuclear Medicine & Ultrasound, Dhaka Medical College, Dhaka. Data were expressed as mean ±SD (Standard deviation). Statistical analysis was done by using SPSS for windows version 17. Unpaired Student's 't' test were used as the tests of significance and p value <0.05 was accepted as the level of significance.

Results:
All the subjects of this study were similar for age & BMI. In this study mean values of serum FT_3 in both the groups were almost similar and within normal range and there is no statistical significant differences. The mean serum FT_4 level was also within normal range but significantly ($p<0.001$) lower in autistic children in comparison to that of normal children. Again, significantly ($p<0.001$) higher levels of serum TSH were found in the autistic

Table I: Serum free triiodothyronine, free thyroxine and thyroid-stimulating hormone levels in both the groups (n=120).

Groups	n	FT_3 (pmol/L)	FT_4 (pmol/L)	TSH (mIU/L)
A-Control	60	4.15±0.87	17.09±2.96	3.15±1.19
B-Study	60	4.24±1.13	13.29±3.55***	10.17±3.72***

Data were expressed as Mean±SD. Unpaired Student's 't' test was performed to compare between groups.
The test of significance was calculated and ***p values <0.05 was accepted as level of significance.

Discussion:

The present study was undertaken to observe some aspects of thyroid function status in children with autism spectrum disorders by estimating serum FT_3, FT_4 and TSH levels. All the parameters were also estimated in apparently healthy age and BMI matched children to find out the baseline data and also for comparison. In this study, thyroid hormone levels in the control group were within physiological limit and almost similar to the findings observed by various investigators from different countries[12,13].

Our study showed that, the mean serum FT_3 levels in both the groups were within normal range and almost similar and no significant difference was observed among the groups. This finding was in agreement with other researchers of different countries[14,15].

The mean serum FT_4 level was also within normal limit but significantly lower in the autistic subjects in comparison to that of the healthy subjects. Similar findings were also made by other investigators[7,8,9]. Again, elevated serum TSH level was found in the autistic children and these observations are in accordance with other research workers[6,10].

It has been suggested that nervous system growth and differentiation are closely correlated with thyroid hormones in the initial developmental stages. Deficiency of this hormone during the first two years of life may produce morphological brain changes that can have significant deleterious behavioral and cognitive effect[9]. In summary, our findings leads to the suggestion that impairment of mental and cognitive development found in autistic children may result from the subclinical hypothyroidism present in these special children.

Conclusion:

From the result of this study, it may be concluded that thyroid hormone deficiency may be one of the non-genetic risk factors associated with autism spectrum disorders. Therefore, routine thyroid test of pregnant mother and new born may be useful for early detection of future risk of development of ASD.

Conflict of Interest: The authors have no conflict of interest to declare.

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