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## Level of Thyroid Stimulating Hormone Concentration in A sample of Hyperactive Versus Pro-social school children in Iraqi City

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### ABSTRACT

**Background:** Attention deficit hyperactivity disorder (ADHD) is a common recognized psychiatric disorder of Childhood and its cause is still unknown. During the last years number of studies have appeared on the subject of relationships between thyroid hormones and psychiatric disease.

**Objective:** To assess the association between thyroid stimulating hormone (TSH) concentrations, for the purpose of comparing the hormone levels among school children with ADHD, and those healthy school children with pro-social traits.

**Subjects & Methods:** A cross sectional study was conducted for the period from the first of June - 2013 to the 31<sup>st</sup> March -2014. The study sample was (100) school children diagnosed with behavioral disorders including ADHD with or without conduct or aggressive disorder. In comparison with (100) school children characterized by pro-social traits as a control group. Assessment of behavioural disorders depended on Rutter behavioral Questionnaire (RBQ), as a behavioral scale used by teachers for assessment of school children behavior. Measurement of serum TSH concentration level was done to school children with ADHD, those with conduct disorder, and to the control group.

**Results:** Out of 100 school children who are diagnosed as having ADHD, 65% were males and 35% were females. School children who were found to have conduct disorder comorbid with ADHD constituted 49%, of them 32% were males and 17% were females. School children diagnosed to have ADHD, without aggressive behavior constituted 33%, and 18% for males and females respectively.

There was a significantly lower TSH level ( $P < 0.05$ ) among school children with pro-social character ( $2.0545 \text{ mIU/L} \pm 3.34410$ ), when compared to ADHD group ( $2.9902 \text{ mIU/L} \pm 1.65301$ ), and those with ADHD and aggressive behavior was ( $2.5590 \text{ mIU/L} \pm 1.43565$ ).

**Keywords:** Hyperactivity disorder; Attention deficit hyperactivity disorder (ADHD); Thyroid stimulating hormone; conduct disorder; Prosocial behavior; Anti-social behavior; Rutter Child Questionnaire (RCQ); Rutter Behaviour Scale (RBS).

### INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is the most common neurodevelopment disorder with childhood onset. It is a complex disorder having multiple causes including genetics as impacted by one's environment, and many different factors play a crucial role in its etiology<sup>1</sup>. This disorder is usually diagnosed in childhood. When difficulties arise during play and school, and it is marked by lack of concentration, short attention span, and physical restlessness<sup>2</sup>, affecting approximately 12% of school-aged children, with higher prevalence in boys than girls<sup>3,4</sup>. During the last years a number of scientific articles have appeared on the subject of relationships between psychiatric disease and thyroid hormones. These studies have demonstrated the presence of numerous changes in the hypothalamo-pituitary-thyroid (HPT) axis, in patients with psychiatric diseases.

Thyroid hormones (TH) are essential for normal development of the human foetal brain<sup>5</sup>, Also it is important for the cognitive function of the child and adult brain<sup>6,7</sup>. However, little is known about their mechanisms of action, they regulate the process of Dendritic and axonal growth, synaptogenesis, neuronal migration, and myelination<sup>8</sup>. Some mechanisms have proposed, suggesting a predominant effect of TH in the hippocampus and prefrontal cortex<sup>9,10</sup>, involving memory and attention functions. In general, patients with hypothyroidism show impaired cognition and generalized neural dysfunction while hypothyroid patients show irritability and anxiety<sup>11,12</sup>. More detailed studies using psycho-behavioural testing in thyroid patients have revealed deficits in memory and learning, attention, motor speed, visuoperceptual and construction skills<sup>13</sup>.

Studies among children with congenital hypothyroidism have also shown a relationship between concentration of TH at birth and neurodevelopment<sup>14</sup>, nevertheless, early treatment of congenital hypothyroidism partially prevents intellectual impairment<sup>15</sup>, even if treated children with congenital hypothyroidism frequently demonstrate impaired Neuromotor, visuospatial, memory, verbal and attention skills<sup>16,17,18</sup>.

The aim of the present study was to assess the association of thyroid stimulating hormone (TSH) concentrations with attention deficit hyperactivity disorder and healthy prosocial children from the primary school children at the age 9 years (4<sup>th</sup> class) to 14 years (end of 6<sup>th</sup> class).

### SUBJECTS AND METHODS

A cross sectional study was conducted for the period from the first of June -2013 to the 31<sup>st</sup> of March-2014. The study sample was selected at random multistage manner, included two study groups were investigated from school children, from classes 4<sup>th</sup>, 5<sup>th</sup>, and 6<sup>th</sup>, their ages were between 9 to 14 years. The study sample was selected from 9-primary schools in Baquba City, center of Diyala Province, these schools were selected randomly.

The study groups included depending on the score of Rutter Child Behaviour Questionnaire (RCBQ), as a scale for diagnosis of behavioral disorders, versus children with prosocial characteristics. Rutter Behaviour Questionnaire (RBQ) for completion by teacher in its original version was developed by Rutter at 1967<sup>19</sup>. The Revised version of CBQ for completion by teacher was developed recently, it consist of 59 items, 39 items for total difficulties (conduct, emotional, hyperactivity) and 20 items for prosocial trait.

First study group diagnosed according to RBQ, as having Attention Deficit Hyperactivity Disorder (ADHD). This group consisted of 100 children, 65% of these were males and 35% were females.

Second study group regarded as a control group, characterized by prosocial behavior, consisted of 100 children, matched for age and gender with first group (65% of these children were males and 35% were females).

Blood Sample was derived from both study sample for measurement of TSH concentration.

The serum was obtained by putting the blood samples in a clean dry plain plastic tube and was allowed to clot at 37°C for 10-25 minutes before centrifugation. Centrifuged at 3000 rpm for 15 minutes, for quantitative determination of Thyrotrophic (TSH) in serum by ELISA.

### RESULTS

Out of 100 studied children with ADHD, 65% were males and 35% were females, as well as the boys were more hyperactive than girls. The TSH level significantly increase in ADHD group 2.7789mIU/L +1.558 than control group or prosocial children 2.0545mIU/L +3.34410, with a significant differences (p<0.05) between the ADHD and control Groups (table- 1).

**Table (1) Statistic comparison between mean TSH among the study groups**

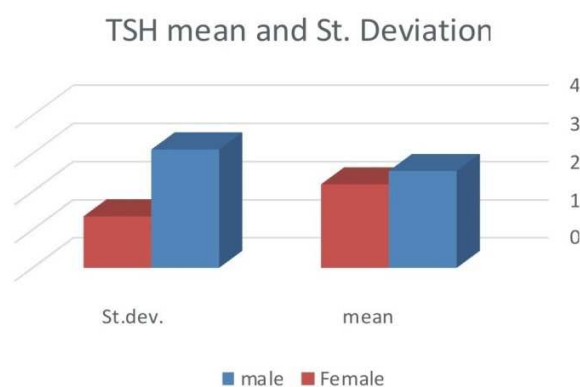
TSH (mIU/L) statistics	ADHD&ADHDwithAggressive (n=100)	Prosocial (n=100)	t	P- Value	Significance
X ±Sd TSH	2.7789±1.558	2.0545±3.34410	1.964	.050	S

Among the one hundred ADHD children, (table- 2), 51% had ADHD symptoms, were 33% males, and 18% were females. While 49% had both ADHD comorbid with Aggression, was found in 32% (32/49) of boys and in 17% (17/49) of girls (figure -1).

**Table (2) Mean and standard deviation of TSH among ADHD study groups and control study group**

Behavior Disorder	Statistic parameters	TSH (mIU/L)
ADHD (n= 51)	Mean	2.9902
	Std. Deviation	1.65301
ADHD+AG (n= 49)	Mean	2.5590
	Std. Deviation	1.43565
Prosocial (n= 100)	Mean	2.0545
	Std. Deviation	3.34410
Total	Mean	2.4167
	Std. Deviation	2.62722

**Fig.1: Mean and standard deviation of TSH (mIU/L) among the study groups according to gender**



In the present study, the mean of serum TSH levels are elevated  $2.9902 \pm 1.65301$  in the ADHD Group than ADHD comorbid with Aggressive, despite that lower  $2.5590 \pm 1.43565$  in the ADHD comorbid type but it was statistically non-significant ( $p < .$ ). The number of children with High serum TSH levels increased in the age group 9- 10 years at the 4<sup>th</sup> class in the ADHD group  $31/51$  ( $3.0138 \pm 1.53455$ ) than in the ADHD comorbid with Aggressive  $25/49$  ( $2.0231 \pm 3.21727$ ) With a significant differences ( $p < .$ ) between these groups, while there was non significant Differences in the mean of serum TSH levels between ADHD group  $2.8454 \pm 1.54831$  than in the ADHD with Aggressive  $2.1763 \pm 1.522$  (table 3), compared to the control or prosocial children Who are matched in the age, gender and class (table 4).

**Table (3) TSH mean's concentration according to the age of the study groups**

TSH (mIU/L) mean $\pm$ Sd	ADHD (n=51)	ADHD & conduct disorder (n=49)	t	P- Value	Significance
9-10 Y	$3.0138 \pm 1.53455$ n=31)	$2.0231 \pm 3.21727$ (n=25)	2.111	.037	S
11-12+>	$2.8445 \pm 1.54831$ n=20)	$2.1763 \pm 1.522$ (n=24)	1.438	0.158	NS

**Table (4) TSH concentration Level according to school children categories**

TSH (mIU/L) concentration Level	School children categories			Total
	ADHD	ADHD & conduct disorder	Prosocial	
Normal	30 58.8%	40 81.6%	98 98.0%	168 84.0%
Abnormal	21 41.2%	9 18.4%	2 2.0%	32 16.0%
Total	51 100.0%	49 100.0%	100 100.0%	200 100.0%

$X^2 = 38.840$   $P < 0.000$  (HS)

## DISCUSSION

ADHD is one of the most common psychiatric problem of childhood in all the parts of the world, In our study, out of the 100 school children with ADHD were involved in this study, males were more affected by ADHD male: female ratio was 1.9:1. These finding are supported by other researchers<sup>20, 21</sup>, and the lower incidence of ADHD among females might be related to having a relatively larger caudate nucleus than males<sup>22, 23</sup>.

In our 100 studied ADHD children the serum TSH levels increased in the age group 9-10 years at the 4<sup>th</sup> when compared with other age groups, also when compared to the control or prosocial group who are similar in the age, with a significant differences between ADHD group and ADHD comorbid with Aggressive.

Weiss et al, (1993) concluded that the prevalence of thyroid hormone abnormalities was higher in children with ADHD than in the normal population.

Thyroid function can be determined either directly by measuring the primary thyroid gland product T4 (preferably as free T4) or indirectly by assessing TSH concentration, sensed by the pituitary<sup>25</sup>.

The results of our study are consistent with the results of other clinical studies among children at a clinic specializing in learning and behavior problems that found an association between TSH concentration and ADHD<sup>26,27,28</sup>. It was found that 51% of the studied children had ADHD, and 49% had both ADHD comorbid with aggression, the percentage of aggression was more among males (75%), while the percentage among females was 25%. This was confirmed by Pataki, who found that 7.9% of boys were Aggressive in comparison to 2.3% in girls<sup>29</sup>. Also explained by American psychiatric association when stated that males are more physically aggressive than females. Quinn and Wigal stated that ADHD often unrecognized some symptoms such as inattentiveness and poor school performance in girl are seen as the hallmark signs of ADHD in females<sup>30</sup>. Which explained partly because female symptoms are not recognized as typical indications of ADHD and may be because these symptoms are less noticeable and less troublesome to adult than males symptoms, the tendency of girls to suffer silently- often means that they bear the burden of untreated ADHD for a much longer time than do boys. In the current study, the mean of serum TSH level was higher in ADHD group than in ADHD group comorbid with conduct or aggressive behavior, with no significant differences between the two groups, also the study showed that about half of the ADHD children are Aggressive, there are several probabilities to why those children are Aggressive, first of all, the areas where they live suffered and still suffering from wars and shelling, this environmental factor may be the cause of their aggression because these environment was polluted by the lead or the gases. Secondly, the type of the diet the children used, may be the cause of the variations in the mean of TSH level, there are other factors such as the genetic background of their children which is not discussed in this study, therefore, El- Baz et al stated that measurement of TSH and T3 should be incorporated in the work up of children in families having ADHD and or Aggression<sup>23</sup>.

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