# THYROID HORMONES PROFILE AMONG CHILDREN WITH ATTENTION DEFICIT HYPER ACTIVITY DISORDER

By

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### ABSTRACT

**Background**: Attention-deficit hyperactivity disorder (ADHD) is considered to have a biologic basis, but the precise cause is unknown. It is one of the neurodevelopmental abnormalities observed frequently in children with generalized resistance to thyroid hormone, suggesting that thyroid abnormalities may be related to ADHD.

Aim of this study: to assess thyroid hormones profile among children with ADHD.

**Methods:** This was a case control cross sectional study, in which 60 ADHD children were recruited from Bab Elsharya outpatient pediatric psychiatry clinic and compared with 28 healthy control children of same age who participated in this research. Serum total T3, total T4, and TSH were assessed with (ELIZA).

**Psychometric procedure:** The Stanford Binet Intelligence Scale, the Arabic version of Conner's Parent Rating Scale-Revised-Long version, and social score were used to calculate social standards of families.

**Laboratory assessment:** Serum total T3, total T4, and TSH were assessed with (ELIZA), in which 60 ADHD children were recruited from Bab Elsharya outpatient pediatric psychiatry clinic and compared with 28 healthy control children of same age who participated in this research.

**Results:** About 80% of the participants were males and 20% were females. Diagnosis according to the Diagnostic and statistical manual of mental disorders, 4th ed. (DSM-IV) showed that 58 (96.7%) of the patients were diagnosed with ADHD combined type by DSM-IV and only one patient(3.3%) had ADHD inattentive type. Forty percent of the patients were from low socioeconomic class, followed by 26.7% from moderate socioeconomic class. There was a statistically significant difference between cases and control groups in all components of Conner's Parent Rating Scale; all cases had higher means than the control group (P = 0.001). There was no significant difference between the study group and their siblings in serum total T3, thyroid-stimulating hormone, T4 (P > 0.05).

Conclusion: Children with ADHD have no thyroid profile abnormalities.

*Key words:* attention-deficit hyperactivity disorder, socioeconomic standard, thyroid hormone profile.

### INTRODUCTION

The diagnosis of Attentionhyperactivity deficit disorder (ADHD) is made in children and adults who show developmentally inappropriate levels of inattention, over activity, and impulsivity; these symptoms cause significant impairment in the individual's functioning in both the home and school or work environment **Psychiatric** (American Association, 2000).

ADHD is considered to have a biologic basis, but the precise cause is unknown. It is one of the neurodevelopmental abnormalities observed frequently in children with generalized resistance to thyroid hormone (GRTH), suggesting that thyroid abnormalities may be related to ADHD (Weiss et al., 1993).

An association has been recognized between behavioral and psychological changes and thyroid dysfunction in humans since the 19th century. In a recent study. 66%of children with ADHD were found to be hypothyroid, and supplementation with thyroxin was largely curative

### (Aronson and Dodds, 2005) (Beaver and Huang, 2003).

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A study in India by (Suresh et al., 1999) concluded that iodine deficiency can cause learning disabilities. poor academic motivation, and impairment of cognition; the same study reported that case reports of thyrotoxicosis ADHD patients rare. in are Symptoms may be subtle, leading to a missed diagnosis. In patients with no characteristic signs of hyperthyroidism. treatment resulted in control of hyperactivity, increased attention span, and improved language patients function in with no characteristic of sign hyperthyroidism (Suresh et al., 1999).

similarity The between of thyroid profile symptoms abnormalities and those of ADHD may attract attention to the possible etiological relationship between these disorders. The prevalence of thyroid dysfunction among patients with ADHD was significantly higher than that among the general population. Identification and treatment of thyroid profile abnormalities are

important considerations when there is an exacerbation of ADHD symptoms in patients whose symptoms had been controlled previously (Weiss et al., 1993). Therefore, we assessed thyroid hormone profile in ADHD patients to examine this etiological relationship.

## PATIENT AND METHODS

This study included 60 Egyptian children diagnosed with ADHD. All of them were selected from Bab Elsharva outpatient pediatric psychiatry clinic during the period from February to May Twenty eight healthy 2018. control children were selected from among normal children of the same age. All the patients ranged in age from 4 to 14 years, sexes, and fulfilled the both Diagnostic and statistical manual of mental disorders, 4th ed., text revision (DSM-IV-TR) diagnostic criteria of ADHD (American **Psychiatric Association**, 2000).

## **Inclusion criteria:**

- 1. Age: (4-14 yrs.) old.
- 2. Sex: both gender (Male & Female).
- 3. DSM IV TR diagnostic criteria of ADHD (American Psychiatric Association, 2000).

## **Exclusion criteria:**

- 1. MR (I-Q below 70 as assessed by Stanford Binnet test).
- 2. Organic etiology.
- 3. Congenital disorders.
- 4. Any chronic medical illness.
- 5. Receiving medical treatment for systemic disorders.

The control group was chosen from normal children os the same age .both the patient and the control group had the same educational and socioeconomic level as well as the same genetic background. All patients had mental retardation (MR) (IO)below 70 as assessed by the Stanford Binet test). organic etiology. Children with congenital disorders, any chronic medical illness, or those receiving medical treatment for systemic disorders were excluded from the study.

# All the studied patient & control were subjected to the following:

# I- semi structural interview:

A specially designed semi structural interview obtained from the Al-Azhar pediatric psychiatry sheet was used to determine demographic data, personal history (prenatal, natal, and childhood history), past history, family history, and mental state examination. The diagnosis was made according to the DSM-IV criteria (American Psychiatric Association, 2000).

### **Π-** Psychometric assessment by:

## A - Stanford Binet Intelligence Scale (Ahmad and Lewis, 1972):

This is the Arabic version of the Stanford Binet Intelligence Scale of general intelligence by (Ahmad and Lewis, 1972). It assesses the following abilities or cognitive areas: memory, comprehension, perception, language abilities, and performance abilities.

These abilities or areas are covered by a variety of subtests that differ according to the age group, ranging from board, picture object identification and at younger ages to memory, vocabulary, absurdities. verbal similarities, and reasoning in older ages.

The score of these subtests is then converted into a figure indicating age' 'mental (the average age of a child achieving that score). Then, mental age is divided by chronological age of the child and multiplied by 100 to arrive at the intelligence quotient or IQ. An IQ of 100 means that child's chronological and the mental ages match. Traditionally, of 90-109 IQ scores are considered average.

B- The Arabic version of Conner's Parent Rating Scale-Revised-Long version (El-Sheikh et al., 2002)

developed This was bv (Conner's et al. 1997), translated by (El-Sheikh et al. 2002), and validated by use in many subsequent researches. It is a paper-and-pencil screening questionnaire designed to be completed by parents to help determine whether children between the ages of 3 and 17 years might have ADHD. It consists of 80 questions, to be answered by parents, each followed by four choices: 0 (not at all), 1 (just a little), 2 (pretty much), or 3 (very much).

## C- Social score to calculate social standards of families (Fahmy and El-Sherbini, 1983)

This is the type of social score used to correlate the social standard with the knowledge attitudes and practices of certain groups with certain health problems related to culture. The model is modified by certain additions of some social indices that include the presence or absence of audiovisual aids of information inside houses. Thus, the indices used were education of the father, education of the mother, per-capita income of family members, crowding index, sanitation in general, family size, and information tools in the house. The total score summed is 37. A total score of 20–25 indicates a low social standard. A middle social standard is determined by a total score of 26–30, whereas high social standard needs total score of 31–37 (Fahmy and El-Sherbini, 1983).

### **III-** Laboratory assessment:

# Of Serum total T3, T4, and TSH by the following technique:

A volume of 3 ml of venous blood was withdrawn from every participant in our study (case and control). Blood was centrifuged, serum was separated and stored at 20°C until assay was performed. Laboratory assessments of serum total T3, total T4, and thyroid stimulating hormone (TSH) were performed using the enzymelinked immuneosorbent assay. Expected normal values are as follows: total T3 (71-207 ng/dl), total T4 (6.43-12.17 ng/dl), and TSH (0.35-5.5 µIU/ml).

### Assay procedure:

Before assay, the reagents were allowed to stand at room temperature (18–26°C). All reagents were gently mixed before use. The desired number of coated strips was placed in the holder. A volume of 50  $\mu$ l of TSH standards, control and patients, were pietted. A volume of 100 µl of ready-touse enzyme conjugate was added to all wells. The plate was covered and incubated for 60 min at room temperature (18–26°C). Liquid was removed from all wells. The wells were washed three times with 300  $\mu$ l. Of 1× wash buffer and blotted on absorbent paper towels. A volume of 100 µl of tetra methyl benzidine (TMB) substrate was added to all wells. Incubation was performed for 15 min at room temperature. A volume of 50 µl of stop solutions were added to all wells and the plate was shaken gently to mix the solution. The absorbance was read enzyme-linked on an immunosorbent assay reader at 450 nm within 15 min after the addition of the stopping solution. Expected references (0.35 - 5.5 μIU/ml).

## Statistical analysis:

The Wilcoxon signed-ranks test was used. The Spearman  $\rho$  method was used to test the correlation between numerical variables. Data were analyzed using SPSS win statistical package version 17 (SPSS Inc., Chicago, Illinois. USA). Numerical data were expressed as mean and SD or median, and range as appropriate. Qualitative data were expressed as frequency and percentage. The c2relation between qualitative variables **(Surwillo, 1980)**. Comparison of categorical variables between the study group and their siblings was carried out using the McNemar test. For quantitative data, comparison between two groups was carried out using the Mann-Whitney Utest (nonparametric t-test). Different scores between the study group and their siblings were compared. A P-value less than 0.05 were considered significant.

### RESULTS

Table (	(1)+	Domographic	charactoristics	of the a	studied groups
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	Ν	%				
Age (Mean ± SD)	8.02	2.3				
Gender						
Male	64	72.2				
Female	24	27.3				
socioeconomic standard of the patients * (Holyachi SK, Santosh A 2013)						
Very low	16	26.7				
Low	24	40				
Moderate	16	26.7				
High	4	6.6				
Residence						
Urban	57	64.8				
Rural	31	35.2				

**Table 1:** shows the socioeconomic standard of the patient groups; about 40% were from a low socioeconomic level, followed by 26.7% from a moderate socioeconomic level and a very low socioeconomic level (26.7%); however, 6.6% were from a high socioeconomic level.

	Cases	Control	
Stanford Binet test	Mean ± SD	Mean ± SD	P value
Memory	77.7 ± 7.8	98.6±4	0.001*
Comprehension	$84.2\pm6.3$	99.7 ± 4.2	0.001*
Perception	$82.5\pm7.5$	$97.9\pm4.4$	0.001*
Language abilities	$79.6\pm9.1$	97.6 ± 3.6	0.001*
Performance abilities	81.4 ± 7.7	97.1 ± 3.2	0.001*
Total IQ	$85.6\pm6.9$	96.6 ± 15.9	0.001*

 Table (2): Results of the IQ test (Stanford Binet Intelligence Scale) in both studied groups.

**Table 2:** In terms of the Stanford Binet test, there were statistically significant differences between the cases and controls in the IQ (P < 0.05). The case group had significantly low IQ compared with the control group in all components and the total score.

 Table (3): Conners' parent rating scale-revised-long version in cases and controls

	Cases	Control	
Subscales	$Mean \pm SD$	Mean ± SD	P value
Oppositional	$78.7 \pm 11.4$	$45.7\pm3.8$	0.001*
Cognitive problems	$76.8 \pm 7.7$	$45.6 \pm 2.8$	0.001*
Hyperactivity	82.1 ± 8.9	$47.4\pm2.6$	0.001*
Anxious-Shy	$67.4 \pm 11.2$	$48.4\pm4.3$	0.001*
Perfectionism	$59.4\pm8.2$	$44.4\pm2$	0.001*
Social Problems	$80.6 \pm 12.3$	48.4 ± 3.1	0.001*

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Psychosomatic	$69.8 \pm 17.3$	$48.6\pm3.4$	0.001*
ADHD index	$74.9\pm5.3$	$45.5\pm2.7$	0.001*
Global index	$86.6\pm4.6$	$46.3\pm2.6$	0.001*
Emotional ability	$78.2\pm9.8$	$46.7\pm2.6$	0.001*
DSM inattention	$71.5\pm7.2$	$44.3 \pm 2.4$	0.001*
DSM hyperactivity	$81.4 \pm 7.1$	$45.8 \pm 2.5$	0.001*
Total Score	$80.4\pm6.6$	45.1 ± 2.5	0.001*

**Table 3:** shows that all cases had higher means than the control group in all components of Conners' Parent Rating Scale with a statistically significant difference (P = 0.001).

 Table (4): Thyroid profile in cases and control groups

	Cases		Control		
Thyroid profile	Mean	SD	Mean	SD	P value
T3 (ng/dl)	149.4	15.4	152.7	16.9	0.732
TSH (ulU/ml)	1.3	0.8	3.2	0.7	0.725
T4 (ng/dl)	9.3	1.1	10	1.3	0.075

**Table 4:** There was no significant difference between the cases and the control group (patient's siblings) regarding serum total T3, TSH, T4 (P > 0.05).

### DISCUSSION

ADHD is considered to have a biologic basis, but the precise cause is unknown. It is one of the neurodevelopmental abnormalities observed frequently in children with GRTH, suggesting that thyroid abnormalities may be related to ADHD (Weiss et al., 1993). The majority of affected children in our study group were males (80%). These findings are consistent with previous studies that show that children diagnosed with ADHD are predominantly males (**Biederman and Faraone**, **2004**).

ADHD is much more common among males than females. It is estimated that boys are two to three times more likely to have ADHD than girls. They are up to nine times more likely than girls to be referred for evaluation and treatment. This might be attributed to the fact that males with ADHD show more externalizing hyperactive disruptive behavior than their female counterparts. Girls usually tend to cluster in the inattentive subtype. Because they are do not show a behavior problem, their difficulties are often overlooked. Boys diagnosed with ADHD are usually clinicreferred because of oppositional, aggressive, and conduct behaviors. They tend to be very disruptive in drawing the classroom, the attention of their teachers (Biederman et al., 2010).

Most of the children in our study were from a low socioeconomic level. Many authors have reported that children affected by psychological disorders tend to be of low socioeconomic status (Castellanos et al., 2002). Among the different possible indicators of socioeconomic status, lower family income alone has repeatedly been shown to be correlated with the risk of ADHD (Graetz et al., 2001).

Diagnosis depends on the presence of three diagnostic criteria: inattentions. hyperactivity, and impulsiveness. Our results showed that all three criteria were present in the 60 children studied, except two children. who did not show hyperactivity.

These findings are consistent with many previous studies that found that the combined type of ADHD is the most common subtype, followed by the predominantly inattentive subtype, followed by the predominantly hyperactive subtype (**Biederman** et al., 2000).

Our results showed that ADHD cases had lower means than control participants for all components of the Stanford Binet Intelligence Scale.

Recently, it has been reported frequently that children with ADHD have on average a lower IQ than children without ADHD.

ADHD symptoms may directly cause an individual to perform

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poorly on the standard test of intelligence (Barkley, 1997).

In terms of the thyroid profile (TSH, T3, T4), the levels of the three hormones in the study group with within normal; no thyroid dysfunction was detected. There was no statistically significant difference between study the group of ADHD patients and their siblings in the total T3, T4, and TSH levels. These results are in agreement with many previous studies that have examined the association between thyroxin and TSH, psychiatric diagnosis, and neurocognitive functioning; most of these studies reported a low prevalence thyroid of concentration abnormalities in psychiatric clinic-referred children (Refetoff, 1994). In addition, (Spencer et al., 1999) reported that most ADHD patients do not thyroid resistance show to addition, hormone (RTH); in patients with ADHD usually have normal thyroid hormone levels.

Another study, in contrast, found that 60% of patients with RTH also have ADHD, pointing to thyroid dysfunction as a potential cause of ADHD (Davis et al., 1995).

Also, our results differed from those of the study of (Hauser et al., 1993), who evaluated the presence and severity of ADHD in 18 families with a history of GRTH. They found that in the study sample, ADHD is associated strongly with GRTH. Symptoms suggestive of this disorder have been reported in patients with GRTH, a disease caused by mutations in the thyroid receptor- $\beta$ gene and characterized by reduced responsiveness of peripheral and pituitary tissues to the actions of thyroid hormone.

stronger In addition. a evidenced relationship was between lower concentrations of free T4 and more frequent mood symptoms and more perhaps ADHD patients may have subtle abnormalities in the hypothalamic-pituitary-adrenal axis. Free T4 may contribute directly toward poor attention, as suggested by studies of children with hypothyroidism (Murphy et al., 1990).

These differences between our study and other studies may be because of the small sample size of our study compared with the previously mentioned studies; in addition, most of the children in the case group had the combined type not the predominate in attentive type or hyperactive-type ADHD, which is reported more in children with thyroid dysfunction.

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It may also be because RTH is not a common disorder.

We faced the following study limitations which are the number of children in the control group was limited to 28 normal children of the same age because of refusal of many parents to complete the test on their normal children. Also, our assessments relied on indirect reports parental and direct interviews with children, but did not include information collected from teachers. Furthermore, our study was carried out on a small sample size of clinic-referred ADHD children who might be non-representative for all children with ADHD.

## CONCLUSION

Children with ADHD have no thyroid profile abnormalities.

### RECOMMENDATIONS

Based on the above data we recommend usage of free T3 and T4 instead of total T3 and T4. Also, we need further more sample size in order to attain further consistency. Moreover, collected information from teachers with indirect and direct parenteral reports is with higher significance.

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قياس هر مونات الغدة الدرقية في أطفال مرضي فرط الحركه المصحوب بقلة الانتباه

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فرط الحركة المصحوبة بنقص الانتباه معروف أنه أحد أكثر الحالات الصحية المزمنة شيوعا لدى الأطفال في سن المدرسة فهو يصيب 3-9% على مستوى العالم.

وجد أن المسببات الدقيقة للتغيرات الهيكلية والوظيفية المؤثرة في فرط الحركة وقلة الانتباه غير معروفة ولكن من المرجح انها ناتجة عن تفاعل بين عوامل جينية وفيسيولوجية وبيئية التي تؤثر على النمو العقلي والعصبي الوظيفي.

إن نقص الأيودين وضعف الغدة الدرقية لدى الأم وكذلك عيوب التكوين الخلقية للغدة الدرقية في المواليد أثناء النمو العقلي مع العوامل الوراثية تساهم في العجز العصبي.

### الهدف من الرسالة:

قياس مستوي هرمونات الغدة الدرقيه في اطفال مرضي فرط الحركة المصحوب المصحوب بقلة الانتباه.

الجزء العملى: العينة والأدوات:

### المجموعة الأولى:

(60 طفل مصرى) تم تشخيصهم كمرضى فرط حركة مصحوباً بنقص الانتباه وفقا للدليل التشخيصى والاحصائى للجمعية الأمريكية للطب النفسى الصورة الرابعة المراجعة ،وقد تم اختيار هم من عيادة الاطفال الأمراض النفسية والعصبيه فى مستشفى با ب الشعريه الجامعي، يتراوح عمر هم من 4-14 سنة من الجنسين (ذكور وإناث) ،ومستوى THYROID HORMONES PROFILE AMONG CHILDREN WITH ATTENTION DEFICIT HYPER ACTIVITY DISORDER Mohamed khalaf abdel-Hamed Abdallah, Mohsen Taha Elkeiy, Kamel Soliman Hamad, Al Hassan Mostafa Zahran

ذك ائهم يتعدى ال (70%) ولا يع انون من أى مسببات عضوية للمرض أو أسرض مزمن،ولا يتناولوا علاج دوائى لأمراض مزمنة.

المجموعة الثانية: (مجموعة ضابطة):

28 طفلا مقابلين للمرضى من الجنسين يتراوح عمر هم من 4-14 سنة وبنفس معايير استبعاد المرض وعلى ألوسابقة لكشف نفسي. استبعاد المرض وعلى ألايكون لديهم تاريخ مرضى سواء كان نفسياً أوسابقة لكشف

الأدوات:

لكلا المجموعتين تم عمل الأتى:

أخذ تاريخ مرضى كامل وتم توقيع كشف طبى عليهم.

2. خضع جميع الأطفال للاختبارات الأتية:

- اختبار ستانفورد بينية:الصورة العربية من اختبار ستانفورد بينية لقياس مستوى الذكاء العام.

- مقياس كونورز لتغيير سلوك الطفل "تقدير الوالدين"الصورة المطولة المراجعة لمعرفة مدى حدة المرض ولتأكيد التشخيص الاكلينيكي.

- قياس المستوى الاجتماعى لعائلات الأطفال المصابين بمرض مزمن باستخدام مقياس فهمى والشربينى 1986.

3. تم أخذ عينات دم لجميع الأطفال لعمل تحليل هرمونات الغدة الدرقية في الدم.

توصلت الدراسة إلى النتائج الأتية:

- أغلب العينةمن الذكور (80%) بينما (75%) من العينة الضابطة من الذكور.

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- أطفال فرط الحركة المصحوبة بنقص الانتباه كانوا من مستوى اجتماعى متوسط (26.7%) ، بينما (6.6%) من العينة من المستوى الاجتماعى المرتفع.

- غالبية المرضى أظهروا النمط المركب من مرض فرط الحركة المصحوب بنقص الانتباه ويليه نمط عدم الانتباه.

- سلوك المعارضة والتحدى وجد فى (30%) من الحالات، بينما حالة واحدة كانت تعانى من مرض سوء سلوك وكذلك حالة واحدة تعانة من مرض المتلازمة (3.3%)، وأربع حالات لم يكن لديهم أمراض نفسية مشتركة (13.3%) بينما (50%) من المرضى من اثنان أو أكثر من الأمراض النفسية المشتركة.

- الأسباب المحتملة فى مرض فرط الحركة المصحوب بنقص الانتباه ماقبل الولادة هى الضغوضات الحياتية للام (30.33%)، مشاكل عائلية (30%) ، مشاكل طبية (26.9%) وهى ارتفاع نسبة السكر فى الدم وإالتهاب رئوى والنقرص بالإضافة لتناول الأم الحامل للعقاقير (33.3%) وكذلك مضاعفات الحمل من اجهاض منذر (16.7%) ، وضغط دم مرتفع مع الحمل (3.1%)، نقص افراز الغدة الدرقية فى حالتين (6.7%).