

STUDY OF TESTOSTERONE LEVEL IN A COHORT OF HYPERACTIVE SCHOOL CHILDREN VERSUS SCHOOL CHILDREN WITH PRO-SOCIAL TRAITS IN IRAQI PROVINCE

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ABSTRACT

Background: The various childhood problems that are often subsumed under the heading of "hyperactivity" occur in various combinations and, apparently, for various reasons. **Objective:** To assess the association between testosterone concentrations, among primary school children with attention deficient hyperactivity disorder (ADHD), versus control school children with pro-social traits. **Subjects & Methods:** A cross sectional study was conducted for the period from the first of April- 2013 to the 31 April-2014. The study sample was one hundred primary school children diagnosed with behavioral disorders including ADHD with or without conduct

disorder, in comparison with (100) control school children characterized with pro-social traits. Assessment of behavioral disorders (ADHD, and conduct) depend on Rutter child behavioral Questionnaire (RCBQ), as a scale used by teachers for assessment of school children behavior, including disorders in behavior, (ADHD and conduct or antisocial behavior), versus pro-social behavior. Measurement of serum testosterone levels was done to the school children with ADHD with or without aggressive behavior and to the controls, pro-social character. **Result:** Testosterone level highly increase 0.6506 ± 0.654 ng/ml for male's school children with ADHD than its level in pro-social control group 0.4492 ± 0.4198 ng/ml. On the other hand ADHD, comorbid aggression group had higher testosterone levels (0.8786 ± 0.8421) ng/ml, than non-aggressive ADHD group (0.4316 ± 0.25689 ng/ml) with a highly significant differences ($p < 0.01$). Eight (24.2%) of 33 ADHD non aggressive males had abnormal testosterone levels but in the aggressive comorbid group 11/33 (34.4%) had

abnormal levels. In contrast testosterone level for control group was abnormal in 5/65 (7.7%), with a highly significant differences ($p < 0.01$) between the disorder types in males and hormone levels. In regard to females it is found that 9/18 (50%), 3(17.6%) of 17 had abnormal testosterone levels for ADHD, and in aggressive comorbid with ADHD. There was no significant differences between the disorder types in females and the hormone levels. Testosterone levels highly increased in ADHD non Aggressive group ($0.6575 \pm 0.5518 \text{ ng/ml}$), ($0.8467 \pm 0.999 \text{ ng/ml}$), for the age 9, 10 years. And 11 years respectively, with significant statistical difference ($p < 0.05$). **Conclusion:** Generally without concentration on the age, it seemed that testosterone levels is more in aggressive children than who have ADHD in comparison with the pro-social children.

KEY WORDS: Attention deficit hyperactivity disorder (ADHD); Testosterone hormone; conduct disorder; Pro-social behavior; Anti-social behavior, Rutter child behavior questioner; Rutter teacher behavior scale.

INTRODUCTION

Childhood problems that are often subsumed under the heading of "hyperactivity" occur in various combinations and, apparently, for various reasons. The designation does not define a homogeneous group of children, does not consistently point to a common cause, and has treatment implications only in the sense that multiple simultaneous approaches must typically be considered¹. Attention-deficit/hyperactivity disorder (ADHD) has prevalence rates ranging From 3 to 9%, depending on sampling strategies and diagnosis criteria ², while 20-50% of children with ADHD continue to show residual symptoms in adulthood ^{3,4}. In children and adolescents who are developing through different stages of social and biological development within a relative short period of life time, their behavior disorders can vary considerably ⁵. In addition, there is evidence that ADHD in childhood plays a role in the later development of other specific disorders and showed that boys with ADHD diagnosis were more likely than controls to develop antisocial Personality disorder and drug abuse syndrome in adulthood. These finding lead Patterson, et.al (6). To hypothesize that ADHD and antisocial behaviors could represent two points of the same process. Furthermore, Fossati, suggested that an association between childhood ADHD symptoms and adult borderline personality disorder^{6, 7}. Changes in the concentration of hormones can have profound effects on mood and behavior in human, and the Variation in hormone levels have been implicated in some psychiatric disorders because some of the patient with major depression show hyperactivity of

the hypothalamic –pituitary-adrenal (HPA) axis characterized by excess secretion of cortisol 8 9 10. Testosterone affects the behavior of adults, but little is known about how it might affect the behavior of children. The few available studies of children have focused on aggression, hyperactivity and other behavior disorders¹¹. For instance Dominance can have a powerful impact on behavior and social functioning and is best measured via testosterone¹² 13. because in the field of social endocrinology that play an important role in aggressive behaviors, no hormone given greater attention than testosterone 14. Testosterone is an androgen, meaning it is masculinizing steroid hormone produced in both men and women by the gonads, adrenal glands and within the brain, although because of the fact that the testes produce testosterone in much larger quantities than other source, men tend to have between seven to ten times as much circulating testosterone as women despite that the great sex difference in circulating levels, but in many cases testosterone has been shown to exert similar influences on social behavior across sexes 15. The aim of the present study was to assess the level of testosterone in school children presented with hyperactivity versus control group with pro-social traits.

Subjects and Methods

A cross sectional study was conducted for the period from the first of April-2013 to the 31 of April-2014. The present study involved 100 hyperactive school children, from classes 4th, 5th, and 6th, their ages were between 9 to 14 years. 65 boys and 35 girls, versus (100) matched school children with pro-social behavior. The study sample was selected from 9- primary schools in Baquba City, center of Diyala Province, these schools were selected randomly. Rutter Child Behaviour Questionnaire (RCBQ), used as a scale for diagnosis of behavioral disorders. Rutter child Behaviour Questionnaire (RC B Q) for completion by teacher in its original version was developed by Rutter at 1967¹⁹. 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 pro-social trait. First study group diagnosed according to RCBQ, as having Attention Deficit Hyperactivity Disorder (ADHD). Blood samples were derived from both study's groups. All blood Sample was carried out in the end of April at a stander time between 8 -10 a.m. in the morning. Blood samples were centrifuged and the serum were frozen until measurement of testosterone level from each study children.

RESULTS

Testosterone levels highly increase (0.6506 ± 0.654 ng/ml) among school children with ADHD than in the pro-social students control group (0.4492 ± 0.41982 ng/ml) who are matched in the age, and gender. With significant statistical differences ($p < 0.01$), (Table 1). Out of 100 ADHD, 49% (49 /100) had ADHD comorbid with aggression. Of the last 32% (32/ 49) were boys and 17% (17/49) were girls. The study showed that the aggressive comorbid with ADHD students had higher Testosterone levels (0.8786 ± 0.84216 ng/ml) than in the ADHD without aggressive behavior. With a highly significant statistical differences ($p < 0.0001$), (Table-2). Among 33 ADHD non aggressive boys, 25 (75.8 %) boys had normal testosterone level. And eight (24.2%) had abnormal level. While among the aggressive comorbid type 21 (65.6%) from 32 boys had normal levels and 11 (34.4%) had abnormal testosterone levels. Versus school children with pro-social characters, boys 60 (92.3%) of 65 had normal level and only 5 (7.7%) with abnormal testosterone level, with a highly significant differences ($p < 0.004$) between the disorder's type in boys and the hormone level (Table 3). The same table showed equal percentage (50%), for normal and abnormal testosterone level among female with ADHD without aggressive character. While for the aggressive comorbid with ADHD only 3 from 17 (17.6%) females had abnormal levels. In regard to the pro-social females, out of 35 only 12 (34.3 %) with abnormal levels. No significant statistical difference was found, ($P = 0.131$). The results reveals that, serum testosterone levels highly significantly increase ($p < 0.01$) in the ADHD non aggressive group (0.6575 ± 0.5518 ng/ml) for the age 9, 10 years, while testosterone level increase (0.8467 ± 0.999 ng/ml) in aggressive comorbid with ADHD students for the age more than 11 years compared with ADHD symptoms group at the same age, with significant statistical difference (Table – 4 and 5).

Table (1): Statistic comparison between mean testosterone among the study groups.

Testosterone statistics	ADHD with & without aggression (n=100)	Pro- social traits (n=100)	t test	P- Value	Significance
mean±Sd (Testosterone)	.6506±.654	.4492 ±.41982	2.592	.01	HS
Range (Testosterone)	0.20 – 5.19	-----	----	-----	-----

Table (2): Mean and standard deviation of testosterone among ADHD study groups

Testosterone statistics	ADHD without aggression (n=51)	ADHD with aggression (n=49)	F test	P- Value	Significance
X ±Sd (Testosterone)	.4316±.25639	.8786±.84216	14.986	.000	HS
Range (Testosterone)	0.20 – 5.19	-----	----	-----	-----

Table (3) Distribution of testosterone Level by gender according to type of behavior disorder the study samples.

Sex	Testosterone Level		Disorder type			X ² -test
			ADHD	ADHD+AD	Pro-social	
Male		Normal	25	21	60	X ² =11.124 P=0.004 (HS)
			75.8%	65.6%	92.3%	
	Abnormal	8	11	5		
		24.2%	34.4%	7.7%		
	Total		33	32	65	
			100.0%	100.0%	100.0%	
Female	Testosterone Level	Normal	9	14	23	X ² =4.062 P=0.131 (NS)
			50.0%	82.4%	65.7%	
	Abnormal	9	3	12		
		50.0%	17.6%	34.3%		
	Total		18	17	35	
			100.0%	100.0%	100.0%	

Table (4) Distribution of testosterone Level according to the type of behavior disorder among the study samples.

Testosterone Level	Disorder type			Total
	ADHD	ADHD+AD	Pro-social	
Normal	34	35	83	152
	66.7%	71.4%	83.0%	76.0%
Abnormal	17	14	17	48
	33.3%	28.6%	17.0%	24.0%
Total	51	49	100	200
	100.0%	100.0%	100.0%	100.0%

Table (5): Testosterone mean's concentration according to the age of the study groups

Testosterone mean \pm Sd	ADHD(n=51)	ADHD+ Agg (n=51)	T	P- Value	Significance
X \pm SdTestosterone of (9-10) n=31)	.6575 \pm .55185 n=31)(.3721 \pm .11084 n=25)(4.138	.000	HS
X \pm SdTestosterone of (11-12+) n=20)(.3960 \pm .14623 n=20)(.8467 \pm .999 n=24)(1.1999	0.05	S

DISCUSSION

To examine the role of testosterone concentration as a part of endocrine factors in children during pre-adolescent or even at the onset of pubertal development with behavior disorders, the mean levels of testosterone were measured in one hundred ADHD students for the purpose of comparing the hormone levels between those groups versus pro-social control group (100 school children), as behavior disorder is concerned. In the current study, 51/100 (51%) had ADHD non aggressive behavior and 49/100 (49%) had ADHD comorbid by aggressive characters. From whole 100 ADHD school children the boys were more Hyperactive 65/100 than girls 35/100. The percentage of Aggression was more among males 32 % (32/49) of

boys and in 17 % (17/49) of girls. This was explained by American psychiatric association when stated that males are more physically aggressive than females¹. Furthermore Quinn and wigal stated that ADHD symptoms are seen as the hallmark signs of ADHD in females, this may be because females symptoms are not recognized as typical indication of ADHD and may be these symptoms are less noticeable and less troublesome to adult than males symptoms²². 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 present study, for the whole 100 ADHD, school children, mean testosterone levels highly increase ($0.6506 \pm 0.654 \text{ ng/ml}$), with a significant differences ($p < 0.01$) than in the school children with pro-social control group ($0.4492 \pm 0.4198 \text{ ng/ml}$) who are matched by the age and gender. This was supported by Chance et al., who found that testosterone levels were higher in the psychiatric than the normal group and reported that, the testosterone was associated with withdrawal and aggression especially after controlling for intelligence¹⁷. Chance et.al, also found that the testosterone was not related directly to cognitive ability, and the boys with less cognitive ability appeared more adversely affected by high testosterone levels, and suggested that testosterone may be useful biological marker for children at risk for disruptive behavior disorders¹⁷. The study showed that children with aggression comorbid with ADHD had higher and significant testosterone Level than non-aggressive children, although there is evidence that both testosterone and cortisol have organizational and active effects on aggressive behavior in human. The available data are inconclusive ¹⁸. Testosterone an important factor in cerebral chemistry as well as involved in the modulation of behaviors by interacting with growth factors, Neurotransmitters, neuropeptide, neuro-active steroids and neuron second messengers. The molecular mechanism by which testosterone regulates human aggressive behavior is not clear. In addition, some studies reported that violent aggressive behaviors of males seem to correlate with the impairment of noradrenergic function, which probably regulate by the gonadal hormones. Our findings are consistent with the results of many studies, which demonstrate that the plasma Testosterone level is higher in male than in female violent offenders at their early life and is Associated with lifetime aggressive behaviors and impulsive aggressiveness ¹⁹. Giotakos et al, stated that the testosterone levels and aggression-impulsivity scores were higher in group of rapists when compared to the controls, and this aggression-impulsivity scores were associated with luteinizing hormone (LH) levels²⁰. And in the recent study they found that the hyperactive hypothalamus-pituitary gonadal (HPG) axis of these persons was associated with their novelty seeking behavior²⁰. Our result showed that the level of hormone increased in children in younger

ages 9, 10 years Specially in those who have ADHD, but the levels of testosterone increased in children older than 11 years old particularly Aggressive group. Ostatnikova, et al, found that salivary Testosterone levels remained stable in pre-pubertal subjects, and no significant increase from The age 6 until 9 years in both sexes. In fact, reported that serum hormone levels correlate with hormone levels in matched saliva samples in a linear fashion 20, 21 . Generally, the study showed that Testosterone levels increased in children in younger ages especially in those who have ADHD, but the level increased in children older than 11 years particularly aggressive boys. Without concentrating on the age, it seemed that the levels of the hormone is more in aggressive children than those who have ADHD in comparison with the children with pro-social features. The current study displayed high percentage of aggression (49%) among children who were already hyperactive, this is may be due to environmental factors in addition to hormonal factors, which contribute for the disruption and aggression where the sample collected born and raise in a hot area, poor security situation, with sectarian challenges affected the areas of current study.

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