

**Original Research Paper**

Proportion of Raised Blood Pressure and Raised Blood Sugar Level in Newly Diagnosed Attention Deficit Hyperactivity Disorder in Children

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ADHD is now considered as a disease spanning the life span. The physical co morbidities of ADHD has not been yet studied adequately. It is unknown whether ADHD is associated with any childhood or adolescent variation in the physiological parameters. The authors have examined the association between ADHD and blood pressure and random blood sugar levels. To define the extent of this hypotheses, the authors performed a cross sectional analysis of blood pressure and random blood sugar level assessment in children newly detected with ADHD. 20.9% of children with ADHD had increased blood pressure (> 90th percentile). Random blood sugar values were normal except for one value, which came as an impaired value. There was positive association between body mass index and systolic blood pressure ($\chi^2 = 4.338$, $p = 0.037$) and correlation with random blood sugar values (Pearson Correlation $r = 0.286$, $p = 0.002$). A significant proportion of children with ADHD has prehypertension. The positive association of increasing blood pressure and blood sugar with increasing body mass index in children with ADHD may indicate a potential biological association between childhood ADHD and adult metabolic syndrome. The retrospective studies on adults with metabolic syndrome should throw light on the causal factors of this world wide epidemic.

INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is one of the most common behavioural disorders of childhood¹. The Centers for Disease Control and Prevention recently reported that nearly 1 in 10 children in the United States aged 4 to 17 years have parent-diagnosed attention-deficit/hyperactivity disorder (ADHD), representing 5.4 million children, half of whom are actively receiving

medication. Criteria for Attention-deficit/hyperactivity disorder as the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision [DSM-IV-TR]), include hyperactivity and inattention, an inability to focus, becoming distracted easily, and making careless errors. Other features include impulsiveness, emotional liability, fidgeting, and excessive talking.

Attention-deficit/hyperactivity disorder is commonly associated with learning disorders and impaired school performance; it may also affect socialization and have psychiatric manifestations as mood disorders, conduct disorders, and bipolar manifestations. Furthermore, manifestations of ADHD commonly continue into adulthood, affecting 3% to 5% of the adult population. Adults with ADHD, compared with adults without ADHD, have an increased risk for substance abuse and antisocial behavior.

ADHD is characterized by pervasive and impairing symptoms of inattention, hyperactivity and impulsivity according to Diagnostic and Statistical Manual V.¹ ADHD is now becoming increasingly diagnosed and studied world-wide. Lifetime prevalence of learning disorders in US children is nearly 10%.³ The CDC reports that the prevalence of parent-reported ADHD among children has increased by more than 20% from 2003 to 2007.⁴ It is clear that hypertension, LDs and ADHD are major challenges faced by this generation of children and their healthcare providers. The multiple short term and long term sequelae makes it a major public health problem. A number of studies have observed an association between Hyperactivity /inattentiveness symptoms and an increased risk of hypertension and type 2 diabetes mellitus in adolescence and adulthood.^{2,3,4,5}

METHODS

Study Design: Hospital based cross sectional study

Study setting: A total of 110 children of 5 to 17 years of age with a DSM IV diagnosis of ADHD were selected randomly from Child Psychiatry OPD. The children included in the study did not have a history of psychiatric and cardiovascular comorbidities. All the study participants were newly diagnosed of ADHD and not taking any drugs for ADHD. Biochemical investigations done in the department of Biochemistry.

Study Period: 1 year

Study population: 110 children of 5-17years of age satisfying the inclusion and exclusion criteria. Inclusion criteria: children of 5-17years of age with a DSM IV diagnosis of ADHD. All the study participants were newly diagnosed of ADHD.

Exclusion criteria: children included in the study did not have a history of psychiatric and cardiovascular comorbidities. They are not taking any drugs for ADHD.

The study started after getting permission from human ethical committee and review board of the institution. A written informed consent was obtained from all the subjects included in the study. Patient details and past history was obtained by oral questionnaire, clinical examination, from case records and by discussing with the physician. BP was checked in the right upper limb in the sitting position. Blood pressures (systolic and diastolic) were measured using calibrated sphygmomanometer with appropriate cuff size. Participants were instructed to remain seated for at least 5 minutes prior to reading. Three separate readings at 30 second intervals were conducted with participants in a seated position with both feet on the floor and legs uncrossed. Average of the 2nd and 3rd reading is used. To interpret the blood pressure of a child, his/her height percentile has to be determined to estimate different percentile values of systolic and diastolic blood pressure. The BP level <90th percentile is normal. The BP measurements between the 90th and 95th percentiles indicate prehypertension. The BP level > 120/80 mm Hg in an adolescent is considered prehypertension. The BP level >95th percentile is hypertension. Hypertension in children is defined as an average systolic and diastolic BP more than 95th percentile for age, gender and height. Biochemical parameters as Random blood sugar was measured. Blood sugar was estimated by Glucose oxidase method after the sample was collected. About 5ml of blood was drawn under aseptic precautions from the cubital vein and collected in a test tube. Serum was separated by centrifugation and kept at -20 oC until analysis was carried out.

STATISTICAL ANALYSIS

The data were entered into a computer using package Microsoft excel. For analysis, statistical package for social sciences (SPSS) version 17 was used. Continuous variables were expressed as mean \pm standard deviation and qualitative data expressed as percentage. Independent t test used for comparing quantitative data between the groups. Categorical variables were compared using chisquare test. A P value of <0.05 is considered statistically significant.

RESULTS

A total of 110 children with ADHD were assessed. The cross sectional analysis revealed that of the 110 children with ADHD, 23(20.9%) had a systolic blood pressure value more than 90th percentile for age, gender and height (Table 1). The diastolic pressure was more than 90th percentile in 27 (24.5 %) of the study population (Table 2).

Random blood sugar levels were normal in 109(99.1%) of these children. Only one child showed an impaired value of random blood sugar (175 mg/dl) (Table 3).

There was a significant association between pre hypertension and BMI ($p=0.037$) in the study subjects (Table5,6). Also, there was a significant positive correlation between body mass index and random blood sugar (Pearson Correlation $r = 0.286$, $p=0.002$) (Table6).

Table 1

Study variables	N	Mean	Standard Deviation
Age(Years)	110	10.9	3.06
BMI(kg/m ²)	110	18.7	4.2
Systolic Blood Pressure	110	105.2	13.6
Diastolic Blood Pressure	110	73.9	8.8
Random Blood sugar	110	95.7	15.3

Table 2

Systolic BP	Frequency	Percentage
>90th	23	20.9
<90th	87	79.1
Total	110	100.0

Table 3

Diastolic BP	Frequency	Percentage
>90th	27	24.5
<90th	83	75.5
Total	110	100.0

Table 4

RBS	Frequency	Percentage
>200	0	0
140 -199	1	0.9
<139	109	99.1
TOTAL	110	100

Table 5

BMI	DBP>90TH	DBP<90TH	TOTAL
>85TH	13(11.8%)	33(30%)	46(41.8%)
<85TH	14(12.7%)	50(45.5%)	64(58.2%)
TOTAL	27(24.5%)	83(75.5%)	110

$$\chi^2 = 0.589 \quad p \text{ value} = 0.443$$

Table:6 – Pearson correlation between BMI and RBS

Other parameters	Pearson correlation	P value
RBS	0.286*	0.002

Correlation is significant at 0.05 level

DISCUSSION

In the present analysis, it was found that overweight in ADHD subjects were significantly associated with increase in systolic blood pressure. Around 23% of these children had an increased systolic blood pressure above the 90th percentile for age, gender and height. The bivariate analysis between the raised systolic blood pressure and body mass index showed a significant association ($p = 0.03$).

According to the International Pediatric Hypertension Association up to 5% of children have primary hypertension.¹ The epidemic of pediatric obesity further highlights this concern as obese children have a 3-fold risk for developing hypertension.² The mechanism linking primary hypertension to learning disorders in children has not yet been investigated. However, inflammation, toxic and heavy metal burden, nutrient deficiencies and an exaggerated stress response should be evaluated. This observation highlights the impor-

tance of blood pressure screening in all children. It has been demonstrated that children with comorbidities such as ADHD and raised BMI may be likely to exhibit blood pressure abnormalities and therefore should not be overlooked with regard to blood pressure screening.² The exact reason for the association between neurocognitive problems and hypertension has not yet been deciphered. Although this is not yet established anatomically in children, adults suffering from chronic hypertension have greater variations in frontal lobe composition ie reduced prefrontal cortex and increased white matter hyper intensities. The importance of understanding the potential impact of hypertension on neurocognition in childhood is that these changes may be reversible with adequate treatment.

In the present study, none of the subjects showed an increased random blood sugar value above 200gm/dl which is the upper limit according to the WHO criteria, though one subject had an RBS value in the “pre- diabetic” range . However a positive correlation was obtained between increasing body mass index and random blood sugar levels (Table 6). This shows that in the background of ADHD, an increased BMI might predispose to a hyperglycaemic state. Sucrose is a potent stimulus for dopamine release. The ingestion of sucrose results in an immediate increase in extracellular dopamine in the nucleus accumbens, and both sucrose intake and extracellular dopamine are enhanced if presynaptic reuptake of dopamine is blocked. The increase in dopamine may increase behavioral responses that can lead to further ingestion of sucrose. This cause an increase in body mass index and random blood sugar levels. This explains the significant positive correlation between body mass index and random blood sugar. In addition there is a reduction in striatal D2 receptors. Furthermore, there is reduced glucose metabolism in the prefrontal cortex of adults with ADHD, consistent with a loss of frontal control mechanisms. Recurrent stimulation of dopamine release may lead to desensitization of the postsynaptic dopamine

signaling pathways, which, in turn, reduces inhibitory signals generated by the frontal cortex, resulting in impulsive behavior and loss of emotional control, and symptoms of ADHD. Finally, there is also a reduction in dopamine metabolites in cerebral spinal fluid samples obtained from children with ADHD.

These observations show that childhood ADHD may be an indicator of the future expression of underlying pathologies including insulin resistance, blood pressure abnormalities and most probably metabolic syndrome. The cause of ADHD is unknown, although recent studies suggest that it may be associated with a disruption in dopamine signaling whereby dopamine D2 receptors are reduced in reward-related brain regions. This same pattern of reduced dopamine-mediated signaling is observed in various reward-deficiency syndromes associated with food or drug addiction, as well as in obesity. While genetic mechanisms are likely contributory to cases of ADHD, the marked frequency of the disorder suggests that other factors are involved in the etiology.

Identifying the etiology of ADHD is paramount for developing better ways to prevent and treat the disorder. There are several potential explanations for the association between ADHD and obesity. First, characteristics associated with ADHD, such as depression or binge eating, may result in obesity. The converse may also be true, that the presence of ADHD may interfere with the ability to lose weight via diet programs or following bariatric surgery. Sugar intake may be driving both ADHD and the risk for obesity. Obese subjects also have fewer striatal D2 receptors, which correlates with reduced glucose metabolism in the frontal and somatosensory cortices. There is also a reduction in dorsal striatal response to palatable food intake, consistent with a lower dopamine response and/or lower D2 receptors. Thus, obese individuals may overeat to compensate for impaired reward responses. Thus, a reduced dopamine-stimulated D2 receptor-mediated response to food may result in the need

to eat more palatable food (to promote dopamine responses) and a greater desire and heightened dopamine activation in response to sight of food (possibly resulting from the inhibition of frontal cortex-dependent executive control).

A number of studies suggest that ADHD may have a genetic basis, and there is increasing evidence to suggest that this may relate to polymorphisms in genes involved in dopamine neurotransmission. Indeed, there is increasing evidence to suggest that ADHD may involve alterations in mesolimbic dopamine signaling. For example, the polymorphism DRD2-TAQ-IA, which results in low striatal D2 receptors, also results in increased risk for alcohol and opioid addiction, obesity, and ADHD. Nevertheless, while the importance of genetics in ADHD is not disputed, the few genetic linkages identified to date can account for only a small percentage of ADHD cases. Thus, it is important for us to consider other possible factors that might cause or predispose individuals to develop ADHD. The dorsolateral prefrontal cortex and medial prefrontal cortex are involved in controlling behavior and motivation, and are altered in subjects with drug addiction. The observation that subjects with low D2 receptors due to polymorphisms in DRD2-TAQ-IA have altered prefrontal lobe metabolism and show a learning disability with the inability to avoid actions with negative consequences also supports a role for a causal connection between D2 receptor density and cortical control behavioral mechanisms. The additional observation that morbidly obese subjects also show altered prefrontal metabolism that correlates with low D2 receptors and addictive behaviors further supports this important link.

CONCLUSION

In a group of children newly detected with ADHD, 20.9% were “pre hypertensive”. The elevation of blood pressure values showed a significance when analysed with body mass index. This indicated that children diagnosed with ADHD had a potential to become hypertensive on

the background of an increasing weight. The blood sugar values also denoted a positive correlation with increasing BMI. This observations suggests a potent indication towards a future metabolic syndrome in these children, if left under recognised.^{1,2} By linking neurocognitive function in the pediatric population with hypertension, this study may help to direct the diagnosis, treatment and ultimately the prevention of these conditions. A causative relationship has not yet been established, and further research is warranted. However, investigating the occurrence of one when presented with the other in a clinical setting seems justified and easily implemented. ADHD is a consequence of the marked increase in intake of added sugars, then public health measures to reduce sugar intake are indicated, especially in young children (aged < 7 years), who are most predisposed to developing ADHD. As ADHD can be associated with impaired school performance, antisocial behavior, and drug addiction, the importance of such an approach could be far reaching.

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