

Prevalence and assessment of biochemical parameters of attention-deficit hyperactivity disorder children in Bangladesh

Abstract

Background and Objectives: This study aimed to evaluate some new biochemical parameters that help ensuring the early and precise diagnosis of attention-deficit hyperactivity disorder (ADHD) in blood plasma.

Design and Settings: A prospective study conducted with patients scheduled for some new biochemical parameters that help ensuring the early and precise diagnosis of ADHD in blood plasma in a Child Development Center of the Chittagong, Bangladesh.

Materials and Methods: The study was carried out at two levels. The first level was questionnaire on personal data and disease history while the second was on biochemical examination of the plasma ammonia and lactate status. A total of 100 children (age range 2 years 4 months to 12 years 6 months, mean age 7 years 5 months) were investigated in this study among 75 were male and 25 were female. This study was conducted in Chittagong Maa-O-Shishu General Hospital, Bangladesh.

Results: We observed that the level of plasma ammonia and lactate were higher in ADHD children (36–60 $\mu\text{mol/L}$; $P < 0.05$ and 22–30 $\mu\text{mol/L}$; $P < 0.05$, respectively) compare to a reference value. The prevalence of ADHD is higher in male (75%) than in female (25%) with a ratio of 3:1. Consanguinity increases the risk of having ADHD in the next generation.

Conclusion: This study concludes that there might be a correlation between ADHD and increased level of plasma ammonia and lactate level, and those might be an important parameter in the diagnosis of ADHD patients.

Key words:

Attention-deficit hyperactivity disorder, biomarkers, consanguinity, hyperammonemia, hyperlactatemia

Introduction

Attention-deficit hyperactivity disorder (ADHD) is a common, multifactorial, clinically diverse, and highly heritable neuropsychiatric disorder that is prevalently seen in children^[1,2] which affect 8–12% of children worldwide.^[3] Its consequences include inattention, hyperactivity, and impulsivity^[4] as well as cognitive deficits and social cognition impairments.^[5] All the way of life, a significant clinical feature pragmatic in ADHD patients is comorbidity with conduct depressive, bipolar, and anxiety disorders.^[4-6] It is one of the most important neurobehavioral disorders that is highly discussed, evaluated, and studied by scientists and psychologists. Diagnostic criteria for this condition have traditionally relied solely on behavioral criteria

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Access this article online

Website: www.jbclinpharm.org	Quick Response Code 
DOI: 10.4103/0976-0105.183261	

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How to cite this article: Hasan CM, Islam MM, Mahib MM, Arju MA. Prevalence and assessment of biochemical parameters of attention-deficit hyperactivity disorder children in Bangladesh. *J Basic Clin Pharma* 2016;7:70-4.

without consideration for potential biochemical underpinning. Several studies on animal and human acquaintances the dysregulation of frontal-subcortical-cerebellar catecholaminergic circuits in the pathophysiology of ADHD and abnormalities of the dopamine transporter lead to impaired neurotransmission shown by molecular imaging studies.^[3] Interestingly, some biochemical changes occur such as the decrease of the levels of norepinephrine, dopamine and serotonin in neostriatum, nucleus accumbens, and frontal cortex.^[7,8] The biochemical marker allows us to provide a useful screening procedure for ADHD. By carefully querying developmentally appropriate criteria such as the childhood onset, persistence, and current presence of these symptoms, ADHD can be diagnosed.^[9] Adult self-report scales, such as the Adult Self-Report Scale, the Wender-Reimherr scale, Brown Attention-Deficit Disorder Scale, and Conners' rating scale may assist in diagnosing adults with ADHD.^[9] Although different diagnosis process is well studied, the use of biochemical markers for ADHD in children is evolving.^[7,10] A primary factor in the development of ADHD is the status of the monoamine system to include serotonin, dopamine, norepinephrine, and epinephrine.^[10]

In this study, we focused on the efficacy of biochemical markers in diagnosing ADHD. We also examined the prevalence of ADHD in the children of Bangladesh in the context of special populations, tolerability, medical screening, and monitoring.

Materials and Methods

Subject collection and study procedure

In total 100 subjects (75% male and 25% female) of 0–12 years (mean age 7 years 5 months, standard deviation 10.5 months) who fulfill the inclusion criteria were included in this study from the Child Development Center of the Chittagong, Maa-O-Shishu General Hospital, Chittagong. By taking consent of parents as well as hospital authority, a detailed history was taken using a predesigned questionnaire and daily follow-up was recorded in a data collection sheet. For the biochemical study, blood samples of studied patients were collected by lab technicians with the help of vein puncture. All the samples were collected in ethylenediaminetetraacetic acid bottles and allow the blood for 15–20 min to clot by leaving it undisturbed at room temperature. After that, the blood samples centrifuged at $1000\text{--}2000 \times g$ [Relative Centrifugal Force = 1.2 r (rpm/1000)] for 10 min and remove the clots. The plasma sample was positioned in the appropriate well of the analyzer. Plasma ammonia and lactate concentration were measured by using Vitros 350 chemistry analyzer.

The significance was tested by the paired *t*-test analysis. Pearson correlation was also performed between plasma ammonia and lactate level in ADHD subjects. Finally, analysis of variance was prepared by using statistical software "Statistical Package for Social Science" (SPSS, Version 18.0 IBM Corporation, NY, USA).

Statement on informed consent of the donors

The volunteer donors were supplied a consent form which informed the title of the research project, and name and detail

contact of investigators as well as purpose of the research. Description of the research mentioning step-by-step brief of the proposed research, inclusion and exclusion criteria of the donors, whether donors will receive any therapy or not, volume of blood to be taken, the possible discomfort of the puncture sites, time required for the blood sampling. The explanation was made on if future use of the research data beyond the current study is anticipated, whether this is a focus group if so the principal investigator should put a procedure in place in which the researchers caution people about the limit on confidentiality. Access to research information regarding who would have access to the collected sample, information regarding retention of sample and schedules for their disposal were also detailed. It was indicated to the consent form that the volunteers might refuse to donate blood at any time. Donor, whether could withdraw his sample data, was disclosed. The sample was restricted for that individual study, not for future research projects was presented in the consent form. Potential harm, injuries, discomforts, or inconvenience associated with donors in this study was added as informed consent statement. If there was known harm to the donors, the potential harm, current knowledge regarding the probability of the occurrence of the harm, clinical importance of the harm; and any relevant knowledge regarding the probability of reversibility, for example, the possibility of bruising or swelling while giving blood, or some other discomforts at the site where blood is drawn and that there might be minimal chance of infection, and that these discomforts were brief and transient were also added. Potential benefits of the donors, not directly, but the society in general or individuals with a similar condition might benefit from the results of this study was explained. Treatment alternative and possibility of the research was described. Confidentiality statement was included in the consent form in the way that "confidentiality will be respected and no information that discloses the identity of the participant will be released or published without consent unless required by law of states. The legal obligation includes a number of circumstances, such as suspected child abuse and infectious disease, expression of suicidal ideas where research documents are ordered to be produced by a court of law and where researchers are obliged to report to the appropriate authorities. In those rare instances where it will not be possible to assure complete confidentiality," the limits on this obligation were carefully explained. Reimbursement issue was also mentioned whether the donors or their parents may be offered money for reasonable out-of-pocket expenses, for example, transportation costs, meals, etc. Finally, detail contact (name, area code and phone number) of investigators was provided in case of any questions of the donors about this study. The consent form was concluded with major questions on above disclosures in yes/no form followed by the signature (with date) of the donor.

Inclusion criteria

Patients with confirmed diagnosis of ADHD are randomly selected as first as diagnosis up to the age 12 years. The inclusion criteria considered in data collection are (1) mental health problems, (2) persistence of hyperactivity and inattention, (3) poor school achievement and a higher rate of disruptive behavior disorders, and (4) the presence of the core problems of inattention, hyperactivity, and impulsivity.

Exclusion criteria

There is more problem to exclude subject only basis on clinical questionnaire and on the basis of some laboratory test. The exclusion criteria are as follows: (1) anxiety states, (2) autism spectrum disorder, (3) schizophrenia or other psychotic disorders, and (4) age more than 12 years.

Results

Prevalence age of attention-deficit hyperactivity disorder in child

Of the 100 subjects of 0–12 years, male children are more susceptible to ADHD (as 75% children were male in our present study), and the symptom of the ADHD is significantly expressed in the mid-age children as 47% of the subjects were in the range of 6–8 years. Comparison of the age distribution of ADHD in studied subjects is shown in Figure 1.

Attention-deficit hyperactivity disorder cause higher plasma ammonia and lactate level

In normal individual with no ADHD, plasma ammonia, and lactate level are 9–33 μmol/L and 6.3–18.90 mg/dl. Of the 100 ADHD subject included in this study, in each case, the level of both is higher than the normal, and the ranges were 36–60 μmol/L and 22–30 mg/dl respectively ($P < 0.05$) [Figure 2].

In ADHD patients, level of both plasma ammonia and lactate increases significantly ($P < 0.05$) [Table 1].

Increasing lactate does not influence the level of ammonia and vice versa

When increasing level of both plasma ammonia and lactate are compared, there were no interrelations between the both of these two biochemical parameter ($P > 0.05$) [Table 2].

Consanguinity increases the prevalence of attention-deficit hyperactivity disorder

In this study, parent’s marital information was taken into consideration. In our study, 13 patients out of 100 were

detected whose parents were bonded by consanguine marriage. Hence, marital relationship within blood relatives increases the risk of ADHD for their progeny.

Modes of delivery also affect the development of attention-deficit hyperactivity disorder

For knowing whether mode of delivery affects the development of ADHD, the information of the ADHD subject’s delivery were considered. Among 100 subjects, only 23% subjects were born in the normal delivery where 77% subjects were born in an obstructive mode indicating that obstructive mode of delivery increase the risk of ADHD occurrence.

Discussion

Despite getting a number of biochemical parameters^[11-13] considered in ADHD, thought of in ADHD, we’ve tried to ascertain the effectuality of some parameters used for diagnosis in our gift studies. Our present studies propose that, as a biological parameter of ADHD, level of both plasma ammonia and lactate increase significantly ($P < 0.05$). As in case of ADHD, alteration of transmission amino acid and level of several neurotransmitters such as norepinephrine, dopamine, and serotonin occur,^[7] which might be a reason to increase ammonia level in ADHD subjects. Hence, increased plasma ammonia level is the indication of altered level of neurotransmitter as well as amino acid in ADHD subjects which can be used to diagnose the ADHD disorder in the child. Lactate could be a by-product of the anaerobic metabolism of aldohexose used for the detection of mitochondrial dysfunction that contains a nice importance as a biomarker in youngsters with attention-deficit disorder.^[14] Various literatures had established that mitochondrial dysfunctions is a part of neuropsychiatric disorders as like as ADHD.^[15,16] According to hypothesis of Russell *et al.*, 2006^[16] impaired astrocytic release of lactate manifest behaviorally as inefficient and inconsistent performance in ADHD patients. As with both plasma ammonia and lactate increases in ADHD subjects, there might have a correlation between increased level of plasma ammonia and lactate in ADHD patients. When correlation studies were carried out using SPSS, it was found that they are very poorly correlated ($P > 0.05$). Hence, there is no relation between the increased levels of ammonia with lactate level in ADHD.

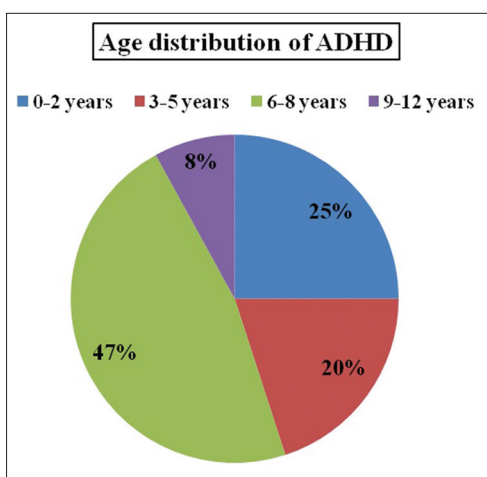


Figure 1: Comparison of age distribution of attention-deficit hyperactivity disorder in studied subjects; most of the subject are at 6–8 years (47%)

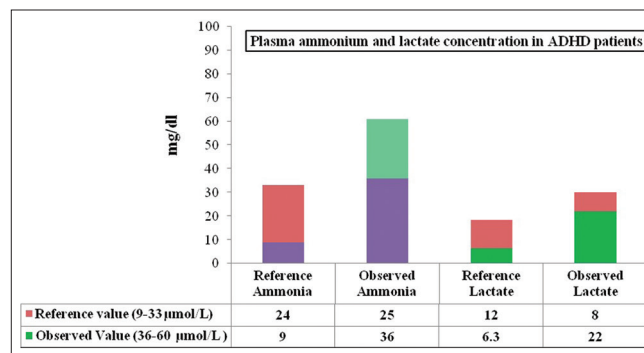


Figure 2: Plasma ammonium and lactate concentration in attention-deficit hyperactivity disorder patient

Table 1: Statistical analysis of ammonia and lactate levels of ADHD subject with normal

Level (in ADHD subject)	t-value	df	Sig. (2-tailed)	Mean difference	95% confidence interval of the difference	
					Lower	Upper
Plasma Ammonium	41.0976	99	0.00 (< 0.05)	24.01	22.8508	25.1692
Plasma Lactate	25.9890	99	0.00 (< 0.05)	5.15	4.7568	5.5432

Here, $P < 0.05$ indicates highly significant. ADHD: Attention-deficit hyperactivity disorder

Table 2: Correlation studies between plasma ammonia and lactate level in ADHD subjects

Correlations		
	Plasma ammonium level	???
Plasma ammonium level		
Pearson correlation	1	
Sig. (2-tailed)		
N	100	
Plasma lactate level		
Pearson correlation	-0.016708602	
Sig. (2-tailed)	0.868946469	> 0.05 (not significant)
N	100	

Here, $P > 0.05$ indicates not significant. ADHD: Attention-deficit hyperactivity disorder

Since the relationship rate is extremely high within the Bangladesh, we tend to offer a trial to search out the connection of minimal brain damage with relationship whether or not it might increase the extent of minimal brain damage within the young kids. As earlier report showed that there's a big increase within the prevalence of minimal brain damage and alternative medicine disorders with a high rate of consanguinity^[17] and our gift study is clearly indicate identical case. However, the sickness is extremely heritable^[1,2] but symptoms of the sickness doesn't onset at terribly starting of life. With the rise of life, the expression of the sickness will increase. This can be due the result the genes whose expression level changes during this sickness causes important level of changes during this age.^[9] Limitation of this study was that the study was dispensed solely at Chattagram, Maa-O-Shishu General Hospital that may be a tertiary level hospital Thus, it is not the representative of the whole population of Asian country. Again, adequate variety of sample was not accessible, and sample size was tiny. This study concludes that there will be a correlation between syndrome and inflated level of plasma ammonia and wet-nurse level, and other people will be an important parameter at intervals the designation of syndrome patients.

Conclusion

The expansion of knowledge in genetics, brain imaging, biochemical and behavioral research is leading to a better understanding of the causes of the disorder, how to prevent it, and how to develop more effective treatments for all age groups. This study found that the prevalence of ADHD in a male child is higher in Bangladesh. Moreover, in the mid-age children (6–8 years), the symptoms are significantly

expressed. Both levels of ammonia and lactate in ADHD subject significantly increased. This two biochemical parameter can be used to diagnose ADHD. Moreover, consanguinity increases the risk of ADHD in children. Though both levels increased in ADHD subjects, but they themselves have no correlation to be increased. Further study will reveal detail mechanism how these two increase during ADHD.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Authors' contributions

CMMH has designed the study and wrote the manuscript. MMI has performed the data collection from hospital. MMRM has performed data analysis and interpretation and modify the manuscript. MACA has supervised the field work, modify the manuscript and also help in collecting data.

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