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Research Article

CLINICAL AND CYTOGENETIC ANALYSIS OF ATTENTION DEFICIT/ HYPERACTIVITY DISORDER (ADHD) IN SOUTH INDIAN POPULATION

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ABSTRACT

The study is to analyze the clinical and cytogenetic investigation on patients with Attention Deficit/ Hyperactivity Disorder (ADHD) from South Indian population. Cytogenetic analysis of 30 patients carried out by using human leukocyte culturing method and clinical analysis were carried out for all the cases with the help of physicians. A significantly higher number of chromosomal aberrations were observed in all the patients when compared with the controls ($p < 0.001$). The detection of chromosomal anomalies as a probable cause of ADHD is very significant in genetic consultations genetic counseling, awareness and management of attention deficit children.

Keywords: ADHD, DSM-IV, Human Leukocyte Culture, Chromosomal aberrations

INTRODUCTION

Attention Deficit/Hyperactivity Disorder is the multifactorial disorder[1]. It is a chronic psychiatric disorder which found in early onset and continuing to have symptoms in adulthood[2]. It normally affects the school-age children up to 3-6% and its symptoms seen in 60% of the patients in adolescence and adulthood globally[3]. ADHD is diagnosed in about two to four times more frequently in boys (92%) than in girls (29%)[4]. Having its three sub types Predominantly Hyperactive-Impulsive, Predominantly Inattentive, Predominantly Hyperactive-impulsive and Inattentive[5], researchers have found that twins and adoption studies shows increased risk of ADHD[6]. Though there are many genes involved in the regulation of ADHD, the mutation of exon 3 on the DRD4 gene located at chromosome 11(11p15.5) of human is primarily responsible for the disorder[7]. The symptoms of ADHD patients may be cumulated as such, child fails to give close attention and makes careless mistakes[8] including learning disability, avoiding to engaging in any task which require mental effort and forgetful in daily activities. Though hyperactivity is characterized by behaviors such as fidgeting, squirming, running about when inappropriate and talking excessively, ADHD is likely to be associated with a number of impairments in many different domains, for instance, these children often exhibit decreased nonverbal and verbal working memory, impaired planning ability and a poor sense of time[9]. Studies on ADHD children frequently report deficient performance on IQ measures in comparison to control children and other studies have found hyperacivity to be negatively related to achievement and IQ measurements[10]. Although many studies comparing ADHD children to normal controls have conducted analyses controlling for IQ, doing so may be questionable in that deficient performance on IQ measures may be directly related to ADHD and the associated impairments in executive functioning[11]. Furthermore, hyperacivity has shown positive relations to problem behaviors[12]. Genetic factors have been postulated as one of the major contributors to the development of ADHD[13]. In this paper we are performing cytogenetic studies carried out by chromosomal aberration analysis and clinical studies based on the features of the patients in order to identify the etiology of the disorder based on chromosomal aspect.

MATERIALS AND METHODS

Subjects

A total of 30 (25 males and 5females) ADHD patients that met DSM-IV criteria (Diagnostic and Statistical Manual of Mental Disorder, fourth edition) [14] were recruited between February and May 2012.

In this study detailed cytogenetic analysis were carried out in all the 30 patients with ADHD disorder with different aged between 4 to 21 years. All the cases of ADHD were classified, based on theirclinical and cytogenetic analysis. The ethics committee of each participating institution approved the study and written informed consent was obtained from all children's their parents and adult subjects. Blood samples were collected and transferred into heparin tubes.

Clinical assessment

All the patients were recruited from the Dr. Rama Rao polyclinic, Kilpauk, Chennai. The diagnosis of ADHD in children was evaluated using the DSM-IV rating scale. Reading and writing performance was evaluated for all the patients.

Cytogenetic analysis

Chromosome preparations were made from phytohemagglutinin (PHA) stimulated peripheral blood lymphocytes following the modified method of Hungerford 1965 and standardized in the biomedical genetics research lab, VIT University. The cytogenetic studies were carried out in all the cases to find out the chromosomal aberrations, including chromosomal breakage, dicentric and ring chromosome. Chromosome preparations were obtained from PHA-stimulated peripheral blood lymphocytes[15]. At least fifty well spread metaphase plates were scored by direct microscopic analysis. Well spread metaphases were photographed under oil immersion objective lens (100X) of Olympus microscope with JAI camera.[16].

Statistical analysis

The samples were coded at the time of preparation and scoring. They were decoded before statistical analysis for comparison. Mean and standard deviation (SD) were calculated. The significances of the differences were analyzed between control and patients. Mean values and standard deviations were computed for the scores and the statistical significance ($P < 0.001$) for chromosomal break and dicentrics.

RESULTS

Clinical analysis

The Clinical analysis were carried out for all the cases of Attention Deficit Hyperactivity Disorder patients observed few clinical variations in Communication, Social Interaction, Sensory, Playing and behavioral problems which were presented in Table 1.

Table 1: The Clinical features of Attention Deficit/ Hyperactivity Disorder (ADHD)

S.no	Age	Sex	Communication Problem	Social Interaction	Sensory Dificulties	Playing Difficulties	Behaviour Problem
1	11	Male	Yes	Yes	Yes	No	Yes
2	10	Male	Yes	No	Yes	Yes	Yes
3	4	Male	Yes	Yes	Yes	Yes	Yes
4	7	Male	Yes	Yes	Yes	No	No
5	19	Male	Yes	Yes	Yes	No	Yes
6	11	Male	Yes	No	Yes	No	Yes
7	8	Male	Yes	No	No	Yes	Yes
8	6	Female	Yes	No	Yes	No	Yes
9	13	Male	Yes	Yes	Yes	No	No
10	5	Male	Yes	No	Yes	Yes	Yes
11	16	Male	Yes	No	Yes	No	Yes
12	16	Female	Yes	Yes	Yes	Yes	Yes
13	8	Female	No	Yes	Yes	No	Yes
14	21	Male	Yes	Yes	Yes	Yes	Yes
15	6	Male	No	Yes	Yes	No	Yes
16	4	Male	Yes	Yes	Yes	No	Yes
17	6	Male	Yes	Yes	Yes	No	No
18	8	Male	Yes	Yes	Yes	Yes	Yes
19	12	Male	No	Yes	No	No	Yes
20	5	Male	Yes	Yes	Yes	Yes	Yes
21	11	Male	Yes	No	Yes	No	No
22	5	Female	Yes	Yes	Yes	Yes	Yes
23	4	Male	No	No	Yes	Yes	Yes
24	12	Male	Yes	Yes	Yes	No	Yes
25	4	Male	Yes	No	No	Yes	Yes
26	6	Male	Yes	Yes	Yes	No	No
27	8	Male	Yes	Yes	Yes	Yes	Yes
28	7	Female	Yes	Yes	Yes	Yes	Yes
29	11	Male	Yes	Yes	No	Yes	No
30	5	Male	Yes	No	Yes	No	Yes

Cytogenetic analysis

The 30 ADHD patients with equally age and sex matched controls were taken for cytogenetic analysis to find out the frequency of chromosomal aberrations. There is significant differences were found in the cytogenetic variables in the frequency of chromosomal breaks and di-centric chromosomes (Table 2). There is significant differences were observed between control and patient samples in the following frequency: The percentage of breaks 1.66 % and total no. of breaks (mean±SD) Control: 0.16 ± 0.37 and patients: 0.83 ± 0.87 ($p<0.001$), Percentage of Di-centric is 1.73 % and total no. of Di-centrics control: 0.16 ± 0.43 and patients: 0.86 ± 0.73 ($p<0.001$), Percentage of Ring chromosome is 0.33% whereas total no. of Ring chromosome control: 00 ± 00 and patients: 0.03 ± 0.18 ($p=0.045$) (Figure 1, 2).

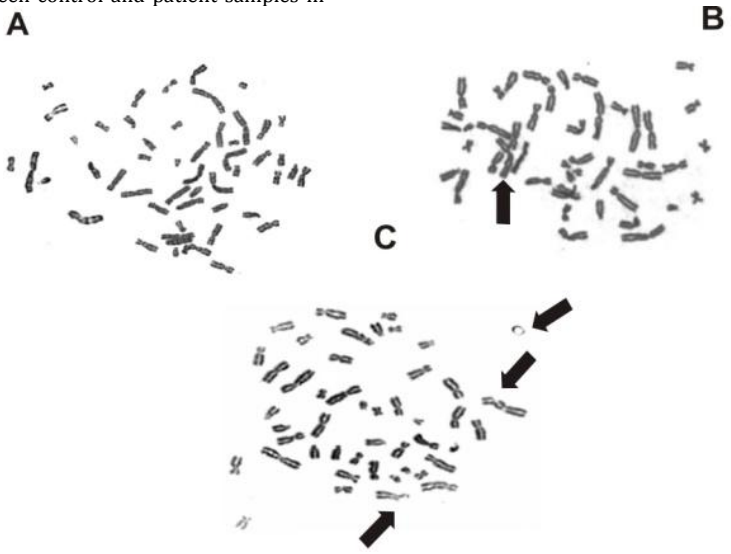

Figure 1: Various types of Chromosome aberrations observed in Attention Deficit Hyperactivity Disorder (ADHD)

(A) Chromosome picture of control sample

(B) Arrow indicates the dicentric chromosome observed in Attention Deficit Hyperactivity Disorder (ADHD)

(C) Arrow indicates the chromosome break and ring chromosome aberrations observed in Attention Deficit Hyperactivity Disorder (ADHD)

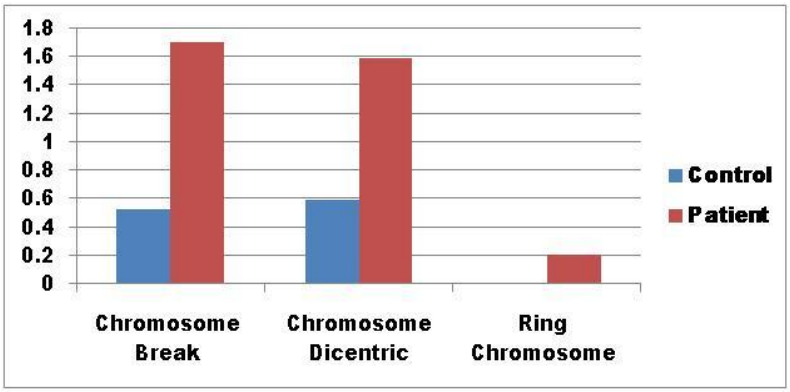

Figure 2: Bar diagram showing the chromosome aberrations observed in Patient and Control samples (Mean ± S.D).

Table 2: The Chromosomal Aberration analysis of Attention Deficit/ Hyperactivity Disorder (ADHD)

S.no	Number of Cells Scored	Chromosome Aberration		Ring Chromosome	Total Number of Aberration	
		Break	Dicentric		No.	%
ADHD 01	50	0	0	1	1	2
ADHD 02	50	0	2	0	2	4
ADHD 03	50	2	0	1	3	6
ADHD 04	50	1	1	0	2	4
ADHD 05	50	1	0	0	1	2
ADHD 06	50	0	2	0	2	4
ADHD 07	50	0	0	0	0	0
ADHD 08	50	2	0	0	2	4
ADHD 09	50	0	1	0	1	2
ADHD 10	50	0	1	0	1	2
ADHD 11	50	1	2	0	3	6
ADHD 12	50	0	1	0	1	2
ADHD 13	50	0	2	0	2	4
ADHD 14	50	2	1	1	4	8
ADHD 15	50	1	1	0	2	4
ADHD 16	50	0	2	0	2	4
ADHD 17	50	3	1	0	4	8
ADHD 18	50	2	0	0	2	4
ADHD 19	50	0	1	0	1	2
ADHD 20	50	0	1	0	1	2
ADHD 21	50	1	1	1	3	6
ADHD 22	50	1	0	0	1	2
ADHD 23	50	1	1	0	2	4
ADHD 24	50	1	2	0	3	6
ADHD 25	50	2	1	0	3	6
ADHD 26	50	0	1	0	1	2
ADHD 27	50	0	0	0	0	0
ADHD 28	50	1	0	0	1	2
ADHD 29	50	1	0	1	2	4
ADHD 30	50	2	1	0	3	6
Total	**1500**	**25**	**26**	**5**	**56**	**112**

DISCUSSION

The global prevalence of Attention Deficit Hyperactivity Disorder is diagnosed at about 3-6% of people under the age of 18. However it is presumed that there is both geographical and local variability among studies. This paper highlights the significance of considering the impact of inattentivity and overactive-impulsivity symptoms among conserved sex ratio and the cytogenetic aspects based on chromosomal nature. The present study examined the percentage of chromosomal aberrations found in ADHD individuals and statistically analysed the overall increased chromosomal abberrations including breaks, dicentric chromosomes and ring chromosomes. However the pattern of the variation of successive abberations from other primary impulsive disorders cannot be evaluated due to the limitations of the available data regarding the long term effects of comorbidity or anticipation. Published studies has already suggested the generalized rate of ADHD as low as 2% and as high as 14% among school aged children. A study in this regard, signifies the nature and prevalence of the impacts on patients with ADHD less than 20 years old due to high frequency of chromosomal abberations and baseline clinical studies[17]. The possible sex differences is assumed to be the consequence of rudimentary biological factors which eventually leads to the males more susceptible to different neurocognitive and developmental disabilities[18]. Further support comes from neuroimaging studies, such as that by; who found that global cerebral glucose metabolism in ADHD girls was 20% lower than in ADHD boys, although this study had very small sample sizes[19]. Furthermore, found fewer structural abnormalities in the brains of girls with ADHD in comparison with those of boys[20]. The assessed preponderance studies of childhood ADHD suggests a great extent of unevenness between male and female ADHD patients, bespeaking the degrees of outnumber males to females with varying ratios[21]. We hope this study might increases effective awareness and appropriate knowledge regarding the cytogenetic scenario of neuro-impulsive disorders among the affected and non-affected population for appropriate diagnosis and proper clinical counseling.

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