

## REVIEW ARTICLE

# CORRELATION OF MAJOR FACTORS AND CO-MORBIDITIES TO ADHD (ATTENTION DEFICIT HYPERACTIVITY DISORDER): A SYSTEMATIC REVIEW

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### Abstract

ADHD (Attention Deficit Hyperactivity Disorder) a neurobehavioral disorder mainly occurs in pediatric age group. It is more prevalent in boys than girls. It is characterized by three common symptoms Inattention, Hyperactivity, and Impulsivity. The impairment of norepinephrine and dopamine neurotransmitter systems is the main cause of ADHD. There are many parameters which trigger this disease. Socio-economic factors, genetic variation, air pollution, or any co-morbid condition like mental retardation, epilepsy, Autistic Spectrum Disorder (ASD) like factors can trigger this disease. Evidences suggested that the age group children between 9 to 11 years are more prone to incidence and/or prevalence of disease. Temperament of the individuals can also leads to ADHD in some children. Various clinical and preclinical studies confirms that the brain is the most vulnerable part of the body for most of the pollutant. Sustained exposure to the vehicular pollution can affect ADHD. There is also some association between the 7-repeat allele of the dopamine D4 receptor gene (DRD4) and ADHD. The parental unipolar or bipolar affective disorder can also lead to childhood ADHD. The cytogenetic analysis shows various types of chromosomal aberrations observed in the ADHD patients. These aberrations include chromosome breaks, chromosome dicentric, and ring chromosome etc. so for effective treatment, it is necessary to prevent as well as to identify the correlation between ADHD and factors which triggered it.

**Keywords:** ADHD, Correlation, Co-morbidities, Factors, Attention Deficit Hyperactivity Disorder,

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## **Introduction**

Attention Deficit Hyperactivity Disorder (ADHD) is the most common neurobehavioral disorder more prevalent in six to thirteen years of age in children [1]. Major three common symptoms of ADHD are inattentiveness, hyperactivity and impulsiveness. Inattention means lack of responsiveness towards stimuli, blunted errors in daily tasks, struggle in focus, being self-absorbed, and forgetfulness. Hyperactivity include violent behaviour, over excitation, altered gate with uncontrolled imagination and impulsivity includes disturbing teachers, sidetracking by calling out, struggling turn writing. Symptoms of ADHD occurs in childhood but also sometimes continue to adolescence [2]. According to symptoms three types of ADHDs are present inattentive, hyperactive-impulsive, and combined type as per the Diagnostic and Statistical Manual of Mental Disorder (DSM IV) from APA (American Psychiatric Association).

Current review enlightens several factors which are correlated to incidence or prevalence of the ADHD. It is essential to find out basic cause which are more prone for occurrence of the disease. It shows significant difference of the ADHD and non ADHD children with various parameters. So it is considerable that some of these factors are trigger factors for the disease. As a result, the child victim of ADHD can suffer from substantial mental illness, for instance difficulty to learn in institution and educational challenges [3], bothersome interactive affiliations with

members within domestic environment, peers, and truncated self-confidence [4].

## **ADHD and Temper: Nature of child**

Exhibition of regular behavioural pattern and perception toward the surrounding is called as Temperament. It comprehends the emotional, motivational, and responsiveness inside nature and works as a mirror in which a child views and communicate with his/her surroundings. Temperament is biologically compelled and obviously associated with inheritable factors which remains steady throughout time and circumstances. Temperament of the child is most crucial contrivance to diagnose ADHD. Two admiring perceptions are mostly applicable for temperament of child during reconnoitering the resemblances as well as variances of the theory with ADHD. Four most appropriate magnitudes to analyze temperament in school going children are; Negative reactivity (the strength and rate at which the child articulates destructive marks), perseverance during allotted task (period of attention), activity (motor conduct), and approach/withdrawal (primary reaction to novel settings) [5]. Previously conducted study reports the existence of 14% populace of children from 883 participants who were having temperament with "high maintenance" profile which include children having hyperactivity, negative reactivity and diminished task tenacity. Rothbart and her colleagues emphasized the association of alteration in provocation and distress with excitement, accomplishment of task, and contemplation [6] where they documented

that attention has both self-regulated and prompted characteristics. The buildup of attentional converging is associated to ability of child to endure attention during the course of drawn-out time. As the child grows up he cultivates the aptitude for self-regulation [6]. If he can't do so that will spoil the career of the child. Child temperament is changed according to the hormone levels in some children but in other cases it is important that neurobehavioral impairment, traumatic condition or any head injury plays a role in child temperament despair. Child temperament is most important to determine for the assessment of mental condition of the child. A Previous study tells that combined subtype ADHD was allied with declined scoring during orientation of task and greater scores upon regular activity [7].

In previous study the pragmatic association of ADHD and temperament was analyzed amongst 70 male children with ADHD (n=35) as well as normal children (n=35) lied within age range between 5-8 years and rated by teachers and parents [8]. McIntosh and Cole-Love clinched that ADHD diagnosed children were having altered temperament and exhibiting hyperactivity, distractibility, and reduced persistence while that was opposite for normal children. Temperament of 8-10 years old 200 children both males and females were evaluated by Bussing et al. and positive responses were found upon Diagnostic Interview Schedule for Children (DISC) for the children with ADHD-combined subtype based on reports obtained by parents [6]. Children found

with combined ADHD subtype obtained considerably greater ratings on the activity level-general dimension and apparently lesser score for coordination of task based paradigms when compared with non-ADHD children. Longitudinal study carried out upon 451 children by Lemery, Essex, and Smider exhibited commonality between magnitudes of behaviour of child upon Questionnaire of temperament, Preschool Behavior Questionnaire as well as the symptoms of ADHD on the MacArthur Health and Behavior Questionnaire [9]. To evaluate ADHD, the investigators utilized the multiple behavior problem related to attention deficit based on inattention and impulsivity subscales. When experimental and theoretical baffled queries were nullified, modest links persisted between the temperament dimensions of activity level, attentional centering, inhibitory control and ADHD symptoms of inattention and impulsivity.

### **Cytogenetic analysis**

Several studies has been carried out to compare normal with ADHD children to monitor IQ (Intelligence Quest). Preceding reports upon ADHD children over and over again reveal declined IQ processes when compared with control children. Additionally more findings suggested negative relationship of hyperactivity with accomplishments and IQ level. It is the matter of quest that whether the deficient IQ based performance has any direct relation with ADHD. Role of genes in ADHD pathology has been accounted. Mutation in exon 3 on DRD4 gene positioned at chromosome 11 of human is

principally accountable for ADHD disorder [10].

Globally 3- 6% population under 18 year age reveal ADHD symptoms. Both local and geographical variations are related with global genetic alteration and prevalence of disease. It is very significant to consider the role of insensitively and overactive-impulsivity indicators among conserved sex ratio and the cytogenetic aspects in association with chromosomal nature. In reported studies ADHD individuals showed abrupt informal alteration in chromosomal arrangement which include ring chromosomes, dicentric chromosomes and nicks in chromosomes. Available reports has by now advocated the general ADHD rate is as low as 2% and as high as 14% among school going children. In respects of this some reports denotes the nature and prevalence ADHD in the children less than 20 years because of high chromosomal aberrations rate. The probable gender variances and several biochemical i.e. hormonal alterations are expected to be the reason by which the males are more vulnerable to many developmental and neuro-cognitive incapacities. Neuroimaging reports have confirmed that girls are 20% less prone to develop ADHD [11]. Additionally, smaller amount of structural irregularities have been stated in the female brain with ADHD when compared with male with ADHD.

### **7-Repeat Allele of the Dopamine D Receptor Gene and ADHD**

All available studies report the association between ADHD and 7-Repeat Allele of the

Dopamine D Receptor gene. Even though availability of several case studies the theory explains DRD4 gene alteration establishes more important correlation with ADHD. Remarkably, in spite of the important meta-analysis reports, the outcomes of merely 2 from 14 family related studies were observed to be important. Additional contemplations advocate role of DRD4 in ADHD pathology. Dopamine and noradrenalin work as DRD4 agonists and their association with ADHD pathophysiology has been identified through both preclinical and clinical studies. Though several genes are associated with psychiatric abnormalities and works in harmonized manner, individual genes exert very little influence upon such illnesses. Even if the study to identify association of correct gene in such pathology is replicated there are very less probability to detect involvement of similar gene. To conduct replications to confirm role of previously detected gene there must be large samples to avoid uncertainties further meta-analytical statistics can resolve conflicting outcomes [8]. This technique helps to inspect whether the collective evidence through all existing knowledge delivers confirmation of statistically significant results in obtained informations. Therefore, to study the supposed connotation between DRD4 7-repeat allele and ADHD, meta-analysis of all existing family-based association and case-control studies are reported. Additional studies are necessary to explain what variant of DRD4 (or some nearby gene) is accountable for this association.

## **ADHD and Pollution**

Exhaustion from transport services is related to respiratory and cardiac disorders in children however only some laboratory studies revealed its neurodegenerative outcome and associated cerebral anomalies in developing Asian countries like India. Human trials have proved that pollution leads to cerebral injury and loss of olfactory activity. The toys, the children play with are enriched with phthalates. Phthalates are industrial chemical added by manufacturers in the toys of children and devices for medical purpose to make them flexible and soft accompanied with some cosmetics to develop aesthetic smell [12]. If the conceiving women inhales such toxic pollutant the upcoming child may suffer from attention insufficiency. Another pollutant is poly acrylic hydrocarbons (PAH) produced after burning of woods, fossils and garbage, found to be moderately fetal for health. Moreover upraised use of motor rides have abundantly elevated environmental carbon dioxide, carbon monoxide and PAH in environment. Recent study carried out by Mortamais et al., 2017 revealed role of PAH in ADHD. Brain imaging study of 242 young students with age group 8-12 years were carried out and it was found that PAH is linked with subclinical alteration in the caudate nucleus and modifies cognitive-behaviour process [13].

## **Food and Mood**

Several findings have revealed that food governs mood of people through alteration in neuro-hormonal make up and energy

requirements. Well-adjusted nutritional diet plan normalizes the mental and physical wellbeing of individuals. Remarkable deviations in youngster's life style led to extreme variations in their routine food consumption nature. A transference from deep-rooted foods to processed, precooked and instant foods is observed in every place of the world and Indian population imitate similar culture blindly. The processed food are prepared in western country as per their need. Indian ancient culture does not allow to do so in Ayurveda. It states that food which is safe to eat is contacted with sunlight at least once. Various aforementioned and current evaluations revealed an emotional and cognitive nature of person is affected the quality and nutritional values of food that the individual consumed. Certain diets can endure good mood while several diets boost debauched tempers or may create minor depression. Mediterranean diet is considered as the most balanced and the healthy eating assortment which are sufficiently enriched with fruits, vegetables, nuts, legumes, fish, cereals, and low fat dairy products and all of them carries important nutrient values. Healthy food creates the vigorous physique and healthy mental wellbeing. Antioxidant enriched fruits i.e. Indian gooseberry, Guava, Grapes, Pomegranate, and several fruits enriched with Vitamin-C prevent hyperactive as well as depressive behaviour by eradicating free radicals formation body and establish regular cellular activity. Children like junk foods which are rich cause of free radicals formation within body. Investigators identified that the people who were

deprived with folic acid were 67 % more prone to undergo depression than those enriched with it. Foods i.e. see foods, whole grain, nuts, legumes and beans are enriched with selenium which retard mild and moderate depression condition. An earlier data, published in the Journal of Trace Elements in Experimental Medicine, 1998; stated that individuals do not selenium rich diet are least are more confused, unsure and anxious than those who are taking it. Flax seeds and walnuts are enriched with omega-3 fatty acids, antioxidants and essential fatty acids which support to fight against depression, normalize mood, retard hyperactive behaviour and promote mental health [14]. Reports published in the British Journal of Nutrition denoted that consumption of food enriched with moderate amount of omega-3 fatty acids supports in execution of better cognitive and motor task as well as development of neuro-behavioural skills. Beverages and foods encompassing sugar and refined flour elevate blood sugar level which is followed by headache and moody crash. Several studies have revealed that ingestion of food consisting of excessive sugar, artificial color, preservatives and saturated fat exacerbate the typical ADHD symptoms in children. Cookies, puffs, dough nut, pastry, and numerous additional bakery foods comprising of Trans fatty acids originates inflammatory alterations in the body which may trigger sluggishness and depression [15].

If the condition is not handled seriously at later stage the ADHD child would be more prone to get low self-confidence, deprived

social interaction and conflicting nature with the parents. So, during treatment of the ADHD children despite considering medical, scholastic and psychosocial interventions, dietary interventions must be considered. Awareness regarding ADHD symptom and diet can help caretakers and parents of the ADHD children to cope up with symptoms of it. An interdisciplinary assertiveness is essential which can be achieved by involvement of health departments, dietary interventions and investigators of scholastic foundations to regulate and manage this illness in an operational way.

### **ADHD and Ethnicity**

Cultural environment surrounding child affects in several ways to the various aspects of central to mental health i.e. personality, language, conduct, emotion, attachment, attention, motivation, traumatic experiences, behavioral expectations and tolerance. Temperament of child is also exaggerated by the marital status of parents. There is diversified culture existed in world's different countries. It is important to find the composite relation between environmental and cultural dynamics to identify the ADHD phenomenon. Attachment and psychodynamic factors have not yet got as much attention that much they should be even though they are more culprit factors for development of ADHD. A child encountered traumatic illness may reveal series of signs identical to ADHD include; anxiety disorders and conduct disorders. Persistent traumatic state for instance negligence and exploitation of child or

failure to gain sheltered affection initially, may lead to form prolonged hyper provocative state in a child which modifies the neuroendocrine actions of cerebral milieu along with emotional, cognitive, and behavioral alterations. Child abuse is mainly succeeded by the cultural environment. The above discussed socioeconomic status of an individual is also the root cause of the economic status of the country. Cultural devotion and responsibility can also affect this disease. Hackett and Hackett addressed more strict expectations of Gujarati-speaking parents toward child behavior and there least tolerance with littler behavioural hitches [16]. Certainly, elevated parenteral expectations lead to exhibit fewer behavioural difficulties in children. Hence, the alterations in the ADHD rate across cultures or time is due to the variances in communal lenience [17].

### **ADHD and Major Mental Co-Morbidities**

Among all ADHD children, 70% all reported for presence of co-morbid conditions like: autistic spectrum disorder (12.2%), mental impedance (28%) or epilepsy ((29.3%) [7]. ADHD children are with at higher risk to conduct substance abuse and mood associated symptoms [18].

### **ADHD and epilepsy**

Population studies support the common occurrence of ADHD and epilepsy co-morbidity. A Review of literature between 1990–2014 reported 20–40% ADHD children to be epileptic [18]. ADHD and

Epilepsy were documented to occur together higher than the expected rates and found to be the common co-morbid illness in infantile ages [20]. Predominance of ADHD in the childhood epileptic victims is 12 to 17%. Most of the concerned factor involved in such circumstances involve genetic susceptibility, dysregulation of noradrenergic system, seizures, subclinical epileptiform discharges, effects of antiepileptic drugs and socio-psychological issues [21].

ADHD is much predominant in early phase of epilepsy patient than normal one [22]. The presence of co-morbidity is identified by interview of parent, medical history, developmental history, family history, and evaluation of neurological symptoms. Boys are reported to be 3 times more susceptible for combined or hyperactive/impulsive ADHD when compared with girls.

### **ADHD and Mental Retardation**

A child with insignificant psychological and intellectual impedance may not be diagnosed as the ADHD until their school years, when parents manifest the indications or cognitive disability, then after resuscitate to the child consultant for mental assessment. In most cases the physician can't consider this as the ADHD and assume that this is due to mental retardation and rarely prescribe the psychostimulants and ADHD remains uneradicated. A study published by Das et al. 1989 reported 33% of high school students both junior and senior were suffered with minor mental hindrance

exhibited ADHD characteristics [23]. Studies upon population suggested that mental retardation is 5-10 times more common in ADHD than in child lacking ADHD [24].

### **ADHD and Autistic Spectrum Disorders (ASDs)**

ASDs are defined by abnormalities in social interaction, communication, and stereotyped or repetitive behaviour [25]. In a recent studies symptoms of ADHD like Inattention and Hyperactivity, are found common in individual diagnosed with ASDs. Current findings report involvement of >50% population from 487 youngsters and juveniles with modest to extreme ASD [4]. As a whole, it is projected that ADHD can arise in 14–80% patients who suffer with ASDs. Even though not being the prominent symptom, ADHD manifestations can be more devastating for the patients in cooperation with both the syndromes [26].

It is extremely difficult to correlate amongst ADHD along with mental retardation, childhood epilepsy as well as autistic spectrum disorders (ASD). Abundant features influence distinction in judgment of dominance and misty associations between these disorders. These relationships are going to be challenging for the researchers to enlighten.

### **Conclusion**

From the above review it can be concluded that there are many physical, chemical,

neurological, cultural, genetical, biological, factors those are in less or more actively can act as etiological factors for the ADHD. These factors are used to understand the disease progression or prevalence in the conditional aspect. The goal of the preventive health care can be fulfilled by this kind of review studies which are helpful in identifying the etiological factors for this disease and open the ways for further going research for researcher. Cultural impact also explains that the measures should be taken with the aim of to decrease the rapid percentage increase in the prevalence of ADHD globally.

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