

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Attention Deficit Hyperactivity Disorder in Children: Overview of Diagnosis, Treatment and Prognosis.

TS Prabhakar¹, R Rekha^{2*}, and NS Vital Rao¹.

¹Department of Pediatrics, Siddhartha Medical College, Vijayawada, Andhra Pradesh, India.

²Department of Food, Nutrition and Dietetics, Andhra University, Visakhapatnam-3, Andhra Pradesh, India.

ABSTRACT

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common childhood-onset psychiatric disorders. It is distinguished by symptoms of inattention, hyperactivity, and impulsivity. ADHD may be accompanied by learning disabilities, depression, anxiety, conduct disorder, and oppositional defiant disorder. Investigators have studied the relation of ADHD to elevated lead levels, abnormal thyroid function, morphologic brain differences, and EEG patterns. With current public awareness of ADHD, pediatricians and health care providers are reporting increases in referral rates of children with suspected ADHD. Numerous rating scales and medical tests for evaluation and diagnosis of ADHD are available, with mixed expert opinion on their usefulness. Parents who are concerned their child may have attention deficit hyperactivity disorder (ADHD) should speak with the child's healthcare provider. Early recognition and treatment of ADHD are important to prevent or limit emotional, academic, and behavioral difficulties.

Keywords: Attention deficit hyperactivity disorder, symptoms, hyperactive, children, treatment,

**Corresponding author*



INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is a medical condition with symptoms of inattention, hyperactivity, and impulsivity. The symptoms affect a child's cognitive, academic, behavioral, emotional, and social functioning, and the condition often continues into adulthood [1]. ADHD is a neuropsychiatric diagnosis for children presenting with significant problems in the central nervous system (CNS) regulation of attention span, impulsiveness, and motor over activity [2].

The prevalence of ADHD among primary school children in India was found to be 11.32%. Prevalence was found to be higher among the males (66.7%) as compared to that of females (33.3%). The prevalence among higher socio-economic group was found to be 16.33% and that among middle socio-economic group was 6.84%. The prevalence was highest in the age group 9 and 10 years [3].

ADHD Causes

Scientists are not sure what causes ADHD, although many studies suggest that genes play a large role [4]. Like many other illnesses, ADHD probably results from a combination of factors. In addition to genetics, researchers are looking at possible environmental factors, and are studying how brain injuries, nutrition, and the social environment might contribute to ADHD.

Genes: Results from several international studies of twins show that ADHD often runs in families. Knowing the genes involved may one day help researchers prevent the disorder before symptoms develop. Learning about specific genes could also lead to better treatments. Children with ADHD who carry a particular version of a certain gene have thinner brain tissue in the areas of the brain associated with attention.

Environmental factors: Studies suggest a potential link between cigarette smoking and alcohol use during pregnancy and ADHD in children. In addition, preschoolers who are exposed to high levels of lead, which can sometimes be found in plumbing fixtures or paint in old buildings, may have a higher risk of developing ADHD.

Brain injuries: Children who have suffered a brain injury may show some behaviors similar to those of ADHD. However, only a small percentage of children with ADHD have suffered a traumatic brain injury.

Sugar: The idea that refined sugar causes ADHD or makes symptoms worse is popular, but more research discounts this theory than supports it [5].

Food additives: Recent British research [5] indicates a possible link between consumption of certain food additives like artificial colors or preservatives, and an increase in activity. Research is under way to confirm the findings and to learn more about how food additives may affect hyperactivity.

Signs and Symptoms

ADHD is a condition that can cause three categories of symptoms: hyperactivity, impulsivity, and inattention. Children with ADHD may have one or more of these symptoms and the symptoms may change in frequency or pattern as the child develops [6]. In most situations, the child has difficulty controlling his or her behavior or attention and may have difficulty anticipating the consequences of his or her behavior. The child does not usually misbehave because he or she is willful or wants to annoy those around him or her. To be diagnosed with the disorder, a child must have symptoms for 6 or more months and to a degree that is greater than other children of the same age.

Children who have symptoms of **hyperactivity** may:

- Fidget and squirm in their seats
- Talk nonstop
- Dash around, touching or playing with anything and everything in sight
- Have trouble sitting still during dinner, school, and story time
- Be constantly in motion

- Have difficulty doing quiet tasks or activities.

These symptoms are usually seen by the time a child is four years old and typically increase over the next three to four years [7]. The symptoms may peak in severity when the child is seven to eight years of age, after which they often begin to decline. By the adolescent years, the hyperactive symptoms may be less noticeable, although ADHD can continue to be present.

Children who have symptoms of impulsivity may [8,9]:

- Be very impatient
- Blurt out inappropriate comments, show their emotions without restraint, and act without regard for consequences
- Have difficulty waiting for things they want or waiting their turns in games
- Often interrupt conversations or others' activities.

Similar to the hyperactive symptoms, impulsive symptoms are typically seen by the time a child is four years old and increase during the next three to four years to peak in severity when the child is seven to eight years of age [10-13]. However, impulsive symptoms usually continue to be a problem throughout the life of the individual.

Children who have symptoms of inattention may:

- Be easily distracted, miss details, forget things, and frequently switch from one activity to another
- Have difficulty focusing on one thing
- Become bored with a task after only a few minutes, unless they are doing something enjoyable
- Have difficulty focusing attention on organizing and completing a task or learning something new
- Have trouble completing or turning in homework assignments, often losing things (e.g., pencils, toys, assignments) needed to complete tasks or activities
- Not seem to listen when spoken to
- Daydream, become easily confused, and move slowly
- Have difficulty processing information as quickly and accurately as others
- Struggle to follow instructions.

Types of ADHD — Three subtypes of ADHD have been identified [14-16]:

Predominantly hyperactive-impulsive: Most symptoms (six or more) are in the hyperactivity-impulsivity categories.

Predominantly inattentive: The majority of symptoms (six or more) are in the inattention category and fewer than six symptoms of hyperactivity-impulsivity are present, although hyperactivity-impulsivity may still be present to some degree.

Combined hyperactive-impulsive and inattentive: Six or more symptoms of inattention and six or more symptoms of hyperactivity-impulsivity are present.

The subtype is determined based upon a child's predominant symptoms, and can change over time.

ADHD Evaluation and Diagnosis:

Diagnosis

ADHD symptoms usually appear early in life, often between the ages of 3 and 6, and because symptoms vary from person to person, the disorder can be hard to diagnose. No single test can diagnose a



child as having ADHD. Instead, a licensed health professional needs to gather information about the child, and his or her behavior and environment. A family may want to first talk with the child's pediatrician. The pediatrician or mental health specialist will first try to rule out other possibilities for the symptoms. For example, certain situations, events, or health conditions may cause temporary behaviors in a child that seem like ADHD [17-20].

Between them, the referring pediatrician and specialist will determine if a child:

- Is experiencing undetected seizures that could be associated with other medical conditions
- Has a middle ear infection that is causing hearing problems
- Has any undetected hearing or vision problems
- Has any medical problems that affect thinking and behavior
- Has any learning disabilities
- Has anxiety or depression, or other psychiatric problems that might cause ADHD-like symptoms
- Has been affected by a significant and sudden change, such as the death of a family member, a divorce, or parent's job loss.

A specialist will also check school and medical records for clues, to see if the child's home or school settings appear unusually stressful or disrupted, and gather information from the child's parents and teachers.

The specialist also will ask:

- Are the behaviors excessive and long-term, and do they affect all aspects of the child's life?
- Do they happen more often in this child compared with the child's peers?
- Are the behaviors a continuous problem or a response to a temporary situation?
- Do the behaviors occur in several settings or only in one place, such as the playground, classroom, or home?

Some children with ADHD also have other illnesses or conditions. For example, they may have one or more of the following:

A learning disability: A child in preschool with a learning disability may have difficulty understanding certain sounds or words or have problems expressing himself or herself in words. A school-aged child may struggle with reading, spelling, writing, and math.

Oppositional defiant disorder: Kids with this condition, in which a child is overly stubborn or rebellious, often argue with adults and refuse to obey rules.

Conduct disorder: This condition includes behaviors in which the child may lie, steal, fight, or bully others. He or she may destroy property, break into homes, or carry or use weapons. These children or teens are also at a higher risk of using illegal substances. Kids with conduct disorder are at risk of getting into trouble at school or with the police.

Anxiety and depression: Treating ADHD may help to decrease anxiety or some forms of depression.

Bipolar disorder: Some children with ADHD may also have this condition in which extreme mood swings go from mania (an extremely high elevated mood) to depression in short periods of time.

Tourette syndrome: Very few children have this brain disorder, but among those who do, many also have ADHD. Some people with Tourette syndrome have nervous tics and repetitive mannerisms, such as eye blinks, facial twitches, or grimacing. Others clear their throats, snort, or sniff frequently, or bark out words inappropriately. These behaviors can be controlled with medication.

Neurobiology of Attention Deficit Hyperactivity Disorder

It is increasingly clear that the etiology of attention deficit hyperactivity disorder (ADHD) is firmly grounded in neurobiological changes in the central nervous system (CNS). The increasing sophistication of modern research tools for genetics, molecular biology, molecular neuropharmacology, and CNS neuroimaging have significantly advanced understanding of the neurobiology of ADHD. Because ADHD is a heterogeneous condition, it most likely has multiple psychosocial and biological causes, and a single neurobiological etiology will probably not be identified.

Research supporting the neurobiological basis for ADHD rests on data from neuropharmacological studies, family-genetic studies, molecular genetics studies, and CNS neuroimaging studies [28-31]. The neuropharmacological data support a central dopamine/norepinephrine dysregulation hypothesis of ADHD [21]. One model to explain the effects of dopamine/noradrenergic medications in ADHD proposes dysregulation in the inhibitory influences of prefrontal cortical activity, predominantly noradrenergic, on subcortical CNS structures that are predominately under dopaminergic control [22]. Medications that have CNS dopamine and/or noradrenergic actions such as stimulants[23], guanfacine[24], clonidine [25], bupropion [26], and tomoxetine [27] are effective in ADHD. The net result is enhanced CNS dopamine and noradrenergic neurotransmission, which appears to be correlated with clinical treatment effects in ADHD.

Using structural and functional magnetic resonance imaging (MRI), a number of studies have examined the prefrontal cortex, basal ganglia, and the cerebellum in children with ADHD [32]. The prefrontal cortex, basal ganglia, and cerebellar vermis in children with ADHD are found to be 5% to 10% smaller than in control children. Functional MRI has shown lower blood flow in the striatum, anterior cingulate, and prefrontal cortex in ADHD children and adults compared with controls.

Treatment of ADHD

This treatment is divided into two major sections — medication treatments for ADHD, psychotherapy and other treatments for ADHD.

Medications

The most common type of medication used for treating ADHD is called a "stimulant." Although it may seem unusual to treat ADHD with a medication considered a stimulant, it actually has a calming effect on children with ADHD [33]. A few other ADHD medications are non-stimulants and work differently than stimulants. For many children, ADHD medications reduce hyperactivity and impulsivity and improve their ability to focus, work, and learn.

However, a one-size-fits-all approach does not apply for all children with ADHD. What works for one child might not work for another. One child might have side effects with a certain medication, while another child may not. Sometimes several different medications or dosages must be tried before finding one that works for a particular child. Any child taking medications must be monitored closely and carefully by caregivers and doctors.

Stimulant medications come in different forms, such as a pill, capsule, liquid, or skin patch. Some medications also come in short-acting, long-acting, or extended release varieties. In each of these varieties, the active ingredient is the same, but it is released differently in the body. Drug treatment for ADHD began decades ago [34]. Some of the best results have been found with the stimulant drugs listed below. "Approved age" means that the drug has been tested and found safe and effective in children of that age.

Another useful category of drugs for adults with ADHD are the antidepressants, either alongside or instead of stimulants [35, 36]. Antidepressants which target the brain chemicals dopamine and norepinephrine are the most effective. These include the older form of antidepressant known as the tricyclics, as well as new antidepressants, such as Venlafaxine (Effexor). The antidepressant Bupropion (Wellbutrin) has been found useful in trials of adult ADHD, and may also help reduce nicotine cravings.



Trade Name	Generic Name	Approved Age
Adderall, Adderall XR	amphetamine (extended release)	3 and older
Concerta	methylphenidate (long acting)	6 and older
Daytrana (patch)	methylphenidate	6 and older
Dexedrine, Dextrostat	dextroamphetamine	3 and older
Focalin	dexmethylphenidate	6 and older
Metadate ER, Metadate CD	methylphenidate (extended release)	6 and older
Ritalin, Ritalin SR, Ritalin LA	methylphenidate (extended release) (long acting)	6 and older
Strattera	atomoxetine	6 and older
Tenex, Intuniv	guanfacine hydrochloride	12 and older
Vyvanse	lisdexamfetamine	6 and older

ADHD Drug Side-effects

The majority of side-effects are minor and do not result in stopping the medication [37]. The most commonly observed side effects are:

- Decreased appetite – often low in the middle of the day and more normal by suppertime. Good nutrition is a priority
- Insomnia – may be relieved by taking the drug earlier in the day, or adding an antidepressant
- Increased anxiety and/or irritability
- Mild stomach aches or headaches
- Tics (more rare)

These medications only control ADHD symptoms on the day they are taken, so it's important to remember that the disorder is not actually cured. While drugs can enable the child to use their skills more easily, an effort is still needed to improve schoolwork or knowledge in other areas. As well as medication, behavioral therapy, emotional counseling, and practical support will also help a person with ADHD cope with the disadvantages of the disorder.

Tips for Coping with ADHD Drug Side Effects

Decreased appetite: If the child's appetite wanes after taking ADHD medicine, give the dose after breakfast so that he or she will eat better in the morning. Serve a large dinner in the evening, when the drug is beginning to wear off. Keep plenty of healthy snacks on hand; a balanced diet with nutritious, higher-calorie foods and drinks will help to offset any weight loss from the ADHD drug. If child's poor appetite lasts for a long period, ask the doctor about reducing the dose or stopping the drug on weekends or summer breaks to allow appetite to return to normal.

Stomach pain or upset: Don't give the medicine on an empty stomach. "For any GI discomfort, taking the medication with or immediately after food will make a very big difference".

Sleep problems: Set up a regular bedtime routine that includes relaxing activities, such as bathing or reading. If a stimulant type of ADHD medication prevents the child from sleeping well, then taking the drug earlier in the day or switching from a long-acting to a shorter-acting form. And reducing the dose or stopping the drug in the afternoon to help sleep at bedtime.



Daytime drowsiness: If the ADHD drug atomoxetine (Strattera) is making the child sleepy during the day, then giving the drug at bedtime instead of in the morning. And lowering the dose or dividing the dose and giving it twice a day.

Heart problems: Since there have been rare reports of serious heart problems in patients taking ADHD drugs. "If there's any history of significant heart problems, the physician may closely monitor, particularly if they're using stimulants

Psychotherapy

Different types of psychotherapy are used for ADHD [38]. Behavioral therapy aims to help a child change his or her behavior. It might involve practical assistance, such as help organizing tasks or completing schoolwork, or working through emotionally difficult events. Behavioral therapy also teaches a child how to monitor his or her own behavior. Learning to give oneself praise or rewards for acting in a desired way, such as controlling anger or thinking before acting, is another goal of behavioral therapy. Parents and teachers also can give positive or negative feedback for certain behaviors. In addition, clear rules, chore lists, and other structured routines can help a child control his or her behavior. Therapists may teach children social skills, such as how to wait their turn, share toys, ask for help, or respond to teasing. Learning to read facial expressions and the tone of voice in others, and how to respond appropriately can also be part of social skills training.

Parents help

Children with ADHD need guidance and understanding from their parents and teachers to reach their full potential and to succeed in school. Before a child is diagnosed, frustration, blame, and anger may have built up within a family. Parents and children may need special help to overcome bad feelings. Mental health professionals can educate parents about ADHD and how it impacts a family. They also will help the child and his or her parents develop new skills, attitudes, and ways of relating to each other.

Parents are also encouraged to share a pleasant or relaxing activity with the child, to notice and point out what the child does well, and to praise the child's strengths and abilities. They may also learn to structure situations in more positive ways. For example, they may restrict the number of playmates to one or two, so that their child does not become over stimulated. Or, if the child has trouble completing tasks, parents can help their child divide large tasks into smaller, more manageable steps. Also, parents may benefit from learning stress-management techniques to increase their own ability to deal with frustration, so that they can respond calmly to their child's behavior.

Tips to Help Kids Stay Organized and Follow Directions

Schedule: Keep the same routine every day, from wake-up time to bedtime. Include time for homework, outdoor play, and indoor activities.

Organize everyday items: Have a place for everything, and keep everything in its place. This includes clothing, backpacks, and toys.

Use homework and notebook organizers: Use organizers for school material and supplies. Stress to your child the importance of writing down assignments and bringing home the necessary books.

Be clear and consistent: Children with ADHD need consistent rules they can understand and follow.

Give praise or rewards when rules are followed: Children with ADHD often receive and expect criticism. Look for good behavior, and praise it.

Complementary and Alternative Treatments for ADHD

Complementary therapies are used along with mainstream medical therapies [39, 40]. Complementary and alternative medicine (CAM) therapies that have been tried for ADHD include vision training, special diets (eg, avoiding sugar, allergy triggers, or particular food additives), megavitamins, herbal

and mineral supplements, EEG biofeedback, and applied kinesiology. These treatments are often used by parents of children with ADHD because they may believe that these treatments "are safer than traditional medicines", "are natural", or "can cure ADHD". Alternative treatments are treatments or products that are not considered to be part of conventional medicine.

The ADHD Diet: What to Eat, What to Avoid

Poor eating habits don't cause attention deficit, but research suggests a strong relationship between ADHD and the food you consume [41]. Find out what foods and supplements make a diet ADD-friendly — and what may make ADHD symptoms worse “many diets are deficient in key vitamins, minerals, and fats that may improve attention and alertness,” that children and adults who have been diagnosed with ADHD be tested for nutritional deficiencies. An ADHD diet that ensures you're getting adequate levels of the right foods optimizes brain function.

Protein: Foods rich in protein — lean beef, pork, poultry, fish, eggs, beans, nuts, soy, and low-fat dairy products — can have beneficial effects on ADD symptoms. Protein-rich foods are used by the body to make neurotransmitters, the chemicals released by brain cells to communicate with each other. Protein can prevent surges in blood sugar, which increase hyperactivity.

Balanced Meals: The child eats a well-balanced diet, including vegetables, complex carbohydrates, fruits, and plenty of protein, then him/her behavior tends to be more consistently under control, and when preparing a meal, half of the plate should be filled with fruits or vegetables, one-fourth with a protein, and one-fourth with carbohydrates. Take several servings of whole grains, which are rich in fiber, each day to prevent blood sugar levels from spiking and then plummeting.

Brain-Boosting Supplements

Zinc, Iron, and Magnesium: Zinc regulates the neurotransmitter dopamine and may make methylphenidate more effective by improving the brain's response to dopamine. Low levels of this mineral correlate with inattention. Iron is also necessary for making dopamine. Low iron levels correlate with cognitive deficits and severe ADHD. Like zinc, magnesium is used to make neurotransmitters involved in attention and concentration, and it has a calming effect on the brain. All three minerals are found in lean meats, poultry, seafood, nuts, soy, and fortified cereals. While diet is the safest way to increase all three mineral levels, a multivitamin/multimineral with iron will ensure that child gets the daily reference value (DRV) of these minerals.

B Vitamins: Studies suggest that giving children who have low levels of B vitamins a supplement improved some IQ scores (by 16 points) and reduced aggression and antisocial behavior. “Vitamin B-6 seems to increase the brain's levels of dopamine, which improves alertness,” says Brown.

Fish Oil for Brain Function

Omega-3 Fatty Acids: Omega-3s are believed to be important in brain and nerve cell function. A new study concluded that daily doses of omega-3s -- found in cold-water, fatty fish, such as sardines, tuna, and salmon -- reduced ADHD symptoms by 50 percent.

Stimulating Herbs

“Herbs may improve blood flow to the brain, increasing alertness while reducing aggressive behavior”.

Ginkgo and Ginseng: “These herbs are cognitive activators”. They act like stimulants, without the side effects of ADHD medication. Typically, adults and children who take ginkgo and ginseng improve on ADHD rating scales, and are less impulsive and distractible.

Pycnogenol: An extract made from French maritime pine bark, pycnogenol was found to improve hyperactivity and sharpen attention, concentration, and visual-motor coordination in students after one month, based on

standardized measures and teacher and parent ratings. The herb is also rich in polyphenols, antioxidants that protect brain cells from free radical damage.

Rhodiola Rosea: Made from a plant of the same name that grows in the Arctic, this herb can improve alertness, attention, and accuracy. It can be too stimulating for young children, and is occasionally beneficial in children ages eight to 12.

Foods to Avoid

High-Sugar Foods and Snacks: Several studies suggest that some ADHD kids are “turned on” by copious amounts of sugar [41]. Read food labels carefully, looking for the following ingredients (code words for sugar): high-fructose corn sweetener, dehydrated cane juice, dextrin, dextrose, maltodextrin, sucrose, molasses, and malt syrup.

Artificial Dyes and Preservatives: Studies suggest that some children with ADHD are adversely affected by food additives. Avoid colorful cereals, like Fruit Loops and Lucky Charms. Cheerios are better, and lower in sugar. Substitute 100 percent fruit juice for soft drinks and fruit punches, most of which are artificially colored and flavored.

Foods That Cause Allergies: According to studies, gluten, wheat, corn, and soy cause some children to lose focus and become more hyperactive. The top eight food allergens are wheat, milk, peanuts, tree nuts, eggs, soy, fish and shellfish.

CONCLUSION

ADHD is one of the most common childhood onset psychiatric disorders that affect 2.0-14.0% of school age children. Boys are more commonly affected by ADHD than girls and the male: female ratio is approximately 3:1 to 4:1. As well as taking medication, different therapies can be useful in treating ADHD in children, teenagers and adults. A growing public awareness of ADHD may have also played a role in the increase in ADHD treatment. Early identification and intervention of this multi factorial neuro-psychiatric condition in the children will help the children improve their academic performance and prevent the development of co-morbid conditions.

REFERENCES

- [1] Diagnostic and Statistical Manual of Mental Disorders, 5th ed. Arlington: American Psychiatric Association; 2013.
- [2] Wolraich M, et al. Pediatrics 2011; 1007: 128-132.
- [3] Suvarna BS, Kamath A. Nepal Med Coll J 2009; 11(1): 1-4.
- [4] Weiler MD, Bernstein JH, Bellinger DC, Waber DP. Child Neuropsychol 2000; 6:218.
- [5] Brogan E, Cragg L, Gilmore C. Arch Dis Child 2014; 99: 834.
- [6] Wijburg FA, Węgrzyn G, Burton BK, Tylki-Szymańska A. Acta Paediatr 2013; 102:462-478.
- [7] Applegate B, Lahey BB, Hart EL. J Am Acad Child Adolesc Psychiatry 1997; 36: 1211.
- [8] Lahey BB, Applegate B, McBurnett K. Am J Psychiatry 1994; 151: 1673.
- [9] Levin FR, Kleber HD. Harv Rev Psychiatry 1995; 2: 246.
- [10] Nigg JT, Blaskey LG, Huang-Pollock CL, Rappley MD. J Am Acad Child Adolesc Psychiatry 2002; 41: 59.
- [11] Weiler MD, Bernstein JH, Bellinger DC, Waber DP.. Child Neuropsychol 2000; 6: 218.
- [12] Carlson CL, Mann M. J Clin Child Adolesc Psychol 2002; 31: 123.
- [13] Brogan E, Cragg L, Gilmore C, et al. Arch Dis Child 2014; 99: 834.
- [14] Lahey BB, Pelham WE, Loney J, et al. Arch Gen Psychiatry 2005; 62: 896.
- [15] Larsson H, Dilshad R, Lichtenstein P, Barker ED. J Child Psychol Psychiatry 2011; 52:954.
- [16] Hinshaw SP, Owens EB, Zalecki C, et al. J Consult Clin Psychol 2012; 80:1041.
- [17] Goldman LS, Genel M, Bezman RJ, Slanetz PJ. J American Medical Association. 1998; 279: 1100.
- [18] Power TJ, Costigan TE, Leff SS, et al. J Clin Child Psychol 2001; 30: 399.
- [19] Rapoport JL, Buchsbaum MS, Zahn TP, et al. Science 1978; 199: 560.
- [20] Pelouquin LJ, Klorman R. J Abnorm Psychol 1986; 95:88.
- [21] Pliszka SR, McCracken, JT, Maas JW. J Am Acad Child Adolesc Psychiatry 1996; 35: 264–272.



- [22] Zametkin AJ, Rapoport JL. *J Am Acad Child Adolesc Psychiatry* 1987; 26:676–686.
- [23] Wilens TE, Spencer TJ. *Child Adolesc Psychiatr Clin N Am* 2000; 9:573–603.
- [24] Scahill L, Chappell, PB, Kim YS, et al. *Am J Psychiatry* 2001; 158:1067–1074.
- [25] Connor DF, Fletcher KE, Swanson JM. *J Am Acad Child Adolesc Psychiatry* 1999; 38:1551–1559.
- [26] Conners CK, Casat CD, Gualtieri CT, et al. *J Am Acad Child Adolesc Psychiatry* 1996; 35:1314–1321.
- [27] Biederman J, Spencer TJ. *J Am Acad Child Adolesc Psychiatry* 2000; 39:1330–1333.
- [28] Cook EH, Stein MA, Krasowski MD. *Am J Hum Genet* 1995; 56:993–998.
- [29] Daly G, Hawi Z, Fitzgerald M. *Mol Psychiatry* 1999; 4:192–196.
- [30] Swanson JM, Flodman P, Kennedy J. *Neurosci Biobehav Rev* 2000; 24:21–25.
- [31] Faraone SV, Doyle AE, Mick E. *Am J Psychiatry* 200; 158:1052–1057.
- [32] Jensen PS. *J Clin N Am* 2000; 9:557–572.
- [33] Wolraich ML, Bard DE, Neas B. *J Dev Behav Pediatr* 2013; 34:83-92.
- [34] Wolraich M, et al. *Pediatrics* 2011; 128:1007-1019.
- [35] Kaplan A, Adesman A. *Curr Opin Pediatr* 2011; 23:684-691.
- [36] Swanson JM, Greenhill LL, Lopez FA. *J Clin Psychiatry* 2006; 67:137.
- [37] Pliszka S. *J Am Acad Child Adolesc Psychiatry* 2007; 46:894.
- [38] Jyothsna S, Akam Venkata, Anuja S. *Indian J Psychiatry*. 2013; 55(4): 338–342.
- [39] Pearl PL, Weiss RE, Stein MA. *Ann N Y Acad Sci* 2001; 97: 931-942.
- [40] Hennessy KD, Green-Hennessy S. *J Ment Health Admin* 1997; 24:340-349.
- [41] Riddle MA, Yershova K, Lazzaretto D. *J Am Acad Child Adolesc Psychiatry* 2013; 52:264.