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### Anxiety Disorder in Children: Review

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#### Abstract

Anxiety is a biological warning mechanism with intense feelings of fear that prepares us for action. It should be differentiated from the normal fear response. Anxiety disorders are one of the most common psychiatric disorders in children and adolescents, but they often go undetected or untreated. Childhood anxiety may be underestimated due to various factors. The prevalence of anxiety in a community depends on many factors, including race, sex, type of the anxiety, and the adequacy of the epidemiological studies. The development of anxiety disorders in children and adolescents involves interplay between heritable factors, developmental factors, cognitive and learning factors, neurobiological factors including genetic, social and environmental factors. Anxiety disorders in children and adolescents are often associated with other psychiatric disorders including other anxiety disorders, depression, attention-deficit hyperactivity disorder (ADHD), oppositional defiant disorder, substance abuse, and other psychiatric disorders. Management of anxiety disorders in children needs and integrative teamwork including cognitive behavioral therapy, mindfulness-based psychotherapies, psychodynamic psychotherapies, and psychopharmacologic treatments.

**Keywords:** Anxiety disorders, Childhood, Prevalence, Comorbidities, Psychotherapy.

#### Introduction

Anxiety is a biological warning mechanism with intense feelings of fear that prepares us for action. It accompanied by somatic complaints indicating hyperactive autonomic nervous system such as palpitation and sweating, and cognitive changes with distortion of perception. It should be differentiated from the normal fear response with the appropriate response to a known threat [1].

The type of fear and its intensity depend on the developmental stage of the child and should seem appropriate to dangers encountered repeatedly during human evolution and may be a part of self-protection system. Infants usually become afraid from

loud noises, being startled and have fear from strangers by the age of 8-10 months. Toddlers usually have fears from imaginary creatures especially in cultures encouraging that. They may be scared from darkness and they usually have normative separation anxiety. Meanwhile, school-age children are usually worried about injury and natural events (e.g., storms, lightening, earthquakes, volcanoes). However, children who become confident and eager to explore novel situations at the age of 5 years usually are immune to have anxiety in later childhood and adolescence. On the other hand, passive and shy children who usually become fearful and try to avoid new situations at the age of 3-5 years are more prone to reveal anxiety later in life. Adolescents usually get fears related to school, social competence, and health issues [2-4]. Table 1 showed the difference between the developmentally accepted anxiety and normal fear from the pathological one.

Anxiety is not typically pathological as it is adaptive in many conditions during childhood, and it is normal for children to feel worried or anxious from time to time, as during starting school or nursery, or moving to a new area. However, anxiety becomes maladaptive when it interferes with functioning. Children with anxiety disorders have higher risks for development of depression, sleep disturbance, peer dysfunction, drug abuse and may persist into adulthood anxiety when left untreated with reduced health-related quality of life [5].

#### Prevalence of Childhood Anxiety

Anxiety disorders are one of the most common psychiatric disorders in children and adolescents, but they often go undetected or untreated. Childhood anxiety may be underestimated due to various factors. The parents may have a confirmation bias about their children abilities and emotions and they are positively biased toward their child's feelings, rendering them in fact blind to their child's inner commotion. They usually overestimate their children's abilities, like performances on math, language or other cognitive tests. At the same time, children below the age of 7 years cannot perfectly express their feelings and behavioral scientists often have to rely on the impressions from parents and other adults [6,7].

**Table 1:** Difference between the developmentally accepted anxiety and normal fear from the pathological one

	Developmentally normal anxiety	Pathological anxiety
<b>Intensity</b>	The degree of distress is realistic according to the child's developmental stage and the object/event	The degree of distress is unrealistic according to the child's developmental stage and the object/event
<b>Impairment:</b> (interfering with the child's daily life)	Do not interfere with daily life:	Interfere with daily life:
A) Social functioning:	able to make friends	unable to make friends
B) Academic functioning:	Does not affect his academic abilities	failing classes
C) Family functioning:	Does not affect the family life	creating conflicts, limiting family choices
<b>Ability to Recover/Coping Skills:</b>	The child able to recover from distress when the event is not present	The child is not able to recover from distress when the event is not present. - The child tend to worry about future occurrences of event/object - The distress occurs across multiple settings

Anxiety disorders are the most common childhood emotional disorders with a prevalence rate of 17-21%; and about 8% may require treatment. The symptoms may vary from transient mild symptoms to full-blown anxiety disorders [1]. Anxiety disorders are common in preschool children, and they follow patterns similar to those in older children. The impact of anxiety symptoms in young children may be clinically significant even if full criteria are not met. However, subclinical anxiety is much more prevalent in the general pediatric population, so that nearly 70% of grade school children report they worry "every now and then" [8].

The prevalence of anxiety in a community depends on many factors, including race, sex, type of the anxiety, and the adequacy of the epidemiological studies. Races showed different prevalence pattern of anxiety. For example, the general prevalence rate of any anxiety disorders in age group between 9-13 years of age was 5.3% in American Indian children, and 5.6% in white American children. These racial differences are related to the genetic origin rather than the environmental factors as the environmental risk factors as poverty, family deviances, and family adversity were more common in the American Indian than in the white American. On the other hand, the parental mental illnesses with genetic roots were more common in parents of the white American than American Indian children [9].

Gender affects both the rate and the type of anxiety. Females have consistently higher prevalence rates of anxiety disorders with more disabling burden than in men. The lifetime and 12-month male: female prevalence ratios of any anxiety disorder were 1:1.7 and 1:1.79, respectively [10]. Girls are more liable to developed specific phobia, panic disorder, agoraphobia, and separation anxiety disorder than boys. The average age at onset of any single anxiety disorder varies widely between studies, but panic disorder often emerges later in the mid-teen years [11, 12]. These significant gender differences are related to differences in socialization process; especially sex-typing and gender roles. Girls are at more risk of continuing psychiatric disorder once they have developed one and at higher risk of developing another psychiatric disorder [13]. The prevalence of anxiety will

also differ according to its type. In a study done by Moffitt et al.; the prevalence of social and simple phobia in adolescents with no reading problems was 3.0% for each, while it was 1.6% for generalized anxiety disorder [14].

### Etiology of Childhood Anxiety

The development of anxiety disorders in children and adolescents involves interplay between heritable factors, developmental factors, cognitive and learning factors, neurobiological factors including genetic factors and social and environmental factors. These factors can increase the risk of or may protect from having anxiety. Risk factors modification and/or enhancement of the protective factors may help to decrease the incidence and prevalence of anxiety disorders in children and adolescents [15].

### Hereditary Factors

Currently, there is growing evidences for the hereditary role in development of anxiety disorders. Most anxious children are born with temperamental predispositions to shyness; often have parents who are anxious. Children of parents with at least one anxiety disorder have a substantially increased risk of having an anxiety disorder and the risk increase when both parents are affected [16]. The heritability effects for each anxiety disorder and anxious traits are usually similar in children, adolescents, and adults. The earlier age of onset for anxiety disorders than many other psychopathologic conditions support the inherent difficulties that could lead to anxiety. However; the large variations in the median age of onset for specific types of anxiety could indicate the role of the developmental shift in the expression of anxiety at different ages [16, 17]. For example; separation anxiety and specific phobia have the earliest onset in childhood, followed by social phobia in early adolescence, and then panic disorders/agoraphobia and generalized anxiety disorder in late adolescence and early adulthood [18]. Monozygotic within-pair correlations were higher than dizygotic correlations for physiological and social anxiety symptoms, suggesting heritable influences on these aspects. Physiological and social anxiety symptoms, which may be related to behavioral inhibition, appear to be genetically influenced. These results are linked to previous findings in older

children and adults [19].

Three main genetic variants have been implicated in development of anxiety. *5-HTTLPR* polymorphism of *SLC6A4* [20] and Val/Met polymorphism of *COMT* [21,22] with panic attacks and Val/Met polymorphism of *BDNF* with a cross-disorder anxiety phenotype [23]. The anxiety disorders exhibit high levels of lifetime co morbidity with one another. Heritable factor does not only affect the prevalence of anxiety but it affects also the associated co morbidities e.g. anxious-misery (with loadings on depression, generalized anxiety, and panic, agoraphobia, social phobia) [24]. Genetic factors can also contribute to the stability of anxiety [25].

### Developmental factors

**Psychobiology:** Anxiety disorders may reflect the individuals' variations in their neural functions. However, the exact amount of effects of many neurobiological factors in predisposing anxiety and anxiety processing are not accurately assessed. Abnormal regulations of neurotransmitters (mainly serotonin, norepinephrine and gamma-aminobutyric acid) in the limbic system may be linked to development of anxiety. A number of medications able to normalize the levels of these neurotransmitters are used to treat anxiety [26]. Abnormal activity of locus ceruleus (with a high number of norepinephrine neurons) and the median raphe nucleus (with a high number of serotonin neurons) appears to be involved in the production of panic attacks [27,28]. Activity of norepinephrine systems in the body and the brain is responsible for many of the physical symptoms of anxiety, such as blushing, sweating and palpitations, which may cause people to become alarmed. However, these systems have also been linked to the production of flashbacks in people with posttraumatic stress disorder [29]. Changes in the brain activities were observed in patients with anxiety. Modern brain-imaging techniques allowed evaluation of the activity of specific areas of the brain in people with anxiety disorders. Abnormalities in cerebral blood flow and metabolism, and possible structural anomalies (e.g., atrophy) in the frontal, occipital and temporal lobes of the brain were observed in some patients with anxiety disorders. However, impairment of the cerebral blood flow could be the result of chronic anxiety rather than being a cause [30]. The amygdala which is involved in the neural circuit of learning to fear a previously neutral/harmless stimulus requires communication with the frontal cortex to form mature fear circuit, including hypothalamic-pituitary-adrenal (HPA) regulation, and reflects highly complex influences on fear mechanism during childhood (e.g., rearing or stress) [31]. Amygdala hypersensitivity was implicated in some forms of anxiety among youth [32]. Increased amygdala responses to fearful facial expressions were found in adolescents with generalized anxiety disorders [33]. The ventral prefrontal regions regulate the affective processing and facilitate proper responses in the presence of affective interference. Prefrontal regulation is especially important during adolescence due to increased reactivity of affective processing systems like the amygdala in response to emotional information compared to children and adults which make them more prone increased incidence and severity of anxiety disorders [34]. It is interesting to observe decreasing in brain function abnormalities with successful

pharmacological or cognitive behavioral intervention [35].

**Environmental Factors:** Environmental factors are likely to play an important part in determining the development of anxiety disorders. Families show intergenerational patterns of psychiatric disorders.

**Parenting style:** The parenting style is an important risk factor for anxiety disorders. Parental anxiety disorder has been associated with increased risk of anxiety disorder in the offspring [36]. Parental overprotection and parental rejection were observed to be significantly associated with increased rates of social phobia in adolescent offspring [37]. Parent-adolescent disagreements were found to indirectly increase the risk for the anxiety and depressive disorders through their direct association with high symptom levels [38]. Anxious parents can model fear and anxiety, reinforce anxious coping behavior, and unwittingly maintain avoidance, despite their desire to help their child. Overprotective, over controlling and overly critical parenting styles that limit the development of autonomy and mastery may also contribute to the development of anxiety disorders in children with temperamental vulnerability [39]. Shyness in infants was found to be positively related to low sociability in families, highlighting the importance of environmental influences in the development of anxiety [40]. The child rearing styles and parental over-control tend to interfere with children's acquisition of effective problem-solving skills, resulting in failure to learn to deal successfully with stressful life experiences. Anxious parents are characterized by relatively high parental control and avoidance [41]. Anxious fathers are more controlling than anxious mothers; while anxious mothers use more punishment and reinforcement of children's dependence in anxiety provoking situations compared to fathers [42].

**Childhood hardship and traumatic events:** Anxiety disorders in children could be triggered by exposure to negative life events. Exposure to natural disasters such as earthquakes, bushfires, and violent storms may increase the rate of anxiety disorders in children. Parent loss may make the children more prone to post-traumatic stress disorder (PTSD) or symptoms. However, parent loss has greater impact in triggering post-traumatic stress disorder than exposure to natural disasters and trauma. This is specially observed in girls, younger children, and children living with a surviving parent who scored high on a measure of posttraumatic stress reported more symptoms [43]. Emotional distress after a natural disaster can persist as long as 10 months that is more evident in girls than boys [44]. However, many anxious children do not necessarily experience elevated rates of negative life events, and many children can survive trauma without clinically significant psychological problems. The effects of environmental stresses are mediated through their effects on parent-child relations [45]. For example, mother's response to a bushfire disaster is the best predictor of post-traumatic phenomena in children following this disaster. The mothers become very anxious and overprotective following the fire and their children tend to exhibit the most post-traumatic symptoms [46]. Anxious parental behavior has been found to influence the degree of distress shown by children during painful medical procedures [47].

**Family social circumstances:** Families with lower education

have higher rates of anxiety disorders than families with a higher education. However, there is little scientific evidence supporting the role of parental education in anxiety pathogenesis. Low household income or unsatisfactory financial situations are associated with higher incidence of anxiety disorders. However, the exact enlightenment is not well elaborated. The degree of urbanization (rural/urban) does not typically correlate with anxiety disorders [48]. Therefore, anxious children cannot be characterized by family size, parental marital status, educational attainment or intelligence [49].

#### **Absence of Protective Factors**

Absence of the protective factors is particularly an important risk factor for development of anxiety disorders. Children's coping skills are considered as protective factors in childhood anxiety disorders. Learning to use active coping strategies, distraction strategies, and problem-focused rather than avoidant-focused coping is useful to decrease anxiety levels [50]. Impaired resilience with decreased ability to succeed in the face of challenges is another risk factor to develop anxiety. Impaired resilience occurs due to a number of factors including absence of active stance toward life, lack of a positive relationship with a significant adult, and weakened persistence. Children supported in their efforts at mastery with positive future expectations and who experience secure parent-child attachments learn how to maintain an active stance toward life and persist in the face of difficulty [51]. Modification of risk factors and enhancement of protective factors helps to reduce the incidence and prevalence of anxiety disorders in children and adolescents [52].

#### **Comorbidities**

Anxiety disorders in children and adolescents are often associated with various psychiatric disorders including other anxiety disorders, depression, attention-deficit hyperactivity disorder (ADHD), oppositional defiant disorder, substance abuse, and other psychiatric disorders. This high comorbidity may reach up to 40% and may influence the functioning and treatment outcome as each disorder has its independent contribution to impaired functioning, particularly in school performance, and is hard to isolate. These comorbidities should be searched for, assessed, and treated concurrently with the anxiety disorder [53]. At the same time, childhood anxiety disorder is considered as a risk factor for development of other types of child psychopathology, such as mood disorders and behavioral problems [54]. Presence of comorbidities makes the diagnosis complicated due to overlapping of the symptoms of anxiety disorders with symptoms of the comorbid conditions, which can lead to misdiagnosis and/or under diagnosis of comorbidity. Inattention, for example, may be present in anxiety, ADHD, depression, learning disorders, and substance abuse. A common clinical phenomenon is the recognition of a comorbid diagnosis once the primary diagnosis is treated and additional symptoms become more evident [15]. Anxiety may also be present with other non-psychiatric organic diseases such as asthma. Bad interpersonal and inter-parental relationships and poor scholastic achievement may be the reasons behind the increased risk of occurrence of anxiety state among children with chronic organic disease [55].

#### **Clinical Manifestations**

Anxiety has a wide spectrum of intensity. For some children and adolescents, anxiety symptoms may present with mild symptoms that can be confused with developmentally appropriate displays of fear, worry, or shyness to a severe symptoms of significant distress that can impair the child functions to enough degrees that warrant the diagnosis of a disorder. About 10% of all children are on the mild self-limited end of the anxiety symptoms continuum, and approximately 2% are at the severe end with major impairment of their daily functions. However, between the two ends many of the symptoms can "overlap" especially in children [56].

#### **Separation anxiety disorder (SAD)**

Despite it can occur at any age group, separation anxiety disorder (SAD) is the most common anxiety disorder found in children and occurs in 2-4% of children and is a strong predictive of adult anxiety disorders, especially panic disorder [57]. It is manifested by excess anxiety of the child when separated from his parents or substitutes, to a degree inappropriate to his developmental level, persists for at least 4 weeks, and may involve feelings of panic. Symptoms may include worries about harm to a loved one, reluctance to go to school, or somatic complaints (e.g., abdominal pain, headache, nausea, and vomiting). Palpitations, dizziness, fainting sensation, and other cardiovascular symptoms are frequent in older children, which could impair their academic, social, and family activities, and producing significant personal or family stress. The affected children feel humiliated and fearful, with low self-esteem. Children may also worry about getting lost or kidnapped [58]. The primary indicators of SAD appear to be separation distress, and avoidance of being alone or sleeping away from their caregivers. Consequently, they are excessively close to their caregivers, not allowing them to be away. At home, they have problems sleeping, and need constant company. Symptoms cause intense distress and significantly interfere with the different aspects of children's and adolescent' lives [59,60]. Separation anxiety disorders can have its root during the neonatal periods. Babies who need neonatal intensive care are more liable to suffer separation anxiety and may have behavior problems in the future life [61].

#### **Generalized anxiety disorder (GAD)**

Generalized anxiety disorder (GAD) affects 2-3% of children. It starts with insidious onset of excessive worry about a wide range of negative possibilities about many things in the child's life and the intense feeling that something wrong will happen. They have irrational, exaggerated fears and worries about several situations [62]. This disorder is rarely diagnosed in infancy and young children when they started to cry with freezing, tantrums, clinging, excessive timidity, and shrinking from contact with new people, with significant distress in unfamiliar social settings. Older children and adolescents may present with physical symptoms of anxiety (e.g., pallor, sweating, tachypnea, tachycardia, restlessness, muscle tension, hyperarousal and recurrent somatic complaints such as abdominal pain or headaches). They are always tense and give the impression that any situation could trigger anxiety. They worry a lot about what other people think of their performance in different areas and

they desperately need to be reassured or calmed down. They can also have perfect ionistic tendencies towards schoolwork. They hardly relax; often have somatic complaints without any apparent cause. They show also avoidance behaviors such as school avoidance or social withdrawal and sleep disturbances [63]. A generalized anxiety disorder diagnosis must include thorough history taking, the use of age-appropriate screening tools, and physical assessment [64].

### **Panic Disorder**

Panic attack is a sudden overwhelming surge of anxiety, stress, and fear. It is quite common, and about one third of people have an attack at least once in a lifetime, usually in a stressful situation or when they are overtired or had too much caffeine. It is also a frequent symptom in psychiatric diseases even outside of panic disorder [65]. Panic disorder preferentially develops in adolescence, more commonly in girls than boys, particularly in subjects who are prone to anxiety or show traits of the “avoiding personality”, but who also have a depressive tendency [66].

Panic disorder can present at different stages of childhood and adolescence except infancy. It is rarely observed in young children. Panic attacks may present in early childhood with extreme distress, intense crying, tantrums, freezing, clinging, or staying close to a familiar person during the attack. The frequency of the attacks increases a lot by the end of adolescence and affects approximately 1-5% of adolescents [67]. The attacks are characterized by exacerbated fear of death associated with numerous autonomic symptoms such as tachycardia, palpitations, sweating, dizziness, shortness of breath, chest pain, sensation of choking or of being smothered, nausea, abdominal pain, tremors and paresthesia with tingling and numbness in extremities, and extreme tension followed by persistent preoccupation with having new attacks [68].

Thirty to 50% of patients have agoraphobia (anxiety about being in places or situations from which escape might be difficult in the event of having an unexpected or situational predisposed panic attack or panic-like symptoms e.g.: closed places such as movie theaters, and crowded places such as start and finish time of classes at schools [69]. The Panic Disorder Severity Scale for Children is a well validated, reliable, and clinically useful for the assessment of panic disorder in children and youth and able to measure the symptoms of panic disorder with or without agoraphobia [70]. Panic attacks in the context of panic disorder are characterized by a greater number and severity of symptoms compared to panic attacks in the context of social anxiety disorder, and were associated with a history of traumatization, inpatient psychiatric treatment, and benzodiazepine use [71].

### **Acute Stress Disorder/Posttraumatic Stress Disorder (PTSD)**

Children are at risk of posttraumatic stress disorder (PTSD) following injury due to pediatric accidental trauma. The symptoms may occur after experience of severe traumatizing event such as actual or threatened death, injury, or threat to the physical integrity of the child or adolescent or to someone close to him/her, or the witnessing of such an event (e.g., sexual abuse or assault, a shooting, an earthquake) [72]. The response occurs in the form of intense fear, helplessness, or horror. In acute stress

disorder symptoms resolve within 1 month of the occurrence of the traumatic event, while in PTSD symptoms are present for more than 1 month afterwards [73]. PTSD is an interaction between a subject, a traumatogenic factor and a social context and is defined as intrusive re-experiencing of the trauma, avoiding traumatic reminders, and persistent physiological arousal [74].

These disorders are not commonly diagnosed in infancy, but may take the form of failure to thrive, feeding problems, or extra fears or aggression in response to stress [75]. In early and middle childhood, it may present as distressing dreams of the event that may change to generalized nightmares of monsters or other threats to self and others. Persistent re-experiencing of the traumatic event through repetitive play, drawing, or storytelling; possible constriction of other play is a common presentation. Physical symptoms are frequently encountered as recurrent abdominal pain, headaches, increased arousal or hyper vigilance; and sleep problems. These children frequently try to avoid any activities related to the traumatic event. They also frequently suffer failure to progress or have regression in their developmental skills, such as toilet learning, language development, socializing, and learning in school; with difficult concentration [76,77]. Adolescents may have distressing dreams of the traumatic event or flashbacks to the traumatic event with persistent re-experiencing of the traumatic event, sometimes through risk-taking behavior with avoidance of activities related to the traumatic event. They may fail to attain adequate academic progression or even regress with difficult concentration. They suffer also lack of thoughts and plans about their future. They may also develop impulsive or aggressive behaviors [78,79].

### **Specific Phobia**

Specific fears are particularly common in childhood and are usually transient during this period. It present with intense or persistent fear (lasting at least for 4 months) triggered by presence or anticipation of the presence of a specific object or exposed to certain situation. Exposure to the object or situation will cause an immediate reaction and physical symptoms that reach the intensity of panic. The child usually cries, has tantrum, or becomes immobile, and “clingy” The child will attempt to severely limit his own activities and his family’s activities to avoid possible exposure to the feared object or situation and could interfere significantly with the child’s or adolescent’s normal routine or functioning [80,81].

### **Social Phobia**

In social phobia, the child feels marked stress with severe and persistent fear in social situations that include people strange to him/her or the child will be in a situation where he/she is under the inspection and observation by others. These situations include but not limited to play dates, large family gatherings, birthday parties, religious ceremonies, and/or collective sharing times at childcare or preschool. The fear must last at least 4 months [82,83]. The physical symptoms of social phobia may reach the intensity of panic when the child or adolescent is in a social situation. These symptoms may lead to school avoidance and/or avoidance of age-appropriate social activities (e.g., sleepovers, school dances). These children usually have significant restriction in lifestyle that could affect important life decisions and prevents

making use of most of the available opportunities. Individuals with social phobia are more likely to show disabilities in school, work, and social life [84].

### Obsessive Compulsive Disorder

Obsessive compulsive disorder (OCD) is a disorder in which obsessions and/or compulsions that cause impairment and distress, and interfere with the child's developmental adaptation, daily activities, and cause marked distress and often disrupt peer and family relationships as well as the school performance [85]. Obsessions present with repetitive, intrusive, and persistent thoughts, ideas, impulses or images that are intrusive, inappropriate and cause marked anxiety or distress. Individuals with obsessions usually attempt to ignore or suppress such thoughts or impulses or to counteract them by other thoughts or actions [86]. Compulsions are repetitive behaviors (such as hand washing, ordering or checking) or mental acts (such as praying, counting, or repeating words) that occur in response to an obsession or in a ritualistic way. It may present in early children when playing or interests take on a compulsive or ritualistic quality (e.g., lining up toys in certain sequences); and interruption of these acts results in intense distress (e.g., refusing to let go of a particular object). Older children and adolescents may present with repetitive physical acts as hand washing, checking and counting rituals, repeating words silently, repetitive praying, hoarding, and arranging objects so that they are "just right". They are over concerned about harm coming to themselves or others if compulsion is not carried out. These symptoms cause significant distress and are severe enough to interfere with functioning, including their school performance [87,88].

### Selective Mutism

It is an uncommon complex anxiety disorder in young children, characterized by inability of the child to talk and communicate effectively in selective stressful social settings. Most commonly, this disorder initially manifests when children fail to speak in school. These children are able to speak and communicate in settings where they are comfortable, secure, and relaxed. Many children with selective mutism have marked trouble in responding or starting communication in a nonverbal manner; therefore social engagement may be compromised in many children when confronted by others or in an overwhelming setting where they sense a feeling of expectation. Selective mutism can result in significant social and academic impairment to the affected children [90,91].

### Impact of Anxiety Disorders on Children' Quality of Life

Generally, there is a poor-quality of life among children suffering anxiety disorder that is observed across all types of anxiety disorders [91]. Symptoms of generalized and separation anxiety disorders have the most significant impact on quality of life [92]. The quality of life is not only affected by the anxiety symptoms but could also be affected by the co morbid conditions such as depression or sleep disorder or by the medications used to control anxiety. Medications may have cognitive or behavioral effects or physically uncomfortable side effects that interfere with school performance. Improved prevention and treatment for anxiety disorders would be impactful both for individual quality of life and for societal productivity. Proper recognition

and management also help to prevent common secondary disorders, such as depression and drugs and/or alcohol abuse. Any intervention should aim to improve the relationships with others, a full and satisfying school and social life, increased self-esteem and improved overall quality of life [93].

### Assessment of Anxiety Disorders in Children

Careful screening for anxiety symptoms and rating the severity of the anxiety symptoms and functional impairment in children and youth with anxiety disorders are of utmost importance. The affected child should have careful assessment for presence of comorbid psychiatric conditions as well as for any systemic medical conditions (e.g., hyperthyroidism) that may mimic anxiety symptoms. Anxiety disorder should also be differentiated from the developmentally appropriate worries, fears, and responses to stressors that are normally observed in children. Finding the root stressors or traumas and their role in contributing to the development or maintenance of anxiety symptoms is an important step for successful treatment by avoiding the anxiety-provoking stimuli [94].

For preschool and young children between 2.5 and 6.5 years, a parent report adapted scale such as Preschool Anxiety Scale can be used [95]. For children older than 8 years, many child self-report screening measures such as Multidimensional Anxiety Scale for Children, Screen for Child Anxiety and Related Emotional Disorders (SCARED), and the Spence Children's Anxiety Scale (SCAS) can be used [96]. For social phobia or social anxiety, the Social Anxiety Scale, the Social Worries Questionnaire, and the social phobia subscale of SCARED are brief screening measures for social phobia/social anxiety symptoms [97].

### Management of Anxiety Disorders in Children

#### Psychological Treatments

**Cognitive Behavioral Therapy (CBT):** Cognitive behavior therapy (CBT) is a group of psychotherapeutic interventions aims to reduce psychological distress and maladaptive behavior by altering cognitive processes. It is based on the underlying hypothesis that affect and behavior are largely the products of cognition and, as such, that cognitive and behavioral interventions can bring changes in thinking, feeling and behavior [98]. Cognitive behavior therapy includes psychoeducation of child and caregivers regarding the nature of anxiety; techniques for managing somatic reactions including relaxation training and diaphragmatic breathing; cognitive restructuring by identifying and challenging anxiety-provoking thoughts; practicing problem-solving for coping with anticipated challenges; systematic exposure to feared situations or stimuli, including imaginal, simulated, and in vivo methods, with special focus on desensitization to feared stimuli; and relapse prevention plans [99].

**Mindfulness-Based Psychotherapies:** Mindfulness-based psychotherapy is rooted in the Far East meditation culture. Mindfulness means paying attention in a particular way: on purpose, in the present moment in a nonjudgmental and nonreactive way. Two approaches in particular are used to increase psychological health: mindfulness-based stress reduction (MBSR) and mindfulness based cognitive behavioral therapy (MBCT) [100, 101].

These methods are beneficial adjunct to outpatient mental health treatment for adolescents [102].

**Psychodynamic Psychotherapies:** Psychodynamic psychotherapy is another treatment option used in clinical practice for a range of common mental disorders in children and adolescents including anxiety. It has been used to treat anxious children since the 1940s [103]. Some reports observed considerable beneficial effects of psychodynamic psychotherapy with phobias or separation anxiety disorder [104].

#### Psychopharmacologic Treatments

Serotonergic antidepressants are used to dampen fear responses in children with anxiety disorders. Selective serotonin reuptake inhibitors (SSRIs) are effective and safe for the acute treatment of anxiety disorders, including generalized anxiety disorder, separation anxiety disorder, and/or social phobia in children and adolescent [105].

**Fluoxetine:** Fluoxetine (SSRI) can significantly improve the anxiety symptoms and is generally well-tolerated. Adverse effects reported include nausea, abdominal pain, drowsiness and headaches. Youths with only one anxiety disorder appeared to respond to lower doses of fluoxetine than those with multiple anxiety disorders [106].

**Fluvoxamine:** Fluvoxamine (SSRI) significantly improves the anxiety symptoms in children and adolescents with mixed anxiety disorders. It is well tolerated, and there were no statistically significant differences in adverse events between placebo-treated patients and those receiving fluvoxamine [107].

**Paroxetine:** Paroxetine (SSRI) becomes an effectiveness treatment in anxiety disorders in children and adolescents. Paroxetine is well-tolerated but can cause decreased appetite, vomiting, insomnia emotional lability and suicidal ideation [108].

**Sertraline:** Sertraline (SSRI) treatment is associated with statistically significant improvements in anxiety symptoms, lower symptom severity with greater improvement. Sertraline at a daily dose of 50 mg is safe and effective in treating generalized anxiety disorder in children and adolescents [109].

**Venlafaxine:** Venlafaxine is one of the serotonin-nor-epinephrine reuptake inhibitor (SNRI) class, which increases the concentrations of the neurotransmitters serotonin and nor-epinephrine in the body and the brain. Venlafaxine significantly improves symptoms of generalized anxiety disorder, panic disorders, as well as Social Anxiety Scale. Side effects of Venlafaxine include anorexia, somnolence, increased heart rate and blood pressure, as well as weight loss. Suicidal ideation/suicide attempt was also reported. Extended-release Venlafaxine may be an effective, well-tolerated short-term treatment for pediatric generalized anxiety disorder [110].

**Duloxetine:** Duloxetine is another a serotonin-norepinephrine reuptake inhibitor (SNRI);effective in treatment of major depressive disorder, generalized anxiety disorder, fibromyalgia and neuropathic pain. Significant side effects included nausea, vomiting, decreased appetite, dizziness, cough, oropharyngeal pain and palpitations [111].

**Tricyclic Antidepressants:** Tricyclic antidepressants, specifically, Clomipramine, were frequently used to treat pediatric anxiety

disorders before the availability of newer antidepressant medications. Their role has subsequently been replaced by the SSRIs and SNRIs. Their side effects include the need for frequent cardiac monitoring, lethality in overdose, and limited clinical experience in pediatric populations [112].

**Benzodiazepines:** Benzodiazepines are psychoactive drugs that bind to the GABAA receptor and enhance the effect of the neurotransmitter gamma-aminobutyric acid (GABA) at the GABA<sub>A</sub> receptor, resulting in sedative, hypnotic, anxiolytic, anticonvulsant, and muscle relaxant properties. It was used for nearly two decades to treat anxiety symptoms in youth despite the limited randomized, controlled studies in few patients [113].

#### Herbal Medicine

The use of herbal remedies is increasing and it is important for the family physicians to ask their patients about such use. Encouraging data support the effectiveness of some of these products, particularly Kava and, to a lesser degree, Inositol. Although none of these supplements or products is free of adverse effects, the potential for benefit seems greater than the risk of harm. The use of omega-3 fatty acids has little therapeutic values in anxiety disorders, and their use should be discouraged, supporting use of more effective treatments [114].

#### Predictors of Treatment Response

There are different factors that can predict the response of children with anxiety to treatment. Demographic factors are very important. Older children have a decreased likelihood of remission of anxiety. Having a first-degree relative with an anxiety disorder is associated with poorer functional outcomes while being Caucasian predicted an increased likelihood to enter remission. At the same time, children with better family functioning are more likely to be in remission. The clinical characteristics of anxiety are also of paramount importance. The type of specific anxiety disorders appears to influence treatment response. The more severe anxiety at baseline is, the poorer the functional outcome and can predict SSRI non-response. The presence and the number of comorbidities can predict the treatment failure. A diagnosis of a comorbid internalizing disorder attenuated the probability of achieving remission at endpoint [94].

#### Conclusion

Anxiety disorders are the most common class of psychological disorder in children and adolescents. Early detection and proper management will help to decrease the possibility of anxiety disorder into adulthood.

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