



## Pediatric depression

Nimmy Davis<sup>1\*</sup>, Alfa Mariyam Thomson<sup>2</sup>, Dr. Abel Abraham Thomas<sup>3</sup>, Dr. Elsey Abraham<sup>4</sup>

<sup>1,2</sup> Fourth Year Pharm D, Nazareth College of Pharmacy, Othara P.O Thiruvalla, Kerala, India

<sup>3</sup> Assistant Professor, Department of Pharmacy Practice, Nazareth College of Pharmacy, Othara, P.O Thiruvalla, Kerala, India

<sup>4</sup> Principal, Nazareth College of Pharmacy Othara, P.O Thiruvalla, Kerala, India

### Abstract

Depression is a sad morbid state that affects nearly all daily activities and has short term as well as long term consequences. Pediatric depression is a subject worth studying since it continues episodically into adulthood. This article summarizes the etiology, clinical presentation and treatment strategies of depression in pediatric population. It also throws a light on etiology of depression in adolescents. Understanding the disorder is crucial for determining the etiologic status, which aids in promoting interventional strategies. The clinical presentation and natural course of the disease are mostly similar in the entire lifespan. However, some variability exists. This variability also exists among gender, as female population is more susceptible to depression. Pediatric depression mostly occurs in situation where the needs of the child are not taken care of as in case of vulnerability and poverty. If early and effective diagnosis is made, then suitable intervention methods can be adopted based on the patient need. This involves psychotherapy, pharmacological treatment and other treatment options.

**Keywords:** pediatric, depression, etiology, clinical presentation, psychotherapy

### 1. Introduction

Depression is defined as the inability to experience pleasure in nearly all daily activities and changes the way the person feels, thinks, and acts. It is a morbid sadness, dejection or melancholy which is realistic and proportionate to personal loss. Pediatric depression affects the life functions of the child, thereby increasing the morbidity and mortality rates. Individual, family and environmental factors are the psychosocial risk factors for childhood depression [2]. Depression earlier was seen as an adult disorder and children were considered developmentally immature to experience depressive disorders. Adolescent low mood was often seen as a part of normal teenage mood swings [3]. Pediatric depression is a common psychiatric condition that continues episodically into adulthood.

The two most prevalent pediatric depressive disorder, are major depressive disorder (mdd) and dysthymic disorder (DD). A major depressive disorder is characterized by one or more depressive episodes without a history of mania, mixed or hypomanic episodes. Dysthymic disorder is characterized by a chronically depressed mood that occurs for most of the day for at least two years [4, 5].

As a biopsychosocial phenomenon, pediatric depression deserves attention, considering the serious, long lasting consequences of the disease to child development, which ranges from physiological changes to the impairment of social, cognitive functions. In the short-term, depressive disorders become a source of psychological suffering for those affected children, whereas in the long-term they compromise social, cognitive, and emotional aspects of child development, thus episodically continuing into adulthood [6]. These depressive episodes are associated with negative consequences later in adolescence such as academic difficulties, risky behavior, self-injury and in adulthood it is associated with lower income levels, higher

divorce rates, suicide tendencies.

The etiological mechanisms that contribute to the onset and maintenance of pediatric depression remain unclear. Individual, family and environmental factors have been documented as psychosocial factors for childhood depression. Individual factors include age, gender, psychological and physical vulnerability, comorbidity with other disorders, emotional disturbance, impaired sociability, low self-esteem and social skill difficulties. Family factors associated with pediatric depression consist of child abuse and marital conflict parental depression. Environmental factors include daily social difficulties, stress, traumatic life events, lack of social support and poor friendships [7]. Symptoms associated with depression can cause significant emotional, physical, cognitive, behavioral, and interpersonal impairment. Poor peer relationships, low self-esteem, and high negative approaches have been strongly associated with depression in pediatric population. Depressed children have been found to demonstrate low rates of social behavior, poor friendship quality, and tend to draw out rejections and negative reactions when interacting with peers. Additionally, depressed children demonstrate sensitivity to negative social cues. Pediatric depression has also been associated with poor self-concept, with children tending to evaluate themselves negatively, to have low expectations for performance, more stringent criteria for failure, and a lower perceived self-competence, depression has also been correlated with a wide range of negative outcomes, such as high rates of suicide, loneliness, social anxiety, and alienation in childhood and adolescence [8, 9].

A diagnosis can be made by a practicing physician. There are various treatments including medication and therapy. Treatment includes education, psychotherapy and medications. Pharmacological treatment depends upon the severity of depression, patient convenience and risks and

benefits [3].

Taking this into consideration, the review is based on the following question: Considering that pediatric depression is an important public health issue, this review aims to assess currently existing evidence taking into consideration, the various aspects -etiology, diagnosis, treatment and prevention of childhood depression [6].

### A. Epidemiology

Several studies have reported that major depressive disorder ranges from 0.4% - 2.5% in children and 0.7 – 9.8% in adolescents. The risk for the disorder starts early in life and continues linearly through adolescence. The risk ranges from 15% to 25%. In the national comorbidity study, in the US, the prevalence of minor depression was 11% in adolescents. Epidemiological studies of community samples have reported the prevalence of MDD in children to range from 0.4–2.5%, while the prevalence of DD has been reported to range from 0.6–1.7%. In total, 23% of children reported depressive symptoms in the “at-risk” and clinical range, and these levels did not differ across sex or grade. However, the number of children exceeding cutoff scores for clinically significant levels of depressive symptoms as assessed by the children’s depression inventory (CDI) has been shown to range from 20 to 24% [7].

Several studies have revealed that females are 2-3 times more likely to develop depression when compared to males. The rate of depression is almost equal in both boys and girls prior to adolescence. However the rates change during early to middle adolescence and this rate continues to adulthood. This difference in rate is due to hormonal changes, stress and response to stress, socialization experiences and difference in interpersonal relationship.

Social status such as income level has a prominent effect on depression. Lower socioeconomic status has a direct effect on depression. Low socioeconomic status is associated with high levels of stress due to family disruption, adverse environmental conditions and financial difficulties [7, 10].

### B. Pathophysiology

#### Brain Abnormalities

Several areas of the human brain are involved in mood functions. Memory, sleep and appetite are commonly disturbed in patients with depression. All cerebral components responsible for these functions are parts of limbic system. These components usually receive signals from neurons that secrete norepinephrine or serotonin or both. Reduced activity of circuits that make use of NE or serotonin may contribute to depression. The prefrontal cortex of the brain is related to emotional responses. Diminished activity of this region may contribute to depression.

Various studies have shown that depressed children had a smaller ratio of frontal lobe volume to cerebral volume. This suggests that alterations in the frontal lobe volume may also lead to depression.

#### Neuroendocrine Abnormalities

Neurotransmitter system abnormalities are important determinants of pathophysiology of pediatric depression. Nobile *et al* found out that serotonin uptake in depressed children is different when compared to a non-depressed child. De Bellis *et al*, in a study, examined nocturnal secretion of adrenocorticotropin, cortisol, growth hormone

and prolactin in a group of depressed pediatric population with comparison to a control group. In the study, it was concluded that depressed children had lower cortisol secretion in the first four hours of sleep. However the levels of cortisol, adrenocorticotropin and prolactin levels did not differ between the two groups [9].

### C. Signs and symptoms

Several empirical data suggests that the clinical signs and symptoms are similar in adults, adolescents and children, even though some developmental differences are observed. To note specifically, hypersomnia has a developmental pattern. It has a higher prevalence in adolescents rather than in children. Suicide attempts also increase with age. Behavioral problems and psychotic complaints are very common during the child’s developmental stage, while they experience less frequent psychotic and melancholic symptoms. In children, psychotic depression is usually manifested by auditory hallucinations. In contrast, in adolescents and adults it is manifested as delusions. Maturation effects and cognitive functions have known to contribute to these differences [7].

A major depressive episode in children and adolescents usually includes at least 5 of the following symptoms during the same 2-week period:

- Depressed (or irritable) mood
- Diminished interest or loss of pleasure in almost all activities
- Sleep disturbance; insomnia or hypersomnia
- Weight change, appetite disturbance, or failure to achieve expected weight gain
- Decreased concentration or indecisiveness
- Suicidal ideation or thoughts of death
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Feelings of worthlessness or inappropriate guilt [9]

Depression is also characterized by atypical features and depressed pediatric population may also experience the following

- Increase in appetite or significant weight gain
- Increased sleep
- Feelings of heaviness in arms or legs
- A long standing interpersonal rejection which may extend far beyond mood disturbance and ultimately result in social or occupational functioning impairment [9].

### Gender Differences

The severity and symptoms of depression vary with respect to gender. Females are usually reported to suffer from high levels of symptoms. Feelings of guilt, failure, increased crying, poor self-esteem and cognitive symptoms are frequent in females, while, anhedonia, social withdrawal and diurnal variation in mood and energy are frequent in males [11, 12].

### Comorbidity

Several studies have shown that about 70% children and adolescents with depression suffer from other psychiatric disorders. 70% children with dysthymic disorder eventually develop major depressive disorder thus resulting in double depression. Other comorbid conditions include disruptive

disorder, anxiety disorder and other substance use disorders. In youth with major depressive disorder and dysthymia may increase the frequency of social and suicidal impairment<sup>[13]</sup>. Depressed students of any age usually portray depressive thoughts and negative attitude about school performance. This negative thinking can lead to “won’t do” tendencies as well as incomplete work in children who are capable of doing their work. According to Verboom *et al.* (2013) as depressive symptoms increase, academic performances decrease. According to Jaycox *et al.* depressed teens have documented low levels of academic efficacy and academic engagement when compared to non-depressed teens. Teenagers may also exhibit self-destructive tendencies. However, each child is a unique individual and experiences and symptoms of depression may also differ<sup>[9]</sup>.

#### **D. Etiological Factors in children and adolescents**

The risk for depression increases episodically during the transition to adolescence from childhood. Adolescence is a crucial developmental stage where biological, psychological and social challenges are faced. It is marked by significant physical maturation changes such as onset of puberty, social cognitive advances such as abstract thinking, interpersonal transitions such as peer relationships and social roles in family.

#### **Family and genetic factors**

Molecular genetic effects have been closely related to early onset depression. Brain derived neurotrophic factor (BDNF) is observed on chromosome 11p14 which is a nerve growth factor that is involved in the regulation of neuronal survival, synaptic plasticity, cellular development, and resistance to stress. BDNF dependent processes have been implicated in the pathophysiology of depressive disorder<sup>[14]</sup>.

#### **Neurobiology**

Neurobiological research in pediatric depression suggests that neurobiological factors change during the course of development, and developmentally influenced neurobiological processes may become disrupted during depressive episodes.

#### **Electrophysiology**

Baseline EEG studies have revealed reduced left frontal electrical activity in infants and adolescents of depressed mothers as well as in adolescents with major depressive disorder. Decreased left frontal EEG activity reflects an underactivation of the approach system and reduced positive emotional expression, which may be a vulnerability marker for depression<sup>[15]</sup>.

EEG sleep measures have shown considerable variability between depressed youngsters and matched controls. Depressed adolescents seem to experience frequent disturbances in circadian rest-activity rhythms, sleep architecture, and RRG rhythms during sleep<sup>[16]</sup>. Baseline EEG sleep patterns differed between depressed adolescents who subsequently had a recurrent unipolar course versus those who developed bipolar illness; adolescents with unipolar course had predominantly rapid eye movement (REM) sleep changes while adolescents with bipolar course had non-REM sleep changes<sup>[16, 17, 18]</sup>.

#### **Neuro endocrine studies**

Depression is linked to altered responses to stress, and numerous studies have documented HPA dysregulation in

adult depression. However depressed children did not display changes in 24-hour Cortisol patterns. Another neuroendocrine marker possibly related to depression is growth hormone, which is secreted by the anterior pituitary and follows a circadian pattern with increased secretion during slow-wave sleep. Although the precise role of growth hormone secretion in depression is not known, it appears to be a marker of central noradrenergic and serotonergic (5-HT) systems. Reduced growth hormone secretion during sleep has been observed in adult depression, but findings in children and adolescents have been variable, with some studies showing no differences whereas others showing reduced or increased secretion<sup>[19, 20]</sup>.

#### **Neuroimaging studies**

Studies that used neuroimaging techniques documented converging lines of evidence. In familial depression, volumetric studies showed reduced left frontal lobe volume. Alterations in amygdala and hippocampal volumes were found in certain studies, although the effects appear to be moderated by anxiety and manic symptoms. In neurochemical studies, pediatric depression documented reduced glutamate and creatinine/phosphocreatinine concentrations in the anterior cingulate, and increased choline concentrations in the left dorsolateral prefrontal cortex<sup>[21, 22]</sup>.

#### **Temperament**

Even though learning and experiences, particularly within the social context is involved in the development and expression of temperament, it is strongly thought to have a genetic origin. Temperament usually characterizes harm avoidance, neuroticism, negative affectivity behavioral inhibition and anxiety. Negative affectivity is the inclination to experience negative emotions. It is characterized by a strong sensitivity to vigilance, emotional distress, negative stimuli, physiological arousal and increased wariness. In contrast, adventure, sociability and the sensitivity towards cues are the characteristics of positive affectivity. Depression is characterized by low levels of positive affectivity and high levels of negative affectivity<sup>[23, 24]</sup>.

#### **Cognitive Vulnerability**

According to cognitive theories of depression, individuals with negative beliefs about the world, self and future will appraise stressors in response to stressful events. Such individuals are more likely to be struck with depression when compared to others who do not have such cognitive styles. There are several types of cognitions that are related to depression. It includes negative automatic thoughts, cognitive distortions, low self-esteem, ruminative response self-control and control related self-efficacy. Several cross sectional studies conducted have shown a strong correlation between depression and negative cognitions. Negative cognitions develop over time and depression becomes stronger with development<sup>[25]</sup>.

#### **Interpersonal Relationships**

Development of secure attachment and social environment are the key principles to the interpersonal theories of depression. Vulnerability to depression arises in families where the child’s need for security, acceptance and comfort are not met. Several studies reveal that families of depressed persons are characterized by problems with communication,

attachment, support and poor child rearing practices. Rejection by family, peers, and teachers also contribute to depression in children as well as adolescents. According to theories of depression, depressed individuals both contribute and react to interpersonal problems [26].

### Stress

Stress may occur as a major life event or as accumulated minor events or as acute or chronic event. Stressful events may be pathological such as in case of an abuse or may be normative as in school transitions. Stress mainly depends on individual actions or at times may be independent on an individual's actions. There is clear link between stress and depression in children. Personal disappointments, child abuse, socioeconomic disadvantage, failures, losses, neglect and interpersonal problems are the negative effects that are associated with depression. Stress associated depression appears to have a strong association in the adolescence rather than in child hood especially in girls. The reasons involve stress reactivity, stress burden and hormonal effects. One theory suggests that recent stress along with childhood stress adds to lifetime stress burden.

### Response to Stress

As it was earlier seen, stress plays an important role in depression. But different individuals vary in the way they respond to stress. And this response can affect their emotional well-being and future adjustments. According to diathesis stress model, depression results from the interaction between stressful events and personal vulnerability. Several studies have documented the interactions between life stress and cognitive styles such as low perceived self-efficacy and negative cognitive styles. Several other types of coping mechanisms like problem solving skills and behavioral styles are related to pediatric depression. There are mainly two types of coping mechanisms: problem focused and emotion focused coping. Problem focused coping mechanisms involve responses which act on the stress source. Emotion focused coping mechanism involves palliative measures that are used to encounter negative emotions which arise from stressful situations. Automatic or involuntary response to any problem is actually a reflection of individual differences in temperament. Engaged coping mechanisms involves cognitive restricting, positive appraisal, problem solving and distractions. In contrast, disengagement responses include self-blame, rumination, avoidance and emotional reaction. Several studies in pediatric populations have documented that high levels of problem focused coping and engaged coping are associated with low levels of depressive symptoms. In contrast, emotion focused coping mechanism, involuntary and disengagement mechanisms are related to high levels of depressive symptoms [27, 28, 29].

### E. Diagnosis

There is no specific diagnosis to identify depression. However, various tests are done to rule out other potential etiologies [9]. The differential diagnosis of depression may include anemia, several cancers, hyper or hypothyroidism, SLE, stroke or other vascular diseases [30].

Laboratory tests may include the following:

- Complete blood count (CBC) with differential
- Serum electrolytes
- Blood urea nitrogen (BUN)

- Creatinine clearance and concentration
- Urine osmolality

### Other tests that may be indicated include the following

- Electroencephalography (EEG)
- Electrocardiography (ECG)
- Liver and thyroid function tests
- Children's Depression Inventory [9]

### F. Treatment

The treatment of childhood depression comprises pharmacotherapy, psychotherapy or the combination. Treatment depends upon various factors such as patient convenience, level of depression, associated risk factors and benefits [31].

#### Step 1: Education

For the treatment to be most successful, both the patient (child) as well as the family should be involved. The more important component of depression treatment is to learn about the disease. Family education is important before treatment decisions are made. It mainly includes the following:

1. The family can learn about the disease, its symptoms and thus can understand how these symptoms affect their daily learning, school works and their relationships. This also aids in recognizing if the symptoms recur in a completely recovered child.
2. The family can learn how to help the child cope up with depression which indeed speeds up the recovery.
3. They can learn how to make the environment more safe for the child specially in case of children who experience suicidal tendencies. [32]

#### Step 2: Psychotherapy

Psychotherapy is also known as counselling or talk therapy. Psychotherapy aims both at the patient and their families to understand their disease, its nature and themselves. It provides a longer lasting response and lower relapse when compared to pharmacotherapy. However, it is less available, more demanding and takes longer time to work than pharmacotherapy. Sessions are usually 30 to 60 minutes long. Usual counselling sessions are conducted for 8 to 10 weeks or longer. This includes how to deal with stress and depressed mood, manage relationships, and strategies to solve problems associated with depression.

During the session, the child talks about its feelings, behavior, relationships and thoughts. The child and the therapist then discuss various ways of taking action, which helps the child cope more effectively with symptoms. The aim of this session is to improve the problem solving skills of the child, thereby increasing their self-confidence [33, 34].

The two most effective methods of psychotherapy are:

- Cognitive behavioral therapy
- Interpersonal psychotherapy

Cognitive behavioral therapy (CBT):- cognitive behavioral therapy is a type of talk therapy in a structured way with a psychotherapist, attending a limited number of sessions. It is a useful tool to address emotional challenges [35]. CBT focuses on the 'here and now' and explores how the individual feels about themselves and others and how behavior is related to these thoughts as seen in fig: 1. The therapist identifies and questions maladaptive thoughts and

helps develop an alternative perspective [34].

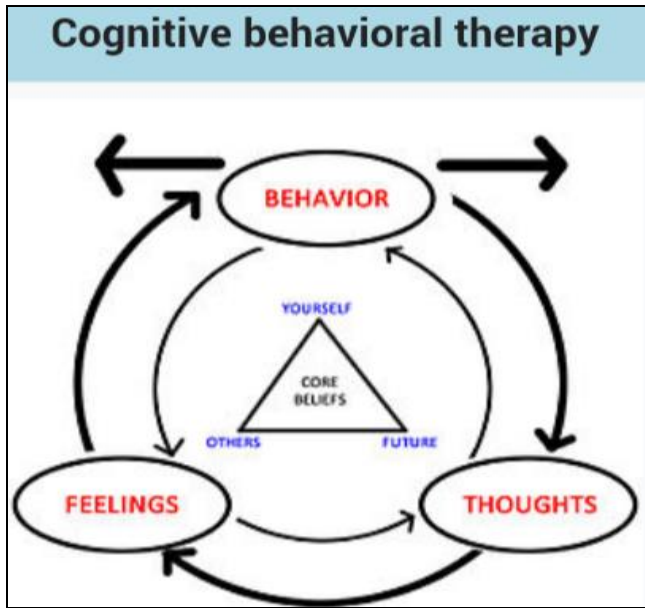


Fig 1: diagram depicting the effect of CBT therapy on emotions, thoughts and behavior [39].

This method aims to help the child identify and rectify the thoughts and behaviors which contribute to depression. It consists of activation of behavioral techniques and methods to improve coping skills, peer relationship, communication skills, solve problems, and regulate emotions [30]. However, there are certain risks associated with CBT. It can explore painful emotions experiences and feelings and the child may feel emotionally uncomfortable or physically drained.

The various steps in CBT include the following steps:

1. Identify troubling situations or conditions.
2. Become aware of thoughts, beliefs and emotions about the problems. This involves interpretation of a situation, events and beliefs.
3. Identify inaccurate or negative thinking. This helps recognize patterns of behavior and thinking that may contribute to depression.
4. Reshape inaccurate or negative thinking [35].

### Interpersonal psychotherapy

This aims at identifying and correcting problems that youth face with other people or any changes such as a move or parental divorce. Individual difficulties are framed in accordance to interpersonal terms and then relationship problems are addressed [36]. It helps mould the interpersonal relationships and adapt to changes in the environment [30]. Younger children benefit more from a therapy known as ‘family – based interpersonal therapy’ that involves the child and its family and discusses mainly on family relationships.

### Dialectical Behavior Therapy

It is usually used to treat children with suicidal thoughts. It emphasizes taking responsibilities and helps examine how to deal with conflicts and negative emotions [36].

### Play Therapy

It involves the use of blocks, toys, puppets, drawings and games to help the child identify and verbalize feelings. The

therapist observes the way the child uses and plays with the material and identifies patterns or themes to understand the child’s problems. This method aims to manage behavior, conflicts and feelings through a combination of play and talk [36].

### Psychodynamic Psychotherapy

This method emphasizes understanding various issues which motivate and influence the child’s thoughts, feelings and behavior. It helps identify the typical behavior of the child, defenses and responses to inner struggles and conflicts. An intensive form of psychodynamic psychotherapy is psychoanalysis and involves several sessions in a week [36].

The initial therapy sessions usually involve identification of factors that contribute to and maintain depression. The later sessions are then focused on therapy which involves changing unproductive behavior patterns. Psychotherapy can be provided by any healthcare professional with appropriate training including psychologists, psychiatrists, nurses and social workers.

### STEP 3: Pharmacological treatment

Children with moderate to severe depression are treated using drugs in addition to psychotherapy. Antidepressants are used to reestablish the normal balance of chemicals in the brain. Selective Serotonin reuptake inhibitor (SSRI’s) is the most widely used drug. The treatment plan is made taking into consideration, its risks, benefits, length and other alternatives.

1. Selective serotonin reuptake inhibitors: they are the first line treatment options for childhood depression mostly due to its minimal side effects and once daily dosing. Fluoxetine, Citalopram, Escitalopram, Fluvoxamine, Paroxetine and Sertraline are commonly in use. Side effects include headache, abdominal pain, nausea, sleep changes or a tendency to bruise. However they resolve within a week or two. A more serious side effect of SSRI’s is serotonin syndrome and symptoms include agitation, hyperthermia and confusions.
2. Atypical antidepressants: they are considered when SSRI’s are not effective or when they cannot be tolerated. Available options include Bupropion, Mirtazapine, Desvenlafaxine and Duloxetine.
3. Tricyclic antidepressants—another group of antidepressants that are rarely used in children due to its numerous side effects. These drugs inhibit norepinephrine and serotonin transporters which mediate active reuptake of biogenic amines NA and serotonin into their respective neurons and thus potentiate them. Imipramine, Amitriptyline, Desipramine, Nortriptyline and clomipramine are the available drugs. TCAs do not appear to be effective in children and younger adolescents. The side effects of TCAs include dry mouth, constipation, nausea, blurred vision, difficult urination, drowsiness, weight gain, and rapid heartbeat

### Maintenance Drug Therapy

Maintenance therapy is considered for children and adolescents who are at high risk for relapse of depression. This may be as long as an year or even longer and is based on the history and patient situations [3, 31, 32,, 33, 37].

#### Step 4: Other Treatment Options

1. Alternative treatments: Alternative treatments for depression include omega 3 fatty acids and St. John's wort. So far, neither extensive studies nor clinical evidences are found regarding these, thus they are not clinically advised.

2. Electroconvulsive therapy: ECT is used to relieve severe depression. During ECT, chemical changes are induced in the brain using electric current. The exact mechanism is not yet understood completely. It is considered as a treatment option in those who do not respond to other treatments and in those who experience delusions. Patients are given an initial dose of general anesthesia to induce sleep and reduce discomfort. Side effects include brief memory loss and confusion [38].

#### Prevention

Prevention programs are aimed at identifying at an early age, the high-risk children showing increased levels of symptoms of depression. Various preventive programs are conducted which would result in positive effects to reduce depressive behaviors, prevent mental health problems and personality dysfunctions in adulthood. School is the ideal place to provide preventive methods to a large number of children before the disorder occurs in full scale. The goal of the prevention is to identify threshold levels of depression to reduce the impact of risk factors and to reinforce the power of protective factors [3].

According to a Dutch non-randomized experimental controlled trial, cognitive behavioral therapy, psycho education, problem solving techniques, relaxation exercise and cognitive restructuring exercises. A 10 weekly session was conducted for children with mild symptoms of depression and was named 'FRIENDS for life'. It is a brief cognitive-behavioral program intervention by classroom teachers. The acronym FRIENDS stands for; Feelings, Remember to relax, I can do it and try my best, Explore solutions, Now reward yourselves, Don't forget to practice, Stay calm.

Another study that used economic modeling techniques showed cost effective preventive measures for preventing childhood depression. This study was focused in Australian population [6].

#### 2. Discussions

Depression in childhood is not merely a mood regulation disorder. Depression is a common condition among children and adolescents, with long lasting detrimental effects on social and occupational functioning, as well as health. It is a condition that almost 8% of children experience. It is a morbid sadness, melancholy that affects the daily activities and changes the way the person feels, thinks and acts. It increases the morbidity and mortality rates. The two major types of pediatric depressive disorder are major depressive disorder and dysthymic disorder.

Depression occurs as a result of brain and neuroendocrine abnormalities. The diminished activity of prefrontal cortex and lower cortisol production are related to these abnormalities. The signs and symptoms of depression in children are similar to that of adults even though there are some developmental differences. In children, psychotic depression is usually manifested as auditory hallucinations. Sleep changes, depressed mood, thoughts of suicide, weight gain, guilt and fatigue are the usual signs and symptoms of

depression. The severity of signs and symptoms depend upon the gender. Females experience greater severity when compared to male population. Poor self-esteem, increased crying is common among girls, while, cognitive symptoms are manifested in boys.

There are various etiological factors that contribute to depression. Brain derived neurotrophic factor (BDNF) observed on chromosome 11p14 which is a nerve growth factor that is implicated in the pathophysiology of depression. Temperament is a factor that has genetic factor. Temperament is characterized by harm, negative thoughts and emotional distress. According to theories of cognitive vulnerabilities, children with negative thoughts will appraise stressors thus eventually; the child will be more susceptible to be struck with depression. Various stress burdens such as child abuse, parental divorce, neglect and various other factors lead to depression in children. Neurobiological studies which involve electrophysiology, neuroendocrine studies and neuroimaging studies have documented various functions of brain that becomes disrupted in depressive disorder. There is no specific diagnosis for depression. MRI scan, PET scan and EEG are usually performed to assess brain abnormalities. The differential diagnosis includes stroke, anemia, cancers and vascular abnormalities.

Treatment involves pharmacotherapy and psychotherapy. Education regarding the severity of disease, treatment and its course and risks and benefits of treatment is provided to the family. Psychotherapy also known as talk therapy is mainly divided into cognitive-behavioral therapy and interpersonal therapy. CBT focuses on identification and rectification of negative thoughts that lead to depression. Dialect psychotherapy, play therapy and psychodynamic psychotherapy are other types of psychotherapy provided to children. Pharmacotherapy includes tricyclic antidepressants, selective serotonin reuptake inhibitors and atypical antipsychotics. SSRI's are the first line treatment choices due to its minimal side effects. Alternative treatment includes use of omega 3 fatty acids and electroconvulsive therapy.

#### 3. Conclusion

Childhood depression is an important health issue and deserves special attention. Over the past decades, considerable advances had been made in the phenology and natural course of the disease. Clinical research has contributed immensely to identify various risk factors associated with pediatric depression and thus, this has resulted in advances in treatment options. Various factors that have been emphasized in the genesis of pediatric depression involve genetics, gene-environment interactions, neurobiology, environmental, interpersonal and cognitive factors. Time is a crucial factor which has been associated with the developmental challenges in pediatric depression, because the brain is sensitive to environmental influences and thus eventually lead to unfolding of depression. Depression compromises further development by interfering in academic achievement, establishing peer relationships and negotiating changes in family relationships. This may further result in additional stress, depression, compromised neurobiological development and other psychopathology. These dynamic processes are the reason why pediatric depression continues throughout the life span. The challenge is the integration of the findings to provide clinical interventions. Early and effective interventions help

interrupt the vicious cycle and allow children to reach their complete potential as adults.

#### 4. Acknowledgement

First and foremost we thank the Almighty. We extend our sincere thanks to the principal of our institution Dr. Elsey Abraham and Dr. Abel Abraham Thomas, guide of this review article for providing necessary information and support in completing the review. We would also like to express our gratitude towards our parents for their support and encouragement.

#### 5. Conflict of Interest

There is no conflict of interest in this review article.

#### 6. Reference

1. Depression. Depression in children and young people: Identification and management in primary, community and secondary care; NICE clinical guidelines, No: 28; National Collaborating Centre for Mental Health [UK]; British Psychological Society. 2005; 10:1-85433-424-7.
2. Joviana Avanci, Simone Assis, Raquel Oliveira, Thiago Pires. Childhood depression. Exploring the association between family violence and other psychosocial factors in low income Brazilian school children; *Child and Adolescent Psychiatry and Mental Health*. 2012; 6:26.
3. Barbara Maughan, Stephan Collishaw, Argyris Stringaris. Depression in childhood and adolescence; *Journal of Canadian Academy of Child and Adolescent Psychiatry*. 2013; 22(1):35-40.
4. Marita McCabe, Lina Ricciardelli, Sophie Banfield. Depressive symptoms and psychosocial functioning in preadolescent children; *depression research and treatment*, 2011.
5. Judith C, Kando Barbara, Wells G, Peggy E, Hayes Depressive disorders; Joseph, Dipiro T. *et al.* Pharmacotherapy a pathophysiological approach, 2002. 5<sup>th</sup> edition; McGraw Hill; page no, 1245.
6. Nadia Nara Rolim Lima. Childhood depression: a systematic review; *neuropsychiatric disease and treatment*, 2013, 1417-1425.
7. Uma Rao, Li-Ann Chen. Characteristics, correlates and outcomes of childhood and adolescent depressive disorders: dialogues in clinical neuroscience. 2009; 11(1):45-62.
8. Emily Dawn Hoerman. Depression in children and adolescents: the role of school professionals; *electronic theses and dissertations*, 2014.
9. Angelo P Giardino. Pediatric depression *Pediatrics Developmental and behavioral articles*, 2017.
10. Rao U. gender differences in depression during the transition to adulthood. *Trends Evidence-Based Neuropsychiatry*. 2002; 4:46-53
11. Masi G, Favilla L, Mucci M, Poli P, Romano R. Depressive symptoms in children and adolescents with dysthymic disorder. *Psychopathology*. 2001; 34:29-35.
12. Bennett DS, Ambrosini PJ, Kudes D, Metz C, Rabinovich H. Gender differences in adolescent depression do symptoms differ for boys and girls? *Journal of Affective Disorders*. 2005; 89:35-44.
13. Essau CA. Comorbidity of depressive disorders among adolescents in community and clinical settings. *Psychiatry journal*. 2008; 158:35-42.
14. Strauss J, Barr CL, George CJ. Association study of brain-derived neurotrophic factor in adults with a history of childhood onset mood disorder. *American Journal of Medical Genetics part B Neuropsychiatric Genetics*. 2004; 1316:16-19.
15. Tomarken AJ, Keener AD. Frontal brain asymmetry and depression: a self-regulatory perspective. *Cognition & Emotion London, UK Psychology Press*, 1998, 387-420.
16. Rao U, Poland RE. Electroencephalographic sleep and hypothalamic pituitary-adrenal changes from episode to recovery in depressed adolescents. *Journal of Child and Adolescent Psychopharmacology*. 2008; 18:607-613.
17. Rao U, Hammen CL, Poland RE. Risk markers for depression in adolescents: sleep and HPA measures. *Neuropsychopharmacology*. In press.
18. Forbes EE, Miller A, Cohn JF, Fox NA, Kovacs M. Affect-modulated startle in adults with childhood-onset depression: relations to bipolar course and number of lifetime depressive episodes. *Psychiatry Research*. 2005; 134:11-25.
19. Mathew SJ, Coplan JD, Goetz RR. Differentiating depressed adolescent 24 h Cortisol secretion in light of their adult clinical outcome. *Neuropsychopharmacology*. 2003; 28:1336-1343.
20. Steiger A. Sleep and endocrine regulation. *Frontiers in Bioscience*. 2003; 8:s358-376.
21. Rosenberg DR, MacMaster FP, Mirza Y, Easter PC. Imaging and neurocircuitry of pediatric major depression. *Clinical Neuropsychiatry Journal of Treatment Evaluation*. 2006; ss3:219-229.
22. Mayberg HS. Defining the neural circuitry of depression: toward a new nosology with therapeutic implications. *Biological Psychiatry*. 2007; 61:729-730.
23. Chorpita BF. The tripartite model and dimensions of anxiety and depression: an examination of structure in a large school sample. *Journal of Abnormal Child Psychology*. 2002; 30:177-190.
24. Rosenbaum JF, Biederman J, Hirshfeld-Becker DR. A controlled study of behavioral inhibition in children of parents with panic disorder and depression. *American Journal of Psychiatry*. 2000; 157:2002-2010.
25. Garber J, Hilsman R. Cognition, stress, and depression in children and adolescents. *Child and Adolescent Psychiatric Clinics of North America*. 1992; 1:129-167.
26. Nolan SA, Flynn C, Garber J. Prospective relations between rejection and depression in young adolescents. *Journal of Personality and Social Psychology*. 2003; 85:745-755.
27. Grant KE. Stressors and child and adolescent psychopathology: measurement issues and prospective effects. *Journal of Clinical Child and Adolescent Psychology*. 2004; 33:412-425.
28. Cole DA. Stress exposure and stress generation in child and adolescent depression a latent trait-state-error approach to longitudinal analyses. *Journal of Abnormal Psychol*. 2006; 115:40-51
29. Rao U, Hammen C, Ortiz LR, Chen LA, Poland RE. Effects of early and recent adverse experiences on adrenal response to psychosocial stress in depressed adolescents. *Biological Psychiatry*. 2008; 64:521-526.
30. Stuart J, Rupke, David Blecke, Marjorie Renfrow. Cognitive therapy for depression; *American Family Physician*. 2006; 73(1):83-86.
31. R Eric Lewandowski. Evidence for management of adolescent depression *Pediatrics* October. 2013; 132:4.

32. Amy H, Cheung Nicole Kozloff, Diane Sacks Pediatric depression an evidence based update on treatment interventions Current psychiatry reports. 2013; 15(8):381
33. Molly S Clark, Kate L, Jansen J. Anthony Cloy Treatment of childhood and adolescent depression; American Family Physician. 2012; 86(5):442-448.
34. Bleakley S, Baldwin D. Anxiety disorders; Roger Walker and Cate Wittlesea Clinical Pharmacy and Therapeutics; 5<sup>th</sup> edition; Churchill Livingstone; Elsevier.
35. <https://www.mayoclinic.org/diseases-conditions/teen-depression/symptoms-causes/syc-20350985>.
36. Psychotherapy for children and adolescents Different types; American Academy of Child and Adolescent Psychiatry, 2017, no:86
37. Drugs used in mental illness: antidepressant and antimanic drugs; KD. Tripathi Essentials of medical pharmacology; 2004; 5<sup>th</sup> edition; Jaypee publishers; page no: 404-414.
38. Nadia NR Lima, Vania B Nascimento, Alberto OA Reis. Electroconvulsive therapy use in adolescents: a systematic review; Annals of General Psychiatry. 2013; 12:17.
39. [https://en.wikipedia.org/wiki/cognitive\\_behavioral\\_therapy](https://en.wikipedia.org/wiki/cognitive_behavioral_therapy)