

# **Clinical Practice Guidelines for Management of Depression in Children and Adolescents**

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## **INTRODUCTION**

Over the last half century, it is now well established that depression can occur at any age and it has been documented as early as infancy. In terms of epidemiology, different studies which have evaluated the prevalence of depression in children and adolescents suggest that the prevalence varies according to the different age groups. Prevalence figures reported for infants vary from 0.5 to 3 % in clinic population, whereas in preschool children the prevalence rate for major depression (1.4%) is reported to be higher than depression not otherwise specified (0.7%) and dysthymia (0.6%). Studies done in community setting suggest prevalence of depression in children to range from 0.4 to 2.5% and among adolescents to be 0.4 to 8.3%. Lifetime prevalence through adolescence is considered to be as high as 20%. Prior to puberty, depression is known to have equal gender representation, however, among adolescents, the male female ratio is 1: 2. Over the years, it has also been understood that depression in children and adolescents is a chronic and relapsing condition, which doesn't remit spontaneously and hence, there is a need to identify and treat the same at the earliest to reduce its long term negative consequences. Childhood depression has been shown to lead to increased risk of poor academic performance, impaired social functioning, suicidal behavior, homicidal ideation, and alcohol/ substance abuse. It is also associated with increased risk of recurrent depressive episodes. Unfortunately, a major proportion of depression in children and adolescents is underdiagnosed and undertreated.

## **SCOPE OF THE GUIDELINES**

Indian Psychiatric Society (IPS) published Clinical Practice Guidelines for management of depression in children and adolescents for the first time in the year 2007. Over the years, more research has accumulated in this area and hence an effort is made to update the previous version of the clinical practice guidelines. These guidelines intend to provide a broad framework for the proper assessment and management of depression in children and adolescents. It is recommended that these guidelines must be read with the previous version. These guidelines must not be considered as a substitute for the professional knowledge and clinical judgement of the treating psychiatrist. It is important to remember that these guidelines are not applicable to any specific treatment setting and will require minor modification to suit to the needs of the children and adolescents in various treatment setting. Accordingly, the recommendations made as part of this guideline may have to be tailored to the needs of the individual patient.

## **ASSESSMENT OF DEPRESSION IN CHILDREN AND ADOLESCENTS**

Assessment of depression in children and adolescents not only involves establishing the diagnosis, but it also involves evaluation of comorbid conditions, considering all the possible differential diagnoses, evaluating psychosocial issues contributing to development and continuation of depression (such as family discord, family psychopathology), risk to life of patient and the ensuing dysfunction etc. It also involves establishing a good therapeutic alliance with the patient and family members and making decision about treatment setting and patient's safety. It is important to remember that assessment is not a one step process, but

it is a continuous process and patient may have to be assessed regularly, as per the need and phase of the treatment.

The complete psychiatric evaluation should include a history of the present illness and current symptoms; evaluation for symptoms of mania or hypomania, a general medical history, history of substance use disorders; a personal history (e.g., psychological development, response to life transitions, and major life events); a social, educational, and family history; a review of the patient's medications, review past treatment history, physical examination, detailed mental status examination and diagnostic tests as indicated. In general, for identification of depression in children and adolescent it is better to collect information from various sources, i.e., patients self report, parental, peer, sibling and teacher report and observation during the clinical interview. The child and parents or other caregivers can be interviewed separately and also together. Multiple interviews may be required to get the full picture of depression. It is suggested that evaluation of children with depression, should involve interview of both the parents and the child. Differences are noted in the parent reports and self reports of depressive symptoms. Parents more often report externalizing symptoms such as irritability, whereas children themselves more often report internalizing symptoms such as low mood.

Wherever possible, developmental perspective should be taken into consideration and play techniques can be used as part of assessment of mental status assessment. It is reported that preschool children with depression show significantly less symbolic play and greater engagement in non-play behavior, such as exploration of toys and interaction with the examiner, than healthy and non-depressed comparison groups. Depressed children also demonstrate less coherence in their play.

As per the prevailing nosological systems, i.e., Diagnostic and Statistical Manual, fifth revision (DSM-5) and International Classification of Diseases, 11<sup>th</sup> Revision (ICD-11), depression must be diagnosed in children and adolescents by using the same diagnostic criteria, as used for other age groups. DSM-5 suggests that the criteria of "presence of depressed mood" can be replaced by 'irritable mood' in children and adolescents. The diagnosis of persistent depressive disorder (equivalent of dysthymia) requires duration of 1 year in contrast to the two-year duration required for adults. However, it is considered that the criteria given in DSM do not address the developmental variations in symptom manifestations, and hence it is required to modify the criteria to pick up depression in children. It is suggested that depression in infants may manifest as failure to thrive, severe psychomotor delay, apathy, sad facial expression and lack of responsiveness to alternative caregivers. It is also important to note that in view of the level of cognitive development, younger children may appear sad but may not be able to verbalize the same. Instead these children may have irritability, which may manifest as frustration and temper tantrums and behavioural problems. Other symptoms indicative of depression in children include increased rejection sensitivity.

Certain cognitive symptoms such as low self-esteem, hopelessness, and depressive guilt, which are seen in patients with depression in other age groups, may not be apparent in children with depression because of lack of cognitive development (i.e. lack of development of abstract thinking). The concern about the future (hopelessness) is more strongly associated with depression in adolescents than in children; whereas guilt is more often seen in children than for adolescents. According to current DSM criteria, patients with depression may present with either an increase or a decrease in appetite/weight from usual. However, it is important to remember that children will have normative increase in appetite and weight and due to this utility of increases in appetite or weight as a clear feature of depression in youth is questionable. It is suggested that although decreases in appetite and weight are associated with depression in children and adolescents, increases are not. It is also suggested that strict

application of 2 week duration criteria may also not be appropriate to very young children. Evidence suggests that preschool children meeting all criteria for MDD independent of the duration criteria exhibit higher levels MDD symptoms and functional impairment than controls. Hence, some of the researchers suggest that rather than focusing on presence of persistent mood symptoms for 2 weeks, in children and adolescents, the clinicians should focus on presence of symptoms for ‘most days than not’. Besides the DSM criteria, evidence suggests that younger children with depression more often manifest with somatic symptoms (headache, abdominal pain and general aches and pains), restlessness, separation anxiety, phobias, and hallucinations. Adolescents with depression are more likely to experience anhedonia, boredom, hopelessness, hypersomnia, weight change (including failure to reach appropriate weight milestones), alcohol or drug use, and suicide attempts.

**Table-1: Assessment of Children and adolescent presenting with Depression**

**Basic assessments**

- Complete history with information from all possible sources
- Interview the child alone
- Physical examination- look for thyroid swelling, evidence for malnutrition or any specific nutritional deficiency
- Mental state examination, if required multiple evaluations over short period of time
- Establish diagnosis according to current diagnostic criteria (do consider features which are commonly seen in children and adolescents with depression)
- Differential diagnosis: consider the possibility of organic causes, medication induced depression and other psychiatric disorders; rule out bipolar disorder
- Consider and evaluate for comorbid psychiatric disorders: Anxiety disorders, Substance use disorder, Personality disorder, Conduct disorder, Oppositional defiant disorder, Attention-deficit hyperkinetic disorder, Dissociative/conversion disorder
- Assess for suicidal behaviour
- Detailed psychosocial evaluation: family discord, family psychopathology
- Assess the level of dysfunction: decline in school performance, school refusal, social interaction
- Assess the severity, specifier, subtype of depression, dysfunction
  - Symptom severity
  - Symptom dimensions (psychotic symptoms, catatonic symptoms, melancholic symptoms, reverse vegetative symptoms and cognitive symptoms)
  - Comorbid physical, psychiatric and substance use conditions
  - Level of functioning and socio-cultural milieu of the patient
- Establish a good therapeutic alliance
- Basic investigations: haemogram, blood sugars and lipid levels, liver functions, renal functions, thyroid function test (if indicated)
- Assessments of caregivers: knowledge and understanding of the illness, attitudes and beliefs regarding treatment, impact of the illness on them, personal and social resources
- Ongoing assessments: response to treatment, side effects, treatment adherence, the impact of patient’s immediate environment, disability assessments, other health- care needs, ease of access and relationship with the treatment team
- Determine about the treatment setting

**Additional/Optional assessments**

- Use of standardized rating scales to rate all aspects of the illness
- Neuroimaging especially in those suspected to have space occupying lesion or other organic conditions like epilepsy, treatment resistant depression

When children manifest psychotic symptoms as part of depression, these are commonly in the form of auditory hallucinations. Adolescents with depression usually report psychotic symptoms in the form of delusions. It is also important to remember that children and adolescents who manifest psychotic symptoms as part of depression have much higher chance of developing bipolar disorder, compared to adults with similar manifestation. There is also some evidence to suggest that seasonal affective disorder may occur in youth, mainly after puberty in adolescent who live in regions with distinct seasons.

Considering the difference in manifestation and developmental or age specific symptoms, it is suggested that evaluation of depression in children and adolescent should cover the acronym “**DUMPS**”. “D” stands for evaluation of duration of symptoms, depressed mood, defiance and disagreeability and distant or withdrawal behaviour. “U”, stands for presence of undeniable drop in educational performance/ grades or interest in school, which are seen quite frequently in young children. Drop in educational attainments arise due to difficulties in concentrating, inability to make decisions and loss of interest and motivation for doing activities that were pleasurable earlier. Accordingly, it is suggested that report cards of several years should be reviewed as this can help in identifying the beginning of decline of grades, or fluctuations with certain seasons (e.g. a drop every winter). Inability to concentrate and complete the work may be particularly burdensome in high school going youth, where much of school work involves writing, doing laboratory assignments, reading and answering questions etc. Children who fall behind in their class often start missing classes or avoid going to school. Accordingly school avoidance should be an alarm for evaluation of depression. “M” stands for morbid and strange behavior which may be actually an indirect manifestation of suicidality. “P” represents pessimism, which is a hallmark of depression in children and adolescents. “S” stands for somatic symptoms, particularly abdominal pain and headaches are common in young people.

**Evaluate for Comorbidity:** In general it is said that comorbidity is the rule rather than the exception in children and adolescents with depression. The commonly seen comorbid conditions include anxiety disorders, substance use disorder, personality disorder, conduct disorder, oppositional defiant disorder, attention-deficit hyperkinetic disorder and dissociative/conversion disorder. The high comorbidity is attributed to the common environmental etiological factors and shared genetic influences between depression and most of the common comorbid disorders.

**Consider the possibility of underlying medical cause:** As in other age groups, it is important to evaluate, whether the depressive symptoms can be attributed to medical illnesses or other psychiatric disorders. The common medical illnesses and psychiatric disorders which need be considered for differential diagnosis are shown in Table-2. Additionally, due importance must be given to intake of medications, as many medications are known to cause depression (see Table-2). In case the symptoms can be better understood and attributed to a medical illness, then the diagnosis of major depressive disorder is not appropriate. Organic diseases, such as hypothyroidism, metabolic abnormalities and space-occupying lesions, should be ruled out in every infant who has depressive symptoms. Considering the fact that depression may be attributed to various physical illnesses, a thorough physical examination must be carried out in all children and adolescents presenting with depressive features. Wherever, there is doubt about any physical illness, help of paediatrician and other specialist should be taken. Identifying depression in the presence of a medical disorder can be at times difficult, especially when the medical disorder is associated with sleep disturbance, change in appetite, somatic symptoms, and lethargy/loss of energy. In such a scenario, clinicians should look for symptoms like feelings of guilt, worthlessness, hopelessness, and thoughts of suicide, which are unlikely to be due to a medical disorder and strongly suggest the presence of major

depression. Depending on the need, various investigations must be carried out. It is important to consider bipolar disorder in the differential diagnosis as use of antidepressants in a child or adolescent with bipolar disorder can lead to switch/behavioural activation. Features which should alert the clinicians for possible bipolar disorder include presence of psychotic features, presence of marked psychomotor retardation, reverse neurovegetative symptoms (excessive sleep and appetite), irritable mood and history of bipolar disorder in family.

Efforts must be made to rule out various psychiatric disorders by focusing on the longitudinal course of the symptoms, presence of other core symptoms of various disorders and severity of symptoms. Further, it is important to remember that many of the psychiatric disorders, considered as differential diagnosis, also co-exist with depression.

**Table-2: Differential diagnosis for depression in children and adolescents**

**Organic Depression**

- Anemia
- Cancer
- Chronic fatigue syndrome
- Hypothyroidism or hyperthyroidism
- Infectious etiologies (e.g., human immunodeficiency virus, hepatitis)
- Inflammatory bowel disease
- Mononucleosis
- Stroke
- Space-occupying lesions of brain
- Temporal Lobe epilepsy
- Nutritional deficiencies, example vitamin deficiency
- Systemic lupus erythematosus or other collagen vascular disease
- Premenstrual dysphoric disorder

**Medication Induced Depression**

- Neuroleptics
- Beta blockers
- Contraceptives
- Corticosteroids
- Isotretinoin
- Stimulants

**Psychiatric Disorders**

- Adjustment disorder with depressed mood
- Acute Stress Reaction
- Bereavement
- Anxiety disorders
- Bipolar disorder
- Dysthymia
- Attention-deficit/hyperactivity disorder
- Specific learning disorder
- Conduct disorder
- Oppositional defiant disorder
- Eating disorders: Anorexia nervosa, Bulimia nervosa
- Personality disorder
- Substance use (e.g., alcohol, heroin)
- Psychotic disorders (e.g., schizophrenia)
- Developmental disorders, like intellectual disability

**Assessment for suicidal behaviour:** One of the most important aspects of assessment of children and adolescent with depression includes assessment of suicidal risk. Clinicians should not underestimate the risk of suicidal behaviour in children and adolescents and must directly inquire about the presence or absence of suicidal ideation, specific plans for self-injury, and any history of actual self-harm or overt threats or gestures. Empirical data suggest that careful inquiry can in fact help to reveal previously unsuspected suicidal ideation or acts. For prepubertal children, inquiry about suicide must be done by taking the developmental perspective into account and attention must be paid to the child's concepts of death, as at times the child may not view death as irreversible. It is important to remember that lack of understanding of irreversibility actually in some cases, increase the risk of a suicide attempt. Questions may begin, with questions like, "Do you ever feel things are so bad that you wish you were dead?", "Do you ever feel like wanting to hurt yourself or do anything to kill yourself?". If patient responds in yes, further inquiry can include questions like, "Have you ever done anything to hurt yourself or to try to kill yourself?". If response to such question is in yes, further inquiry should focus on about what was done and the outcome of such an act along with any possible precipitants and context of the ideation or action.

It is also important to assess the motivation and intent of any attempt if present in the past and the clinician should remember that it is not the method per se, but the subject own understanding of lethality which is more important. History of multiple attempts in the past, persistent suicidal ideation, and high intent are associated with repetition of attempts and completion of suicide in future. Other factors which should be taken into consideration are psychological and interpersonal situation, family and interpersonal relations, comorbidity, chronicity of depression, risk taking behaviours, impulsivity, aggression and hostility, presence of auditory hallucinations commanding the child to hurt or kill him or her, history of physical and sexual abuses and failure (in exams and love). Assessment of suicidal risk is not complete without the evaluation of availability of lethal means (potentially lethal drugs, access to guns). The availability of firearms in particular magnifies the risk of completed suicide, because attempts with firearms are far more lethal than most other means used by adolescents.

**Evaluate the level of Dysfunction:** It is also very important to evaluate the level of dysfunction in terms of academic performance, family functioning and peer relationship. It is also important to understand the child's support system as it forms the backbone of the treatment plan to be carried out. While evaluating the support system, it is important to remember that, it is not the number which matters, but it is the comfort level of the child with that adult which matters. At times, although both the parents may be available, but one may be overcritical and other may be sulking his/her guilt. In such cases it is important to educate the parents, and they may also be evaluated for psychiatric morbidity.

**Use of Rating Scales:** Wherever possible, unstructured assessments need to be supplemented by use of standardized rating scales. Investigations need to be carried out depending on the assessment. In general neuroimaging is not indicated in children and adolescents with depression. However, neuroimaging may be considered in patients suspected to have intracranial space occupying lesions or other intracranial pathology.

**Assessment of knowledge and understanding of the disorders:** Assessment should also include evaluation of knowledge and understanding about the disorder among the patients and their parents/caregivers/family members. Additionally it is important to evaluate the attitudes and beliefs regarding treatment of both patient and caregivers. It is also important to understand the personal and social resources of the caregivers and the impact of the illness on the caregivers.

**Develop therapeutic alliance:** While carrying out the assessment, clinicians should focus on developing a good therapeutic alliance with the child and family, as early as possible, to

ensure involvement of the patient and family in the treatment over the period of time. The most important component for development of a good therapeutic alliance is paying attention to the concerns of patients and their families as well as their wishes for treatment. Management of the therapeutic alliance should also include awareness of transference and counter-transference issues, even if these are not directly addressed in treatment.

**Ongoing Assessment:** It is important to remember that assessment is an ongoing process and after starting of treatment it is important to continuously assess the response to treatment, adverse effects of medications, medication and treatment adherence, the impact of patient's immediate environment on patient's illness, disability assessments, other health-care needs and ease of access and relationship with the treatment team. Other issues which must be considered include caregiver burden, stigma experienced/perceived by the patient/caregiver and coping abilities of both patient and the caregivers. Appropriate interventions must be carried out to address the emerging issues during the course of the treatment.

### **FORMULATING A TREATMENT PLAN (FIGURE-1)**

Formulation of treatment plan involves deciding about treatment setting, determining the type of psychological treatment and type of medications to be used. Both patients and caregivers be actively consulted while preparing the treatment plan. The treatment plan formulated should be feasible, flexible and practical to address the needs of the patients and caregivers. Clinician should continuously work with the patient and the caregivers and keep on re-evaluating the treatment plan and make necessary modifications.

### **DETERMINE A TREATMENT SETTING**

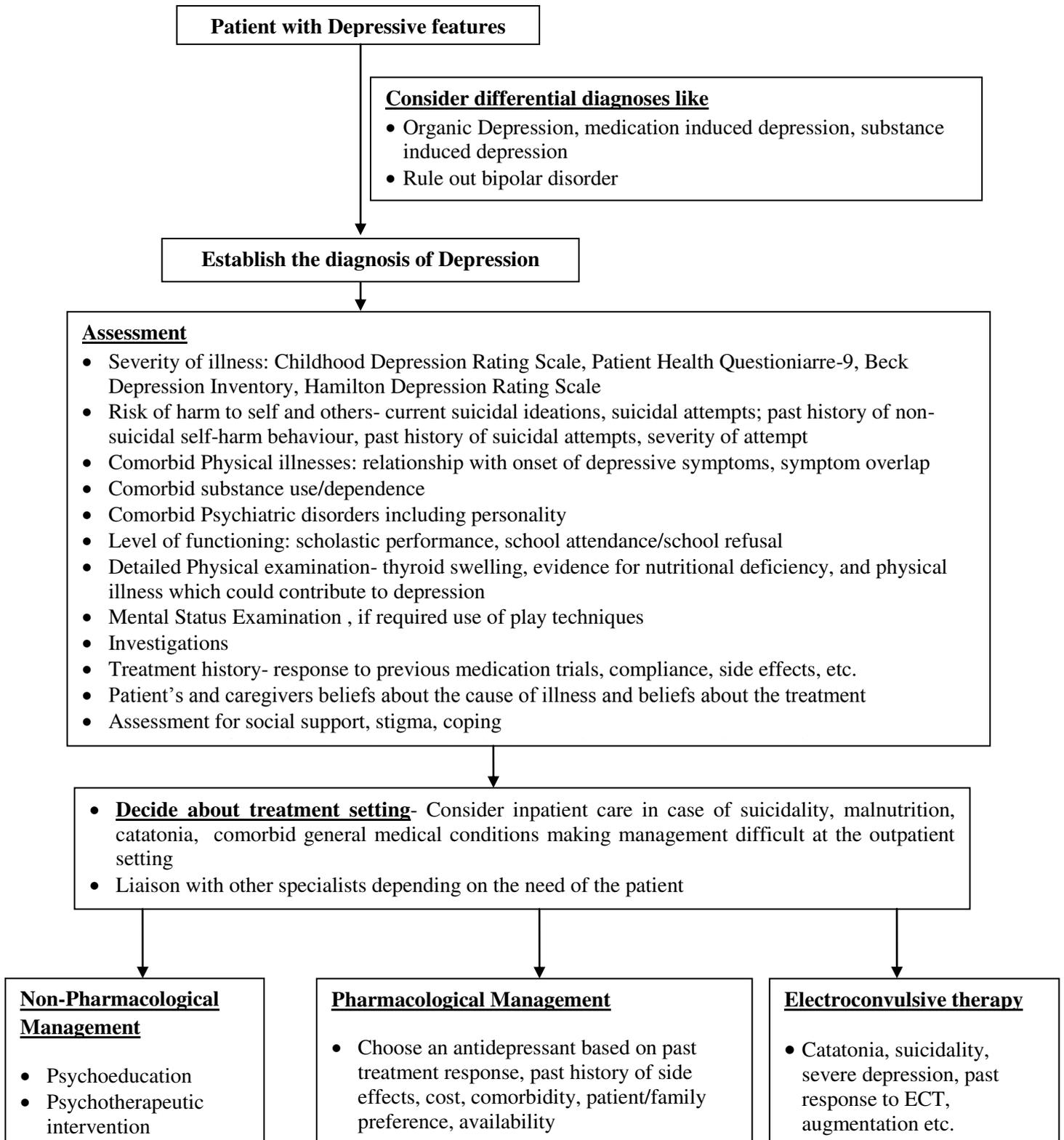
Depression in children and adolescents need to be provided in the least restrictive treatment environment which is safe and effective for a given patient. Determination of treatment setting should take into consideration: clinical the severity of symptoms, available support from parents' and other family members, motivation for treatment, and family's ability to ensure safety of the patient. Children and adolescents with suicidal or homicidal ideation, intention or a plan require close monitoring. Hospitalisation is usually indicated for patients who are considered to pose a serious threat of harm to themselves or others. Other indications for inpatient care are shown in table-3.

**Table-3: Indications for admission in children and adolescents with depression**

<ol style="list-style-type: none"><li>1. Those who express suicidal ideas of a definite sort, or who have made a attempt of suicide</li><li>2. Those who harm themselves, or threaten to harm others</li><li>3. Subjects who have problems with treatment compliance or delivery, leading to unduly protracted treatment</li><li>4. Those who require electroconvulsive therapy</li><li>5. Those who neglect themselves substantially, particularly their food intake</li><li>6. Those who require removal from a hostile social environment</li></ol>
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However, it is important to remember than for providing inpatient care, provisions of Mental Health Care Act, 2017 (MHCA, 2017) need to be followed.

**Figure-1: Initial Evaluation and Management Plan for Depression in Children and Adolescents**



## **MONITOR THE STATUS AND SAFETY OF PATIENT**

Over the course of treatment, clinical picture of patient may change, with emergence of certain new symptoms and subsidence of existing symptoms. It is important to monitor the patients for the emergence of or change in destructive impulses towards self or others. If anytime during the course, patient is considered to be at high risk, than hospitalization or more intensive treatment should be considered. Significant changes in a patient's psychiatric status or the emergence of new symptoms may also at times warrant a diagnostic re-evaluation of the patient.

## **PROVIDE PSYCHOEDUCATION TO THE PATIENT AND FAMILY**

Psychoeducation is one of the most important components of management of depression in children and adolescents. It not only helps the patients and their families, but it also helps the clinician. Psychoeducation makes the patient and family become informed partners in the treatment decisions and enhances the treatment adherence. Education about depression also helps in formulating a treatment plan, decreases parental self-blame (*"I'm not a good parent"*) and blame of the child (*"He's manipulative,"* or *"He's lazy"*). Psychoeducation should be offered to all family members because the symptom of depression (e.g., lack of interest, fatigue, irritability, and isolation) can affects each of them. At times, family members and friends take the patient's behaviors personally or otherwise become emotionally over involved, causing more stress, guilt or anger for the patient to cope with. Supportive and understanding relationships improve the patient's and family's global functioning and treatment outcome. Furthermore, it appears that educating parents about their child's depression helps them identify their own depressive symptoms and potential need for treatment.

## **ENHANCE TREATMENT ADHERENCE**

The key to the successful treatment of depression is adherence to treatment plans. Hence, it is very important for the clinician to educate the patient and family about the need of regular follow up and drug compliance. Measures which can improve the medication adherence are given in Table-4.

**Table-4: Measures which can improve medication compliance**

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| <ul style="list-style-type: none"><li>• Explain the patient/family members as to when and how often to take medicines</li><li>• Preferably give once a day dosing</li><li>• Prescribe minimum number of tablets</li><li>• Always ask the patient/caregivers about kind of formulation (e.g. tablet, capsule etc) which they/patient would prefer to take</li><li>• Check the whole prescription to avoid duplication of medication</li><li>• Explain the patient/caregivers that the beneficial effect will be seen only after 2- 4 weeks of intake of medications</li><li>• Explain the patient/caregiver the need to take medication even after feeling better</li><li>• Explain the patients/caregivers asks about the side effects</li><li>• Explain the patient/caregivers as to what to do- if side effects are encountered</li><li>• Encourage the patient/caregivers to report side effects</li><li>• Explain to the patient/caregivers about the need to consult with psychiatrist before discontinuing medications</li></ul> |
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## **WORK WITH THE PATIENT AND CAREGIVERS TO ADDRESS THE ISSUES OF RELAPSE**

Fluctuation of symptoms is common in depression and patients and their families should be educated about the significant risk of relapse. They should be educated to identify the early

signs and symptoms of new episodes. Families should also be asked to seek adequate treatment early in the course of a new episode to decrease the likelihood of a full-blown relapse or complication.

### **TREATMENT OPTIONS FOR MANAGEMENT FOR DEPRESSION**

Treatment options for management of depression in children and adolescents include psychotherapies, antidepressants, electroconvulsive therapy (ECT) and other somatic treatments like repetitive transcranial magnetic stimulation (rTMS).

***Psychotherapeutic interventions:*** Various psychotherapeutic interventions as such cognitive therapy, psychotherapy, art therapy, drama therapy and family therapy have been used in the management of depression in children and adolescents. These interventions have been evaluated in the form of individual and group interventions. Cognitive-behavioural therapies (CBT) attempt to address the cognitive distortions in depressed children and adolescents. In CBT, child is the focus of treatment and therapists play an active role in treatment to form a collaborative relationship to solve problems. The therapist teaches the child to monitor and keep a record of thoughts and behaviour; there is emphasis on diary-keeping and on homework assignments and treatment consists of behavioural techniques (activity scheduling) and cognitive strategies (cognitive restructuring). Studies which have evaluated CBT for management of depression in children suggest that in short-term CBT is better than no treatment. With respect to efficacy of CBT among adolescents with depression, there is conflicting evidence to draw any definite conclusion. Some studies suggest that CBT is an efficacious treatment for depressed teens and is superior to interventions like family therapy and supportive counselling, whereas, other studies showing the efficacy of CBT similar to placebo. Studies which have compared combination of CBT and medication with medication alone, suggest that combination is more effective than the medication alone. A recent meta-analysis which included 9 studies evaluating the efficacy of CBT in children and adolescents with depression showed that CBT was better than no treatment, but it was not found to be better than wait list or placebo. This study further showed that efficacy of CBT was better in those without comorbidity and without parental involvement. The number of CBT sessions in a treatment course in these studies has varied from 5 to 16 sessions, however the meta-analysis suggest that number of sessions does not have significant influence on the efficacy. Another review of efficacy trials suggest that CBT is more efficacious in adolescents (13-24years) than in children (aged  $\leq 13$  years).

In view of association of depression in children and adolescents with problems in relationship, interpersonal therapies have also been evaluated for management of depression in children and adolescents. Addressing the issues in the interpersonal context can contribute to the alleviation of the child's depressive symptoms, regardless of the personality organization or biological vulnerability of the individual. The main goals of interpersonal therapy (IPT) are to identify and treat the depressive symptoms and address the interpersonal problems associated with the onset of depression. A meta-analysis which included data of 538 participants from 7 randomised controlled trials showed that, when compared with controlled conditions (Placebo, wait listed or Treatment as usual), IPT had significantly superior effective in reducing depressive symptoms and leading to response/remission, for all cause discontinuation rates and improvement in quality of life/functional improvement. Another meta-analysis included 10 studies comprising of 766 participants evaluated the efficacy of IPT among adolescents with depression reported that IPT-A, was significantly superior to control or treatment as usual in reducing depressive symptoms among adolescents. In view of the association of depression in children with family pathology, including mental illness and dysfunctional family relationships, many authors suggest role of family therapy in management of childhood depression.

***Use of Antidepressants:*** Efficacy of many antidepressants has been evaluated in randomized controlled trials in children and adolescents. The antidepressants which have been evaluated in children and adolescents include imipramine, des-imipramine, clomipramine, nortriptyline, amitriptyline, fluoxetine, paroxetine, escitalopram, sertraline, duloxetine, venlafaxine, nefazodone and mirtazapine. Randomized controlled for most of these antidepressants have been negative. A recent network meta-analysis, which included data on 14 antidepressants from 34 trials involving 5260 participants, concluded that only fluoxetine was significantly better than placebo. This meta-analysis also concluded that fluoxetine was better tolerated than duloxetine and imipramine. Similarly, tolerability of citalopram and paroxetine was significantly better than imipramine. A Cochrane review, which included 19 randomised control trials, which evaluated the efficacy of newer antidepressants in management of depression in 3335 children and adolescents, concluded that in general there is no difference between antidepressants and placebo in terms of efficacy. However, in view of the risk associated with untreated depression, the authors concluded that fluoxetine might be the medication of first choice. Further the authors concluded that use of antidepressants was associated with increased risk of suicidal behaviour, compared to placebo.

The multicentric National Institute of Mental Health (NIMH) funded study, i.e., Treating Adolescent Depression Study (TADS), which compared the use of fluoxetine alone, cognitive behavioral therapy (CBT) alone, or combination of both concluded that combination of CBT and fluoxetine offered the highest treatment response rates and this was followed by response rate to fluoxetine alone. CBT alone was not found to be efficacious. Response rate to fluoxetine alone was 61 % as measured by CGI-I Scores compared to only 35% with placebo ( $p = 0.001$ ). Response rate to combination of fluoxetine and CBT was 71%. Hence, it is not surprising that fluoxetine is the only drug approved by US FDA for the treatment of depression in children and adolescents. The predictor of good response to treatment in the TADS study included being younger, less chronically depressed, having higher functioning, less hopeless with less suicidal ideation, fewer melancholic features, fewer comorbid diagnoses, and greater expectations of improvement with treatment. In this study combined treatment, under no condition was less effective than monotherapy. In terms of remission rates, data from TADS study suggests that remission rate are significantly higher with combination treatment (37%) when compared to the other treatment groups (fluoxetine- 23%; CBT -16%; placebo-17%), with odds ratios of 2.1 for combination group versus fluoxetine, 3.3 for combination group versus CBT, and 3.0 for combination group versus placebo. Escitalopram has been evaluated in 2 recent multicentric trials. These 2 double blind randomised control trials included adolescents aged 12 to 17 years, who were treated with escitalopram 10 to 20 mg/day. These trials showed that escitalopram was superior to placebo and was well tolerated. One of these trials also showed that the response and remission rates were significantly higher with escitalopram. There was no significant difference between the escitalopram and placebo groups in terms of treatment emergent suicidal behaviour.

Among the various antidepressants, Food and Drug Administration (FDA), of United States has approved use of fluoxetine in children aged 8 years or above and use of escitalopram in children 12 years or above.

Many studies have also compared the efficacy of antidepressants versus psychological treatment versus combined treatment. A Cochrane review which evaluated these studies showed that there is limited evidence to suggest that antidepressant medication is more effective than psychotherapy in terms of immediate post-intervention remission rates. Further the authors concluded that the evidence is limited to say that combination treatment was more effective than antidepressant alone in achieving higher remission rates and there is no evidence to suggest that combination treatment was better than psychological therapy alone. Further, the existing data suggest that use of antidepressants is

associated with higher suicidal behaviour. The authors concluded that overall the evidence is limited to draw any conclusions.

One of the major controversies with respect to use of antidepressants among children and adolescents is the risk of suicidal behaviour. Based on the available data of possible increase in risk of suicidal behaviour with antidepressants, FDA has issued a black box warning against use of antidepressants among children and adolescents. Accordingly cautious approaches need to be considered while using antidepressants among children and adolescents, and they must be closely monitored for any treatment emergent suicidal behaviour.

Another important issue while using antidepressants among children and adolescents is medication induced behavioural activation which is characterised by symptoms of irritability, agitated and aggressive behaviour, anxiety symptoms (i.e., features of panic attacks), restlessness, hostility, akathisia, hypomania/mania and emergence of psychotic symptoms. There is some evidence to suggest that antidepressant associated behavioural activation is associated with use of higher doses of medications. Hence, it is suggested that children and adolescents receiving antidepressants must be closely monitored while starting antidepressant medication and during the period of change of doses of antidepressant medications.

***Electroconvulsive therapy:*** ECT is not the first line treatment in the management of depression in children and adolescents. In general most of the available data is in the form of retrospective studies and these studies suggest the ECT is effective in children and adolescents with depression. With response rates reported in the range of 64-100%. In a review Rey and Walter<sup>170</sup> reviewed 60 studies involving 396 patients younger than 18 years of age (only 5 of these were younger than 12 years) and reported 63% remission rate for the patients with depression. Three quarters of patients with catatonic conditions, regardless of the underlying psychiatric morbidity, showed a significant improvement with ECT. They also concluded that ECT was administered almost always after other treatments have failed and when a patient's symptoms are incapacitating or life threatening and a considerable improvement with ECT was seen in approximately 90% of adolescents with depression who were resistant to pharmacotherapy. In 2 other reviews done by Ghaziuddin et al (2004) and Stein et al (2006) which included other available studies and case reports the efficacy of ECT in depression ranged from 60% to 100%. Side effects like fatality, premature termination of treatment and prolonged seizures are rarely reported with use of ECT in children and adolescents. Studies which have evaluated the long term cognitive side effects of ECT also report no significant difference between children and adolescents who are treated with ECT and control group subject.

**Treatment Resistant Depression:** There is limited data on management of treatment resistant depression among adolescents. A multicentric randomised study, named "Treatment of SSRI-Resistant Depression in Adolescents (TORDIA)", has evaluated 334 patients aged 12 to 18 years, diagnosed with major depression of moderate severity, who did not respond to an adequate trial of an SSRI (i.e., a trial of at least 8 weeks, of which in the last 4 weeks patient received a dose of at least 40 mg/day of fluoxetine or its equivalent). These patients were randomised to receive a different SSRI or venlafaxine, with or without CBT for 24 weeks. Outcome of the study was determined by using Clinical Global Impressions (CGI)-Improvement scale and Children's Depression Rating Scale-Revised (CDRS-R) scale. A CGI-improvement score of 2 or less and a reduction in CDRS-R score by 50% were considered as indicators of efficacy. At 12 weeks, CBT plus switch to venlafaxine or second SSRI was found to have higher response rate than switch to medication alone. Over there was no difference in the efficacy of venlafaxine and second SSRI. There was no difference between the two antidepressant groups in terms of suicidal behaviour as an adverse effect, but compared to SSRIs, venlafaxine was associated with higher rise in diastolic blood pressure

and pulse rate and dermatological problems. Further analysis of data showed that higher plasma level of antidepressants was associated with better response. Second phase of TORDIA trial was an open trial in which those who did not respond to first treatment were changed to second treatment at 12 weeks and then evaluated at the end of 24 weeks. Those who responded to treatment at the first phase were continued on the same treatment during the second phase too. It was seen that at 24 weeks, patients who demonstrated clinical response at 12 weeks had higher remission rate and shorter time to remission. Remission rate was higher for patients with lower baseline depression, hopelessness, and self-reported anxiety. Remission was also predicted by lower depression, hopelessness, anxiety, suicidal ideation, family conflict, and absence of comorbid dysthymia, anxiety, and drug/alcohol use and impairment at 12 weeks. Of those who responded by week 12, one-fifth (19.6%) experienced relapse by week 24. Long term follow-up at 72 weeks of patients recruited to the TORDIA study showed that 61.1% of the patients achieved remission. The remission rates and time to remission were not affected by the treatment received during the first 12 weeks. However compared to patients who received venlafaxine those who received SSRI had more rapid decline in depressive symptoms and suicidal ideations as per the self-report. Factors which were associated with lack of remission included higher severity of depression at the baseline, higher level of dysfunction at the baseline and use of alcohol/drug at the baseline. Among patients who had achieved remission at week 24, one-fourth (25.4%) relapsed in subsequent 1 year.

#### **PHASES OF ILLNESS/TREATMENT**

As in other age groups, management of depression in children and adolescents can also be broadly divided into three phases, i.e., acute phase, continuation phase and maintenance phase. Maintenance phase treatment is usually considered when patient has recurrent depressive disorder.

#### **ACUTE PHASE TREATMENT**

The goal of acute phase management is to effectively treat depression to achieve remission, treat comorbid disorders, to promote social and emotional adjustment, to improve self-esteem, to relieve family distress and to prevent relapse. Treatment should also lead to reduction of dysfunction and improvement in quality of life of the child along with improvement of family functioning.

Irrespective of the specific treatment modality used, all the patients and their parents must be provided adequate psychoeducation (Table-5).

#### **Table-5: Basic components of Psychoeducation**

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| <ul style="list-style-type: none"> <li>• Assessing the basic knowledge of the patient and caregivers about aetiology, treatment and prognosis</li> <li>• Explaining the patient and caregivers about the signs and symptoms of depression</li> <li>• Explaining the patient and caregivers about the diagnosis of depression</li> <li>• Explaining the impact of untreated depression on school attendance and academic functioning</li> <li>• Explain that depression is a medical disorder which is treatable</li> <li>• Explain the role of the parents and teachers in recovery</li> <li>• Addressing the common misconceptions about depression</li> <li>• Explain about the lag period of onset of action</li> <li>• While using antidepressants explain the risk of suicidal behaviour and the precautions to be taken</li> <li>• Provide information about aetiology, with special emphasis on explaining the role of interpersonal conflicts, family pathology etc</li> <li>• Provide information about treatment options, their efficacy/effectiveness, side effects,</li> </ul> |
|--|

duration of use

- Discuss about importance of medication and treatment compliance
- Provide information about possible course and long term outcome
- Discuss about problems of substance abuse, interpersonal conflict, stress etc
- Discuss about how to deal with day today stress
- Discuss about communication patterns, problem solving etc
- Enhancing adaptive coping to deal with persistent/residual symptoms
- Discuss about relapse and how to identify the early signs of relapse
- Encourage healthy life styles

**Selection of initial treatment:** Selection of initial treatment modality is often guided by severity of depression, number of prior episodes, chronicity of depression, subtype, age of the patient, contextual factors like family conflict, academic problems and exposure to negative life events, compliance with treatment in the past, previous response to treatment, and patient's and family's motivation for treatment and response to a particular treatment in family member. However, one of the most important factors in selecting a particular treatment modality is family and patient's preference. It is seen that at times a socially phobic patient may refuse group therapy and an anxious parent or patient may refuse medications as the first line of treatment, so alternate treatments may be required. Besides the patient, family and clinical variables it is also important to take into consideration the clinicians factors before determining the initial treatment modality. The clinician factors include clinician availability, motivation, and expertise with a specific therapy. Hence, the decision to initiate medication versus specific psychotherapy should be made jointly by the clinician and adequately informed parents (guardians) with assent from the child.

For mild to moderate depression, psychotherapy is considered to be preferred initial modality of treatment. Selection of specific type of psychotherapy will depend on clinician's experience and comfort along with the patient's needs. CBT should be preferably be used in children and adolescents with cognitive distortions and comorbid anxiety disorders. IPT may be beneficial in presence of stressors like separation from parents, authority concerns with parents and teachers, loss or death of relatives or friends etc. In a country like India, where few clinicians have expertise and time to carry out CBT or IPT, supportive psychotherapy may also be useful.

Antidepressant medications may be used for children and adolescents with moderate depression in which psychotherapy is not feasible, severe depression with or without psychotic symptoms and depression that fails to respond to an adequate trial of psychotherapy. For patients requiring pharmacotherapy, SSRIs, especially fluoxetine should be considered as the first choice in patients aged 8 years or more. It has maximum support in treating depression in children and adolescents, and it is the only antidepressant found to be efficacious in more than one acute trial. Hence, fluoxetine should be the first line treatment unless reasons like potential drug interactions, family resistance, prior lack of response with an adequate dose and trial preclude its use. In such cases, escitalopram or sertraline can be considered. Escitalopram has been evaluated in children aged 12 or more and has been reported to be efficacious and safe. Other alternative first line antidepressant includes sertraline. However, before prescribing antidepressant, parents and other caregivers must be provided information about the potential risks and benefits and informed consent to start the medication must be taken from the parents. Parents and patient should be explained about side effects, dose, the timing of therapeutic effect, and the danger of overdose. Patients who are at risk of committing suicide, it is recommended that parents should be given the responsibility for storing and administering medications, especially during the acute and during the first 2 to 4 months after complete remission. It is also important that parents need

to be made aware of possible role of SSRIs with regard to suicidality and they should be asked to be vigilant and should monitor the patient's behaviour. At present, there is no indication for baseline laboratory tests before and during the administration of SSRIs.

When used, SSRIs should be started in low doses (usually half the starting dose of adults) and gradually titrated to achieve a balance between symptom control and avoidance of side effects. When used, fluoxetine can be started in the dose of 10 mg daily and this can be increased to 20 mg daily after 1 week if there are no side-effects. There is little evidence regarding the effectiveness of doses higher than 20 mg daily.

It is important to remember that depression in children and adolescents often occurs in psychosocial context and hence besides using antidepressants associated environmental and social problems should be addressed with supportive measures. Combined treatment increases the likelihood of remission and also improves self-esteem, coping skills, and adaptive strategies of the patient and improves family and peer relationships.

Further in case of psychotherapy or pharmacotherapy, specific interventions should be provided to parents and other caregivers to help them effectively manage the child's irritability, defiance, isolation, or other behavioral problems. If any of the parent or significant family member has any mental problem, it should be addressed.

While patient is treated with antidepressant, it is advisable to see the patient once in 1-2 weeks, because this will help the clinician to monitor the patient's depression status (improvement or worsening), emergence of suicidality if any, monitor bothersome adverse effects and to adjust dose accordingly and increase patient adherence to treatment. During follow-up it is recommended that severity of depression should be monitored objectively using various clinicians and self rated scales.

**Adequate trial:** There is no consensus with regard to an adequate trial in children and adolescents, and it is extrapolated from the adult data. Once an antidepressant is started, patients should be treated with adequate and tolerable doses for at least 4 to 6 weeks. If patient shows no response, by 4 weeks, the clinician should increase the dose to maximum tolerable dose, with close monitoring of side effects. If patient shows partial response with minimal or no side effects by 4-6 weeks, the clinician should wait till 8 weeks and increase the dose to maximum tolerable dose before considering failure of response. However, these recommendations should be applied cautiously, because the SSRIs possess a relatively flat dose-response curve, suggesting that maximal clinical response may be achieved at minimum effective doses. Therefore, adequate time should be allowed for clinical response, and frequent, early dose adjustment should be avoided.

**Non-response or partial response to initial trial:** There is some data for adolescents to suggest that adolescent who doesn't respond to an adequate trial of SSRI may benefit from second SSRI. If patient was initially treated with fluoxetine, then it can be stopped immediately and the second antidepressant can be built-up slowly; but if initially the patient was treated with some other SSRI, then cross tapering should be done. If the patient experienced intolerable side effects with SSRI (e.g., nausea, excessive restlessness, agitation) during the first trial, then the second SSRI should be started at lower doses. If patient was initially treated with psychotherapy, and did not show any response, then he should be either started on an SSRI or alternate form of psychotherapy should be considered.

If the patient shows partial response to the initial SSRI trial, augmentation strategy can be used. The potential advantages of augmentation versus switching to another antidepressant monotherapy include no need for discontinuation of initial antidepressant, less lag time for response, partial responders continue to receive treatment without interruption, and treatment of breakthrough symptoms is possible. The best augmenting agent for children and adolescents who fail to respond to SSRIs or are partial responders remains to be determined. However, there is some data to suggest that combination treatment with antidepressant and

CBT is possibly superior to antidepressant only. Based on adult data and expert opinion, augmentation may be a useful strategy for youths who have shown initial response with optimal dosing, but who have not achieved remission and augmentation recommendations from adult data can be extrapolated. Available evidence suggests that compared to medication alone, a combination of CBT and fluoxetine is more efficacious.

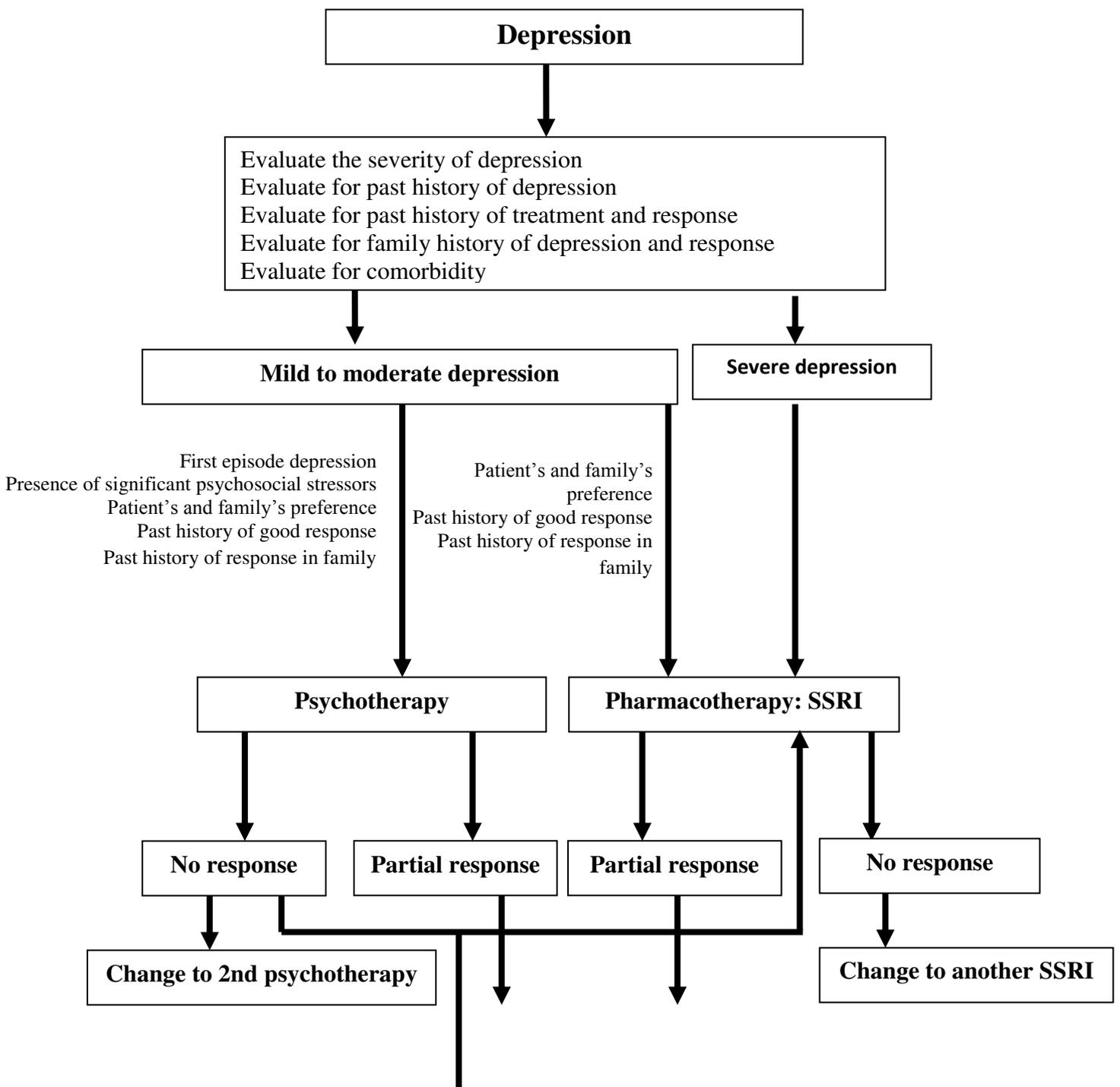
***Failure to respond to 2 antidepressant trials:*** If the patient fails to respond to second SSRI trial, then it is important to re-evaluate the diagnosis, comorbidity, non-compliance and other psychosocial factors which may be contributing to non-response. The adequacy of psychotherapeutic interventions should also be checked and all the possible modifications which can improve the condition should be made. With all these measures, if it is clear that diagnosis is clear and other contributing factors have been addressed and patient still fails to respond to second SSRI, based on adult data, it is recommended to switch to venlafaxine, bupropion or mirtazapine.

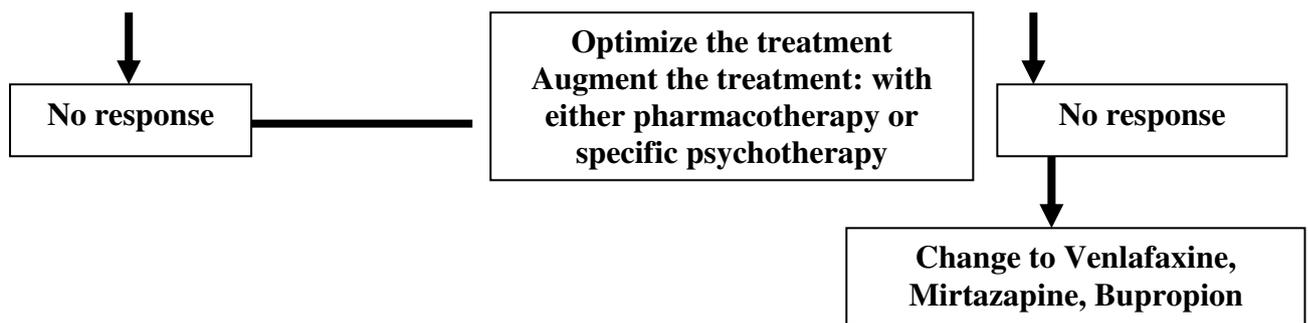
Electroconvulsive therapy (ECT) should be usually considered in patients who fail to respond to 2 adequate antidepressants trails or in other clinical situations where ECT is consider to be life saving (refusal to eat or drink, severe suicidality, catatonia) or where other treatment modalities cannot be used. According to MHCA, unmodified ECT cannot be administered and use of ECT in minors, should be done with the informed consent of the guardian and prior permission of the Mental Health Review Board.

**Table-7: Indications for ECT in children and adolescents**

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| <ul style="list-style-type: none"><li>• Severe, persistent major depression with or without psychotic features, including catatonia</li><li>• Symptoms are severe, persistent, and significantly disabling which may be in the form of life-threatening symptoms such as the refusal to eat or drink and severe suicidality</li><li>• Failure to respond to at least two adequate trials of appropriate antidepressant agents accompanied by other appropriate treatment modalities.</li><li>• ECT may be considered earlier in cases if adequate medication trials are not possible because of the patient's inability to tolerate the antidepressant, the adolescent is grossly incapacitated and thus cannot take medication, or waiting for a response to a psychopharmacological treatment may endanger the life of the adolescent.</li></ul> |
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**Figure -1: Treatment algorithm of Depression in children and adolescents**





### **TREATMENT IN CONTINUATION PHASE**

Although there is not much data about treatment of depression during the continuation phase in children and adolescent, but considering the high rate of relapse and recurrence of depression, continuation therapy is recommended for all children and adolescents for at least 6 to 12 months after resolution of symptoms during the acute phase treatment. The frequency of visits during the continuation phase can be once a month, however, exact frequency should be determined by the clinical status of the patient, level of functioning, available support systems, presence or absence of environmental stressors and ability of the patient to deal with the same, motivation for treatment, and the presence of comorbid psychiatric or medical disorders. If psychotherapy was used during the acute phase of treatment, then the same must be continued, however, the frequency of sessions can vary depending on the need of the patient. If patient was initially treated with antidepressants then it is generally recommended to continue with the same dose of antidepressant as used for the management of acute phase. If the patient was treated with a combination of antidepressants and nonspecific psychotherapy during the acute phase of treatment, then they can be provided specific psychotherapy depending on the patient's suitability.

### **TREATMENT IN MAINTENANCE PHASE**

Usually, maintenance therapy is not indicated after the first episode. The initiation and duration of maintenance treatment should be a collaborative decision between the patient, family and clinician with appropriate consideration of patient and family's preference as well as the risk factors for recurrence. Whether to give maintenance treatment is determined by the number of previous episodes, severity of the present and previous depressive episodes (e.g., suicidality, psychosis, functional impairment), presence of comorbid disorders, side effects of treatment, and patient's and family preference. Environmental factors, such as family stability (e.g., divorce, illness, job loss, or homelessness), family psychopathology, appropriateness of school placement and contraindications for treatment, also must be taken into consideration before deciding about the maintenance treatment. As there is no sufficient data about the maintenance treatment in children and adolescents, based on the adult literature, it is recommended that patients with two (if episodes are characterized by psychotic symptoms) or three episodes of depression, severe suicidality, severe dysfunction during the episodes, family history of affective disorders and history of treatment-resistance should receive maintenance treatment.

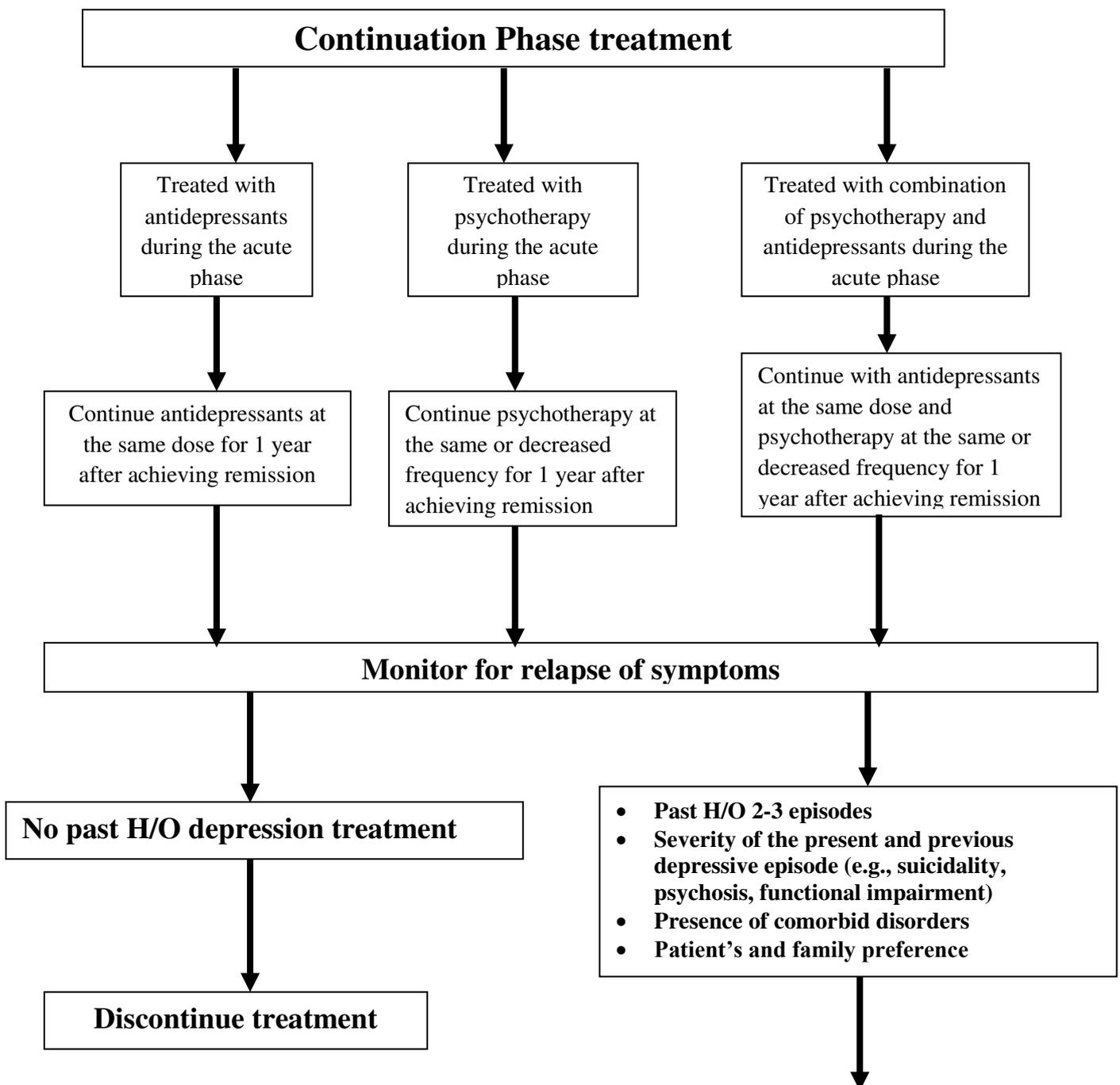
The optimal duration of maintenance medication is not well established but depending on risk factors, it is generally believed to be between 3 years to lifetime.

Unless there is a contraindication, the psychotherapeutic or pharmacological treatments that were efficacious to induce the remission during the acute phase of treatment are used for

maintenance therapy. It is important to note that the long-term effects of antidepressant medications on the maturation and development of children have not been studied. The clinician and the patient's family should weigh the risks and benefits of maintenance antidepressants against the possible consequences of relapses.

During the maintenance phase children and adolescents need to be monitored at least once a month to once in 3 months, based on the clinical status, environmental stressors, level of functioning and available social support.

**Figure -2: Treatment algorithm for continuation phase of depression in children and adolescents**



## Maintenance Treatment

### **DISCONTINUATION OF TREATMENT**

After the completion of the continuation phase treatment after the first episode of depression, medications can be discontinued slowly over the period of few weeks to avoid withdrawal effects. Fluoxetine is known to have long elimination half-life. Before tapering off medication, tapering schedule, withdrawal symptoms and relapse must be discussed with the patient and the family. Because the chances of relapse are very high during the first 8 months after stopping treatment, patients should be seen every 2 to 4 months during this period. If symptoms recur, then promptly previously effective treatment need to be reinstated.

### **MANAGEMENT OF CLINICAL FEATURES THAT REQUIRE SPECIAL ATTENTION**

**Suicidal Ideation and/or Suicide Attempts:** Management of suicidality in children and adolescents requires proper assessment, monitoring and resolution of the same. Patients, who are at high risk of suicide, need to be managed as inpatients. If admission is refused, then the family should be advised to implement the high risk management at home and all potentially lethal agents, especially firearms and toxic medications should be kept away from the patient's access. If family conflict is present, family therapy needs to be considered. If the patient has hopelessness and cognitive distortions then proper psychoeducation and use of principles of CBT need to be considered. Antidepressants need to be considered if the depression is severe enough to cause significant impairment in patient's participation in psychotherapy, or if the patient worsens or fails to improve with psychotherapy alone. ECT may be considered in patients with severe suicidality and those who have not responded to other modality of treatments.

**Psychotic Depression:** Antipsychotics need to be added to antidepressant for psychotic depression. There is no data in adolescents which can specifically help to select a particular antipsychotic, but generally atypical antipsychotics are preferred. However, it is to be remembered that use of antipsychotics is associated with the increased risk of tardive dyskinesia, weight gain and hormonal changes. Hence, it is advised to taper off antipsychotics following remission of psychotic symptoms. It is important to remember that presence of psychotic symptoms in depression is an indicator of possible development of bipolar disorder, and clinicians should be alert to this possibility, particularly if antidepressants are prescribed.

**Atypical Depression:** Psychotherapy and pharmacotherapy are used frequently, although data specific for management of atypical depression in children and adolescents is not available.

**Treatment-Resistant Depression:** If an adolescent presents with treatment-resistant depression, proper evaluation of treatment failure should be done, which should include re-evaluation of the diagnosis, assessment of dose of antidepressant used in the past, length of drug trial, length of psychotherapy, compliance with medication, psychiatric comorbidity

(anxiety, dysthymia, substance use, and personality disorders), comorbid medical illnesses, undetected bipolar depression, exposure to chronic or severe life events, such as sexual abuse, that may require different modalities of therapy. There is meagre evidence to suggest that adolescents with treatment resistant depression may respond to ECT.

Because of lack of data, several psychopharmacological strategies have been recommended for adults with TRD may be applicable to youth: optimization (extending the initial medication trial and/or adjusting the dose), and switching to another agent in the same or a different class of medications, augmentation or combination (e.g., lithium, T3). Each strategy should be implemented in a systematic fashion with proper education of the patient and family, and support to reduce the potential for the patient to become hopeless.

**Comorbid anxiety disorders:** Anxiety disorders or anxiety symptoms are frequently associated with depressive disorders, and treatment with SSRIs tends to address both sets of symptoms. It has also been seen that patients with comorbid anxiety disorders respond better to CBT.

**Comorbid ADHD:** Management of comorbiddepression and ADHD can be very challenging and selection of treatment modality depends on the relative severity of both the conditions. Psychostimulants may be used as the first line agents, if the ADHD is more severe than depression. If both depressive and ADHD symptoms improve with stimulant, then psychostimulants can be continued. However, if depression doesn't respond to psychostimulant, then it is advisable to consider antidepressant. Once depression improves with SSRI it is advisable to re-evaluate the patient for ADHD symptoms and if these are present, patient should be managed according to guidelines for ADHD. However, if depression is more severe, it should be treated before ADHD. If both depressive and ADHD symptoms adequately improve, then the same treatment should be continued. If only depressive symptoms improve and ADHD symptoms continue then the patient should be treated according to guidelines for ADHD. Irrespective of the severity of depressive symptoms, psychosocial interventions must be carried out for both the disorders.

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