

Depression-let's Look !

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Definition:

Depression is one kind of mood disorder, more than sadness causing a persistent feeling of sadness and loss of interest. It is an irrational or abnormal expression of emotion persisting more than two weeks, mostly of unknown cause, imparting functional impairment and needing treatment According to World Health Organization (WHO) (WHO-2012) depression has following characteristics: a. depressed mood, b. loss of interest or pleasure, decreased energy, feeling of guilt and or low self-worth, disturbed sleep and or appetite, f. poor concentration.

Sadness: Sadness is a common emotion of short duration, having a cause not causing functional impairment and donot need treatment.

History:

Hippocrates described a syndrome of melancholia as a distinct disease with particular mental & physical symptoms. Derived from the Latin verb deprimere, in 14th century, "to depress" The first version of the DSM (DSM-I, 1952) contained depressive reaction and the DSM-II (1968) depressive neurosis. In 20th century, researchers theorized that depression was caused by a chemical imbalance in neurotransmitters in the brain, altering monoamine neurotransmitter levels and affecting depressive symptoms

Diagnostic Criteria:DSM 5 (Diagnostic & statistical manual of mental disorder, 5th edition 2013)

According to the American Psychiatric Association's diagnostic criteria for Major Depressive Disorder, a person must experience five or more symptoms (at least one of the first two) below for a continuous period of at least two weeks.

- Feelings of sadness, hopelessness, depressed mood
- Loss of interest or pleasure in activities that used to be enjoyable
- Change in weight or appetite (either increase or decrease)

- Change in activity: psychomotor agitation (being more active than usual) or psychomotor retardation (being less active than usual)
- Insomnia (difficulty sleeping) or sleeping too much
- Feeling tired or not having any energy
- Feelings of guilt or worthlessness
- Difficulties concentrating and paying attention
- Thoughts of death or suicide.

Most symptoms must be present every day or nearly every day and must cause significant distress or problems in daily life functioning. People with a depressive illness cannot merely "pull themselves together" and get better.

Depression Statistics

- More than 1 out of 20 Americans of 12 years of age and older reported to have depression (female: male 2:1) in 2009-2012. In Bangladesh: 4.6% (WHO-NIMH survey, 2003-2005) have depression. Every day 3000 (every year 800000) people of the world commit suicide, mostly due to depression (WHO)

Types of depression- there is no general agreement but it has been classified as-

Classification of depressive disorder (DSM5)

- Disruptive mood dysregulation disorder (diagnosed in children and adolescents).
- Major depressive disorder (including major depressive episode)
- Persistent depressive disorder (dysthymia)
- Premenstrual dysphoric disorder(PMDD)
- Substance/medication-induced depressive disorder
- Depressive disorder due to another medical condition
- Other specified depressive disorder
- Unspecified depressive disorder

Depression (**major depressive disorder or clinical depression**) is a common but serious mood disorder. It

causes severe symptoms that affect how you feel, think, and handle daily activities, such as sleeping, eating, or working. To be diagnosed with depression, the symptoms must be present for at least two weeks.

Some forms of depression are slightly different, or they may develop under unique circumstances, such as:

- **Persistent depressive disorder** (also called dysthymia) is a depressed mood that lasts for at least two years. A person diagnosed with persistent depressive disorder may have episodes of major depression along with periods of less severe symptoms.
- **Perinatal depression** is much more serious than the “baby blues” (relatively mild depressive and anxiety symptoms that typically clear within two weeks after delivery) that many women experience after giving birth. Women with perinatal depression experience full-blown major depression during pregnancy or after delivery (postpartum depression). The feelings of extreme sadness, anxiety, and exhaustion that accompany perinatal depression may make it difficult for these new mothers to complete daily care activities for themselves and/or for their babies.
- **Psychotic depression** occurs when a person has severe depression plus some form of psychosis, such as having disturbing false fixed beliefs (delusions) or hearing or seeing upsetting things that others cannot hear or see (hallucinations). The psychotic symptoms typically have a depressive “theme,” such as delusions of guilt, poverty, or illness.
- **Seasonal affective disorder** is characterized by the onset of depression during the winter months, when there is less natural sunlight. This depression generally lifts during spring and summer. Winter depression, typically accompanied by social withdrawal, increased sleep, and weight gain, predictably returns every year in seasonal affective disorder.
- **Bipolar disorder** is different from depression, but it is included in this list is because someone with bipolar disorder experiences episodes of extremely low moods that meet the criteria for major depression (called “bipolar depression”). But a person with bipolar disorder also experiences extreme high – euphoric or irritable – moods called “mania” or a less severe form called “hypomania.”

Sub types of Major Depressive disorder may be:

Mild, moderate, severe, with psychotic features, in partial remission, in full remission or unspecified

Pathology physiology

Important neurotransmitters—chemicals that brain cells use to communicate—appear to be out of balance viz: Neurobiology :Neurotransmitters: Mono amine, Nor adrenaline, Dopamine function. Likewise endocrine abnormality and abnormal immune function have some role. (Endocrine:HPA axis,thyroid function;Immune system eg inhibition of immune functioning by glucocorticoids)

Research indicates that depressive illnesses are disorders of the brain. Brain-imaging technologies have shown that the brains of people who have depression look different than those of people without depression. The parts of the brain responsible for regulating mood, thinking, sleep, appetite, and behavior appear to function abnormally

CT scan and MRI have found a number of abnormalities in the patients with long lasting major depressive disorders (MDD) (these investigations are not indicated for diagnosis) like-

- a. Enlarged lateral ventricles
- b. Decreased hippocampal volume
- c. Decreased volume of basal ganglia structures
- d. Decreased grey matter volume of subgenual prefrontal cortex
- e. Increased Amygdala volume whereas

PET scan shows - Altered cerebral blood flow and metabolism in - prefrontal cortex, anterior cingulate cortex, Amygdala and thalamus and Caudate nucleus

But these images do not reveal why the depression has occurred.

Etiology: not always known. Current research suggests that depression is caused by a combination of genetic, biological, environmental and psychological factors.

Predisposing factors:

- Genetic: More in 1st degree relatives both in bipolar and unipolar probands. Liability to MDD and generalized anxiety disorder (GAD) involves same genes but different environmental risk factors. It's a combined action of several genes known as polygenic inheritance. Patient with depression often seem to have high level of anxiety pre-morbidly (Personality).

Precipitating & perpetuating factors:

1. Early environment: a. Deprivation from maternal affection b. parental separation c. family discord

d. physical or sexual abuse e. parenting style
f. postnatal maternal depression.

2. Social environment: a. stressful life events b. prolonged stress c. nonspecific stressors

Depression can happen at any age, but often begins in adulthood. Depression is now recognized as occurring in children and adolescents, although it sometimes presents with more prominent irritability than low mood. Many chronic mood and anxiety disorders in adults begin as high levels of anxiety in children.

Depression, especially in midlife or older adults, can co-occur with other serious medical illnesses, such as diabetes, cancer, heart disease, and Parkinson's disease. These conditions are often worse when depression is present. Sometimes medications taken for these physical illnesses may cause side effects that contribute to depression.

Medications possibly associated with depressive symptoms:

Anticonvulsants (e.g., phenobarbitone), anti-hypertensive agents (e.g., lipophilic beta blockers), antiarrhythmic drugs (e.g., digitalis), antibiotics (e.g., dapsone), anti cholesterol lowering drugs (e.g., statins), cancer chemotherapy agents (e.g., methotrexate), H₂ blockers (e.g., cimetidine)

Depression in Women

During Pregnancy (Baby blues syndrome) Lasts for few days to weeks: 60%-85% pregnant mother experience this; usually does not need treatment)

Woman experience: mood swings, anxiety, sadness, irritability, crying, decreased concentration, trouble sleeping.

Post partum depression: Just after delivery or within few weeks (needs treatment). It is characterized by loss of appetite, insomnia, intense irritability and anger, overwhelming fatigue, Loss of interest in sex, lack of joy in life, feelings of shame, guilt or inadequacy, severe mood swings, difficulty bonding with baby, withdrawal from family and friends, thoughts of harming herself or baby.

Women experience depression about twice as often as men. Biological, life cycle, hormonal, and other factors unique to women may be linked to their higher depression rate. Researchers have shown that hormones directly affect brain chemistry that controls emotions

and mood. Some women may be susceptible to a severe form of premenstrual syndrome called premenstrual dysphoric disorder (PMDD). Women affected by PMDD typically experience depression, anxiety, irritability, and mood swings the week before menstruation, in such a way that interferes with their normal functioning. Women with debilitating PMDD do not necessarily have unusual hormone changes, but they do have different responses to these changes.

Women are particularly vulnerable to depression after giving birth, when hormonal and physical changes, along with the new responsibility of caring for a newborn, can be overwhelming. Many new mothers experience a brief episode of the "baby blues," but some will develop postpartum depression, a much more serious condition. Some studies suggest that women who experience postpartum depression have had prior depressive episodes.

Depression in Men

Research and clinical evidence reveal that while both women and men can develop the standard symptoms of depression, they often experience depression differently and may have different ways of coping with the symptoms. Men may be more willing to acknowledge fatigue, irritability, loss of interest in work or hobbies, and sleep disturbances rather than feelings of sadness, worthlessness, and excessive guilt. Depression can also affect the physical health in men differently from women. One study shows that, although depression is associated with an increased risk of coronary heart disease in both men and women, only men suffer a high death rate.

More than four times as many men as women die by suicide in the United States, even though women make more suicide attempts during their lives. Even if a man realizes that he is depressed, he may be less willing than a woman to seek help.

Depression in the Elderly

Some people have the mistaken idea that it is normal for the elderly to feel depressed. On the contrary, older people feel satisfied with their lives. In addition, older adults may have more medical conditions such as heart disease, stroke or cancer, which may cause depressive symptoms, or they may be taking medications with side effects that contribute to depression. Some older adults may experience what doctors call vascular depression,

also called arteriosclerotic depression or subcortical ischemic depression. Vascular depression may result when blood vessels become less flexible. Those with vascular depression may have, or be at risk for, a co-existing cardiovascular illness or stroke. The majority of older adults with depression improve when they receive treatment with an antidepressant, psychotherapy, or a combination of both.

Precipitating factors: a. Due to loneliness - “**Empty nest syndrome**”, Death of spouse, apart from children. b. Lack of employment. c. Perceive as family/social burden. d. Dependency. e. Chronic illness and disability: DM, HTN, Parkinson’s, Stroke, CKD, Arthritis etc. e. History of Previous Depression

Signs Symptoms of Depression in elderly: Memory problems, confusion, social withdrawal, loss of appetite, weight loss, vague complaints of pain, inability to sleep, Irritability, Delusions (fixed false beliefs), hallucinations, persistent and vague complaint, help-seeking, moving in a more slow manner, demanding behavior.

Management: Two parts

1. Assessment (history, physical examination, mental state examination, laboratory tests).
2. Treatment:

Laboratory test

(Usually needed): Complete blood count, bio-chemistry profile (electrolytes, blood urea nitrogen, creatinine, glucose) and thyroid function (T3, T4, TSH)

(Sometimes needed): Electrocardiogram, folate level, serum calcium level, vitamin B12 level, serum level of digoxin or theophylline (if taking either medication) and urinalysis

Treatments:

1. General (Food & nutrition, assurance to family and caregivers, documentation)
2. Specific: Pharmacological - Biological, Electroconvulsive Therapy : Non- Pharmacological (Psycho-Social): Cognitive therapy, Cognitive behavior therapy

Where indicated: (Non- Pharmacological)

- In case of mild and moderate depression
- In special condition where drugs are relatively contraindicated (Early pregnancy, lactating mother, Other drug interaction etc)
- When patient refused to take medicine

Most Common Psychosocial Interventions for Depression

Psychotherapy: 1. Cognitive-behavioral therapy 2. Interpersonal therapy 3. Problem-solving therapy 4. Supportive therapy

Psychosocial intervention:

1. Activities and exercise
2. Bereavement groups
3. Family counseling
4. Participation in social events
5. Psychoeducation
6. Celebrate past and present positive life events

Pharmacological treatment (Anti depressant drug)

Antidepressants work to normalize naturally occurring brain chemicals called neurotransmitters, notably serotonin and norepinephrine or dopamine.

Indications are: a. A past history of moderate or severe depression b. Subthreshold depressive symptoms that have been present for a long period (typically at least 2 years) c. Subthreshold depressive symptoms or mild depression that persists after other interventions And d. In Major Depressive Disorder (Combination of antidepressant medication and a high-intensity psychological intervention (CBT-cognitive behavior therapy or IPT-interpersonal therapy) are highly recommended).

Drug classifications

- SSRI (selective serotonin receptor uptake inhibitor): Fluoxetine, Fluvoxamine, Sertraline, Paroxetine, Escitalopram, Citalopram
- SNRIs (Serotonin and norepinephrine reuptake inhibitor): Atypical antidepressants: Bupropion, Duloxetine, Venlafaxine, Mirtazapine
- TCAs-ic: Amitriptyline, Clomipramine, Desipramine, Doxepin, Imipramine, Nortriptyline
- MAOIs- Monoamine oxidase inhibitors : Phenelzine, Tranylcypromine, Isocarboxazid, Selegiline

Drugs of choice: NICE guideline suggests SSRIs for first choice. Titrate and assess efficacy for 2 weeks and after 2 weeks if no response-Increase the dose. If effective, continue for 6-9 months after recovery

If poorly tolerated: Switch to different drugs and if non responsive for 3-4 weeks : Consider treatment for resistant depression

The newest and most popular medications are called selective serotonin reuptake inhibitors (SSRIs).

Serotonin and norepinephrine reuptake inhibitors (SNRIs) are similar to SSRIs. However, medications affect everyone differently so “no one-size-fits-all” approach to medication exists..

For all classes of antidepressants, patients must take regular doses for at least three to four weeks before they are likely to experience a full therapeutic effect. They should continue taking the medication for the time specified by their doctor, even if they are feeling better, in order to prevent a relapse of the depression. Medication should be stopped only under a doctor’s supervision. Some medications need to be gradually stopped to give the body time to adjust. Although antidepressants are not habit-forming or addictive, abruptly ending an antidepressant can cause withdrawal symptoms or lead to a relapse.

Though SSRI and other antidepressant are relatively safe based on the thorough review the FDA was prompted, in 2005, to adopt a “black box” warning label on all antidepressant medications to alert the public about the potential increased risk of suicidal thinking or attempts in children and adolescents taking antidepressants. In 2007, the FDA proposed that makers of all antidepressant medications extend the warning to include young adults up through age 24. A “black box” warning is the most serious type of warning on prescription drug labeling.

Side Effects

Antidepressants may cause mild and, usually, temporary side effects (sometimes referred to as adverse effects) in some people. These are -

- Dry mouth—it is helpful to drink sips of water, chew sugarless gum and clean teeth daily.

- Constipation—eat bran cereals, prunes, fruit and vegetables.
- Bladder problems
- Sexual problems-sexual functioning may change.
- Blurred vision—this will pass soon and will not usually necessitate new glasses.
- Dizziness—rising from the bed or chair slowly is helpful.
- Drowsiness as a daytime problem—this usually passes soon..

The most common side effects associated with SSRIs and SNRIs include:

- Headache-this usually goes away.
- Nausea-this is also temporary, but even when it occurs, it is transient after each dose.
- Nervousness and insomnia (trouble falling asleep or waking often during the night)—these may occur during the first few weeks; dosage reductions or time will usually resolve them.
- Agitation (feeling jittery)—if this happens for the first time after the drug is taken and is more than transient, the doctor should be notified.

Psychotherapies

Many forms of psychotherapy, including some short-term (10- to 20-week) and other regimens are longer-term, depending on the needs of the individual.

Two main types of psychotherapies - cognitive-behavioral therapy (CBT) and interpersonal therapy (IPT) - have been shown to be effective in treating depression.

Phase	Duration	Goal
Acute	Approx. 3 months	To achieve complete recovery from signs and symptoms of acute depressive episode (i.e., remission)
Continuation	4-6 months	To prevent relapse as patient’s depressive symptoms continue to decline and his or her functionality improves
Maintenance	<ul style="list-style-type: none"> • 3 months or longer, depending on patient’s needs • Over the age of 70, usually 12-24 months or lifetime if more than 2 episodes 	<ul style="list-style-type: none"> • To prevent recurrence of a new depressive episode • Relapse occurs in 40-60%

Studies have indicated that for adolescents, a combination of medication and psychotherapy may be the most effective approach to treating major depression and reducing the likelihood for recurrence.

Electroconvulsive therapy (ECT) is useful, particularly for individuals whose depression is severe or life threatening, or for those who cannot take antidepressant medication. ECT often is effective in cases where antidepressant medications do not provide sufficient relief of symptoms. In recent years, ECT has been much improved.

Indications for ECT

a. Severe Depression with food refusal, b. Suicidal attempts/thoughts c. Post partum depression d. In case of pregnancy (Where Antidepressants are contraindicated) d. Depression with psychotic features.

Depression in special situations:

Depression and diabetes: In case of diabetic patients the prevalence of depression is more than normal population (9% to 60%). Presence of depression having negative impact in diabetes control and high risk of heart diseases

- Drugs: Use SSRIs : First choice fluoxetine .SNRIs also safe (Duloxetine) and Avoid TCA and MAOIs to prevent weight gain and blood sugar control with special attention to Mirtazipinie which cause weight gain and is diabetogenic

Depression in pregnancy and lactation : in Pregnancy and lactation: Nortriptyline, Amitriptyline, Imipramine, Fluoxetine are recommended. Paroxetine, Venlafaxine to be avoided

**SSRIs may increase the risk of Persistent Pulmonary Hypertension of Newborn*

*In case of **Breast feeding**: Sertraline is the first choice*

In hepatic impairment: Recommended: Imipramine (Start with 25 mg/day). Paroxetine, Citalopram (Start with 10mg/day) and Avoid: Amitriptyline, Sertraline, Fluoxetine.

In renal impairment: Citalopram and Sertraline is recommended, dose reduction and/or drug-dose interval may need to change. Lithium to be avoided

Key points to know

- A single episode of depression should be treated for at least 6–9 months after remission
- The risk of recurrence of depressive illness is high and increases with each episode
- Those who have had multiple episodes may require treatment for many years .The chances of staying well are greatly increased by taking antidepressants.
- Antidepressants are effective, not addictive, not known to lose their efficacy over time, not known to cause new long-term side effects

How Family and Friends Can Help the Depressed Person

If you know someone who is depressed, it affects you too. The most important thing anyone can do for the depressed person is to help him or her get an appropriate diagnosis and treatment. You may need to make an appointment on behalf of your friend or relative and go with her to see the doctor. Encourage him to stay in treatment, or to seek different treatment if no improvement occurs after six to eight weeks.

The second most important thing is to offer emotional support. This involves understanding, patience, affection and encouragement. Engage the depressed person in conversation and listen carefully. Do not dismiss feelings expressed, but point out realities and offer hope. Do not ignore remarks about suicide. Report them to the depressed person's therapist. Invite the depressed person for walks, outings, to the movies and other activities. Keep trying if he declines, but don't push her to take on too much too soon. . Remind your friend or relative that with time and treatment, the depression will lift.

Depression is not an uncommon disease in our clinical practice. Apprehension and timely intervention may help complete remission of the enigma.