Depression: A Review

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ABSTRACT

Depression is a major mood disorder characterized by an experience of inadequacy, despondency, reduced activity, pessimism, anhedonia, and disappointment in which those signs and symptoms critically disrupt and adversely affect the depressive person’s life, sometimes more chance to attempt suicide as a result. This search for a prolonged understanding of the reasons for depression, and the developing effective treatment, is relatively significant. Clinical and pre-scientific research recommend stress as a key feather in the pathophysiology of depression.
INTRODUCTION

Depression is a common psychiatric disorder that presents with feelings of guilt, low self-worth, depressed mood, loss of interest or pleasure, decreased energy, disturbed sleep or appetite, and poor concentration as some of the problems that represent the common mental disorder called depression. Then, depression often comes with symptoms of anxiety. The bipolar affective disease normally includes each manic and depressive episode separated through intervals of regular mood. These problems can become chronic or recurrent and lead to substantial impairments in a person's ability to take care of his or her everyday responsibilities. At its points, depression can lead to suicide. Almost 1 million lives are misplaced yearly because of suicide, which interprets to 3000 suicide deaths each day. For every person who completes suicide, 20 or more may attempt to end his or her life[1]. The majority of the patients prefer advice from a psychiatrist due to depression. The community still believes that the medication for patients with depression would go for lifelong and it's due to their weakness in personality and they cure themselves by themselves. What others see in patients as a myth related to depression and these myths are created mostly by underqualified counselors, faith healers, and non-medical experts of their interest and largely by society. The increased awareness and approaches to the psychiatrist results in the increased no of patients and not necessarily a rise in the prevalence. Nowadays treatment for depression becomes easier because of newer medications, better facilities, and increased responses of the patients to treatment[2].

Types of depression:

like other diseases depressive illness also has a different kinds of forms:

(1) Major depression is expressed by a combination of symptoms like obstruction in doing work, difficulty to sleep eat and loss of interest in participation or to enjoy pleasurable activities. This type of depression can occur in a lifetime twice or several times.

(2) Dysthymia: a less severe type that can include long-term chronic symptoms but not disable but it can keep you from full-term functioning and happiness or from feeling good. Patients with dysthymia may experience major depressive episodes.

(3) Manic depression is also known as bipolar which is not common as other forms of depression it includes cycles of depression and elation or mania, sometimes the patients rapidly and dramatically change the mood, in a depressed cycle the patient has one or any
other symptoms of depressive illness, and in mania cycle the patient experience the symptoms of mania which may affect the thinking, judgment and social behavior that may result in serious problems\cite{1,3}.

**Symptoms of depression:**

Patients with depression or mania may experience every symptom some may experience a few symptoms and the severity of the symptoms may vary from individuals to individual\cite{4,5}. Which includes:

1. Depression: anxious or empty mood and persistent sad
2. A feeling of hopelessness and negative thoughts
3. Worthlessness, helplessness
4. No interest in enjoying pleasure, not interest in hobbies and other activities that one can enjoy.
5. Difficulty in sleeping, or oversleeping
6. Decreased intake of food, loss of weight.
7. Increased intake of food or weight gain.
8. Feeling of tiredness, fatigue, being slowed down.
9. Death or suicidal thoughts and attempts.
10. Decrease in concentration, difficulty in making decisions.
11. Common physical symptoms such as headache, digestive disorder, and chronic pain do not respond to treatment\cite{6}.

**Causes of depression:**

Which includes environmental factors and genetic factors:

**Environmental factors:**

Events include traumatic conditions, stress, childhood difficulty (abuse), these situations can happen to anyone at any time in everyone's life. These are considered factors outside of
society. Some researchers explain that these events are sociological or psycho-social events that can affect the patient health or mind. They also explain that the events or experiences in everyone’s life may affect mental health. These experiences may influence the patients’ thoughts emotions and behavior, these experiences may be from their past relationships, childhood abuse, and past crises. The key factor for the development of depression in individuals is based on how they react to these environmental events or experiences in their day-to-day life [7].

(1) **Stress**: most researchers believe that stress has a direct relation to the development of depression, but the stress may be negative or positive, development of depression depends on how the individual’s body or mind reacts to the stressful event. Negative stress includes loss of loved ones, loss of job, relation breakups, and divorce. Positive stress involves planning for the wedding, getting new jobs, moving to a new city. Both these stress from environmental factors can lead to the development of depression [8].

(2) **Traumatic events**: many studies show that most of the peoples have experienced this type of events before the development of the events. Traumatic events improve, loss of loved ones, any serious medical illness, or unexpected financial loss. These events in life can even destroy the control of sense and stability in a person’s life and may lead to emotional stress.

(3) **Childhood difficulties**: Persons with severe difficulties in childhood may have an increased chance of developing depression. The most common childhood difficulties include sexual harassment, parental separation, physical harassment, dysfunctional upbringing, and mental illness in one or both of the parents. One of the most difficult situations for the children is the separation or death of the parents before the age of 11. There is a greater chance of developing depression in children who had experienced these events [9,10].

(4) **Synthetic chemicals**: in our day-to-day life every one using so many synthetic chemicals in the form of preservatives, addictive and hormones that are used in food products. Pesticides which are air sprayed and other water pollutants are also involved. Many studies show that air and water pollution alone can cause cancer and other serious health issues these events can lead to developing depression. Synthetic chemicals and pollutants are now closely related and linked together in developing depression [11].

(5) **Noise pollution**: which may lead to the development of aggression. Hypertension, hearing difficulty, raised stress level, difficulty in sleep that may lead to depression panic
attacks, and difficulty in remembering. An increase in noise pollution may result in major cardiac disorders and increased blood pressure. Patients with depressive tendency become more susceptible if the patient has prolonged exposure to noise pollution [12].

(6) **Electrical pollution:** our environment is surrounded by radio waves so everywhere we go; we are exposed to these waves. The electrical devices work by electrical radio waves and these kinds of waves can develop depression. Unlike other environmental causes, the waves can’t see, hear, and cannot be tasted but these waves can induce a negative effect in our mind [13].

(7) **Natural and catastrophic disasters:** which include hurricanes, earthquakes, forest fires, and even man-made disasters such as bombings which can push a more susceptible patient to the major depressive condition [14].

**Genetic factors:**

Most of the genetic-based studies of mood disorder mainly focused on the functional polymorphisms in the loci which encodes the serotonin transporter (SLC6A4), serotonin 2A receptor (5HTR2A), tyrosine hydrolase, tryptophan hydrolase 1, and catechol-o-methyltransferase (COMT) [15].

It’s known that depressive illnesses run through families but nowadays it's not fully known and people may inherit or be susceptible to illness or maybe the environmental factors may be the main reason for the developing illness. So, researchers say that the illness may be inherited based on their studies, which appears to be a vulnerability to depression this means that if the person's close relatives who had depressive illness may increase the chance to inherit a tendency to develop the illness [16,17].

I. Bipolar disorder has a greater genetic influence, in those with bipolar disorder, 50% of their parent (one or both) had a history of clinical depressive illness, chance for developing clinical depression in children is 25% if the mother or father had a bipolar depression if both the parents had bipolar depression the chance for getting depression is 75%, siblings of those with bipolar disorder are 8-18 times more likely to develop bipolar disorder, 2-10 times are more likely to develop the major depressive disorder than others with no siblings [18].

Studies conducted in identical twins, genetic influence on depression is mainly based on the research work on identical twins. They are very helpful to the research work because they
share the same genetic code and if any one of them is depressive the other has a chance of developing clinical depression is approximately 76%. Are the twins are raised apart from each other both have a chance of developing depression (67%) because of the strong and same genetic influence if this happens i.e.; one becomes depressive other may develop a depressive illness which shows that the illness is likely to be entirely genetic. Not only the genetic factors the environmental factors are also a part of developing illness[19].

Studies are also done in the fraternal twins, in identical twins they share almost the same genetic code and they look similar but, in these twins, they share only 50% of their genetic code and don’t look similar so if one the twin is depressed the chance for developing the illness in other is only 19%[20,21].

**Pathophysiology**

The pathophysiology of depression is not fully understood but some theories are developed based on depressive conditions. Current theories are the monoaminergic system, immunological dysfunction, circadian rhythm, and structural or functional abnormalities of emotional circuits.

The monoamine theory is mainly based on the efficacy of monoaminergic drug-using treatment of depression. The primary causes of depression are the insufficient activity of monoamine neurotransmitters in a depressive person. Some of the evidence-based on the monoamine theories are first, depletion of tryptophan and precursor of serotonin, monoamine can lead to depression; this suggested that reduced serotonin neurotransmitter is important in depression[22]. Second, the correlation between polymorphism in the 5HT-TLPR gene and depression risk in serotonin receptors. Third, reduced size of locus coeruleus, reduction in the activity of thyroxin hydroxylase, increased density of alpha-2 adrenergic receptor it’s may decrease adrenergic neurotransmitters in depression[23]. However, this theory concept is inconsistent with the truth that serotonin depletion does not cause depressive treble in healthy persons, the reality that antidepressants immediately up the level of monoamines, however, this takes weeks to work, and the existence of atypical antidepressants which not target this pathway[24].

Immune system abnormalities also influence depression by increasing the cytokine level and it generates sickness behavior. We suggested a nonsteroidal anti-inflammatory agent, and
cytokine inhibitor for normalizing cytokine level after successful depressive treatment, if the patient has immune system abnormalities in depression [25].

**Diagnosis**

Rating scales aren't used to diagnose depression, however, they indicate the severity of signs for some time, so a depressive person who scores above a given cut-off point then it can easily evaluate for a depressive level diagnosis. Several score scales are used for this purpose. Some rating scale includes the Hamilton Rating Scale for Depression, the Beck Depression Inventory or the Suicide Behaviors Questionnaire-Revised [26].

**DSM and ICD criteria**

The most used criteria for diagnosis depressive conditions are DSM (diagnosis and statistical manual of mental disorder) and ICD (international statistical classification of disease) which uses recurrent depressive disorder for the repeated episode [27], both DSM and ICD are measured by using typical depressive symptoms. In ICD-10 has three typical depressive symptoms (depressive mood, reduced energy, and anhedonia) these are used for diagnosing depression. According to DSM-5 mainly they have two depressive symptoms (depressive mood and anhedonia (loss of interest)).

Major depressive disorder, mainly classified as a mood disorder based on DSM-5 criteria. The diagnosis of depression is a score based on the presence of single or recurrent major depressive episodes. Further qualifiers are used to categorize each episode itself and the path of the disorder. The class Unspecified Depressive Disorder is diagnosed if the depressive episode's manifestation does not meet the criteria for a major depressive episode [28].

**Major depressive episodes**

A major depressive episode is classified by the presence of depressive mood in the patient persist for at least two weeks. Episodes are categorized as mild (few symptoms in minimum criteria) and moderate or severe (marked impact score on social and occupational functioning). If the patient has psychotic features it is commonly referred to as psychotic depression and its automatically rated as a severe episode [28].

**Subtypes**

The DSM-5 further classified six subtypes are:
• “Melancholic depression” (loss of pleasure in most activity, worsening of symptoms in the morning hour, early morning walking, excessive weight loss, and excessive guilt).

• “Atypical depression” (paradoxical anhedonia, significant weight gain, and increased appetite, hypersomnia, and sensation of heaviness in limb known as leaden paralysis).

• “Catatonic depression” (its rare and severe form of major depression mainly disturb motor behaviors other symptoms are, a person is mute and almost stuporous and exhibits purposeless).

• “Depression with anxious distress” (risk of suicide of depressed individual with anxiety)

• “Depression with peripartum onset” (intense, sustained and sometimes disabling depression experienced by women after giving birth or while a woman is pregnant).

• “Seasonal affective disorder” (it is the depression in which depressive episodes come on in the autumn or winter, and resolve in spring) [29,30].

Prevention

Preventive efforts may also result in decreases in the level of the condition of between 22 and 38%. Two major preventive Behavioral interventions are (interpersonal therapy) and (cognitive-behavioral therapy) is more effective in preventing new-onset depression. Because such interventions seem to be more effective when delivered to each person or small group, it's been advised that they can be capable of attaining their big target audience that most efficiently through the Internet [31].

Treatment:

In the case of mild depression either medication or psychotherapy is more effective when compared with moderate or severe depression which requires an approach of both medication and psychotherapy [32].

Drug therapy: first-line drug therapy is antidepressants about 60-65% of patients effectively respond to first antidepressants. Selection of antidepressants can be done by matching the patients’ symptoms with the side effects, physical condition, mental strength, psychiatric conditions, and no specific antidepressant agent is superior to another based on efficacy or its onset of action and their previous response. Cost-effective treatments can be done by
prescribing the drugs in their generic form. Fluoxetine and Citalopram are the agents mostly preferred by the UMHS. The patients with antidepressant medication should be closely monitored because of the chance for worsening depression and suicidality at the beginning of treatment or an alternation in the dose $^{[33]}$.

The effect of antidepressants therapy is based on their activity on the neurotransmitters and neurotransmission. Based on the Monoamine hypothesis, depression is caused by the activity in the brain of monoamines which include dopamine, serotonin, and norepinephrine $^{[34]}$. In the 1950s Monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants were discovered as effective treatments for depression. In 1965 based on these findings and other supporting studies and evidence, Led Joseph Schildkraut published his paper on the topic “The Catecholamine Hypothesis of Affective Disorder” $^{[35,36]}$.

MAOIs stop the degradation of the monoamines neurotransmitters dopamine, serotonin, and norepinephrine by blocking the monoamine oxidase enzyme which results in the increased concentration of these neurotransmitters and an increase in the neurotransmission $^{[37]}$. Tricyclic antidepressants block the reuptake of these neurotransmitters. These days the most common antidepressants are selective serotonin reuptake inhibitors (SSRIs) which block the reuptake of serotonin thereby increasing the level of serotonin in brain synapses $^{[38]}$. MAOIs, Tricyclic antidepressants, and (SSRIs) may raise the level of serotonin and other antidepressants block the binding of serotonin with 5-HT$_{2A}$ receptors and suggesting simply that serotonin is a happy hormone. The fact is that use of other antidepressants present in the bloodstream and the raised level of the serotonin, then the patient may feel bad or worsening of the depression for the first few days or week of the initial treatment. The explanation for this fact is that 5-HT$_{2A}$ developed as a saturation signal (patients with 5-HT$_{2A}$ antagonist may gain weight), and by making the animals stop looking for food and mates, etc., and ask them to hunt or search for predators $^{[39]}$. In some terrifying situations, it will be helpful for the animals not to feel hungry even if they need to eat this can be achieved by the stimulation of 5-HT$_{2A}$ receptors, but if the terrifying situation lasts for a long time, then the animal starts to eat and mate again the fact is situation survived by the animal is not so dangerous than they felt. The number of 5-HT$_{2A}$ receptors decreased by a process known as downregulation and through this, the animal go back to normal behavior. This suggests that there are 2 ways to relieve anxiety in humans with serotonergic drugs i.e., by blocking the stimulation of 5-HT$_{2}$ receptors or by overstimulating them until they are minimized via tolerance $^{[40,41]}$.
Frequent visits: In the initial period of treatment the patient requires frequent visits to evaluate the response to intervention, suicidal thoughts side effects, and psychosocial support systems.

Continuation therapy: Continuing the treatment may reduce the incidence of recurrence of major depression (9-12 months after the acute symptoms are fixed), based on the patient’s history of relapse and other clinical factors the lifetime drug therapy or long-term maintenance therapy are determined [42,43].

Patient support (education): Patient education and their support for the treatment are also important if the patient is not cooperating and resistance to the treatment or diagnosis of the illness may be a serious problem. So, the patients should be well educated about the condition about the treatment plans about outcomes, and also the family members should support the provide them confidence which will be more helpful for the treatment [43].

Prolonged treatment and side effects:

Antidepressants are the first-line agents for the depressive episodes in the acute phase and help to resolve the symptoms but if it is untreated the condition or the symptoms may become more worsen. In long-term use, the brain starts to work as compensation for the drug-induced changes with a process called oppositional tolerance. The brain tries to redevelop the normal balance of production, release, and reuptake of the neurotransmitters. The fact is that if the medication boosts up the level of serotonin in the brain, then the neurobiology of the system tries to reduce the production of the neurotransmitter, in other words, the use of antidepressants for a long period the brain creates a system to blocks or cancel its effects, i.e., use of antidepressants itself may cause problems [44]. At the same time, there is evidence stating that the sudden stoppage of antidepressants in patients who are taking the medication for a long period may develop withdrawal symptoms to drugs and some may don’t have any effects and continue to recurring depressive illness. If the treatment is restarted as a result these patients can develop a permanently recurring illness. This is tardive dysphoria [45,46].

Alternative Treatment

There is no proof of any alternative treatment for depression. Entought some people with depression get relaxation by using home remedies, mainly reduce depressive symptoms such as anxiety, physical pain, and changing roles. If you considering using home remedy use should seek advice from a health care provider [47].
Some of the alternative treatments are massage therapy, yoga, meditation, relaxation, acupuncture, herbal remedies, aromatherapy, chiropractic treatment, guided imagery, etc. [48]

Meditation is now defined as an altered state of consciousness. It is a type of rest that, not like sleep, is entered into purposely. Meditation is normally practiced regularly for at least 10 mins every day. While the body is in a relaxed state, the thoughts are cleared using specializing in one thought -- occasionally a word, a phrase, or a specific scene.

Relaxation is marked through reduced muscle stress and respiration, decrease heart rate and lower blood pressure and improved circulation. The relaxation lowers the activity of the sympathetic nervous system by meditation. In addition to lowering the heart rate and decreasing the blood pressure this change also can lead to i. Decreased sweat production, ii. Decreased oxygen consumption, iii. Decreased catecholamine production (chemical substances related to the strain and stress), iv. lower cortisol production (stress hormone) [49].

Different types of exercising can decrease stress, and lower depression. Exercise also can boom your energy, balance, and flexibility. In general, a workout is safe, effective, and improves your health conditions.

CONCLUSION

Depression is a severe medical condition and public health concern. Although the development of depression is due to an understanding of difficulty, trigger factors, and treatment of the disorder is important for promoting affected individuals. There is also a need to study the course and duration of continuation treatment of depressive disorder person. These studies must evaluate the cost-effective treatment which can be easy use without difficulty in the primary care treatment for depression.

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