



## Depression – A Review

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### ABSTRACT

Depression is a disorder characterized by feelings of inadequacy, hopelessness, depression, hopelessness, anhedonia and sadness when these symptoms are severely disturbed and negatively affect a person's health, sometimes to the point that suicide is attempted or had no effect. The need for increased guidance on the causes of depression, as well as the development of additional therapies, is especially important. Clinical and pre-clinical studies show that stress is a leading mediator in the pathophysiology of depression.

**Keywords:** Depression, neurotransmitters, stress, treatment, anti depressants

### Introduction

According to WHO estimates, depression will be the second leading cause of illness in another decade, one in five women, and 12 men will be depressed. Not only adults but also 2 percent of schoolchildren, and 5 percent of teens also suffer from depression, and these are often undetectable. Depression has become a very common cause for people to come to a psychiatrist, or the general opinion that all mental disorders are depression<sup>1-2</sup>. What one sees in many patients is a myth related to depression. People still believe that it is because of a weakness in the personality, or that one can cure oneself, or that a drug will last a lifetime and is only a relief. All of these are myths, and are mainly created by religious healers, or unqualified counselors, and non-medical professionals because of their interest, and especially people who do not know the public. Increased awareness, as well as the approach of psychiatrists, has been a major factor in the increase in the number of patients and not the increase in the number. With new medicines, and better services, treatment for depression has become easier, and more people are responding well to treatment, and they are returning to normal functioning as soon as possible

### Types of depression

Depression comes in many forms, as do many other illnesses: i. Depression is characterized by a combination of symptoms that impair the ability to work, sleep, eat and enjoy activities that were once fun. These debilitating episodes of disability can occur once, twice or several times in life. ii. Dysthymia, a type of severe depression, includes chronic, incurable symptoms that do not disfigure, but end up working on "full steam" or feeling better. Sometimes people with dysthymia also experience major episodes of depression. iii. Manic-depressant or bipolar disorder is almost as common as other types of depressive disorders. It includes cycles of depression and happiness or insanity. Sometimes mood swings are dramatic and fast, but they are usually slow. When you are in a depressed cycle, a person may have any or all of the other symptoms of depression. If you are in a manic cycle, any or all of the symptoms listed under mania can be detected. Mania often affects the thinking, judgment, and behavior of the public in ways that can cause serious problems and embarrassment

### Prevalence – World scenario and Indian scenario:

Depression is the most common mental illness reported in many community-based studies. It is also reported as a single outpatient clinic site and in courses seen in a variety of medical and surgical settings. It is also reported to be the most common mental illness in adults in all various settings. Studies in India have also shown that health events during the pre-depression phase play a major role in depression. (Table 1) Research on women also highlighted the importance of identifying risk factors such as cohabitation, marital discord and sexual coercion<sup>6-7</sup> There is a need to continue research into factors such as cost, attitude toward treatment, adherence to rules, compliance and neurobiological relationships. There is also a need to study the course of depressive disorders in India in order to determine the need and duration of ongoing treatment. Studies should also examine the most cost-effective treatments that can be easily used in a primary care setting to effectively manage stress.

**Table**

.The Indian Council of Medical research, a collaborative project at four centres (Bikaner, Goa, Patiala and Vellore) and the outcome

ICMRDiscriptiveCategories	Bikaner N=68%	Goa N=85%	Vellore N=68%	Patiala N=102%	All centers N=323%
Predominantly Depressed type	5.8	11.7	11.8	17.7	11.8

**Symptoms of depression:**

Not every depressed person or man experiences all the symptoms. Some may experience a few symptoms, others many. Also, the severity of symptoms may vary in people11-14 Depression: i. a continuing state of sadness, anxiety or emptiness, ii. feelings of despair, hopelessness, iii. guilt, worthless, helpless, iv. loss of interest or pleasure in hobbies and activities you once enjoyed, including sex, v. insomnia, waking up in the morning or falling asleep, vi. appetite or weight loss or overeating and weight gain, vii. weight loss, fatigue, slowing down, viii. thoughts of death or suicide, suicide attempts, ix. restlessness, irritability, x. difficulty concentrating, remembering or making decisions, xi. persistent symptoms that do not respond to treatment, such as headaches, digestive disorders, and chronic pain

**Causes of disease – Environmental factors and Gene component***Genetic Causes of Depression*

Most published studies of genetic modification of mood disorders have focused on the functioning of polymorphisms (genetic variation of DNA that alters the expression and / or function of a genetic product) in loci encoding the serotonin transporter (SLC6A4), serotonin 2A receptor (5HTR2A), tyty TH) (a dopamine-binding enzyme), tryptophan hydroxylase 1 (TPH1) (serotonin synthesis), and catechol-o-methyltransferase (COMT) (dopamine catabolism15It has long been known that depressive disorders can work in families , but until recently it was not fully known whether humans inherited these diseases or what other environmental factors were the real cause. ”Depression researchers have been able to determine that to some degree, depressive disorders can be inherited. as an inherited tendency to to improve illness. It does not mean that we are made for depression16-17.Bipolar disorder has a strong genetic influence. Of those with bipolar disorder, about 50% of them have a parent with a history of clinical depression. When a mother or father has bipolar disorder, their child will have a 25% chance of developing some form of clinical depression. If both parents have bipolar disorder, the chance of their child also developing moderate mental illness is between 50% and 75%. Brothers and sisters of those with bipolar disorder are eight to 18 times more likely to have bipolar disorder, and two to ten times more likely to have major depression than others without such children.

**Twin Studies:** Much we know about the genetic impact of clinical depression is based on research done by identical twins. The same twins are very useful for researchers as they both have exactly the same genetic code. It has been found that when one of the same twins is depressed the other will have clinical stress of about 76% of the time. When the same twins are raised apart from each other, both will be stressed about 67% of the time. Because both twins are under a lot of stress, which means that they have a strong genetic makeup. In the event that when one twin is clinically depressed and the other is constantly depressed, then clinical depression may be entirely genetic. However, because the ratio of both identical twins growing up to depression is close to 100% this tells us that there are other factors that contribute to a person's risk of depression. This may include natural factors such as childhood experiences, current stresses, traumatic events, exposure to substances, medical conditions, etc.19.The study was also conducted on twin brothers. Unlike identical twins who have the same genetic code, these children share about 50% of their genes and do not look alike. Studies have shown that when one of the twin brothers is depressed, the other suffers from depression at about 19 percent of the time. This is still a high level of stress compared to general general levels, and points to genetic influence on the development of clinical depression

*Environmental Causes of Depression*

The natural causes of depression include events such as stress, traumatic events, and childhood difficulties. These are events that can happen to anyone and happen in our daily lives. They are considered to be factors outside of us. Some researchers refer to these events as social or psychological factors because they are an “organization” or “combination” of social events and the functioning and functioning of the human brain. Researchers have known for some time that the experiences (events) we have in our lives can also affect our mental health. People's thoughts, feelings, and behavior are influenced by what happens in the past in their lives. These experiences can include past relationships, child development and past problems. The key to developing clinical depression in some people seems to be their response to various environmental issues or aspects in their daily lives.

Depression: There seems to be a very complex relationship between stressful situations, the mental and physical response to stress, and the development of clinical depression. Many researchers believe that for some people, there is a direct link between stress and depression. Interestingly, this depression can be both positive and negative. Examples of negative stress are losing a loved one, losing a job, losing a relationship and getting a divorce. Examples of good stress are planning a wedding, preparing for a new job, and moving to a new city. Both negative and positive pressures from environmental events can precede the increase in pressure

***Traumatic Events:***

It is true that many people have experienced a traumatic event before the onset of depression. Traumatic events in people's lives include the loss of a loved one, serious health problems, divorce, or serious financial loss. These types of events can destroy a sense of control and stability in a person's life, which often leads to emotional distress.

***Childhood Difficulties:***

It has long been known that people with severe childhood problems have higher rates of clinical depression. The most common childhood problems include sexual, emotional, or physical abuse, dysfunctional parenting, parental separation, and mental illness for one or both parents. One of the most difficult emotional events for a child to endure the separation or death of a parent before the age of eleven<sup>25-26</sup>. Children who have experienced this event and show high levels of depression.

***Synthetic Chemicals:***

Every day we take synthetic chemicals from everywhere. From preservatives, supplements and hormones found and added to many of our diets, pesticides and air and water pollution too. Studies have shown that air and water pollution alone can cause cancer and other diseases. Synthetic chemicals and pollution are now widely regarded as a link between depression and Major Depression episodes

***Noise Pollution:***

Noise pollution has been linked to aggression, high blood pressure, increased levels of stress, tinnitus, nausea and vomiting, sleep disturbances. In particular, tinnitus is associated with severe depression, panic attacks and forgetfulness. Frequent exposure to noise pollution has also been linked to cardiovascular disease and increased blood pressure. A person with a tendency to depression who may be at greater risk for depression by prolonged exposure to noise pollution

***Electrical Pollution:***

We are always surrounded by radio waves wherever we go. Many of the electronics we use work with radio waves and these radio waves have been found to cause depression and irritability. The exact causes of why they are not yet known and unlike other types of natural causes of stress, electrical pollution cannot be seen, heard, tasted, or heard. However, it can have a detrimental effect on our mental and physical health

***Natural and Catastrophic Disasters:***

Natural and catastrophic natural disasters, such as hurricanes, earthquakes, or fires, even man-made disasters such as bombs and war can depress a person already at high risk of depression 30 of nature.

***Treatment***

Minor depression can be successfully treated with medication or psychotherapy. Medium to severe depression may require a combination of medication and psychotherapy

***Drug Treatment:***

50-65% of patients respond to the first antidepressant. No one antidepressant agent is superior to another in efficacy or response time. Selection can be guided by comparing patient symptoms with a profile of side effects, the presence of medical and psychiatric disorders, and pre-existing reactions. Related costs can be considered (e.g., generics). UMHS's preferred agents are Fluoxetine (generic) and citalapram (Celexa ®) 33. Patients treated with antidepressants should be closely monitored for an increase in depression or suicide, especially at the beginning of treatment or when the dose increases or decreases. The effects of anti-depressants treatment are believed to be due to their effects on neurotransmitters and neurotransmission. The Monoamine Hypothesis is a biological belief that stress is caused by the underlying activity of the brain's monoamine receptors, such as dopamine, serotonin, and norepinephrine. In the 1950's monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants were mistakenly found to be effective in treating depression. These findings and other supporting evidence led Joseph Schildkraut to publish his paper entitled "The Catecholamine Hypothesis of Affective Disorders" in 1965. Schildkraut included low levels of stress neurotransmitters. Studies of other psychiatric disorders such as schizophrenia have also found that very little activity of certain neurotransmitters is linked to these problems<sup>34,35,36</sup>. The hypothesis has been the focus of research in fields such as pathophysiology and pharmacotherapy for over 25 years.

of monoamine neurotransmitters serotonin, norepinephrine, and dopamine by blocking the enzyme monoamine oxidase, leading to an increase in the concentration of these neurotransmitters in the brain and a very small increase in neurotransmission, dopamine. Today the most common antidepressants are selective serotonin reuptake inhibitors (SSRIs), which inhibit serotonin reuptake (thereby increasing the level of active serotonin in

brain synapses). Some novel anti-depressants affect norepinephrine reactivation, or different receptors in the neurotransmitter hormone. In fact, when previous antibodies increase in the blood and serotonin levels increase, it is common for the patient to feel worse in the first few weeks of treatment. One explanation for this is that 5-HT<sub>2A</sub> receptors evolve as a signal of saturation (people who use 5-HT<sub>2A</sub> antagonists tend to gain weight), telling the animal to stop looking for food, mate, etc., and to start hunting for predators<sup>41</sup>. In a threatening situation it is helpful for the animal not to feel hungry even if it needs food. Stimulation of 5-HT<sub>2A</sub> receptors will achieve that. But if the threat is to last a long time the animal needs to start eating and mating again - the fact that it survived shows that the threat was not as dangerous as the animal felt. Thus the number of 5-HT<sub>2A</sub> receptors decreases through a process known as down regulation and the animal returns to its normal behavior. This suggests that there are two ways to alleviate anxiety in humans with serotonergic drugs: by inhibiting the activation of 5-HT<sub>2A</sub> receptors or by reactivating them until they decrease tolerance. Promoting or blocking different receptors in the cell affects genetic expression. Recent findings have shown that neurogenesis, and thus, changes in brain morphogenesis, mediate the effects of antidepressant drugs. Another hypothesis is that antidepressants may have long-term effects due to the stimulation of neurogenesis in the hippocampus, an effect found in mice. Some animal studies suggest that antiretroviral drugs may affect gene expression in brain cells, by influencing "genetic clocks". Other studies suggest that the onset of delayed clinical outcomes from antidepressants indicates the involvement of mutant mutations in antidepressant effects. Rodent studies have consistently demonstrated the regulation of a 3, 5-cyclic adenosine monophosphate (cAMP) system caused by a variety of chronic but not potent antidepressant therapies, including serotonin and norepinephrine uptake inhibitors, monoamine oxidase inhibitors, tricyclic antidepressants, lithium and electroconvulsions. cAMP is synthesized from adenosine 5-triphosphate (ATP) by adenylyl cyclase and is synthesized by cyclic nucleotide phosphodiesterases (PDEs) 46-47. The data also suggest that anti-depressants can measure neural plasticity in long-term management. Another theory about the cause of stress is that it is characterized by an overactive hypothalamic-pituitary-adrenal (HPA axis) similar to the neuro-endocrine (cortisol) stress response. These HPA axis contribute to the formation of depressive symptoms, and anti-depressants serve to control the activity of HPA axis<sup>48,49,50</sup>.

#### ***Frequent Initial Visits:***

Patients need regular visits before treatment to assess response to intervention, suicidal ideation, side effects, and psychosocial support programs.

#### ***Continuation Therapy:***

Continuous treatment (9-12 months after the resolution of severe symptoms) reduces the incidence of recurrence of major depression. Long-term retention or lifelong drug treatment should be considered for selected patients based on their history of recurrence and other clinical features.

#### ***Education/Support:***

Education and patience are important. Social stigma and patient resistance in diagnosing depression continues to be a problem

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### **Side effects for Prolong Treatment**

Anti-depressants are important in treating depressive episodes in a critical phase where untreated symptoms are in a very serious condition. With prolonged use, however, the brain begins to function to compensate for the changes caused by drugs through a process called antidepressants. The brain attempts to establish a normal balance in the production, release and reuptake of neurotransmitters - as does the entire body system when its normal function is disrupted. The idea is that when a drug automatically improves brain levels of serotonin or norepinephrine, systemic neurobiology responds by reducing its neurotransmitter production. In other words, if the use of antidepressant continues long enough, the brain will develop a system to cancel its effect. There is a possibility that the use of the anti-depressant itself may cause a problem. There is a certain neurobiological response that may lead to the emergence of high levels of resistance to treatment. In addition, there is evidence that stopping antidepressants in people who do not respond to them can lead to a change in symptoms as the brain compensates and, in this case, drug withdrawal. For some people, however, stopping the treatment has no effect. They continue to experience recurrent depression. If antidepressant treatment is restored as a response, these patients may develop a recurrent chronic illness. This is obvious dysphoria.

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### **Alternative Treatments for Depression**

There is no evidence that any other treatment or home remedy is effective in treating moderate to severe depression. However, some people with mild depression can benefit from home remedies by getting more rest. It can also help to cope with other causes of stress, such as grief, anxiety, shifting roles, and even physical pain. If you have depression and are considering using another treatment, it is important to seek the advice of a health care provider. Examples of other therapies include: Acupuncture, Aromatherapy, Biofeedback, Chiropractic Treatment, Guided Imagery, Remedies, Hypnosis, Massage Therapy, Meditation, Relaxation, Yoga, etc. Meditation is sometimes described as a transformed state of consciousness. It is a form of relaxation that, unlike sleep, is deliberately entered into. Meditation is usually done for at least 10 minutes each day. While the body is at rest, the mind is cleared up by focusing on one thought - sometimes a word, a phrase, or a specific group. A relaxed response called meditation slows down the sensory nervous system. In addition to reducing heart rate and lowering

blood pressure, this response can also lead to: i. Decreased sweat production, ii. Decreased oxygen consumption, iii. Decreased catecholamine production (chemicals associated with a stress response). iv. Decreased production of cortisol (stress hormone) 58 Different types of exercise can reduce stress, relax you, and reduce depression. Exercise can increase your strength, balance, and flexibility. Generally, exercise is a safe, effective, and easy way to improve your well-being. Music therapy has been shown to be an effective non-drug use for people of all ages that helps reduce fear, anxiety, depression, or depression. . Music can be thought of as a natural tree of peace for the human spirit. Pythagoras, in the sixth century B.C. philosopher and mathematician, it is thought that he pioneered music therapy. During World War II, the Veterans' hospitals consisted of volunteers playing for soldiers who wounded their music. The results were so positive that the VA added music treatment programs. In a simple way, all you need to do is install a music player on a CD player or mp3 player with headphones. Then choose music - from New Age "status" music to classical music - that suits your personal needs, feelings, and preferences.

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### **Application of Modern Technology for Diagnosis and Treatment – Under Development - Hypothesis**

The search for safe, effective and fast antidepressants may also benefit patients who are currently resistant to treatment. Significant progress in new antidepressant development has been slow, with no significant serotonin selective reuptake inhibitors (SSRIs) being introduced over the years. 5 years ago. Although SSRI therapeutic effects are associated with fewer side effects and higher doses than first- and second-generation antidepressants, their main mechanism of action, prevention of neurotransmitter, is certainly not new. Before considering certain drug categories, several methods that need to be considered. The discussion of antidepressant treatment depends on which patients are being taken under this broader diagnostic phase and what diagnostic measures and procedures are accepted as indicating a reasonable anti-depressant effect. The diagnostic methods used in most recent disease studies show a population that sometimes shows a high placebo response rate (> 50%), requiring a large number of studies (over 100) to show greater therapeutic benefit over a new anti-depressant placebo. In these areas, even established anti-depressants such as imipramine sometimes do not appear to be significantly higher than placebo. European and U.S. studies An antidepressant drug that can be based on comparisons with conventional tricyclics alone may not reveal the difference, which promotes the equal effectiveness of the new drug. However, a judgment may be warranted with respect to claims of effectiveness if adequate comparisons with the placebo group are not available. Potential differences in clinical outcomes of patients studied in the U.S. compared to European settings should also be considered in evaluating response data. In addition, other psychotherapeutic agents such as alprazolam and trazodone have sometimes been referred to as broad-spectrum antidepressants that have been reported to be equivalent to first-generation tricyclic or other anti-depressants in some studies and as a result, are considered equally. successfully under severe stress, outpatients. There is no doubt that most experienced physicians would consider using alprazolam or trazodone as a basic treatment for a patient who is not as active in depression as seeking medical attention. On the other hand, recent comparisons provide hard evidence of negligence that certain agents [e.g., non-reactive monoamine oxidase (MAO) inhibitors] may be superior to tricyclic antidepressants in stress groups such as bipolar or atypical depression. All of this highlights the uncertainty surrounding the selection and evaluation of new treatments for depressed patients and their associated disorders. effects of drugs. However, this method of treatment does not answer the question, as many species of animals have multiple limitations for the detection of novel antidepressants, from the cycle (e.g., experiments simply showing biochemical properties of common drugs) to failure to detect any activity of certain suspended agents. (e.g., the inability of MAO inhibitors to reverse the lack of ineffective prevention). Although some widely used behavioral paradigms (e.g., self-help paradigm have been studied, forced swimming tests, and stress reduction caused by locomotor activity) have found positive results in many currently used anti-depressant drugs, false results and falsehoods found. other novel combinations. Only clinical trials can clearly establish the use of a new combination in the treatment of depression, whether described in small or large, and a strong case can be made for the clinical findings involved in finding the most effective antidepressants to date have been identified. Ultimately, we must rely on the perception of competent physicians who use well-directed communities to find new and effective alternative therapies in much-needed areas, rather than drug and placebo variants established only in large trials with fewer underperforming patients. was performed, it was shown that an antidepressant-like effect of the potent administration of Withaferin-A, was linked to the conversion of nNOS. Pre-treatment of mice with small amounts of nNOS inhibitor and Withaferin-A produced an antidepressant-like effect. Withaferin-A has been shown to be effective in selective 5-HT reuptake inhibitors (SSRIs) for severe depression, drug-resistant stress and severe depression. Various behavioral, biological, and molecular studies have been performed to determine the exact mechanism of the antidepressant effect of Withaferin-A. Studies show that previous treatment in mice with different nNOS inhibitors produces an antidepressant-like action with a small active dose of Withaferin-A. However, more studies are needed to determine the molecular mechanisms of Withaferin-A action in the nNOS, as well as other mechanisms that may be involved in their function such as repression.

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### **Conclusion**

Depression is a serious health condition and a serious public health concern. Although the increase in stress may be due to a combination of factors, understanding the consequences, potential causes, and treatment of the disease is important in promoting the well-being of the people affected. There is also a need to study the course of existing stress disorders land to determine the need and duration of ongoing treatment. Studies should also evaluate cost-effective treatment models that can be easily used in primary care settings to effectively treat depression.

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