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The Critical Overview and Provisions of a Survivor in the Depressive Condition

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Abstract

Depression is a psychotic disorder that can lead to emotional and psychological problems, including depressed mood, loss of interest or pleasure, losing energy and concentration, worthlessness feelings or inappropriate responsibility, loss of appetite and libido, insomnia, and persistent thoughts of death or suicide. The foremost reasons behind this deficiency of monoamine transmitters' Serotonion, Noradrenaline, Dopamine. There are various types of factors leading to depression such as social, economic, cultural and environmental factors. The massive quantity of synthetic drugs used for quick action as treat depressive conditions. In advance period of serious obsessional with the modern medication system, people have strong believes on the ancient medication systems such as Ayurveda, Siddha, and Unani management because of the herbal drugs that may produced very slight adverse effects. This article also discussed the global burden of depression, pathophysiology, diagnosis and management of various types of depression.

Keywords: Depression; MAO-A; Noradrenaline; Serotonin; Major depressive disorder

Introduction

Depression is a kind of psychological disorder that causes changes in mood, thoughts, behavior and physical health [1]. Among the worldwide listing of diseases, depression is one of the top five diseases. Globally, it is estimated to be the second-leading causes of disability till the year 2020. Earlier studies have shown that about 80% to 90% of peoples suffered from the depression reported as symptoms of anxiety [2-4].

World Health Organization estimated that around 350 million individuals have been affected by major depressive disorders [5]. Lifetime prevalence rates of major depressive disorders as high as 25% for females and an estimated lifetime prevalence rate of 12% for males in US population as estimates through the Diagnostic and Statistical Manual of Mental Disorders [6].

Types of depression

The types of depression are explained as follow:

Major depressive disorder

Persistent depression

Depressive psychosis

Perinatal depression

Premenstrual dysphoric disorder

Seasonal depression

Situational depression

Atypical depression

Major depressive disorder: It is a normal type of psychiatric disease with rates of non-responsiveness to antidepressants. As per NMHS (2015) in India one out of twenty people above 18 years of age suffered from major depressive disorder [7].

Persistent depressive disorder: It is chronic depression and lasts for two years or takes more time. Persistent depression might not feel as intense as major depression, but it can still strain relationships and make difficult in daily tasks [8,9].

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Depressive psychosis: Some people with major depression have also gone through periods of losing touch with reality called as psychosis. It can involve hallucinations and delusions, in cooperation of these together is consider as the major depressive disorder [10].

Perinatal depression: This type of depression is peripartum onset, occurs during pregnancy or within four weeks of childbirth. It's often called postpartum depression but only applies to depression after giving birth [11]. Depression during pregnancy and after childbirth adversely affects the growth and development of the progeny. In case of hormonal changes that occur during pregnancy and childbirth can trigger change in the brain leading to mood swings [12,13].

Premenstrual dysphoric disorder (PMDD): This disease is a type of Premenstrual Syndrome (PMS) having both physical and psychological symptoms; collectively PMDD symptoms tend to be mostly psychosomatic [14].

Seasonal depression/affective disorder: This type of depression is related to seasonal changes. The majority of people tend to happen during the winter season. Symptoms often begin in the fall, as days start to get shorter and continue through the winter [15].

Situational depression: This type of disorder is very common in primary care, but epidemiological studies reported that the rates of this disorder ranging from 1% to 18% among people with mental health problems [16].

Atypical depression (AD): It refers to depression that temporarily goes away in response to positive events [17]. According to West and Dally the first definition of AD as a preferentially Monoamine Oxidase Inhibitor (MAOI) responsive [18].

Sign and symptoms

Despondency, gloom or grief, difficulty in sleeping or sleeping too much, lack of energy and fatigue, loss of appetite or overeating, loss of interest in formerly pleasurable activities, loss of concentration and inability to make decisions, feelings of hopelessness, constant worry & anxiety, thoughts about self-harm, and suicidal tendency [19,20].

Epidemiology

Depression is a widespread disorder that is widely distributed through society in all ages and socio-economic classes in the entire population across the world and 450 million people suffer from several types of mental or behavioral related disorders [21]. The lifetime rate of depression is to be high as 14% to 17% and the one-year prevalence is 4% to 8%. Another hand the rate of major depressive disorder among women are 10% to 25% and for men 5% to 12% [22]. The depression is more common in females than males, in young adults than elderly people and in less-educated and lower-income populations [23,24].

Globally, depression is the principal provider to non-fatal health loss, accounting for 7.5% of global Years Lived with Disability (YLDs) and 2.0% of global Disability-Adjusted Life Years (DALYs) in 2015. Depressive disorders accounted for almost 1/3 of the total DALYs caused by mental and substance use disorder (Figure 1). It is estimated to be the second leading cause of disease burden globally and the third leading cause of disease burden in Low and Middle Income Countries (LMICs) by 2030 as per Global Health Estimates 2015 [25].

Burden of depression in India

In India about 57 million people (estimate globally around 18%) affected by depression [26]. The Indian depression survey reported that in between 1990 and 2013 the burden of depression, increased by 67% Near to 2025, DALYs attributable to depression is predictable to rise roughly 2.6 million (22.5%) due to increasing population growth and aging [27,28]. According to the population-based studies, it is expected that the problem of depression is much higher ranging from 1.8% to 39.6% [29-33].

Mortality rate through depression

Mortality rate of people having depression is much more (1.52 times) than the general population, this suffering is due to untreated mental or awful physical health condition [34]. In addition, studies of depression have shown the probability of deaths from suicide among whose suffer from depressed hospitalized patients to be 15%. Certain condition and particular risk groups are also increased this rate as in the case of farmer suicides [35,36].

Risk factors associated with depression

There are multiple factors responsible for depression with complex mechanisms having no single identifiable cause. Evidence revealed that several biological, social, economic, cultural and environmental factors showing faulty adaptation in any individual responsible for depression (Figure 2). One thing may also develop depression in any person due to the loss of a loved one, or it may clarify in the background of multiple social or financial tensions [37].

Biological factors related to depression: It depend on two biological factors, one is genetic factors and other non-genetic or environmental factors [38]. A significant relationship between genetic vulnerability to depression and early childhood disturbing experiences is known to exist [39].

Psychological factors related to depression: Psychological factors depend on familial background i.e., contact to unhelpful parental influences such as a critical parental style during early childhood may give rise to negative feelings about their self. The long-term consequences of partition or early loss of the maternal attachment relationship may include depression [40].

Social factors related to depression: Distress social relationships such as familial, marital and parental relationships have been connected with the commencement depression [39]. Familial and intimate partner violence among women is the most common in India and other low and middle income countries [41,42]. The existing impact of modernization, urbanization, migration, globalization and ensuing loss of family and social support systems, leading to social isolation [43].

Cultural factors related to depression: Culture plays an important role in the depression, such as religious conviction, caste, beliefs, attitudes, interpretations and symptom thresholds, which diverge across people with depression often, have features related to various socio-cultural [44].

Financial factors related to depression: Person suffering from acute (sudden economic crisis) or chronic (poor income households) financial contrarieties are more liable to developing depression like behaviors or depression [45].

Pathophysiology

This is based on measurement of various types of indirect markers,

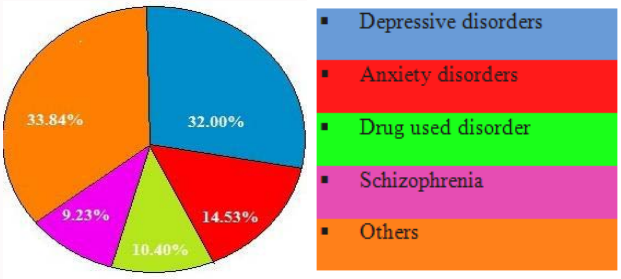

Figure 1: Global disability-adjusted life years due to mental and various types of exploitation.

post-mortem studies, and neuroimaging methods as follows;

Neural circuitry of depression

In the pathogenesis of depression, the Nucleus Accumbens (NAc) and the Ventral Tegmental Area (VTA) play an important role in depression condition? Both NAc and VTA are situated in the mesolimbic dopamine system. These brain regions mediate the recompense response to congenial stimulus such as food, sex, and drugs and dysfunction in compensate circuit of brain [46-48].

Stress response circuits

In this theory, the constant pressure and hyperactivity of the Hypothalamic-Pituitary-Adrenal (HPA) axis is causing chronic hypercortisolemia. The structural and functional brain abnormalities have been recognized in depressed patients with elevated levels of corticosteroids. There are two region of brain are effected, one is Amygdala involved in largely flexible emotional reaction and to some degree of stress response [49,50]. The second region of the brain shown to reduce in size with long time administration of corticosteroids in the hippocampus held to use as an inhibitory signal to the HPA axis [51].

Alteration of an Antioxidant system in brain

The long time stress has been exposed to modify the expression of such types of genes regulating antioxidant systems, such as Superoxide Dismutase (SOD), catalase, glutathione peroxidase, glutathione reductase, and NADPH oxidase [52].

The biogenic monoamine theory

The any types of dysfunction occur in the serotonergic system that has been leads to mood and anxiety disorders. The first antidepressant drugs worked by reviving the diminished monoamine activity in the brain, which is originate by this biogenic monoamine hypothesis worked by reviving the diminished monoamine activity in the brain [53,54].

Inflammation and depression

The current popularity affected by inflammatory depression disorder reported that the pro-inflammatory (IL6, IL1 CRP, TNF-α) marker level is to be elevated as in compare normal range in human. An increase in pro-inflammatory cytokines results in a lack of neuronal plasticity neurodegeneration. In the laboratory scale the depression can be induced in the animal model by administration of (IFN)-α, which is central inflammatory cytokine that has been shown to produce depression [55-57]. The pro-inflammatory can also interfere with the activity of growth factors which result in reduced neurogenesis as the immune changes can damage glial cells of the brain and neurons [58].

Neurotrophic hypothesis

The neutrophic factors are fundamental molecular controller of neuronal development and flexibility. Various types of neurotrophic factors are responsible for degenerate of certain prefrontal cortex areas and hippocampcal area in depressed patient. In addition to decreased levels of NGF, BDNF [59-62].

Hormones and depression

Thyroid hormones: In the neurodegenerative and psychiatric conditions the Thyroid Hormones (TH) are imbalances. Thyroid hormones are playing an essential role in the brain development, maturation and have been shown to promote neurogenesis, in the hippocampus region. Hypothyroidism is associated to depressive-like symptoms in that it impaired hippocampus neurogenesis [63,64].

Estrogen involvement: Low estrogen level in the menstrual cycle can cause depression in female vulnerability and may occur in the postpartum and after the onset during the menopause. Estrogen hormone is modulating mood by growing the rate of deprivation of MAO and intraneuronal 5-HT transport system [65,66].

Vasopressin and depression: The level of arginine and vasopressin hormone is to be high in patients then the patient suffering from mental disorder [67]. Arginine and vasopressin played an important role in the regulation of depression response, one of the major features of depression, which work together with chronic renal failure at the elevated level in the pituitary to control the release of ACTH. High arginine vasopressin concentrations were also linked with psychomotor and mental retardation with the major depressive disorder in the depressed patient [68-70].

Allegation of the circadian rhythm in depression: The diminished stage of melatonergic signaling in the brain is due to delayed circadian rhythm leads to depression, the patients may clear with late onset of sleep, complexity in maintenance of sleepiness and early morning awakening. This given a way to the discovery of new antidepressant agent, agomelatine, which acts on melatonin and serotonin receptors on the suprachiasmatic nucleus. Disturbance of circadian rhythm is also proposed to make persons vulnerable to depression [71-73].

Diagnosis

Some types of questions are helps to the doctors to determine the high sever of the depression such as taking history and ask about symptoms to the patient. The Hamilton depression rating level (scale), use for the checking of depression condition.

The other diagnoses of depression are the low level of neurotransmitters serotonin, dopamine, and norepinephrine. Various things might potentially go wrong with this process in the brain physiology and lead to a neurotransmitter deficit may potentially include;

- Inadequate of the various types of neurotransmitter (serotonin) is produced.
- Inadequate receptor sites to obtain different types of the neurotransmitter.
- The neurotransmitter is being full back up rapidly into the presynaptic before it can reach receptor sites.
- Molecules that help in the formation of neurotransmitters, such as specific enzymes, may be in small supply.

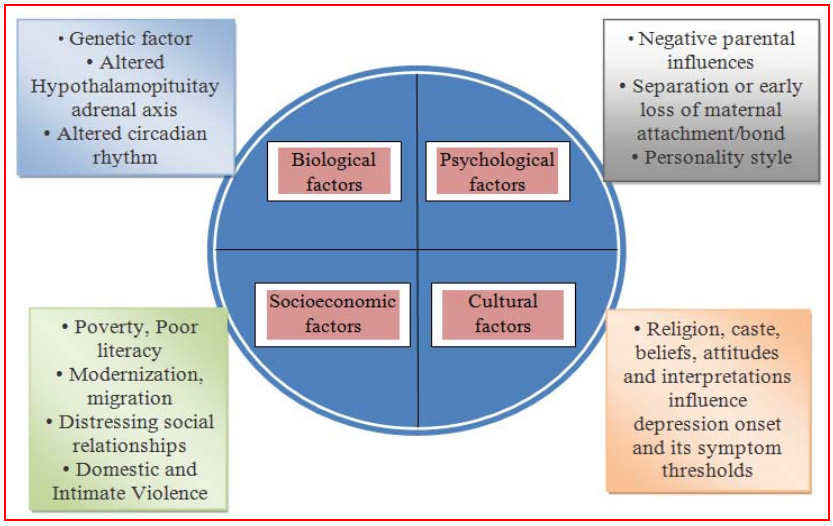

Figure 2: Risk factors associated with depression.

Table 1: Allopathic treatment medication of depression.

Class of Antidepressant	Antidepressant Drug
Selective Serotonin Reuptake Inhibitors (SSRI)	Citalopram, Escitalopram, Paroxetine, Fluoxetine
Tricyclic Antidepressant (TCA), tertiary	Amitriptyline Clomipramine, Imipramine
TCAs, secondary	Desipramine, Nortriptyline
Norepinephrine Reuptake Inhibitors (NRI)	Reboxetine
Serotonin-Norepinephrine Reuptake Inhibitors (SNRI)	Duloxetine, Venlafaxine
Monoamine Oxidase A Inhibitor (MAOI)	Moclobemide
Noradrenergic and Specific Serotonergic Antidepressant (NaSSA)	Mianserine, Mirtazapine
Norepinephrine-dopamine reuptake inhibitors	Bupropion
Selective serotonin reuptake enhancers	Tianeptine
MT1 and MT2 agonist, 5- HT2 antagonist	Agomelatine
Serotonin antagonist and reuptake inhibitors	Etoperidone, Nefazodone

- If there is fall down anywhere along the pathway, neurotransmitter supplies may not be adequate as needed. Insufficient supplies may then lead to depression [74,75].

Prevention

There are different types of preventive tips available for the prevention of depression and mental illness. Do not drink alcohol or use illegal drugs. These substances can lead depression and may lead to thoughts of suicide in the depression patient.

There are following tips may to be help in feeling better to the depression patient:

- Get daily exercise
- Maintain good sleep habits (sleep at night)
- Attempt activities that bring pleasures
- Get involved in group activities
- Sharing feeling to someone about any topic
- Always think positively

Treatment and Management

Treatments and management depend on the symptoms and severity of depression. Standard treatments include pharmacotherapy, psychotherapy, and their combination. Moreover, severe and drug-resistant depression is commonly treated with ECT or Transcranial Magnetic Stimulation (TMS) [76].

Appointment in behavioral activation using motivational interviewing

Advise an increase in activities such as Adding 20 minutes of exercise 3 to 4 times per week

- Improving diet
- Enhance communal activities
- Participate in pleasant activities

Pharmacotherapy

Iproniazide is the first antidepressants drug, which was discovered by suddenly, during insightful clinical observations, Iproniazide basically developed for the treatment of tuberculosis showed mood stimulation like effects. As well as, imipramine, a suspected antipsychotic drug showed antidepressant activity (Table 1) [77-79].

Light therapy

Light therapy is approved by FDA, in the light therapy; basically use a light box in the dark months of the year (September to March).

The light intensity is about 10,000 lux for 30 minutes in every morning. These therapy basically use for seasonal depression [80].

Electroconvulsive therapy (ECT)

ECT can get better in mood those suffering from severe depression or suicidal thoughts, that patient who cannot get enhanced with other treatments the use ECT, it most effective treatment for the depression. Generally in the electroconvulsive therapy, a convulsion is induced by applying an electrical current via a wire 0.3 mm to 1 mm (width) absolute frequency is not more than 20 Hz to 120 Hz, duration of the stimulus about 0.5 sec to 8 sec to the surface of the head of the patient [81,82].

Transcranial magnetic therapy (TMS)

In this therapy used magnetic impulses to stimulate nerve cells of the brain. Depolarization of cortical neurons by the use of magnetic current that passes via a metal coil applied to the scalp of the patient during the therapy. TMS resulting in increasing levels of dopamine and serotonin [81,83].

Herbal plants used for the treatment of depression

The herbal drugs have a rational alternative for the management and treatment of mental disorders such as insomnia, depression, and anxiety among prosperity of others. Under developing antidepressants drugs from herbal sources appear to be a realistic approach due to their beneficial effects and lower side effects. *Hypericum perforatum* was commonly known as St. John's wort is the single herbal antidepressant that has been approved for the clinical management of mild to moderate cases of depression. Hypericin and hyperforin are flavonoids which are already being there in hypericum that are claimed to be responsible for the antidepressant activity [84]. Herbal treatment still remains to be the first line treatment option for nearly 80% of the population. Plants such as *Justicia odora*, *Whitiana somnifera*, *Calpurnia aurea,* and *Asparagus leptocladodius* have traditionally been used for the treatment of depression [85].

Conclusion

The study concluded that the depression is a major burden for the health-care system worldwide if it does not diagnose and manage initially, may alter critical condition for the survivor, and some time leads to death. The rate of major depressive disorders for lifetime is more common in women 10% to 25%, than in men 5% to 12%. The different outward appearance of depression ranges from mild to extremely severe situations as similar to psychotic depression shows symptoms such as hallucinations and delusions in patients with depressive disorder. The diverse of depression theories presented by world class physicians in respect to pathogenesis on the basis of quantitative measurement of indirect markers, investigation research study and neuro-imaging techniques. In addition, selections of best management options and treatment goals for suppression of such type of disorders have been developed over the decades with various types of therapies i.e., pharmacotherapy, psychotherapy, counseling of patients and somatic therapy frequently employed for the treatment of depression. Science ancient time, the herbal treatment medication system has been also played a significant role to manage the mental disorders.

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References

1. Behera P, Sharan P, Mishra AK, Nongkynrih B, Kant S, Gupta SK, Prevalence and determinants of depression among elderly persons in a rural community from northern India. Natl Med J India. 2016;29(3):129-35.
2. Fekadu N, Shibeshi W, Engidawork E. Major Depressive Disorder: Pathophysiology and Clinical Management. J Depress Anxiety. 2017;6(1):1-7.
3. Fißler M, Quante A. A case series on the use of lavendula oil capsules in patients suffering from major depressive disorder and symptoms of psychomotor agitation, insomnia and anxiety. Complement Ther Med. 2014;22(1):63-9.
4. Abelaira HM, Réus GZ, Quevedo J. Animal models as tools to study the pathophysiology of depression. Braz J Psychiatry. 2013;35:S112-20.
5. Thapar A, Collishaw S, Pine DS, Thapar AK. Depression in adolescence. Lancet. 2012;379(9820):1056-67.
6. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th edn. 2000;11-8.
7. Grover S, Dutt A, Avasthi A. An overview of Indian research in depression. Indian J Psychiatry. 2010;52:S178-88.
8. Sansone R, Correll T. Dysthymic disorder: The persistent depression. Psychiatry. 2005;9:1-2.
9. Hilty DM, Leamon MH, Lim RF, Kelly RH, Hales RE. A review of bipolar disorder in adults. Psychiatry (Edgmont). 2006;3(9):43-55.
10. Swartz C, Shorter E. Psychotic depression. Cambridge University Press; 32nd Avenue: New York. 2007;55-8.
11. Chaudron LH. Postpartum depression: what pediatricians need to know? Pediatr Rev. 2003;24(5):154-61.
12. Flanagan T, Avalos LA. Perinatal Obstetric Office Depression Screening and Treatment: Implementation in a Health Care System. Obstet Gynecol. 2016;127(5):911-5.
13. Pearlstein T. Perinatal depression: treatment options and dilemmas. J Psychiatry Neurosci. 2008;33(4):302-18.
14. Accortt EE, Kogan AV, Allen JJB. Personal history of major depression may put women at risk for premenstrual dysphoric symptomatology. J Affect Disord. 2013;150(3):1234-7.
15. Baghai TC, Eser D, Möller HJ. Effects of different antidepressant treatments on the core of depression. Dialogues Clin Neurosci. 2008;10(3):309-20.
16. Casey P, Bailey S. Adjustment disorders: the state of the art. World Psychiatry. 2011;10(1):11-8.
17. Singh T, Williams K. Atypical Depression. Psychiatry. 2006;3(4):33-9.
18. Łojko D, Rybakowski JK. Atypical depression: current perspectives. Neuropsychiatr Dis Treat. 2017;13:2447-56.
19. Kennedy SH. Core symptoms of major depressive disorder: relevance to diagnosis and treatment. Dialogues Clin Neurosci. 2008;10(3):271-7.
20. Saveanu RV, Nemeroff CB. Etiology of depression: genetic and environmental factors. Psychiatr Clin North Am. 2012;35(1):51-71.
21. Umadevi P, Murugan S, Suganthi SJ, Subakanmani S. Evaluation of antidepressant like activity of cucurbita pepo seed extracts in rats. Int J Curr Pharm Res. 2011;3(1):108-13.
22. Garriock HA. Genetics of major depressive disorder in treatment resistance and tryptophan depletion. University of Arizona. 2006;2:70-8.
23. Kessler RC, Bromet EJ. The epidemiology of depression across cultures. Annu Rev Public Health. 2013;34:119-38.
24. El-Refaey H, Amri H. Effects of Antidepressants on Behavioral Assessment

in Adolescent Rats. Bahrain Medical Bulletin. 2011;33(2):83-9.

25. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med. 2006;3(11):e442.

26. Depression and other common mental disorders: global health estimates. Geneva: World Health Organization; 2017.

27. Schatzberg AF. New approaches to managing psychotic depression. J Clin Psychiatry. 2003;64:19-23.

28. Charlson FJ, Baxter AJ, Cheng HG, Shidhaye R, Whiteford HA. The burden of mental, neurological, and substance use disorders in China and India: a systematic analysis of community representative epidemiological studies. Lancet. 2016;388(10042):376-89.

29. Sengupta P, Benjamin AI. Prevalence of depression and associated risk factors among the elderly in urban and rural field practice areas of a tertiary care institution in Ludhiana. Indian J Public Health. 2015;59(1):3-8.

30. Reddy NB, Pallavi M, Reddy NN, Reddy CS, Singh RK, Pirabu RA. Psychological Morbidity Status Among the Rural Geriatric Population of Tamil Nadu, India: A Cross-sectional Study. Indian J Psychol Med. 2012;34(3):227-31.

31. Sathyanarayana Rao TSS, Darshan MS, Tandon A, Raman R, Karthik KN, Saraswathi N, et al. Suttur study: An epidemiological study of psychiatric disorders in south Indian rural population. Indian J Psychiatry. 2014;56(3):238-45.

32. Shidhaye R, Gangale S, Patel V. Prevalence and treatment coverage for depression: a population-based survey in Vidarbha, India. Soc Psychiatry Psychiatr Epidemiol. 2016;51(7):993-1003.

33. Mathias K, Goicolea I, Kermode M, Singh L, Shidhaye R, Sebastian MS. Cross-sectional study of depression and help-seeking in Uttarakhand, North India. BMJ Open. 2015;5(11):e008992.

34. Cuijpers P, Vogelzangs N, Twisk J, Kleiboer A, Li J, Penninx BW. Comprehensive Meta-Analysis of Excess Mortality in Depression in the General Community versus Patients with Specific Illnesses. Am J Psychiatry. 2014;171(4):453-62.

35. Bhise MC, Behere PB. Risk factors for farmers' suicides in central rural India: Matched case–control psychological autopsy study. Indian J Psychol Med. 2016;38(6):560-6.

36. Manoranjitham SD, Rajkumar AP, Thangadurai P, Prasad J, Jayakaran R, Jacob KS. Risk factors for suicide in rural south India. Br J Psychiatry. 2010;196(1):26-30.

37. Shi Y, Yang D, Zeng Y, Wu W. Risk Factors for Post-stroke Depression: A Meta-analysis. Front Aging Neurosci. 2017;9:218.

38. Sullivan PF, Neale MC, Kendler KS. Genetic epidemiology of major depression: review and meta-analysis. Am J Psychiatry. 2000;157(10):1552-62.

39. Bauwens F, Pardoen D, Staner L, Dramaix M, Mendlewicz J. Social adjustment and the course of affective illness: a one-year controlled longitudinal study involving bipolar and unipolar outpatients. Depress Anxiety. 1998;8(2):50-7.

40. Yang L, Zhao Y, Wang Y, Liu L, Zhang X, Li B, et al. The Effects of Psychological Stress on Depression. Curr Neuropharmacol. 2015;13(4):494-504.

41. Varma D, Chandra PS, Thomas T, Carey MP. Intimate Partner Violence and Sexual Coercion among Pregnant Women in India: Relationship with Depression and Post- Traumatic Stress Disorder. J Affect Disord. 2007;102(1-3):227-35.

42. Haqqi S, Faizi A, Haqqi S. Prevalence of Domestic Violence and associated Depression in married women at a Tertiary care hospital in Karachi. Procedia–Soc Behav Sci. 2010;5:1090-7.

43. Chen J, Chen S, Landry PF. Urbanization and Mental Health in China: Linking the 2010 Population Census with a Cross-Sectional Survey. Int J Environ Res Public Health. 2015;12(8):9012-24.

44. Jacob KS. Social context and mental health, distress and illness: critical yet disregarded by psychiatric diagnosis and classification. Indian J Soc Psychiatry. 2016;32(3):243-8.

45. Freeman A, Tyrovolas S, Koyanagi A, Chatterji S, Leonardi M, Ayuso-Mateos JL, et al. The role of socio-economic status in depression: results from the COURAGE (aging survey in Europe). BMC Public Health. 2016;16(1):1098.

46. Krishnan V, Nestler EJ. The molecular neurobiology of depression. Nature. 2008;455(7215):894-902.

47. Nestler EJ, Carlezon WA. The mesolimbic dopamine reward circuit in depression. Biol Psychiatry. 2006;59(12):1151-9.

48. Ressler KJ, Nemeroff CB. Role of norepinephrine in the pathophysiology and treatment of mood disorders. Biol Psychiatry. 1999;46(9):1219-33.

49. Bouhuys AL, Bos EH, Geerts E, van Os TW, Ormel J. The association between levels of cortisol secretion and fear perception in patients with remitted depression predicts recurrence. J Nerv Ment Dis. 2006;194(7):478-84.

50. Brown S, Woolston J, Frol B. Amygdala volume in patients receiving chronic corticosteroid therapy. Biol Psychiatry. 2008;63(7):705-9.

51. Aan Het Rot M, Mathew Sj, Charney Ds. Neurobiological mechanisms in major depressive disorder. Cmaj. 2009;180(3):305-13.

52. Seo JS, Park JY, Choi J, Kim TK, Shin JH, Lee JK, et al. NADPH oxidase mediates depressive behavior induced by chronic stress in mice. J Neurosci. 2012;32(28):9690-9.

53. Cowen PJ. Serotonin and depression: pathophysiological mechanism or marketing myth? Trends Pharmacol Sci. 2008;29(9):433-6.

54. Saldanha D, Kumar N, Ryali VSSR, Srivastava K, Pawar AA. Serum serotonin abnormality in depression. Med J Armed Forces India. 2009;65(2):108-12.

55. Kopschina Feltes P, Doorduin J, Klein HC, Juárez-Orozco LE, Dierckx RA, Moriguchi-Jeckel CM, et al. Anti-inflammatory treatment for major depressive disorder: implications for patients with an elevated immune profile and non-responders to standard antidepressant therapy. J Psychopharmacol. 2017;31(9):1149-65.

56. Dolati K, Rakhshandeh H, Shafei MN. Evaluation of antidepressant effect of ethanolic extract of Rosa damascene using forced swimming test. Avicenna J Phytomed. 2011;2(1):46-51.

57. Vogelzangs N, Duivis H, Beekman A, Kluft C, Neuteboom J, Hoogendijk W, et al. Association of depressive disorders, depression characteristics and antidepressant medication with inflammation. Transl Psychiatry. 2012;2:e79.

58. Audet MC, Anisman H. Interplay between pro-inflammatory cytokines and growth factors in depressive illnesses. Front Cell Neurosci. 2013;7:68.

59. Bocchio-Chiavetto L, Miniussi C, Zanardini R, Gazzoli A, Bignotti S, Specchia C, et al. 5-HTTLPR and BDNF Val66Met polymorphisms and response to TMS treatment in drug resistant depression. Neurosci Lett. 2008;437(2):130-4.

60. Angelucci F, Brene` S, Mathe AA. BDNF in schizophrenia, depression and corresponding animal models. Mol Psychiatry. 2005;10(4):345-52.

61. Heldt S, Stanek L, Chhatwal J, Ressler K. Hippocampus-specific deletion of BDNF in adult mice impairs spatial memory and extinction of aversive memories. Mol Psychiatry. 2007;12(7):656-70.

62. Molendijk M, Bus B, Spinhoven P, Penninx B, Kenis G, Prickaerts J, et al. Serum levels of brain-derived neurotrophic factor in major depressive disorder: state–trait issues, clinical features and pharmacological treatment. Mol Psychiatry. 2011;16(11):1088-95.

63. Montero-Pedrazuela A, Venero C, Lavado-Autric R, Fernández-Lamo I, García-Verdugo JM, Bernal J, et al. Modulation of adult hippocampal neurogenesis by thyroid hormones: implications in depressive-like behavior. Mol Psychiatry. 2006;11(4):361-71.

64. Alkemade A, Unmehopa UA, Brouwer JP, Hoogendijk WJ, Wiersinga WM, Swaab DF, et al. Decreased thyrotropin releasing hormone gene expression in the hypothalamic paraventricular nucleus of patients with major depression. Mol Psychiatry. 2003;8(10):838-9.

65. Douma SL, Husband C, O'Donnell ME, Barwin BN, Woodend AK. Estrogen-related mood disorders: reproductive life cycle factors. ANS Adv Nurs Sci. 2005;28(4):364-75.

66. Krishnan V, Nestler EJ. Linking molecules to mood: new insight into the biology of depression. Am J Psychiatry. 2010;167(11):1305-20.

67. Van West D, Del-Favero J, Aulchenko Y, Oswald P, Souery D, Forsgren T, et al. A major SNP haplotype of the arginine vasopressin 1B receptor protects against recurrent major depression. Mol Psychiatry. 2004;9(3):287-92.

68. Gold PW, Goodwin FK, Post RM, Robertson GL. Vasopressin function in depression and mania [proceedings]. Psychopharmacol Bull. 1981;17(1):7-9.

69. De Winter RF, van Hemert AM, DeRijk RH, Zwinderman KH, Frankhuijzen-Sierevogel AC, Wiegant VM, et al. Anxious–retarded depression: relation with plasma vasopressin and cortisol. Neuropsychopharmacology. 2003;28(1):140-7.

70. van Londen L, Kerkhof GA, van den Berg F, Goekoop JG, Zwinderman KH, Frankhuijzen-Sierevogel AC, et al. Plasma arginine vasopressin and motor activity in major depression. Biol Psychiatry. 1998;43(3):196-204.

71. Verster GC. Melatonin and its agonists, circadian rhythms and psychiatry. Afr J Psychiatry (Johannesbg). 2009;12(1):42-6.

72. Girish MB, Bhuvana K, Nagesh Raju G, Sarala N. A novel atypical antidepressant drug: Agomelatine – A review. Int J Pharm Biomed Res. 2010;1(3):113-6.

73. Soria V, Urretavizcaya M. [Circadian rhythms and depression]. Actas Esp Psiquiatr. 2009;37(4):222-32.

74. Markus MacGill, Timothy J. Legg. What is depression and what can I do about it? 2017.

75. Smith KM, Renshaw PF, Bilello J. The diagnosis of depression: current and emerging methods. Compr Psychiatry. 2013;54(1):1-6.

76. Holtzheimer PE, Nemeroff CB. Novel targets for antidepressant therapies. Curr Psychiatry Rep. 2008;10(6):465-73.

77. Nieuwsma JA, Trivedi RB, McDuffie J, Kronish I, Benjamin D, Williams JW. Brief psychotherapy for depression: a systematic review and meta-analysis. Int J Psychiatry Med. 2012;43(2):129-51.

78. Yildiz A, Gonul AS, Tamam L. Mechanism of actions of antidepressants: Beyond the receptors. Bull Clin Psychopharmacol. 2002;12:194-200.

79. Kasper S, Hamon M. Beyond the monoaminergic hypothesis: Agomelatine, a new antidepressant with an innovative mechanism of action. World J Biol Psychiatry. 2009;10(2):117-26.

80. Eniola K, Bacigalupo A, Mounsey A. PURLs: Light therapy for nonseasonal major depressive disorder? J Fam Pract. 2016;65(7):486-8.

81. Eitan R, Lerer B. Nonpharmacological, somatic treatments of depression: electroconvulsive therapy and novel brain stimulation modalities. Dialogues Clin Neurosci. 2006;8(2):241-58.

82. Cusin C, Dougherty DD. Somatic therapies for treatment-resistant depression: ECT, TMS, VNS, DBS. Biol Mood Anxiety Disord. 2012;2:14.

83. Gotto J, Rapaport MH. Treatment options in treatment-resistant depression. Primary Psychiatry 2005;12(2):42-50.

84. Klemens J. Herbs used for psychotropic or Behaviour modifying activity. J Am Association Integrative Med. 2006;1:1-9.

85. Mesfin F, Demissew S, Teklehaymanot T. An ethnobotanical study of medicinal plants in Wonago Woreda, SNNPR, Ethiopia. J Ethnobiol Ethnomed. 2009;5:28.