CLINICAL ESTIMATION OF IMPLICATIVE FACTORS ALONGWITH TREATMENT OF DEPRESSION BY USING PHQ-9 SCORE ANALYSIS

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ABSTRACT

Depression is a mental health condition marked by ongoing feelings of grief, loss of energy and difficulty dealing with daily life activities. Aim of this study is to assess the implicative factors, prevalence and treatment trend of depression. A prospective cross-sectional study was conducted in the department of psychiatry of Civil Hospital, Sialkot, Pakistan. Data of 55 depressive patients was taken and filled in a well-structured questionnaire during face to face interview. Majority of the depressive patients were from the age category of 21-30 years (n=20, 36.4%). Females (n=39, 70.9%) were more affected by depression than males (n=16, 29.1%) with more prevalence in unmarried people (n=33, 60%) and in urban population (n=42, 76.4%). Most of the depressive patients were of graduation level (n=34, 61.8%) and were students (n=20, 36.3%). A number of depressive patients were suffering from hypertension (n=5, 9.1%). The risk factor with the highest prevalence among the depressive patients was socioeconomic status including both middle and low class (n=36, 65.5%), followed by stressful situations (n=34, 61.8%), irregular sleep (n=31, 56.4%), unemployment (n=30, 54.5%), lack of exercise (n=20, 36.4%), mental traumatic events (n=15, 27.3%), genetic factors (n=9, 16.4%) and physical traumatic events (n=3, 5.5%). Patient Health Questionnaire-9 (PHQ-9) scores show that equal number of moderate (n=16, 29.1%) and severely moderate depressive patients (n=16, 29.1%) were reported, followed by mild depression (n=15, 27.3%), minimal depression (n=6, 10.9%) and severe depression (n=2, 3.6%). Majority of the depressive patients were receiving counselling (n=49, 89.1%) along with cognitive behavioral therapy (n=17, 30.9%). Most of the patients were

taking escitalopram (n=12, 21.8%), followed by fluoxetine (n=6, 10.9%), venlafaxine (n=03, 5.5%), fluvoxamine (n=3, 5.5%), sertraline (n=2, 3.6%), quetiapine (n=2, 3.6%), dosulephine HCl (2, 3.6%), paroxetine (n=2, 3.6%), fluphenazine/nortriptyline (n=1, 1.8%), lithium carbonate (n=1, 1.8%) and mirtazapine (n=1, 1.8%).

Keywords: Depression, female, socioeconomic status, stressful situations, severity, counselling, SSRIs.

INTRODUCTION
Depression is a predominant psychiatric disorder that affects how we feel and how we think about ourselves and the world around us. Characterized by impairments in cognition, emotional regulation, memory, motoric function, motivation, and neurovegetative symptom, it is responsible for more 'years lost' to disability than any other condition worldwide (Kircanski *et al.,* 2012). Yet depression is widely undiagnosed and untreated because of stigma, lack of effective therapies and insufficient mental-health resources (Smith & De Torres, 2014). Although the prevalence of depression varies considerably globally, depression commonly has its onset in the late twenties (Massie, 2004) Most clinical and epidemiological studies of depression have found higher prevalence rates among females than males (Angst *et al.,* 2002). Depression is a pervasive constellation of mental disorders that has a multifactorial etiology including neurobiological, psychosocial and pathophysiologic factors such as alterations in brain concentrations of neuropeptides, neurotransmitters, and neurophysiological and neuroendocrine abnormalities, traumatic life events, chronic stresses, and lack of appropriate social support systems (Ehlers *et al.,* 1988). Research has implicated several mechanisms involved in the pathogenesis of depression including altered serotonergic, noradrenergic, dopaminergic, and glutamatergic systems, increased inflammation, HPA axis abnormalities, vascular changes, and decreased neurogenesis and neuroplasticity. (Caspi *et al.,* 2010).

A group of treatment options has been developed to combat depression over the decades. Non-pharmacological interventions for depression include psychotherapy, behavior modification, and implementation of positive lifestyle habits (i.e., physical fitness, nutrition, stress reduction, establishing a strong social network) (Houle *et al.,* 2013). About half of moderate-to-severe episodes of depression improve with antidepressant treatment and is recommended as an initial treatment choice for patients with mild to moderate major depressive disorder and certainly should be provided for those with severe major depressive disorder (Armstrong, 2011). During the past several decades, there has been great progress in the development of newer generation antidepressants possessing various modes of action in the use of pharmacotherapeutic agents for treating depression (Citrome, 2016).

METHODOLOGY
Study Design
A prospective cross-sectional study was conducted on depressive patients. The implicative factors, prevalence and treatments trends of depression were assessed in patients suffering from depression. Study was conducted in the Department of Psychiatry of Civil Hospital, Sialkot, Pakistan. Data was collected from outpatients visiting the above mentioned hospital located in Sialkot, Pakistan. The data was collected from August 2020 - September 2020. Total duration of data collection was 1 month.

Sample Size
For the completion of our research work, data of 55 depressive patients was taken. The determination of coverage of social analyses, time resources and finances are important factors in data collection. Hence, it normally does not cover every individual in the study being investigated. Ideal sample size is a vital element in any type of research in order to estimate the total number of samples required for the detection of significant variations in clinical parameters, therapeutic effects and associations after data collection.

Patient Selection

Patients of all age groups were selected randomly from various socioeconomic, demographic and regional societies. Limitation of our research work in patient's selection was that the patients were only eligible if they were either the residents of the city Sialkot or its Tehsils i.e. Daska, Sambrial, Pasrur. To minimize selection bias in the research project, we reported all the patients for whom treatment follow-up data was available, without the imposition of any other criteria. A total of 55 patients from all age groups were involved without gender differentiation. There was no limitation of religion or ethnicity in the research work.

The selected patients of depression willingly participated in the research project and consent forms were signed in both English and Urdu for legal approaches. Epidemiologic studies showed that roughly 40%–50% of the risk for depression is genetic. This makes depression a highly heritable disorder. Yet, the search for specific genes that confer this risk has been unsatisfying, with no genetic anomaly being identified to date with certainty, with lack of substantive molecular genetic findings (Akiskal, 2000). Due to the genetic association of depression, family history of patients was also considered.

Study Tool and Data Collection Procedure

Well-structured questionnaire was prepared, analyzed and then filled during face to face interview with the patient. All the relevant questions including demographic characteristics, clinical manifestation of depression, past medical history of depression, family history of depression and complications were asked and recorded during the interview. Demographic characteristics included age, gender, marital status, area of residence, residential status, socioeconomic status, education and occupation. Age groups of ≤ 20 years, 21-30 years, 31-40 years, 41-50 years, 51-60 years, ≥ 60 years were included. Patients from all socioeconomic classes including lower, middle and upper class were considered during the study. The scores from Patient Health Questionnaire (PHQ-9) were calculated and recorded after questioning from the patients.

Information was taken from each depressive patient verbally, according to the data collection form. After the demographic data, past medical history and family medical history of depression was noted. Comorbidity of other diseases was also noted. Patient Health Questionnaire (PHQ-9) was filled during the interview and scores from the questionnaire were calculated and recorded for the assessment of depression severity in the patients.

Ethical Considerations

Data was collected after the ethical approval of Civil Hospital, Sialkot. A verbal consent of each depressive patient in the department of psychiatry was taken before data collection and all types of personal information was kept confidential and used only for research purpose.

Validity of Questionnaire

Face validity is the degree to which the appearance of a questionnaire is assessed, whether it is professional or poorly constructed. After designing the questionnaire, it was sent to senior professionals from clinical sector working at Civil Hospital, Sialkot. It was done by my supervisor. Validity is one of the main concern with research. Content validity refers to the extent to which the content on the questionnaire is fairly representative of the data it seeks to measure.

Inclusion and Exclusion Criteria

The inclusion and exclusion criteria for patient selection is described on next page.

Inclusion Criteria

- Patients with selective age groups were included.
- Patients with depression in district Sialkot were included.
- All patients with socioeconomic status were included.

Exclusion Criteria

- Patients outside the premises of Sialkot were excluded
- Patients not suffering from depression were excluded.
- People with unethical belief in this study were excluded.

Data Analysis

The data was analyzed and interpreted after collection from patients in different hospitals and clinics of Sialkot by the utilization of various investigational laboratory tests. The graphs were plotted on Microsoft Excel spread sheet after performing calculations to analyze the implicative factors, prevalence and treatment trends of depression in Sialkot.

RESULTS

Assessment of Demographic Characteristics of Depression

For the completion of our research work, data of 55 depressive patients was taken. Depression can develop at any age and from the results, it was observed that depression generally develops during teen age and can also affect people above 60 years. However, majority of the depressive patients were from the age category of 21-30 years (n=20, 36.4%) rather than ≤ 20 years (n=19, 29.1%), 31-40 years (n=13, 23.6%), 41-50 years (n=1, 1.8%), 51-60 years (n=4, 7.2%) and ≥ 60 years (n=1, 1.8%). Sex stratified prevalence was also calculated among the depressive patients which showed that females (n=39, 70.9%) were more affected by depression than males (n=16, 29.1%). Unmarried people (n=33, 60%) were highly affected by depression in comparison to married (n=19, 34.5%) and widowed (n=3, 5.5%). Area of residence was considered and a high prevalence was observed in urban population (n=42, 76.4%) as compared to rural population (n=13, 23.6%). High prevalence was observed in patients with own houses (n=48, 87.3%) than rental houses (n=7, 12.7%). Socioeconomic status plays a vital role as an implicative factor of depression and is the cause of depression in majority of the population. From the results, it was concluded that people belonging to middle class (n=30,54.5%) were more affected by depression with a comparatively high prevalence in upper class (n=19, 34.5%) as compared to lower class (n=6, 10.9%). Likewise, education level of depressive patients was also recorded in which most of the depressive patients were of graduation level (n=34, 61.8%), followed by intermediate (n=9, 16.4%), under matriculation (n=5, 9.1%), post-graduation (n=4, 7.3%) and matriculation (n=3, 5.5%). Majority of the depressive patients were students (n=20, 36.3%) while some of the patients were either employed (n=13, 23.6%) or unemployed (n=10, 18.2%). A small number of housewives (n=12, 21.8%) were also suffering from depression.

Table 1: Demographics of Depressive Patients

Parameter	Frequency (n=55)	Percentage (%)
Age		
≤ 20 years	16	29.1
21-30 years	20	36.4
31-40 years	13	23.6
41-50 years	01	1.8
51-60 years	04	7.2
≥ 60 years	01	1.8
Gender		
Male	16	29.1
Female	39	70.9
Marital Status		
Married	19	34.5
Unmarried	33	60
Widowed	03	5.5
Area of Residence		
Urban	42	76.4
Rural	13	23.6

Residential Status		
Own House	48	87.3
Rental House	07	12.7
Socioeconomic Status		
Upper Class	19	34.5
Middle Class	30	54.5
Lower Class	06	10.9
Education		
Under Matriculation	05	9.1
Matriculation	03	5.5
Intermediate	09	16.4
Graduation	34	61.8
Post-graduation	04	7.3
Occupational Status		
Employed	13	23.6
Unemployed	10	18.2
Student	20	36.3
Housewife	12	21.8
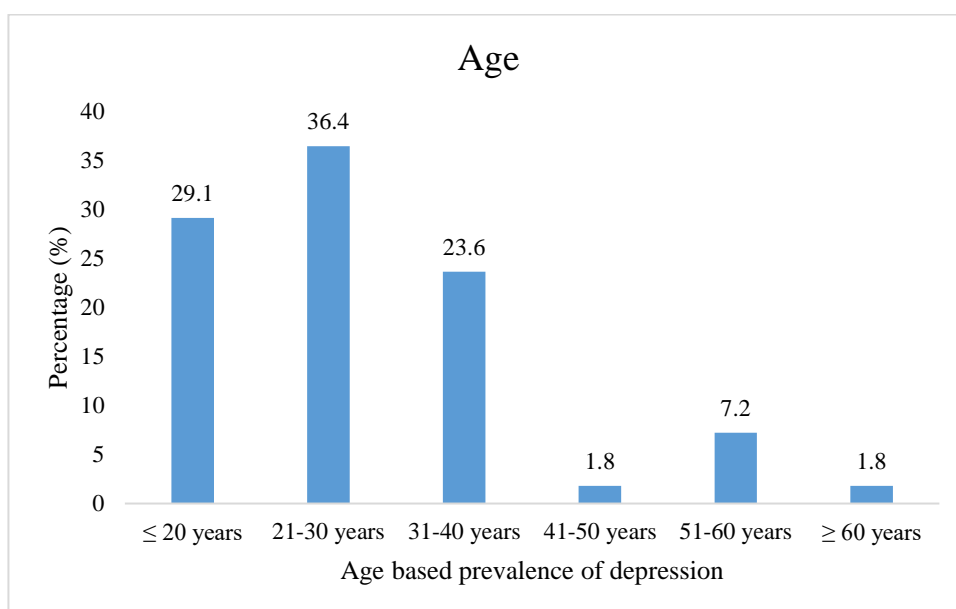
Figure 1: Age based prevalence of depression
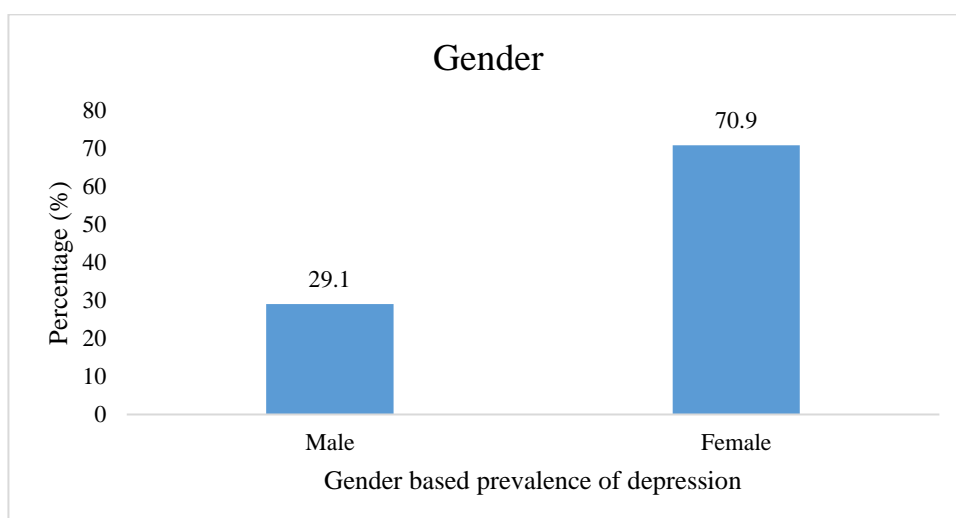
Figure 2: Gender based prevalence of depression
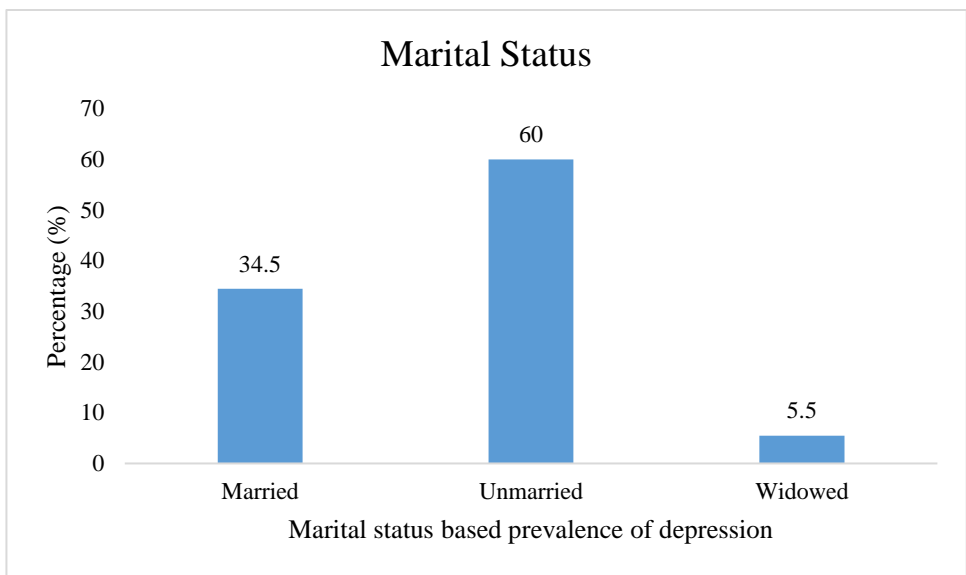
Marital Status

Figure 3: Marital status based prevalence of depression

Area of Residence
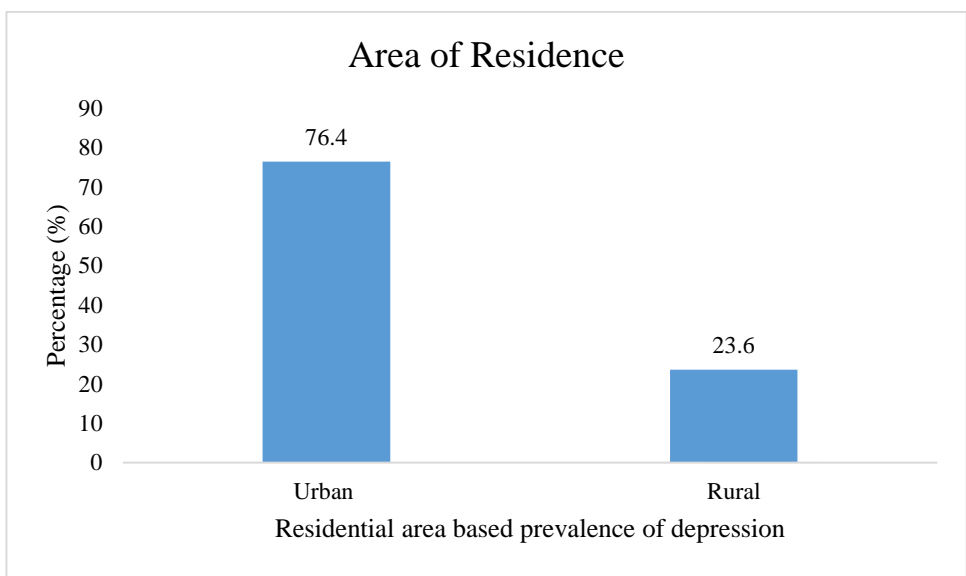
Figure 4: Residential area based prevalence of depression
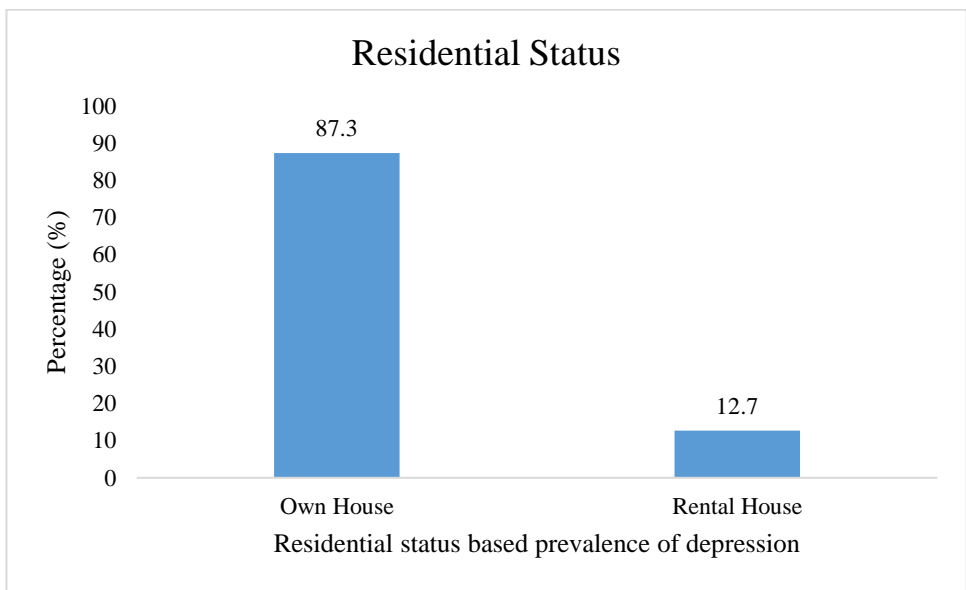
Residential Status

Figure 5: Residential status based prevalence of depression
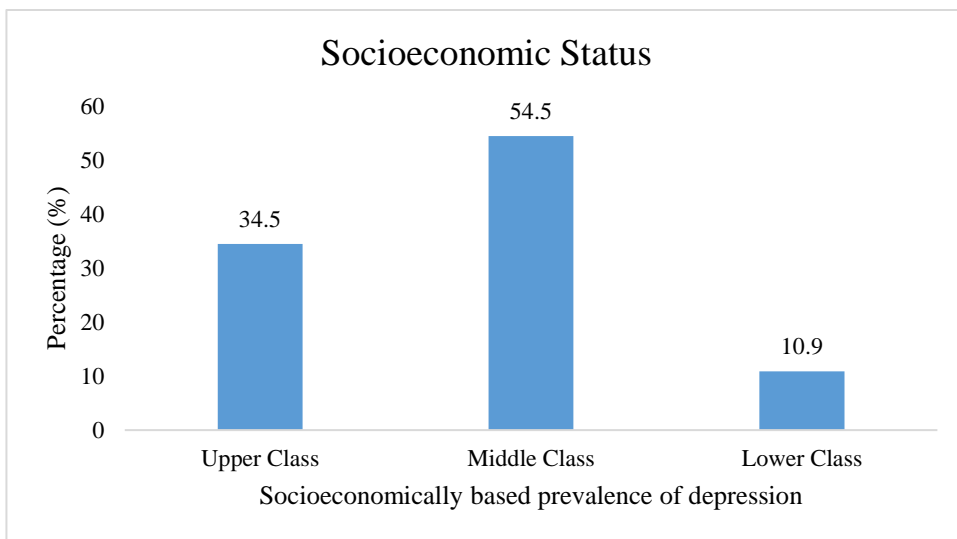
Figure 6: Socioeconomically based prevalence of depression
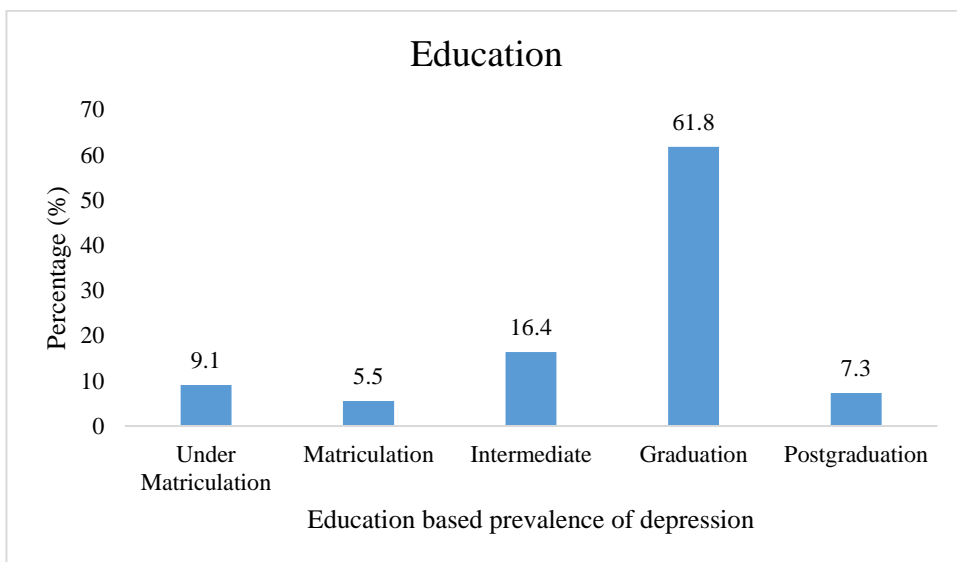

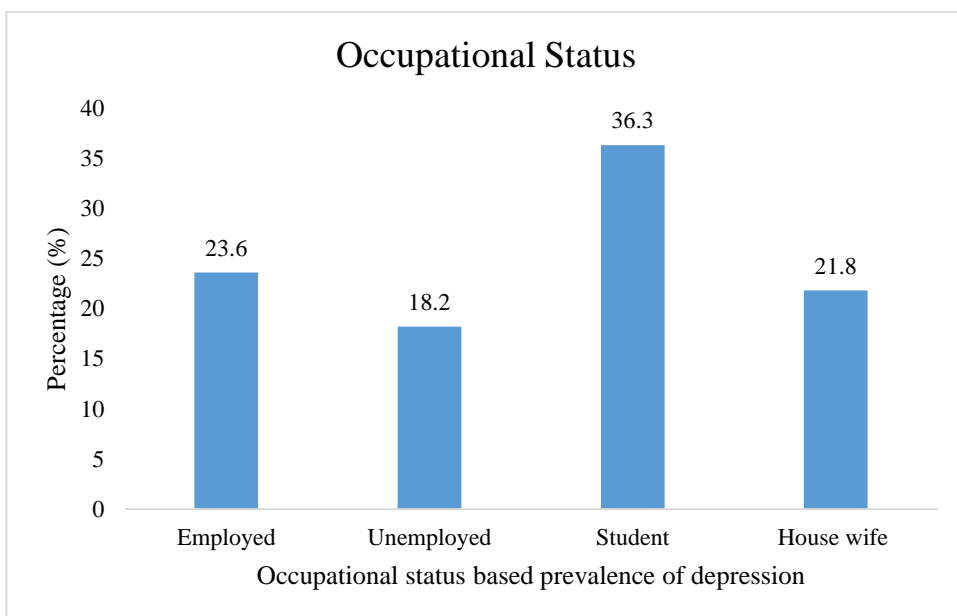**Figure 7: Education based prevalence of depression**

Figure 8: Occupational status-based prevalence of depression

Assessment of Patient History of Depression and Comorbidities

Data from 55 patients was collected and their past and family history of depression was recorded. Most of the patients did not have any past history of depression (n=48, 87.3%) while some were diagnosed with depression in the past (n=7, 12.7%). Majority of the depressive patients did not have any family member diagnosed with depression (n=46, 83.6%) however, some of the patients had family members i.e. mother, father etc. diagnosed with depression (n=9, 16.4%). Comorbid diseases can play a part in the development of depression. A number of depressive patients were suffering from hypertension (n=5, 9.1%) whereas other comorbid diseases such as peptic ulcer (n=4, 7.3%), rheumatoid arthritis (n=3, 5.5%), diabetes (n=2, 3.6%), polycystic ovarian syndrome (n=2, 3.6%), epilepsy (n=1, 1.8%), eczema (n=1, 1.8%) were also reported in the patients although in less frequency.

Table 2: Patient history of Depression and Comorbidities

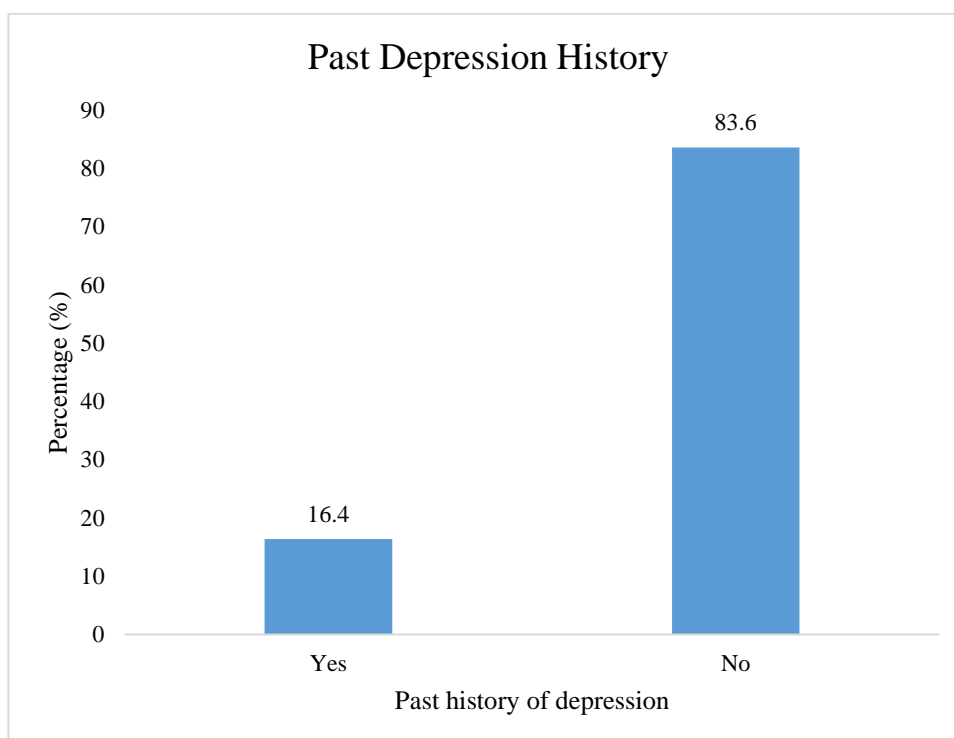| Parameter	Frequency (n=55)	Percentage (%)
Past History of Depression		
Yes	07	12.7
No	48	87.3
Family History of Depression		
Yes	09	16.4
No	46	83.6
Comorbidities		
Hypertension	5	9.1
Diabetes	2	3.6
Epilepsy	1	1.8
Polycystic Ovary Syndrome (PCOS)	2	3.6
Eczema	1	1.8
Peptic Ulcer	4	7.3
Rheumatoid Arthritis	3	5.5

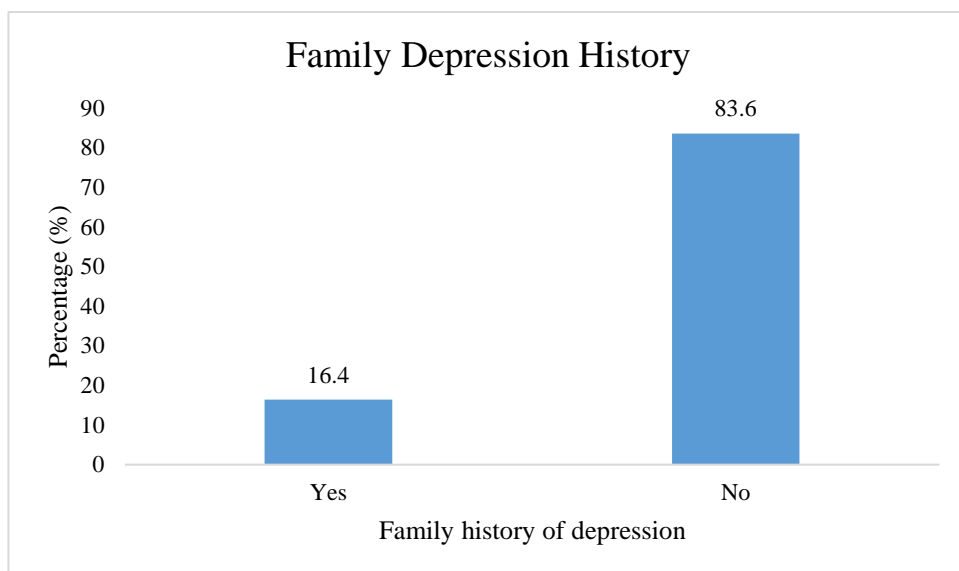**Figure 9: Patient's past history of depression**

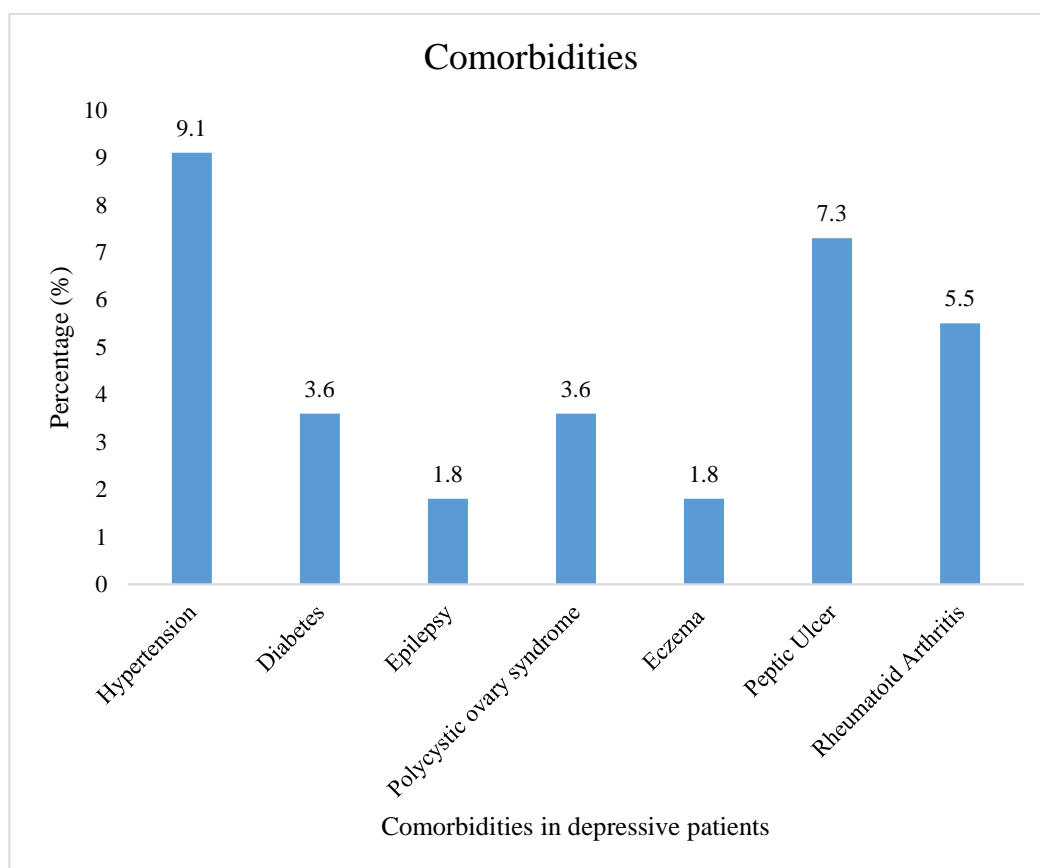**Figure 10: Patient's family history of depression**

Figure 11: Comorbidities in depressive patients

Assessment of Implicative Factors of Depression

Data from 55 depressive patients was taken and the implicative factors involved in the development and progression of depression were assessed and recorded. The risk factor with the highest prevalence among the depressive patients was socioeconomic status including both middle and low class (n=36, 65.5%), followed by stressful situations (n=34, 61.8%), irregular sleep (n=31, 56.4%), unemployment (n=30, 54.5%), lack of exercise (n=20, 36.4%), mental traumatic events (n=15, 27.3%), genetic factors (n=9, 16.4%) and physical traumatic events (n=3, 5.5%).

Table 3: Implicative Factors of Depression

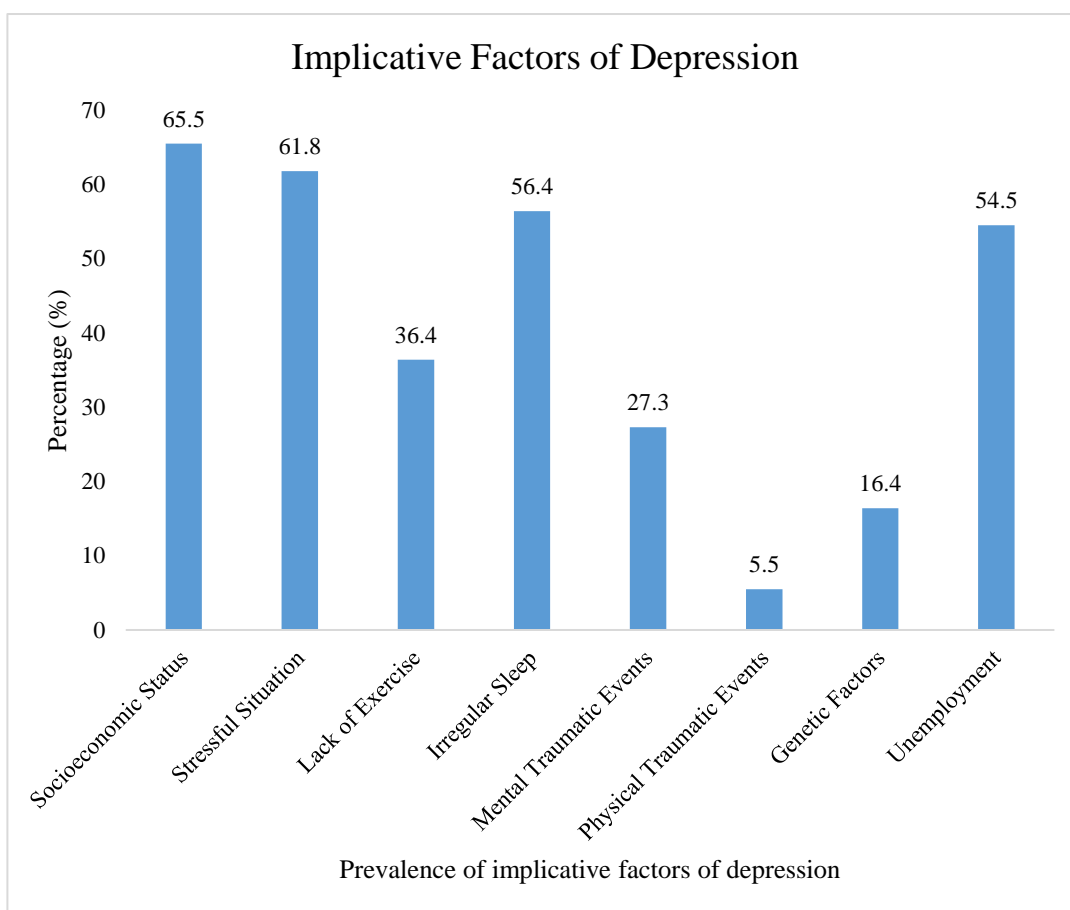| Parameters	Frequency (n=55)	Percentage (%)
Socioeconomic Status (Low to Middle Class)	36	65.5
Stressful Situation	34	61.8
Lack of Exercise	20	36.4
Irregular Sleep	31	56.4
Mental Traumatic Events	15	27.3
Physical Traumatic Events	03	5.5
Genetic Factors	09	16.4
Unemployment	30	54.5

Figure 12: Prevalence of implicative factors of depression

Assessment of Severity of Depression in Patients according to PHQ-9 scores

For the completion of our research work, data of 55 depressive patients was taken and severity of depression was assessed in accordance to PHQ-9 scores. Equal number of depressive patients were observed and reported in the categories of moderate (n=16, 29.1%) and severely moderate depression (n=16, 29.1%), followed by mild depression (n=15, 27.3%), minimal depression (n=6, 10.9%) and severe depression (n=2, 3.6%).

Table 4: Severity of Depression in Patients according to PHQ-9 scores

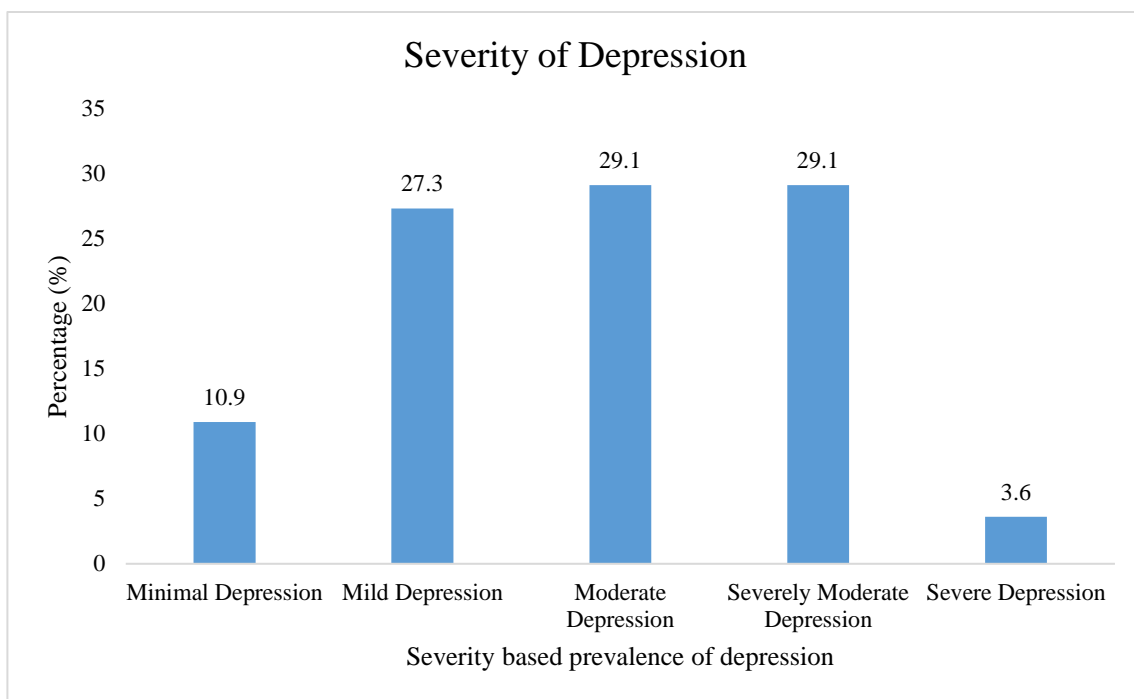| Parameter	Scores	Frequency (n=55)	Percentage (%)
Severity of Depression			
Minimal Depression	1-4	06	10.9
Mild Depression	5-9	15	27.3
Moderate Depression	10-15	16	29.1
Severely Moderate Depression	16-20	16	29.1
Severe Depression	20-27	02	3.6

Severity of Depression

Figure 13: Severity based prevalence of depression

Assessment of Treatment of Depression

For the completion of our research work, data of 55 depressive patients was taken. Treatment was not given for minimal depression while mildly depressed patients were only given non-pharmacological treatment including counselling and cognitive behavioral therapy (CBT). Both non-pharmacological and pharmacological treatment was given to patients suffering from moderate, severely moderate and severe depression. Majority of the depressive patients were receiving counselling (n=49, 89.1%) while some were also getting cognitive behavioral therapy (n=17, 30.9%). From the data collected, it was assessed that majority of the patients were taking escitalopram (n=12, 21.8%), a selective serotonin reuptake inhibitor for the treatment of depression, followed by fluoxetine (n=6, 10.9%), venlafaxine (n=03, 5.5%), fluvoxamine (n=3, 5.5%), sertraline (n=2, 3.6%), quetiapine (n=2, 3.6%), dosulephine HCl (2, 3.6%), paroxetine (n=2, 3.6%), fluphenazine/nortriptyline (n=1, 1.8%), lithium carbonate (n=1, 1.8%) and mirtazapine (n=1, 1.8%) along with clonazepam (n=5, 9.1%) for insomnia and propranolol (n=5, 9.1%) for increased heart rate and palpitations.

Table 5: Mode of Treatment in Depressive Patients

Parameter	Frequency (n=55)	Percentage (%)
Non Pharmacological Treatment		
Counselling	49	89.1
Cognitive Behavioral Therapy (CBT)	17	30.9
Pharmacological Treatment		
Escitalopram	12	21.8
Fluoxetine	06	10.9
Venlafaxine	03	5.5
Sertraline	02	3.6
Fluvoxamine	03	5.5
Quetiapine	02	3.6
Lithium Carbonate	01	1.8
Mirtazapine	01	1.8
Dosulepine HCl	02	3.6
Paroxetine	02	3.6
Fluphenazine/Nortriptyline	01	1.8
Clonazepam	05	9.1
Propranolol	05	9.1

Treatment of Depression

Figure 14: Non Pharmacological treatment of depression
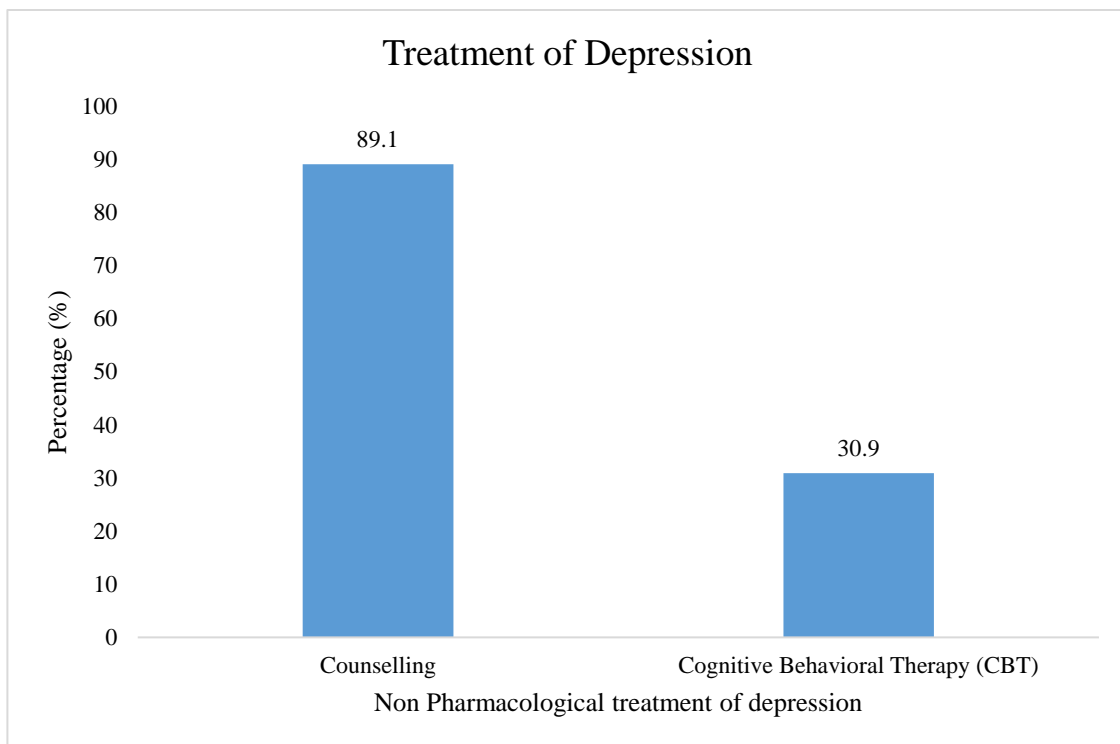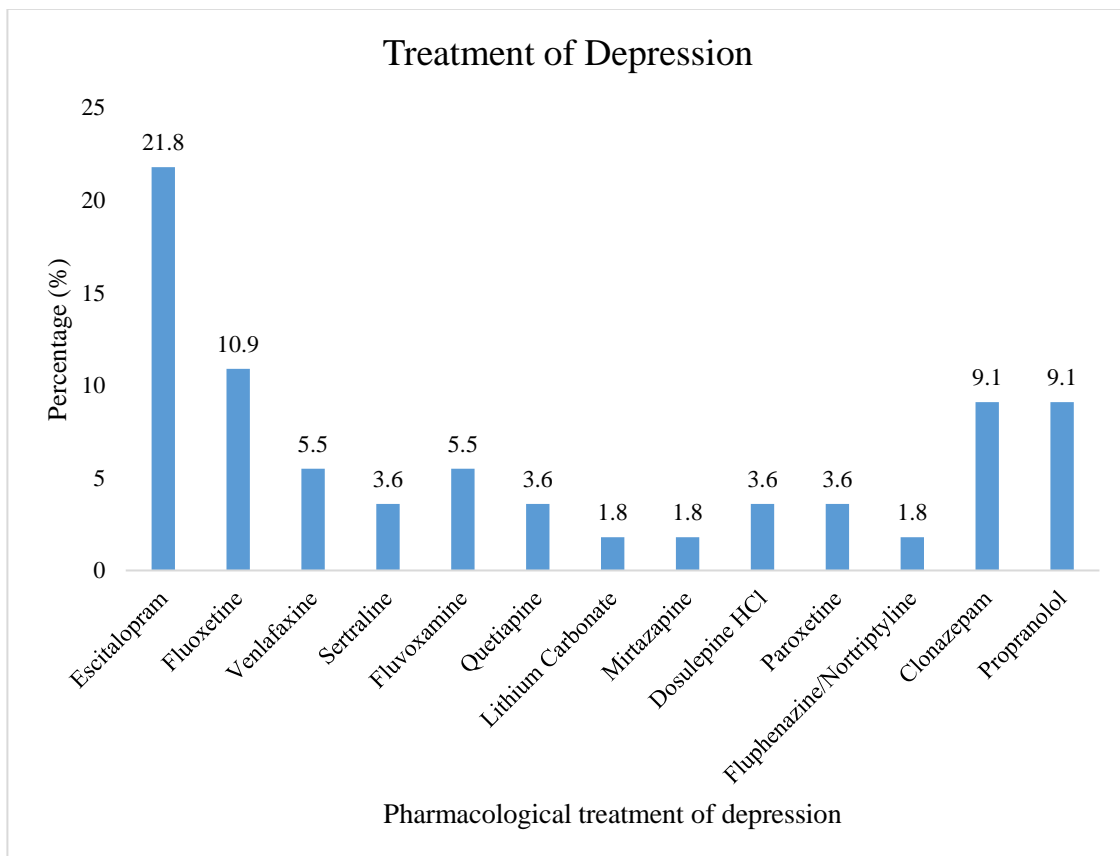
Treatment of Depression

Figure 15: Pharmacological treatment of depression

DISCUSSION

Depression is a common mental disorder affecting more than 350 million people worldwide. It is characterized by persistent sadness and a lack of interest or pleasure in previously satisfying or enjoyable activities. It can also disturb sleep and appetite; fatigue and poor concentration are common. The effects of depression can be long-term or recurrent and can dramatically affect a

person's ability to function and live a satisfying life. Distribution of age in the incidence of depression differs among studies depending on the sample studied, measurement and methods used. The association between depression and age has been given significant research attention, but the results are ambiguous. According to our survey, age group of 21-30 (n=20, 36.4%) had the highest prevalence of depression than any other age groups.

Similarly, age differences in depression was studied in the National Comorbidity Survey Replication, a national survey of the US household population in 2010 and according to the survey, depression was more prevalent in the above mentioned age group as compared to other age groups (Kessler *et al.,* 2010). Although many studies of depressive disorders show an initial rise across age groups, followed by a descent, this pattern is by no means universal and the peak age for prevalence varies significantly from study to study. The study of gender differences in depression has received increasing attention in recent years and has emerged as an important area of focus as one of the most reliable findings in the social epidemiology of mental health is the gender gap in depression.

In our survey, depression was more prevalent in women (n=39, 70.9%) than men. Data from the National Comorbidity Survey, a population-based epidemiological study, in the 10 countries surveyed (United States, Canada, Puerto Rico, France, West Germany, Italy, Lebanon, Taiwan, Korea, and New Zealand) showed that the prevalence of depression was higher in women as compared to men (Noble, 2005). Several biological processes are assumed to be involved in the susceptibility of women to depression, including genetically determined vulnerability, hormonal variations related to various aspects of reproductive function, and an undue sensitivity to such hormonal fluctuations in brain systems that facilitate depressive states. Psychosocial events such as role-stress, victimization, sex-specific socialization, internalization coping style, and disadvantaged social status have all been considered to be contributors to the increased susceptibility of women to depression. The comorbidity of depression and hypertension (HTN) is common and hypertensive patients are found to have higher chance of suffering from depression therefore, complicating the management of both conditions. Hypertensive patients with co-morbid depression lead to lack of adherence to treatment, absent to follow up and poor compliance to lifestyle modification. Hence, it is very important to assess prevalence of depression among hypertension. In our survey, comorbidity of depression and hypertension was higher (n=5, 9.1%) as compared to other comorbid diseases. According to literature, a study performed in 2005 acknowledged an increase in the prevalence of depression in hypertensive patients. Several causative factors have been proposed to elucidate this association, such as autonomic nervous system dysfunction, and more recently, genetic influences.

The clinical significance of this study is clear, since depressive symptomatology is related with poor BP control in hypertensive patients and with the development of complications of hypertension (Scalco *et al.,* 2005). Given the high prevalence and considerable burden of depression, substantial research has focused on the factors underlying depression. As one of the important environmental factors affecting many aspects of individuals' development, behavioral evidence proposes that family socioeconomic status (SES) has a powerful impact on physical and mental health, such as depression. According to our survey, prevalence of depression was higher in middle and lower class (n=36, 65.5%) as compared to upper class. These results were relatable to a study carried out in Germany in 2017 which illustrated the association of depression with low socioeconomic status (Hoebel *et al.,* 2017).

Within the past 20 years, depression research has given increasing attention to the possibility of complex and mutual relations between stress and depression. Not only does stress increase risk for depression, but depression, in turn, also increases vulnerability to stressful events which can provoke or trigger depression episodes in vulnerable individuals. Major life stressors, especially those involving interpersonal stress and social rejection, are amongst the strongest proximal risk factors for depression. According to our study, stressful situations (n=34, 61.8%) were noted to be a prominent factor in the development of depression. A study performed in 2015 indicated that stress can initiate mental and probably biological processes that increase risk for depression. The more stressful life events a person experiences, the more he or she is susceptible for developing depression (Plieger *et al.,* 2015). Unemployment and job loss have long been reported to be linked with impaired mental

health. According to our survey, depression was prevalent in unemployed individuals (n=30, 54.5%) as compared to employed. These results were relatable to a study performed in Germany in 2018 which provided evidence that unemployment is associated with higher risk of depression (Zuelke *et al.,* 2018). Being unemployed has been shown to be related to reduced psychosocial wellbeing and life satisfaction and increases the risk of affective disorders such as depression. In light of the global financial crisis, the associations between employment status and mental health have gained renewed attention. Sleep and depression interact in a complex manner, and while insomnia increases the susceptibility to depression, depression is often associated with altered circadian and social rhythms. According to our study, irregular sleep (n=31, 56.4%) played a substantial role in the development of depression in individuals. These results are relatable to the study performed in 2005 in Tennessee that reaffirmed the close relationship of insomnia with depression (Taylor *et al.,* 2005).

Insomnia has predictive significance in depression, and therapeutic strategies that target disturbances in circadian rhythm contribute in its management. It is essential to determine the severity of depression in patient as it influences treatment decision-making and is used in treatment guideline recommendations. According to our survey, moderate (n=16, 29.1%) and severely moderate depression was more prevalent among the patients. These results were similar to the study performed in 2012 in Alaska regarding the prevalence of depression severity (Dillard *et al.,* 2012). Counselling is an acknowledged psychological therapy that is often used in the management of common mental disorders such as anxiety and depression. It is associated with modest progress in short-term outcome compared with common general practitioner care, and hence is a useful addition to mental health services in primary care. In our study, majority of the people suffering from mild, moderate and severe depression were receiving counselling (n=49, 89.1%).

According to literature, a study performed in United Kingdom indicated that the depressive patients who received counselling were more likely to have improved psychological symptom levels than those who did not receive counselling. Depressive patients who received counselling tended to be more satisfied with their treatment (Rowland *et al.,* 2001). Cognitive–behavioral therapy (CBT) for depression is one of the best investigated treatments in all of medicine for the treatment of mild, moderate, and severe depression. CBT is a type of psychotherapy in which thought patterns are modified in order to change moods and behaviors. According to our study, Cognitive Behavioral Therapy (n=17, 30.9%) was used alongside counselling in moderate, severely moderate and severely depressed patients. A study performed in 2012 revealed CBT to be a valuable treatment for mild, moderate, and severe forms of depression. It was equally effective and more long-lasting than medication alone, and the combination of medication and CBT increased the response rate (Sudak, 2012). Although pharmacological and psychological interventions are both effective for depression, antidepressant drugs remain the mainstay of treatment. During the last 20 years, selective serotonin reuptake inhibitors (SSRIs) have increasingly become the most commonly prescribed antidepressants. Escitalopram, the last SSRI introduced in the market, is the pure S-enantiomer of the racemic citalopram appears to be suitable as first-line antidepressant treatment for moderate to severe depression.

According to our study, along with counselling and CBT, escitalopram (n=12, 21.8%) was given to majority of the depressed patients. In a survey performed in 2009, escitalopram was shown to be significantly more effective than other anti-depressive agents in the treatment of depression (Cipriani *et al.,* 2009). Similarly, fluoxetine (n=6, 10.9%) was also given to the patients for the treatment of moderate and severely moderate depression. According to literature, a randomized trial performed in 2002 showed that fluoxetine daily appeared to be well tolerated and effective for acute treatment of depression in outpatients (Emslie *et al.,* 2002).

CONCLUSION
Depression, overwhelming sadness and hopelessness, is responsible for a substantial proportion of the global disease burden and is a major cause of suicide worldwide. Depression was more prevalent in patients with age ranging from 21-30 years. Majority of the depressed patients were female in

contrast to males. Various implicative factors were involved in the development of depression such as low socioeconomic status, stressful situations, unemployment and irregular sleep. Patient Health Questionnaire-9 (PHQ-9) was used for the diagnosis of depression and severity of depression was determined based on the scoring in Patient Health Questionnaire-9. Counselling and Cognitive Behavioral Therapy (CBT) was given to mild, moderate, severely moderate and severely depressed patients. Moderate, severely moderate and severely depressed patients were also receiving pharmacological treatment in which escitalopram and fluoxetine were mostly prescribed.

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