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Original Article

Detection, Management Approach of Depression and Antidepressant Utilization in Adult Patients: Results of a Cross-Sectional Survey

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Editorial Viewpoint

- Depression with its varied presentation is commonly first diagnosed by physicians.
- This large cross-sectional study shows high prevalence of depression in employed educated adults.
- Escitalopram was the most preferred antidepressant in all the studied age groups.

Abstract

Aim: The study was conducted to understand the demographics, prevalence of co-morbid conditions and treatment modalities of depression.

Methods: A cross-sectional, nationwide observational study was conducted to understand the management pattern of depression in India. Depression was majorly diagnosed with DSM-IV TR criteria.

Results: The data of 2276 Indian patients across 18 states were collected through 135 mental health professionals. The study population was predominantly from urban (81.2%) area. The prevalence of uneducated and employed patients in the study was 7.2% and 54.6% respectively. The main co-morbidities observed were diabetes, hypertension, anxiety and insomnia. Overall, escitalopram monotherapy was used in 67.2% patients. Escitalopram was found to be the preferred antidepressant in patients with co-morbid conditions including hypertension and diabetes. Counseling was the most common non-pharmacological therapy practiced.

Conclusion: This large cross sectional study in real life settings demonstrates high prevalence of depression among employed and educated adult Indian patients. Hypertension and diabetes are the two most common co-morbidities in patients with depression. Escitalopram is commonly used and preferred antidepressant in all studied age groups and even in co-morbid depression.

Introduction

Depression is a common condition worldwide and one of the major public health issues.¹ It poses significant health burden given the lifetime prevalence of all depressive disorders over 20%.¹ Fortunately, depression is a treatable condition; however many times it remains under-diagnosed¹ and under-treated leading to morbidities. In country like India, where there is scarcity of psychiatrists,¹ patients often present to physicians with non-classical symptoms of depression. Hence, it is important that the physicians recognize and treat the depressive disorder appropriately. Despite extensive research on depression, little is currently known about the nationwide demographic data of depression and diagnosis methods used in real life settings in India.

Depression management constitutes non-pharmacological and pharmacological options. Antidepressant drugs have a remarkable impact on symptom improvement as well as improvement of the quality of life. However, drug utilization in actual clinical practice need continuous study. In India, drug utilization studies of psychotropic drugs^{2,3} have been performed but there is no study of depression at national level. The national level data could be useful for physicians in understanding overall treatment pattern of depressive disorders. With this background, the present study was conducted to understand demographics of patients diagnosed with Major Depressive Disorder (MDD), presence of co-morbid conditions in patients with depression and treatment paradigms for depression with/without co-morbid conditions.

Table 1a: Demographic data and clinical characteristics of patients with depression (n=2276)

Characteristics	N (%) / Mean (SD)
Mean age (years)	41.5 (11.8)
Male	54.9%
BMI (kg/m ²)	24.2 (4.4)
Urban	81.2%

Table 1b: Education and employment status of patients with depression (n=2276)

Characteristics	%
No formal education	7.2%
Educated	92.8%
Primary education	12.4%
Secondary education	22.2%
Higher secondary education	14.9%
Graduates	32.9%
Postgraduates	10.4%
Employed	54.6%

Methods

In this cross-sectional, observational study patients with depression were enrolled over a recruitment period of December 2013 to November 2014. The patients across India were chosen to represent all geographical areas and different demographic population. Psychiatrists and physicians with experience in the management of depression working in either clinics or hospitals across India were invited to join this study. The eligible patients were consecutively presenting diagnosed cases of major depressive disorder (MDD) of either sex aged between 18 and 65 years and willing to sign the patient authorization form. Diagnosis of MDD was either done with DSMIV-TR or other clinical criteria. The healthcare professionals' filled information in a web based case report form. The information collected was based on questionnaire in English language

containing items on demographic details (age, gender, education and employment status and state of residence), co-existing medical conditions, family history of mental illness, presence or history of any other major medical illness and questions related to the management of depression. The safety was evaluated by recording adverse event.

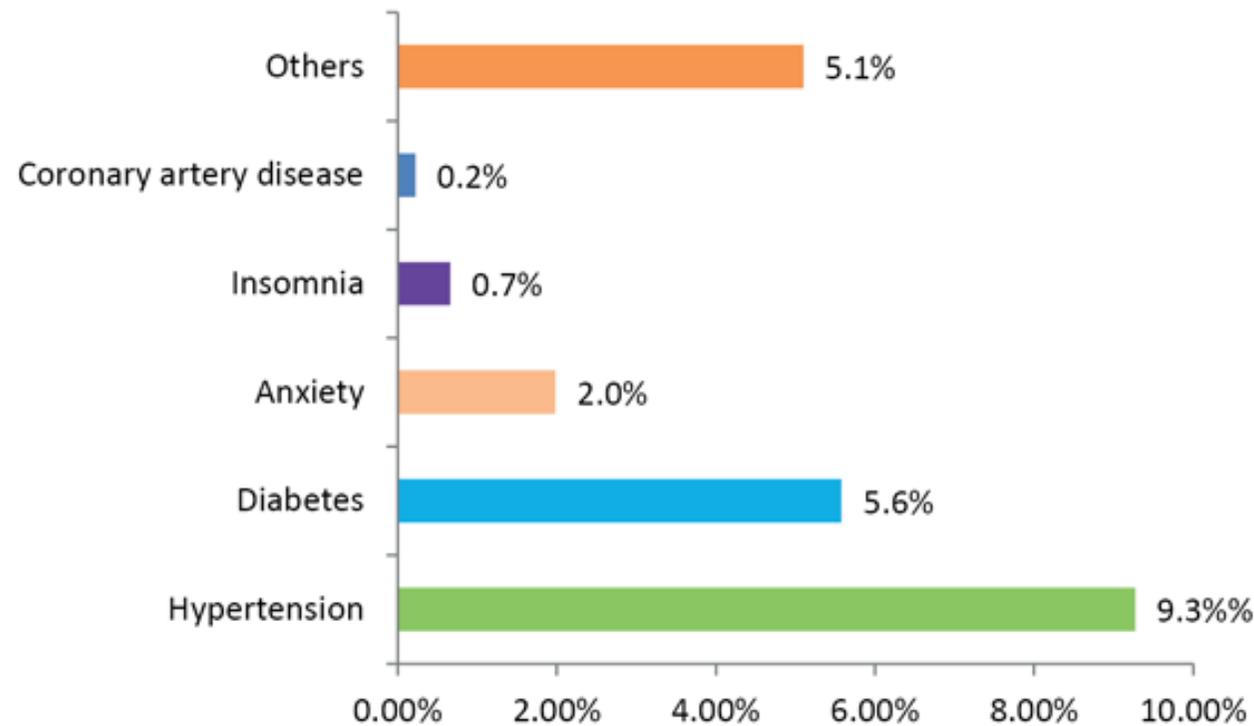


Fig. 1: Prevalence of ongoing co-morbidities in depression

Based on the WHO4 recommendation for a cross-sectional survey to investigate drug use in health facilities, we included more than 600 patients. Convenience samples of consecutive patients were used in the study.

Statistical Analysis

Continuous variables are summarized using frequency, mean, standard deviation, and minimum and maximum while categorical variables are summarized using frequency and percentage.

Ethics Approvals

After approval of the protocol by Ethics Committee, the study was conducted in compliance with the protocol, ethical principles of International Conference on Harmonization of Technical Requirements for Registration of Pharmaceutical for Human Use –Good Clinical Practice (ICH-GCP) guidelines that have their origins in the Declaration of Helsinki, Indian regulatory and guidelines [Indian Council of Medical Research (ICMR) and Indian GCP guidelines] and Indian GCP guidelines. Eligible patients were included after taking written consent.

Results

Characteristics of Study Participants

We recruited 2276 patients with depression from 135 centers across 18 states of the country. The four states which mainly contributed study population were Maharashtra (14.7%), Andhra Pradesh (14.2%), Haryana (11.9%) and Delhi (10.1%). The patients were also enrolled from Uttar Pradesh, Gujarat, Rajasthan, Kerala, Madhya Pradesh, West Bengal, Punjab, Orissa, Karnataka, Bihar, Jammu and Kashmir, Himachal Pradesh, Tamil Nadu and Manipur. The mean age of study population was 41.5 (+11.8) years. The study included 54.9% male and 45.1% female population. The study population predominantly constituted urban patients (81.2%). The other demographic details are given in Table 1a.

Only 7.2% patients were uneducated. Almost one third of patients were graduates and 22.2% had secondary education (Table 1b) while 54.6% patients were employed. Family history of depression was present only in 0.1%.

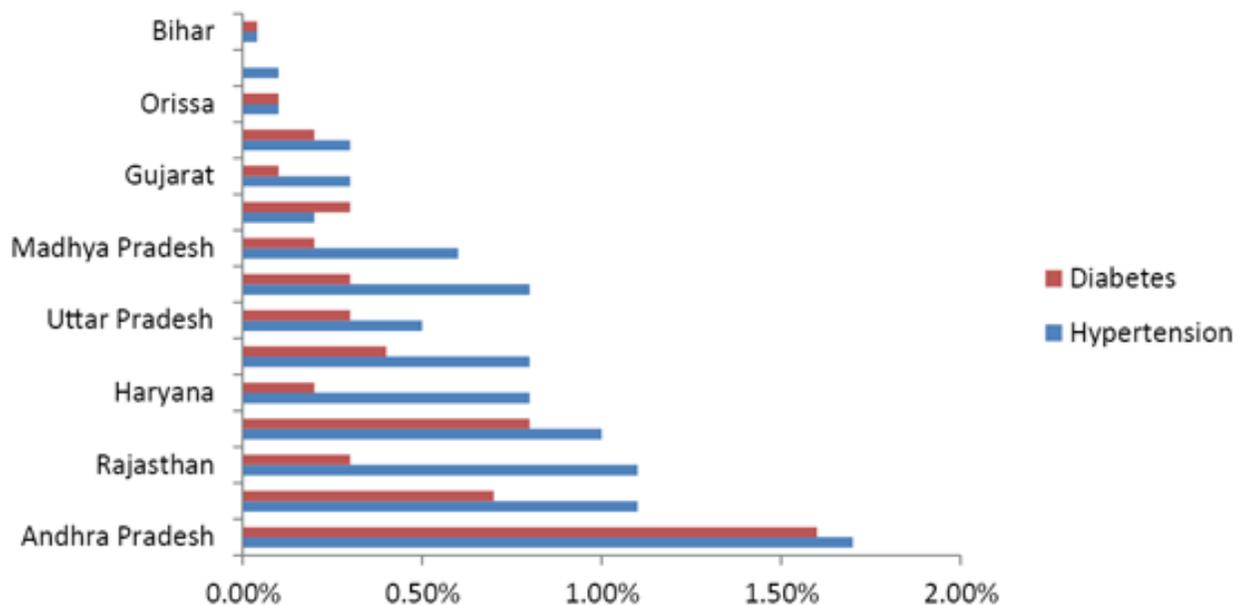


Fig. 2: State wise prevalence of hypertension and diabetes among patients with depression

Diagnosis of Depression by Healthcare Professionals

Diagnosis of depression was performed with DSMIV-TR criteria in 1701 (74.7%) patients while 575 (25.3%) were patients diagnosed with other criteria. Major depression was present in all patients. Dysthymia or mild chronic depression and seasonal affective disorder was observed in 0.4% and 0.5% patients respectively while bipolar disorder (manic depression), atypical depression and psychotic depression was seen in 0.1% patients each.

Co-morbidities in Depression

A total of 25.5% patients had prior medical illness or surgical history while alcohol and tobacco consumption was reported in 0.7% and 0.4% patients, respectively. The prevalence of ongoing hypertension, diabetes, anxiety, insomnia and coronary artery disease was 9.3%, 5.6%, 2%, 0.7% and 0.2% patients respectively while other conditions were present in 5.1% (Figure 1). The mean duration of hypertension and diabetes in these patients was 4.0 (± 4.8) and 5.1 (± 5.3) years. Family history of depression was noted only in three patients.

Of the patients having hypertension 54% were male and 46% were female. Similarly, among having diabetes 48.8% were male and 51.2% were female. The state wise distribution of hypertension and diabetes among patients with depression showed prevalence of hypertension and diabetes in Andhra Pradesh among 1.7% and 1.6%

patients respectively. The prevalence of hypertension in Maharashtra, Rajasthan and Delhi was 1.1%, 1.1%, and 1% respectively (Figure 2). The prevalence of hypertension and diabetes in depression observed in other states was less than 1%.

Management of depression

Non-pharmacological management

The most common non-pharmacological therapy i.e. counseling was used in 32.6% while cognitive behavioral therapy (CBT), exercise therapy, electroconvulsive therapy and other therapies were used in 13.7%, 9.2%, 0.5% and 44% patients respectively (Table 2).

Table 2: Non-pharmacological management

Type of therapy	N (%)
Counseling	779 (32.6%)
Cognitive behavioral therapy	328 (13.7%)
Exercise therapy	219 (9.2%)
Electro-convulsive therapy	13 (0.5%)
Others	1050 (44%)

Table 3: Gender wise use of drugs

Antidepressant	Male	Female
	Antidepressants	
Escitalopram	858 (56.3%)	667 (43.7%)
Sertraline	89 (46.8%)	101 (53.2%)
Desvenlafaxine	95 (53.4%)	83 (46.4%)
Paroxetine	66 (56.9%)	50 (43.1%)
Mirtazapine	58 (52.7%)	52 (47.3%)

Pharmacological Treatment

In terms of antidepressant monotherapy, escitalopram was used as monotherapy in 67.2% patients while sertraline, desvenlafaxine, paroxetine and mirtazepine and were used as monotherapy in 8.4%, 7.8%, 5.1% and 4.8% patients respectively. Clonazepam and lorazepam was used in 37.5% and 4.2% patients respectively. A total of 41 patients were prescribed combination therapy of antidepressants. Escitalopram plus clonazepam was prescribed among 21 patients. Flupentixol plus melitracen and triple drug combination (imipramine, chlordiazepoxide and trifluoperazine) was prescribed in 14 and three patients each. Gender wise use of antidepressants is given in Table 3.

In patients with depression with hypertension, escitalopram was used in 59.2% patients while, clonazepam and sertraline were used in 34.6% and 13.7% patients respectively. Paroxetine, desvenlafaxine, amitriptyline, mirtazapine and fluoxetine were used in 9%, 8.1%, 7.1%, 6.6% and 6.2% cases respectively. In patients with depression associated with diabetes, escitalopram was used in 68.5% patients while clonazepam, sertraline, desvenlafaxine, amitriptyline, fluoxetine and mirtazepine were used in 30.7%, 9.5%, 7.9%, 6.3%, 4.7% and 3.9% respectively. In depression with anxiety, escitalopram was used in 66.7%, clonazepam in 46.7%, mirtazapine in 20% and sertraline in 13.3% patients. In depression with insomnia, escitalopram, clonazepam, mirtazapine, were used in 73.3%, 33.3% and 20% patients respectively while desvenlafaxine, paroxetine and zolpidem were used in 13.3% each.

Table 4: Age-group-wise usage of antidepressants

Antidepressant	18-24 years (n=153) N (%)	25-30 years (n=326) N (%)	31-40 years (n=670) N (%)	>40 years (n=1105) N (%)
Escitalopram	103 (67.3%)	232 (71.2%)	465 (69.4%)	730 (66.1%)
Clonazepam	58 (37.9%)	122 (37.4%)	257 (38.4%)	416 (37.6%)
Sertraline	11 (7.2%)	25 (7.7%)	59 (8.8%)	96 (8.7%)
Desvenlafaxine	9 (5.9%)	20 (6.1%)	51 (7.6%)	98 (8.9%)
Paroxetine	9 (5.9%)	19 (5.8%)	38 (5.7%)	51 (4.6%)
Mirtazapine	10 (6.5%)	14 (4.3%)	35 (5.2%)	51 (4.6%)
Lorazepam	5 (3.3%)	14 (4.3%)	28 (4.2%)	48 (4.3%)

Escitalopram was used in 67.3%, 71.2%, 69.4% and 66.1% patients in the age group of 18-24 years, 25-30 years, 31-40 years and more than 40 years of age group respectively. Age group wise use of other commonly used antidepressants is shown in Table 4. Clonazepam was used in the same age groups in 37.9%, 37.4%, 38.4% and 37.6% patients respectively.

Only 12 (0.5%) patients reported 14 adverse events of which 42.9% were of mild severity. The most common adverse event was dizziness. No serious adverse event was reported in the study. Majority (92.8%) of the adverse events did not have causal relationship with the treatment modalities while only one event was possibly related to the study treatment. Out of 14 adverse events, 50% required treatment.

Discussion

With an objective of understanding the disease pattern and its management in Indian setting, we conducted this cross sectional study and evaluated the demographic profile, associated co-morbid medical illnesses and treatment modalities of depression. The five major states contributing to our study population were Maharashtra, Andhra Pradesh, Haryana, Delhi and Uttar Pradesh. Our study findings of high prevalence of depression in urban population are in accordance with Sengupta and colleagues.⁵

Depression has negative impact on personal level, family level as well on the society and in turn on the country level. With adverse mental and emotional wellbeing, depression lowers the quality of life and affects productivity at workplace. Fifty five percent of our study population was employed which underscores the importance of diagnosis of depression in working population due to risk of economic impact on the country. Depression is commonly associated with comorbidities. Cardiac and metabolic disorders are associated with mental diseases.⁶ An association between major depression and cardiovascular disease has been established.⁷ We observed hypertension and diabetes as the two most common comorbidities in Indian patients with depression. Over nine percent was hypertensive making it the most common comorbidity in our study population. Depression independently has shown to be associated with carotid intima media thickness.⁸ Presence of hypertension may augment the carotid intima media thickness and lead to severe complications; hence it is imperative to control both depression and hypertension to avoid complications.

Both diabetes and depression are common diseases. Depression is common in patients with diabetes and vice versa because of the bidirectional relationship between depression and metabolic syndrome.⁹ Diabetes associated depression is a significant burden. In our study, diabetes mellitus was found to be the second most common comorbidity followed by hypertension. In a study conducted by Joesph and colleagues 31% patients with type 2 diabetes had moderate depression while 14.3% had severe depression.¹⁰ Depression in diabetes is associated with poor outcomes. ¹¹ In our study population, 5.6% had diabetes. In patients with diabetes mellitus, treatment of depression is important for effective and sustained glycemic improvement. Depression may result in poor glycemic control and screening for depressive symptoms could be useful for identifying patients requiring additional support.¹²

State wise variation in regards to co-morbidities revealed highest prevalence of both hypertension and diabetes among patients with depression in patients from Andhra Pradesh. The patients from Maharashtra, Rajasthan and Delhi also showed high prevalence of hypertension in these patients.

Counseling was the most common-non-pharmacological method practiced in close to one third of patients with depression. Survey results¹³ showed that counseling is done by primary care physicians only in 40% patients. Our findings are somewhat similar to these results. According to our study results, uniformly in all studied age groups and both genders, selective serotonin reuptake inhibitors (SSRIs) were the most commonly prescribed antidepressants possibly because of their advantage in terms of side effect profile and better tolerability compared to most tricyclic antidepressants.¹⁴ This finding is in accordance with other survey result.² Indian Psychiatric Society multicentric study has showed that escitalopram is the most commonly used antidepressant.³

In patients with depression associated with hypertension, escitalopram was found to be the most common antidepressant and was used in 59% patients. Tricyclic antidepressants (TCAs) are not the suitable choice of agents in hypertensive patients due to risk of rise in blood pressure. ¹⁵ Amitriptyline, a TCA was used only in 7.1% patients with depression with comorbid hypertension. Selective serotonin reuptake inhibitors could be the suitable antidepressant option in diabetes because they may also improve glycemic control.¹³ Escitalopram is one such agents which can be used for the management of depression in diabetes patients with beneficial effect on the glycemic control. In an Indian study treatment of depression in diabetes patients showed clinically and statistically significant reduction of fasting as well as postprandial blood sugar values.¹⁶ In accordance with the results of this study, 68.5% patients with depression associated with diabetes in current study were also treated with escitalopram. Antidepressant associated side effects can have an impact on the management of depression due to discomfort to the patients and possibility of non-adherence to the treatment with potential of relapse or recurrence of symptoms. In an observational, prospective study Lucca and colleagues reported incidence of adverse reactions to

antidepressants to 42.3%.¹⁷ Our finding is strikingly contrast as we observed the adverse event rate of just 0.53%. There are two possible explanations to these observations. The study done by Lucca et al was in a tertiary care teaching hospital where largely referred patients are treated and hence, possibly they may be receiving other drugs along with antidepressants. Secondly, their study was prospective in nature, hence patient reporting adverse event during any of the visits gets added to the incidence; however ours was cross sectional and single visit study. We reported only patients reporting adverse events at that moment. One of the reasons for this low side effect is cross sectional questionnaire based reporting. Receptor selectivity and site of action helps in predicting adverse events associated with antidepressants.¹⁸ Escitalopram being the most selective o SSRI antidepressants without high affinity to other receptors has favorable tolerability profile. The efficacy and safety results suggest that escitalopram may have an improved benefit–risk ratio compared to other antidepressants.¹⁹ Overall, escitalopram seems to be the preferred agent across age groups studied in this study and even in all comorbidities reported in the study. Clonazepam is another drug which is seen very commonly used in patients with depression anxiety and insomnia. Characteristics such as long half-life and higher potency are possible reason for its preference compared to other drugs in the benzodiazepine class.²⁰ Combination of clonazepam with SSRIs might amplify the response in depression.

Strengths and Limitations

One of the major strengths of our study was to be able to recruit large number of patients from all geographic areas of India. The results of this study provide overall demographic profile of patient with depression and its real life management approach which could be useful for the healthcare professionals engaged in the treatment of depression. Use of convenience sampling was a limitation of the present study. Being a cross sectional study without follow up, there is high chance that adverse events could be under-reported. The study population was predominantly educated people and patients from urban area, hence does not reflect data from rural and illiterate patients. The results should be carefully interpreted considering these limitations. Nonetheless, the study provides good insights about demographic parameters, comorbidities and approach towards depression management in Indian patients.

Conclusion

Depression is more commonly observed in patients with 40 years of age and above and more so in educated and employed population. Hypertension and diabetes are the two most common co-morbidities in Indian patients with depression. Escitalopram is the preferred antidepressant for the treatment of major depression in both genders and even in patients with comorbid conditions. Counseling is the most commonly used but underutilized non-pharmacological treatment option.

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