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Original Research Article

Physical comorbidity and its impact on symptom profile of depression in Indian setting 2 (COSPO-DEP-2 study)

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ABSTRACT

Background: The objective of the study was to determine the symptom profile and prevalence of comorbidities and to understand the prescription patterns of antidepressants among depression patients in India.

Methods: The real-world, retrospective, observational COSPO-DEP-2 study was conducted at various centres across India between April 2021 and March 2022.

Results: Data of 7288 patients with depression was analyzed. The mean (SD) age of the patients was 45.1 (11.9) years. Majority of the patients were males (54.2%) and literate (92.7%); 53.1% were unemployed; 14.5% were unmarried and other 8.8% patients were divorced or separated. Almost equal proportion of patients were from urban and rural areas. A family history of psychiatric disorder was present in 14.9% patients. More than half (57.3%) of the patients presented with first episode of depression. Mild depression was present in 38.87% patients, moderate depression in 38.06% patients and severe depression in 23.07% patients. Diabetes was the most common comorbid condition (31.5%) followed by hypertension (26.6%), migraine (24.6%), and chronic pain (16.6%). Majority (54%) of patients were prescribed combination of pharmacotherapy with psychotherapy. The most commonly prescribed drug for depression management was escitalopram (57.5%) followed by benzodiazepines (38.7%). Escitalopram was also the most commonly prescribed drug in patients with depression having comorbidities.

Conclusions: Depression is common among both genders and more commonly seen among unemployed people and in those with family history of depression. The commonly reported comorbidities include diabetes, hypertension, migraine and chronic pain. Escitalopram is the most commonly used agent followed by benzodiazepines among patients of depression with or without comorbidities.

Keywords: Depression, Antidepressants, Comorbidities, Treatment, Escitalopram

INTRODUCTION

Depression is a common illness affecting approximately 280 million people globally.¹ Global Burden of Disease report estimates the prevalence of unipolar depressive episodes to be 1.9% for men and 3.2% for women.² According to a population-based study conducted in India, prevalence of depression is estimated to be 15.1%.³ According to a study conducted at 14 sites

by World Health Organization (WHO), the most common diagnosis in primary care was depression.⁴

Association of depression with medical comorbidities may be understood in many ways. Depression may predate the onset of a medical illnesses and can present as an early symptom of medical illnesses, such as an early sign of Parkinson's disease.⁵ Alternatively, depression may be a risk factor for the development of certain medical

disorders, like coronary heart disease, myocardial infarction, diabetes mellitus, malignancies and others.^{6,7} Depression may also contribute to the pathogenesis of other diseases, such as late-life depression caused or exacerbated by cerebrovascular disease.⁸ This infers a bidirectional association of depression with medical illness leading to a negative impact on the onset, course, prognosis, and treatment of both conditions.⁹

With scarcity of information available on depression and its association to physical disorders, this real-world observational study was conducted to determine the symptom profile and prevalence of comorbidities in patients with depression in India. The study also intended to understand the prescription patterns of anti-depressants among depression patients attending psychiatric clinics or hospitals in India.

METHODS

Study design

The real-world, retrospective, cross-sectional, observational COSPO-DEP-2 (physical COMorbidity and its impact on Symptom PrOfile of DEPRESSION in Indian setting-2) study was conducted at multiple study centres including hospitals, clinics, and health care institutes in India. Patients were selected based on treating clinician's discretion, and no additional evaluation or investigations were performed during data capture in this study. The patient data was collected by physicians or psychiatrists between April 2021 and March 2022.

Study variables

Patients were selected based on treating physician's or psychiatrist's discretion, and no additional evaluation or investigations were performed during data capture. The demographic parameters included age, gender, marital status, family history of mental disorder, and socioeconomic status variables, which included education, and locality of residence. Disease related variables included frequency of depressive disorders, severity of symptoms as per International Classification of Diseases (ICD)-10 diagnosis, total duration of illness, mode of onset, precipitating event, management approach and prescribed drug(s). Details of associated comorbidities and their management were also documented.

Sample size and statistical analysis

In this real-world study, patients' data was collected retrospectively without any predetermined sample size. The study did not test any hypothesis and only the observations from patient's records were analyzed. The data was collected from various centers across India and appropriate statistical analysis was performed at Lambda Therapeutic Research Ltd., Ahmedabad, India. Demographic and baseline characteristics were summarized using descriptive statistics. Categorical

variables were summarized with frequency and percentage. Continuous variables were summarized with count, mean, and standard deviation. Graphical presentation of data was done using pie chart/bar chart as appropriate. Statistical analyses were performed using SAS[®] version 9.4 (SAS Institute Inc., USA).

Ethics statement

The study was conducted after due approval from ACEAS independent ethics committee, Ahmedabad, India. This was a retrospective study without patient identifiers; hence, the informed consent of patients was not taken.

There was no confidentiality breach of the data during its analysis and interpretation.

RESULTS

Data of 7288 patients with depression from various centres across India between April 2021 and March 2022 were analyzed.

Table 1 provides the demographic details of patients enrolled in this study. The mean (SD) age of the patients was 45.1 (11.9) years. Gender distribution showed that majority of the patients were males (54.2%) while females constituted 45.8% of the population. The mean age was 46 and 44 years for male and female patients, respectively.

The majority (92.7%) of patients were literate, 51% patients were graduate/post-graduate, and 22.5% patients completed high school. The socio-economic distribution revealed that 36.1% patients belonged to middle class, while 30% patients were from upper middle class. More than half (53.1%) of the patients were unemployed, majority of the patients (55.5%) were living in joint family, and almost half of the patients (51.7%) were residing in the urban locations. Around 14.5% of the patients were unmarried and 8.8% patients were divorced or separated.

Family history of mental disorder

Majority (85.14%, n=6205) of the patients did not have any family history of psychiatric disorder, while 14.86% (n=1083) patients had positive family history of psychiatric disorder. In the family history, mood/affective disorder was the most common psychiatric disorder (8.05%, n=587). Other psychiatric disorders were psychotic disorders (6.96%, 507) followed by anxiety disorder, personality disorder and alcoholism.

Proportion of patients according to episode (first episode depression/ recurrent depressive disorder)

More than half (57.3%, n=4179 patients) of the patients presented with first episode of depression, while 42.5% (n=3109) patients had history of recurrent episodes of depression.

Severity of disease

The categorisation of depressed patients according to the severity of depression by ICD-10 classification revealed that 38.9% patients had mild depressive episode, 38% patients had moderate depression and 23.1% patients had severe depression (Table 2). Of 23.1% patients who had severe depression, almost 3/4th (77.6%) patients had concomitant psychotic symptoms.

Table 1: Demographic characteristics of patients.

Parameter	All patients (n=7288)
Age, years, mean (SD)	45.1 (11.9)
Gender, n (%)	
Men	3950 (54.2)
Women	3338 (45.8)
Education status, n (%)	
Illiterate	532 (7.3)
Primary school	1402 (19.2)
High school	1641 (22.5)
Graduate	2842 (39.0)
Post-graduate	871 (12.0)
Socio-economic status, n (%)	
Labourer class	372 (5.1)
Lower middle class	1648 (22.6)
Middle class	2633 (36.1)
Upper middle class	2188 (30.0)
Affluent	447 (6.1)
Employment status, n (%)	
Employed	3421 (46.9)
Unemployed	3867 (53.1)
Type of family, n (%)	
Joint	4045 (55.5)
Nuclear	3243 (44.5)
Locality, n (%)	
Rural	3521 (48.3)
Urban	3767 (51.7)
Marital status, n (%)	
Divorced/separated	638 (8.8)
Married	5591 (76.7)
Single	1059 (14.5)

SD: standard deviation

Duration of depression

The majority (58.3%, n=4251) of patients had the duration of depression between 1 to 6 months, while 26.8% (n=1954) patients had depression for >6 months, and only 14.9% (n=1083) patients had depression for <1 month.

Mode of onset

More than half of the patients with depression (51.71%, n=3769) had acute onset of depression, while others had

subacute (21.39%, n=1559), abrupt (18.44%, n=1344), or insidious (8.45%, n=616) onset of depression symptoms.

Precipitating factor for current episode was not present in about half of the patients (52.55%) with depression, while 47.45% patients with depression were reported to have the presence of some or other precipitating factor.

Comorbid conditions in depression patients

Diabetes was the most common comorbid condition (31.5%) followed by hypertension (26.6%), migraine (24.6%), and chronic pain (16.6%) (Figure 1).

Treatment

Majority of the patients (54%, n=3971) received a combination of pharmacotherapy with psychotherapy for the management of their depression, whereas pharmacotherapy alone was given to 35% (n=2518) and psychotherapy alone to 11% (n=799) of the patients.

Of the 6489 patients who received pharmacotherapy either alone or in combination with psychotherapy, 64% of patients were prescribed >2 drugs for managing their depression.

The most commonly prescribed drug for depression management was escitalopram (57.5%) followed by benzodiazepines (38.7%), sertraline (13.6%), nortriptyline (12.9%), amitriptyline (12.51%), duloxetine (12.5%), fluoxetine (n=12.2%), desvenlafaxine (9.3%), and monoamine oxidase (MAO) inhibitors (6.7%) (Figure 2).

Preference of drugs among depression patients with comorbid conditions

In patients with depression having comorbidities, escitalopram was the most commonly prescribed drug irrespective of the comorbid condition followed by benzodiazepines (BZDs).

After escitalopram and BZDs, the commonly prescribed drugs were sertraline, nortriptyline and fluoxetine in patients with diabetes as comorbidity; sertraline, fluoxetine, and duloxetine in patients with hypertension as comorbidity; amitriptyline, nortriptyline, sertraline in patients with migraine; and duloxetine, nortriptyline and amitriptyline in patients with chronic pain as comorbidity (Figure 3).

Among patients with asthma, after escitalopram and BZDs, sertraline was the next commonly prescribed medication followed by fluoxetine.

Similarly, in stroke patients also, escitalopram and BZDs were followed by sertraline and amitriptyline.

Table 2: Patient distribution as per severity of disease and recurrence.

Patients with depression	First episode depression (n=4179), n (%)	Recurrent depressive disorder (n=3109), n (%)	All patients (n=7288), n (%)
Mild depressive episode with or without somatic syndrome	1885 (45.2)	948 (30.5)	2833 (38.9)
Moderate depressive episode with or without somatic syndrome	1602 (38.3)	1172 (37.7)	2774 (38.0)
Severe depressive episode with psychotic symptoms	159 (3.8)	217 (7.0)	376 (5.2)
Severe depressive episode without psychotic symptoms	533 (12.8)	772 (24.8)	1305 (18.0)

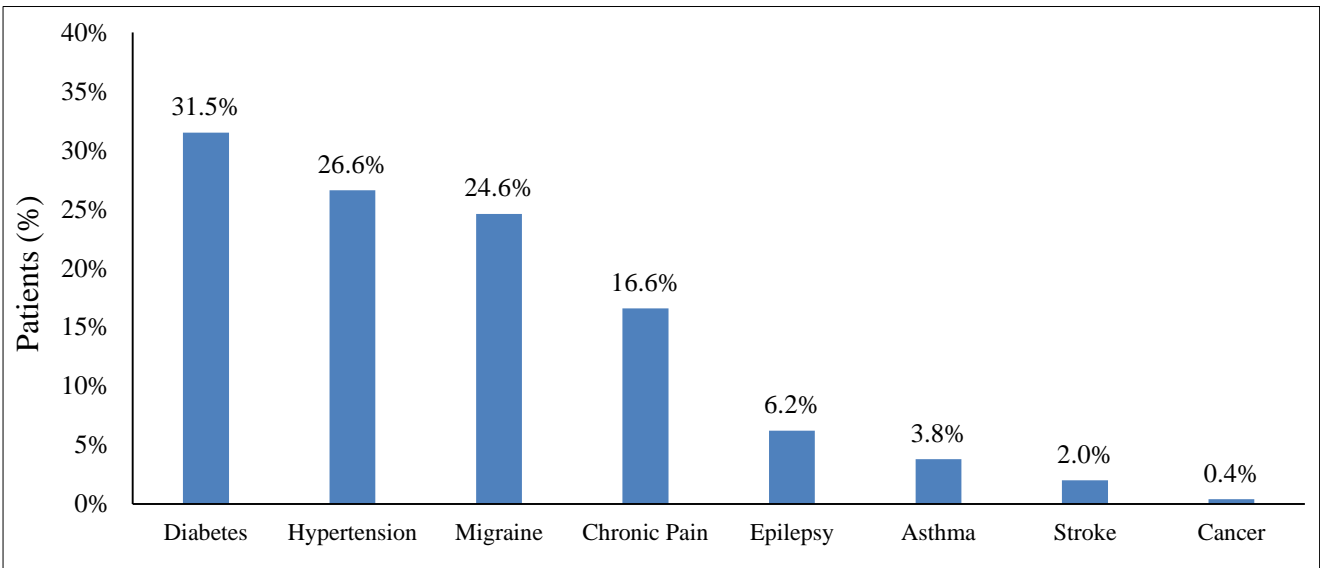


Figure 1: Patients with depression having comorbidities.

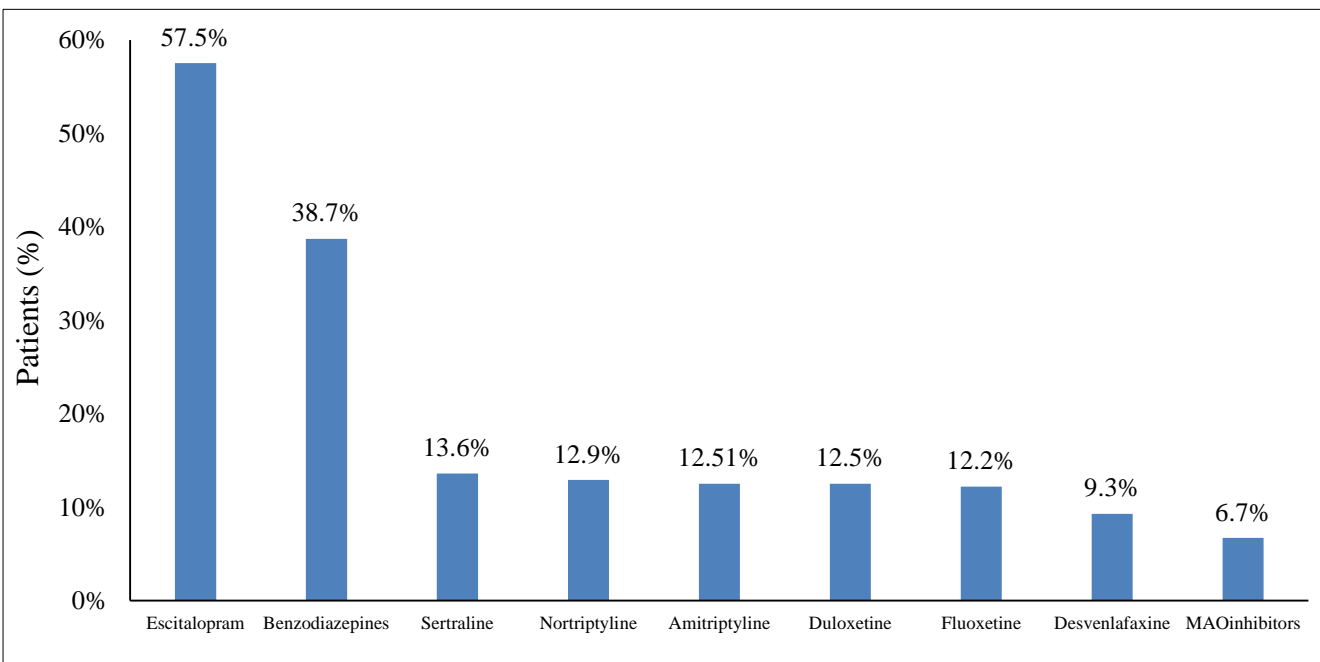


Figure 2: Drugs prescribed for management of depression.

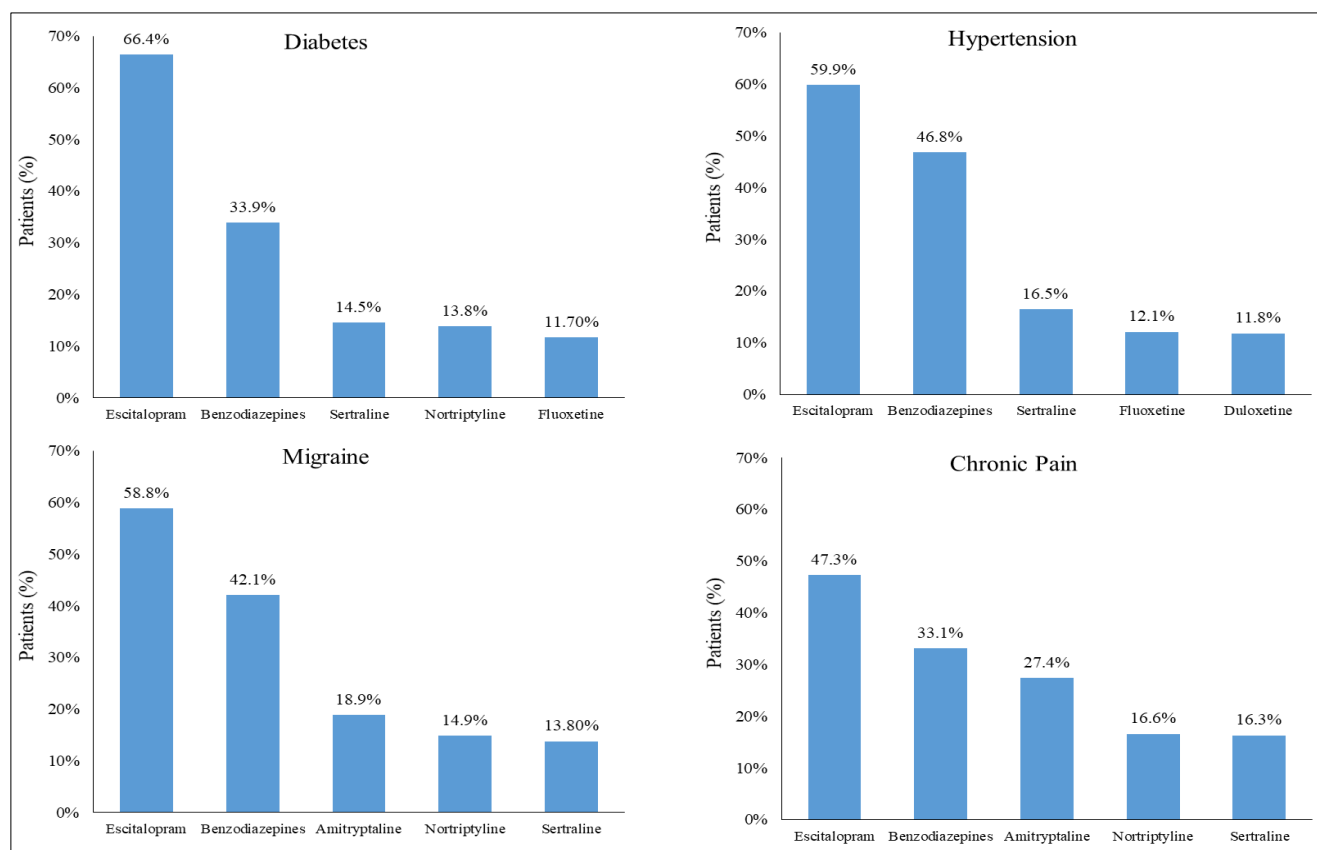


Figure 3: Preference of drugs for depression patients with common comorbid conditions.

DISCUSSION

Depression is common, often chronic and/or recurrent condition associated with significant morbidity and mortality. Data of a total 7488 patients with depression across India were analysed in this real-world observational study. Unlike other studies, the present study reported a higher prevalence of depression in males (54.2%) as compared to females (45.8%).¹⁰ The overall mean (SD) age of the study patients was 45.1 (11.9) years. Majority of the study patients (60.1%) were from middle and upper middle class. A number of studies have shown that economic hardship increases depression among adults in various age groups or age related statuses.¹¹ The contradictory finding in current study may probably be due to more contribution to patient data from private clinics/hospitals where the proportion of low income group patients is comparatively less.

Earlier studies have documented that higher education is associated with a reduced likelihood of depression, majority of the patients (92.7%) in the present study were literate with about 51% patients having graduate to post graduate level of education.¹² However, few studies have reported that people from disadvantaged backgrounds realize a greater protective effect from higher education than people from advantaged backgrounds.¹³ Studies have reported that unemployment can lead to a higher prevalence of depressive symptoms and major depressive

disorder.¹⁴ More than half (53.1%) of depressed patients were unemployed in this study. An association exists between family disruption, particularly divorce, and subsequent depression that is independent of socioeconomic status.¹⁵ This study reported majority (55.5%) of the patients living in a joint family. About 14.5% of the patients were unmarried and 8.8% patients were divorced or separated. The distribution of patients among rural (48.3%) and urban (51.7%) areas was nearly similar as reported by several studies.^{16,17}

More than half (57.3%) of cohort in this study presented with first episode of depression. Severity of depression classified by ICD-10 depicted that 76.9% had mild to moderate depression. About 23.1% patients had an episode of severe depression, of which, almost three forth (77.5%) had concomitant psychotic symptoms as well.

Experiencing negative life events and psychiatric disorders are higher for the severely depressed, psychosomatic and cognitive-emotional classes, compared to the non-depressed class.¹⁸ Treatment outcomes have a significant relationship with severity and duration of index episode.¹⁹ In the present study, 58.3%, had duration of depression between 1-6 months. More than half of the patients (51.71%) had acute onset of the depression, and no precipitating factor was present in about half of the patients.

Diabetes and depression are serious chronic diseases that negatively affect quality of life, increase functional disability, and reduce life expectancy.²⁰ According to few researchers, depression is a consequence of diabetes, perhaps due to the burden of chronic disease or because of the biochemical changes that occur in diabetes.²¹ Another line of researchers, indicate that depressive symptoms are risk factors for the development of diabetes due to decline in health-maintenance behaviours among depressed persons, or biochemical changes associated with depression.^{22,23} In the present study, the most common associated comorbidities with depression included diabetes, hypertension, migraine and chronic pain. Depression in hypertensive patients is associated with poorer health status which includes poor quality of life and treatment compliances, increased medical sources and mortality.²⁴ Migraine and depression often coexist, and their comorbidity may be caused by shared aetiologies.²⁵

Pharmacotherapy and psychotherapy are generally effective treatments for depression.²⁶ In this study, more than half of the patients were prescribed combination of pharmacotherapy and psychotherapy. Although, long-term effects of combined therapy are not well known, as per a meta-analysis, combined therapy results in better outcomes versus antidepressant drugs alone.²⁷ Escitalopram and benzodiazepines were the most commonly prescribed drugs for management of depression in current study. Besides, they were the most prescribed drugs for depression in patients with comorbid conditions. Currently, escitalopram, a selective serotonin-reuptake inhibitor, is an effective first-line option in the management of patients with major depression, including severe forms, and various anxiety disorders.^{28, 29} The multiple metabolic degrading pathways of escitalopram, minimize its drug interactions. It has good tolerance, relatively fast onset of action, and has cost-effectiveness and cost-utility advantages over other antidepressants.³⁰ Although antidepressants are known to be clinically superior to benzodiazepines alone in treating depression, few guidelines suggest the role for benzodiazepines as a combination therapy for a time-limited period if anxiety or insomnia are also present.³¹⁻³³ In comparison to other SSRIs, sertraline inhibits serotonin and dopamine uptake without inhibiting norepinephrine uptake, monoamine oxidase activity or exhibiting anticholinergic activity.^{34,35} Sertraline has minimal inhibitory effects on the major cytochrome P450 (CYP450) enzymes.³⁶ In the present study, sertraline was the third choice for patients with comorbid diabetes, hypertension, asthma, and stroke. Study patients with comorbid migraine, received amitriptyline as the third choice. The 2012 evidence-based guideline update for pharmacologic treatment for episodic migraine prevention in adults, by the American headache society and American Academy of Neurology, endorsed two anti-depressants viz., amitriptyline and venlafaxine for the prevention of migraine.^{37, 38} The presence of depression in chronic pain complicates the afflicted individual's course of illness and adaptation as well.³⁹ Depressed patients with acute or chronic pain tend to rate their pain severity higher than

those without depression.⁴⁰ Since duloxetine simultaneously influences both serotonin and norepinephrine, it exerts some analgesic effect.⁴¹ In the present study, in patients with comorbid chronic pain, duloxetine was the third choice. The strength of this real-world study is the inclusion of patients across the country over a period of one year. However, since treatment outcomes were not included, it limits the study.

CONCLUSION

Depression is common among both genders and more commonly seen among unemployed people and those with family history of depression. The most common associated comorbidities included diabetes, hypertension, migraine and chronic pain. The most prescribed drugs for depression included escitalopram and benzodiazepines. The study findings are expected to assist in better understanding of depression and its management.

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Conflict of interest: Dr. Pragna Patel, Dr. Meera Kacha, Dr. Amit B. Jain, and Dr. Nilanj Dave are employees of Intas Pharmaceuticals Limited, Ahmedabad, Gujarat, India

Ethical approval: The study was approved by the ACEAS Independent Ethics Committee, Ahmedabad, India

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