Original Article

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Prevalence, Severity and Determinants of Depression in Patients with Type 2 Diabetes Mellitus

Internal Medicine Section

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ABSTRACT

Introduction: Patients with Type 2 Diabetes Mellitus (T2DM) are at higher risk to develop depression. Depression in turn adversely affects glycaemic control and increases the risk of diabetes-related complications and mortality. There is a large variation among Indian studies on prevalence of depression in T2DM and associated risk factors.

Aim: To assess the prevalence, severity, and determinants of depression among patients with T2DM.

Materials and Methods: The study was conducted at a Tertiary Care Hospital during February 2018-February 2019, in North-Indian state of Uttarakhand. Study subjects were patients with T2DM, age >18 years. Based on exclusion and inclusion criterias, a total sample of 290 patients were studied. Presence of depression was assessed using Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria. Hamilton Depression Rating Scale (HAM-D) was used to estimate the severity of depression. Unpaired t-test and Mann-Whitney U test were used to compare continuous variables between subjects with and without depression. Chi-Square test was used to analyse categorical data. Binary logistic regression analysis was used to study the association between likelihood of depression and predictor variables.

Results: Among 290 (155 males and 135 females, mean age of all subjects 58.2±11.08 years) study subjects with T2DM, 64 (22.1%) were found to have depression using DSM-5 criteria. Out of these 64 patients with depression, 46 were detected to have mild depression, 14 moderate depression and 4 severe depression using HAM-D scale. Subjects with T2DM and depression had: higher proportion of females (62.5% vs. 42.0%; p-value 0.004); lower literacy level (53.1% vs. 67.3%; p-value 0.037); higher frequency of diabetic retinopathy (85.9% vs. 62.8%; p-value <0.001) and diabetic kidney disease (43.8% vs. 27.4%; p-value 0.013); higher Fasting Plasma Glucose (FPG) (217.7±94.62 vs. 190.0±76.45 mg/dL; p-value 0.040); and lower haemoglobin (10.8±2.49 vs. 11.7±2.37 gm/dL; p-value 0.010) compared to the subjects without depression. On binary logistic regression analysis, female gender (OR 2.457, 95% CI 1.368-4.413, p-value 0.003) and diabetic retinopathy (OR 3.842, 95% CI 1.788-8.255, p-value 0.001) remained significantly associated with likelihood of depression.

Conclusion: Depression was present in one-fifth of the study subjects with T2DM. Majority of them had mild depression. Female gender and diabetic retinopathy were associated with increased likelihood of depression.

Keywords: Diagnostic and statistical manual of mental disorders-fifth edition, Diabetic kidney disease, Diabetic retinopathy, Hamilton depression rating scale

INTRODUCTION

Diabetes Mellitus (DM) is a major public health challenge worldwide [1]. According to recent estimates, DM affects 7.3% of the Indian population [2]. Patients with DM are more susceptible to develop mental health problems. Depression is twice as common in patients with DM as in general population [3]. Interestingly, diabetes and depression share a unique two-way relationship.

Diabetes may place a person at higher risk of developing depression due to: (i) impaired quality of life; (ii) financial stress of managing a chronic progressive illness; (iii) disabilities arising out of micro and macrovascular diabetic complications; and (iv) diabetes related neurohormonal and neurotransmitter changes in brain [3].

On the other hand, data from the prospective studies indicate that depression increases the risk of development of diabetes [4,5]. Among patients with established DM, depression is associated with increased blood glucose levels [6]. Patients with depression may find it difficult to achieve glycaemic control due to reduced motivation level and self-care behaviour, diminished physical activity, poor adherence to the medical treatment, and hormonal changes [3,7]. Depression is also associated with increased risk of diabetes-related complications and mortality [8,9]. Thus, depression may act as an impediment in comprehensive management of DM.

Data from randomised controlled trials suggest that treatment of depression using cognitive behaviour therapy or anti-depressants in patients with DM may lead to improvement in glycaemic control [10,11].

Studies from India have found prevalence of depression widely ranging from 8-84% among patients with T2DM [12-24]. In addition there has been considerable variation among these studies regarding risk factors for depression in subjects with T2DM. The present study aimed to determine prevalence of depression, its severity and risk factors among patients with T2DM, attending a tertiary care teaching hospital in state of Uttarakhand, India.

MATERIALS AND METHODS

This study was a cross-sectional observational study with convenient sampling design. The study was conducted during February 2018-February 2019 in the Department of General Medicine at a Tertiary Care Teaching Hospital in the state of Uttarakhand, India. The study protocol was approved by the Institutional Ethics Committee (SRHU/Reg/Int/2018-285). Written informed consent was obtained from the study subjects.

The calculated sample size was 288, selecting 95% confidence interval, precision of 5% and expected prevalence of 25% based on earlier studies [13,14].

Inclusion criteria: Outpatients and Inpatients with T2DM, age more than 18 years.

Exclusion criteria: (i) patients previously diagnosed with major psychiatric illness or receiving antidepressants; (ii) patients with altered sensorium or critically ill patients; (iii) pregnancy; and (iv) patients diagnosed with HIV infection, tuberculosis, chronic liver disease or malignancy.

The DSM-5 criteria were used to diagnose clinical depression in study subjects [25]. Briefly, the study subjects were assessed for the presence of eight symptoms described in DSM-5 criteria that suggest the presence of clinical depression. To diagnose an individual as having clinical depression, he or she must be experiencing at least five out of these eight symptoms during the same 2-week period and at least one of the symptoms should be either depressed mood or loss of interest in almost all activities. In addition, these symptoms should result in significant distress in social, occupation or other important areas of functioning. Besides this, episode of depression should not be attributable to effects of a substance or other medical or psychiatric disorder.

Study subjects diagnosed to have depression according to DSM-5 criteria were further evaluated for severity of depression. Severity of depression was assessed using HAM-D [26]. HAM-D consisted of 17 items each of which carried scores ranging from 0 to 2 (eight items) or 0 to 4 (nine items). Study subjects with depression were categorised according to the total score obtained on HAM-D as follows: (i) mild depression=8-13; (ii) moderate depression=14-18; (iii) severe depression=19-22; and (iv) very severe depression ≥23.

FPG, Post-Prandial Plasma Glucose (PPG), glycated haemoglobin (HbA1c), serum creatinine and qualitative urine protein tests were performed in NABL (National Accreditation Board for Testing and Calibration Laboratories) certified laboratory. HbA1c assay was performed using Boronate affinity chromatography method. Plasma glucose and serum creatinine were measured using enzymatic hexokinase method and alkaline kinetic picrate method, respectively on UniCel DxC auto-analyser. Dipstick test for urine protein was performed using UroColor Uristix®. All subjects were evaluated by Ophthalmologist for presence of diabetic retinopathy. Patients were diagnosed to have diabetic retinopathy when specific lesions were detected at dilated fundoscopy. Patients were classified to have diabetic kidney disease if estimated glomerular filtration rate using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was less than 60 mL per minute per 1.73 square meter of body surface area and urine dipstick examination was positive for albuminuria.

STATISTICAL ANALYSIS

The data was collected and entered in MS Excel 2010 spread sheet. Statistical analysis was performed using IBM® SPSS® Statistics Version 22. Continuous data was compared between 2 groups using unpaired t-test (parametric data) and Mann-Whitney U test (non-parametric data). Categorical data was analysed using Chi-Square test. The association between likelihood of depression and predictor variables was examined using binary logistic regression analysis.

RESULTS

The study included two hundred and ninety subjects with T2DM. Age of the study subjects was 58.2±11.08 years (range=28-89 years). One hundred and fifty-five subjects (53.4%) were males and 135 (46.6%) were females. Socio-demographic and clinical parameters of the study subjects are shown in [Table/Fig-1,2], respectively.

Prevalence and severity of depression: Sixty-four (22.1%) among 290 study subjects were found to have depression using DSM-5 criteria. Patients with depression (n=64) were further classified into mild, moderate and severe depression using HAM-D. Among 64 patients with T2DM and depression, 46 (71.9%) were found to have mild depression, 14 (21.9%) with moderate depression and 4 (6.3%) with severe depression [Table/Fig-3]. None of the study subjects was detected to have very severe depression.

Variable	Results, n (%) or (Mean±SD)
Age (years)	58.2±11.08
Gender (male: female)	155 (53.4%): 135 (46.6%)
Marital status (married: *single)	269 (92.8%): 21 (7.2%)
Type of family (joint: nuclear)	178 (61.4%): 112 (38.6 %)
Smoking	76 (26.2%)
Alcohol consumption	34 (11.7%)
Education	
Illiterate	104 (35.9%)
12th standard	134 (46.2%)
Graduation and higher education	52 (17.9%)
Occupation	
Professional work	39 (13.4%)
Skilled workers	27 (9.3%)
Unskilled workers	68 (23.4%)
Housewives	119 (41.0%)
Retired from work	37 (12.8%)
Per capita income (rupees) mean±SD	72000±84000

[Table/Fig-1]: Socio-demographic parameters of the study subjects with T2DM (n=290).
Continuous variables are expressed as mean±SD except per capita income which is expressed as median±inter-quartile range. Categorical variables are expressed as frequencies (percentage). *Single subjects include those who were unmarried/divorced/widow/widower

Variable	Results, n (%) or (Mean±SD)
Height (cm)	160.1±8.47
Weight (kg)	62.6±10.18
Body mass index (BMI) (kg/sqm) mean±SD	24.5±3.77
Family history of DM	56 (19.3%)
Duration of DM (years)	9.6±7.36
Hypertension	132 (45.5%)
Coronary artery disease	48 (16.6%)
Diabetic retinopathy	197 (67.9 %)
Diabetic kidney disease	90 (31.0 %)
Insulin therapy	60 (20.7 %)
FPG (mg/dL)	196.8±81.40
PPG (mg/dL)	245.0±91.35
HbA1c (%)	8.9±2.34
Haemoglobin (gm/dL)	11.5±2.43
Serum creatinine (mg/dL)	1.1±1.4

[Table/Fig-2]: Clinical parameters of the study subjects with T2DM (n=290).
Continuous variables are expressed as mean±SD except for serum creatinine which is expressed as median±interquartile range. Categorical variables are expressed as frequencies (percentage); BMI: Body mass index; DM: Diabetes mellitus; T2DM: Type 2 diabetes mellitus; FPG: Fasting plasma glucose; PPG: Post-prandial glucose; HbA1c: Haemoglobin A1c

Comparison of demographic and clinical parameters between subjects with T2DM with and without depression: Subjects with T2DM and depression had higher proportion of females (62.5% vs. 42.0%; p-value 0.004), lower literacy level (53.1% vs. 67.3%; p-value 0.037), higher frequency of diabetic retinopathy (85.9% vs. 62.8%; p-value <0.001) and diabetic kidney disease (43.8% vs.27.4%; p-value 0.013), higher FPG (217.7±94.62 vs. 190.0±76.45 mg/dL; p-value 0.040) and lower haemoglobin (10.8±2.49 vs. 11.7±2.37 gm/dL; p-value 0.010) compared to the subjects without depression [Table/Fig-3,4]. The study did not find significant difference between two groups with respect to occupation of the study subjects (p-value 0.076).

On binary logistic regression analysis, only female gender (OR 2.457, 95% CI 1.368-4.413, p-value 0.003) and diabetic retinopathy (OR

Variable	With depression (n=64)	Without depression (n=226)	p-value
Age (years)	60.1±10.30	57.6±11.25	0.107
Gender (male:female)	24:40	131:95	**0.004**
Marital status (married: *single)	56:8	213:13	0.066
Type of family (joint:nuclear)	46:18	132:94	0.051
Smoking	15 (23.4%)	61 (27.0%)	0.568
Alcohol consumption	6 (9.4%)	28 (12.4%)	0.508
Literate	34 (53.1%)	152 (67.3%)	**0.037**
Per capita income (rupees)	80714±84000	72000±84429	0.809

[Table/Fig-3]: Comparison of socio-demographic variables between T2DM subjects with and without depression.
*Single subjects include those who were unmarried/divorced/widow/widower. Unpaired t-test was used to compare continuous variables between two groups except for the per capita income which was compared using Mann-Whitney U test. Chi-Square test was used to compare the categorical variables between two groups

Variable	With depression (n=64)	Without depression (n=226)	p-value
BMI (kg/sqm)	24.4±4.14	24.5±3.67	0.870
Duration of DM (years)	10.8±7.14	9.2±7.40	0.129
Family history of T2DM	12 (18.8%)	44 (19.5%)	0.898
Hypertension	33 (51.6%)	99 (43.8%)	0.271
Coronary artery disease	15 (23.4%)	33 (14.6%)	0.093
Diabetic retinopathy	55 (85.9 %)	142 (62.8%)	**<0.001**
Diabetic kidney disease	28 (43.8 %)	62 (27.4%)	**0.013**
Insulin therapy	16 (25.0%)	44 (19.5%)	0.335
FPG (mg/dL)	217.7±94.62	190.0±76.45	**0.040**
PPG (mg/dL)	264.4±112.36	239.5±83.95	0.104
HbA1c %	9.1±2.50	8.9±2.30	0.548
Haemoglobin (gm/dL)	10.8±2.49	11.7±2.37	**0.010**

[Table/Fig-4]: Comparison of clinical parameters between T2DM study subjects with and without depression.
Continuous variables are expressed as mean±SD. Categorical variables are expressed as frequencies (percentage). Unpaired t-test was used to compare continuous variables between two groups whereas the categorical variables were compared using Chi-Square test. BMI: Body mass index; DM: Diabetes mellitus; T2DM: Type 2 diabetes mellitus; FPG: Fasting plasma glucose; PPG: Post-prandial glucose; HbA1c: Haemoglobin A1c

3.842, 95% CI 1.788-8.255, p-value 0.001) remained significantly associated with likelihood of depression.

Factors associated with severity of depression: Subjects with mild depression had higher per capita income compared to those with moderate and severe depression (88636±80000 vs. 36000±45171 rupees, p-value 0.013). Both the groups were comparable with respect to rest of the demographic and clinical parameters.

DISCUSSION

Co-occurrence of T2DM and depression may pose significant challenge for management of both the conditions. The present study assessed the prevalence, severity and associated factors of depression.

The mean age of the study subjects was 58.2 years, similar to the earlier published studies from India [15-24]. This observation may be a reflection of the fact that in India, highest prevalence of DM is observed in age-group of 55 years and above [2]. The average duration of diabetes in study cohort was nine-and-half years similar to the studies by Raval A et al., Balhara YP and Sagar R, and Siddiqui S et al., [15,16,20]. Forty-six percent of the study subjects had hypertension, whereas diabetic retinopathy and diabetic kidney disease were detected in two-thirds and one-third of the study subjects, respectively.

Using DSM-5 criteria, 64 (22.1 %) of the 290 study subjects with T2DM were found to have depression. There is wide variation in prevalence of depression among patients with T2DM, reported from India. According to a recent systematic review, Indian studies have found prevalence of depression ranging from 8-84% in patients with T2DM [12]. Variables such as: (i) community vs. hospital-based study; (ii) methods adopted to diagnose depression; (iii) socio-economic background of the study subjects; and (iv) diabetes-related factors (duration, glycaemic control, complications), may have contributed to such large difference in prevalence of depression observed in Indian studies. The prevalence of depression in patients with T2DM detected in the present study is similar to that seen by Poongothai S et al., Guruprasad KG et al., and Rajput R et al., [13,14,23]. In a community-based study in Chennai, Poongothai S et al., found depression in 23.4% of the subjects with T2DM. Guruprasad KG et al., from Karnataka and Rajput R et al., from Haryana, in hospital-based studies, detected depression in approximately one-fourth of their study cohorts with T2DM [13,14,23].

In this study, subjects with T2DM and depression were observed to have: (i) higher proportion of females; (ii) lower literacy rate; (iii) higher frequency of diabetic retinopathy and diabetic kidney disease; (iv) higher FPG; and (v) lower haemoglobin levels compared to those without depression. On binary logistic regression analysis, the likelihood of depression remained strongly associated with female gender and diabetic retinopathy.

Association between depression and female gender among patients with T2DM has also been observed previously [19,22,24]. Adverse experiences during childhood, higher sensitivity towards life-events, hormonal milieu, lesser family and social support may contribute to higher prevalence of depression in females [27]. Lower literacy rate observed in subjects with T2DM and depression, has also been reported by Guruprasad KG et al., and Victor R et al., [14,22]. A meta-analysis by Lorant V et al., also showed association between depression and lower education level [28].

Higher frequency of diabetic retinopathy and diabetic kidney disease among subjects with depression as seen in this study, has also been reported in earlier studies from India [13,15,17,23]. de Groot M et al., in a meta-analysis of 27 studies involving 5374 subjects, also observed significant association between depressive symptoms and diabetic complications [8]. Diabetic micro and macrovascular complications may increase functional disability, impair quality of life, enhance pill load, increase frequency of investigations, hospital visits, and financial burden, and create more dependence on family members, thus adding to the risk of depression. On the other hand, patients with depression, due to reduced adherence to medical treatment [3,29] and sub-optimal glycaemic control [6], may become more prone to develop diabetes-related complications.

In the present study, patients with depression had higher FPG as compared to those without depression. Similar findings were reported by Bajaj S et al., and Siddiqui S et al., [17,20]. In a meta-analysis of 24 studies, Lustman PJ et al., have also observed significant association between depression and hyperglycaemia [6]. Poor glycaemic control in patients with T2DM and depression has been attributed to lesser compliance to the anti-diabetic medications and alterations in hypothalamus-pituitary-adrenal axis [3,7].

Subjects with T2DM and depression were found to have lower haemoglobin values compared to those without depression. Association between depression and anemia has been reported in a large cohort of otherwise healthy individuals previously [30]. However, in the present study, higher proportion of females in the group with depression might have contributed to the lower haemoglobin levels in this group.

Among 64 subjects with T2DM and depression, 46 (71.9%), 14 (21.9%) and 4 (6.3%) subjects were having mild, moderate and severe depression, respectively. Patients with moderate and severe depression had lower per capita income compared to those with mild depression. Joseph N et al., and Sharma P et al., from India have previously reported association between depression and lower socio-economic status in patients with T2DM [19,31]. Expenditure incurred

upon anti-diabetic medications, diabetes-related complications and co-morbid conditions is substantial. A large component of this expense needs to be borne by patient himself. Lower per-capita income in subjects with DM and depression may thus lead to added psychological stress and higher severity of depression.

Limitation(s)

Being a hospital-based study with convenient sampling design, the observations cannot be extrapolated to the general population. Hospital-based studies are also susceptible to selection bias as sick patients and those with complications are more likely to visit tertiary care hospital. Second, this is a cross-sectional study; thus, causal link cannot be established between depression and associated variables.

CONCLUSION(S)

The present study from a tertiary care teaching hospital in the state of Uttarakhand found depression in approximately one-fourth of the study subjects with T2DM. Female gender and diabetic retinopathy are significant risk factors for depression in patients with T2DM. Lower per capita income is associated with higher severity of depression. Identification and treatment of depression in patients with T2DM may help to improve their quality of life, sense of psycho-social wellbeing, glycaemic control and may also contribute in prevention of diabetes related complications.

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