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Prevalence & determinants of depression in type 2 diabetes patients in a tertiary care centre

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***Background & objectives*: Depression is common among people with diabetes and it is associated with poor outcomes. This study was carried out to investigate the prevalence and determinants of depression in patients with established type 2 diabetes (T2DM) attending a tertiary care hospital in north India.**

***Methods*: Patients with established T2DM were evaluated for depression by administering the nine-item PHQ-9 (Hindi version). Binary logistic regression model was used to examine association between predictor variables and risk of depression. Results were expressed as odds ratio and 95 per cent confidence interval. Cronbach alpha was calculated to assess internal consistency of PHQ-9.**

***Results*: Patients with T2DM (n=300) were evaluated [147(49%) male and 153(51%) female]. The median duration of diabetes (IQ) was 8(4-13) yrs. Of the study patients, 68 (23%) met the criteria for major depression, 54 (18%) for moderate depression and the remaining 178 (59%) had no clinically significant depression. Depression was strongly associated with age >54 yr (OR 1.26, 95% CI 1.02-1.67; *P*<0.05), central obesity (OR 1.34, 95% CI 1.04-1.64; *P*<0.001), neuropathy (OR 1.94, 95% CI 1.03-3.66; *P*=0.002), nephropathy (OR 1.81, 95% CI 1.02-3.21; *P*=0.041), peripheral vascular disease (OR 6.08, 95% CI 1.07-34.6; *P*=0.042), diabetic foot disease (OR 2.32, 95% CI 1.06-5.86; *P*<0.001) and pill burden (>4) (OR 1.27, 95%CI 1.01-1.44; *P*=0.035). However, the likelihood of depression was not significant with duration of diabetes and insulin use.**

***Interpretation & conclusion*: This study showed high prevalence of depression in patients with T2DM. The risk factors for depression were age, central obesity, diabetic complications particularly neuropathy and diabetic foot disease and increased pill burden.**

Key words Depression - diabetic complications - pill burden - T2DM

Diabetes is a chronic disease which affects virtually every organ in the human system. The World Health Organization projected that 300 million people will suffer from diabetes by 2025[1]. India has the largest number of diabetic population in the world and it is expected that there will be 69.9 million diabetic populations in India by 2025[1].

Depression is common among people with diabetes[2], and it is associated with worse diabetes outcomes[3,4]. The prevalence of depression is higher in patients with diabetes who have long-term complications[4,5]. Compared with patients with diabetes alone, patients with depression and diabetes have been shown to have poorer self-management and poor adherence to antidiabetic, lipid-lowering and antihypertensive treatment[6]. They are more likely to have higher cardiovascular risk factors like smoking, obesity, sedentary lifestyle, and uncontrolled hyperglycaemia[5]. Depression may be an important barrier to effective diabetes management. Patients with depression and diabetes are more likely to have higher macrovascular and microvascular complications[4] and higher mortality rates[7].

While depression may contribute to poor diabetes-related outcomes, diabetes and its complications may also contribute to poor depression outcomes[6,8,9]. The available data regarding the prevalence of depression in type 2 diabetes (T2DM) patients in India are limited. We investigated the prevalence and determinants of depression in patients with T2DM attending a tertiary care hospital in north India, and its relationship with glycaemic control, diabetic complications, demographic and socio-economic factors was examined.

Material & Methods

This cross-sectional study was carried out from June 2008 to March 2009 at the Nehru Hospital, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh. All consecutive patients with T2DM attending the Endocrinology Outpatient Clinic in Nehru Hospital, were evaluated. Informed and written consent was obtained from all the participants. The study protocol was approved by the Institute's Ethics Committee. Patients with established T2DM as defined by American Diabetes Association (ADA 1997) criteria[10] were examined consecutively for depression by PHQ-9 (a subset of the Patients Health Questionnaire)[11]. Further, Social, demographical and clinical variables were also assessed.

Depression was assessed by administering the nine-item PHQ-9, a self report version of PRIME-MD[11] which assesses the presence of major depressive disorder using modified Diagnostic and Statistical Manual, Fourth edition (DSM-IV) criteria. There is good agreement reported between the PHQ diagnosis and those of independent psychiatry health professionals (for the diagnosis of any one or more PHQ disorder, kappa=0.65; overall accuracy, 85%; sensitivity, 75%; specificity, 90%)[12,13]. In this study Hindi version of PHQ-9 was used. It has been validated in Indian population and is considered to be reliable tool for diagnosis of depression[14]. The PHQ-9 is a dual instrument that is used to establish a provisional depressive disorder as well as it provides a symptoms severity score. For the diagnosis of depression, we defined clinical significant depression as: a PHQ-9 score of 8-9 as minor depression, a PHQ-9 score of 10 or greater as moderate depression; a score of 15 or more and one of the two cardinal symptoms (either depressed mood or anhedonia) as definite major depression[12,13]. Patients who did not understand the questionnaires or deaf or not able to answer (*i.e.*, unconscious) or on wheel chair were excluded.

Anthropometric measurements: Standing body height (to the nearest 0.1 cm) was measured with a commercial stadiometer. A digital scale, with an accuracy of ± 100 g, was used to measure body weight (BW). The waist circumference (WC) was measured in a horizontal plane, midway between the inferior margin of the ribs and the superior border of the iliac crest. The measurements were taken thrice and the mean was taken as the final reading. Body mass index (BMI) (kg/m^2) was calculated by dividing weight (in kilograms) by the square of height (in meters), as a measure of total adiposity.

Systolic and diastolic blood pressure (SBP & DBP) was measured twice at an interval of 3 min in the sitting position after a 15 min rest, and the mean was taken. Blood samples (3 ml) were drawn after 8-12 h overnight fasting for the measurement of lipid profile [total cholesterol (TC), high density lipoprotein (HDL) cholesterol, and triglycerides (TG)] and fasting plasma glucose (FPG) levels. Plasma glucose was measured using the glucose oxidase method[15], serum total cholesterol[16] and triglycerides[17] by standard enzymatic procedures and HDL cholesterol[18] by direct assay method.

Neuropathy was evaluated by history and of clinical examination using 10 g monofilament, vibration sense by biothesiometer (VPT at great toe >25 mV were considered significant) and ankle reflex[19]. Incipient nephropathy was diagnosed by Micral test[20] and it was presumed to be present if any two readings out of three of urinary albumin to creatinine ratio were ranging from 30 to 300 µg/mg. Clinical nephropathy was evaluated by the estimation of 24 h urine protein and it was present if urine proteins were more than 500 mg/total volume of urine[21]. Ophthalmologist diagnosed retinopathy by detailed fundus examination and was classified according to Diabetic Retinopathy Study (DRS) and Early Treatment Diabetic Retinopathy Study (ETDRS)[22]. Coronary artery disease (CAD) was diagnosed by history of angina or myocardial infarction or documented by previous treatment records. Interpretation of ECG was recorded as per Minnesota codes. Peripheral vascular disease (PVD) was diagnosed by definitive history of intermittent claudication or if two or more peripheral pulses were absent in both feet. The grading was done according to ankle brachial index (ABI) by Doppler Study [Multi Duplex(R)-II (Huntleigh Diagnostics - UK)]. PVD was diagnosed when ankle brachial index was less than 0.9.

Statistical analysis: Data were reported as the mean ± SD or percentages, for skewed data median (Interquartile range) was reported. Differences in characteristics between participants were tested with unpaired *t* test for normally distributed variables, with the Wilcoxon rank sum test for skewed variables, and with the chi-square test or fisher exact test for categorical variables. The significance level was set at 5 per cent. Binary logistic regression model was used to examine association between predictor variables (as captured by data capturing form) and risk of depression. The main model consists of following predictor variables: demographic variables age, gender, obesity, clinical variables like diabetic complications, blood pressure and duration of disease, *etc*. Results were expressed as odds ratio (OR) and 95 per cent confidence intervals (CI). Cronbach alpha was calculated to assess internal consistency of PHQ-9. All statistical analyses were carried out using Statistical Package for Social Sciences (SSPS) (Version 17.0, USA).

Results & Discussion

A total of 300 T2DM patients including 147 (49%) men and 153 (51%) women were evaluated. The mean age ± SD of patients was 54.2 ± 10 yr. The median (interquartile range) duration of diabetes was 8 (4-13) yr. Among the patients, 205 (68%) were hypertensive and the median duration of hypertension was 3 (0.7-8) yr . Microvascular (85% men vs. 69% women, P<0.001) and macrovascular complications (27% men vs. 13% women, P<0.001), both were higher in men (Table I). Of the patients assessed, 68 (23%) patients fulfilled the criteria for severe depression, 54 (18%) for moderate depression and 178 (59%) patients had no clinically significant depression. Internal consistency of PHQ-9 was evaluated using Cronbach alpha. Cronbach alpha was 0.84 indicating good consistency of this psychometric scale (PHQ-9) in the study population.

This study showed that more than one third of patients with T2DM were ailing from moderate to severe depression. The prevalence of depression in T2DM patients in our study was 41 per cent. The data regarding the prevalence of depression in patients with T2DM from India are scarce. However, studies from USA and UK reported the prevalence of depression in patients with T2DM varying from 30 to 83 per cent[23,24]. A small study from Iran reported 55 per cent prevalence of depression in patients with T2DM[25]. Similarly, a meta analysis by Anderson *et al*[26] identified the prevalence of depression in diabetes ranging from 8 to 61 per cent.

The likelihood of depression was significantly higher with age ≥54 yr (OR 1.26, 95% CI 1.02, 1.67; P<0.05). Depression was most strongly associated with monthly income >5000 INR (OR 1.22, 95% CI 1.03-1.41; P<0.001), greater waist circumference (OR 1.34, 95% CI 1.04-1.64; P<0.001), neuropathy (OR 1.94, 95% CI 1.03-3.66; P=0.002), nephropathy (OR 1.81, 95% CI 1.02-3.21; P=0.041), peripheral vascular disease (OR 6.08, 95% CI 1.07-34.6; P=0.042), diabetic foot (OR 2.32, 95% CI 1.06-5.86; P<0.001) and pill burden >4 (OR 1.27, 95% CI 1.01-1.44; P=0.035). However, the likelihood of depression was not significant with gender, duration of diabetes, duration of hypertension, rural *vs.* urban residence, education, hyperglycaemia, hypertension, insulin use, retinopathy as well as cerebrovascular disease (Table II).

Advancing age is usually associated with depression as has been shown in earlier studies[5,24] and more so in patients with T2DM, as was also observed in our study. The data regarding the predilection of gender with depression are conflicting[27-29]. Studies from the West have suggested the higher prevalence of depression in women as compared to men[30,31]. The higher prevalence of depression in women is influenced by adverse experiences, sociocultural roles, psychological attributes, biological factors including hormones and poor social support as these are the major determinants for higher prevalence of depression in women. One of the reasons of lack of gender predilection in our study may be due to lesser diabetes related complications in women as compared to men and relatively better social fabric and support. Another important variable which showed strong association with T2DM was central obesity. There is a strong and robust association between obesity and depression as many studies have

Table I. Demographic and clinical characteristics of patients with T2DM

Characteristics	Overall 300 (100%)	Male 147 (49%)	Female 153 (51%)
Age (yr)	54.2 ± 10.0	55.1 ± 9.2	54.4 ± 11.5
DOD (yr)+	8 (4-13)	8 (4-15)	7.5 (4-12)
DHTN (yr)+	3 (0.7-8)	3 (0.5-8)	3 (1-9)
BMI (kg/m^2)+	25.4 (22.3-29.0)	23.9 (21.7-27.1)	26.5 (23.4-31.2)**
Waist (cm)	91.7 ± 12.3	91.3 ± 12.6	92.2 ± 11.8
FPG (mg/dl)+	149 (115-198)	133 (110-177)	156 (118-208)*
PPPG (mg/dl)+	206 (159-265)	200 (154-250)	216 (168-268)
HbA_{1c} (%)	9.0 ± 2.3	8.7 ± 2.1	9.4 ± 2.5
TC (mg/dl)	180.6 ± 50.8	174.7 ± 49.2	187.4 ± 51.9
HDL (mg/dl)	47.8 ± 20.2	47.7 ± 20.6	47.9 ± 19.7
LDL (mg/dl)	101.4 ± 34.5	94.6 ± 33.5	109.0 ± 4.2*
TG (mg/dl)+	177 (148-210)	140 (103-194)	170 (120-239)*
Complications n (%)			
Microvascular	231 (77)	125 (85)	106 (69)**
Complications any			
Neuropathy	194 (65)	112 (76)	82 (54)**
Nephropathy	106 (35)	56 (38)	50 (33)**
Retinopathy	116 (39)	65 (44)	51 (33)**
Non Proliferative	47 (16)	16 (11)	31 (20)**
Proliferative	69 (23)	49 (33)	20 (13)**
Macrovascular	60 (20)	40 (27)	20 (13)**
Complications any			
CAD	31 (10)	19 (13)	12 (8)**
PVD	13 (4)	10 (7)	3 (2)*
Stroke	7 (2)	5 (3)	2 (1)**
Diabetic foot	21 (7)	18 (12)	3 (2)
Amputation	10 (3)	10 (7)	0 (0)**

P *<0.05, **<0.001 compared to male. Values are mean ± SD. +median (interquartile range)
DOD, duration of diabetes; DHTN, duration of hypertension; BMI, body mass index; CAD, coronary artery disease; PVD, peripheral vascular disease

reported earlier[5,32,33]. Altered body image associated with obesity and co-morbidities further perpetuate the depression. The increasing incidence of T2DM in part, is due to increase in prevalence of obesity therefore obesity, depression and diabetes make it vicious in genesis of disease and poses a challenge in management as well.

There are conflicting reports regarding the association between glycaemic control and depression[3,5,26]. Poor glycaemic control may result in depression and *vice versa* depression may result in poor glycaemic control. However, in our study there was no difference in HbA_{1c} level in patients with and without depression. As expected the number of prescribed medicines had a bearing on patients' behaviour and in our study a strong association between depression and pill burden was seen similar to literature[5].

The DM complications strongly influence the outcome and both micro- and macrovascular complications were observed associated with higher prevalence of depression particularly neuropathy, nephropathy and diabetic foot disease. Similar to our findings weak association with retinopathy was reported by Nailboff and Rosenthal[34]. Association of diabetic foot disease showed a strong association with depression irrespective of aetiology, whether it was neuropathic or neuroischemic foot disease. This happens because patients become invalid because of foot disease, treatment cost, prolonged hospital stay and subsequently poor rehabilitation make it worst among all the diabetic complications. The limitations of this study included its cross-sectional nature, hence, causal relationships between depression and variables could not be assumed, and small sample size.

Table II. Binary logistic regression analyses showing risk factors associated with depression in T2DM patients

Risk factors	Odds ratio (95% CI)	*P* value
Age (≤54 vs. >54 yr)	1.26 (1.02-1.67)	<0.05
Gender (Male *vs*. Female)	1.11 (0.63-1.95)	0.70
Duration of diabetes (≤9 *vs*. >9 yr)	1.03 (0.79-1.34)	0.23
Duration of hypertension (≤3 *vs*. >3 yr)	0.87 (0.67-1.07)	0.56
Area of residence (Rural *vs*. Urban)	0.76 (0.44-1.34)	0.35
Income (≤5000 *vs*. >5000 INR/month)	1.22 (1.03-1.41)	<0.001
Education (literate *vs*. illiterate)	1.12 (0.93-1.46)	0.07
BMI (≤25 *vs*. >25 kg/m^2)	1.21 (0.98-1.35)	0.05
Waist*	1.34 (1.04-1.64)	<0.001
HbA$_{1c}$ (≤7 *vs*. >7 %)	1.82 (0.92-3.12)	0.09
SBP (≤130 *vs*. > 130 mmHg)	1.23 (0.89-1.45)	0.35
DBP (≤80 *vs*. >80 mmHg)	1.01 (0.99-1.03)	0.24
Neuropathy	1.94 (1.03-3.66)	0.002
Nephropathy	1.81 (1.02-3.21)	0.041
Retinopathy	1.18 (0.78-1.79)	0.43
Microvascular complications any	2.39 (1.14-5.04)	0.022
CAD	2.07 (0.95-4.51)	0.066
PVD	6.08 (1.07-34.6)	0.042
CVA	1.71 (0.28-10.5)	0.561
Diabetic foot	2.32 (1.06-5.86)	<0.001
Macrovascular complications any	2.27 (1.20-4.30)	0.012
Dyslipidaemia**	0.57 (0.18-1.85)	0.355
Insulin use	1.08 (0.60-1.95)	0.796
Number of prescribed medicine (≤4 *vs*.>4)	1.27 (1.01-1.44)	0.035

*Waist (for male ≤ 80 *vs*.>80 cm and female ≤90 *vs*. >90 cm, sex adjusted odds ratio was calculated); **Dyslipidaemia is defined as TC and TG >150 mg/dl or LDL >100 mg/dl or HDL <40 mg/dl for male and <50mg/dl for female. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; CAD, coronary artery disease; PVD, peripheral vascular disease; CVA, cerebrovascular accident

In conclusion, our study showed high prevalence of depression in patients with T2DM. The risk factors for depression were age, central obesity, diabetic complications particularly neuropathy and diabetic foot disease and increased pill burden. The depression and diabetes are causally related and deserves attention from clinicians to ensure better management.

***Conflict of interest*:** None.

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