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ORIGINAL PAPER

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Prevalence of depression in Indian patients with type 2 diabetes mellitus and/or hypertension: DEPTH Study

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ABSTRACT

Introduction. Depression, a common psychiatric mood disorder, is a leading cause of disability and a significant contributor to the overall global burden of disease.

Aim. To determine the prevalence of depression in patients with controlled and uncontrolled type-2 diabetes mellitus (T2DM) and/or hypertension (HTN) in India. The association of depression with socio-demographic profile and clinical risk factors was also assessed.

Material and methods. In this cross-sectional epidemiological study, T2DM and/or HTN patients attending outpatient department at tertiary care hospitals and private clinics across 54 cities in India were enrolled. The primary outcome measure was to determine the prevalence of depression in T2DM, HTN and T2DM + HTN patients. Association of depression with patients' demography, socio-economic status, anxiety, and clinically diagnosed insomnia were also investigated.

Results. Of 1829 patients, the prevalence of depression in T2DM, HTN and T2DM+HTN cases were found to be 51.03%, 46.94% and 48.64%, respectively. A higher proportion of patients with uncontrolled T2DM and HTN reported depression (T2DM: 77.64% vs. 22.36%; HTN: 72.49% vs. 27.51%). There was a significant association between anxiety and severity of depression across all indications ($p<0.0001$). Depression was significantly associated with complications in T2DM ($p=0.0001$) and comorbidities in T2DM + HTN ($p=0.0023$) cases.

Conclusion. Depression is highly prevalent and has a direct significant association with various socio-demographic variables and anxiety in Indian patients with T2DM and/or HTN.

Keywords. comorbidity, diabetes, depression, hypertension; prevalence, type 2 diabetes mellitus

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Introduction

Depression, a common psychiatric mood disorder, is a leading cause of disability and a significant contributor to the overall global burden of disease. Worldwide, it affects around 350 million people with a lifetime risk of 7%.[1] It is estimated that by 2020, depression is projected to increase up to 5.7% of the total disease burden and would be the second leading cause of disability-adjusted life years.[2] In India, approximately 57 million people are affected by depression which contributes approximately 18% of the global estimate.[3] Multiple risk factors such as stressful life events, social or financial stresses, cultural and environmental factors, family history or enduring medical conditions play a critical role in the development of depression.

There is enough compelling evidence to demonstrate the strong bidirectional relationship between depression and chronic illnesses in the community.[4] Depression is a negative prognostic indicator in many chronic medical diseases. Hypertension (HTN) and type-2 diabetes mellitus (T2DM), two most common non-communicable chronic illnesses, are shown to serve as a risk factor for depression.[5] Data from previous studies indicate depression as a comorbidity in approximately 39-41% of T2DM and 15-40.1% of HTN patients.[6-10] The risk of depression was 1.8 times higher in diabetics compared to non-diabetics.[11] Major depression, also termed as major depressive disorder, was reported in one of eight individuals with diabetes, while one fifth may have a less severe form of depressive symptoms.[12]

Type-2 diabetes and HTN often co-exist due to substantial overlap with respect to their etiology, disease mechanisms and complications including microvascular and macrovascular disorders.[13] In the US, HTN occurs in approximately 50% to 80% of patients with T2DM, while in India, around 20.6% patients were co-existent with both diseases.[14] Both T2DM and HTN patients are more susceptible to psychological distress, especially depression, which may further lead to poor self-management and treatment compliance, alterations in behavioral, dietary and lifestyle habits, and escalation in the rate of morbidity and mortality.[15-25] This intermingling of the symptoms of diabetes and depression, termed as "diapression", needs to be addressed in an integrated manner to improve patient care.[12] In addition to depression, anxiety also tends to affect the outcome of these two diseases.[26] The American Diabetes Association (ADA) and the International Diabetes Federation recommends regular screening for depression in diabetics.[25,27] Furthermore, ADA recommends annual screening of depression in all patients with diabetes, particularly in those with a self-reported history.[27]

In view of the availability of limited data and association of depression with an increased likelihood of T2DM/HTN-related complications, the relationship between T2DM/HTN and depression requires careful deliberation. Hence, the present study assessed the prevalence of depression in these patients, given that cases of T2DM, HTN and their co-occurrence are rapidly increasing which may upsurge the overall rate of depression in Indian population. We also investigated the association of depression with socio-demographic factors, anxiety, and clinically diagnosed insomnia.

Material and methods

Patient and Setting

This was a cross-sectional, epidemiological, multi-centric study. Patients (between 18-60 years, both inclusive), with documented history of T2DM and/or HTN since ≥ 5 years, attending the outpatient department of a tertiary care set-up/private clinics were enrolled between May to Oct 2017 across 54 cities in India. This study recruited controlled and uncontrolled T2DM and HTN patients in the ratio of 30:70 within each primary disease group. Patients diagnosed with any other psychiatric disorders, alcohol dependence or drug abuse, severe cardiac, hepatic, neurological and renal diseases were excluded from the study. Additionally, pregnant or lactating women, patients with a history of any clinical evidence of malignancies, exacerbation of chronic illnesses, severe and acute infections, complicated infections or participation in any other intervention trial within 30 days prior to screening were also excluded from the study.

The study protocol was approved by Conscience independent ethics committee, Ahmedabad, India. The study was conducted in accordance with the principles of Declaration of Helsinki, International Conference on Harmonization Good Clinical Practice (ICHGCP) guidelines, and Indian regulatory guidelines (Indian Council of Medical Research and Indian GCP guidelines). All patients provided written consent in the patient authorization form to participate in the study.

Survey Method and Data Collection

Patients meeting the eligibility criteria were enrolled and a unique identification number was assigned to each patient. The demographic details, socioeconomic status (based on modified Kuppuswamy's scale)[28], and family history of patients were recorded at the day of enrolment. The duration and complications of T2DM and/or HTN, associated comorbidities and related complications, physical examination, vital signs, laboratory details (if available) were also recorded. Details of clinically diagnosed insomnia based on the past medical records and concomitant medications were captured. Study assessment tools like Patient Health Questionnaire-9 scale (PHQ-9) and Generalized Anxiety Disorder 7-item (GAD-7) (defined under "Study Assessment Tools") were administered to assess depression and anx-

iety, respectively. All the study-related observations were documented in case report form by the investigator or his/her qualified designee. The study monitors ensured that the data is complete and genuine and the patient's safety and rights are well-protected.

Study Definitions

Diabetic patients with glycosylated hemoglobin (HbA1c) ≥7% or postprandial blood glucose (PPG) ≥180 mg/dL were considered as uncontrolled and those with HbA1c <7% or PPG <180 mg/dL were considered as controlled patients.[27]

A subject's blood pressure was measured once, however, if elevated, a repeat BP was taken 5 min later. Patients with an average systolic BP (SBP) ≥140 mmHg or an average diastolic BP (DBP) ≥90 mmHg were considered as uncontrolled hypertensive patients. Patients with an average SBP <140 mmHg or an average DBP <90 mmHg, based on physician's discretion were considered as controlled hypertensive patients.[29]

Patients were categorized into obese and non-obese category based on their BMIs. A BMI of <17.5 kg/m^2 indicated underweight, 17.5-22.9 kg/m^2 as normal weight, 23-27.9 kg/m^2 as overweight and >28 kg/m^2 as obese (class 1).[30]

Study Assessment Tools

Prime MD PHQ-9: The PHQ-9 is used to screen, monitor, diagnose, and measure the severity of depressive symptoms. The 9-item questionnaire ranges from 0 to 27 and can be scored from 0 (not at all) to 3 (nearly every day). The present study assessed major depressive syndrome and other depressive symptoms in patients.[31] Patients were said to have not categorized depression if the symptoms did not fulfil the criteria of either major depressive syndrome and other depressive symptoms. A score of <5 indicates "no symptoms of depression", score 5-9 as "mild", 10-14 as "moderate depression", 15-19 as "moderately severe depression" and ≥20 as "severe depression".

Generalized Anxiety Disorder (GAD)-7: It is a self-reported questionnaire to identify probable cases of GAD and measure the severity of GAD symptoms. The GAD-7 items included: 1) nervousness; 2) inability to stop worrying; 3) excessive worry; 4) restlessness; 5) difficulty in relaxing; 6) easy irritation; and 7) fear of something awful happening. Response categories were "not at all", "several days", "more than half the days", and "nearly every day", scored as 0, 1, 2, and 3, respectively. The total score of GAD-7 ranges from 0 to 21. A score of 0-4 indicates "no symptoms of anxiety", score 5-9 as "mild anxiety", 10-14 as "moderate anxiety", and 15-21 as "severe anxiety".[32]

Study Outcomes

The primary outcome was to determine the prevalence of depression in patients with T2DM, HTN and both T2DM+HTN (controlled and uncontrolled cases). The other outcome measures were to identify the association between depression and patients' demographic profile, socio-economic status (based on modified Kuppuswamy's scale), lifestyle parameters, anxiety, clinically diagnosed insomnia, co-morbidities and complications.

Statistical Analyses

Assuming 27% prevalence rate of depression in patients with T2DM and HTN, the sample size was estimated to be 936 in both indications to estimate the prevalence rate with 3% error margin and 95% level of significance.[33,34] Descriptive statistics were used in the study. The continuous variables were analyzed by independent Analysis of Variance and categorical variables by Chi-square Test/Fisher exact test at 5% level of significance. All the data were analyzed using Statistical Analysis System (SAS)® version 9.4.

Results

Patient Disposition

A total of 1829 (97.70%), out of 1872 screened patients, completed the study (T2DM: 631 [33.71%]; HTN: 573 [30.61%]; T2DM+HTN: 625 [33.39%]). The remaining 43 (2.30%) patients were screen failures.

Table 1. Demographic details*

Variable	HTN (N=573)	T2DM (N=631)	HTN +T2DM (N=625)	Total (N=1829)
Gender				
Male, n (%)	295 (51.48)	315 (49.92)	319 (51.04)	929 (50.79)
Female, n (%)	278 (48.52)	316 (50.08)	306 (48.96)	900 (49.21)
Age (Years), mean±SD	50.31±8.00	49.95±8.25	53.12±6.51	51.14±7.75
BMI (kg/m^2), mean±SD	27.51±4.65	27.33±4.54	28.05±4.69	27.63±4.63
Marital Status, n (%)				
Married	560 (97.73)	609 (96.51)	614 (98.24)	1783 (97.48)
Single	4 (0.70)	7 (1.11)	5 (0.80)	16 (0.87)
Divorced	1 (0.17)	1 (0.16)	0	2 (0.11)
Widowed	8 (1.40)	14 (2.22)	6 (0.96)	28 (1.53)
Duration of Disease, n (%)				
5-10 years	542 (85.90)	474 (82.72)	475 (76.00)	1491 (81.52)
>10 years	86 (13.63)	93 (16.23)	55 (8.80)	234 (12.79)

* BMI, body mass index; HTN, hypertension; SD, standard deviation; T2DM, type 2 diabetes mellitus

A higher proportion of patients with T2DM and HTN had uncontrolled disease in comparison to controlled disease (T2DM: 77.64% vs. 22.36%; HTN: 72.49% vs. 27.51%). The mean ± SD age and BMI of the overall population were 51.14 ± 7.75 years and 27.63 ±

Table 2. Prevalence of Depression in T2DM, HTN and T2DM+HTN using Prime MD PHQ-9 (Score ≥5)

Depression Diagnosed	T2DM			HTN			T2DM+HTN
	Number (%) of Patients, 95% Confidence Interval						
	Control	Uncontrolled	Total (N=322)	Control	Uncontrolled	Total (N=269)	Total (N=304)
Major Depressive syndrome	6 (1.86), 0.39:3.34	14 (4.35), 2.12:6.58	20 (6.21), 3.57:8.85	8 (2.97), 0.94:5.00	16 (5.95), 3.12:8.77	24 (8.92), 5.52:12.33	52 (17.11), 12.87:21.34
Other Depressive symptoms	16 (4.97), 2.60:7.34	86 (26.71), 21.88:31.54	102 (31.68), 26.60:36.76	25 (9.29), 5.82:12.76	75 (27.88), 22.52:33.24	100 (37.17), 31.40:42.95	95 (31.25), 26.04:36.46
Not Categorized	50 (15.53), 11.57:19.48	150 (46.58), 41.14:52.03	200 (62.11), 56.81:67.41	41 (15.24), 10.95:19.54	104 (38.66), 32.84:44.48	145 (53.90), 47.95:59.86	157 (51.64), 46.03:57.26
Total	**72 (22.36), 17.81:26.91**	**250 (77.64), 73.09:82.19**	**322 (100.00), 100.00:100.00**	**74 (27.51), 22.17:32.85**	**195 (72.49), 67.15:77.83**	**269 (100.00), 100.00:100.00**	**304 (100.00), 100.00:100.00**

Table 3. Depression severity in HTN+T2DM cases

Depression Severity	Number (%) of Patients			
	Control HTN + Control T2DM (N=80)	Control HTN + Uncontrolled T2DM (N=109)	Uncontrolled HTN + Control T2DM (N=119)	Uncontrolled HTN + Uncontrolled T2DM (N=317)
None	51 (63.75)	49 (44.95)	76 (63.87)	145 (45.74)
Mild depression	19 (23.75)	35 (32.11)	33 (27.73)	109 (34.38)
Moderate depression	8 (10.00)	21 (19.27)	9 (7.56)	49 (15.46)
Moderately severe depression	2 (2.50)	4 (3.67)	1 (0.84)	13 (4.10)
Severe depression	0	0	0	1 (0.32)

4.63 kg/m^2, respectively. There was a similar distribution of men (50.79%) and women (49.21%) within the study. A significantly higher proportion of patients had T2DM and/or HTN since 5-10 years in comparison to >10 years (81.52% vs 12.79%, p< 0.0001) (Table 1). Four hundred and twenty-three (23.13%) patients (T2DM: 135; HTN: 161; T2DM+HTN: 127) had a significant family history of T2DM and/or HTN.

Prevalence of Depression

Approximately half (48.9%; 895/1829) of the overall population suffered from depression (score of ≥5 in the MD PHQ-9), including 322 (51.03%) patients with T2DM, 269 (46.94%) patients with HTN and 304 (48.64%) patients with T2DM+HTN. Majority of T2DM and/or HTN patients had not categorized depression. Of the other two categories of depression, a greater proportion of patients had "other depressive symptoms" compared to "major depressive syndrome" across all indications. In overall, a higher proportion of depressive patients with T2DM and HTN had an "uncontrolled" versus "controlled" nature of the disease. No statistically significant association was reported between different categories of depression (major depressive syndrome and other depressive symptoms) and controlled/uncontrolled T2DM or HTN (Table 2). A direct significant association was noted between severity of depression and controlled/uncontrolled T2DM and/or HTN cases (p<0.0001) (Table 3).

Association of Depression with Socio-demographic and Clinical Factors

Demographic profile

There was no significant association between gender and depression in T2DM and/or HTN patients. A significant association was observed between BMI and different types of depression in T2DM (p=0.0015) patients. The higher proportion of patients with T2DM and/or HTN with depression were overweight or obese (class 1). A significant association was reported between age and depression in patients with HTN (p=0.0386) while no such significant association was reported in T2DM or T2DM+HTN cases (Table 4).

Lifestyle parameters

There was a significant association between exercise and depression in T2DM+HTN patients (p=0.0243) but no such association was reported in T2DM and HTN patients. No significant association was reported between physical activity or alcohol consumption and depression. A significant association was reported between smoking habits and depression in patients with T2DM (p=0.0044) and T2DM+HTN (p=0.0169) (Table 4).

Socio-economic Status

There was a significant association between socioeconomic status and depression in patients with T2DM (p=0.0324) and T2DM + HTN (p=0.0006). The higher proportion of patients in the upper middle class reported depression across all indications (T2DM: 45.03%;

Table 4. Association of Depression with independent variables in HTN, T2DM and HTN+T2DM

	T2DM				HTN				T2DM+HTN			
Variable	**1 (N=20)**	**2 (N=102)**	**3 (N=200)**	**Total (N=322)**	**1 (N=24)**	**2 (N=100)**	**3 (N=145)**	**Total (N=269)**	**1 (N=52)**	**2 (N=95)**	**3 (N=157)**	**Total (N=304)**
Gender, n (%)												
Male	14 (4.35)	45 (13.98)	97 (30.12)	156 (48.45)	13 (4.83)	48 (17.84)	65 (24.16)	126 (46.84)	21 (6.91)	49 (16.12)	83 (27.30)	153 (50.33)
Female	6 (1.86)	57 (17.70)	103 (31.99)	166 (51.55)	11 (4.09)	52 (19.33)	80 (29.74)	143 (53.16)	31 (10.20)	46 (15.13)	74 (24.34)	151 (49.67)
Age (Years) Mean±SD	54.05 ±6.79	52.65 ±7.65	51.49 ±7.17	52.01 ±7.32	50.75 ±6.83	53.57 ±7.16	51.37 ±7.19	52.13 ±7.21	53.69 ±6.21	54.38 ±5.69	53.80 ±5.82	53.96 ±5.84
BMI (kg/m²), n (%)												
< 17.5	0	1 (0.31)	1 (0.31)	2 (0.62)	0	0	1 (0.37)	1 (0.37)	0	0	0	0
17.5 – 22.9	5 (1.55)	22 (6.83)	22 (6.83)	49 (15.22)	3 (1.12)	11(4.09)	18 (6.69)	32 (11.90)	2 (0.66)	12 (3.95)	15 (4.93)	29 (9.54)
23.0 – 27.9	7 (2.17)	54 (16.77)	76 (23.60)	137 (42.55)	12 (4.46)	44 (16.36)	70 (26.02)	126 (46.84)	23 (7.57)	46 (15.13)	65 (21.38)	134 (44.08)
>28	8 (2.48)	25 (7.76)	101 (31.37)	134 (41.61)	9 (3.35)	45 (16.73)	56 (20.82)	110 (40.89)	27 (8.88)	37 (12.17)	77 (25.33)	141 (46.38)
Lifestyle parameters, n (%)												
Does the patient exercise regularly												
Yes	3 (0.93)	27 (8.39)	47 (14.60)	77 (23.91)	8 (2.97)	36 (13.38)	34 (12.64)	78 (29.00)	27 (8.88)	36 (11.84)	87 (28.62)	150 (49.34)
No	17 (5.28)	75 (23.29)	153 (47.52)	245 (76.09)	16 (5.95)	64 (23.79)	111 (41.26)	191 (71.00)	25 (8.22)	59 (19.41)	70 (23.03)	154 (50.66)
Brisk walking	3 (0.93)	15 (4.66)	32 (9.94)	50 (15.53)	7 (2.60)	27 (10.04)	23 (8.55)	57 (21.19)	18 (5.92)	26 (8.55)	71 (23.36)	115 (37.83)
Cardio	0	0	1 (0.31)	1 (0.31)	-	-	-	-	1(0.33)	1 (0.33)	0	2 (0.66)
Jogg/running	0	5 (1.55)	9 (2.80)	14 (4.35)	0	5 (1.86)	6 (2.23)	11 (4.09)	2 (0.66)	2 (0.66)	5 (1.64)	9 (2.96)
Swimming	-	-	-	-	0	0	1 (0.37)	1 (0.37)	-	-	-	-
Heavy Weight	-	-	-	-	-	-	-	-	1(0.33)	0	0	1 (0.33)
Yoga	0	8 (2.48)	7 (2.17)	15 (4.66)	0	5 (1.86)	4 (1.49)	9 (3.35)	6 (1.97)	8 (2.63)	18 (5.92)	32 (10.53)
Cervical exercise	-	-	-	-	0	0	1 (0.37)	1 (0.37)	-	-	-	-
Cycling	-	-	-	-	1 (0.37)	0	1 (0.37)	2 (0.74)	0	0	2 (0.66)	2 (0.66)
Walking	0	1 (0.31)	1 (0.31)	2 (0.62)	0	1 (0.37)	2 (0.74)	3 (1.12)	2 (0.66)	1 (0.33)	2 (0.66)	5 (1.64)
Leg exerciser	-	-	-	-	-	-	-	-	0	1 (0.33)	0	1 (0.33)

Variable	T2DM				HTN				T2DM+HTN			
	1 (N=20)	2 (N=102)	3 (N=200)	Total (N=322)	1 (N=24)	2 (N=100)	3 (N=145)	Total (N=269)	1 (N=52)	2 (N=95)	3 (N=157)	Total (N=304)
Alcohol consumption, n (%)												
Yes	2 (0.62)	15 (4.66)	19 (5.90)	36 (11.18)	4 (1.49)	9 (3.35)	19 (7.06)	32 (11.90)	4 (1.32)	5 (1.64)	11 (3.62)	20 (6.58)
No	18 (5.59)	87 (27.02)	181 (56.21)	286 (88.82)	20 (7.43)	91 (33.83)	126 (46.84)	237 (88.10)	48 (15.79)	90 (29.61)	146 (48.03)	284 (93.42)
Smoking habits, n (%)												
Never smoked	20 (6.21)	77 (23.91)	177 (54.97)	274 (85.09)	16 (5.95)	78 (29.00)	123 (45.72)	217 (80.67)	46 (15.13)	72 (23.68)	138 (45.39)	256 (84.21)
Former smoker	0	8 (2.48)	12 (3.73)	20 (6.21)	4 (1.49)	9 (3.35)	13 (4.83)	26 (9.67)	4 (1.32)	9 (2.96)	13 (4.28)	26 (8.55)
Current smoker	0	17 (5.28)	11 (3.42)	28 (8.70)	4 (1.49)	13 (4.83)	9 (3.35)	26 (9.67)	2 (0.66)	14 (4.61)	6 (1.97)	22 (7.24)
Duration (Years), Mean±SD	-	20.71 ±7.28	18.64 ±8.10	19.89 ± 7.53	25.50 ±4.20	20.69 ±6.36	17.89 ±7.89	20.4 6±6.95	26.00 ±5.66	20.86 ±6.57	24.67 ±4.97	22.36 ±6.20
Socio-economic status, n (%)												
Lower	1 (0.31)	4(1.24)	30 (9.32)	35 (10.87)	3 (1.12)	11 (4.09)	19 (7.06)	33 (12.27)	3 (0.99)	2 (0.66)	3 (0.99)	8 (2.63)
Upper Lower	6 (1.86)	14 (4.35)	43 (13.3)	63 (19.57)	5 (1.86)	12 (4.46)	24 (8.92)	41 (15.24)	6 (1.97)	10 (3.29)	44 (14.47)	60 (19.74)
Lower Middle	3 (0.93)	19 (5.90)	32 (9.94)	54 (16.77)	7 (2.60)	18 (6.69)	31 (11.52)	56 (20.82)	16 (5.26)	27 (8.88)	39 (12.83)	82 (26.97)
Upper Middle	8 (2.48)	5 (18.01)	79 (24.53)	145 (45.03)	7 (2.60)	49 (18.22)	60 (22.30)	116 (43.12)	25 (8.22)	47 (15.46)	46 (15.13)	118 (38.82)
Upper	2 (0.62)	7 (2.17)	16 (4.97)	25 (7.76)	2 (0.74)	10 (3.72)	11 (4.09)	23 (8.55)	2 (0.66)	9 (2.96)	25 (8.22)	36 (11.84)

HTN: 43.12%; T2DM+HTN: 38.82%) (Table 4). Furthermore, a significantly greater proportion of depressive patients had monthly family income between 18,498 and 36,996 (in Indian National Rupees) in patients with T2DM (29.50%; p<0.0001), HTN (28.25%; p=0.0329) and T2DM + HTN (31.91%; p=0.0011) (data not shown).

Anxiety

There was a statistically significant association between severity of depression and anxiety scores across all indications (p<0.0001; Table 5).

Insomnia

A higher proportion of patients with depression had insomnia (versus no insomnia) across all the indications (T2DM: 5.23% vs. 4.12%; HTN: 10.12% vs. 3.49%; T2DM+HTN: 9.28% vs. 3.84%). However, the association was found to be non-significant (Table 5).

Comorbidities and Complications

Dyslipidemia was the most common comorbidity reported in patients with T2DM (24.22%), HTN (14.87%) and T2DM+HTN (27.30%). The proportion of dyslipidemic patients with other depressive symptoms was higher in comparison to patients with major depressive syndrome across all the indications (T2DM: 5.28% vs. 1.86%; HTN: 5.95% vs. 1.12%; T2DM+HTN: 9.54% vs. 5.59%).

Among patients with HTN and depression, the most common complications reported (> 10%) were angina (13.01%) and heart failure (11.15%). Diabetic neuropathy (13.35%) was the most common complications reported among patients with T2DM and depression. Depression was found to be significantly associated with complications in T2DM (p=0.0001) and comorbidities in T2DM + HTN (p=0.0023) cases. In addition, the complications of HTN have also shown a significant association with depression in T2DM + HTN patients (p=0.0246) (data not shown).

Discussion

The co-occurrence of depression in patients with T2DM and HTN is well-known and has been reported in wide array of literature.[11,26] Depression is usually associated with poor disease control, adverse health outcomes in patients with T2DM/HTN.[22,34]

In the current study, more than 45% of the patients with T2DM (51.03%), HTN (46.94%) and T2DM+HTN (48.64%) reported depression (score of ≥5 in the MD PHQ-9). In comparison to our results, previous studies have reported a lesser prevalence of depression in both T2DM (23.4% to 42.2%) and HTN (15% to 40.1%) patients.[6-10,35-38] Majority of the patients with depression had uncontrolled nature of the disease (T2DM: 77.64%; HTN: 72.49%); indicating an association between depression and poorly managed disease conditions. The higher proportion of patients did not fulfil the criteria of either "major depression" or "other depressive symptoms" across all indications. This might be due to fact that substantially larger proportion of patients in our study had none to mild severe depression (>70%). This study further reports that patients meeting the criteria of "other depressive symptoms" were higher in comparison to those with "major depression" across all clinical conditions (T2DM: 31.68% vs. 6.21%; HTN: 37.17% vs. 8.92% and T2DM+HTN: 31.25% vs. 17.11%). These findings were in concordance with the earlier published literature where a higher proportion of diabetics reported to have "other depressive symptoms" in comparison to "major depression" (20% vs. 12.5%).[39] A systematic diagnosis of depression using established screening tools and treatment initiation without commensurate increase in clinical duration should be devised for an improved therapeutic outcome in HTN and T2DM patients. Furthermore, a call for integrated clinical approach for assessment and management of major depression should be more emphasized in patients with both T2DM and HTN.

Socioeconomic status was significantly associated with depression in T2DM and T2DM + HTN cases. Our results were in agreement with earlier findings where socio-demographics was postulated as a risk factor for cases of depression in DM and HTN patients.[10,40] In the study, a significant association between BMI and depression was observed in T2DM patients (p=0.0015), however, the majority of patients across each indication were overweight or obese (class 1). Similar results were reported by Barnes et al (2015) in which depression was found to be significantly associated with elevated BMI.[41] Hence, the obesity status of T2DM and/or HTN patients should be documented and efforts should be made to identify the disease progress and initiate timely, and effective treatment for improved outcomes. In addition, poor lifestyle also serves as a predisposing factor for depression and worsens self-management of T2DM and HTN. In the present study, more than 70% of the patients with depression and T2DM/HTN did not exercise regularly, making them more susceptible to disease-related complications and comorbidities.

Depressive T2DM patients are more likely to develop comorbidities and complications than the non-depressive patients.[42] In our study, depression was significantly correlated with associated complications in T2DM patients (p=0.0001). Additionally, depression was significantly associated with comorbidities (p=0.0023) and complications of HTN (p=0.0246) in T2DM + HTN patients. This could be due to the fact that depression activates the hypothalamic-pituitary-adrenal axis, sympathetic nervous system, proinflammatory and proco-

Table 5. Association of Depression with Anxiety (GAD-7 scores) and insomnia in patients with HTN, T2DM and HTN+T2DM

Depression	Anxiety (GAD-Score)					Diagnosed with insomnia clinically	
	No Symptoms	Mild	Moderate	Severe	Total	Yes	No
HTN, n (%)							
None	254 (44.33)	45 (7.85)	4 (0.70)	1 (0.17)	304 (53.05)	12 (2.09)	3 (0.52)
Mild	59 (10.30)	132 (23.04)	15 (2.62)	1 (0.17)	207 (36.13)	28 (4.89)	11(1.92)
Moderate	2 (0.35)	23 (4.01)	22 (3.84)	2 (0.35)	49 (8.55)	13 (2.27)	3 (0.52)
Moderately Severe	0	2 (0.35)	6 (1.05)	2 (0.35)	10 (1.75)	4 (0.70)	2 (0.35)
Severe	1 (0.17)	0	0	2 (0.35)	3 (0.52)	1 (0.17)	1 (0.17)
Total	**316 (55.15)**	**202 (35.25)**	**47 (8.20)**	**8 (1.40)**	**573 (100)**	**58 (10.12)**	**20 (3.49)**
T2DM, n (%)							
None	275 (43.58)	32 (5.07)	2 (0.32)	0	309 (48.97)	8 (1.27)	3 (0.48)
Mild	89 (14.10)	151 (23.93)	13 (2.06)	3 (0.48)	256 (40.57)	16 (2.54)	14 (2.22)
Moderate	4 (0.63)	28 (4.44)	20 (3.17)	4 (0.63)	56 (8.87)	8 (1.27)	7 (1.11)
Moderately Severe	0	2 (0.32)	7 (1.11)	1 (0.16)	10 (1.58)	1 (0.16)	2 (0.32)
Severe	0	0	0	0	0	0	0
Total	**368 (58.32)**	**213 (33.76)**	**42 (6.66)**	**8 (1.27)**	**631 (100)**	**33 (5.23)**	**26 (4.12)**
T2DM+HTN, n (%)							
None	298 (47.68)	19 (3.04)	4 (0.64)	0	321 (51.36)	8 (1.28)	5 (0.80)
Mild	59 (9.44)	120 (19.20)	15 (2.40)	2(0.32)	196 (31.36)	19 (3.04)	11 (1.76)
Moderate	2 (0.32)	41 (6.56)	40 (6.40)	4 (0.64)	87 (13.92)	26 (4.16)	7 (1.12)
Moderately Severe	0	3 (0.48)	9 (1.44)	8 (1.28)	20 (3.20)	5 (0.80)	1 (0.16)
Severe	0	0	0	1 (0.16)	1 (0.16)	0	0
Total	**359 (57.44)**	**183 (29.28)**	**68 (10.88)**	**15 (2.40)**	**625 (100)**	**58 (9.28)**	**24 (3.84)**

agulation responses which in turn increases cortisol secretion, catecholamine release, cytokines and platelet/endothelial cell adhesion molecule-1. These mediators may play a vital role in disease progression in depressive patients with coexisting T2DM and HTN.[22] However, no significant association was reported between depression and comorbidities/complications in patients with HTN.

As stated, we noted substantially higher proportion of depressive patients in uncontrolled T2DM and HTN cases in our study. Previous studies have also shown that uncontrolled diabetes increases the risk of diabetic complications which in turn enhances depressive symptoms in T2DM patients.[43,44] On the other hand, depression was found to be a risk factor for poor blood pressure control in HTN patients.[45] There is still no consensus regarding the true nature of the relationship between depressive symptoms and uncontrolled nature of disease, which remains to be elucidated in well-designed studies. However, the current finding suggests that depression management may require an additional strategy of optimizing the disease control, which also reduces the risk of complications in both T2DM and HTN patients. A better understanding of the relationship may help clinicians to address the affective conditions that may lead to more comprehensive management of depression.

Quality of sleep plays a vital role in reducing the risk of DM and HTN.[46] Poor sleep quality and altered circadian rhythms increase depression and insulin resistance.[26,47] In our study, more than 5% of the patients with depression suffered from insomnia (T2DM: 5.23%, HTN: 10.12%; T2DM+HTN: 9.28%).

Anxiety, in addition to depression, serves an important role in the outcome of any disease.[26] A significant association was observed between depression and anxiety across all the indications ($p<0.0001$). Since, majority of our patients had none to mild depression, the prevalence of no or mild anxiety was reported in a higher proportion of patients.[48]

Clinical Implication

Depression has been identified as a cause and a consequence of T2DM and HTN. The presence of depression worsens the disease condition, deteriorate the symptoms and impacts self-care in patients with T2DM and HTN and vice versa. People with depression are more likely to be sedentary and eat diet that is rich in saturated fats and refined sugars and avoid fruit and vegetables, which may further aggravate the risk of developing T2DM and HTN.[49] Furthermore, depression significantly affects treatment adherence and patients tend to miss medical appointments, takes erratic diet, skips exercise and medications and avoid self-care; further deteriorating disease management and exacerbating the severity of depressive symptoms.[17,50] Clinicians and other healthcare professionals in T2DM and/or HTN setting(s) should be made aware of concurrent depression and must undertake subjective and objective assessments of depression. Patients with T2DM+HTN, who are at risk of complications or have predominant physical symptoms or an uncontrolled disease must undergo regular screening for depression. This would enable clinicians to have an adequate management of T2DM and HTN in patients with comorbid depression and offer them better disease control by preventing long-term complications. It is very critical to take care of depressive symptoms in patients with T2DM and/or HTN as psychological treatment of depressive symptoms would not only improve T2DM and HTN-related complications but would also improve anxiety and patient well-being.

Strength and Limitations

Our study has few strengths and limitations. This was a first of its kind study conducted across different geographical regions of 54 cities in India. The study highlighted the burden of depression in patients with controlled and uncontrolled T2DM and HTN and has identified the various risk factors associated with development or aggravation of depressive symptoms in the most common metabolic disorders. Validated and widely used questionnaires were used to assess the severity of depression (Prime MD PHQ-9) and anxiety (GAD-7), which ensured the credibility of our findings. There are few limitations of this study as well. Firstly, no comparator group was included to see the viability of the study results. Additionally, no longitudinal assessment was done to evaluate the changes in depression, anxiety and other factors from baseline. Nevertheless, this study provides the first nationwide data on the prevalence of depression in patients with T2DM and/or HTN. Further longitudinal studies are warranted to ascertain the long-term association of depression with these metabolic disorders and to assess its impact on disease progression and vice versa.

Conclusion

The current study indicates an increased prevalence of depressive disorders in patients with T2DM (51.03%), HTN (46.94%) and T2DM+HTN (48.64%) in conjunction with anxiety and sleep disturbances. There was a direct significant association between depression and socioeconomic status, education, occupation, physical activity in patients with T2DM and/or HTN. Depression care in patients with T2DM and/or HTN is critical as it worsens the disease condition and increases the T2DM and HTN-related complications, anxiety and deteriorates the patient well-being. Patients who are on high-risk should undergo regular screening for depression and management under comprehensive mental healthcare systems.

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