Original Article

Occurrence and Predictors of Depression and Poor Quality of Life among Patients with Type-2 Diabetes: A Northern India Perspective

Prerna Bahety, Gunjan Agarwal[1], Deepak Khandelwal[2], Deep Dutta[3], Sanjay Kalra[4], Pankaj Taparia[5], Vikas Singhal[6]

Departments of Family Medicine, [1]Medicine and [2]Endocrinology, Maharaja Agrasen Hospital, [3]Department of Endocrinology, Venkateshwar Hospital, New Delhi, [4]Department of Endocrinology, Bharti Hospital, Karnal, Haryana, Departments of [5]Neurology and [6]Psychiatry, Maharaja Agrasen Hospital, New Delhi, India

Abstract

Background and Aims: Globally, depression has been linked to Type-2 diabetes mellitus (T2DM). However, similar data from India are scant. This study evaluated the occurrence and predictors of depression and health-related quality of life (QOL) in patients with T2DM as compared to healthy controls. **Materials and Methods:** One hundred adults with T2DM without prior diagnosis of depression and 100 matched controls were evaluated. Depression was assessed using Patient Health Questionnaire-9. World Health Organization QOL Brief (WHO-QOL-BREF) was used to assess QOL. Demography, anthropometry, biochemical parameters of diabetes control, and microvascular and macrovascular complications in patients were recorded. **Results:** Depression was significantly more common in T2DM (63%) as compared to controls (48%) (odds ratio [OR] - 1.84 [1.04, 3.24]; $P = 0.03$). In T2DM, depression was higher in patients with disease duration >5 years (OR = 2.66; $P = 0.02$), glycated hemoglobin >7% (OR = 3.45; $P = 0.004$), retinopathy (OR - 3.56; $P = 0.03$), and nephropathy (OR - 4.11; $P = 0.07$). Occurrence of depression was significantly higher among the patients with macrovascular complications, namely, coronary artery disease (17.4%; $P = 0.000006$), cerebrovascular disease (14.2%; $P = 0.0006$), and peripheral vascular disease (7.9%; $P = 0.05$). Insulin users had higher depression as compared to patients using only oral antihyperglycemic medications ($P = 0.034$). Patient with depression had significantly low QOL. The WHO-QOL for all the domains was significantly lower in T2DM with microvascular and macrovascular complications, as compared to those without. **Conclusion:** Indian T2DM had higher prevalence of depression and lower QOL as compared to controls, which was associated with poor glycemic control and higher end-organ damage. Public health measures are required to create more awareness for managing depression in diabetes.

Keywords: Depression, diabetes, diabetes complications, glycemic control, quality of life

Introduction

World Health Organization (WHO) has defined health from a new perspective, stating that "health is defined not only by the absence of disease and infirmity but also by the presence of physical, mental, and social well-being."[1] India is currently considered as diabetes capital of the world looking into the alarming rise in the prevalence of diabetes mellitus (DM) in Indian population.[2,3] DM brings a lot of complications with it, one among which is depression. Worldwide, it is a very commonly encountered problem and has been found to be associated with poor glycemic control and also poor quality of life (QOL) in patients with diabetes.[4]

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Meta-analyses and systematic literature reviews have revealed that individuals with DM have a 2-fold increased risk of developing depression when compared to their nondiabetic counterparts.[4-6] According to some studies, approximately 30% of people with DM have depressive symptomatology and more than 10% have major depression.[7-9]

Address for correspondence: Dr. Deepak Khandelwal, Department of Endocrinology, Maharaja Agrasen Hospital, Punjabi Bagh, New Delhi - 110 026, India.
E-mail: khandelwalaiims@gmail.com

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Patients with diabetes need to put in extra efforts every day to match with the metabolic state of the individuals without diabetes, which significantly impacts the QOL of the individual.[4,5] It is the psychosocial behavior and mental status of person with diabetes that affects the self-care behavior and ultimately, long-term glycemic control, the risk of developing long-term complications, and QOL. Cause of depression in diabetes may be multifactorial, ranging from increased pill count of medicines, associated obesity, associated end-organ damages and comorbidities which may lead to decreased self-care such as lack of exercise, and increased substance abuse (alcohol and smoking).[10] The productivity and growth of a country depend on the health-related QOL (HRQOL) of its people and the psychosocial factors have a potent effect on the physical health outcomes. Hence, having assessing tool for QOL is a must.

Relation between depression and diabetes is a self-perpetuating cycle resulting in adverse long-term glycemic control further worsening the risk of developing long-term complications/end-organ damage, QOL, increased hospitalization, and even mortality.

However, in spite of considerable data from the western world, there are limited data regarding the burden of depression and QOL in Indians with diabetes. Our study evaluated the occurrence of depression and its relation with glycemic control, microvascular and macrovascular complications in Type-2 DM (T2DM). We also assessed QOL in patients with T2DM as compared to healthy controls.

Materials and Methods

A case–control study was conducted in the Outpatient Department of Endocrinology and Medicine clinic at Maharaja Agrasen Hospital, Punjabi Bagh, Delhi, a 400-bedded teaching, superspecialty, National Accreditation Board for Hospitals and Healthcare Providers and Joint Commission International accredited hospital serving patients from both urban and rural areas. The study was approved by the Institutional Ethics Committee.

Consenting T2DM adults aged ≥30 years and <80 years of age diagnosed with diabetes according to the American Diabetes Association criteria for at least 1 year, with the absence of diagnosis of depression/anxiety before the diagnosis of DM on the basis of history or previous records were included in the study. Age- and sex-matched apparently healthy controls were taken in a ratio of 1:1. Controls were recruited from both the hospital and the community. The hospital controls were the apparently healthy relatives of the patients admitted for any illness and also hospital staff.

Excluded patients included those who refused to give their consent for the study, individuals with diabetes other than T2DM (T1DM, pancreatic diabetes, secondary diabetes among others), pregnant women, those with severe comorbid physical illness or cognitive impairment that could affect their response, i.e., patients with other significant medical illnesses that were not related to DM such as asthma, chronic obstructive pulmonary disease, patients with current psychiatric disorders other than depression on the basis of history or previous medical records, and patients with the current history of substance abuse.

Methods of data collection

Patients of T2DM visiting the endocrinology and medicine outpatient department for a routine check-up and meeting the inclusion criteria were considered for the study. The study and its procedure were explained to the patients, and written informed consent was taken from all the individuals who were willing to participate. The assessments were conducted in accordance with the regular clinical practice and institutional protocols. Laboratory investigations were done as a part of routine clinical practice, and the data were captured and used for analysis. Details of age, gender, presence or absence of various microvascular and macrovascular complications were noted, and clinical variables such as body mass index (BMI), blood pressure, and laboratory investigations such as fasting and postprandial blood glucose and glycated hemoglobin (HbA1c) were recorded.

The Patient Health Questionnaire-9 (PHQ-9) is the depression module, which scores each of the nine Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria as "0" (not at all) to "3" (nearly every day). It has been validated for use in primary care.[11] PHQ-9 scores were used to determine the occurrence of depression in cases as well as controls. For the diagnosis of depression, we used PHQ-9 score as follows: 0–4, no depression; 5–9, mild depression; 10–14, moderate depression; 15–19, moderately severe depression; and 20–27, severe depression. However, to make it simpler, we merged the last two groups and defined depression as follows: 0–4, no depression; 5–9, mild depression; 10–14, moderate depression; and ≥15, severe depression.[11]

WHO-QOL-BREF scale was used for data collection on HRQOL. This is a shorter version of the original WHO-QOL-100 and consists of 26 items that are scored over four major domains, namely, physical, psychological, social relationships and environment. The responses of the WHO-QOL-BREF are scored in a Likert scale fashion from 1 to 5, with higher scores denoting higher QOL and vice versa. The WHO-QOL-BREF was chosen for this study because it contains domains of life function critical to HRQOL, and as a generic scale, it provides information that is comparable across patient groups and populations with different languages and culture. In addition, because of its brevity, it took a relatively shorter time to administer (about 6 min in this study) which made it appropriate for use in busy clinics like ours.[12]

Statistical analysis

Statistical analysis was performed with the help of Epi Info (TM) 3.5.3 (Atlanta, GA, USA). Epi Info is a trademark of the Centers for Disease Control and Prevention. Normality of the distribution of variables was assessed using the Kolmogorov–Smirnov test. Independent *t*-test and Wilcoxon rank-sum test were carried out for normally distributed and

skewed variables, respectively. Chi-square tests were used for categorical variables. Pearson's or Spearman's correlation coefficient was calculated for normally distributed and skewed variables, respectively. Descriptive statistical analysis was performed to calculate the means with corresponding standard deviations (SDs). Test of proportion was used to find the standard normal deviate (*Z*) to compare the difference proportions, and Chi-square test was performed to find the associations. Odds ratio (OR) with 95% confidence interval had been calculated to find the risk factors. Pearson's correlation coefficient was calculated to find the correlation between variables. $P < 0.05$ was taken to be statistically significant.

Results

A total of 100 cases and 100 controls were enrolled in the study. In the study, males and females in the case and control groups were 48 and 52 and 47 and 53, respectively. The mean age (mean ± SD) of the cases was 56.09 ± 5.92 years and that of the controls was 56.15 ± 7.88 years. Two groups were matched for their age, sex, and BMI [Table 1]. The occurrence of microvascular and macrovascular chronic complications among the study participants has been elaborated in Table 2. Most common chronic complications among patients with diabetes were retinopathy (23%), followed by nephropathy (13%). Established coronary artery disease (CAD) was present in 11% of T2DM patients in our study.

The occurrence of depression in T2DM patients and controls in our study was 63% and 48%, respectively ($\chi^2 = 4.55$; OR - 1.84 [1.04, 3.24]; $P = 0.03$) [Figure 1]. Significantly higher proportion of T2DM individuals had moderate and severe depression (41.0%) as compared to controls (28.0%); [Figure 2]. Mean PHQ-9 score of T2DM individuals was significantly higher than controls [Table 3]. Furthermore, mean WHO-QOL score for all domains of T2DM individuals was significantly lower than controls [Table 3].

Depression was significantly more in T2DM patients having disease duration ≥5 years as compared to disease duration <5 years ($\chi^2 = 4.90$; OR = 2.66 [1.10, 6.43]; $P = 0.02$) [Figure 3]. Depression was also significantly more in T2DM patients having poor glycemic control (HbA1c >7) in comparison with individuals with fair glycemic control (HbA1c ≤7) (OR = 3.45 [1.46, 8.16]; $P = 0.004$) [Figure 4].

The risk of depression was 3.5 times more among the patients with retinopathy (OR - 3.5625 [1.1069, 11.4656]; $P = 0.03$; statistically significant), 4.11 times more among the patients with nephropathy (OR - 4.11 [0.86, 19.54]; $P = 0.07$; approached statistical significance), and 2.13 times more among the patients with neuropathy (OR - 2.13 [0.54, 8.33]; $P = 0.27$; not significant), as compared to patients without retinopathy, nephropathy, and neuropathy, respectively. Fisher's exact test showed that occurrence of depression was significantly higher among the patients with CAD (17.4%; $P = 0.000006$), cerebrovascular accident (CVA)/transient ischemic attack (TIA) (14.2%; $P = 0.0006$), and peripheral vascular disease (PVD) (7.9%; $P = 0.05$), as compared to those without CAD (0%), CVA/TIA (0%), and PVD (0%), respectively.

The mean WHO-QOL for all the domains was lower of the patients with nephropathy in comparison with patients without nephropathy. However, it was not significant for all the domains. The mean WHO-QOL for all the domains were lower of the patients with neuropathy in comparison with patients without neuropathy ($P < 0.01$).The WHO-QOL for all the domains was significantly lower in T2DM with at least any one of the microvascular or macrovascular complications as compared to those without any of these complications (except for domain 4) [Figure 5]. After adjusting the confounding factors,

Table 1: Comparison of baseline parameters of patients with type-2 diabetes and healthy controls

Baseline parameters	Cases (T2DM) (*n*=100)	Controls (*n*=100)	*P*
Age (years), mean±SD	56.09±5.92	56.15±7.88	0.95
Male:female	48:52	47:53	0.88
BMI (kg/m^2), mean±SD	26.68±2.02	26.23±2.43	0.15

T2DM: Type 2 diabetes mellitus, SD: Standard deviation, BMI: Body mass index

Table 2: Presence of chronic complications in study participants with type 2 diabetes

Complications	Cases (*n*=100) (%)
Retinopathy	23 (23.0)
Nephropathy	13 (13.0)
Neuropathy	14 (14.0)
CAD	11 (11.0)
CVA/TIA	9 (9.0)
PVD	5 (5.0)

CAD: Coronary artery disease, CVA: Cerebrovascular accident, TIA: Transient ischemic attack, PVD: Peripheral vascular disease

Table 3: Distribution of Patient Health Questionnaire-9 score and quality of life score of different domains of the two groups

Parameters	Cases (T2DM) (*n*=100)	Control (*n*=100)	*P*
PHQ-9 (mean±SD)	9.70±6.73	7.13±4.69	<0.0001*
WHO-QOL domain 1 (mean±SD)	64.14±24.58	71.43±20.56	0.012*
WHO-QOL domain 2 (mean±SD)	64.24±24.81	71.02±20.88	0.019*
WHO-QOL domain 3 (mean±SD)	65.19±24.51	71.42±18.13	0.042*
WHO-QOL domain 4 (mean±SD)	62.90±25.72	70.51±19.60	0.019*

*Statistically significant. T2DM: Type 2 diabetes mellitus, PHQ-9: Patient Health Questionnaire-9, QOL: Quality of life, WHO-QOL: World Health Organization quality of life score, SD: Standard deviation

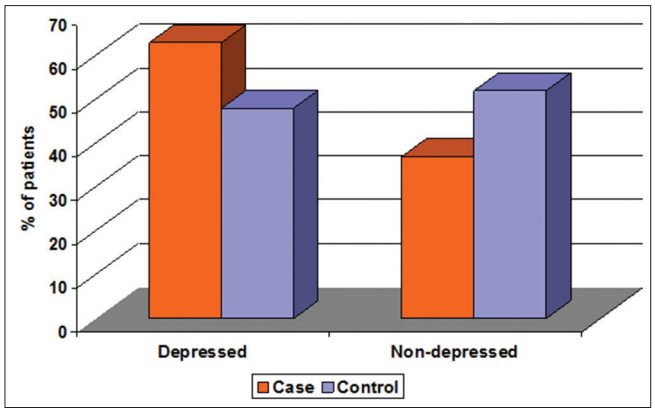

Figure 1: The risk of depression was 1.84 times among the individuals with Type 2 diabetes mellitus (cases) as compared to the controls (Odds ratio - 1.84 [1.04, 3.24]; $P = 0.03$)

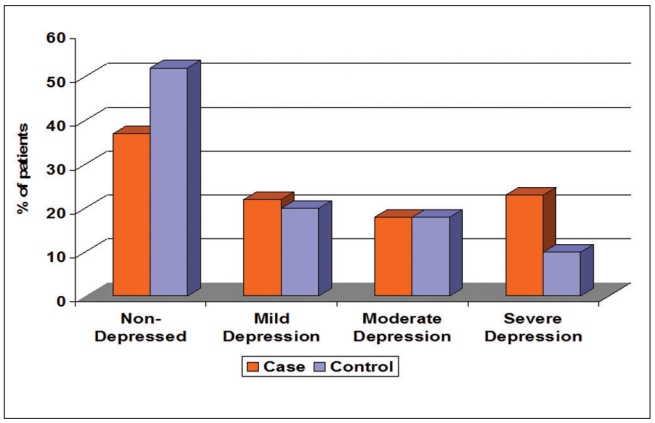

Figure 2: Distribution of various grades of depression among Type 2 diabetes mellitus individuals (cases) and healthy controls

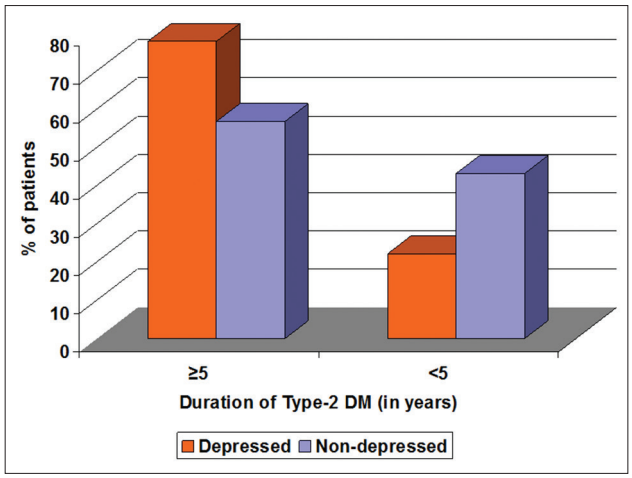

Figure 3: Frequency of depression among subjects with Type 2 diabetes mellitus with disease duration ≥5 years as compared to those with disease duration <5 years

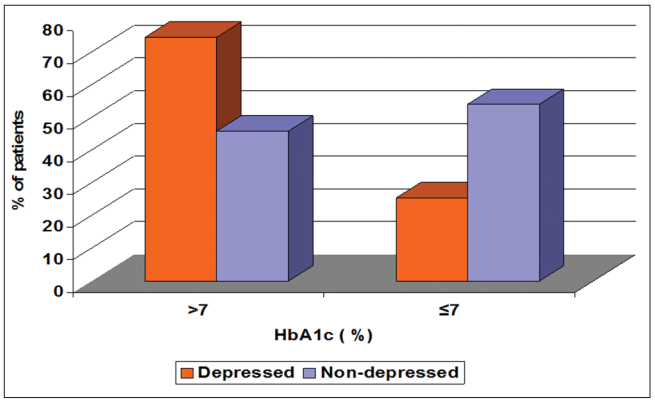

Figure 4: Frequency of depression among Type 2 diabetes mellitus individuals with poor glycemic control (glycated hemoglobin >7) in comparison with individuals with fair glycemic control (glycated hemoglobin ≤7)

multiple logistic regression showed that the risk of depression was 1.27 times more for patients with T2DM (OR - 1.27 [1.07, 2.29; $P = 0.04$]), as compared to those without.

The risk of depression was 1.15 times among the T2DM patients with >2 class of oral hypoglycemic agents (OHAs) use as compared to the T2DM patients with ≤2 class of OHAs use (OR - 1.15 (0.30, 4.37); $P = 0.83$). Proportions of patients with depression among insulin users were higher than insulin nonusers ($P = 0.034$). All seven T2DM individuals on insulin therapy were depressed, while 56 out of 93 T2DM individuals were depressed who were only on oral antihyperglycemic medications. There was no significant correlation between episodes of hypoglycemia and presence of depression of individuals with T2DM ($P = 0.22$).

Discussion

Our study showed that depression is a common comorbid health problem in T2DM outpatients, which was significantly more common as compared to matched healthy controls. The risk of depression was significantly more in T2DM patients with longer duration of diabetes (≥5 years), patients with poor glycemic control (HbA1C >7) and among insulin users.

Prevalence of T2DM has increased exponentially in recent years around the globe. The age group between 45 and 64 years constituted the major diabetes population in the developing countries while age group 65 years and above were mainly involved in the developed countries,[13] thus affecting most productive population worst in developing countries. Depression is also highly prevalent just like diabetes. At any given time, about 340 million people globally suffer from depression.[14] WHO documents that depression is associated with greatest number of morbid years in the form of disabilities from the diseases that are nonfatal and chronic. They account for around 12% of burdensome years with disability.[15] Globally, depressive disorders are the fourth leading cause of disease burden in women and seventh leading cause in men.[15]

In our study, the risk of depression was significantly higher (1.84 times) among individuals with T2DM as compared to controls. Furthermore, risk of depression was

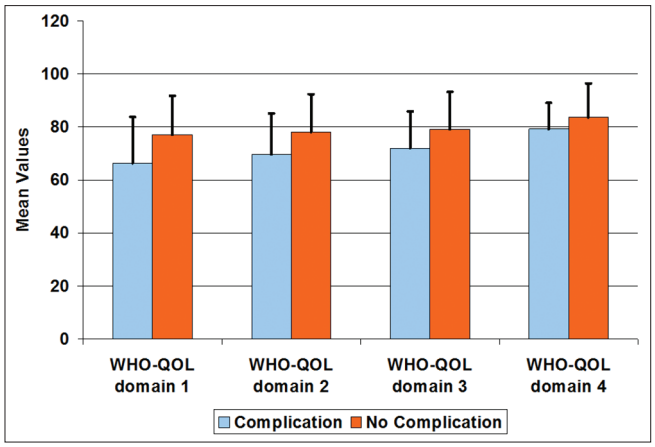

Figure 5: World Health Organization quality of life score for all the domains in Type 2 diabetes mellitus individuals with any chronic micro/macro-vascular complications in comparison with individuals without any of these complications. Statistically, significant for all domains, except domain 4

significantly more (2.66 times) among T2DM patients with disease duration ≥5 years as compared to those with disease duration <5 years. Previous meta-analysis has also shown the prevalence of depression significantly higher among patients with diabetes as compared to those without diabetes.[5] Goldney *et al*. have also shown in their study that the prevalence of depression in the patient with diabetes was 24% compared with 17% in people without diabetes.[16]

Increased use of different types of oral antidiabetes medication was not linked to increased occurrence of depression among patients with T2DM in our study. However, insulin use for diabetes management was observed to be linked with a higher occurrence of depression. However, it must be realized that insulin cannot be directly linked to depression. It is likely that patients who were receiving insulin for diabetes management perhaps had more severe/advanced disease, more associated comorbidities and complications which necessitated insulin use, which could have had an impact on the occurrence of depression. The end-organ damage and comorbidities in insulin users were not assessed separately and is a limitation of this study.

Impact of depression on diabetes management can be highlighted by the observation of Kalsekar *et al*., who reported significantly lower adherence to OHAs in patients with depression as compared to those without depression.[17,18] However, interestingly in another study, Arshad and Alvi showed that glycemic control and type of treatment did not predict depression.[19] Heterogeneity in the patient profile evaluated in different studies may explain these differences.

In our study, there was a significant correlation between poor glycemic control and presence of depression in individuals with T2DM. The risk of depression was 3.45 times more among the T2DM patients with HbA1c >7% as compared to those with HbA1c ≤7%. A longitudinal study in individuals with T2DM by Richardson *et al*. observed a higher HbA1c among patients with associated depression at all-time points compared to patients without depression.[20]

Patients with T2DM and depression had significantly poorer QOL in our study as compared to those without depression. In addition, significant inverse correlation was found between PHQ-9 score and WHO-QOL domain 2, WHO-QOL domain 3, and WHO-QOL domain 4 scores in T2DM individuals. Goldney *et al*., also in their study, showed a clear difference in the QOL scores for the diabetes and depression group when compared with the diabetes group without depression.[16] Eren *et al*. found that the presence of depression resulted in a significant deterioration in QOL in individuals with T2DM.[21] Similar results were obtained in a population-based US survey in 2004 where lower HRQOL was observed in patients with T2DM and those at high risk for T2DM (3–5 diabetes-related risk factors).[22] Jain *et al*. in their study also showed that QOL is poor in diabetes individuals as compared to nondiabetes population.[23]

Our study showed a significant correlation between retinopathy and presence of depression in T2DM individuals. Risk of depression was 3.5 times more among the patients with retinopathy as compared to the patients without retinopathy. The proportion of individuals with depression was significantly higher among subjects with T2DM who had CAD, CVA/TIA, and PVD than individuals without these macrovascular complications. T2DM individuals with diabetic complications are more depressed than without complications.[24] Yoshida *et al*. reported that the presence of microvascular complications, specifically neuropathy, was associated with depression independent of age, gender, marital status, social support, pain, perception of general health, diabetes type, duration of diabetes, HbA1c, and insulin requirement.[25] Lloyd *et al*., in their study, showed that even mild diabetes complications have a significant impact on patients' QOL.[26] In our study, the mean of WHO-QOL for all the domains was lower for the patients with complications in comparison with patients without complications. Our study also showed that lower QOL is seen in patients with poor glycemic control in diabetics. This has also been shown by Jacobson that early and aggressive intensive therapy leading to improved glycemic control is likely to reduce the impact of diabetes on the QOL.[27]

Conclusion

This study showed that depression is a common comorbid health problem in T2DM patients of Delhi and its occurrence was even higher in patients with longer duration of diabetes (≥5 years), poor glycemic control (HbA1C >7) and among insulin users. QOL was strongly linked with depression, and QOL was significantly lower in patients with T2DM. Further, the presence of complications was related to poor QOL in T2DM. The observation of this study has grave practical importance from the Indian perspective. Onset of T2DM in India is nearly 2 decades earlier than the Caucasians. With

the current prevalence of T2DM of 9%–10%, an additional 12%–15% of the population having prediabetes, with the highest annual global rates of prediabetes progression to T2DM (18%, vs. 2.5% in the USA), India is not only a ticking time bomb of diabetes but also depression.[28-30] Hence, special public health initiatives are needed to tackle depression among Indians with diabetes, which will have an overall beneficial impact on diabetes control and QOL.

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Conflicts of interest

There are no conflicts of interest.

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