

Depressive comorbidity in type 2 Diabetes: Prevalence and associated factors

Comorbidité dépressive dans la diabète type 2: Prévalence et facteurs associés

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ABSTRACT

Background: The comorbidity diabetes depression is frequent and would have a synergistic effect. Depression is underdiagnosed in diabetology consultations.

Methods: This was a cross-sectional study that included 102 outpatients with type 2 Diabetes mellitus (T2DM) recruited during April and May 2019. A pre-established form was filled out from the interview of the patients and the medical file review. Depression, Therapeutic adherence, self-esteem, temperament, satisfaction of treatment, quality of life and physical activity were assessed by validated questionnaires.

Results: The average age of the patients was 53.4 ± 8.5 years, sex-ratio was 0.7. 76.5% have exhibited depressive symptoms; 51% of the patients have had moderate to severe depression. Depression was associated with female gender ($p=0.04$) and psychiatric family history ($p=0.01$). Patients with depression have had significantly higher HbA1c levels ($p=0.05$) and significantly lower HDL-C levels ($p=0.05$). Regarding psychosocial factors, depression was associated with low self-esteem ($p=0.005$) and significantly higher scores of depressive ($p=0.002$) and cyclothymic ($p=0.003$) temperaments. Depression was also associated with significantly lower treatment satisfaction ($p=0.01$) and poor quality of life. In multivariate study, factors independently associated with depression were female gender, low HDL-C, quality of life score without diabetes and low self-esteem score.

Discussion: The limitations were the relative low number of patients, the auto-questionnaire for the assessment of depression, a recruitment of patients not including a first line health care facility and the absence of prospective aspect. This study showed, despite limitations, that depression is frequent in patients with T2DM and was associated with several sociodemographic, anamnestic, clinical and psychological characteristics.

Key words: Type 2 diabetes; Depression; Blood glucose control; Quality of life; Self-esteem; Treatment satisfaction

RÉSUMÉ

Introduction : La comorbidité diabète dépression est fréquente et aurait un effet synergique. La dépression est sous-diagnostiquée dans les consultations de diabétologie.

Méthodes : Il s'agit d'une étude transversale qui a inclus 102 patients ambulatoires atteints de Diabète de type 2 (DT2) recrutés durant les mois d'avril et mai 2019. Un formulaire pré-établi a été rempli à partir de l'entretien avec les patients et de l'examen du dossier médical. La dépression, l'observance thérapeutique, l'estime de soi, le tempérament, la satisfaction du traitement, la qualité de vie et l'activité physique ont été évalués par des questionnaires validés.

Résultats : L'âge moyen des patients était de $53,4 \pm 8,5$ ans, le sex-ratio était de 0,7. 76,5 % ont présenté des symptômes dépressifs ; 51% des patients avaient une dépression modérée à sévère. La dépression était associée au sexe féminin ($p = 0,04$) et aux antécédents familiaux psychiatriques ($p = 0,01$). Les patients souffrant de dépression avaient des taux d'HbA1c significativement plus élevés ($p = 0,05$) et des taux de HDL-C significativement plus bas ($p = 0,05$). En ce qui concerne les facteurs psychosociaux, la dépression était associée à une faible estime de soi ($p = 0,005$) et à des scores significativement plus élevés de tempéraments dépressifs ($p = 0,002$) et cyclothymiques ($p = 0,003$). La dépression était également associée à une satisfaction au traitement significativement plus faible ($p = 0,01$) et à une mauvaise qualité de vie. Dans l'étude multivariée, les facteurs indépendamment associés à la dépression étaient le sexe féminin, un faible taux de HDL-C, un score bas de qualité de vie sans diabète et un faible score d'estime de soi.

Discussion : Les limites de l'étude étaient le nombre relativement faible de patients, l'auto-questionnaire pour l'évaluation de la dépression, un recrutement de patients n'incluant pas de structure de soins de première ligne et l'absence d'aspect prospectif. Cette étude a montré, malgré ses limites, que la dépression était fréquente chez les patients atteints de DT2 et était associée à plusieurs caractéristiques sociodémographiques, anamnestiques, cliniques et psychologiques.

Mots clés : diabète de type 2 ; Dépression ; Contrôle glycémique ; Qualité de vie ; estime de soi ; Satisfaction du traitement

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INTRODUCTION

Diabetes and depression are among the most frequent chronic diseases. The global prevalence of diabetes in adults over 18 years old has increased from 4.7% in 1980 to 8.5% in 2014. Diabetes is associated with significant morbidity and mortality. It is a major cause of blindness, kidney failure, cardiovascular accidents, and lower limbs amputation. In 2019, it was estimated that 1.5 million deaths were directly related to diabetes[1]. As for depression, its prevalence was estimated at 15%. It is the leading cause of disability worldwide according to the World Health Organization (WHO) and contributes significantly to the global burden of disease[2]. The relationship between diabetes and depression has been widely established in the literature[3]. However, data from Tunisia and North Africa remain relatively limited. The risk of diabetes for patients with depressive disorders was estimated at 17% in untreated patients, this risk raised to 25% in patients on antidepressants regardless of other risk factors [4]. In addition, the risk of diabetes' complications was higher in case of depressive symptoms[5]. The WHO Global Mental Health Survey has shown that depression-diabetes comorbidity leads to even greater alterations in health than adding the two disorders' complications[2]. Comorbid depression in patients with diabetes participating in a disease management program was associated with an increased risk for all-cause mortality over a two-year period of approximately 36% to 38%, depending on the definition of depression that was used [6]. These results suggest a synergistic effect between depression and diabetes generating an additional negative effect beyond the simple addition of the negative effects of each of the two conditions.

The aims of this study were:

- To determine the frequency of depression in a population of patients with type 2 diabetes mellitus (T2D).
- To study the factors associated with depression in patients with T2DM.

METHODS

This was a cross-sectional study carried out during the months of April and May 2019 at theXXX diabetology outpatient clinic.

The study included a population of patients with T2DM, followed at the XXX diabetology outpatient clinic during the months of April and May 2019.

→ Inclusion criteria

- Age between 18 and 65 years old.
- Type 2 diabetes.

→ Non-inclusion criteria

- Patients under psychotropic treatment.
- Inability to consent (psychotic disorders, mood disorders with psychotic features, dementia).
- Patients with life-threatening disease (neoplasia, unstable coronary disease...).

- Patients unable to answer questionnaires.
- Pregnant women.
- Non-cooperative subjects.

The evaluation of epidemiological and clinical characteristics was carried out using a pre-established questionnaire collecting anamnestic, clinical and therapeutic characteristics.

Concerning the biological parameters of the patients, glycemic balance was evaluated by

- the glycated hemoglobin referring to the recommendations of the American Diabetes Association (ADA) of 2021[7]. Referring to these recommendations, the thresholds of normal glycated hemoglobin were:

- <7% without significant hypoglycemia
- Less stringent A1C goals (such as 8% [64mmol/mol]) maybe appropriate for patients with limited life expectancy, or where the harms of treatment are greater than the benefits.

- The fasting blood sugar

- Lipid panel: Triglycerides, total cholesterol, HDL-cholesterol and LDL-cholesterol. Dyslipidemia has been defined based on the 2014 ADA recommendations:

- Hypertriglyceridemia: TG > 1.7 mmol / l
- Hypo HDL-C: HDL-C < 1.3 mmol/l for women and < 1 mmol/l for men

- Hyper LDL-C: LDL > 1.8 mmol/l in subjects without cardiovascular disease and > 1.8 mmol/l in subjects with cardiovascular disease and those at very high risk of cardiovascular disease [8].

- Kidney function was assessed by the dosage of 24-hour microalbuminuria and serum creatinine with calculation of creatinine clearance.

Depression was assessed by the Beck's inventory scale in its short form(9); the threshold values were fixed at 4 for mild depression, at 8 for moderate depression, and at 16 for severe depression as recommended by the authors [9]. Self-esteem was evaluated by the Rosenberg's scale of self-esteem [10], the temperament by the TEMPS-A (Temperament Evaluation of Memphis, Pisa, Paris and San Diego-autoquestionnaire) [11], and the quality of life was measured by Audit of Diabetes Dependent Quality of Life (ADDQoL) [12]. The treatment adherence was evaluated by the Morisky medication adherence scale [13], satisfaction of treatment by the "Diabetes Treatment Satisfaction Questionnaire" (DTSQ) [14]. The physical activity was appreciated by the International Physical Activity Questionnaire [15].

Statistical analysis was made by the software SPSS® for Windows®, version 21.0. The independent factor was the presence of depression, which divided the study sample in two groups: patients with moderate to severe depression versus patients without depression or with mild depression. the Chi square test and the Student's t-test were used for the between-group analysis. The statistical significance was set at 5%.

Ethical considerations

The ethics committee of the National Institute of Nutrition and Food Technology have approved the protocol of this study. Informed consent to participate in the study was obtained from participants. The Blood samples were

taken as part of the biological monitoring of diabetes and not specifically for the study.

RESULTS

After applying the inclusion and non-inclusion criteria, 102 patients with T2DM were included in the study. The mean age was 53.4 ± 8.5 years with extremes of 27 to 65 years. The sex-ratio was 0.7; 83.3% of the patients were married; 51% had secondary school level; 39.2% were unemployed; 55.9% had an average socioeconomic level. Regarding medical history, 77.5% had a family history of diabetes while 4.9% had a personal history of depression.

Prevalence of depression

Depressive symptoms were present in 76.5% of the patients, including 42.2% with moderate and 8.8% with severe symptoms (table 1).

Table 1. Prevalence of depression

Depressive symptoms	None	Mild	Moderate	Severe
Prevalence	23.50%	25.50%	42.20%	8.80%

Clinical characteristics of diabetes

The mean age at diabetes onset was 42.10 ± 8.68 years. Average duration of diabetes was 11.23 ± 7.08 years. Based on HBA1c and ADA recommendations, 74.5% of patients had unbalanced diabetes. Fasting blood glucose was ≥ 7.2 mmol/l in 75.5% of patients. Concerning the complications of diabetes, 64.7% have never had metabolic complications, 71.6% have had at least one degenerative complication. Regarding comorbidities, 44.1% of the patients were obese (BMI ≥ 30), dyslipidemia was observed in 61.8% of the patients, hypertension in 29%, and hypothyroidism in 2.9%, the latter being stabilized under thyroid hormone therapy. Physical activity was low for 62.4% of the patients and moderate for 37.6%.

Almost half of the patients (44.1%) were on oral antidiabetic drugs (OAD), 23.5% on insulin and 32.4% on a combination of insulin and OAD; 42.2% of the patients were hospitalized at least once for diabetes. According to the scores of the Morisky et al. questionnaire, treatment adherence was low in 42.1% of cases, medium in 47.1% and high in 10.8%. The mean score of the Diabetes Treatment Satisfaction Questionnaire was 29.1 ± 6.1 .

Therapeutic characteristics of diabetes

Almost half of the patients (44.1%) were on oral antidiabetics; 23.5% on insulin and 32.4% on insulin and oral antidiabetics combination. According to the scores of the Morisky questionnaire, treatment adherence was low in 42.1% of cases, moderate in 47.1% and high in 10.8%. Almost half of patients (42.2%) had been hospitalized at least once for diabetes.

Psychological characteristics

According to Rosenberg scale, self-esteem was low to very low for 69.3% of the patients. The quality of life, assessed by the ADDQoL, was bad in average. The highest scores on TEMPS-A were for hyperthymic temperament and cyclothymic temperament.

Factors associated with depression

Sociodemographic factors

In the study sample, moderate to severe depressive symptoms were significantly more frequent in female (60% vs 38.1% in male; $p = 0.04$) and in patients with a psychiatric family history (76.2% vs 44.4% in patients without psychiatric family history; $p = 0.01$).

Clinical and biological factors

Moderate to severe depressive symptoms were associated with higher rates of glycated hemoglobin (HBA1c) and lower rates of HDL-C (table 2).

Depression was not associated with the presence of degenerative ($p = 0.19$) or metabolic complications ($p = 1$).

Table 2. Correlation between clinical and biological characteristics and depression in Type 2 Diabetes Mellitus

	Patients with mild to severe depressive symptoms (mean $\pm$ SD)	Patients without or with minor depressive symptoms (mean $\pm$ SD)	p
Duration of diabetes	11.48 $\pm$ 6.90	10.98 $\pm$ 7.32	0.72
Age of onset	41.65 $\pm$ 8.15	42.58 $\pm$ 9.26	0.59
BMI	29.60 $\pm$ 4.65	28.72 $\pm$ 4.86	0.35
Waist circumference	104.86 $\pm$ 10.05	101.66 $\pm$ 9.96	0.10
HBA1C	9.32 $\pm$ 1.83	8.63 $\pm$ 1.66	<u>0.05</u>
TC	4.77 $\pm$ 1.29	4.74 $\pm$ 1.02	0.90
LDL-C	1.14 $\pm$ 0.39	1.09 $\pm$ 0.32	0.46
HDL-C	1.11 $\pm$ 0.25	1.25 $\pm$ 0.41	<u>0.05</u>
TG	1.67 $\pm$ 1.34	1.45 $\pm$ 1.08	0.38

BMI: Body Mass Index; HBA1c: Glycated Hemoglobin; TC: Total Cholesterol; LDL-C: LDL Cholesterol; HDL-C: HDL-Cholesterol; TG: triglycerides

Psychological factors

Moderate to severe depressive symptoms were associated with low self-esteem; 82.7% of patients with moderate to severe depressive symptoms had low self-esteem vs 55.1% of the patients with minor or without depressive symptoms ($p = 0.005$).

Patient with moderate to severe depressive symptoms had higher scores of depressive and cyclothymic temperaments (table 3).

Table 3. Relationship between temperaments and depression in patients with Type 2 Diabetes Mellitus.

	Patients with mild to severe depressive symptoms (mean $\pm$ SD)	Patients without or with minor depressive symptoms (mean $\pm$ SD)	p
Cyclothymic	4.90 $\pm$ 2.51	3.24 $\pm$ 2.93	<u>0.003</u>
Depressive	2.77 $\pm$ 1.73	1.74 $\pm$ 1.56	<u>0.002</u>
Irritable	2.51 $\pm$ 2	2.22 $\pm$ 2.08	0.46
hyperthymic	5.78 $\pm$ 1.08	5.21 $\pm$ 1.74	0.70
Anxious	1.81 $\pm$ 1.05	1.46 $\pm$ 0.99	0.09

Moderate to severe depressive symptoms were associated with a bad quality of life with lower quality of life scores (table 4).

Table 4. Relationship between quality of life and depression in patients with Type 2 Diabetes Mellitus

	Patients with mild to severe depressive symptoms (mean±SD)	Patients without or with minor depressive symptoms (mean±SD)	p
General, quality of life scores	-1.73± 1.66	-1.02± 1.75	0.04
Quality of life without diabetes scores	25.11± 12.76	-17.78± 13	0.005
Composite quality of life scores	59.69± 35.31	-42.18± 33.02	0.01

Physical activity

Moderate to severe depressive symptoms were not associated with low physical activity ($p=0.24$).

Therapeutic factors and treatment satisfaction

No association was found between moderate to severe depression and treatment-related factors. Specifically, these symptoms were not associated with insulin use ($p=0.55$) or the number of hospitalizations ($p=0.34$). Depression was not associated to treatment adherence score evaluated with Morisky scale ($p=0.06$).

According to DTSQ, patients with moderate to severe depressive symptoms had lower treatment satisfaction scores (27.61 ± 6.75 vs. 30.62 ± 4.86 ; $t=2.58$; $p=0.01$).

Multivariate analysis

A binary logistic regression analysis was conducted with the presence of moderate to severe depression as the dependent variable. Independent variables included sex, family history of diabetes, family psychiatric history, waist circumference, HbA1c, HDL-C level, degenerative complications, self-esteem score, overall quality of life score, quality of life score excluding diabetes, composite quality of life score, DTSQ general satisfaction score, physical activity score, cyclothymic temperament score, and depressive temperament score. The analysis revealed that moderate to severe depression was independently associated with female sex, lower HDL-C levels, lower quality of life scores (excluding diabetes), and lower self-esteem scores (table 5).

Table 5. Factors independently associated with moderate to severe depression : Multivariate analysis

	standardized coefficient beta	Confidence interval	p
Sex	0.34	(0.13; 0.91)	0.03
HDL-C	0.18	(0.04; 0.76)	0.02
the quality-of-life without diabetes score	0.96	(0.93; 0.99)	0.03
self-esteem score	0.73	(0.61; 0.88)	<0.001

Discussion

In our study population, the mean age of patients was 53.4 ± 8.5 years, with a sex ratio of 0.7. Overall, 76.5% of participants exhibited depressive symptoms, and 51% presented with moderate to severe depression. Univariate analyses showed that depression was significantly associated with female gender, a positive psychiatric family history, higher HbA1c levels, and lower HDL-C levels. On a psychosocial level, depression was linked to lower self-esteem, higher depressive and cyclothymic temperament scores, reduced treatment satisfaction, and poorer quality of life. In the multivariate analysis, independent predictors of depression included female gender, low HDL-C, impaired diabetes-independent quality of life, and low self-esteem.

51% of patients had moderate to severe depression. It is currently admitted that the prevalence of depression is high among people with diabetes. Depression was twice as common in people with type 1 and type 2 diabetes than in the general population. It affected 10-20% of adults with diabetes[16,17]. According to a recent metanalysis, the point prevalence of major depressive disorder was 14.5% (95% CI 7.9-25.3; $I^2=99.65$). People with T2DM were more likely to have major depressive disorder compared with the general population (odds ratio 1.73, 95% CI 1.38-2.16)[18]. In the International Prevalence and Treatment of Diabetes and Depression (INTERPRET-DD) study, a collaborative study carried out in 14 countries, Looyd et al. founded that the prevalence of current major depressive disorder was 10.6% among 2783 people with T2DM, and 17.0% reported moderate to severe levels of depressive symptoms[19].

Some studies, though, concluded that depression was not more prevalent in patients with T2DM[20,21]. They have shown that the risk of depression is not higher in people with diabetes who are unaware of the diagnosis. A meta-analysis found that the prevalence of depression in people with unrecognized diabetes did not differ significantly from that in people with normal glucose metabolism (OR 0.94; 95% CI: 0, 71-1.25)[22]. Icks et al. found an increased odds of developing high depressive symptoms in participants with diagnosed diabetes. However, the odds ratios decreased when considering comorbidities and other covariates. Interestingly, in participants with previously undetected diabetes, the odds was not increased, even 10 years after detection of diabetes[23]. The international diabetes management practices study, conducted in 21 developing countries, of which Tunisia, found that 33.1% of the patients with T2DM reported depressive symptoms, 22.1% reported mild symptoms, 9.9% moderate and 1.2% severe symptoms (PHQ-9 score ≥ 20)[24].

A meta-analysis by Mezuk B et al. concluded that the effect of depression on the increased risk of developing T2DM tended to be stronger than the effect of T2DM on the increased risk of developing depression[25]. For the same authors, the relative risk was highest for patients with a depressive disorder on antidepressant medication[25]. A three-year prospective study by Pan et al., with analysis controlled for age and BMI, showed

that the use of selective serotonin reuptake inhibitors or tricyclic antidepressants was associated with an increased risk of developing T2DM[26].

In our study, regarding sociodemographic characteristics, depression was associated with female sex, lower educational level. There was no association between age, socioeconomic level and the presence of depression. In most studies, depression in T2DM was associated with female sex and low educational level [19,27–29]. Regarding the age factor, most studies reported that advanced age was a risk factor for depression, but, for the population of patients with diabetes, it was found that depression was less common in older cohorts[6].

Clinically, depression was associated with higher rates of HbA1c. Many longitudinal studies on T2DM have indicated that depression was associated with poor glycemic control[30–32]. In a longitudinal study of three waves of follow-up of a community sample, depression scores and diabetes distress scores were significantly associated with levels of glycemic control (HbA1c) over time [33]. Lustman et al. analyzed data from 24 studies and found that depression was significantly associated with hyperglycemia ($p < 0.0001$)[29]. Effect sizes were similar (0.22 vs. 0.18) and statistically significant in the subset where depression was the independent variable ($N = 7$) and the subset where glycemic control was the independent variable ($N = 6$). This result supports the hypothesis of a reciprocal interaction in which depression causes hyperglycemia and hyperglycemia causes depression[29].

In our study, the presence of depression was not associated with the presence of degenerative or metabolic complications. In a large prospective study by Lin et al.[33], major depressive disorder in subjects with T2DM was associated with an increased risk of microvascular and macrovascular complications at five years of follow-up. In addition, a meta-analysis of 27 cross-sectional studies by de Groot et al. showed that depression was associated with a significantly increased risk of microvascular and macrovascular complications ($p < 0.001$)[5]. Depression was also associated with a higher death rate[34–35].

In our study, no association was found between depression and BMI. For lipid profile parameters, depression was linked with lower levels of HDL-C. A meta-analysis by Luppino et al. examined the longitudinal relationship between overweight, obesity and depression and found a two-way correlation. Obese people had a 55% increased risk of developing depression, and people with depression had a 58% increased risk of developing obesity[36]. Metabolic syndrome is another risk factor for developing type 2 diabetes. Metabolic syndrome is particularly frequent in psychotic disorders and mood disorders[37–38]. Skilton et al found that rates of depression were higher in people with metabolic syndrome than in healthy controls[39]. Lower levels of HDL-C were generally associated with suicidal behaviors [37,40–41].

For psychosocial factors, depression was associated with poor quality of life. It was also associated with low self-esteem and lower treatment satisfaction. Several

cross-sectional studies and cohort studies have found that people with T2DM-depression comorbidity had a significantly more impaired quality of life than patients with T2DM without depression[42–43]. Regarding self-esteem, the presence of depression in people with T2DM was associated with a lower sense of self-efficacy[44]. People with low self-esteem were less likely to follow a diet in T2DM [45]. For treatment adherence, studies have generally found depression to be associated with poor diabetes self-management, including poor diet and poor medication adherence[46–48].

Finally, the presence of depression was associated with higher scores for depressive and cyclothymic temperaments. In addition to clinical and subclinical depressive states, psychological dimensions related to depressive temperament, such as neuroticism, have also been shown to be risk factors for depression[49]. In addition, high level of neuroticism and depressive temperament were associated with dysfunctional regulation of the hypothalamic-pituitary-adrenal system[50].

The high prevalence of depression among patients with diabetes in this study underlines the need for systematic screening, with particular attention to women and individuals with a psychiatric family history. Since depression was associated with poorer metabolic control (higher HbA1c, lower HDL-C) and reduced quality of life, a multidisciplinary care approach is recommended. Clinicians should incorporate psychosocial assessment into diabetes management, addressing self-esteem, treatment satisfaction, and temperament-related vulnerabilities. Multidisciplinary collaboration between endocrinologists and psychiatrists can improve both psychological well-being and metabolic outcomes.

Strengths:

This study addresses the clinically relevant comorbidity of T2DM and depression, using validated instruments to assess biological, psychosocial, and behavioral factors. A multifactorial approach and multivariate analysis strengthen the reliability of the findings and reveal independent associations. The results have clear clinical relevance, supporting targeted depression screening in diabetic patients.

Limitations:

This study is limited by a small sample size, use of a self-reported depression questionnaire, exclusion of primary care settings in recruitment, and its cross-sectional design.

CONCLUSION

Depression is common in patients with T2DM and is associated with female gender, low self-esteem, low quality of life and adverse metabolic markers. Routine screening and integrated psychosocial care are essential to improve outcomes. Further studies with larger, more diverse populations and longitudinal designs are

warranted to clarify causal relationships and inform targeted interventions.

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