Comorbidity of Depression and Type 2 Diabetes in Egypt

Results from the International Prevalence and Treatment of Diabetes and Depression (INTERPRET-DD) Study

Tarek Okasha[1], Bassem Murad Mostafa[2], Islam Ibrahim[1], Ahmed Adel Abdelgawad[1], Cathy E. Lloyd[3], Norman Sartorius[4], Hussien Elkholy[1]

1 Okasha Institute of Psychiatry, Neurology and Psychiatry Department, Faculty of Medicine, Ain Shams University, Egypt

2 Internal Medicine and Endocrinology Department, Faculty of Medicine, Ain Shams University, Egypt

3 Faculty of Health, Wellbeing and Social Care, The Open University, UK

4 Association for the Improvement of Mental Health Programmes (AMH), Geneva, Switzerland

Abstract

Background: Diabetes mellitus and depression are serious common diseases, and the number of people with both conditions is rising steadily. Depression in people with diabetes mellitus results in poorer prognosis through different mechanisms. On the other hand, the presence of diabetes in individuals with depression increases functional impairment that is associated with depression.

Aims: The study is aimed at assessing the prevalence and factors associated with depression among adults with type 2 diabetes mellitus attending a diabetes clinic in Cairo, Egypt.

Methods: A cross-sectional study was conducted among adult patients with diabetes type 2 attending a diabetes clinic in the endocrinology department in Ain Shams University Teaching Hospital, Cairo, Egypt. Data were collected through face-to-face interviews by trained psychiatrists and from patients' records.

Results: The prevalence of depression among diabetic patients was 21.8% (95% CI 15.6%-29.1%). Depression was more common among younger age groups and those with a higher level of education. There was no significant difference between those with lifetime depression compared to those without depression regarding physical health complications.

Conclusions: The prevalence of depression among patients with type 2 diabetes is high. Given the impact of co-morbid diabetes and depression, diabetic patients should be routinely screened for the latter condition.

Keywords:

Diabetes Mellitus, Type 2 diabetes, Depression

Corresponding author:

Hussien Elkholy

h.elkholy@med.asu.edu.eg

Introduction

Diabetes mellitus (DM) is a chronic metabolic disease, characterized by disturbance in the metabolism of carbohydrates, lipids and amino acids leading to a persistent elevation of blood glucose, either as a result of decreased insulin secretion, or due to a reduction to insulin sensitivity of the body cells **(Goyal et al,2023).** According to the International Diabetes Federation "Diabetes Mellitus" is one of the most common chronic conditions in the world. The prevalence of diabetes mellitus has increased dramatically over the last years secondary to increasing obesity and sedentary lifestyle which resulted in diabetes to become the 8th cause of disability adjusted life years (DALYS) **(International Diabetes Federation, 2021).** In 2021, approximately 537 million adults (20-79 years) have been living with diabetes. The total number of people living with diabetes is projected to rise to 643 million by 2030 and 783 million by 2045 respectively **(International Diabetes Federation, 2021).**

It is reported that 3 in 4 adults with diabetes live in low- and middle-income countries **(Naskar et al., 2017).** Prevalence may vary depending on the socioeconomic level of the country, the ethnic subgroup, diagnostic criteria, and the clinical characteristics of the diabetic population **(King et al. 1998).** The Arab world (North Africa, Middle East, and Gulf area) specifically is expected to have the second highest increase in percentage of people with DM in 2030 compared to other parts of the world **(Sweileh et al, 2014).**

Depressive disorder is another prevalent condition experienced by an estimated 3.8% of the population. This includes 5% of adults (4% among men and 6% among women), and 5.7% of adults older than 60 years. Approximately 280 million people in the world have depression **(World Health Organization [WHO], 2023).** Depression is about 50% more common among women than among men. **(Woody et al., 2017).**

Relationship between diabetes and depression

Around 300 years ago, Thomas Willis (British Physician) suggested a probable relationship by stating that diabetes mellitus was the consequence of a ''period of sadness'' **(Nicolau & Masmiquel, 2013).** Since then, many studies have agreed that an association exists between diabetes and depression. Moreover, literature on this topic has increased over the past decade.

Diabetes and depression appear to display an etiological bidirectionality. Prevalence of depression is higher in people having diabetes compared to those without diabetes **(Briganti et al., 2019).** On the other hand, **Tabák et al. (2014)** have reported that patients with depression show an elevated risk to develop diabetes. It is worth noting that in combination, these two chronic conditions result in 4.5 times higher healthcare costs than for diabetes patients without depression **(Markowitz et al., 2011; Naskar et al., 2017).**

Many studies concluded that the comorbidity of diabetes and depression is associated with higher mortality rates **(Hofmann et al, 2013).** Moreover, studies show that such comorbidity increases diabetes related complications. For example, **Lin and colleagues (2004)** showed that people with diabetes and comorbid depression had a 36% increased risk of developing microvascular complications such as renal impairment, retinopathy and foot ulcers, compared to individuals with

diabetes without depression. Furthermore, a 25% higher risk of developing macrovascular complications, such as cardiac and neurological events was reported **(Richardson et al., 2008).**

There are three suggested explanations for the increased depression prevalence in people with diabetes. The first possible reason is the psychosocial impact involved in being diagnosed with diabetes **(Das et al., 2013)** including the extensive fear of developing long term complications of diabetes and changes in lifestyle needed to maintain good metabolic control. However, increased prevalence of depression even in people with undiagnosed diabetes makes the psychosocial theory insufficient as the only cause for such an increase. Various biochemical changes secondary to diabetes form the basis of a biological hypothesis for the increased depression prevalence in diabetic patients **(Ducat 2014).** According to this hypothesis, increased inflammatory cytokines, hyperglycemia, and hyperinsulinism contribute to a low-grade chronic inflammation state. The passage of these cytokines to the central nervous system may result in development of depression by increasing cytokine synthesis by microglial cells, the activation of macrophage-like cells in periventricular areas, decreased neuroplasticity, adrenal axis hyperactivation. and decreased volume of the brain such as hippocampus and amygdala, Thirdly, depression and diabetes may present coincidently without relation between the two conditions **(Ismail, 2010; Lloyd et al., 2005).**

On the other hand, there are two potential reasons for increased prevalence of diabetes among depressed patients. Firstly, it has been suggested that the increased risk of developing diabetes in subjects with depression may be explained by the lifestyles present in depressed patients. Depression is associated with poor dietary habits, abnormal sleep patterns and a more sedentary lifestyle **(Palinkas et al., 1991).** On the contrary, the biological hypothesis also attempts to explain the increased incidence of diabetes in subjects with depression through the increased synthesis of proinflammatory cytokines (interleukin-1 and interleukin-6) in the central nervous system that results in systemic inflammation due to the passage of these substances through the blood-brain barrier. This leads to insulin resistance and eventually diabetes **(Barglow et al., 1984; Gold et al., 1988; Palinkas et al., 1991).**

Diabetes and Depression in Egypt

Egypt is located in North Africa with Arabic and Mediterranean roots with a population above 100 million in 2021 (**Abouzid et al., 2022; CAPMAS,2023).** Interestingly, the Egyptian physician "Hesy-Ra" first described diabetes in approximately 3000 BC, but diabetes was further described in details as "plentiful urine" in the Upper Egyptian Ebers Papyrus dating back to 1550 BC (**Hegazi et al., 2015).**

In Egypt, diabetes is a fast-expanding concern. According to the International Diabetes Federation (IDF), Egypt ranks ninth in the prevalence of diabetes worldwide, the prevalence of among Egyptian adults being 15.2%, **(International Diabetes Federation, 2021)** which may be underestimated as reports indicate that 43% of patients with diabetes and most people with prediabetes in Egypt are likely undiagnosed **(Al-Rubeaan, 2010).** It is alarming that diabetes prevalence in Egypt has increased rapidly within a relatively short period from approximately 4.4 million in 2007 to 7.5 million in 2013. It is expected this number will jump up to 13.1 million by 2035 **(Whiting et al., 2011)**. Therefore, diabetes should be thoroughly explored in terms of its risk factors, prevention, treatment, and consequences. Moreover, the general population should be aware of and well informed about all aspects of diabetes.

Prevalence rates of depression in Egypt varied over the years and between different studies. In a 1988 survey of a community sample from an urban and rural population in Egypt, reported a rate of 15.3% **(Okasha et al, 1988**), while the preliminary National Survey of Prevalence of Mental Disorders

in Egypt reported rates as low as 2.7% in 2003 **(Ghanem et al,2009)**. Prevalence rate of 3.5% in 2015 was reported by the WHO **(World Health Organization [WHO], 2017).** However, a recent a recent systematic review by Odejimi et al.**(2020)** reported that the prevalence of depression among older adults ranges between 23.7 and 74.5% **(Abdel-Wahab et al, 2022).**

Study objectives

The aim of this study was to examine the prevalence and correlates of depressive disorders in adults with Type 2 diabetes attending secondary care facilities in Cairo, Egypt. The data formed part of International Prevalence and Treatment of Diabetes and Depression (INTERPRET-DD) study in 17 countries across the globe.

Methods

This study was part of the International Prevalence and Treatment of Diabetes and Depression Study (INTERPRET-DD) and a detailed description of the methodology can be found in ***Lloyd et al. (2015)*****.** The study was a cross-sectional, single interview study that included consecutive patients with type 2 diabetes , aged 18 – 60 years, attending the Diabetes Clinic of Ain Shams University Hospitals. Ain Shams University Hospitals are one of the largest tertiary hospitals in Egypt. It has approximately 2300 beds, 5000 physicians and serving more than three quarters of a million patients annually. The Ain Shams Hospitals consists of 8 Hospitals (Diabetes clinic is in one of them) and 6 specialized centers including the Okasha institute of Psychiatry. The hospitals accept patients from all over the country, including urban and rural areas. The hospitals provide service as inpatients, outpatients clinic and virtually through the telemedicine clinics.

Type 2 diabetes is defined according to WHO criteria (random plasma glucose ≥ 11.1 mmol/l or fasting plasma glucose ≥ 7.0 mmol/l or 2–hour plasma glucose ≥ 11.1 mmol/l).

Prior to interview the site investigators completed an information form for each eligible individual. This form included information from medical records, such as age, duration of diabetes, family history of diabetes and presence/history of diabetes complications. The latter included cardiovascular disease, retinopathy, peripheral neuropathy, peripheral vascular disease and renal disease and associated disorders. Most recent measurements of blood pressure, HbA_{1c}, height and weight were also recorded. A diagnosis of current major depressive disorder (MDD) was made at the interview so that the proximity of clinical records did not differ. Participants were asked if they lived in what they considered to be a rural or an urban area, and reported their highest level of education (defined as no formal, some/completed primary, some/completed secondary school, or higher education, which was defined as any college, postgraduate or professional training). Marital status was defined as married/cohabiting vs being single/widowed/divorced which, for our analyses, was dichotomized into living alone vs not living alone. Participants were also asked if they considered that they had a regular income.

Each participant was asked to complete the Patient Health Questionnaire (PHQ-9). The PHQ-9 consists of nine items on a four-point Likert-type scale **(Kroenke et al., 2001).** It has good sensitivity and specificity with regard to identifying cases of depression as well as being sensitive to change over time, and has been used in a number of different countries (Kroenke et al., 2001). Moderate/severe depressive symptomatology was defined as PHQ-9 scores > 9, as this was a research study rather than clinical practice, in which a significant level of symptoms would usually be considered to be PHQ-9 scores >15 (**Petrak et al., 2015).** All questionnaires were completed using standard self-complete methods in the appropriate language, or assisted one-to-one collection, with the questions read out by the researcher and answered by the participant. Where no existing

translation/cultural adaptation of the questionnaire was available it was adapted using standard forward/back translation procedures.

A psychiatric interview was subsequently conducted by a trained interviewer using the Mini International Neuropsychiatric Interview (MINI plus- V5) **(Sheehan et al., 1998)** Arabic version **(Ghanem et al., 1999)**. Depression was defined at interview as a current (within 2 weeks) diagnosis of MDD in accordance with the criteria given in the International Classification of Diseases 10 classification (and the corresponding criteria of MDDs in the DSM-IV). Previous MDD, lifetime (i.e. either current or previous MDD) and recurrent MDD (i.e. with both current and previous MDD) were also diagnosed at the interview. For the purpose of the analysis in this study, we compared those diagnosed with lifetime depression to those without a diagnosis.

Ethical approval

Prior to commencing the study, ethical approval was obtained from the Institute of Psychiatry, Ain Shams University (currently known as Okasha Institute of Psychiatry). Ethical approval also was obtained from the Open University, UK, where the data were stored for analysis.

Statistical analysis

SPSS was used to analyze data **(Rubin & Schenker, 1986)**. Descriptive statistics are reported, along with univariate (t-test, chi-squared test, Wilcoxon rank-sum test) analyses to examine the differences between those with and without lifetime MDD.

The present study is the first of its kind to use both a clinical interview as well as a screening instrument to detect clinical depression and depressive symptoms, and to also record the diagnoses of diabetes complications contained in medical records kept by leading centers of care for people with diabetes.

3. Results

A total of 200 patients were approached to be interviewed as planned and 143 consented and were included, achieving a response rate of 71 %. Around 77 % of the respondents were female. Out of the total study participants, 64% were not living alone. About 60 % had attended secondary school or above. The majority of the study participants (54.9%) were urban residents. More than 92% of participants had a positive family history of diabetes. Half of the participants were on one diabetic control medication and the rest were on two or more. Most of the participants were non-smokers (78.9% never smoked and 4.9% were past smokers). This could be explained by the majority of the sample being females and smoking being less common and culturally unacceptable amongst them. Almost all the sample (97.9%) reported either never or rarely exercising.

In the study sample, the prevalence of lifetime depression was 21.8% (95% CI 15.6%-29.1%). **Table 1** shows the prevalence of current, recurrent, and past depression according to the MINI diagnosis.

Table 1: prevalence of depression among sample of patients with Type 2 diabetes

	N (%)	95.0% CI
MAJOR DEPRESSIVE DISORDER (Current)	29 (20.42%)	14.43% - 27.61%
MAJOR DEPRESSIVE DISORDER (Recurrent)	18 (12.68%)	7.97% - 18.88%
MAJOR DEPRESSIVE DISORDER (Past)	21 (14.79%)	9.68% - 21.31%
MAJOR DEPRESSIVE DISORDER (Lifetime)	31 (21.83%)	15.65% - 29.15%

In the study sample, depression was more common among those of a younger age (Mean ± SD = 46.48 ± 8.73) compared to those without a diagnosis of depression (Mean ± SD= 50.16 ± 8.54, p value 0.037). Moreover, depression was more common on those with a higher level of education (P value 0.028). This could possibly be due to their understanding of diabetes risk and complications. There were no significant differences regarding the rest of collected factors (sex, living status, family income status, location of residence, accessibility of health services in the local area, family history of diabetes, and family history of mood disorders and number of diabetic medications) between the group with depression and the group without (Table 2).

Table 2: Relation between sociodemographic factors, family history, availability of services and depression in Type 2 diabetes patients

		No MDD	MDD overall (current, recurrent, past)	Test of sig.		
		Mean ± SD	Mean ± SD	value	p value	sig.
AGE		50.16 ± 8.54	46.48 ± 8.73	t = 2.11	0.037	S
		N (%)	N (%)			
Sex	Female	83 (75.45%)	25 (80.65%)	χ^2 =0.36	0.547	NS
	Male	27 (24.55%)	6 (19.35%)			
Highest level of education attained	0	15 (13.51%)	2 (6.45%)	χ^2 =9.14	0.028	S
	1	33 (29.73%)	4 (12.9%)			
	2	35 (31.53%)	9 (29.03%)			
	3	28 (25.23%)	16 (51.61%)			
Living status	Not living alone	70 (63.06%)	21 (67.74%)	χ^2 =0.23	0.631	NS
	living alone	41 (36.94%)	10 (32.26%)			
Family income status	No regular income	45 (40.54%)	11 (35.48%)	χ^2 =0.26	0.611	NS
	Regular income	66 (59.46%)	20 (64.52%)			
Location of Residence	rural / village	53 (47.75%)	11 (35.48%)	χ^2 =1.47	0.225	NS
	Urban	58 (52.25%)	20 (64.52%)			
Are there health services accessible in participant's local area?	no	53 (48.18%)	11 (35.48%)	χ^2 =1.57	0.21	NS
	yes	57 (51.82%)	20 (64.52%)			
Family History of Diabetes	No family history	11 (9.91%)	0 (0%)	χ^2 =7.06	0.07	NS
	Diabetes in 1st degree relative	42 (37.84%)	11 (35.48%)			
	Diabetes in 2nd degree relative	36 (32.43%)	8 (25.81%)			
	Diabetes in both 1st & 2nd degree relative	22 (19.82%)	12 (38.71%)			
Family History of Mood Disorders	no	108 (97.3%)	30 (96.8%)	Fisher exact test	1	NS
	yes	3 (2.7%)	1 (96.8%)			
Number of DM medications	1	51 (45.95%)	21 (67.74%)	χ^2 =5.21	0.074	NS
	2	54 (48.65%)	8 (25.81%)			
	3	6 (5.41%)	2 (6.45%)			

On the other hand, lifetime depression (current, recurrent, or past) with significantly related to shorter duration of diabetes (Means ± SD; No MDD 9.06 ± 5.50, MDD 6.07 ± 3.70, p <0.001).

There were no significant differences between the “depression” and “no depression” groups regarding diabetic control reflected by the most recent HbA1c results (Mean ± SD No MDD 9.73 ± 1.71, MDD 9.95 ± 2.32 , p value 0.618), diabetic complications (Figure 1) or physical health comorbidities (Figure 2). This could be due to the small sample size.

Figure 1: Diabetic complications in Type 2 diabetes patients with and without depression.

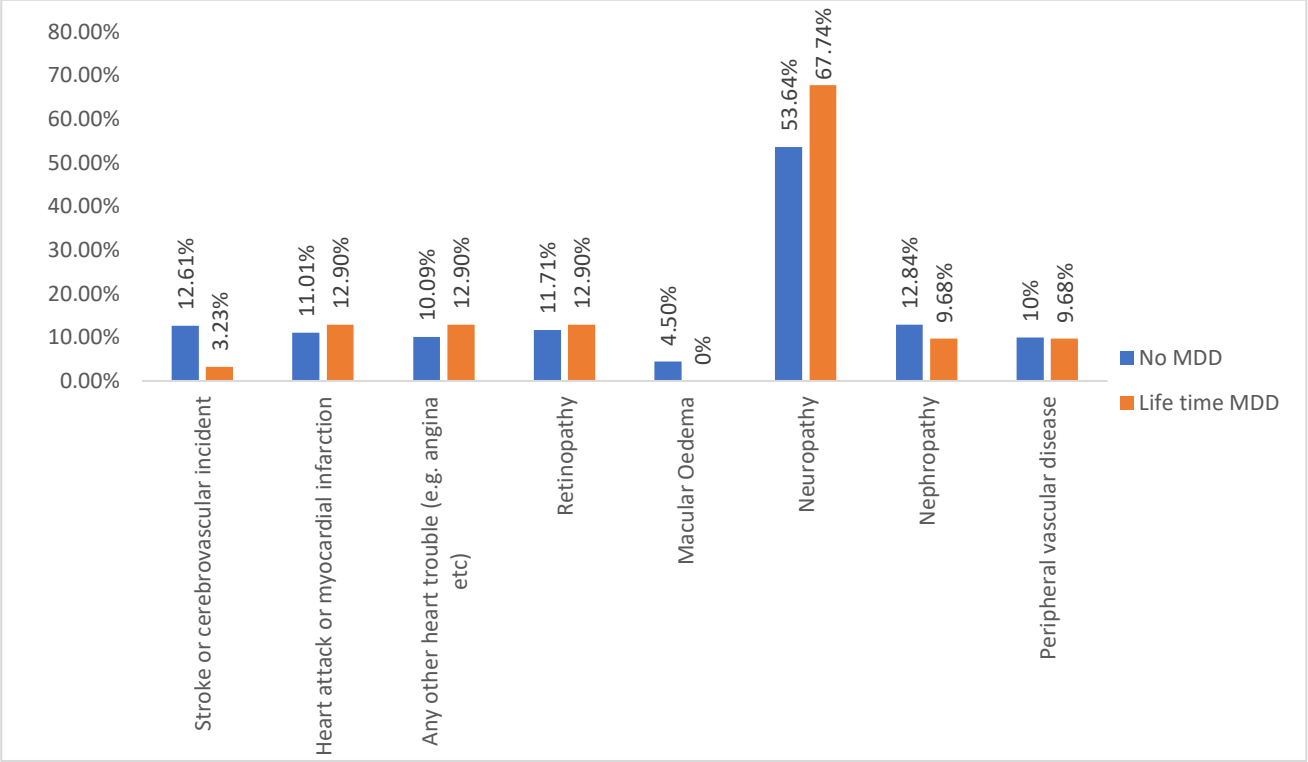
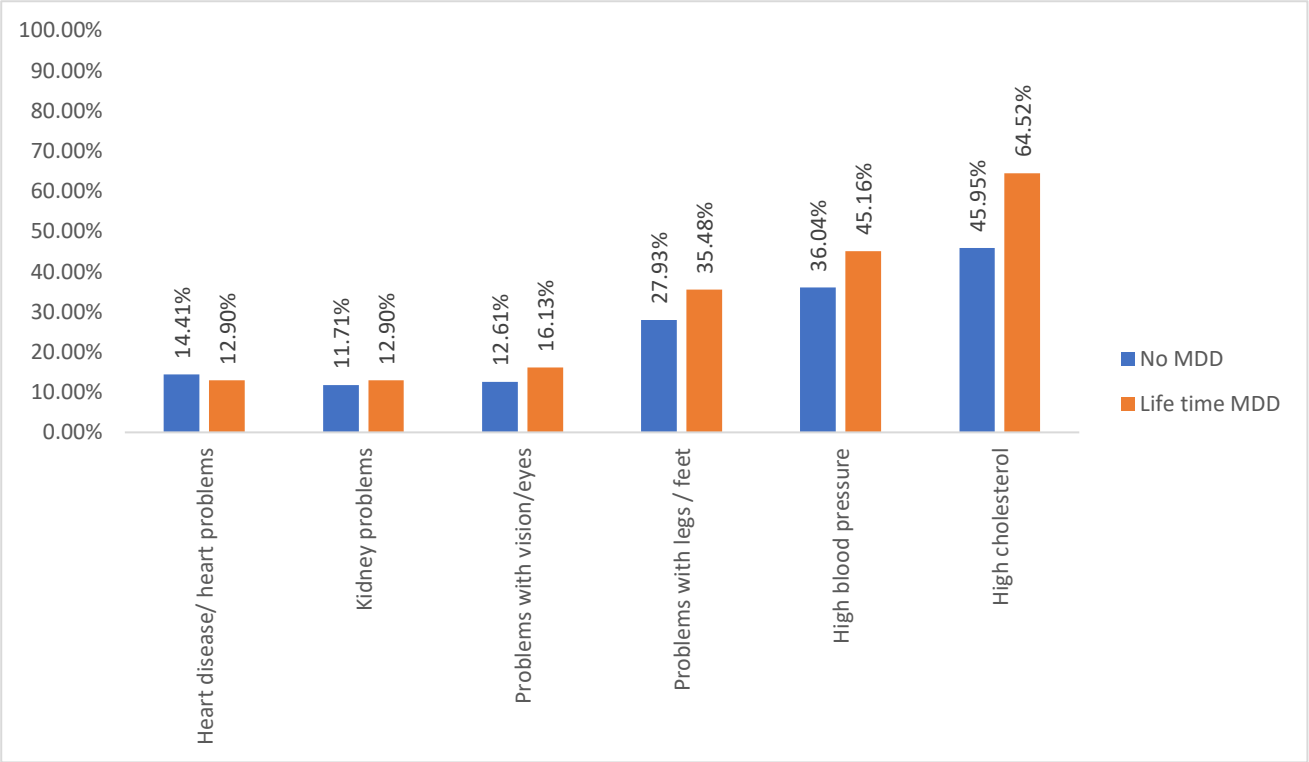


Figure 2: Physical health comorbidities in Type 2 diabetes patients with and without depression.



4. Discussion

This study aimed to assess the prevalence of depression among patients with Type 2 diabetes followed up at the Ain Shams university hospital, Cairo, Egypt. The findings revealed that the prevalence of current depression among the study participants was 21.8%, this magnitude being almost similar to the findings of studies conducted previously in Egypt which found prevalence rates of depression to be 17.5 % and 18 % respectively **(Roshdy et al., 2022, Shehatah et al., 2010)**, but markedly different from another two Egyptian studies which report 9% and 74 % respectively **(Sayed et al., 2022, El-Shafie et al., 2011) .** A recent multicenter study reported depression in 34.2% of the sample. However, the study included both patients with diabetes type I and II (Abd-Elgawad,2023).

This great variation in results is possibly explained by the different tools used to measure depression and sociocultural and behavioral-related factors among study participants.

This variation in prevalence rates has been found in other Arab countries, African countries and worldwide. For example, a study in Jordan reported a prevalence rate of undiagnosed depression among Jordanian diabetic patients was 19.7% **(Al-Amer et al., 2011)** while other Palestinian and Saudi Arabian studies have reported a prevalence of 40 % and 49% respectively **(El Mahalli, 2015; Sweileh et al., 2014).**

Our results are similar to other studies conducted in African countries, for example Mosaku **et al. (2008)** reported a similar prevalence of depression in Nigerian diabetic patients while an Ethiopian study reported a prevalence of 43.6% **(Dejene, 2014)**, with a study in Tanzania found a rate of 87% **(Khan et al., 2019).**

In a recent large Brazilian study a similar prevalence of depression in diabetic patients to be around 22.5% **(Briganti et al., 2019).** However, **Ganasegeran et al. (2014)** found major depression in 40% of a sample of Malaysian diabetic patients which is higher than in this study.

Studying associated risk factors of depression among diabetic patients is important in order to initiate early treatment which results in improving clinical outcomes and reducing resource utilization **(Katon et al., 2009).** The current study found that female patients were more depressed than male patients though the difference was non-significant, possible due to the small sample size. Our findings are consistent with a recent Austrian study composed of more than 123232 diabetic patients and reported a higher prevalence of depression in females **(Deischinger et al., 2020),** which could be explained by hormonal changes females experiencing during different phases of their life **(Albert, 2015).**

Duration of diabetes is also associated with the development of depression in this study and as reported by other researchers **(Asefa et al., 2020, El Mahalli, 2015).** This could be explained by the fact that increased duration of diabetes is known to increase the risk of developing complications and the consequent health care costs which result in more susceptibility to developing depression. However, in our study, we noted that diabetes duration was shorter in those with depression. It is not clear whether this has a cultural or social root or related to the stress of being diagnosed with limited education about diabetes or support provision.

Contrary to most studies (**Khan et al., 2019; Sweileh et al., 2014, El Mahalli, 2015) ,** our results did not find a significant association between development of diabetic complications and depression. This could be due to our small sample size, which was not large enough to produce significant results.

Conclusion and Recommendations

Depression is one of the least mentioned complications associated with diabetes despite its prevalence. The study results showed that more than one fifth of the sample suffered from depression at some point. Younger age, higher education and duration of diabetes were all associated with a higher risk of having depression. Based on these findings, routine screening for depression should be part of diabetes management and a multidisciplinary, holistic, person-centred approach to care which includes psychiatric and psychological assessment and management. Egypt is one of the countries that have adapted the WHO mental health Gap Action Programme (mhGAP) and have been training professionals in primary healthcare settings on various mental health issues. This creates a good opportunity to integrate at least a basic level of screening for mood symptoms in primary healthcare settings and facilitate managing present symptoms early or refer to more specialized services. On the other hand, as this is study was conducted in a tertiary setting, we would recommend that assessment for depression becomes an integral part of the service provided especially consultation of liaison psychiatry is easier. Moreover, being a tertiary hospital, more complex cases are expected to be seen. Despite not being able to detect the association between complications and depression, other researchers had which should also be considered in this recommendation.

Larger studies are needed to be able to generalize the results and also to further investigate the unexpected finding regarding the duration of diabetes, and the association with diabetes complication, with in depth consideration of cultural and social implications of diabetes.

Limitations of the study.

We employed a cross-sectional study design; therefore, the temporal relationship between the predictors and outcome variables is not clear. Moreover, the small number of the sample, and the study being conducted in one clinic -despite that the clinic accepts patients from different governorates- generalizing the results to the whole population is difficult, thus our results should

be interpreted cautiously. Some associations detected by other researchers (e.g. with diabetic complications) were not noticed in this study, which could also be due to the small sample size.

Authors Contribution

TO is the site's primary investigator and was involved in every step. BMM is the endocrinologist who was responsible for the physical health assessments in the study. HE and AAA were the site coordinators. BMM, HE, AAA and II were responsible for data collection and assessing the subjects physically (BMM) and from the mental health perspective (HE, AAA and II). All authors contributed equally to data reviewing and analysis. HE and II produced the first draft of this article. CEL and NS are the INTERPRET-DD primary investigators and project leads. All authors revised the article and contributed to the final version of the manuscript.

Acknowledgments

Authors would like to thank all the patients who agreed to take part in the study. Authors are also grateful to Dr Sara Abdel Hamid, Dr. Omar Yehia and Dr. Safi Mohammed for their contribution in collecting data.

Conflict of interest:

None of the authors have any conflicting interests to declare in relation to this work.

References

- Abd-Elgawad, M., Abdelsattar, N. K., Genedy, G. T., Madeeh, A. K., Khamis, M., Ryaad, M., Hassaan, W. H., Abdullah, E. A., Mustafa, M. G., Assar, A., Farhat, A. M., Soliman, Y., Shrestha, A. B., & Taha, A. M. (2023). Prevalence of depression and anxiety among diabetic patients in Egypt: A cross-sectional study. *Medicine*, *102*(46), e35988. https://doi.org/10.1097/MD.0000000000035988
- Abdel-Wahab, M. et al. (2022) 'Clinical guidelines of the Egyptian Psychiatric Association for the management of treatment-resistant unipolar depression in Egypt', Frontiers in Psychiatry, 13. doi:10.3389/fpsyt.2022.797150.
- Abouzid, M. R., Ali, K., Elkhawas, I., & Elshafei, S. M. (2022). An overview of diabetes mellitus in Egypt and the significance of integrating preventive cardiology in diabetes management. Cureus. https://doi.org/10.7759/cureus.27066
- Al-Amer, R. M., Sobeh, M. M., Zayed, A. A., & Al-domi, H. A. (2011). Depression among adults with diabetes in Jordan: Risk factors and relationship to blood sugar control. Journal of Diabetes and Its Complications, 25(4), 247–252. https://doi.org/10.1016/j.jdiacomp.2011.03.001
- Al-Rubeaan, K. (2010). Type 2 diabetes mellitus red zone. International Journal of Diabetes Mellitus, 2(1), 1–2. https://doi.org/10.1016/j.ijdm.2009.12.009
- Albert, P. R. (2015). Why is depression more prevalent in women? Journal of Psychiatry and Neuroscience, 40(4), 219–221. https://doi.org/10.1503/jpn.150205
- Alzahrani, A., Alghamdi, A., Alqarni, T., Alshareef, R., & Alzahrani, A. (2019). Prevalence and predictors of depression, anxiety, and stress symptoms among patients with type II diabetes attending primary healthcare centers in the Western Region of Saudi Arabia: A cross-sectional study. International Journal of Mental Health Systems, 13(1). https://doi.org/10.1186/s13033-019-0307-6
- Anderson, R. J., Freedland, K. E., Clouse, R. E., & Lustman, P. J. (2001). The prevalence of comorbid depression in adults with diabetes. Diabetes Care, 24(6), 1069–1078. https://doi.org/10.2337/diacare.24.6.1069
- Asefa, A., Zewudie, A., Henok, A., Mamo, Y., & Nigussie, T. (2020). Depression and its associated factors among diabetes mellitus patients attending selected hospitals in southwest Ethiopia: A cross-sectional study. Psychiatry Journal, 2020, 1–8. https://doi.org/10.1155/2020/6486030
- Ballinger, G. A. (2004). Using generalized estimating equations for longitudinal data analysis. Organizational Research Methods, 7(2), 127–150. https://doi.org/10.1177/1094428104263672
- Barglow, P., Hatcher, R., Edidin, D. V., & Sloan-Rossiter, D. (1984). Stress and metabolic control in diabetes: Psychosomatic evidence and evaluation of methods. Psychosomatic Medicine, 46(2), 127–144. https://doi.org/10.1097/00006842-198403000-00005
- Briganti, C. P., Silva, M. T., Almeida, J. V., & Bergamaschi, C. D. (2019). Association between diabetes mellitus and depressive symptoms in the Brazilian population. Revista de Saúde Pública, 53, 5. https://doi.org/10.11606/s1518-8787.2019053000608
- Capmas. (2023). Central Agency for Public Mobilization and Statistics. https://www.capmas.gov.eg/HomePage.aspx

- Clouse, R. E., Lustman, P. J., Freedland, K. E., Griffith, L. S., McGill, J. B., & Carney, R. M. (2003). Depression and coronary heart disease in women with diabetes. Psychosomatic Medicine, 65(3), 376–383. https://doi.org/10.1097/01.psy.0000041624.96580.1f
- Das, R., Singh, O., Thakurta, R. G., Khandakar, M. R., Ali, S. N., Mallick, A. K., Roy, P., & Bhattacharrya, A. K. (2013). Prevalence of depression in patients with type II diabetes mellitus and its impact on quality of life. Indian Journal of Psychological Medicine, 35(3), 284–289. https://doi.org/10.4103/0253-7176.119502
- de Groot, M., Anderson, R., Freedland, K. E., Clouse, R. E., & Lustman, P. J. (2001). Association of Depression and Diabetes Complications: A meta-analysis. Psychosomatic Medicine, 63(4), 619–630. https://doi.org/10.1097/00006842-200107000-00015
- Deischinger, C., Dervic, E., Leutner, M., Kosi-Trebotic, L., Klimek, P., Kautzky, A., & Kautzky-Willer, A. (2020). Diabetes mellitus is associated with a higher risk for major depressive disorder in women than in men. BMJ Open Diabetes Research & Care, 8(1). https://doi.org/10.1136/bmjdrc-2020-001430
- Dejene, S. (2014). Depression and diabetes in Jimma University Specialized Hospital, Southwest Ethiopia. Journal of Psychiatry, 17(3). https://doi.org/10.4172/psychiatry.1000126
- Demyttenaere, K., Bruffaerts, R., Posada-Villa, J., Gasquet, I., Kovess, V., Lepine, J. P., Angermeyer, M. C., Bernert, S., de Girolamo, G., Morosini, P., Polidori, G., Kikkawa, T., Kawakami, N., Ono, Y., Takeshima, T., Uda, H., Karam, E. G., Fayyad, J. A., Karam, A. N., Mneimneh, Z. N., … WHO World Mental Health Survey Consortium (2004). Prevalence, severity, and unmet need for treatment of mental disorders in the World Health Organization World Mental Health Surveys. JAMA, 291(21), 2581–2590. https://doi.org/10.1001/jama.291.21.2581
- Ducat, L., Philipson, L. H., & Anderson, B. J. (2014). The mental health comorbidities of diabetes. JAMA, 312(7), 691. https://doi.org/10.1001/jama.2014.8040
- El Mahalli, A. A. (2015). Prevalence and predictors of depression among type 2 diabetes mellitus outpatients in eastern province , Saudi Arabia. International Journal of Health Sciences, 9(2), 121–127. https://doi.org/10.12816/0024105
- El-Shafie, T. M., El-Saghier, E. O., & Ramadan, I. K. (2011). Depression among type 2 diabetic patients. The Egyptian Journal of Hospital Medicine, 44(1), 258–271. https://doi.org/10.21608/ejhm.2011.16406
- Fung, A. C., Tse, G., Cheng, H. L., Lau, E. S., Luk, A., Ozaki, R., So, T. T., Wong, R. Y., Tsoh, J., Chow, E., Wing, Y. K., Chan, J. C., & Kong, A. P. (2018). Depressive symptoms, co-morbidities, and glycemic control in Hong Kong Chinese elderly patients with type 2 diabetes mellitus. Frontiers in Endocrinology, 9. https://doi.org/10.3389/fendo.2018.00261
- Ganasegeran, K., Renganathan, P., Manaf, R. A., & Al-Dubai, S. A. (2014). Factors associated with anxiety and depression among type 2 diabetes outpatients in Malaysia: A descriptive cross-sectional single-centre study. BMJ Open, 4(4). https://doi.org/10.1136/bmjopen-2014-004794
- Ghanem MH, Ibrahim M, El Behairy AA, El Merghany H. (1999): Mini International Neuropsychiatric Interview for children/adolescents (MINI Kid); Arabic version, 1st ed. Cairo, Egypt: Department of Neuropsychiatry, Faculty of Medicine, AinShams University; 1999.

- Ghanem, M., Gadallah, M., Meky, F. A., Mourad, S., & El-Kholy, G. (2009). National Survey of Prevalence of Mental Disorders in Egypt: preliminary survey. Eastern Mediterranean health journal = La revue de sante de la Mediterranee orientale = al-Majallah al-sihhiyah li-sharq al-mutawassit, 15(1), 65–75.
- Gold, P. W., Goodwin, F. K., & Chrousos, G. P. (1988). Clinical and biochemical manifestations of depression. Relation to the neurobiology of stress (1). The New England journal of medicine, 319(6), 348–353. https://doi.org/10.1056/NEJM198808113190606
- Goyal, R., Singhal, M., & Jialal, I. (2023). Type 2 Diabetes. In StatPearls. StatPearls Publishing.
- Hegazi, R., El-Gamal, M., Abdel-Hady, N., & Hamdy, O. (2015). Epidemiology of and Risk Factors for Type 2 Diabetes in Egypt. Annals of global health, 81(6), 814–820. https://doi.org/10.1016/j.aogh.2015.12.011
- Hofmann, M., Köhler, B., Leichsenring, F., & Kruse, J. (2013). Depression as a risk factor for mortality in individuals with diabetes: a meta-analysis of prospective studies. PloS one, 8(11), e79809. https://doi.org/10.1371/journal.pone.0079809
- International Diabetes Federation. (2021) IDF Diabetes Atlas, 10th edn. Brussels,Belgium. Available at: https://www.diabetesatlas.org
- Ismail K. (2010). Unravelling the pathogenesis of the depression - diabetes link. In Katon W, Maj M and Sartorius N (Ed.), Depression and diabetes (pp: 29-61). Wiley-Blackwell.
- Katon, W., Russo, J., Lin, E. H., Heckbert, S. R., Ciechanowski, P., Ludman, E. J., & Von Korff, M. (2009). Depression and diabetes: factors associated with major depression at five-year follow-up. Psychosomatics, 50(6), 570–579. https://doi.org/10.1176/appi.psy.50.6.570
- Khan, Z. D., Lutale, J., & Moledina, S. M. (2019). Prevalence of Depression and Associated Factors among Diabetic Patients in an Outpatient Diabetes Clinic. Psychiatry journal, 2019, 2083196. https://doi.org/10.1155/2019/2083196
- King, H., Aubert, R. E., & Herman, W. H. (1998). Global burden of diabetes, 1995–2025: Prevalence, numerical estimates, and projections. Diabetes Care, 21(9), 1414–1431. https://doi.org/10.2337/diacare.21.9.1414
- Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: validity of a brief depression severity measure. Journal of general internal medicine, 16(9), 606–613. https://doi.org/10.1046/j.1525-1497.2001.016009606.x
- Lin, E. H. B., Katon, W., Von Korff, M., Rutter, C., Simon, G. E., Oliver, M., Ciechanowski, P., Ludman, E. J., Bush, T., & Young, B. (2004). Relationship of depression and diabetes self-care, medication adherence, and preventive care. Diabetes Care, 27(9), 2154–2160. https://doi.org/10.2337/diacare.27.9.2154
- Lloyd, C. E., Sartorius, N., Cimino, L. C., Alvarez, A., Guinzbourg de Braude, M., Rabbani, G., Uddin Ahmed, H., Papelbaum, M., Regina de Freitas, S., Ji, L., Yu, X., Gaebel, W., Müssig, K., Chaturvedi, S. K., Srikanta, S. S., Burti, L., Bulgari, V., Musau, A., Ndetei, D., Heinze, G., … Mankovsky, B. (2015). The INTERPRET-DD study of diabetes and depression: a protocol. Diabetic medicine : a journal of the British Diabetic Association, 32(7), 925–934. https://doi.org/10.1111/dme.12719
- Lloyd, C., Smith, J., & Weinger, K. (2005). Stress and diabetes: A review of the links. Diabetes Spectrum, 18(2), 121–127. https://doi.org/10.2337/diaspect.18.2.121

- Markowitz, S. M., Gonzalez, J. S., Wilkinson, J. L., & Safren, S. A. (2011). A review of treating depression in diabetes: emerging findings. Psychosomatics, 52(1), 1–18. https://doi.org/10.1016/j.psym.2010.11.007
- Mosaku, K., Kolawole, B., Mume, C., & Ikem, R. (2008). Depression, anxiety and quality of life among diabetic patients: a comparative study. Journal of the National Medical Association, 100(1), 73–78. https://doi.org/10.1016/s0027-9684(15)31178-0
- Naskar, S., Victor, R., & Nath, K. (2017). Depression in diabetes mellitus-A comprehensive systematic review of literature from an Indian perspective. Asian journal of psychiatry, 27, 85–100. https://doi.org/10.1016/j.ajp.2017.02.018
- Nicolau, J., & Masmiquel, L. (2013). Diabetes mellitus y trastorno depresivo, un mal binomio [Diabetes mellitus and depressive disorder, an undesirable association]. Endocrinologia y nutricion : organo de la Sociedad Espanola de Endocrinologia y Nutricion, 60(10), 583–589. https://doi.org/10.1016/j.endonu.2013.01.011
- Odejimi O, Tadros G, Sabry N. A systematic review of the prevalence of mental and neurocognitive disorders amongst older adults' populace in Egypt. Middle East Curr Psychiatry. (2020) 27:47. doi: 10.1186/s43045-020-00055-8
- Okasha, A., Khalil, A. H., El Fiky, M. R., et al (1988) Prevalence of depressive disorders in a sample of rural and urban Egyptian communities. Egyptian Journal of Psychiatry, 2, 167–181.
- Palinkas, L. A., Barrett-Connor, E., & Wingard, D. L. (1991). Type 2 diabetes and depressive symptoms in older adults: a population-based study. Diabetic medicine : a journal of the British Diabetic Association, 8(6), 532–539. https://doi.org/10.1111/j.1464-5491.1991.tb01646.x
- Petrak, F., Baumeister, H., Skinner, T. C., Brown, A., & Holt, R. I. G. (2015). Depression and diabetes: treatment and health-care delivery. The lancet. Diabetes & endocrinology, 3(6), 472–485. https://doi.org/10.1016/S2213-8587(15)00045-5
- Richardson, L. K., Egede, L. E., Mueller, M., Echols, C. L., & Gebregziabher, M. (2008). Longitudinal effects of depression on glycemic control in veterans with Type 2 diabetes. General hospital psychiatry, 30(6), 509–514. https://doi.org/10.1016/j.genhosppsych.2008.07.001
- Rubin, D. B., & Schenker, N. (1986). Multiple imputation for interval estimation from simple random samples with ignorable nonresponse. Journal of the American Statistical Association, 81(394), 366–374. https://doi.org/10.1080/01621459.1986.10478280
- Roshdy, E. A., Ahmed, M. M., Hasan, M. D., & Ahmed, W. M. (2022). Depressive symptoms, dementia and glycemic control in Egyptian elderly patients with type 2 diabetes mellitus. The Medical Journal of Cairo University, 90(3), 253–259. https://doi.org/10.21608/mjcu.2022.234972
- Sayed Ahmed, H. A., Fouad, A. M., Elotla, S. F., Joudeh, A. I., Mostafa, M., Shah, A., Shah, J., & Mohamed, S. F. (2022). Prevalence and Associated Factors of Diabetes Distress, Depression and Anxiety Among Primary Care Patients With Type 2 Diabetes During the COVID-19 Pandemic in Egypt: A Cross-Sectional Study. Frontiers in psychiatry, 13, 937973. https://doi.org/10.3389/fpsyt.2022.937973
- Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., & Dunbar, G. C. (1998). The Mini-International Neuropsychiatric Interview

(M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. The Journal of clinical psychiatry, 59 Suppl 20, 22–57.

- Shehatah, A., Rabie, M. A., & Al-Shahry, A. (2010). Prevalence and correlates of depressive disorders in elderly with type 2 diabetes in primary health care settings. Journal of affective disorders, 123(1-3), 197–201. https://doi.org/10.1016/j.jad.2009.09.002
- Sweileh WM, Abu-Hadeed HM, Al-Jabi SW, Zyoud SH. Prevalence of depression among people with type 2 diabetes mellitus: a cross sectional study in Palestine. BMC Public Health. 2014 Feb 13;14:163. doi: 10.1186/1471-2458-14-163. PMID: 24524353; PMCID: PMC3929146.
- Tabák, A. G., Akbaraly, T. N., Batty, G. D., & Kivimäki, M. (2014). Depression and type 2 diabetes: a causal association?. The lancet. Diabetes & endocrinology, 2(3), 236–245. https://doi.org/10.1016/S2213-8587(13)70139-6
- Whiting, D. R., Guariguata, L., Weil, C., & Shaw, J. (2011). IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes research and clinical practice, 94(3), 311–321. https://doi.org/10.1016/j.diabres.2011.10.029
- Woody, C. A., Ferrari, A. J., Siskind, D. J., Whiteford, H. A., & Harris, M. G. (2017). A systematic review and meta-regression of the prevalence and incidence of perinatal depression. Journal of affective disorders, 219, 86–92. https://doi.org/10.1016/j.jad.2017.05.003
- World Health Organization. (2023, March 31). Depressive disorder (depression). World Health Organization. https://www.who.int/news-room/fact-sheets/detail/depression
- World Health Organization. (2017). Depression and other common mental disorders: global health estimates (No. WHO/MSD/MER/2017.2). World Health Organization.