ORIGINAL ARTICLE

Prevalence of Anxiety and Depression in Patients with Type 2 Diabetes Mellitus

Nauman Ismat Butt[1*], Muhammad Hasnain[1], Huzaifa Nadeem[1], Tashia Malik[2], Barak Waris[1], Osama Habib[1] and Muhammad Atif Qureshi[1]

[1]*Department of Medicine & Allied, Azra Naheed Medical College, Superior University, Lahore, Pakistan*
[2]*Department of Medicine, Jinnah Hospital, Allama Iqbal Medical College, Lahore, Pakistan*

Abstract

Background: This study investigates the prevalence of depression and anxiety among type 2 diabetes mellitus (T2DM) patients in Pakistan, focusing on socio-demographic factors and co-morbidities. Understanding these mental health issues is crucial for improving diabetes management and patient outcomes, particularly in a country with limited mental health resources.

Objective: To determine the frequencies of anxiety and depression in patients with T2DM presenting in medicine outpatient clinics.

Methods: A cross-sectional study was conducted at Chaudhary Muhammad Akram Teaching and Research Hospital, Azra Naheed Medical College, Superior University Lahore, from February to October 2024. The study was performed in outpatient clinics of the medicine department. A total of 216 T2DM patients were enrolled using non-probability consecutive sampling. Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS). Demographic data and diabetes-related variables were also collected. Statistical analysis was performed using SPSS version 23.0, with chi-square tests post-stratification keeping p-value <0.05 as significant.

Results: Mean age was 53.7±13.0 years, with a majority being female (61.1%). Poor diabetes control was reported in 176 (81.5%) patients. Anxiety was seen in 44 (20.4%) patients, with higher levels in females than males (p<0.001). Depression was found in 54 (25.0%) patients, with significantly higher rates in females compared to males (p<0.001), and in those with chronic kidney disease (p=0.007).

Conclusion: This study highlights the high frequency of anxiety and depression among T2DM patients, especially in females and those with chronic kidney disease. These findings underscore the need for integrated mental health care in diabetes management, including routine screening and targeted interventions for high-risk groups.

Keywords: *Type 2 diabetes mellitus (T2DM), anxiety, depression, hospital anxiety and depression scale (HADS), HbA1c, observational study, cross-sectional study, Pakistan.*

INTRODUCTION

Diabetes mellitus (DM) is a prevalent chronic metabolic disorder that is rising globally, with approximately 285 million people affected, a number projected to reach 438 million by 2030, with over 70% of cases in developing countries [1]. People with DM face serious complications such as cardiovascular disease, kidney failure, neuropathy, and blindness, which severely impact their quality of life and contribute to high healthcare costs, estimated at USD 850 billion globally in 2017 [2]. Type 2 diabetes is increasingly common in both high- and low-income countries, but the rise is expected to be more significant in low-income regions due to factors like urbanization, dietary changes, and limited access to healthcare [3, 4]. This rise is driven by factors such as urbanization, changes in diet, and limited access to early diagnosis and effective treatment. The growing diabetes epidemic, particularly in resource-poor settings, highlights the need for better preventive measures, early detection, and more efficient management strategies [4].

**Corresponding author: Nauman Ismat Butt, Department of Medicine & Allied, Azra Naheed Medical College, Superior University, Lahore, Pakistan, E-mail: nauman_ib@yahoo.com*
Received: November 10, 2024; Revised: January 16, 2025; Accepted: February 18, 2025
DOI: https://doi.org/10.37184/lnjpc.2707-3521.7.47

Studies have shown that depression is more common in insulin-dependent diabetic individuals, as they typically have more advanced disease and require more intensive treatment [5]. Depression rates increase as diabetes progresses and complications like neuropathy and sexual dysfunction emerge [6]. Neuropathy and nephropathy are strong predictors of depression in diabetic patients, who are almost twice as likely to experience depression and anxiety compared to the general population [7]. There is evidence linking depression and diabetes through dysregulation of the hypothalamic-pituitary-adrenal axis, with elevated cortisol levels worsening metabolic dysfunctions such as insulin resistance [8]. Depression, a leading cause of disability affecting 300 million people globally [9], is twice as likely to occur in individuals with both diabetes and depression than in those with either condition alone [10].

The increased cortisol levels in depression lead to further metabolic issues, complicating diabetes management and resulting in poorer glycemic control, impaired self-care, and reduced quality of life [11, 12]. This dual burden poses challenges for clinicians, as both conditions exacerbate each other, leading to higher HbA1c levels and unstable blood sugar control [13]. The emotional

strain of depression can interfere with adherence to treatment and lifestyle recommendations, worsening glycemic control, impairing self-care, and lowering quality of life, which in turn raises healthcare costs. The coexistence of diabetes and depression poses significant challenges for clinicians, as both conditions amplify each other's effects. Effective diabetes management must therefore include attention to mental health, and identifying those at risk for depression to improve patient outcomes and quality of life [13].

A study in the United Kingdom found that about one-third of diabetic individuals experience anxiety, and one-quarter suffer from depression, which aligns with findings from similar research [14, 15]. Although studies in developed countries have explored the link between diabetes and mental health, research in Pakistan is limited. This study aims to investigate the prevalence of depression and anxiety among type 2 diabetic patients presenting in outpatient medicine clinics. Understanding these mental health issues is critical for improving diabetes management and overall patient outcomes, particularly in a country with limited mental health resources, and for informing more effective healthcare policies and interventions. This study aims to fill the gap in research on the frequencies of anxiety and depression in patients with T2DM presenting in medicine outpatient clinics in Pakistan, where mental health resources are limited. Mental health significantly affects diabetes management, adherence to treatment, and overall quality of life, helping to inform targeted interventions and improve patient outcomes.

METHODOLOGY

The present cross-sectional study was conducted at the outpatient clinics of the Department of Medicine, Chaudhary Muhammad Akram Teaching and Research Hospital, affiliated with Azra Naheed Medical College, Superior University Lahore, from February 2024 to October 2024. The research was approved by the Ethical Review Board, Ref. No. IRB/ANMC/2024/04 dated 15th February 2024. Keeping a confidence interval of 95% with a margin of error of 6%, a sample size of 214 was required using the expected frequency of anxiety as 27.6% in patients with type 2 diabetes mellitus [16]. Keeping a confidence interval of 95% with a margin of error of 6%, a sample size of 207 was required using the expected frequency of depression as 26.3% in patients with type 2 diabetes mellitus [16]. Therefore to study the frequency of both anxiety and depression, we enrolled 216 patients of type 2 diabetes mellitus in our study. Detailed informed consent was taken from each patient before inclusion in the study. Using a non-probability consecutive sampling technique, the study included participants with type 2 diabetes mellitus, of both genders, while excluding patients with type 1 diabetes mellitus, steroid use, malignancy, pregnancy/post-partum, or those with pre-existing psychiatric disorders to minimize bias. Type 2 Diabetes Mellitus was defined as patients with HbA1c of greater than 6.5%, or two blood glucose random readings of ≥200mg/dl, or previous history of diabetes diagnosis, or taking anti-hyperglycemic medicines.

To evaluate anxiety and depression, the Hospital Anxiety and Depression Scale (HADS) was used. This 14-item self-administered tool is divided into two subscales, each containing seven items, to measure anxiety and depression [17]. Each item is rated on a four-point Likert scale, and the total score determines the severity: a score of 0-7 indicates no anxiety/depression, 8-10 suggests moderate levels, and 11-21 indicates severe anxiety/depression. In addition to HADS, a demographic form was created to collect information on variables such as age, gender, employment and marital status, diabetes duration, diabetes control, and presence/absence of ischemic heart disease and chronic renal disease.

All the data were analyzed using SPSS version 23.0, with descriptive statistics (mean and standard deviation) for continuous variables, and frequencies and percentages for categorical variables. Chi-square tests were used post-stratification, with a significance level set at p-value ≤0.05.

RESULTS

In this study, 216 patients with type 2 diabetes mellitus were enrolled to determine the frequency of anxiety and depression, with a majority of females as demonstrated in Table **1**. The mean age of the participants was 53.7±13.0 years, with 110 (50.9%) patients aged 52 years or more. In terms of employment status, 114 (52.8%) were unemployed. The majority of participants were married.

Table 1: Demographic and clinical variables.

Variables	Groups	Frequency	Percentage
Gender	Female	132	61.1
	Male	84	38.9
Age (years)	51 or less	106	49.1
	52 or more	110	50.9
Employment Status	Employed	102	47.2
	Unemployed	114	52.8
Marital Status	Married	200	92.6
	Unmarried	16	7.4
Diabetes Duration (years)	5 or less	108	50.0
	6 or more	108	50.0
Diabetes Control	Good/Controlled	40	18.5
	Poor/Uncontrolled	176	81.5
Ischemic Heart Disease	Present	24	11.1
	Absent	192	88.9
Chronic Kidney Disease	Present	18	8.3
	Absent	198	91.7
HADS Anxiety Score	Normal (0-7)	130	60.2
	Borderline (8-10)	42	19.4
	Abnormal (11-21)	44	20.4
HADS Depression Score	Normal (0-7)	110	50.9
	Borderline (8-10)	52	24.1
	Abnormal (11-21)	54	25.0

Table 2: Stratification of data with regards to HADS anxiety score.

Variables	Groups	HADS Anxiety Score			p-value
		0-7 Normal n(%)	8-10 Borderline n(%)	11-21 Abnormal n(%)	
Gender	Female	66 (50.0)	34 (25.8)	32 (24.2)	*<0.001
	Male	64 (76.2)	08 (9.5)	12 (14.3)	
Age (years)	51 or less	58 (54.8)	24 (22.6)	24 (22.6)	0.265
	52 or more	72 (65.5)	18 (16.4)	20 (18.1)	
Employment Status	Employed	62 (60.8)	20 (19.6)	20 (19.6)	0.966
	Unemployed	68 (59.6)	22 (19.3)	24 (21.1)	
Marital Status	Married	120 (60.0)	40 (20.0)	40 (20.0)	0.731
	Unmarried	10 (62.5)	02 (12.5)	04 (25.0)	
Diabetes Duration (years)	5 or less	62 (57.4)	24 (22.2)	22 (20.4)	0.567
	6 or more	68 (63.0)	18 (16.6)	22 (20.4)	
Diabetes Control	Good/Controlled	22 (55.0)	12 (30.0)	06 (15.0)	0.155
	Poor/Uncontrolled	108 (61.4)	30 (17.0)	38 (21.6)	
Ischemic Heart Disease	Present	14 (58.4)	02 (8.3)	08 (33.3)	0.138
	Absent	116 (60.4)	40 (20.8)	36 (18.8)	
Chronic Kidney Disease	Present	10 (55.6)	02 (11.1)	06 (33.3)	0.303
	Absent	120 (60.6)	40 (20.2)	38 (19.2)	

*Significant at p<0.05

Table 3: Stratification of data with regards to HADS depression score.

Variables	Groups	HADS Depression Score			p-value
		0-7 Normal n(%)	8-10 Borderline n(%)	11-21 Abnormal n(%)	
Gender	Female	54 (40.9)	32 (24.3)	46 (34.8)	*<0.001
	Male	56 (66.7)	20 (23.8)	08 (9.5)	
Age (years)	51 or less	44 (41.5)	34 (32.1)	28 (26.4)	*0.009
	52 or more	66 (60.0)	18 (16.4)	26 (23.6)	
Employment Satus	Employed	52 (51.0)	28 (27.5)	22 (21.5)	0.401
	Unemployed	58 (50.8)	24 (21.1)	32 (28.1)	
Marital Status	Married	102 (51.0)	50 (25.0)	48 (24.0)	0.360
	Unmarried	08 (50.0)	02 (12.5)	06 (37.5)	
Diabetes Duration (years)	5 or less	52 (48.2)	28 (25.9)	28 (25.9)	0.702
	6 or more	58 (53.7)	24 (22.2)	26 (24.1)	
Diabetes Control	Good/Controlled	20 (50.0)	14 (35.0)	06 (15.0)	0.110
	Poor/Uncontrolled	90 (51.1)	38 (21.6)	48 (27.3)	
Ischemic Heart Disease	Present	14 (58.3)	04 (16.7)	06 (25.0)	0.636
	Absent	96 (50.0)	48 (25.0)	48 (25.0)	
Chronic Kidney Disease	Present	06 (33.3)	02 (11.1)	10 (55.6)	*0.007
	Absent	104 (52.5)	50 (25.3)	44 (22.2)	

*Significant at p<0.05

The mean diabetes duration was 6.8±6.2 years, with half of the participants (108, 50.0%) having 5 or fewer years of diabetes. Mean HbA1c (%) was 9.5±2.7 and a large proportion of participants reported poor/uncontrolled diabetes. Ischemic heart disease (IHD) was present in 24 (11.1%) patients while chronic kidney disease (CKD) was reported in 18 (8.3%) as depicted in Table **1**.

The mean HADS anxiety score was 6.8±4.6 while the mean HADS depression score was 7.9±4.3. Regarding psychological outcomes, anxiety levels as assessed by the HADS Anxiety scale demonstrated that 42 (19.4%) patients were in the borderline anxiety category and 44 (20.4%) had abnormal anxiety scores. Similarly, depression levels measured by the HADS Depression scale showed that 52 (24.1%) had borderline depression and 54 (25.0%) had abnormal depression scores as demonstrated in Table **1**.

On stratification of data with regards to HADS anxiety score, a statistical significance of anxiety was seen with gender. Anxiety was seen in 32 (24.4%) females

compared to 12 (14.3%) males having a p-value <0.01. No statistical association of anxiety was seen with age (p-value 0.265), employment status (p-value 0.966), marital status (p-value 0.731), diabetes duration (p-value 0.567), diabetes control (p-value 0.155), ischemic heart disease (p-value 0.138) or chronic kidney disease (p-value 0.303) as shown in Table **2**.

On stratification of data with regards to HADS depression score, a statistical significance of depression was seen with gender, age, and chronic kidney disease. Depression was seen in 46 (34.8%) females compared to 08 (9.5%) males (p<0.001). Depression was reported in 28 (26.4%) patients aged 51 years or less as opposed to 26 (23.6%) patients aged 52 years or more (p=0.009). Depression was seen in 10 (55.6%) patients with chronic kidney disease compared to 44 (22.2%) patients without CKD (p=0.007). No statistical association of depression was seen with employment status (p=0.401), marital status (p=0.360), diabetes duration (p=0.702), diabetes control (p=0.110), or ischemic heart disease (p=0.636) as shown in Table **3**.

DISCUSSION

Our findings align with previous studies that report a higher prevalence of depression and anxiety among female diabetic patients, as well as a strong association between these mental health issues and the presence of co-morbidities such as CKD. The results of the present study highlight a significant association between gender and both anxiety and depression in patients with type 2 diabetes. Specifically, females were more likely to experience both anxiety and depression compared to males, with a stronger prevalence of depression observed in females (34.8%) compared to males (9.5%). Additionally, CKD was a major factor contributing to the higher incidence of depression, with more than half (55.6%) of patients with CKD reporting depressive symptoms. Similar to Dehesh *et al.,* Masmoudi *et al.* and Al-Mohaimeed, we observed a notably higher prevalence of depression in females and those with CKD, which could be attributed to gender-specific biological, hormonal, and social factors that may influence mental health [18,19]. Age was also associated with depression, as younger patients (≤51 years) were more likely to experience depressive symptoms than older patients (≥52 years). This is consistent with findings from other studies, suggesting that younger diabetic patients may face greater emotional and psychological stress due to challenges related to early disease onset and longer-term management. However, no significant associations were found between psychological distress and other factors such as employment, marital status, diabetes duration, or control. Our study's lack of significant associations with employment, marital status, or diabetes duration may reflect differences in patient populations or suggest that other unmeasured factors, such as socioeconomic status or access to healthcare, could play a more pivotal role in influencing mental health outcomes. These findings suggest that addressing gender differences and comorbidities like CKD could be crucial in managing mental health in diabetic patients. Dehesh *et al.* reported depression in 59% and anxiety in 62% of the 1500 diabetic patients enrolled, with anxiety linked to high FBS, LDL-C, TG, hypertension, diabetic complications, and low physical activity, while depression was associated with female gender, older age, high BMI, high FBS, LDL-C, low HDL-C, high TG, high HbA1c, hypertension, and low physical activity [18]. A study in Tunisia found that 40% of elderly diabetics experienced anxiety and 22% had depression, while Masmoudi *et al.* reported higher rates of depression (44%) and anxiety (58%) in their cohort of diabetic patients [18, 20]. The prevalence of depressive and anxiety disorders was 43% and 50% respectively in the study by Alami-Hassani *et al.,* with significant associations identified between these mental health conditions and demographic, economic, medical, and diabetes-related factors including age, gender, professional activity, co-morbidities, family history, the type, complications and treatment of diabetes mellitus [21]. In contrast, research from Western countries indicates a somewhat lower prevalence, using the HADS scale to report 32% of diabetics as depressed and 22% as anxious [21]. In Asian studies, the prevalence of depression in diabetic patients ranges from 17% to 44%, while anxiety affects between 4% and 58% of individuals. Al-Mohaimeed reported anxiety and depression in 43.6% and 34.8% of diabetic patients [19]. Rajput *et al.* reported the frequency of depression at 26.3% and anxiety at 27.6% in patients with type 2 diabetes mellitus [16]. Severe depression and anxiety had a strong association with female gender, age, insulin use, and the presence of diabetes complications including nephropathy, retinopathy, and ischemic heart disease [16].

Deischinger *et al.* highlighted that diabetes mellitus exacerbates the gender gap in depression, with women being more likely to develop depression than men, particularly between the ages of 40 and 49 years [22]. The higher prevalence of depression in women with diabetes may be linked to factors such as hormonal fluctuations, obesity, alcohol use, and cardiovascular diseases, which increase the risk for depression [22, 23]. Additionally, women tend to visit healthcare providers more often than men, leading to higher rates of depression diagnosis. Men, in contrast, may be less likely to report symptoms or seek help, which may lead to underdiagnosis of depression [22, 24]. Therefore addressing gender-specific factors, including diabetes-related distress and obesity, could help narrow the gender gap in depression among diabetic patients. In the study by Chireh *et al.* over 10 years, the incidence of major depressive disorder was 4.1%, while 10.1% of participants developed diabetes [25]. Depression was particularly linked to female gender, family stress, traumatic events, and chronic or heart disease while diabetes was more common with advancing age and non-white ethnicity [25]. It has been

reported that interventions like group therapy, online treatments, and psychotherapy are highly effective in improving depression in diabetes mellitus, while the impact on glycemic control was more mixed [25, 26]. Pharmacological treatments and group therapy show significant effects on glycemic control, but exercise and online interventions do not [27, 28]. For patients with subthreshold depression, psychotherapy was most effective, while psychoeducation offered no advantages over usual care [29]. Collaborative care has been recommended for patients with complex, multimorbid conditions [30, 31]. The potential for metformin to also improve depressive symptoms has been noted, suggesting avenues for future research [32].

The present study has several limitations, including its cross-sectional design, which limits the ability to draw causal conclusions, and its single-center setting, which may restrict the generalizability of the findings. This selection bias limited the diversity of the sample. Additionally, sampling bias may have been introduced if certain groups, such as those with more severe diabetes or those actively seeking mental health support, were overrepresented. The exclusion of patients with pre-existing psychiatric conditions may also have overlooked a significant subgroup that could benefit from mental health support. Additionally, information and response bias is another concern, as the reliance on self-reported data through the HADS questionnaire might have led to inaccurate reporting of anxiety and depression symptoms, either due to social desirability bias or a lack of awareness of mental health issues. Recall bias could also have influenced participants' ability to accurately report past experiences with mental health symptoms. Furthermore, reporting bias could have played a role, as participants may have underreported symptoms due to the stigma surrounding mental health. Finally, confounding bias may have arisen from unaccounted factors, such as medication use or other health conditions, which could have influenced both diabetes management and mental health outcomes. The study did not consider other potentially important socio-demographic factors, such as income or family support that might influence mental health outcomes. It should also be noted that clinic-based samples may not accurately represent the broader diabetic population, as they are more likely to include patients with more severe or complicated cases, potentially leading to an overestimation of anxiety and depression prevalence. Moreover, the study does not address whether the mental health challenges observed in diabetic patients are specifically more pronounced compared to those with other chronic conditions. Many long-term illnesses, including cardiovascular disease, chronic respiratory conditions, and kidney disease, are also commonly associated with elevated levels of mood disorders. Therefore, without comparisons to other chronic conditions, it is difficult to determine whether the mental health burden in diabetes is particularly noteworthy or part of a broader trend seen in individuals with long-term health conditions. Future studies should aim to minimize these biases through more rigorous sampling methods, objective measures, and control for confounding variables. Future research should consider longitudinal studies to establish causal relationships and multi-center designs to increase the diversity and generalizability of the results. It is also recommended that future studies explore a broader range of socio-demographic factors and include patients with pre-existing psychiatric conditions to better understand the full spectrum of mental health challenges in diabetic patients. Furthermore, integrating mental health screening and intervention into routine diabetes care, especially for high-risk groups such as females and those with comorbidities like CKD, could improve overall patient outcomes. Lastly, investigating the impact of cultural attitudes towards mental health in Pakistan could provide valuable insights for developing culturally sensitive mental health interventions for diabetic patients.

CONCLUSION

In conclusion, this study highlights the high prevalence of anxiety and depression in patients with type 2 diabetes, particularly among females and those with CKD. It emphasizes the need for targeted mental health interventions, especially in high-risk groups, to improve overall care. The strong link between depression and comorbidities like CKD calls for a holistic approach to diabetes management, addressing both physical and mental health. Regular psychological screening should be integrated into routine care. Further research is needed to explore causal relationships and socio-demographic factors influencing mental health in this population.

ETHICS APPROVAL

The research was approved by Ethical Review Board of Azra Naheed Medical College, Superior University Lahore, Ref. No. IRB/ANMC/2024/04 dated 15th February 2024. All procedures performed in studies involving human participants were following the ethical standards of the institutional and/ or national research committee and the Helsinki Declaration.

CONSENT FOR PUBLICATION

Detailed informed consent was taken from each patient before inclusion in the study.

AVAILABILITY OF DATA

Data generated or analyzed during this study are available from the corresponding author upon reasonable request.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

Declared none.

AUTHORS' CONTRIBUTION

This study was conceived and designed by NIB, MH, OH and MAQ. NIB, HN, TM and BW did the initial literature research. NIB, MH and HN did the data collection, assembly and patient assessment. Data analysis and interpretation were done by NIB, TM and BW. NIB, MH, HN and BW were involved in manuscript writing. TM, OH and MAQ did the final critical review and corrections. NIB is the corresponding author on behalf of all other authors.

REFERENCES

1. Baena-Díez JM, Peñafiel J, Subirana I, Ramos R, Elosua R, Marín-Ibañez A, *et al.* Risk of cause-specific death in individuals with diabetes: A competing risks analysis. Diabetes Care 2016; 39(11): 1987-95. DOI: https://doi.org/10.2337/dc16-0614
2. Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, *et al.* IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract 2018; 138: 271-81. DOI: https://doi.org/10.1016/j.diabres.2018.02.023
3. Kaiser AB, Zhang N, van der Pluijm WO. Global prevalence of type 2 diabetes over the next ten years (2018-2028). Diabetes 2018; 67(11): 1234-41.
4. Butt NI, Ghoauri MSA, Waris U, Sabeh D, Qaisar F. Frequency of restless legs syndrome in Pakistani patients with type 2 diabetes mellitus. Cureus 2024; 16(6): e62624. DOI: https://doi.org/10.7759/cureus.62624
5. Li C, Ford ES, Strine TW, Mokdad AH. Prevalence of depression among U.S. adults with diabetes: Findings from the 2006 behavioral risk factor surveillance system. Diabetes Care 2008; 31(1): 105-7. DOI: https://doi.org/10.2337/dc07-1154
6. de Groot M, Anderson R, Freedland KE, Clouse RE, Lustman PJ. Association of depression and diabetes complications: A meta-analysis. Psychosom Med 2001; 63(4): 619-30. DOI: https://doi.org/10.1097/00006842-200107000-00015
7. Tovilla-Zárate C, Juárez-Rojop I, Peralta Jimenez Y, Jiménez MA, Vázquez S, Bermúdez-Ocaña D, *et al.* Prevalence of anxiety and depression among outpatients with type 2 diabetes in the Mexican population. PLoS One 2012; 7(5): e36887. DOI: https://doi.org/10.1371/journal.pone.0036887
8. Trento M, Raballo M, Trevisan M, Sicuro J, Passera P, Cirio L, *et al.* A cross-sectional survey of depression, anxiety, and cognitive function in patients with type 2 diabetes. Acta Diabetol 2012; 49(3): 199-203. DOI: https://doi.org/10.1007/s00592-011-0275-z
9. World Health Organization. Depression [Internet]. Geneva: World Health Organization; 2018 [cited 2019 Mar 7]. Available from: https: //www.who.int/news-room/fact-sheets/detail/depression
10. Butt NI, Ghoauri MSA, Waris U, Sabeh D, Qaisar F, Imran A. Prevalence of adhesive capsulitis in patients with type 2 diabetes mellitus: A single-center cross-sectional study from Pakistan. Cureus 2024; 16(10): e70675. DOI: https://doi.org/10.7759/cureus.70675
11. van der Feltz-Cornelis C, Allen SF, Holt RIG, Roberts R, Nouwen A, Sartorius N. Treatment for comorbid depressive disorder or subthreshold depression in diabetes mellitus: Systematic review and meta-analysis. Brain Behav 2021; 11(2): e01981. DOI: https://doi.org/10.1002/brb3.1981
12. Li S, Yang D, Zhou X, Chen L, Liu L, Lin R, *et al.* Neurological and metabolic related pathophysiologies and treatment of comorbid diabetes with depression. CNS Neurosci Ther 2024; 30(4): e14497. DOI: https://doi.org/10.1111/cns.14497
13. Khan P, Qayyum N, Malik F, Khan T, Khan M, Tahir A. Incidence of anxiety and depression among patients with type 2 diabetes and the predicting factors. Cureus 2019; 11(3): e4254. DOI: https://doi.org/10.7759/cureus.4254
14. Boettiger DC, Lin TK, Almansour M, Hamza MM, Alsukait R, Herbst CH, *et al.* Projected impact of population aging on non-communicable disease burden and costs in the Kingdom of Saudi Arabia, 2020-2030. BMC Health Serv Res 2023; 23(1): 1381. DOI: https://doi.org/10.1186/s12913-023-10309-w
15. Chowdhry MAT, Butt NI, Shakeel H, Gondal MNF, Saeed H. Tahir H. Is lack of patient knowledge a cause of poorly controlled diabetes mellitus? PJMHS 2021; 15(9): 2302-4. DOI: https: //doi.org/10.53350/pjmhs211592302
16. Rajput R, Gehlawat P, Gehlan D, Gupta R, Rajput M. Prevalence and predictors of depression and anxiety in patients of diabetes mellitus in a tertiary care center. Indian J Endocrinol Metab 2016; 20(6): 746-51. DOI: https://doi.org/10.4103/2230-8210.192924
17. Stern AF. The hospital anxiety and depression scale. Occup Med (Lond) 2014; 64(5): 393-4. DOI: https://doi.org/10.1093/occmed/kqu024
18. Dehesh T, Dehesh P, Shojaei S. Prevalence and associated factors of anxiety and depression among patients with type 2 diabetes in Kerman, Southern Iran. Diabetes Metab Syndr Obes 2020; 13: 1509-17. DOI: https://doi.org/10.2147/DMSO.S249385
19. Al-Mohaimeed AA. Prevalence and factors associated with anxiety and depression among type 2 diabetes in Qassim: A descriptive cross-sectional study. J Taibah Univ Med Sci 2017; 12(5): 430-6. DOI: https://doi.org/10.1016/j.jtumed.2017.04.002
20. Masmoudi J, Damak R, Zouari H, Ouali U, Mechri A, Zouari N, *et al.* Prevalence and impact of anxiety and depression on type 2 diabetes in tunisian patients over sixty years old. Depress Res Treat 2013; 2013: 341782. DOI: https://doi.org/10.1155/2013/341782
21. Alami-Hassani C, Abaïnou L, Douali W, Idrissi A, Elhadri S, Laffinti MA, *et al.* The prevalence of anxiety and depressive disorders in patients with diabetes. World J Adv Res Rev 2023; 18(3): 1091-7. DOI: https://doi.org/10.30574/wjarr.2023.18.3.1067
22. Deischinger C, Dervic E, Leutner M, Kosi-Trebotic L, Klimek P, Kautzky A, *et al.* Diabetes mellitus is associated with a higher risk for major depressive disorder in women than in men. BMJ Open Diabetes Res Care 2020; 8(1): e001430. DOI: https://doi.org/10.1136/bmjdrc-2020-001430
23. Kwong ASF, Manley D, Timpson NJ, Pearson RM, Heron J, Sallis H, *et al.* Identifying critical points of trajectories of depressive symptoms from childhood to young adulthood. J Youth Adolesc 2019; 48(4): 815-27. DOI: https://doi.org/10.1007/s10964-018-0976-5
24. Gronich N, Saliba W, Schwartz JB. Prevalence and proportion by age and sex of chronic health conditions in a large healthcare system. PLoS One 2024; 19(9): e0308031. DOI: https://doi.org/10.1371/journal.pone.0308031
25. Chireh B, D'Arcy C. Shared and unique risk factors for depression and diabetes mellitus in a longitudinal study, implications for prevention: An analysis of a longitudinal population sample aged ≥ 45 years. Ther Adv Endocrinol Metab 2019; 10: 2042018819865828. DOI: https://doi.org/10.1177/2042018819865828
26. van der Feltz-Cornelis C, Allen SF, Holt RIG, Roberts R, Nouwen A, Sartorius N. Treatment for comorbid depressive disorder or subthreshold depression in diabetes mellitus: Systematic review and meta-analysis. Brain Behav 2021; 11(2): e01981. DOI: https://doi.org/10.1002/brb3.1981
27. de Groot M, Shubrook JH, Hornsby WG Jr, Pillay Y, Mather KJ, Fitzpatrick K, *et al.* Program ACTIVE II: Outcomes from a randomized, multistate community-based depression treatment for

rural and urban adults with type 2 diabetes. Diabetes Care 2019; 42(7): 1185-93.
DOI: https://doi.org/10.2337/dc18-2400

28. Che T, Teng X, Huang Q, Mu Y, Tang X, Mu X, *et al.* Agomelatine *versus* fluoxetine in glycemic control and treating depressive and anxiety symptoms in type 2 diabetes mellitus subjects: A single-blind randomized controlled trial. Neuropsychiatr Dis Treat 2018; 14: 1527-33.
DOI: https://doi.org/10.2147/NDT.S167608
29. Arteaga-Henríquez G, Simon MS, Burger B, Weidinger E, Wijkhuijs A, Arolt V, *et al.* Low-grade inflammation as a predictor of antidepressant and anti-inflammatory therapy response in MDD Patients: A systematic review of the literature in combination with an analysis of experimental data collected in the EU-MOODINFLAME Consortium. Front Psychiatry 2019; 10: 458.
DOI: https://doi.org/10.3389/fpsyt.2019.00458
30. Habib O, Ashaq F, Butt NI, Ashraf HH, Mahmood K, Anser A. Prevalence of depression and anxiety in chronic kidney disease patients. PJMHS 2022; 16(6): 236-8.
DOI: https://doi.org/10.53350/pjmhs22166236
31. van Eck van der Sluijs JF, Castelijns H, Eijsbroek V, Rijnders CAT, van Marwijk HWJ, van der Feltz-Cornelis CM. Illness burden and physical outcomes associated with collaborative care in patients with comorbid depressive disorder in chronic medical conditions: A systematic review and meta-analysis. Gen Hosp Psychiatry 2018; 50: 1-14.
DOI: https://doi.org/10.1016/j.genhosppsych.2017.08.003
32. Wei L, Hui Y, Jinxi W, Shihui L, Hongping L, Jian L, *et al.* Zuogui Jiangtang Jieyu prescription improves diabetes-related depression by modulation of gut microbiota and neuroinflammation in hippocampus. Heliyon 2024; 10(21): e39291.
DOI: https://doi.org/10.1016/j.heliyon.2024.e39291