

Prevalence and Impact of Psychological Disorders on Pharmacotherapy of Diabetic Patients in Low Resource Settings: A Prospective Assessment in Primary Healthcare Settings

Kiran Shahbaz¹, Alamgeer¹, Vibhu Paudyal^{2,3}, Maryam Zubair⁴, Maryam Zahra Safdar⁵, Momina Tahir⁵, Laraib Akram⁵, Salamat Ali⁵

¹Department of Pharmacology, University College of Pharmacy, University of the Punjab, Lahore, Pakistan; ²Institute of Clinical Sciences, University of Birmingham, Edgbaston, Birmingham, UK; ³Florence Nightingale Faculty of Nursing, Midwifery and Palliative Care, King's College London, London, UK; ⁴Faculty of Experimental Medicine, Orebro University, Orebro, Sweden; ⁵Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, GC University Faisalabad, Faisalabad, Pakistan

Correspondence: Salamat Ali, Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, GC University Faisalabad, Faisalabad, Pakistan, Tel +00-92-3004189052; +00-92-041-9201036, Email drsalamat@gcuf.edu.pk

Background: Prevalence of psychological disorders among individuals with diabetes is significantly higher as compared to the general population.

Aim: This study aimed to assess the prevalence and impact of psychological disorders on pharmacotherapy of diabetes patients.

Methodology: This cross-sectional study was conducted at two primary care hospitals in Pakistan from April to June 2023. The nine-item Patient Health Care Questionnaire (PHQ-9) scale was used to assess depression in the study's population, and its effects on pharmacotherapy of diabetes. Chi-square test was used to evaluate relationship between ordinal variables/categorical variables and depression whereas; Student's *t*-test was used to assess the relationship between numerical variables with depression.

Results: A total of 320 patients were assessed, comprising 120 (37.5%) males and 200 (62.5%) females, with a mean age of 52.5 (SD ± 11.8) years. The average duration of diabetes is 7.0 (SD ± 5.4). The average PHQ-9 score was 8.3 (SD ± 5.5). Depression was found to be prevalent in 43.7% of the study population. Gender (female) (*p*-value 0.002), advanced age (*p*-value 0.002), lower income (*p*-value 0.001), education levels (*p*-value 0.001), longer duration of diabetes (*p*-value 0.001), poor diabetes control according to BSR value (*p*-value 0.001), usage of injectable insulin (*p*-value 0.005), and concomitant diseases (*p*-value 0.001) were found to be independently linked with depression. Significant association was observed between depression and treatment adherence (*p*-value 0.0025), number of missed doses (*p*-value 0.045), and difficulty in diabetes management (*p*-value 0.0015).

Conclusion: Our study highlights significant prevalence of depression in study population and the prevalent depression negatively impacts on treatment adherence. It also revealed that depression complicates diabetes management resulting in poor medication adherence, poor diabetes control and diabetes related complications, making diabetes control more challenging and difficult.

Keywords: psychological disorders, diabetes, pharmacotherapy, PHQ-9

Introduction

Individuals with diabetes face a twofold increased likelihood of being diagnosed with depression compared to the general population.¹ In recent decades, there has been a global increase in the prevalence of diabetes among adults.² According to IDF, the global prevalence of diabetes was estimated to be around 536.6 million in the year 2021. This figure is expected to undergo a substantial increase, reaching approximately 783.2 million by the year 2045.³ Pakistan holds third global ranking in terms of diabetes prevalence.⁴

The prevalence of psychological disorders among patients with diabetes is greater than that observed in the general population.⁵ Depression impacts roughly one in every five diabetes patients. This prevalence is around three times higher

than the anticipated rate of depression in the general population.⁶ Some studies suggest that around 40% of patients with diabetes experience elevated levels of depressive symptoms.⁶ The Prevalence of psychiatric disorders in Pakistan is much higher in comparison to western countries.⁷

Despite the high prevalence of depression in individuals with diabetes, it often remains undiagnosed, and only one-third of depressed diabetic patients receive a diagnosis and treatment.⁸ Depression and type-2 diabetes may also have common biological basis.⁵ Meta-analyses of the available literature have demonstrated a consistent relationship between depression and hyperglycemia,⁹ an elevated risk of diabetes complications,¹⁰ non-adherence to diabetes therapy¹¹ and increased risk of deaths.^{12,13}

Depression also influence the progression of diabetes and has been associated with inadequate self-management,¹⁴ failure to attain clinical goals,¹⁵ contributes to an increased burden of diabetes symptoms,¹⁶ reduced quality of life,¹⁷ high economic burden,¹⁸ increased number of missed doses of diabetic medications^{19,20} and perceived functional limitation of diabetes.²¹

Existence of depressive symptoms has also been identified as a potential factor linked to inadequate glycemic control.⁹ Poor glycemic control, in turn, increases the risk of developing complications like stroke, cardiovascular incidents, amputation, and chronic kidney disease among individuals with diabetes.²²

In Pakistan, patient with diabetes and depression exhibit significantly poor glycemic control, likely due to lower adherence to recommended self-care activities. Patients with longer illness duration and diabetes related complications, reported inadequate adherence to prescribed medication therapy, which correlated with poor glycemic control.²³ Many diabetes patients in Pakistan also lack essential information necessary to improve medication adherence due to limited access to health care providers.²⁴

In Pakistan, the National Action Plan for Non-Communicable Diseases Prevention and Control emphasizes prevention and management but lacks implementation, particularly at primary healthcare facilities. Rural health centers and sub-district hospitals lack standard guidelines and resources for diabetes care, with specialist only available at district level hospitals. The referral system is weak, leading to inadequate diabetes management and care for associated complications.²⁵

Collaborative care is also uncommon in Pakistani healthcare system, with limited physician-pharmacist interaction in designing therapeutic regimes and barriers to pharmacists providing clinical services. Consequently, diabetes patients often lack necessary education to improve medication adherence.²⁴

High prevalence of psychological disorder in diabetic patients not only disrupts glucose metabolism but also impacts behavioral risk factors including insufficient physical activity and the consumption of high calorie diets which contribute to obesity and further exacerbate glucose-related issues.²⁰ Limited reports are available that highlight the existence of psychological disorders in diabetic population and associated relationship between psychological disorders and pharmacotherapy in diabetic patients. Most studies on depression among people with diabetes were conducted in specialized diabetes care centers. To our knowledge, few studies have examined the prevalence and impact of depression in diabetics in rural center. Therefore, this study was designed to assess the prevalence and impact of depression on the pharmacotherapy of diabetic patients. This study will provide valuable insight for diabetologist and allied health professionals to include direct monitoring of diabetic patients with depression at resource limited healthcare settings.

Aim

This study aimed to assess the prevalence and impact of psychological disorders on pharmacotherapy of diabetes patients.

Ethics Approval

Ethical approval was taken from the Chairman of the Bioethics Committee at the University of the Punjab, Lahore (Reference No. 3265). Additionally, we obtained permission to carry out the study from THQ Hospital Pasrur (NO.HR/1457/THQ/PSR), and from THQ Hospital Daska (No. 3765/E. I). The PHQ-9 questionnaire was adopted after the necessary permission from the principal author. Permission to use the PHQ-9 scale was sought from the principal author via email, and the acknowledgeable response confirmed that the scale is now accessible in public domain for non-commercial research purpose. Therefore, the study complies with the Declaration of Helsinki.

Methodology

Study Design and Setting

The study design was observational cross sectional study. The methodology adopted for the conduct of this study followed the Equator's checklist of observational studies. STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines were followed to conduct the current study. The study was undertaken at two primary healthcare settings of Punjab province of Pakistan including Tehsil Headquarter Hospital Pasrur and Tehsil Headquarter Hospital Daska (70 and 150 bedded hospitals respectively) from April to June 2023.

Inclusion and Exclusion Criteria

The patients who were enrolled at the non-communicable disease (NCD) centers of above two hospitals for the management and follow-up of type-2 diabetes mellitus (BSR value greater than 200mg/dl) approached from vicinity of these hospitals in Out Patient Doors (OPDs) were enrolled. Patients aged 18 years or above, diagnosed of having type-2 diabetes mellitus (prior to their visit to the diabetes outpatient facility) were included. Pregnant women and anyone deemed seriously ill by the care taking medical professional were excluded from the study.

Study Variables

Demographic details and treatment-related information were collected from patients on a pre-designed validated questionnaire. The demography included parameters such as age, gender, educational background, income level, residential location (urban or rural), diabetes history, duration of the disease, family history of diabetes, blood sugar random (BSR) value, number of hospital admissions, and any diabetes-related complications. The Pharmacotherapy variables included parameters such as adherence, any side effect experienced, modification to diabetes treatment plan and number of missed doses.

Psychological disorders were assessed using the Patient Health Questionnaire-9 (PHQ-9) scale. The PHQ-9 questionnaire is a validated tool consisting of nine items, each corresponding to one of the nine depression criteria outlined in the DSM-IV. These nine items of questionnaire address aspects such as lack of interest or pleasure in activities, feeling of hopelessness, sleep disturbances, fatigue, change in appetite, negative self-perception, difficulty concentrating, physical restlessness and suicidal ideation.

Data Collection Tool and Procedure

A data collection form was designed to gather demographic information and diabetes-specific history from patients and the data was collected through face-to-face interviews.

Patients were asked to recall any depressive symptoms they experienced over the preceding 2 weeks and provide responses on a four-point Likert scale, ranging from 0 (not at all) to 3 (nearly every day). When compared to structured interviews by mental health professionals, a PHQ-9 score of ≥ 10 was identified as the most effective threshold for diagnosing major depression, demonstrating both high sensitivity and specificity at 88%.²⁶ A cut of point of greater than 10 is also optimal for epidemiological research as it includes a broader range of participants, who may have depressive disorders, ensuring a more comprehensive representation of the population potential's depression severity.²⁷ The PHQ-9 is widely recognized as one of the most commonly used depression screening instruments, particularly in primary care settings.

Patients who scored 10 or higher on the PHQ-9 questionnaire were further asked about their psychological disorder treatment. Those individuals who had been prescribed medication for psychological disorders were interviewed in detail regarding how these disorders affected their blood glucose levels, diabetes treatment plan, adherence to treatment, instances of missed doses, and any encountered side effects. This comprehensive evaluation aimed to assess the impact of psychological disorders on the pharmacotherapy of diabetic patients.

Patients may inaccurately recall their medical history and potentially under-report or over report psychological symptoms. To minimize this bias, the study employed a rigorous data collection approach. Data were exclusively

collected by two trained interviewers and a validated questionnaire tool was employed to accurately assess the presence and severity of depressive symptoms.

Sample Size

The study employed a non-probability convenience sampling technique. The sample size was calculated using Raosoft formula taking 95% level of confidence and $\pm 05\%$ margin of error. Using this formula, we have calculated minimum sample size as 320 patients. The study included all the diabetic patients who visited NCD (non-communicable Disease) clinic of selected primary healthcare hospitals. All the participants were elaborated regarding the purpose of study prior to the conduct. Figure 1 shows a flow chart scheme of study population and final recruited patients.

Data Analysis

Data analysis was carried out using the IBM SPSS Statistics version 27.0. Simple descriptive statistics was applied on demographic variables. Chi-square test was used to assess the relationship between ordinal variables/categorical variables and depression whereas; Student's *t*-test was used to assess the relationship between numerical variables with depression. A *p*-value ≤ 0.05 was considered statistically significant.

Results

A total of 320 patients (200 females, 120 males) with average age 52.48 (SD \pm 11.76) years were included in the study. The maximum participants were female (62.5%). The average duration of diabetes is 7.03 (SD \pm 5.39). The majority of patients 30.6% (*n*=98) were suffering from the illness for 1–5 years' duration and most of the patients 40.3% (*n*=129) had blood sugar level (BSR value) greater than 125 mg/dl while 32.8% (*n*=105) of the patients had blood sugar random (BSR value) greater than 300mg/dl. The 71.3% (*n*=228) participants manage their diabetes using injectable insulin, 17.8% (*n*=57) individual uses oral hypoglycemic agents and 6.6% (*n*=21) individual uses Insulin + oral hypoglycemic agents (Table 1).

The prevalence of psychological disorders specifically depression was 43.7%, using the commonly accepted cut-off value of 10. The distribution of PHQ-9 severity cut-off values was as follows: none/minimal depression 33.1% (*n*=106), mild 23.1% (*n*=74), moderate 28.1% (*n*=90), moderately severe 13.1% (*n*=42), and severe 2.5% (*n*=08). Figure 2 details the prevalence of disorders.

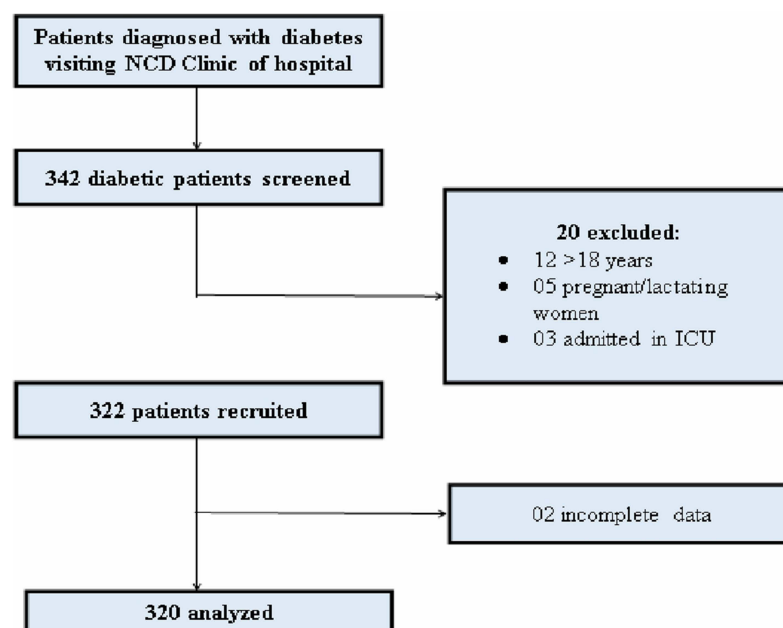


Figure 1 A flow chart showing scheme of study population and final recruited patients.

Abbreviations: *NCD, Non-communicable disease; ICU, Intensive care unit.

Table 1 Demographic Characteristics of Participants and Relevant Variables

Sr no.	Variables	Categories	Frequency	Percentage
1.	Gender	Male	120	37.5%
		Female	200	62.5%
2.	Age	22–39	43	13.4%
		40–59	184	57.5%
		60–79	91	28.4%
		>80	2	0.6%
3.	Diabetes History	Less than 1 Year	58	18.1%
		1–5 year	98	30.6%
		5–10 year	71	22.2%
		More than 10 Year	93	29.1%
4.	BSR Value	Below 125mg/dl	84	26.3%
		Greater than 125mg/dl	129	40.3%
		Greater than 300mg/dl	105	32.8%
		Greater than 500mg/dl	2	0.6%
5.	Diabetes Management	Oral Hypoglycemic agents	57	17.8%
		Injectable (Insulin)	228	71.3%
		Injectable (GLP 1 analogue)	1	0.3%
		Insulin + Oral hypoglycemic agents	21	6.6%
		Only life style modification	1	0.3%
		Life style modification + Drugs	12	3.8%

Abbreviation: BSR, Blood sugar random.

Table 2 describes the impact of various variables on the occurrence of depression (**Table 2**). A significant correlation between gender and the prevalence of depression, with women being more commonly affected by depression than men (p -value = 0.005). Furthermore, individuals with a diabetes duration exceeding 10 years' have higher BSR value (greater than 300) and were found to be at a higher risk of experiencing depression when compared to those who have controlled diabetes (P -value; <0.001).

Individual who has BSR value greater than 300 also most commonly suffer from comorbid diseases/diabetes related complications, consequently increasing their susceptibility to depression (P -value; <0.001). Patients who administer

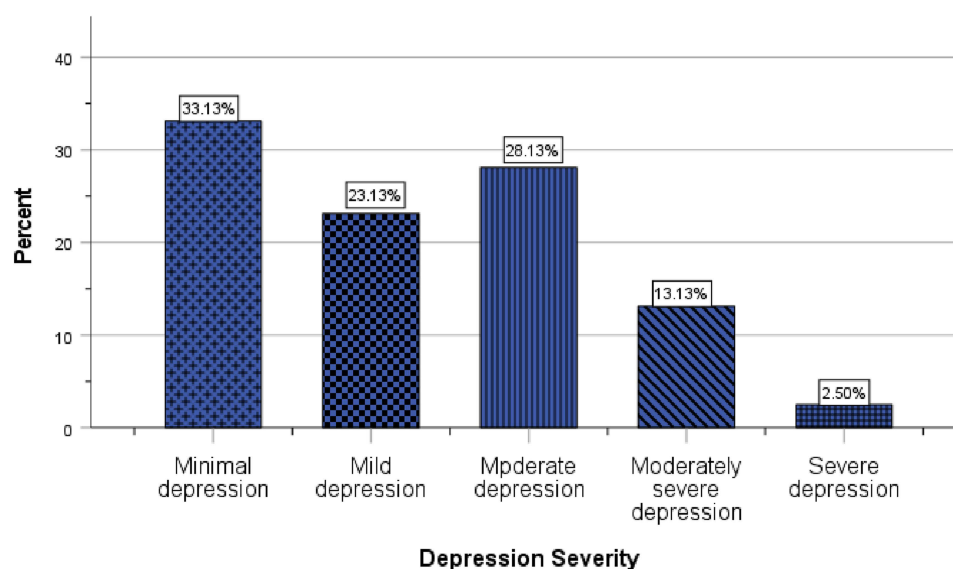
**Figure 2** Frequency of depression severity among study participants.

Table 2 Effect of Demographic Variables on Psychological Disorders

Sr. No.	Variables	Categories	Moderate	Moderately severe	Severe	P-value
1.	Gender	Male	32	10	2	0.005
		Female	58	32	6	
2.	Diabetes History	Less than 1 Year	12	0	1	<0.001
		1–5 year	21	11	2	
		5–10 year	25	12	0	
		More than 10 Year	32	19	5	
3.	BSR Value	Below 125mg/dl	10	0	0	<0.001
		Greater than 125mg/dl	35	16	1	
		Greater than 300mg/dl	44	28	6	
		Greater than 500mg/dl	1	0	1	<0.001
4.	Diabetic Complications	Restless leg syndrome (RLS)	47	27	6	
		Amputation	5	2	1	
		Retinopathy	11	7	0	
		Nephropathy	2	2	2	
		Heart Disease	18	12	2	
5.	Diabetes Management	No complication	9	3	0	<0.001
		Oral Hypoglycemic agents	4	1	0	
		Injectable (Insulin)	74	36	4	
		Injectable (GLP I analogue)	0	0	0	
		Insulin + Oral hypoglycemic agents	10	5	4	
		Only life style modification	0	0	0	
		Life style modification + Drugs	2	0	0	

Abbreviation: BSR, Blood sugar random.

injectable insulin twice daily had also significant level of depression as compared to the patient who use oral hypoglycemic agents to control/manage their diabetes.

Among the total number of individuals (320) in the study, a notable 43.7% experienced symptoms of depression. Only a small proportion, just 11.3% of the study individuals, were formally diagnosed with depression and subsequently prescribed anti-depressants for its management.

A statistically significant association was found between depression and treatment adherence. Approximately 7.5% (n=24) of the study individuals reported experiencing difficulties in strictly adhering to their prescribed diabetes treatment regime. There is also a significant correlation identified between number of missed doses in diabetes treatment and the presence of depression, as 3.8% (n=12) indicated a specific number of missed doses. About 8.1% (n=26) of these patients felt that their psychological disorders had a tangible effect on their ability to manage their diabetes appropriately. Table 3 shows data about the effect of psychological disorders on pharmacotherapy of diabetes.

Table 3 Effect of Psychological Disorders on Pharmacotherapy of Diabetic Patients

Sr.No.	Categories	Frequency	Percent	Confidence Interval (95%)	P-value
1.	Treatment adherence	24	7.5%	0.250–1.083	0.002
2.	Number of missed doses	12	3.8%	0.009–0.908	0.05
3.	Effect on blood sugar level	7	2.2%	–0.612–1.041	0.61
4.	Side effect of psychological disorder therapy	6	1.9%	–0.628–1.129	0.58
5.	Effect of psychological disorder on diabetes management	26	8.1%	0.298–1.163	0.001

Discussion

The rising global prevalence of diabetes has exacerbated the challenge of managing this chronic condition, particularly due to the frequent occurrence of psychological issues in this population. To address this concern, our study was carried out within the Pakistani population to determine the prevalence and impact of depression among individuals with diabetes mellitus and to assess the effect of depression on the pharmacotherapy of diabetic patients.

Our findings revealed a significant prevalence of depression, affecting approximately 43.7% of the study participants. These results are consistent with previous research conducted in Pakistan and other regions.

The findings of a study conducted in Pakistan on the prevalence of depression among diabetic patients reports depression prevalence rate of about 40%,²⁸ While a similar study in Karachi, reported 43.5%.²⁹ In South Africa, a semi-rural clinic study found that 45.9% of individuals with diabetes were experiencing depression.³⁰ In Iran, another study reported a prevalence of 47.6%³¹ and a study by Thour et al found a 41% prevalence.³² The variability in depression prevalence across studies can be attributed to factors including variation in screening scale used to assess symptoms and diverse settings.

Our study revealed that females were more commonly affected by depression than males, this finding aligns with studies conducted in previous studies undertaken in United States.³³ Researchers have also found significant relationship between age and depression.³⁴ This is in line with our study findings that also revealed that increased age as an independent risk factor for depression. The study also revealed a connection between depression and low educational attainment and income levels, which corresponds with findings in previous studies.^{35,36}

Our study identified a correlation between the duration of diabetes and the development of depression, aligning with findings from other research studies.^{34,37} Poor glycemic control was also strongly linked to depression in our results. This finding is in line with previous research studies conducted in America.³⁸

Our study also found a significant relationship between the presence of other chronic conditions, such as hypertension or asthma, and an elevated risk of depression aligning with previous research.³⁹ Additionally, presence of complications like nephropathy, neuropathy, and diabetic foot along with other comorbid conditions can significantly raise the risk of developing of depression. The development of depression can also be influenced by functional limitations stemming from complications like retinopathy and amputation.⁴⁰

A significant correlation was also found between the frequency of hospital admissions due to diabetes-related complications and the presence of depression, consistent with earlier research indicating higher rates of anxiety and depression among hospitalized individuals.^{41,42}

We also observed that patients using insulin or a combination of insulin and oral hypoglycemic agents exhibited higher rates of depression in comparison to those who were solely relying on oral hypoglycemic agents, consistent with previous research.^{43,44}

Results of our study revealed that patients with depression had significantly lower adherence to diabetes medication therapy compared to patients without depression. These findings align with previous studies, indicating that individual with diabetes and depression tend to have poorer medication adherence.¹⁹ Consistently, other research has shown that individuals with elevated depressive symptom scores tend to exhibit lower adherence to their diabetes medication regimens in comparison to those with lower depressive symptom scores.^{45,46}

Depression also raises the frequency of missed doses. Similar findings were observed in another study, where depression was linked to memory loss. This association may cause people to forget to take their medications on time.⁴⁷

The findings of our study emphasize the importance of assessing depression as a fundamental component of evaluating diabetic patients, aligning with recommendations from the American Diabetic Association that advocates for the screening and assessment of depression in all individuals with type 2 diabetes mellitus.⁴⁸ Furthermore, our study highlights the crucial role of diabetic educators in offering guidance and education to individuals with diabetes. They play a vital role in dispelling myths and addressing false beliefs related to diabetes management, especially in resource-limited settings. It is crucial to make sure that people with depression are promptly sent to psychiatrists for counselling and therapy. This proactive approach is essential in preventing a vicious loop where non-compliance with anti-diabetic medications leads to poor diabetes control, which, in turn, exacerbates depression. Collaborative care and support from

healthcare professionals in both diabetes and mental health fields are essential to improve overall health outcomes for individuals with diabetes and depression.²⁸ Integrated care approaches could potentially alleviate the challenges faced by diabetic patients with depression and improve their quality of life.

Strength and Limitation

The strength of our study include a manageable sample size, high response rate and its inclusivity, which allowed participants of all literacy levels to participate.³⁶

Our study has also some limitations as well. Firstly, the absence of a control group for comparison. Secondly, we utilized the patient health questionnaire (PHQ-9) to measure depression at a single point in time, lacking of follow up data. Thirdly, we focused on a specific subset of individuals diagnosed with psychological disorder. So, our interviews regarding adherence to diabetes medication and instance of missed doses were only conducted with this restricted cohort and the investigation was only carried out in two government hospitals, which limits the ability to generalize study findings.

Conclusions

This study highlights a high prevalence of depression in diabetic population. A culminating strong association was assessed between diabetes and depression. Furthermore, it is observed that depression exacerbates the therapy of diabetes, contributing to poorly controlled diabetes and subsequent complications. Finally, the psychological disorders hinder adherence to diabetes medication, consequently intensifying the challenges associated with diabetes management.

Future Research and Recommendations

Routine monitoring of diabetic patients with depression in primary care settings is strongly recommended to enable early detection and timely intervention. Specialized training for diabetic educators is essential to effectively support patients dealing with both diabetes and depression. More importantly, patients should be educated about the bidirectional relationship between diabetes and depression, emphasizing the importance of managing both conditions together. Furthermore, continuous research into innovative interventions, treatments, and technologies is crucial for optimizing the management of diabetes and depression together.

Impact Statements

- Data from low resourced settings substantiate a significant relationship between depression and diabetes. Alarmingly, untreated psychological disorders impact the pharmacotherapy of diabetes.
- There is a dire need to develop integrated strategies to address both conditions simultaneously.
- It is imperative to initiate specialized programmes for personalized care of diabetic-depression comorbid population and relevant skill development of dealing healthcare professionals.

Data Sharing Statement

On demand statistical sheets, and dataset will be available from the corresponding authors available at drsalamatali@g-cuf.edu.pk.

Ethics Approval and Patients' Consent

The study complies with the Declaration of Helsinki. The necessary ethical permission was obtained from the Chairman of the Bioethics Committee at the University of the Punjab, Lahore (Reference No. 3265). Additionally, we sought permission to collect data from THQ Hospital Pasrur (NO.HR/1457/THQ/PSR), and from THQ Hospital Daska (No. 3765/E. I). The PHQ-9 questionnaire was adopted after the necessary permission from the principal author. An informed verbal and written consent was taken from study participants at time of data collection.

Consent to Publish

All authors have given their consent for prompt publishing of research work. All the participants were elaborated regarding the purpose of study prior to the conduct.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study has not utilized any funding during or for the whole conduct.

Disclosure

The authors declare no conflicts of interest in this work.

References

- Smith KJ, B  land M, Clyde M, et al. Association of diabetes with anxiety: a systematic review and meta-analysis. *J Psychosom Res.* 2013;74(2):89–99. doi:10.1016/j.jpsychores.2012.11.013
- Beagley J, Guariguata L, Weil C, et al. Global estimates of undiagnosed diabetes in adults. *Diabetes Res Clin Pract.* 2014;103(2):150–160. doi:10.1016/j.diabres.2013.11.001
- Sun H, Saeedi P, Karuranga S, et al. IDF diabetes Atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract.* 2022;183:109119. doi:10.1016/j.diabres.2021.109119
- Meo SA, Zia I, Bukhari IA, et al. Type 2 diabetes mellitus in Pakistan: current prevalence and future forecast. *JPM. J Pak Med Assoc.* 2016;66(12):1637–1642.
- Moulton CD, Pickup JC, Ismail K. The link between depression and diabetes: the search for shared mechanisms. *Lancet Diabetes Endocrinol.* 2015;3(6):461–471. doi:10.1016/S2213-8587(15)00134-5
- Gavard JA, Lustman PJ, Clouse RE. Prevalence of depression in adults with diabetes: an epidemiological evaluation. *Diabetes Care.* 1993;16(8):1167–1178. doi:10.2337/diacare.16.8.1167
- Mirza I, Jenkins R. Risk factors, prevalence, and treatment of anxiety and depressive disorders in Pakistan: systematic review. *BMJ.* 2004;328(7443):794. doi:10.1136/bmj.328.7443.794
- Lustman PJ, Clouse RE, Alrakawi A, Rubin EH, Gelenberger AJ. Treatment of major depression in adults with diabetes: a primary care perspective. *Clin Diabetes.* 1997;15(3):122–128.
- Lustman PJ, Anderson RJ, Freedland KE, et al. Depression and poor glycemic control: a meta-analytic review of the literature. *Diabetes Care.* 2000;23(7):934–942. doi:10.2337/diacare.23.7.934
- De Groot M, Anderson R, Freedland KE, et al. Association of depression and diabetes complications: a meta-analysis. *Psychosomatic Med.* 2001;63(4):619–630. doi:10.1097/00006842-200107000-00015
- Gonzalez JS, Peyrot M, McCarl LA, et al. Depression and diabetes treatment nonadherence: a meta-analysis. *Diabetes Care.* 2008;31(12):2398–2403. doi:10.2337/dc08-1341
- Black SA, Markides KS, Ray LA. Depression predicts increased incidence of adverse health outcomes in older Mexican Americans with type 2 diabetes. *Diabetes Care.* 2003;26(10):2822–2828. doi:10.2337/diacare.26.10.2822
- Zhang X, Norris SL, Gregg EW, Cheng YJ, Beckles G, Kahn HS. Depressive symptoms and mortality among persons with and without diabetes. *Am J Epidemiol.* 2005;161(7):652–660. doi:10.1093/aje/kwi089
- Van Tilburg MA, McCaskill CC, Lane JD, et al. Depressed mood is a factor in glycemic control in type 1 diabetes. *Psychosomatic Med.* 2001;63(4):551–555. doi:10.1097/00006842-200107000-00005
- Rush WA, Whitebird RR, Rush MR, et al. Depression in patients with diabetes: does it impact clinical goals? *J Am Board Family Med.* 2008;21(5):392–397. doi:10.3122/jabfm.2008.05.070101
- Ludman EJ, Katon W, Russo J, et al. Depression and diabetes symptom burden. *Gen Hosp Psychiatry.* 2004;26(6):430–436. doi:10.1016/j.genhosppsych.2004.08.010
- Ali S, Stone M, Skinner TC, et al. The association between depression and health-related quality of life in people with type 2 diabetes: a systematic literature review. *Diabetes/Metab Res Rev.* 2010;26(2):75–89. doi:10.1002/dmrr.1065
- Le TK, Able SL, Lage MJ. Resource use among patients with diabetes, diabetic neuropathy, or diabetes with depression. *Cost Eff Resour Allocation.* 2006;4(1):1–9. doi:10.1186/1478-7547-4-18
- Lin EH, Katon W, Von Korff M, et al. Relationship of depression and diabetes self-care, medication adherence, and preventive care. *Diabetes Care.* 2004;27(9):2154–2160. doi:10.2337/diacare.27.9.2154
- Gonzalez JS, Safren SA, Cagliero E, et al. Depression, self-care, and medication adherence in type 2 diabetes: relationships across the full range of symptom severity. *Diabetes Care.* 2007;30(9):2222–2227. doi:10.2337/dc07-0158
- Fisher L, Chesla CA, Mullan JT, et al. Contributors to depression in Latino and European-American patients with type 2 diabetes. *Diabetes Care.* 2001;24(10):1751–1757. doi:10.2337/diacare.24.10.1751

22. Esposti LD, Saragoni S, Buda S, Sturani A, Esposti ED. Glycemic control and diabetes-related health care costs in type 2 diabetes; retrospective analysis based on clinical and administrative databases. *Clinicoecon Outcomes Res.* **2013**;193–201. doi:10.2147/CEOR.S41846
23. Zuberi SI, Syed EU, Bhatti JA. Association of depression with treatment outcomes in type 2 diabetes mellitus: a cross-sectional study from Karachi. *Pak BMC Psychiatry.* **2011**;11(1):27. doi:10.1186/1471-244X-11-27
24. Iqbal Q, Bashir S, Iqbal J, et al. Assessment of medication adherence among type 2 diabetic patients in Quetta city. *Pak Postgrad Med J.* **2017**;129(6):637–643. doi:10.1080/00325481.2017.1328251
25. Khan MA, Walley JD, Khan N, et al. Effectiveness of an integrated diabetes care package at primary healthcare facilities: a cluster randomised trial in Pakistan. *BJGP Open.* **2018**;2(4):bjgpopen18X101618. doi:10.3399/bjgpopen18X101618
26. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med.* **2001**;16(9):606–613. doi:10.1046/j.1525-1497.2001.016009606.x
27. van Steenberg-Weijnenburg KM, de Vroeghe L, Ploeger RR, et al. Validation of the PHQ-9 as a screening instrument for depression in diabetes patients in specialized outpatient clinics. *BMC Health Serv Res.* **2010**;10(1):235. doi:10.1186/1472-6963-10-235
28. Zhang X, Norris SL, Gregg EW, Cheng YJ, Beckles G, Kahn HS. Frequency of depression in patients with type 2 diabetes mellitus and its relationship with glycemic control and diabetic microvascular complications. *Cureus.* **2019**;11(7).
29. Khuwaja AK, Lalani S, Dhanani R, et al. Anxiety and depression among outpatients with type 2 diabetes: a multi-centre study of prevalence and associated factors. *Diabetol Metab Syndr.* **2010**;2(1):72. doi:10.1186/1758-5996-2-72
30. Kagee A, Martin L. Symptoms of depression and anxiety among a sample of South African patients living with HIV. *AIDS Care.* **2010**;22(2):159–165. doi:10.1080/09540120903111445
31. Khamseh ME, Baradaran HR, Javanbakht A, et al. Comparison of the CES-D and PHQ-9 depression scales in people with type 2 diabetes in Tehran, Iran. *BMC Psychiatry.* **2011**;11(1):1–6. doi:10.1186/1471-244X-11-61
32. Thour A, Das S, Sehrawat T, et al. Depression among patients with diabetes mellitus in North India evaluated using patient health questionnaire-9. *Indian J Endocrinol Metab.* **2015**;19(2):252–255. doi:10.4103/2230-8210.149318
33. Culbertson FM. Depression and gender: an international review. *Am Psychologist.* **1997**;52(1):25. doi:10.1037/0003-066X.52.1.25
34. Almawi W, Tamim H, Al-Sayed N, et al. Association of comorbid depression, anxiety, and stress disorders with type 2 diabetes in Bahrain, a country with a very high prevalence of type 2 diabetes. *J Endocrinol Invest.* **2008**;31(11):1020–1024. doi:10.1007/BF03345642
35. Madkhali JM, Hakami AA, Dallak AH, et al. Prevalence and associated factors of depression among patients with diabetes at Jazan Province, Saudi Arabia: a cross-sectional study. *Psychiatry J.* **2019**;2019:6160927. doi:10.1155/2019/6160927
36. Roy T, Lloyd CE, Parvin M, et al. Prevalence of co-morbid depression in out-patients with type 2 diabetes mellitus in Bangladesh. *BMC Psychiatry.* **2012**;12(1):1–10. doi:10.1186/1471-244X-12-123
37. Iype T, Shaji SK, Balakrishnan A, et al. Cognition in type 2 diabetes: association with vascular risk factors, complications of diabetes and depression. *Ann Indian Acad Neurol.* **2009**;12(1):25. doi:10.4103/0972-2327.48848
38. Marcelo P. *Depression, Glycemic Control and Type 2 Diabetes.* BMC; **2011**.
39. Nasser J, Habib F, Hasan M, Khalil N. Prevalence of depression among people with diabetes attending diabetes clinics at primary health settings. *Bahrain Med Bull.* **2009**;31:1–7.
40. Pouwer F, Beekman ATF, Nijpels G, et al. Rates and risks for co-morbid depression in patients with Type 2 diabetes mellitus: results from a community-based study. *Diabetologia.* **2003**;46(7):892–898. doi:10.1007/s00125-003-1124-6
41. AlBekairy A, AbuRuz S, Alsabani B, et al. Exploring factors associated with depression and anxiety among hospitalized patients with type 2 diabetes mellitus. *Med Princ Pract.* **2017**;26(6):547–553. doi:10.1159/000484929
42. Al-Amer RM, Sobeh MM, Zayed AA, et al. Depression among adults with diabetes in Jordan: risk factors and relationship to blood sugar control. *J diabet complicat.* **2011**;25(4):247–252. doi:10.1016/j.jdiacomp.2011.03.001
43. Papelbaum M, Moreira RO, Coutinho W, et al. Depression, glycemic control and type 2 diabetes. *Diabetol Metab Syndr.* **2011**;3(1):1–4. doi:10.1186/1758-5996-3-26
44. Bai X, Liu Z, Li Z, et al. The association between insulin therapy and depression in patients with type 2 diabetes mellitus: a meta-analysis. *BMJ open.* **2018**;8(11):e020062. doi:10.1136/bmjopen-2017-020062
45. Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. *Arch Intern Med.* **2000**;160(21):3278–3285. doi:10.1001/archinte.160.21.3278
46. Kilbourne AM, Reynolds CF, Good CB, et al. How does depression influence diabetes medication adherence in older patients? *Am J Geriatric Psychiatry.* **2005**;13(3):202–210. doi:10.1097/00019442-200503000-00005
47. Ainsworth P. *Understanding Depression.* Univ. Press of Mississippi; **2009**.
48. Association AD. American diabetes association standards of medical care in diabetes–2017. *Diabetes Care.* **2017**;40(Suppl. 1):S1.

Patient Preference and Adherence

Dovepress

Publish your work in this journal

Patient Preference and Adherence is an international, peer-reviewed, open access journal that focusing on the growing importance of patient preference and adherence throughout the therapeutic continuum. Patient satisfaction, acceptability, quality of life, compliance, persistence and their role in developing new therapeutic modalities and compounds to optimize clinical outcomes for existing disease states are major areas of interest for the journal. This journal has been accepted for indexing on PubMed Central. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/patient-preference-and-adherence-journal>