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Editorial

Examining the Psychological Burden of Diabetes Mellitus: The Association and Relationship between Depression, Anxiety, and Diabetes Mellitus. A Systematic Review

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Abstract

Diabetes Mellitus is a global health issue, and the rising prevalence of depression and anxiety among individuals with diabetes poses a significant concern. Metabolic disturbances in diabetes can potentially impact psychological well-being. The study aims to determine the prevalence of depression, and anxiety, and explore the relationship between these mental health conditions and diabetes. A comprehensive search was conducted on PubMed and Google Scholar using MeSH terms and keywords. Articles were selected based on predefined inclusion criteria, and a rigorous quality assessment was performed by two independent authors. Cross-sectional, case-control, systematic reviews, and meta-analysis studies investigating the association between diabetes mellitus, depression, and anxiety were included. After careful quality appraisal, twelve articles were selected for inclusion in the study. These studies were of high quality, some have limitations and a moderate risk of bias. The findings consistently demonstrated a strong association between depression, anxiety, and diabetes mellitus, supported by physiological, biochemical, and anatomical alterations observed in these conditions. The evidence from the included studies supports the coexistence of diabetes, depression, and anxiety. Individuals with diabetes have a higher prevalence of depression and anxiety compared to healthy individuals. All the studies affirm the relationship between diabetes and psychological disorders or disturbance. However, further research is warranted to establish the precise relationship between depression, anxiety, and diabetes and to elucidate the underlying mechanisms through which these mental health conditions may contribute to the development of diabetes mellitus.

Keywords: Diabetes Mellitus OR Hyperglycaemia AND Depression AND Anxiety AND Stress.

Introduction

Diabetes is Polygenic Syndrome that affects multiple organs and is caused by high fasting blood glucose levels and insulin deficiency. Type 1 Diabetes Mellitus (T1D) is insulin-dependent and typically develops in juveniles. Type 2 Diabetes (T2D) commonly occurs in individuals over the age of 35 [1]. According to the international diabetes federation, there were 537 million adults aged 20-79 years worldwide living with diabetes in 2021 [2].

Depression was found to prevail in 3.8% of the population, with a higher prevalence in females than males. Among adults, the prevalence of depression is 5.0%, and 5.7% in people older than 60 years [3]. Globally, anxiety disorders affect 301 million people [4]. Given the significant number of individuals affected by both disorders, a bi-directional relationship has been observed, with diabetes, depression, and anxiety acting as risk factors for each other. The prevalence of depression is twice as high in diabetic patients compared to healthy individuals [5]. Poor mental health can be defined as a strong risk factor associated with an increased risk of diabetes [6]. Depression prevails more highly in people with diabetes than in those without [7], which may be due to biologically induced changes by diabetes like lifestyle limitations, worst quality of life, worsened blood glucose level, and feeling of suffering from chronic disease can cause poor mental health affecting both mind and body [8]. Depression and T2D have an impact on patients with poor compliance, poor self-care, worse quality of life [9], and a higher risk of dementia [10]. The acute and chronic complications of diabetes mellitus can also contribute to anxiety and fear among diabetic patients [11].

The physiological relationship between psychiatric comorbidities and metabolic control is not yet fully understood. Hormonal changes associated with stress in the hypothalamic-pituitary-adrenal axis, as well as high blood glucose levels resulting in elevated levels of catecholamines and cortisol, may also contribute to inflammation, structure alteration in the hippocampus, weight gain and may potentially share etiological factors [9]. Studies have indicated that a longer duration of diabetes and suboptimal glycemic control is associated with depressive symptoms, while anxiety symptoms are associated with high HbA1c levels, insulin pump therapy, and infrequent glucose monitoring [10]. In patients with T2D, structural and functional

abnormalities in the brain, such as alteration in white matter tracts like the corpus callosum, have been observed, potentially leading to dementia, cognitive decline, stroke, and emotional disturbances [5,12]. Additionally, some tentative evidence suggests an association between high C-Reactive protein levels, inflammatory states, anxiety, depression, and T2D [13].

Although several studies have been conducted to assess the prevalence of depression in diabetes mellitus the result was found to be inconsistent. Additionally, previous studies lack consensus but defined various risk factors associated with depression in diabetes patients.

This study aims to investigate, find the gaps in the literature and assess the relationship between diabetes mellitus and anxiety and depression. It seeks to determine whether individuals with diabetes are at risk of developing depression and anxiety and vice versa. It also aims to provide insight relationship between diabetes mellitus, depression, and anxiety.

Methodology And Results

Methodology

The Systematic Review was carried out by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) [14].

Databases

The Articles for systematic review were collected from Google Scholar and the search engine PubMed. The Article was last searched on 13. Nov.2022.

Keywords and MeSH

Using keywords and the MeSH strategy articles were collected that show relationship between diabetes mellitus, depression, and anxiety. 241 articles were collected in total.

The keyword and MeSH keyword used were the following: Diabetes Mellitus OR Hyperglycaemia OR Polygenic Syndrome OR Insulin-dependent diabetes OR Diabetic Ketoacidosis(DKA) OR Ketonemia OR Glycated Haemoglobin OR Non-Insulin dependent diabetes OR Pancreatic β cells OR insulitis OR Hypertriacylglycerolemia AND Young Adults OR Teenager AND Depression OR Reduced energy OR less self-esteem AND Anxiety OR stress AND ((("Diabetes Mellitus"[Mesh]) AND "Diabetes Mellitus/psychology"[Mesh]) AND "Depression"[Mesh]) AND "Anxiety"[Mesh] AND ("Diabetes Mellitus"[MeSH Terms] OR "Diabetes Mellitus") AND ("Anxiety"[MeSH Terms] OR "Angst" OR "Anxiety" OR "Anxiousness" OR "Hypervigilance" OR "Nervousness" OR "Social Anxiety") AND ("Anxiety Disorders"[MeSH Terms] OR "Anxiety Disorders" OR "Anxiety Neuroses" OR "Anxiety States, Neurotic" OR "Neuroses, Anxiety") AND ("Humans"[MeSH Terms] OR "Homo sapiens" OR "Humans".

Eligibility Criteria and Study Selection

Screening, data selection, extraction, and quality assessment were done independently by two Authors Zahra Ali (ZA) and Abdelrahman Abaza (AA). The data were collected from electronic databases and duplicates were removed from Excel. The studies were analyzed and only relevant articles were selected for quality appraisal. The studies by both reviewers were combined and disagreements were resolved by consensus.

Inclusion and Exclusion Criteria

Inclusion Criteria	*Exclusion Criteria*
Peer-reviewed articles were included.	Non-Relevant articles were excluded.
Only articles with full text were included.	Animal studies and editorials were removed.
Studies that estimated the relationship between anxiety, depression, and diabetes mellitus and were relevant to the research question were included.	Gestational diabetic cases were excluded from the review.
Articles that received high-quality appraisal scores were included in the review.	Articles that received low-quality appraisal scores, indicating potential methodological flaws or limitations, were excluded from the review.
Only articles in the English language were included.	Grey literature, unpublished articles, and non-peer-reviewed articles were excluded from the review.

Data Extraction and Quality Assessment Tools

Two authors independently performed data extraction of selected studies. The following characteristics and variables were investigated using a standardized quality assessment tool: Study design, Number of participants, baseline characteristics of participants, including the association of diabetes with altered white matter structure, serum levels of high-sensitivity C-reactive protein, insulin manipulation, depression, anxiety, and comorbidities. The number of study participants, study outcomes, and whether the study was funded by a pharmaceutical company.

Two investigators (ZA, AA) evaluated the risk of bias using quality assessment tools: For case-control studies Table 1 (SEE TABLE 1): Quality Assessment Tool of Case-Control Studies using Newcastle-Ottawa Scale. Table 2 (SEE TABLE 2): Quality Assessment of Systematic Reviews and Meta-Analysis using AMSTAR

checklist, and for Cross Section Studies. Table 3 (SEE TABLE 3): Quality Assessment of Cross-sectional Studies using AXIS Scale. Only studies with good quality were included. Disagreements were discussed and resolved by consensus.

Table 1: Quality Assessment Tool of Case-Control Studies using the Newcastle-Ottawa Scale.

Study	Selection	Comparability	Exposure	Overall (Max 9)
Dogan et al. (2019) [11].	★★★	★★	★★	7, High Quality
Almeida et al. (2018) [17].	★★★	★	★★	6, Moderate Quality

Table 2: Quality Assessment of Systematic Reviews and Meta-Analysis using the AMSTAR checklist.

	Liu et al. (2022) [5]	Smith et al. (2018) [6]	Ni et al. (2021) [7]	Zhou et al. (2021) [12]	Rechenberg et al. (2021) [15]	Graham et al. (2020) [16]
Study Design	Yes	Yes	Yes	Yes	Yes	Yes
Search Strategy	Yes	Yes	Yes	Yes	Yes	Yes
Grey literature included	No	No	No	No	No	No
Data Extraction	Yes	Yes	Yes	Yes	Yes	Yes
Risk of Bias Assessment	Yes	Yes	Yes	No	No	Yes
Statistical Analysis	Yes	Yes	Yes	Yes	No	Yes
Results	Yes	Yes	Yes	Yes	Yes	Yes
Included studies and characteristics	Yes	Yes	Yes	Yes	Yes	Yes
Risk of Bias	Yes	Yes	Yes	Yes	Yes	Yes
Meta-Analysis	Yes	Yes	No	Yes	No	Yes
Conflict of interest	Yes	Yes	Yes	Yes	Yes	Yes
Source of funding mentioned	Yes	Yes	No	Yes	No	Yes
The rationale of the study provided	Yes	Yes	Yes	Yes	Yes	Yes
Original research question	Yes	Yes	Yes	Yes	Yes	Yes
Multiple reviewer selection and Data extraction.	Yes	Yes	Yes	Yes	Yes	Yes
Selective outcome reporting	Yes	Yes	Yes	Yes	Yes	Yes
Overall Results	Good	Good	Good	Good	Good	Good

Table 3. Quality Assessment of Cross-sectional Studies Using the AXIS Scale. Characteristic of Cross-sectional Studies.

Questions	Yang et al. (2022) [8]	Yang Qian et al. (2020) [13]	Berger et al. (2019) [18]	Nguyen et al. (2020) [19]
Introduction				
Objects/ Aims	Yes	Yes	Yes	Yes
Methods				
Sample size justified	Yes	Yes	Yes	Yes
Population	Yes	No	Yes	Yes
Appropriate sample selection	Yes	Yes	Yes	Yes
Study design	Yes	Yes	Yes	Yes
Selection Process	Yes	Yes	Yes	Yes
Addressing non-Respondents	Yes	Yes	Yes	Yes
Risk factors and outcomes according to the aim of the study	Yes	Yes	Yes	No
Risk and outcomes measure using the correct measurement	Yes	Yes	No	Yes
Statistical significance	Yes	Yes	Yes	Yes
Accurate method explanation	Yes	Yes	Yes	Yes
Results				
Basic data adequately described	Yes	Yes	Yes	Yes
Non-Response bias	No	Yes	No	Yes
Information about non-respondents	No	Yes	No	No
Results internally consistent	Yes	Yes	No	Yes

Results presented for all analyses	Yes	Yes	No	Yes
Discussion				
Discussion and conclusion justifiable	Yes	Yes	Yes	Yes
Limitations mentioned	Yes	Yes	Yes	Yes
Other				
Funding source and conflict of interest defined	Yes	Yes	Yes	Yes
Ethical Approval/ Consent from the patient	Yes	Yes	Yes	Yes
Sample collection	Partially mentioned	Recruited participants from a general hospital	Random selection of 21 out of 28 centers.	Adolescents age 12-18 years with T1D and their parents involved in diabetic care.
Data collection	The data the collection method is described clearly.	Questionnaires, physical examinations, and medical records. Clinical data collection includes HbA1c, temperature, serum hs-CRP level, B.P, Fasting plasma glucose, HDL cholesterol, Triglycerides, use of anti-hypertensive medications, and recent acute infection.	Questionnaires and diagnostic interviews.	Questionnaires and diagnostic interviews. Relevant demographic and clinical characteristics of adolescents.
Statistical analysis	A clear description of the statistical method is mentioned.	Descriptive statistics, independent t-tests, chi-square tests, spearman correlation, multiple linear regression, kruskal-wallis tests, Benjamini-Hochberg correction.	Poisson and linear regression models.	Descriptive statistics, chi-square tests, and regression analyses.
Results	Blood glucose level fluctuations and disturb sleep quality were associated with the high prevalence of depression and anxiety in T2D.	Associations were found between serum hs-C-Reactive Protein levels and symptoms like depression and anxiety.T2D is sex-specific with females only demonstrating a positive association.	Association of insulin manipulation and comorbidity.	Mood and anxiety disorders are common in adolescents with T1D.
Overall Assessment	Good	Good quality	Good quality study with a robust methodology.	Good.

Results

Literature search and study selection

Google Scholar's "Prevalence and Relationship of Diabetes with Depression, Anxiety and Stress" produced 76,000 results. Additional filters were applied which yielded 74,000 articles. Only 121 papers met the inclusion criteria as other papers were not relevant to the inclusion criteria. Some articles were obtained by applying the Snowball technique. A total of 241 studies were collected from electronic databases of which 120 were selected from PubMed by applying the MeSH strategy. After removing duplicates 175 articles were obtained.

After reviewing the titles and abstracts, 128 articles were removed as they do not meet the inclusion criteria. Subsequently, 47 articles were included for preparation for full-text screening. However, 11 of these articles were not available in full text for review.

A total of 25 articles were subjected to quality appraisal using assessment tools. Among these, 12 articles were deemed to be of good quality, scoring more than 70% on the quality assessment tools. The PRISMA flow diagram in Figure 1 presents the evaluation process and summarizes the article selection.

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart data extraction process.

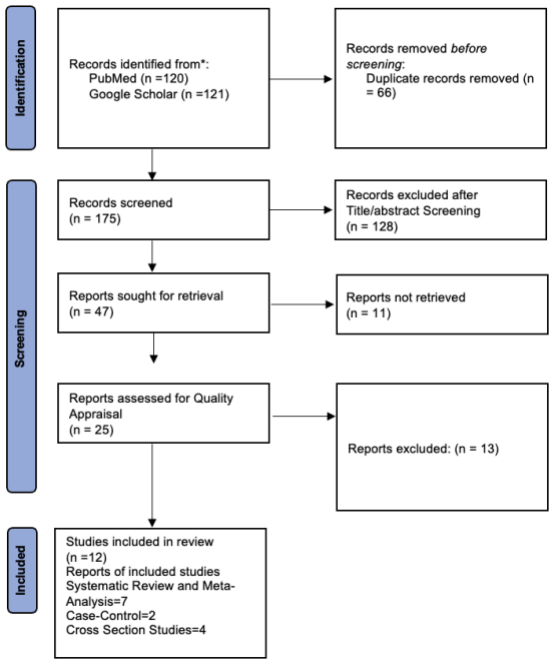

Table 4 (SEE Table 4) provides information on the aims, outcomes of the included studies, and their risk of bias and limitations. To provide further insights, baseline characteristics of the included studies Table 5 (SEE Table 5) summarizes the result of all the included systematic reviews, and meta-analyses and provides the results and characteristics of participants of case-controls and cross-sectional studies.

Table 4

Artides	Risk of bias/ Limitations	Aims	Outcomes
Liu et al. (2022) [5]	Low risk of bias	To develop the updated epidemiology data about depression in T2D patients and explore potential risk factors associated with depression and T2D patients in China.	25.9% of T2D showed depression and anxiety.
Smith et al. (2018) [6]	Low	The longitudinal association between diabetes and anxiety examines anxiety as a risk factor for incident diabetes and diabetes as a risk factor for incident anxiety in adults 16 years or older.	Anxiety is a risk factor for incident diabetes.
Ni et al. (2021) [7]	Low	Demonstrate the beneficial effect of mindful-based intervention in diabetic patients with depression and diabetic-related stress.	Mindful Based Intervention can be beneficial in diabetic patients with depression, diabetic related stress.
Yang et al. (2022) [8]	Low	Assess the psychological condition of diabetic patients and identify potential risk factors for a poor mental state, focusing association between blood glucose fluctuations and depression and anxiety in individuals with T2D.	Blood glucose level fluctuations and disturb sleep quality were associated with the high prevalence of depression and anxiety in T2DM.
Dogan et al. (2019) [11]	Low	Compared psychiatric symptom frequency in patients with T1D, T2D, and non-diabetic controls.	Diabetic groups showed a high rate of psychiatric symptoms.
Zhou et al. (2021) [12]	Low	Provides insights into the relationship between T2D, white matter microstructure, and cognitive and emotional outcomes, paving the way for further research in this field.	T2D patients have microstructural changes in the white matter tracts.T2D can cause alteration in white matter, associated with cognitive deficits and emotion.
Yang Qian et al. (2020) [13]	Low	Investigate the association between serum high-sensitivity C-reactive levels and symptoms of depression and anxiety in T2D while considering potential sex differences.	Associations were found between serum hs-C-Reactive Protein levels and symptoms like depression and anxiety.T2D is sex-specific with females only demonstrating a positive association.
Rechenberg et al. (2021) [15]	Moderate	Synthesize the use of Cognitive behavior therapy in adolescents with T1D, assess its effectiveness on physical and psychosocial outcomes, and explore differences in outcomes based on the type or method of Cognitive behavior therapy delivery	T1D are at high risk for psychosocial problems that in turn negatively affect their diabetes management.
Graham et al. (2020) [16]	Moderate	Determine if different measures of depression are differentially associated with the increase in T2D. Also, examine the association between anti-depressant use and T2D risk.	Depression can cause a high risk of diabetes. The use of antidepressants is considered a risk for depression and is associated with an increased risk of T2D.
Almeida et al. (2018) [17]	Moderate	Assess psychiatric diagnoses in a Brazilian sample of adolescents with and without T1D and examine the factors associated with the presence of psychiatric disorders.	The prevalence of psychiatric disorders in adult T1D patients was considerably high.
Berger et al. (2018) [18]	Moderate	Assess the association between intentional insulin manipulation and psychiatry comorbidity, metabolic control, diabetes complications (severe hypoglycemia, hospital admissions due to diabetic ketoacidosis), and outpatient visits.	Psychiatric disorders were associated with insulin handling and manipulation, in female patients especially.
Nguyen et al. (2020) [19]	Low	It aims to examine the relationship between demographic and clinical characteristics, adolescent diabetes distress, and parental distress with the severity of anxiety and depressive symptoms in adolescents with T1D.	Mood and anxiety disorders are common in adolescents with T1D.

Table 5: Baseline Characteristics of Included Systematic Reviews, Meta-Analysis, Case-controls and Cross-sectional studies.

Rechenberg et al. (2021) [15]	Zhou et al. (2021) [12]	Ni et al. (2021) [7]	Smith et al. (2018) [6]	Liu et al.(2022) [5]	Systematic Reviews	References
T1D	T2D	T1D and T2D	T1D and T2D	T2D		Types of Diabetes
≤18 years of age No gender restriction	-	>18 years No Gender restriction	>16 or over Non-Diabetics and undiagnosed	Chinese adults (≥18 years). No Gender restriction.		Age
Psychosocial	Depression	-	Psychiatric Disorders			Comorbidities
T1D patients have 2 to 3 times higher anxiety and depression.	-	-	Young People with T1D had 2.5 times increased hazard of developing Anxiety over 26 years. and diabetes was associated with 2.6 times increased likelihood of having an anxiety disorder.	T2D patients show depression and Anxiety.		Prevalence of Depression and Anxiety

Yang et al. (2022) [8]	References Cross-sectional studies	Almeida et al. (2018) [17].	Dogan et al. (2019) [11].	References Case-control studies	Graham et al. (2020) [16]
		11-16 years	20-60 years	Age	T2D
182		81	208	Number of participants	18 or older
T2D		45/ 36.	70/70(T1D), 68(T2D).	Control/ diabetics group	-
Comorbidity group diagnosed with Anxiety and depression.		The main diagnoses that were present among the majority of participants were depression, anxiety, and neurological disorders.	Symptoms of psychic disorders in diabetic patients prevail more than in the control group	Prevalence of depression and anxiety	All Measures of depression are nearly related to a high risk of T2D.

Yang Qian et al. (2020) [13]	120-18 years old	392	T2D	Anxiety and depression prevail.
Berger et al. (2019) [18]	10-22 years	241	T2D	Depression rates were four times higher, and female patients were at higher risk for psychiatric disorders.
Nguyen et al. (2020) [19]	18 years or older	320	T1D	Presence of anxiety disorder among adolescents.

Risk of Bias

The risk of bias in the included articles was assessed using appropriate quality appraisal tools shown in Tables 3, 4, and 5. Some articles have a moderate risk of bias, and a few articles were of high quality and have a low risk of bias. The articles also have certain limitations. The results of which are evaluated in Tables 1, 3, 4, and 5.

Characteristics of Participants in the included studies

The sample characteristic of case-control studies by Almeida et al. (2018) included 81 participants, with 36 T1D and 45 without (controls). The groups were homogenously distributed regarding sex, age, socioeconomic status, and nutritional status. There was no significant difference between T1D and control groups regarding gender, age, body mass index, family, per capita income, and parental education. The overall prevalence of mental disorders in the sample was 22.2%. Mental disorders were more frequent in patients with T1D compared to controls: 30.56% vs 15.56%. Among participants with psychiatric disorders, 16.67% had two concomitant diagnoses. The most prevalent psychiatric diagnosis was depression, anxiety, and developmental disorders. Of the total sample, 32.5% had undergone some kind of psychological counseling prior to the study, and 6.17% had consulted with psychiatry. Disease duration and mean HbA1c did not show a significant association with the presence of psychiatric co-morbidity. The sensitivity and specificity of the strength and difficulties questionnaire (SDQ), compared to the development and well-being assessment (DAWBA), were 54.5% and 72% for parents, and 80% and 96% for adolescents respectively. The positive predictive value for SDQ questions for parents was 46.1% and 88.9% for adolescents, while the negative predictive value for parents was 78% and 92.3% for adolescents. The agreement of the SDQ questionnaire with DAWBA was 12% for parents and 78% for adolescents.

A case-control conducted by Dogan et al. (2019) included 70 T1D, 68 T2D patients, and 70 non-diabetic control patients. There were no significant demographic differences in the three groups. Further evaluation and results are presented in Figures 2 and 3 and Table 2.

Figure 2

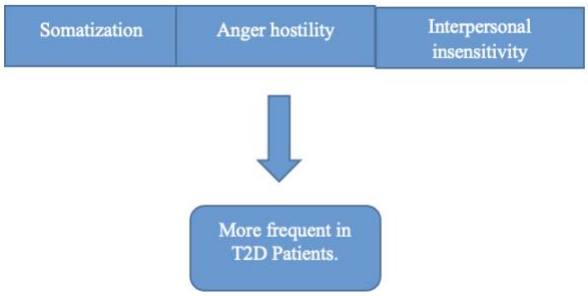

Figure 3

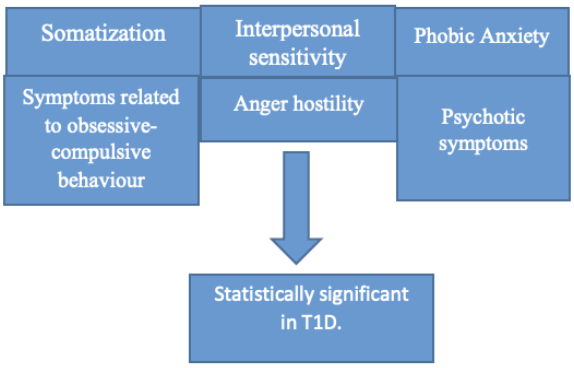

Figure 2 and 3 by Primary author and not copied from an external source.

Discussion

The study's primary aim was to examine the prevalence and relationship between diabetes mellitus, depression, and anxiety. The goal was to understand how diabetes affects the mental and psychological health of the patient by altering the body's physiology. Additionally,

we tried to assess whether depression and anxiety could be the potential cause of diabetes mellitus.

Diabetes Mellitus can be a risk factor for the prevalence of depression and anxiety and viceversa. Studies have reported a 44.05% prevalence of emotional distress in individuals with diabetes [8], and adolescents with T1D show a 37% presence of psychiatric disorders. In terms of gender differences, females showed a 33.4% prevalence of depression, while males showed a rate of 28.0% [5]. The results by Yang Qian et al. in a cross-sectional study suggest that sex moderates these associations. Elevated hs-C-reactive proteins (which are significant for clinical symptoms of depression and anxiety) in female patients are associated with a high prevalence of depression. Age in females also plays a role, as post-menopausal women over 60 years of age produce a decreased amount of estrogen, which can lead to increased inflammation and a higher likelihood of depression and anxiety. There was a strong link between serums hs-CRP and symptoms of anxiety in female patients with T2D. However, male patients did not show a similar positive trend. The lack of association between serum hs-CRP and depression score in male patients may be attributed to their relatively physical activity levels and lower prevalence of metabolic syndrome in the study sample. It also suggests that increasing moderate exercise and lowering the prevalence of metabolic syndrome may decrease the level of inflammation-induced mood disorders among patients with T2D [5,13].

Emotional states and endocrinological disorders may contribute to gender differences in diabetic patients [8]. Hyperglycemia in di and certain molecular and metabolic changes, can disturb glucose metabolism and impact brain cell functions, leading to cognitive decline. [20] High Hb1Ac levels are associated with depressive symptoms, especially in females [21]. T2D patients using insulin, particularly those with poor glycemic control and advanced diabetes are more likely to develop depression [5]. Insulin therapy can have negative side effects, such as weight gain, hypoglycemia, and pain, which can contribute to depression and anxiety. These psychological issues, adjustment difficulties, and poor physical health resulting from insulin injection play a role [22]. The prevalence of depression in T1D is reported as 29.3% in one study and 26.6% in another study involving youth with T1D [18]. T1D patients who have higher rates of internalizing disorder associated with insulin manipulation. These patients exhibit depression rates four times higher, three times rates of specific phobic, and double the rates of social phobia compared to patients who adhere to insulin therapy. Eating disorders are also associated with insulin manipulation. Insulin manipulation shows a strong association with metabolic control and diabetes complications, highlighting the role of behavior and adherence problems as mediating factors in metabolic deterioration and diabetes complications [23]. Insulin purging, which involves skipping insulin for weight loss purposes, denial of diabetes, hiding from others, fear of hypoglycemia, and self-destructive behavior, has shown an association with psychiatric disorders. Diabetes-specific symptoms in depressive disorders include using less insulin, reduced energy, decreased self-care, self-destructive intentions, and even suicidal tendencies [24,25]. Avoidance behaviors, such as skipping or reducing insulin due to hypoglycemic fear and social phobia, can contribute to depression and anxiety. Insulin manipulation, behavior problems, and adherence issue play a role in metabolic deterioration. Female patients have a higher risk of insulin manipulation and psychiatric disorders [18]. The standard deviation of blood glucose fluctuation is significantly associated with the prevalence of depression and anxiety. Healthy healthcare patterns and good sleep quality have been found to improve depressive symptoms. On the other hand, poor sleep quality and sleep disorders cause depression and anxiety [9].

Studies Indicate atrophy to the hippocampus, temporal lobe, and orbitofrontal regions in T2D. These are the regions of the cortex that plays an important cognitive role in memory, learning, and decision-making [26,27]. Neuroimaging studies have demonstrated structural and functional abnormalities in the brains of individuals with T2D. Disruption in white matter in the inferior frontal-occipital fasciculus left inferior longitudinal fasciculus, and left uncinated fasciculus might be related to cognitive dysfunction in T2D. Microstructure changes in the inferior network, white matter alteration, and decreased fractional anisotropy observed in the corpus callosum are found constantly in patients with major depressive disorder, cognitive impairment, and emotional disturbance in T2D [12,16]. Additionally, the microstructure alteration of white matter commissure corpus callosum, which connects the cerebral hemispheres, is involved in communication and processes between the two cerebral hemispheres [28]. A decreased fractional anisotropy in the left olfactory cortex and the emergence of prodromal symptoms are associated with olfactory function [29,30]. White matter alteration is also associated with obesity-related conditions, including cardiovascular risk factors such as metabolic syndrome [31].

Anxiety has been associated with an increased incidence of diabetes, although the link lacks comprehensive evidence [32]. Different measures of depression show an 11% increase in diabetic cases. Patients diagnosed with depression using standardized diagnostic interview have a 65% increased risk of diabetes, but the relationship between depression and new-onset diabetes lack comprehensive evidence [16,33]. However, various measures of depression are strongly associated with increased risk factors for T2D. Depression defined by antidepressants is associated with a 33% increased risk of T2D but remains uncertain if antidepressants themselves are the cause. Depression is attributed to an 18% increased risk of T2D [16]. Depression is attributed to an 18% increase in the risk of T2D [6]. Factors such as increased activity of the hypothalamic-pituitary-adrenal axis, chronic inflammation, poor dietary care, and physical inactivity

contribute, are factors, but the mechanism connecting depression and the measures that cause diabetes [34]. From studies, T2D patients showed a high prevalence of anger hostility, somatization, and sensitivity compared to the control group. Overall, 42.5% of diabetic patients, had at least one psychiatric problem, with generalized anxiety being the most common (prevalence of 21%) followed by ongoing depression (5.5%) and social phobia (7%). Similar psychiatric disorders were also found in T1D patients [11,35]. No statistical difference was found between T1D and T2D patients in terms of psychiatric symptoms. [35]. A meta-analysis of 248 studies up to 2018, reported the global prevalence of depression in T2D as 28% [36].
Berger et al. (2019) interviewed 241 young T1D patients to assess psychiatric co-morbidity and adherence to insulin therapy. They found that the prevalence of psychiatric co-morbidity in T1D patients was 29.3%. The adherent group showed a 17.5% rate of psychiatric co-morbidity, similar to the rates in children and adolescents without chronic disease [37]. The Manipulated-Group had a higher rate of 46.5%, suggesting that insulin manipulation may be a risk factor for psychiatric disorders, particularly eating disorders. Female patients were at higher risk for psychiatric disorders and insulin manipulation, consistent with previous studies [27,38,39].
Dogan et al. (2019) conducted a case-control study in Turkey analyzing the psychiatric symptoms of diabetic patients. They found a higher prevalence of psychiatric disorders in diabetic patients compared to the general population, including social anxiety, agoraphobia, panic, and mood disorder. High glucose levels and diabetic complications were identified as independent risk factors for psychiatric disorders. No statistically significant difference was found between T1D and T2D patients, and distinct symptom patterns were seen when compared to the control group. The study utilized the revised symptom screening test (SCL-90-R) to evaluate various psychiatric symptoms beyond depression and anxiety [11].

Cognitive behavior therapy is recognized as the gold standard psycho-therapeutic approach for managing anxiety and depressive symptoms [40,41,42,43,44,45]. It is a short-term skill that incorporates restructuring, relaxation, training, and exposure therapy and can be delivered in person and online. Implementing cognitive behavior therapy can be helpful in T1D adolescents with anxiety and depressive symptoms to lead to better and improved diabetic outcomes [41,46,47,48].

Limitations
There are certain limitations in studies the number of refusals to participate in cross-sectional studies, especially by male patients. Large samples and multicentre studies are needed to further explore the causal relationship between glucose fluctuations and emotional disorders in T2D. Small sample size and moderate risk of bias in various studies.

Conclusion
The evidence from multiple studies highlights a significant prevalence of depression and anxiety among diabetic patients. These findings suggest a close association between these mental health conditions and diabetes. However, further research is needed to establish this relationship's exact nature and underlying mechanisms. Although several studies suggest a potential causal link between high depression rates and the development of diabetes, comprehensive large-scale investigations are necessary to elucidate the underlying pathophysiology of depression and anxiety as contributing factors to the incidence of diabetes. Understanding this relationship more comprehensively can lead to improved management strategies and interventions that address both the physical and mental well-being of individuals with diabetes.

Conflict of interest
The Authors Disclose no conflict of interest.

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