

## Incidence of Depression in patients with Type 2 Diabetes Mellitus

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### ABSTRACT

**Introduction:** Depression and diabetes are both chronic devastating conditions & their co-occurrence has been associated with poor outcomes. The link between depression and type 2 diabetes is bidirectional, significant candidate pathways include the innate inflammatory response, the hypothalamic-pituitary-adrenal (HPA) axis, and insulin resistance, which all interrelate with each other. In formerly undiagnosed diabetic patients, depression had a higher prevalence and might be due to an unfavorable or stressful lifestyle such as condensed physical activity, socioeconomic scarcity, social adversity, unhealthy diet. In this study, the emphasis was made on screening for depression in patients with T2DM.

**Aim of the study:** To investigate the incidence of Depression in Patients with T2DM.

**Objectives of the study:** To obtain demographic details, to assess the depression levels, and to establish the relation based on the severity of depression in T2DM patients.

**Methodology:** It is a prospective observational study design, the patient health questionnaire (PHQ-9) was used to assess depression in 387 patients aged between 30-80 years. Venous blood was collected to assess fasting blood sugar (FBS), post-lunch blood sugar (PLBS) and Glycated hemoglobin (HbA1c).

**Results:** The PHQ-9 revealed that 182 patients (47%) are minimal in depression severity followed by 169 patients (38.5%) are mild in depression severity. Female gender, increased age, obese patients, and longer duration of diabetes was associated with increased odds of depression. Whereas, being married was protective and was associated with decreased odds of depression.

**Conclusion:** In our study, we found the majority of subjects with minimal severity of depression when correlated between depression and T2DM. When HbA1c levels are compared, patients with higher levels of HbA1c are presented by subjects with moderate levels of depression.

**Keywords:** Type 2 Diabetes mellitus; HbA1c; Depression; Patient health questionnaire-9; Depression severity.

### Introduction

Depression is a common and potentially debilitating mental illness characterized by a sense of inadequacy, despondency, decreased activity, pessimism, disturbed sleep or appetite, anhedonia and sadness, where these symptoms severely disrupt and adversely affect a person's life.<sup>1</sup> It is a chronic illness that distresses around 340 million individuals at any given time world wide.<sup>2</sup> The occurrence of diabetes mellitus has grasped epidemic levels worldwide ensuing massive human, economic and social costs globally. Presently, 415,000,000 public are existing with diabetes, 75% of who live in developing nations especially India, Bangladesh, Central African Republic; this figure has been anticipated to rise to 642,000,000 by 2040.<sup>3</sup> A connotation amongst depression and diabetes was recognized in the early 17<sup>th</sup> century, diabetes frequently seemed in persons who had experienced earlier life stresses or grief.<sup>4</sup>

The association amongst depression and T2DM

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is bidirectional: T2DM is linked with a roughly 20% amplified risk of occurrence of depression and depression is linked with a 60% amplified risk of occurrence of T2DM.<sup>5,6</sup> The linkage between depression and T2DM is that the psychological burden of living with a chronic disorder inclines patient to depression, and depression in patients with T2DM is allied with deprived self-care activities.<sup>7</sup> A meta-analysis presented an augmented risk of depression in patients diagnosed with diabetes compared with undiagnosed diabetes patients.<sup>8</sup> This finding stipulates that stress, together with an awareness of the challenges and potential complications related to diabetes, can cause depression.<sup>9</sup> The physiological burden related to the diabetes diagnosis may cause emotional distress, loss of interest and energy, and poor concentration, resulting to a depressive state.

Significant biological factors are related to the hypothalamic-pituitary-adrenal (HPA) axis dysfunction. Stimulation of the HPA axis increases the assembly of cortisol, a stress hormone, by the endocrine. Excess cortisol ends up in increasing glucose and insulin resistance; chronic elevation of cortisol increases the danger of metabolic syndrome, which elevates the risk of T2DM. Stress can activate the sympathetic system, increasing cortisol. Furthermore, the inflammatory system is activated as a result of this cascade and produces proinflammatory cytokines, which are postulated to steer to insulin resistance.<sup>10, 11</sup> Cortisol and cytokines induce negative changes within the monoamine system and hippocampus, worsening depressive symptoms.<sup>12,13</sup>

The cognitive-behavioral model suggests that the burden of T2DM ends up in low mood and negative thoughts about diabetes, which worsens diabetes self-care. Such negative thoughts and behaviors will be recognized and modified with cognitive-behavioral therapy (CBT), which slightly improves mood and glycemic control in patients with T2DM.<sup>14</sup> Furthermore, in developing countries including India, there's a scarcity of information on the burden of depression among diabetes patients.<sup>15,16</sup>

In this multicentric study, we investigated the association between glycaemic control and depression among T2DM patients attending tertiary hospital and primary care clinic facility in Warangal, India.

## Methodology

The study was a Prospective Observational study

design, conducted at Sri Bhadrakali Diabetic Care Clinic, Samraksha Diabetes & Thyroid Super Speciality Hospital and Mahatma Gandhi Memorial Hospital in Warangal, India. 427 diabetic patients were assessed for eligibility, of which 387 participants met the inclusion criteria, aged amid 30 and 80 years were registered into the study by organized random sampling of consenting patient visiting the clinic/hospital. Patients with type 1 diabetes and other chronic diseases such as osteoarthritis, cancer, multiple sclerosis, pregnant women and individuals aged <30 years at diagnosis or patients >80 years were excluded from the study. In addition, patients with other causes of depression such as loss of a close family member within the past 4 months and medication history of depression or manic/hypomanic episode then diabetes were excluded from the study. The socio-demographic characteristics such as age, gender, education, employment, as well as the clinical data like duration of diabetes, diabetes medication, hypertension and antihypertensive medication were collected using structured questionnaires. Depression was screened using PHQ-9. The PHQ-9 is an instrument that has been validated in diabetes patients for the detection of general depressive symptoms.<sup>17</sup> The PHQ-9 assesses how often the respondent has experienced specific symptoms over the past 2 weeks, assigning values of 0 to 3 points (0 - not at all, 1 - several days, 2 - more than half of the days, 3 - nearly every day).<sup>18</sup> Major depressive disorder was defined as the presence of at least five symptoms, reported for more than half the days in the past 2 weeks, including depressed mood or anhedonia, as well as the thought of suicide or better dead.<sup>19</sup> Blood pressure was measured after 5 min rest using an automated digital blood pressure monitor (Omron 907XL pro, Healthcare, Inc., Vernon Hills, IL), with the patients seated comfortably with a back support and arm resting on a table. FBS and PLBS were done by using GOD-POD method in which the normal values were taken as 60-110mg/dl and 110-160mg/dl respectively. Body weight was measured with a Seca 740 scale. Venous blood was drawn from each participant for the measurement of HbA1c using the boronate affinity chromatography method on PDQ Plus HPLC autoanalyzer (Primus Diagnostics, Trinity Biotech, Ireland). Good glycaemic control was defined as HbA1c of less than 7%.<sup>20</sup>

## Statistical analysis:

Descriptive statistics (mean+ S.D) were used to analyze the data.

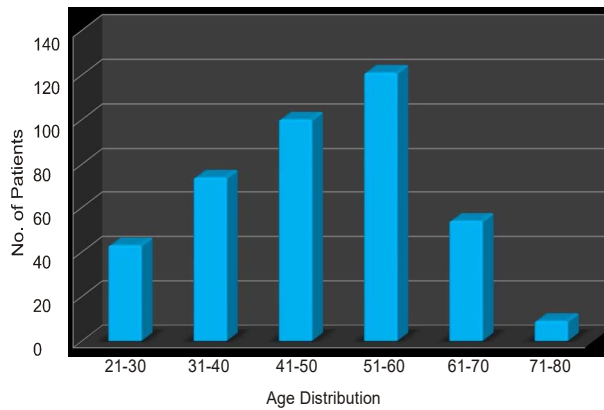
**Results**

In our study population a total of 427 participants with type 2 DM were enrolled but only 387 participants met the inclusion criteria.

(Find the Fig. 1-8 and Tables. 1-8 to correlate with results).

**Table 1:** Age Distribution

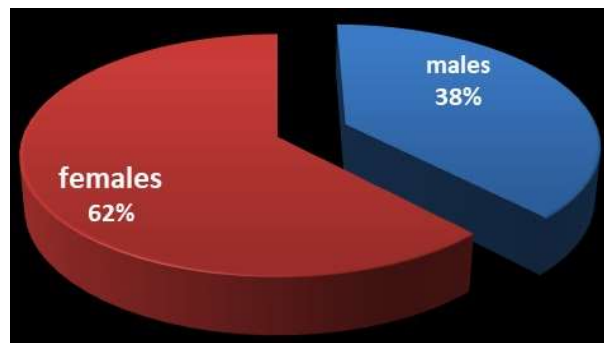
Class interval	No. of patients
21-30	43
31-40	74
41-50	100
51-60	121
61-70	54
71-80	9



As its noticeable a greater number of type 2 diabetic patients are in between the age group of 41-60yrs. The highest in amid 41-50yrs (31.2%) followed by age groups of 51-60yrs (25.8%), 31-40yrs (19.1%), 61-70yrs (13.9%), 21-30yrs (11.1%) and the least in age groups of 71-80yrs (2.32%)

**Table 2:** Gender Distribution

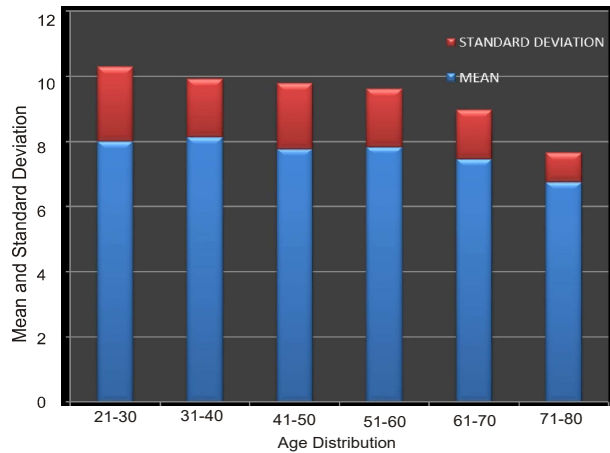
Gender	No. of Patients	Percentage
Males	147	38%
Females	240	62%



of the participants,147 (38%) and 240 (62%) were males and females respectively. High representation of females was present.

**Table 3:** Mean & Standard Deviations of HbA1c levels in age distribution.

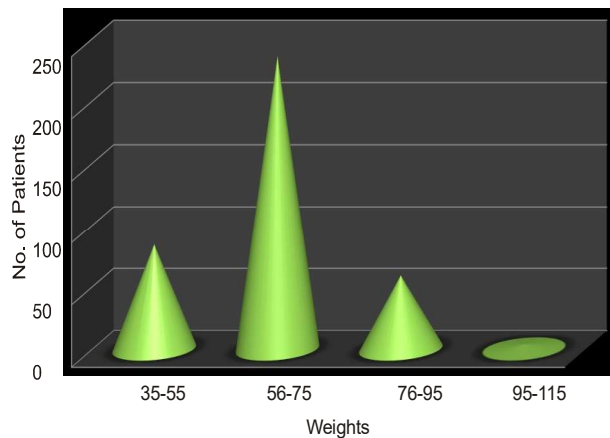
Age	Mean	Standard Deviation
21-30	8.02	2.27
31-40	8.13	1.8
41-50	7.78	2.02
51-60	7.84	1.79
61-70	7.45	1.49
71-80	6.75	0.9



There is no significant difference of mean and Standard Deviation between age groups.

**Table 4:** Weight Distribution

Class Interval	No. Of Patients
35-55	84
56-75	236
76-95	59
96-115	4

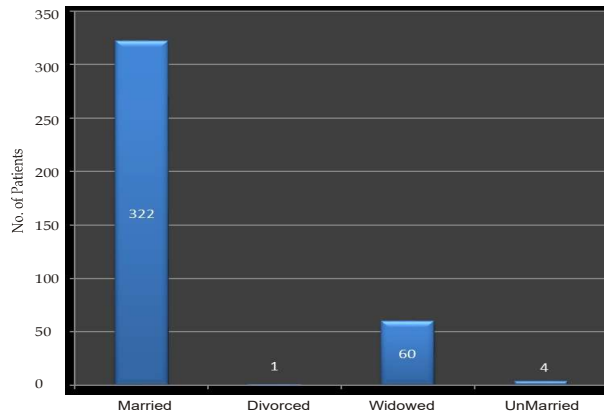


Weights of the patients were done using manual weighing machine, in which patients weighed

between 56-75 Kgs were more.

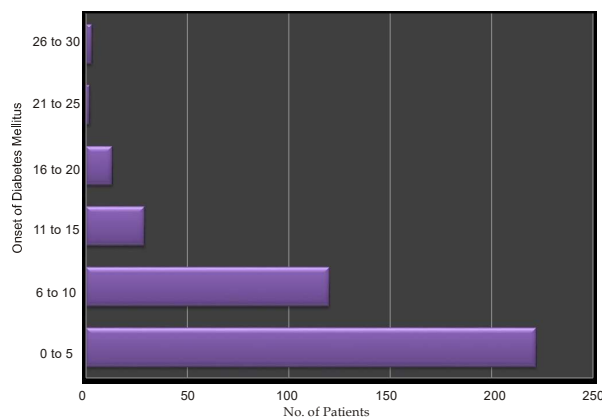
Table 5: Marital status

Marital Status	No. of Patients
Married	322
Divorced	1
Widowed	60
Unmarried	4



In our study population, greater number of the subjects were married (83.2%) compared to widowed (15.5%), unmarried (1.03%) and very least number were divorced (0.25%).

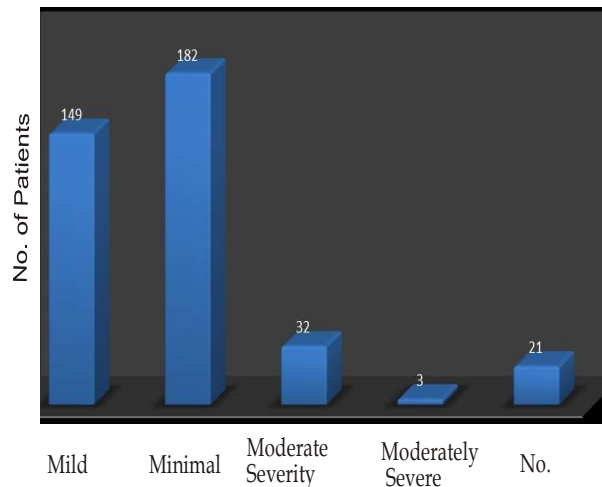
Class Interval	No. of Patients
0 to 5	222
6 to 10	120
11 to 15	29
16 to 20	13
21 to 25	2
26 to 30	3



The number of newly diagnosed patients with T2DM were 222 in a period of 5 years

Table 7: depression severity

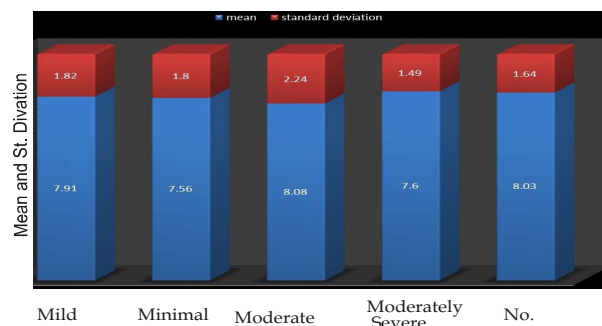
Depression severity	No. of patients
Mild	149
Minimal	182
Moderate	32
Moderately severe	3
No depression	21



When the subjects were examined for severity of depression results demonstrated that the minimal severity (47%) accounted for a higher risk then followed by mild (38.5%) than moderate (8.2%) and moderately severe (0.77%). The subjects assessed with no depression were (5.42%)

Table 8: hba1c level significance in depression severity.

Depression severity	Mean	Standard deviation
Minimal	7.91	1.82
Mild	7.56	1.8
Moderate	8.08	2.24
Moderately severe	7.6	1.49
No depression	8.03	1.64



The HbA1c levels were compared between the depression scores of the patients using standard deviation and mean.

### *Discussion*

The risk of evolving depression in the diabetic population was found to be double in comparison to the non-diabetic population.<sup>21</sup> In several studies, the variance of the sociocultural background of participants may need to be attributed to the differences in depression patterns. In many studies' diverse assessment tools with fluctuating sensitivity and specificity are used for screening of depression.<sup>22</sup> Limited studies in Africa have assessed the incidence of depression and its effects on patients with diabetes.<sup>23</sup> Over-all, the presence of diabetes and depression globally has been revealed to differ by the socioeconomic status of populations considered.<sup>24</sup> Probable elucidations aimed toward the observation comprise a better level of gender variations, social diffidence, lower level of education, a greater level of poverty and financial constraints among individuals. Female gender, unmarried status and a lower level of education, all of which have socioeconomic insinuations, were related to depression during this study.<sup>25</sup>

In a systematic review from the European depression in diabetes (EDID) research consortium study it was reported that in older adults, the comorbidity expects an earlier occurrence of complications. Individually diabetes and depression decrease the standard of life, but together they need a further negative effect. Due to the negative effects on health, the rise in complications, both diseases must be known in a private, and treated concurrently, to decrease depression, and to healthier control of diabetes.<sup>26</sup> In our research group we reported that a higher prevalence of depression in patients with type 2 diabetes mellitus was in increasing age.

The risk for incident diabetes was consistently higher among women, but not men, with more depressive symptoms. Sex Differences in the Association between Depression, Anxiety, and Type 2 Diabetes Mellitus an epidemiological research study examined the potential for sex interactions are vital because it has been hypothesized that stress and poor psychological state might portend different health outcomes for ladies than men. Several possible explanations exist, like sex differences in coping mechanisms or differential biological responses to depression or anxiety including inflammatory response and/or hypothalamic-pituitary-adrenal (HPA) axis dysregulation.<sup>27</sup> Gender distribution was high and

therefore, the prevalence of depression is reported within the female population (62%) than the male population (38%).

SV Bădescu et al. in their article reviewed that a robust association between depression in patients in their forties with orally treated diabetes was found, compared to patients in their seventies. On the contrary, insulin therapy in the elderly people with T2DM led to the development of glycemic control.<sup>28</sup> Hence, the finding of HbA1c levels in age distribution found that increasing age has better glycemic control.

An article published by global diabetes community in the UK proposes that individuals with diabetes, inadequate insulin averts the body from receiving glucose from the blood into the body's cells to use as energy. Once this ensues, the body starts burning fat and muscle for energy, instigating a drop by complete body weight. Unpredicted weight loss is usually observed in persons with DM. This hypothesis suggests in our study that a greater number of patients have maintained a mean weight of up to 75 kgs.<sup>29</sup>

A data from the longitudinal Canadian National Population Health surveyed that the additional intrusion which may aid inconsiderate depression is a legal status that is significant to the epidemiology of psychiatric disorders. Specifically, the high frequency of major depression in persons with separated, divorced, or widowed status has been well recognized. Though, the literature is alienated on whether marital trouble leads to major depression and/or the other way around. During this research study the larger proportion was married and therefore, the connotation between divorce, widow and the better emotional role was also unusual. This might flow from the sampling bias as there have been just one divorced and 60 widowed patients in the study.<sup>30</sup>

Analyzes of recent statistical data by Yanling Wu et al. studied among persons with a positive case history of diabetes, the disease is understood to occur earlier, and obesity has been reported to play a key role in its early onset. These results are concordant with those of this study, which presented that the high number of groups had a better rate of the positive case history of diabetes, higher BMI, and better HOMA-IR than the further group.<sup>31</sup>

Data from the PHQ-9 Validity of a Brief Depression Severity Measure research study, totaling patients provide strong evidence for the validity of the PHQ-9 as a quick measure of

depression severity. Our analysis of the entire range of PHQ-9 scores accompaniments because the PHQ-9 is progressively used as an incessant measure of depression severity, it's obliging to spot the likelihood of a serious or sub-threshold clinical depression at various cut points. PHQ-9 scoring of 5, 10, 15, and 20 signifies mild, moderate, moderately severe, and severe depression. During this analysis, we diagnosed that the high number of populations were with minimal depression (182 patients) followed by mild depression (149 patients) during a group of people.<sup>32</sup> Once depression is identified during a diabetic patient, the goal would be to treat both diseases at an equivalent time. Petrak et al. suggested treating depression as urgency because the response to medication is usually seen in 2-4 weeks for antidepressants, whereas, the development in glycemic control and levels of HbA1c requires some months to settle. Theory suggests that HbA1c levels are maintained accordingly, deprive of depression severity.<sup>33</sup>

### Conclusion

It is vital to acknowledge opportunities to attenuate the impact of comorbid depression and diabetes as this bidirectional association has major consequences for patients. Depression is commonest among patients with T2DM and it has been found that females (62%) are more at the risk of depression than males (38%). The subjects with minimal severity of depression were high compared with mild severity when correlated between depression and T2DM. When HbA1c levels are compared, patients with higher levels of HbA1c are presented by subjects with moderate levels of depression.

In patients with T2DM, depression remains underdiagnosed and a very important aspect for the endocrinologist would be the cognizance of this fairly common co-morbidity. The ADA guidelines recommend that diabetic patients be regularly screened for psychosocial problems (e.g., depression) with the Patient Health Questionnaire PHQ-9, or any other legalized screening tool. Consequently, ADA guidelines mentioned collaborative-care interventions show effectiveness in comorbid depression and diabetes, leading to increased self-care, a much better quality of life, treatment satisfaction, and healthier glycemic control. The management of diabetes and depression is often challenging given the multifaceted interplay between them, CBT, pharmacotherapy, and collaborative care may result in cost savings and improve patient self-care

and functionality.

### Statements

#### 7.1 Acknowledgements

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#### 7.2 Ethical approval

Ethical clearance was obtained from Institutional Human Ethics Committee of Kakatiya Medical College and IHEC number is KIEC/KMC/NCT/NIS/2018/P32 and each patient provided written voluntary informed consent after the rationale and the procedure of the study were thoroughly explained them in their local language also. Patients found to be depressed were referred to the Psychiatry department for further assessment and possible management.

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7.4 *Competing interests: The authors declare that they have no competing interests.*

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#### 7.6 Author's contribution:

All the authors contributed equally to this research work. The manuscript has been read and approved by all the authors, that the requirements for authorship as stated earlier in this document have been met, and that each author believes that the manuscript represents honest work.

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