Review Article

Diabetes mellitus and suicide

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ABSTRACT

Relationship of diabetes mellitus (DM) with metal health disorders such as depression has been explored extensively in the published literatures. However, association of diabetes mellitus with suicidal tendencies has been evaluated less extensively. The present narrative review aimed to assess the literature relating to diabetes mellitus and suicide. As a part of the review, Pubmed and Google Scholar databases were searched for English language peer reviewed published studies with keywords relating to diabetes and suicide. Additional references were identified using cross-references. The available literature suggests that suicidal ideas and attempts are more frequent in patients with diabetes mellitus than healthy or medically ill controls. Although, a few studies report evidence to the contrary. Suicide accounts for a large proportion of deaths in patients with diabetes mellitus type I (T1DM), and their mortality rate is higher than that of age matched control population. Psychological morbidity, including depression, precedes suicidal ideas and attempts; though many other factors can be hypothesized to impact and modulate this association. A common method of suicide attempt in patients with diabetes includes uses of high doses of insulin and its congeners or medications to treat the disease. Regular screening and prompt treatment of depression and suicidality is suggested for patients with DM.

Key words: Depression, diabetes mellitus, insulin, suicidal behaviour

Introduction

Diabetes mellitus (DM) is a medical disorder which affects an increasing large proportion of the population across different age groups.[1,2] Though it is prevalent globally, it poses a particular health challenge in resource constrained low and middle income countries.[3,4] The two commonest forms of the disorder, diabetes Type I (T1DM) and Type II (T2DM) have different pathophysiological mechanisms. DM affects multiple organ systems and is associated with poor quality of life and even reduced life expectancy.[5,6]

It has been suggested that diabetes (both T1DM and T2DM) is associated with increased occurrence of certain psychiatric disorders.[7-10] Suicidal ideas as well as suicide attempts are potentially life threatening psychiatric emergencies that occur more frequently in patients with DM than in the general population. Many studies have focused on the relationship that DM shares with psychiatric disorders, especially depressive disorder.[9-12] However, fewer studies have focused upon understanding suicidality among individuals with DM. This narrative review was conducted to understand the existing literatures on relationship between diabetes and suicide. We aimed at reviewing the literature on rates of occurrence of suicidal ideas and attempts in patients with diabetes, the risk factors for suicidality, the common and unique methods for suicidal attempts in such patients, and management of such patients.

Access this article online	
Quick Response Code:	Website: www.ijem.in
	DOI: 10.4103/2230-8210.137487

Methodology of the review

Searches for relevant literatures were carried out using electronic databases. Pubmed (including Pubmed Central) and Google Scholar were used to identify published studies. Searches were carried out using Medical Subject Headings (MeSH) terms 'Diabetes mellitus' and 'Suicide'. Additional searches were carried out using related

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keywords of 'suicidal behaviors' and 'self harm' along with DM. The searches were carried out in December 2013. The initial search yielded 165 abstracts. Articles were evaluated and were classified according to the broad subject related to suicidality in DM. Further studies were identified using cross-references from the identified text and by going through the related citations. Only English language peer reviewed articles were included as a part of this review.

The full-texts of the identified studies were obtained and assessed for their content. The manuscripts were categorized according to broad themes like epidemiology, elaboration of risk factors for suicide, and management issues. Relevant data were extracted from the articles and incorporated in the narrative. Discrepancies in the interpretation of the literatures were resolved through mutual discussion between the authors.

Occurrence of suicidal thoughts and attempts in diabetes

The studies that have assessed the occurrence of suicidal ideas, attempts and deaths in patients with DM have been summarized in [Table 1].

Studies have assessed suicidal ideations using different tools including structured interview schedules such as Mini International Neuropsychaitric Interview (MINI),[13,18] rating scales (such as Beck Depression Scale suicidality item),[22] and a single question relating to suicidal ideations.[14,16] The size of the population assessed have varied from less than 100[23] to over 80,000.[14] Studies have come mainly from Scandinavian countries and USA,[10,17,20-28] though there are few studies from other countries too.[13,15,18,19,29,30]

The rates of suicidal ideation and suicidal attempt has been reported to be as high as 26.4%[23] and 13.3%,[20] respectively. Some of the studies focusing on suicidal

Table 1: Studies assessing occurrence of suicidal behaviour in patients with Diabetes Mellitus

Study	Type of study	Population	Country	Findings
Suicidal ideas and attempts				
Ceretta *et al.*, 2012[13]	Case control	3141	Brazil	Suicide risk according to MINI in 13.1% in patients with DM as compared to 2.1% in controls
Fuller Thompson and Sawyer[14]	Observational	82,675	Canada	Lifetime suicidal ideation in Type 1 DM at 15.0% and Type II DM at 9.4%. Age and sex adjusted odds ratio of Type 1 DM at 1.61
Pompili *et al.*, 2009[15]	Case control	100	Italy	Patients with diabetes showed greater hopelessness and suicide ideation than internal-medicine outpatients
Han *et al.*, 2013[16]	Observational	17,065	Korea	Suicidal ideation in 24.2% of diabetics compared to 16.5% in the non-diabetic population (suicidality assessed though a single question)
Bot *et al.*, 2013[17]	Observational	646	Netherlands	11.0% of the patients with DM had suicidal ideation with PHQ 9 (8.3% for type I DM, 13.2% for Type II DM)
Igwe *et al.*, 2013[18]	Case control	540	Nigeria	6.3% of those with DM had suicidal risk compared to 7.8% in essential hypertension group according to MINI
Radobuljac *et al.*, 2009[19]	Case control	625	Slovenia	The healthy control group trended toward higher lifetime prevalence of all suicidal behaviors and self-injurious behavior
Roy *et al.*, 2010[20]	Case control	816	USA	Suicide attempt rate in African American patients with Type I diabetes was 13.3% as compared to 3.5% in controls (P<0.001)
Myers *et al.*, 2013 [21]	Observational	145	USA	9.2% of the patients had attempted suicide. Most of those who attempted had a diagnosis of depression
Roy and Roy, 2006[22]	Observational	459	USA	No significant relationship between serum cholesterol levels and either total Beck Depression Inventory (BDI) scores or BDI scores on the item measuring current suicidal ideation
Goldston *et al.*, 1997[23]	Observational	91	USA	Interview Schedule for Children showed one year and lifetime prevalence of suicidal ideation to be 12.1% and 26.4% respectively
Completed suicides				
Patterson *et al.*, 2007[24]	Retrospective	28887	Multiple	11/141 (7.8%) deaths in patients with Type I DM due to suicide (SMR of 1.1)
Kyvik *et al.*[25]	Retrospective	1,682	Netherlands	In type I DM in males - 12 suicidal deaths (SMR of 1.6)
Joner and Patrick, 1991[26]	Cohort	1908	Norway	Of the cohort of Type 1 DM patients followed up for 8 years, 20/1908 died, out of which 8 (40%) due to suicide
Dahlquist and Kallen, 2005[27]	Case control	456	Sweden	9.0% deaths in diabetes group were suicides as compared to 13.6% deaths in control population in a registry based case-control study
Wibell *et al.*[28]	Retrospective	58	Sweden	17.2% of 58 deaths in 15-34 age group of DM patients due to suicide. SMR of 2.0 in males
Swerdlow and Jones[29]	Cohort	3090	UK	0.55% of the total deaths due to suicide (SMR of 1.46 and 1.98 in males and females respectively)
Feltbower *et al.*, 2008[30]	Retrospective	4,246	UK	6/108 (5.5%) deaths due suicides in a register of 4,246 individuals with type 1 DM (SMR 2.5)

CI: Confidence Interval, DM: Diabetes mellitus, MINI: Mini international neuropsychiatric interview, OR: Odds ratio, PHQ-9: Patient health questionnaire (9 item version), SMR: Standardized mortality rate

ideation and attempts in patients with DM have found that suicidal risk is higher in patients with diabetes.[13-16,20] However, two studies have found that patients with diabetes had lower rate of suicidal ideation as compared to healthy controls[19] and patients with other medical disorder.[18] Depression has been reported to be the most common psychiatric disorder in persons with DM who attempted suicide.[21]

Data about suicide completers among the patients with DM have primarily come from cohort studies and studies based on health registries. The proportion of cases reported to be due to suicide has varied from 0.55%[29] to as high as 40%.[26] Most of the studies which have reported rates of suicides in T1DM population has given vales in the range of 5-15%.[24,30] The low rate found in one specific study[29] could be ascribed to the fact that this study looked exclusively at T2DM cases where mortality can result due to a host of medical complications due to diabetes or other concurrent medical illnesses. Standardized mortality rate (SMR) provide a better approximation in such situations as it looks at comparison with the age specific mortality. There too, diabetes has been associated with SMR of more than one, which suggests greater mortality rates in this population especially males.[24,25,28,30]

Factors that influence suicidality in diabetes

Many demographic variables have been explored for putative association with suicidality in patients with DM. Males seems to have a greater risk in completing suicides.[28] In a sample of patients from Nigeria, lower education was associated with increased suicidality.[18] Relation of glycemic control with suicidality has been evaluated in one study.[17] The study conducted on 646 patients with DM found suicidality to be significantly associated with poorer glycemic control.

Depressive cognition has been associated with suicidal ideation in patients with DM. A large Korean study has shown that depression acts synergistically with diabetes in increasing the chances of having suicidal ideations.[16] Similar findings have been observed in other studies.[15,20] Other psychological factors like stress have also been suggested to play a role in suicidal ideations and attempts in patients with DM.[31] Multivariate analyses has showed that female sex, severity of childhood abuse, history of alcohol abuse, and depression were significantly and independently associated with having attempted suicide.[20]

The literatures relating to risk factors for suicidal behavior among patients with DM is not very extensive. However, it has been reported that probably risk factors related to suicide in general and those of chronic medical illnesses do apply in context of DM as well. Risk factors can be inherent to the patient's characteristics like coping skills, personality profile, additional psychiatric illness including depression and alcohol use disorder, and presence of hopelessness. Past history of suicide attempt and family history of completed suicide present additional risk factors. This is compounded by illness related and situational risk factors like lack of social support, adverse life events, exacerbation of the illness and gradual accrual of diabetes related complications. Access to means of self harm is another factor which determines whether a suicidal plan is executed or not. A range of risk factors and protective factors determine the overall suicidal risk in a particular patient and the reader is referred to more comprehensive sources for understanding of suicide risk factors in general.[32,33] [Figure 1] provides a simplistic model of how different factors aggregate to confer suicidal risk.

Characteristics pertaining to means of suicide attempts

Patients with DM present some unique characteristics of suicide attempts. It has been seen that insulin is used quite frequently in the suicidal. This can be ascribed to easy availability and accessibility to a potentially lethal means of suicide in the form of injectable insulin.[34] Subcutaneous or intravenous injection of insulin can cause hypoglycemia which can cause death if it is severe and lasts for a prolonged period of time. Biguanides, like metformin, can cause lactic acidosis when taken in larger than necessary amounts. [Table 2] provides a list of the medications that have been used for suicidal attempts.

As evident from the table, insulin has been widely used in suicidal self-harm attempts in patients with DM. Probably, the first report of use of high dose of insulin with a suicidal intent in a diabetes patient dates back to 1934 when a 50-year-old female patient consumed 400 U of insulin apparently being depressed due to financial issues.[53] Subsequently, there have been reported cases of suicidal self-administration of insulin where the patients had recovered fully after prompt medical treatment.[37-39] Not only regular insulin, but its congeners like insulin glargine and lispro have also been used for self-harm attempt.[40-43] Use of insulin as a means of suicidal attempt seems to be more common in patients with T1DM than T2DM.[44] This could be due to the fact that T1DM can only be treated with insulin and consequently is more regularly accessible to these patients. For treatment of patients with T2DM, many other pharmacological agents are prescribed which cannot be administered through an invasive route.[54]

Information about the use of oral anti-diabetic mediations for self harm has come mainly from case reports. Oral

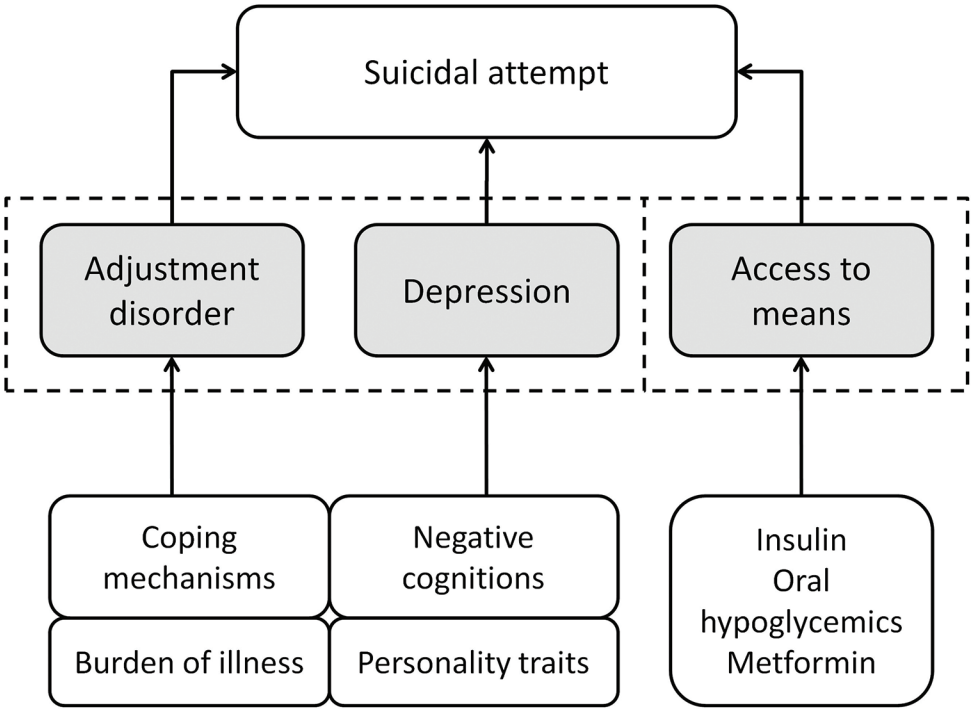

Figure 1: A simplistic model to explain how different factors aggregate towards risk of suicidal behaviour

Table 2: Medications for diabetes treatment that have been reported to be used for suicidal attempts

Medication	Method
Gliclazide	Patient developed renal failure after consumption of 28 g of gliclazide (a sulfonylurea)[35] Underwent hemodialysis and survived
Glipizide	Used in conjunction with Insulin.[36] Fatal outcome
Insulin	Many reports from over the world. Both regular insulin [37-39] and other formulations (insulin glargine,[40-43] lispro[41]). Hypoglycemia occurs and can be managed successfully by using dextrose infusion.[37,41] Can have fatal outcome if untreated.[44]
Liraglutide	Subcutaneous injection of 72 mg of Liraglutide (a GLP-1 receptor agonist).[45] No hypoglycemia. Non fatal outcome
Metformin	Many cases. Development of lactic acidosis. [46-50] Treated with hemofiltration or dialysis. Fatal[50] as well as non fatal[46,47] outcome
Phenformin	Consumption of excess doses (850 mg) associated with recurrent vomiting.[51] No hypoglycemia and managed conservatively
Sitagliptin	Ingestion of 1700 mg of sitagliptin (Dipeptidyl peptidase-4 inhibitor).[52] No hypoglycemia. Non fatal outcome

GLP-1: Glucagon-like peptide-1

medications like glipizide and gliclazide have been used for attempted suicide in patient with DM.[35,36] Metformin has been used in massive quantities with an intent to self-harm in a few patients.[46-50] Use of excess doses of metformin results in lactic acidosis which may result in cardiac arrest[47,50] and even death.[50] Hemodialysis or hemofiltration have been used to correct lactic acidosis in these situations. Other medications that have been used in excess quantities with suicidal intent include liraglutide, phenformin, and sitagliptin.[45,51,52]

Apart from the above, suicidal attempts in patients with DM have involved excess consumption of sugary substances leading to hygerglycemic state. A case of fatal self-induced hyperglycemia by drinking excess amounts of sugared tea has been reported for a 15–year-old boy with diabetes.[55] Similarly, a case of fatality has been reported with the use of sugary solution in a patient with DM.[56] There have been reports of use of other medications, notably psychotropics, like antidepressants and antipsychotics, for suicidal attempt by patients with DM.[44]

Danger of abuse of antidiabetic therapy for suicidal attempts is not confined to the patient, but even extends to the other family members who live along with the patient. Use of insulin and other medications for treatment of DM has also been described in family members who had taken the patient's medications for suicidal attempt.[57-59]

Management of suicidality in diabetes mellitus

Management of suicidality among patients with DM begins with proper assessment and evaluation. Depression and adjustment problems are common in patients with DM and require attention. Suicide risk assessment can be conducted as a part of screening for depression or otherwise. Many brief screening questionnaires for depression like Primary Health Questionnaire-9 (PHQ- 9)[60] and Beck Depression Inventory (BDI)[61] have questions relating to suicidal

ideation. Specifically asking about current suicidal ideas directly (and not in a roundabout indirect manner) is useful. It has been seen that asking about suicidal ideas do not implant such ideas in the person assessed, but missing on such questioning due to hesitation on the part of the therapist may lead to missed opportunities to screen for suicidal behavior. Specific instruments to assess suicidality are also available for comprehensive assessment of patients with suicidal ideation[62,63] SAD PERSONS is a mnemonic that can be used for remembering the risk factors for suicide and includes male sex, older age, depression, previous attempt, ethanol abuse, rational thinking loss (hopelessness), social supports lack, organized plan, no spouse and, sickness (presence of medical illness).

Suicidality tends to occur in presence of a diagnosable psychiatric illness or psychological stress. It is important to conduct a detailed psychiatric evaluation to assess for the presence of disorders like depression, anxiety disorders, substance use disorders, and personality disorders. Presence of psychosocial stressors and social supports can be helpful in guiding treatment. Medical history focusing on complications due to diabetes and other medical co-morbidities should be documented and treatment reviewed. Adherence to treatment in the past and the present can give pointers towards presence of underlying depression.[64]

In case a diagnosis of depression is made in patients with diabetes showing suicidality, appropriate treatment should be initiated. Management options would include both pharmacotherapy and psychotherapy.[65,66] Attention must be paid towards drug interactions and impact of the psychotropic medications on glucose levels. Some of the Selective Serotonin Reuptake Inhibitors (SSRIs) would be preferred choice as they improve glycemic control, while Tricyclic Antidepressants (TCAs) and mirtazapine should be avoided.[67] Second generation antipsychotics usually have the propensity to cause impaired glucose metabolism and first generation antipsychotics should be preferred when antipsychotics need to be given for control of psychotic symptoms.[68]

Certain precautions need to be taken for patients who exhibit suicidal risk. High risk management needs to be instituted for patients having suicidal risk. This may include hospitalization, 24-hour surveillance and monitoring, and avoidance of potentially fatal articles like sharps and medications in the vicinity of the patient. Medications for the treatment of diabetes like insulin and oral hypoglycemic agents should be supervised and kept away from easy accessibility of the patient. Suicide risk assessment should be conducted frequently and high risk precautions should continue till risk is deemed to be consistently low.

Management of patients who have attempted self-harm in recent past should be given priority as an emergency. They should be triaged according to the present condition and anticipated complications. If a patient has consumed excess doses of oral hypoglycemic agent or injected insulin in large amounts, then regular blood sugar monitoring should be conducted. Dextrose infusion is utilized to prevent blood glucose from falling too low.[37,38] In some situations, insulin levels can be monitored over time to determine the critical period and when the dextrose infusions can be slowly tapered away. Lactic acidosis is a potential problem for patients who have been receiving biguanides like metformin.[48,49] Hemodialysis and hemofiltration can be used in cases of excess consumption of metformin. Supportive measures like fluid correction and electrolyte balance should continue for the management of the patient. After stabilization of the patient, a psychiatric consultation should be sought for assessment and management. The salient features of management of patients with suicidality in patients with DM are highlighted in Table 3.

Conclusion

Suicidal thoughts and behaviors are a clinical and public health challenge in patients with DM. There are studies to suggest that DM is associated with greater frequency of suicidal thoughts and attempts, though there are a couple of studies which report to the contrary. The standardized mortality ratio due to suicide seems to be higher for patients with DM. Easy access to lethal means in the form of insulin and oral hypoglycemic agents seems to make attempt easy. Regular screening for suicidal ideas and appropriate psychiatric management of the symptoms can help in reducing potentially fatal outcomes.

Table 3: Highlights of the management of patients with suicidality

Suicide risk assessment using a screening instrument and/or a detailed psychiatric interview
Assess for psychiatric illness like depression and substance use disorder
Appropriate treatment for the psychiatric conditions
Suicide prevention measures when suicide risk is moderate to high
In case of suicide attempt, triage and initiate specific treatment

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Cite this article as: Sarkar S, Balhara YS. Diabetes mellitus and suicide. Indian J Endocr Metab 2014;18:468-74.

Source of Support: Nil, **Conflict of Interest:** None declared.