Review Article

Diabetes and psychiatric disorders

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ABSTRACT

Interface of diabetes and psychiatry has fascinated both endocrinologists and mental health professionals for years. Diabetes and psychiatric disorders share a bidirectional association -- both influencing each other in multiple ways. The current article addresses different aspects of this interface. The interaction of diabetes and psychiatric disorders has been discussed with regard to aetio-pathogenesis, clinical presentation, and management. In spite of a multifaceted interaction between the two the issue remains largely unstudied in India.

Key words: Diabetes, psychiatric disorders, psychotropic medications

Introduction

The interface of diabetes and psychiatry has fascinated both endocrinologists and mental health professionals for years. Way back in 17th century Thomas Willis speculated that diabetes was caused by "*long sorrow and other depressions.*" Sir Henry Maudsley commented that "Diabetes is a disease which often shows itself in families in which insanity prevails" in "The Pathology of Mind" published in 1879. Insulin coma therapy was used as a psychiatric treatment within a decade of isolation of insulin. Over the past few decades this interface has been studied more extensively with greater scientific rigor.

Diabetes and psychiatric disorders share a bidirectional association - both influencing each other in multiple ways. The current article addresses different aspects of this interface. General issues pertaining to the topic would be described first. Subsequently salient features of individual psychiatric disorder would be presented.

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Patterns of co-occurrence of diabetes and psychiatric disorders

Comorbidity of diabetes and psychiatric disorders can present in different patterns. First, the two can present as independent conditions with no apparent direct connection. In such a scenario both are outcome of independent and parallel pathogenic pathways. Second, the course of diabetes can be complicated by emergence of psychiatric disorders. In such cases diabetes contributes to the pathogenesis of psychiatric disorders. Various biological and psychological factors mediate the emergence of psychiatric disorders in such context. Third, certain psychiatric disorders like depression and schizophrenia act as significant independent risk factors for development of diabetes. Fourth, there could be an overlap between the clinical presentation of hypoglycemic and ketoacidosis episodes and conditions such as panic attacks. Fifth, impaired glucose tolerance and diabetes could emerge as a side effect of the medications used for psychiatric disorders. Treatment of psychiatric disorders could influence diabetes care in other ways also as discussed in subsequent sections [Box 1].

Diabetes and psychiatric disorders interact in other ways as well. Certain substances of abuse such as tobacco and alcohol can alter the pharmacokinetics of the oral hypoglycemic agents. Moreover, the presence of a comorbid psychiatric disorder like depression could interfere with the management of diabetes by influencing treatment adherence. Similarly certain disorders such as

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Box 1: Interaction between diabetes and psychiatric disorders

- Present as cooccurring independent conditions with no apparent direct connection
- Diabetes as a risk factor for development of psychiatric disorders
- Psychiatric disorders as risk factors for emergence of diabetes
- Overlapping clinical presentation of diabetes and psychiatric disorders
- Interaction of medications
- Impaired treatment adherence

phobia of needles and injections can present difficulties with investigations and treatment processes such as blood glucose testing and insulin injection. Also patients with psychiatric disorders are less likely to seek treatment. Such delays would postpone detection of co-occurring diabetes as well.

Implications of co-occurrence of diabetes and psychiatric disorders

Co-occurring psychiatric disorders in patients with diabetes are associated with impaired quality of life,[1] increased cost of care,[2] poor treatment adherence,[3] poor glycemia control (evidenced by elevated HbA1c levels),[4] increased emergency room visits due to diabetic ketoacidosis,[5] higher frequency of hospitalization, and higher rate of absenteeism.[6] Additionally there is an increase in cost of medical care. Cost of care for non-mental health conditions among patients with co-occurring psychiatric disorders and endocrinal disorders is twofold or even higher (depending on the treatment setting) than the population without co-occurring psychiatric disorders.[7]

Diagnosing psychiatric disorders among patients with diabetes

One of the biggest challenges in management of psychiatric disorders among those suffering from diabetes is the low rates of detection. Up to 45% of the cases of mental disorder and severe psychological distress go undetected among patients being treated for diabetes.[8] This is a result of both patient and physician-related factors. Physicians should be aware of the possible co-morbid psychiatric disorders likely to be associated with diabetes. As highlighted in the subsequent sections psychiatric co-morbidity is not uncommon in those suffering from diabetes. Consequently these patients should be regularly screened for common psychiatric disorders. Brief instruments such as patient health questionnaire (PHQ) and symptom checklist-90 (SCL-90) are sensitive, time efficient, and well-validated screening tools for common psychiatric disorders like depression and anxiety. Scales such as Hospital Anxiety and Depression Scale (HADS) could be used to further quantify the severity of anxiety and depression in this population. It is imperative to screen those suffering with diabetes for emergence of psychiatric disorders and vice versa. Since there could be some overlap between the physical features of diabetes and psychiatric disorders it is important to look for the behavioral and cognitive features of psychiatric disorders.

Psychiatric disorders could be diagnosed using two of the most commonly used nosological systems. These are the International Statistical Classification of Diseases and Related Health Conditions- 10 (ICD-10) of World Health Organization (WHO) and Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) of American Psychiatric Association (APA). In spite of certain dissimilarities, there is a substantial overlap between these two manuals. ICD-10, the more widely used of the two, makes use of the alpha-neumaric coding system for different psychiatric disorders. Psychiatric disorders are coded in chapter F of ICD-10. The chapter is further divided into 10 categories from 00-09 with each housing a particular group of psychiatric diagnoses [Table 1]. There is a brief primary care version of ICD-10 that is aimed at assisting the primary care physicians in diagnosing psychiatric disorders.

Some of the psychiatric disorders of particular relevance with regard to diabetes include delirium, substance use disorders, depression, anxiety, psychotic illness like schizophrenia, eating disorders.

The subsequent section presents an overview of these psychiatric conditions in the context of diabetes.

Delirium

Delirium in diabetes could be a manifestation of hypoglycemic episodes[9] or diabetic ketoacidosis. Delirium represents the severe end of the spectrum of clinical manifestation of these phases. Patients with diabetes suffering from co-morbid psychiatric disorders are more likely to experience hypoglycemic delirium. Because of use of overlapping terminology in the literature it is difficult to estimate the exact prevalence of delirium in diabetes based on current nosological systems. However, episodes of hypoglycemia[10] and diabetic ketoacidosis[11] are not uncommon in diabetes and consequently delirium is also not an infrequent occurrence. Delirium is associated with various adverse outcomes including increased hospital stay, increased cognitive and functional deterioration, morbidity and mortality.[12,13]

Delirium in diabetes could present as hypoactive or hyperactive delirium. The patient is excited, talking

Table 1: List of categories of psychiatric disorders (mental and behavioral disorders) in ICD-10

Category code	Name of category		Disorders included#
F00-F09	Organic, including symptomatic, mental disorders		Delirium Dementia Mental disorders due to brain damage and dysfunction and to physical conditions
F10–F19	Mental and behavioral disorders due to psychoactive substance use		Tobacco use disorders Alcohol use disorders
F20-F29	Schizophrenia, schizotypal, and delusional disorders		Schizophrenia Persistent delusional disorder
F30-F39	Mood (affective) disorders		Depressive disorder Bipolar affective disorder
F40-F48	Neurotic, stress-related, and somatoform disorders	Phobic anxiety disorders Generalized anxiety disorder Panic disorder Obsessive-compulsive disorder	
F50-F59	Behavioral syndromes associated with physiological disturbances and physical factors		Eating disorders Sexual dysfunction
F60-F69	Disorders of adult personality and behavior		
F70-F79	Mental retardation		
F80-F89	Disorders of psychological development		Autism
F90-F98	Behavioral and emotional disorders with onset usually occurring in childhood and adolescence		Hyperkinetic disorders Conduct disorders

ICD-10- International Statistical Classification of Diseases and Related Health Conditions- 10, #The list is not exhaustive.

irrelevantly and moving around aimlessly in hyperactive delirium. On the contrary, calmness and reduced psychomotor activity predominates the clinical picture in hypoactive variety. Additionally, disorientation, confusion, and altered sensorium are shared by both these forms. Other clinical features of delirium include perceptual disturbances such as hallucinations, sleep-wake cycle disturbances and thought disturbance. The usual course is waxing and waning interspersed with lucid intervals.

Early identification is crucial to the outcome of delirium. The main stay of treatment is correction of the underlying cause with supportive care. Low-dose dopaminergic antagonists (also known as typical antipsychotics) could be used for control of behavioral disturbance. It is recommended to use high potency medications such as haloperidol. Since the clinical picture can vary rapidly it is important to assess the patient at frequent intervals and modify the treatment plan accordingly [Box 2].

Box 2: Delirium in diabetes: salient features

- Manifestation of hypoglycemic episodes or diabetic ketoacidosis
- Types: hypoactive, hyperactive, or a combination thereof
- Potentially life threatening with high mortality rates
- Early identification crucial to outcome
- Correct the underlying cause, i.e., hypoglycemia/ ketoacidosis
- Close supervision and supportive care is main stay of treatment
- Ensure patient safety
- Low-dose high potency typical antipsychotics (e.g., haloperidol) can be used for behavioral control
- Nonpharmacological interventions such as providing clock, calendar in the ward/ICU; repeated reorientation to time/place/person
- Mini-Mental Status Examination (MMSE), Delirium Rating Scale (DRS) can be used to assess the progress

Substance abuse: tobacco

Tobacco can be used in smoking (cigarettes, biri, hooka, cigar) and smokeless forms (gutkha, tobacco powder, khaini, snuff). The prevalence of smoking among those having diabetes has been found to be comparable to that of the general population in studies from western settings.[14]

Cigarette smoking is an independent, modifiable risk factor for development of diabetes. It is associated with increased risk of diabetes in a dose-response manner.[15,16] Although evidence is less compelling but smokeless tobacco use has also been associated with increased risk of development of type 2 diabetes.[17]

Cigarette smoking increases this risk for diabetic nephropathy, retinopathy, and neuropathy (strongest association in type 1 diabetes) as well as that of macrovascular complications, coronary heart disease (CHD), stroke, and peripheral vascular disease (strongest association in type 2 diabetes).[18] Severe periodontal conditions and oral symptoms are more common among those diabetics who chew gutkha.[19]

The proposed hypotheses on the role of smoking in causation of diabetes include smoking-induced hyperglycemia, hyperinsulinemia, and elevated blood pressure;[20] smoking induced impaired endothelial function;[21] pro-diabetogenic action of components of tobacco smoke (e.g., cadmium).[22]

In diabetes care, smoking cessation is of utmost importance to facilitate glycemia control and limit the development of diabetic complications. However smoking (tobacco) cessation is a challenging job, more so in those having diabetes.[23] Early smoking cessation reduces the risk of development of type 2 diabetes to the nonsmoker level.[24] Smoking cessation is an effective intervention in the early course of microvascular and macrovascular complications. Smoking cessation also reduces the risk of coronary heart disease and mortality among these patients.[25]

Every patient should be offered advice on quitting. There are various pharmacological and nonpharmacological interventions for tobacco use. The medications available for use in India include nicotine replacement therapy (NRT) in form of gums, vareniclnie, bupropion, clonidine, and nortryptiline [Table 2]. These medications should be used under clinical supervision because of certain uncommon but potentially severe side effects such as seizures with bupropion and suicidal behavior with varenicline.

It is important to ask each patient for his/her tobacco use status and advice against tobacco. This is of special importance among adolescents with diabetes as most of them initiate tobacco use after being diagnosed with diabetes.[26] Box 3 presents an outline of the plan of action for a physician for helping a diabetic quit tobacco use.

The clinicians must be prepared for the possible weight gain and increased risk of type 2 diabetes following smoking cessations.[27] However, these effects are either transitory or could be easily managed with life style modifications and behavioral interventions.[28] Hence, when smokers quit, they should be advised on weight management and be monitored for diabetes in the years soon after quitting. Additionally since tobacco smoke is an inducer of various isoforms of the cytochrome P450 system, it is recommended to monitor the possible change in dose requirement of various oral hypoglycemic agents that are metabolized by the enzyme system.

Substance abuse: alcohol

Prevalence of alcohol use in diabetic population has been reported to be around 50--60% in epidemiological surveys and treatment seeking population.[29,30] The relation between alcohol consumption and diabetes remains controversial. While consumption in higher amounts is associated with an increased risk of type 2 diabetes, consumption in low to moderate amounts has been found to be protective in some studies.[31] Glucose intolerance can develop in alcoholics due to alcohol induced acute pancreatitits as well.

One of the commonest and serious concerns associated with use of alcohol in diabetes is emergence of hypoglycemia. It could be alcohol-induced fasting hypoglycemia, potentiation of drug-induced hypoglycemia, or reactive hypoglycemia in susceptible individuals. Additionally alcohol consumption may impair individual's ability to recognize emergence

Table 2: Pharmacotherapies for management of tobacco dependence

Drug[#]	Mechanism of action	Side effects/contraindications/ recommendations
First line therapies		
Nicotine replacement therapy (NRT): available as gums (2 mg/ 4 mg per piece) and patches	Prevents withdrawals associated with abstinence from tobacco products Addresses craving Avoids the harmful consequence of the nonnicotine products present in tobacco products	*Common side effects:* mild and transient and include mouth soreness, hiccups, and jaw ache, local skin reaction Use with caution among cardiovascular disorder patients
Varenciline	Partial agonist at alpha 2, beta 4 nicotinic receptors	Use associated with increased risk of suicidal behavior and cardiovascular events
Bupropion (sustained release)	Blockage of reuptake of dopamine and norepinephrine	Preferred for comorbid depression and/or weight concerns *Contraindications:* history of seizure disorder, eating disorder; use of an monoamine (MAO) inhibitor in past 14 days
Second line therapies		
Clonidine	Alpha 2 adrenergic receptor agonist	*Common side effects:* dry mouth, drowsiness, dizziness, hypotension, and sedation To be used with caution in hypertensive patients specially during induction and withdrawal phases
Nortriptyline	Tricyclic antidepressant	*Common side effects:* sedation, dry mouth, blurred vision, urinary retention, lightheadedness, tremors. Overdose may produce cardiotoxic effects
Combination therapies		
Bupropion (sustained release) and NRT		
Combination NRT		

[#]Safety and efficacy of these treatments for pregnant smokers remain unknown. Pregnant smokers should be encouraged to quit without medication.

Box 3: Recommendation for prevention and treatment of tobacco use

Make tobacco use history an essential part of evaluation
Assess each patient about use of tobacco products
Recommend quitting for users and advise nonusers not to start
Educate each patient on harms associated with tobacco use
Severity of dependence can be rated using the Fagerstrom test for nicotine dependence (FTND) – smoking and smokeless forms
Follow the 5 As and 5 Rs
Refer patients for specialized care

5 As in tobacco cessation	5 Rs in tobacco cessation
Ask every patient on every visit about tobacco use status	Relevance of quitting specific to the patient
Advise strongly all users to quit	Risks with continued use specific to the patient
Assess the patient's willingness to quit	Rewards of quitting specific to the patient
Assist patients in their efforts to quit	Roadblocks to quitting specific to the patient
Arrange a follow-up close around the quit date	Repetition of the previous steps

Box 4: Recommendations with regard to alcohol use among diabetics

- Assess all patients for alcohol use
- Use brief screening questionnaire like CAGE
- Advise nonusers to not to start and users to abstain/use in moderation
- Educate each patient on harms associated with alcohol use
- People using insulin or insulin secretagogues should be made aware of delayed hypoglycemia that can occur up to 24 hours after drinking alcohol
- People with type 1 diabetes should be made aware of the risk of morning hypoglycemia if alcohol is consumed 2–3 hours after the previous evening's meal
- Alcohol should be limited to 1–2 drinks per day (less than 14 standard drinks/ week for men and less than 9 standard drinks/ week for women)

CAGE questionnaire to assess problem drinking:

- Have you ever felt the need to Cut down on your drinking?
- Have people Annoyed you by criticizing your drinking?
- Have you ever felt Guilty about drinking?
- Have you ever felt you needed a drink first thing in the morning (Eye-opener) to steady your nerves or to get rid of a hangover?

Two or more yes responses suggest problem drinking and the patient should be referred for detailed evaluation

of such episode and intervene appropriately. Heavy alcohol consumption can precipitate diabetic ketoacidosis. Being a cause of peripheral neuropathy and retinopathy independently, co-occurring diabetes and alcohol use can have synergistic effect for these complications.[32] It has been seen that alcohol consumption is inversely associated with adherence to diabetes self-care behaviors.

Concomitant use of chlorpropamide (a sulfonylurea agent) and alcohol could lead to disulfiram-ethanol type of reaction. It is characterized by facial flushing, warmth, headache, nausea, vomiting, sweating, or thirst within minutes of consuming alcohol. Also, alcohol consumption may lead to excessive weight gain and elevated glucose levels. Alcohol can also alter the metabolism of oral hypoglycemic agents. Metformin is contraindicated in those actively using alcohol for the fear of lactic acidosis. Additionally alcohol induced hepatopathy requires a dose reduction for oral hypoglycemics metabolized in liver.

Similar to tobacco use all patients with diabetes should be screened for alcohol use [Box 4]. Those who have not yet started should be advised to continue to be sober. Those with problematic alcohol use should be advised to practice abstinence or at least use in moderation. Brief screening tools available to identify individuals with problem drinking. One such tool is a CAGE questionnaire which is an acronym for four simple questions aimed at screening problem drinking.

Diabetics having problem drinking (binge drinking, alcohol abuse, or alcohol dependence) should be offered individualized comprehensive interventions. Some of the commonly used medications in management of alcohol dependence include disulfiram, acamprosate, naltrexone, and topiramate. Table 3 provides a brief overview of these medications.

Additionally, such individuals can be offered nonpharmacological interventions such as brief intervention, motivation enhancement therapy, self-help group such as alcohol anonymous and relapse prevention.

Mood disorders

Mood disorders include depressive disorders, dysthymia, and bipolar affective disorders (BPAD). Co-occurrence of diabetes and depression has been established in clinical as well as general population studies.[33] This co-occurrence is associated with increased impairment as well as mortality.[34] Risk of developing depression is 50-100% higher among patients with diabetes compared to that among the general population.[35] The prevalence of diabetes among BPAD patients has been found to be increased (in hospital based studies) or equal (in epidemiological surveys) to that observed in the general population.[36,37]

Emergence of depression in diabetes is associated with increased complications, mortality rates, and healthcare costs.[38-40]

Depression and diabetes share a bidirectional causal association. Depression has been postulated to play a causal role in emergence of diabetes. A recent metaanalysis has reported that depressed individuals have a 60% increased risk of developing diabetes.[41] A specific association has been found between risk of developing diabetes and

Table 3: Pharmacotherapies for management of alcohol dependence

Drug[#]	Mechanism of action	Side effects/contraindications/recommendations
Disulfiram	Irreversible inhibition of enzyme acetaldehyde dehydrogenase (ALDH)	*Common side effects:* Transient mild drowsiness, fatigue, impotence, headache, acneiform eruptions, allergic dermatitis, and a metallic or garlic-like aftertaste *Absolute contraindications:* consent not given, cerebral damage, hypersensitivity reaction Diabetes is a relative contraindication for its use Not to be used with chlorpropamide for fear of disulfiram-ethanol type reaction
Acamprosate	Enhancement of GABAergic neurotransmission and reduction of glutamatergic neurotransmission	*Common side effects:* transient diarrhea, headaches, dizziness, and pruritis Safe in hepatoptahy as not metabolized in liver
Naltrexone	Opioid-receptor antagonism	*Common side effects:* nausea, headache, anxiety, sedation Causes dose dependent hepatotoxicity
Topiramate	Antagonism of glutamate and facilitation of gamma-aminobutyric acid (GABA)	*Common side effects:* dizziness and somnolence, ataxia, impaired concentration, confusion, fatigue, paresthesias, speech difficulties, diplopia, and nausea
Selective serotonin reuptake inhibitors (SSRIs)	Inhibition of serotonine reuptake at pre synaptic level	Limited evidence for their use
Combination therapies		
Combination of naltrexone with acamprosate		
Combination of acamprosate or naltrexone with disulfiram		
Combination of pharmacotherapy and nonpharmacological interventions		

[#]Safety and efficacy of these treatments for pregnant women remain unproven.

nonsevere depression, persistent depression, and untreated depression.[42]

Similarly, diabetes has been recognized as a "depressogenic" condition.[43] Biochemical changes (including neuro-endocrinal changes such as hypercortisolemia, leptin activity in limbic system, altered glucose transportation, proinflamatory cytokines) associated with diabetes or its treatment, psychological factors (such as stress associated with living with diabetes, poor treatment adherence), and behavioral factors (sedentary lifestyles, smoking, overeating) have been implicated in this causal association.[44] There is a modest association between use of most antidepressants and incidence of diabetes with long-term use of antidepressants at moderate or higher doses increasing risk of diabetes by almost twofold.[45] Similarly factors such as poor diet, habitual inactivity, excessive nicotine use, psychotropic medications used for treatment of bipolar disorder have been implicated in association between BPAD and diabetes.

Tricyclic antidepressants (TCAs), selective serotonine reuptake inhibitors (SSRIs), selective serotonin, and norepinepherine reuptake inhibitors, serotonin modulators are the commonly used medications for depression. All of these have been associated with an increased risk of development of diabetes following intermittent as well as continued long-term use [Box 5].[46] Although the findings are preliminary and the studies reflecting these findings have methodological limitations, they call for a cautious approach while using these medications in this population group. A stronger evidence base is available for mood stabilizers and antipsychotics used in management of bipolar disorders with regard to metabolic derangements. Interestingly the association between antipsychotics and diabetes was recognized soon after their introduction as reflected in the use of term "phenothiazine diabetes" in 1960s.[47] Introduction of newer atypical antipsychotic has attracted much attention for their metabolic and cardiovascular side effects.[48] These medications are associated with an increased risk of weight gain and impaired glucose tolerance. The risk of these side effects varies within the atypical antipsychotics with clozapine and olanzapine most likely to cause them [Box 6].[49] Similarly mood stabilizers such as lithium and sodium valproate are associated with weight gain and impaired glycemia control.

Nonpharmacological interventions such as cognitive behavior therapy and interpersonal therapy can be used either alone or in combination with pharmacotherapies.

Anxiety disorders

The prevalence of anxiety disorders among patients with diabetes is considerably higher compared to the general population.[50] Anxiety symptoms have been found to be significant risk factors for development of diabetes.[51] Negative correlations have been observed between prevalence of anxiety disorders and levels of HbA1c.[52]

The prevalence rate of generalized anxiety disorder (GAD)

Box 5: General principles of management of mood and anxiety disorders in diabetes

- Screen for the presence of mood and anxiety disorders at every visit
- Emergence of depressive and anxiety features should not be ignored
- High risk groups (e.g., females for depression; adolescents for needle phobia) should be evaluated more rigorously
- Screening instruments such as Patient Health Questionnaire (PHQ) and Symptom Checklist – 90 (SCL-90) can be used for screening purposes
- Effective pharmacotherapies are available for these disorders
- Possibility of weight gain and impaired glycemia control must be kept in mind while selecting the drug; chose medication with less potential to cause such derangements
- Advice on strategies on weight control to all the patients
- It is preferable to use drugs in combination with psychotherapeutic interventions such as CBT, ERP, etc.
- Milder forms of depression and anxiety, especially in children, adolescents, and pregnant females can be managed by psychotherapeutic techniques alone.
- Psychotherapeutic interventions help improve compliance and reduce stress-induced counter-regulatory hormones thereby having salutary effects on diabetes control

Box 6: Pharmacotherapy for depression and anxiety disorders in diabetes

- Increased risk of hyperglycemia and diabetes with TCAs, SSRIs, selective serotonin, and norepinepherine reuptake inhibitors, serotonin modulators
- Medication-induced weight gain is one of the possible mechanisms
- Hyperglycemic effects of noradrenergic activity of antidepressants are another possible mechanism
- SSRIs, buproprion, mirtazapine, nefazodone have comparatively lesser noradrenergic effects
- Benzodiazepines (such as alprazolam) also have a direct effect on glycemia control
- Beta blockers such as propranolol should be avoided as they interfere with normal physiological warning signs of hypoglycemic episode

has been found to be around three times higher than that reported in the general population. However, rates of panic disorder, obsessive compulsive disorder (OCD), post-traumatic stress disorder (PTSD), and agoraphobia have been found to be within the range of those reported in community studies.[53]

Relation of anxiety disorders and diabetes has not been explored as systematically and extensively as that of depression and diabetes. Anxiety in the context of diabetes has been studied mostly in association with depression.

Needle and injection phobia and phobia of hypoglycemic episode are two conditions associated with diabetes.[54] Patients with these conditions are likely to miss glucose monitoring or even insulin dose administration in severe cases. Also they might maintain a state of chronic hyperglycemia for the fear of developing a hypoglycemic episode.

Clinical features such as sweating, anxiety, tremor, tachycardia, and confusion are shared by both hypoglycemic episodes and anxiety disorders. This could present a diagnostic challenge especially among individuals having phobia of hypoglycemic episodes. Chronically anxious individuals may be more likely either to fail to perceive the initial warning signs of hypoglycemia or to confuse these with anxiety.

Medications used in management of anxiety disorders such as SSRIs, benzodiazepines, and beta adrenergic blockers could potentially interfere with glycemia control and normal physiological warning signs of an impending hypoglycemic episode.

Schizophrenia and other psychotic disorders

Association of psychotic disorders (including schizophrenia) and diabetes is well established. Overall risk of type 2 diabetes in people with schizophrenia is between two and four times that in the general population.[55] Family history of type 2 diabetes is significantly higher even among the first-degree relatives of patients of schizophrenia. Similarly, a positive family history may increase the risk of developing diabetes in individuals with schizophrenia up to threefold.[56] It has been shown that people with diabetes and schizophrenia have higher mortality rates than individuals with diabetes alone.[57] Additionally, the presence of type 2 diabetes is associated with increased mortality risk in patients with schizophrenia.

Schizophrenia is associated with impaired glucose tolerance and insulin resistance. The prevalence of impaired glucose tolerance in people with schizophrenia may be as high as 30%, depending upon age. The likely contributors to increased risk of diabetes in schizophrenia include both genetic and environmental factors. Physical inactivity, poor diet, poor healthcare, and treatment with antipsychotic medications are some of these factors. There are some preliminary reports that suggest that schizophrenia is an independent risk factor for diabetes.[58] Moreover schizophrenia is associated with a treatment nonadherence rate to the tune of 50%. This has significant management implications for such individuals. The association between antipsychotic medications and diabetes has been presented in Table 4. Table 5 presents the guidelines for managing diabetes risks in people with schizophrenia.

The information presented here is based primarily on the literature from the western settings. Interface of diabetes and psychiatry has received little attention in India. As noted by Sridhar there are little published data

Table 4: Propensity of psychotropics to cause weight gain and impairment of glycemia control

Parameter	Group of medications	High risk	Intermediate risk	Low risk	Findings inconsistent
Weight gain	Antidepressants	TCAs (amitryptiline> nortryptiline) MAOI (Phenelzine) Mirtazapine	SSRIs (Paroxetine> Sertraline/ Fluoxetine/ Citalopram/ Fluvoxamine)	Bupropion[#] Serotonine antagonists[#] (Nefazodone)	Venlafaxine
	Antipsychotics	Clozapine Olanzapine	Low potential typical (Chlorpromazine) Risperidone Quetiapine	High potency typical (Haloperidol) Ziprasidone Aripiprazole	
	Mood stabilizers	Lithium Divalproex sodium	Carbamazepine	Oxcarbazepine Topiramate[$]	
Impaired glycemia control	Antidepressants	TCAs (Amitryptiline> Nortryptiline) Paroxetine Fluvoxamine Venlafaxine	Sertraline Fluoxetine	MAOI ^	
	Antipsychotics	Clozapine Olanzapine	Risperidone Quetiapine	High potency atypical (Haloperidol) Ziprasidone Aripiprazole	
	Mood stabilizers	Divalproex sodium Lithium		Topiramate ^	

[#]Associated with slight weight loss in some studies, [$]Causes weight loss, ^ Associated with decrease in plasma glucose

Table 5: Guidelines for managing diabetes risks in people with schizophrenia[#]

Drug-naive patients starting an antipsychotic treatment (A)	Nondiabetic patients on antipsychotic treatment (B)	Diabetic patients established on antipsychotic treatment (C)
• Baseline random (or fasting) plasma glucose and glycosylated hemoglobin (HbA_{1c}) test • Repeat 4 months after initiating or changing an antipsychotic • If normal, repeat random (or fasting) glucose annually • If abnormal, refer to column C	• Ask about symptoms of hyperglycemia • Test random (or fasting) plasma glucose levels annually	• Endocrinologist to continue to manage the diabetes • Psychiatrist to continue to manage schizophrenia • Co-ordination between the two

[#]Based on "Schizophrenia and Diabetes 2003" Expert Consensus Meeting, Dublin, 3–4 October 2003: consensus summary. The British Journal of Psychiatry (2004) 184: S112-S114

from India on the coexistence of diabetes and psychiatric illness.[59] A few studies have explored the prevalence of depression and anxiety among patients with diabetes in specific settings only. Psychosocial outcomes including well-being in persons with diabetes have also been studied.[60] There is a need to study these issues in the Indian context as attitudes and concepts vary across cultures and impact on these interactions. A special emphasis should be placed on prospective studies to elucidate the link between various psychiatric disorders and diabetes. The role of stigma in seeking help for comorbid psychiatric disorders among patients with diabetes requires special attention. The potential role of the family in management of these individuals needs to be tapped fully. This is an area which should be explored specifically in studies as the family structure in the Indian context differs from that in the west.

Another important issue with significant management implications among individuals having both diabetes and psychiatric disorders is that of treatment adherence. Psychological, cognitive, and emotional issues associated with psychiatric disorders make the issue complicated. Individuals with comorbid diabetes and psychiatric illness are more likely to receive poor diabetes care. Poor treatment adherence is seen with both medication use as well as investigations.[61] Self-management is an essential component of diabetes care. The presence of comorbid psychiatric illness can make self-management difficult to implement. It has also been seen that increased healthcare utilization for comorbid psychiatric disorder could improve treatment adherence for diabetes as well.[62] Psychological approaches can help improve the therapeutic adherence in diabetes care. It is important to see patients and care givers as important stake holders in management plan. They should be involved in the decision-making process. The patients should be entrusted with the responsibility of shared decision making.

Interaction of diabetes and psychiatric disorders is multifaceted and an increase in understanding of the same would help endocrinologist and psychiatrists alike to serve this cohort effectively and comprehensively.

References

1. Goldney RD, Phillips PJ, Fisher LJ, Wilson DH. Diabetes, depression, and quality of life: a population study. Diabetes Care 2004;27: 1066-70.
2. Hutter N, Schnurr A, Baumeister H. Healthcare costs in patients with diabetes mellitus and comorbid mental disorders--a systematic review. Diabetologia 2010;53:2470-9.
3. Gonzalez JS, Safren SA, Cagliero E, Wexler DJ, Delahanty L, Wittenberg E, *et al*. Depression, self-care, and medication adherence in type 2 diabetes: relationships across the full range of symptom severity. Diabetes Care 2007;30:2222-7.
4. Lustman PJ, Anderson RJ, Freedland KE, de Groot M, Carney RM, Clouse RE. Depression and poor glycemic control: a meta-analytic review of the literature. Diabetes Care 2000;23:934-42
5. Bryden KS, Dunger DB, Mayou RA, Peveler RC, Neil HA. Poor prognosis of young adults with type 1 diabetes: a longitudinal study. Diabetes Care 2003;26:1052-7.
6. Das-Munshi J, Stewart R, Ismail K, Bebbington PE, Jenkins R, Prince MJ. Diabetes, common mental disorders, and disability: findings from the UK National Psychiatric Morbidity Survey. Psychosom Med 2007;69:543-50
7. Centorrino F, Mark TL, Talamo A, Oh K, Chang J. Health and economic burden of metabolic comorbidity among individuals with bipolar disorder. J Clin Psychopharmacol 2009;29:595-600.
8. Li C, Ford ES, Zhao G, Balluz LS, Berry JT, Mokdad AH. Undertreatment of mental health problems in adults with diagnosed diabetes and serious psychological distress: the behavioral risk factor surveillance system, 2007. Diabetes Care 2010;33:1061-64.
9. Lewis R. Diabetic emergencies: Part 1. Hypoglycaemia. Accid Emerg Nurs 1999;7:190-6.
10. Boland E, Monsod T, Delucia M, Brandt CA, Fernando S, Tamborlane WV. Limitations of conventional methods of self-monitoring of blood glucose. Diabetes Care 2001;24:1858-62.
11. Kitabchi AE, Umpierrez GE, Murphy MB, Barrett EJ, Kreisberg RA, Malone JI, *et al*. Management of hyperglycemic crises in patients with diabetes. Diabetes Care 2001;24:131-53.
12. MacLullich AM, Beaglehole A, Hall RJ, Meagher DJ. Delirium and long-term cognitive impairment. Int Rev Psychiatry 2009;21:30-42.
13. Han JH, Shintani A, Eden S, Morandi A, Solberg LM, Schnelle J, *et al*. Delirium in the emergency department: an independent predictor of death within 6 months. Ann Emerg Med 2010;56: 244-52.e1.
14. Ford ES, Mokdad AH, Gregg EW. Trends in cigarette smoking among US adults with diabetes: findings from the Behavioral Risk Factor Surveillance System. Prev Med 2004;39:1238-42.
15. Foy CG, Bell RA, Farmer DF, Goff DC Jr, Wagenknecht LE. Smoking and incidence of diabetes among U.S. adults: findings from the Insulin Resistance Atherosclerosis Study. Diabetes Care 2005;28:2501-7.
16. Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J. Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. JAMA 2007;298:2654-64.
17. Persson PG, Carlsson S, Svanström L, Ostenson CG, Efendic S, Grill V. Cigarette smoking, oral moist snuff use and glucose intolerance. J Intern Med 2000;248:103-10.
18. Eliasson B. Cigarette smoking and diabetes. Prog Cardiovasc Dis 2003;45:405-13.
19. Javed F, Altamash M, Klinge B, Engström PE. Periodontal conditions and oral symptoms in gutka-chewers with and without type 2 diabetes. Acta Odontol Scand 2008;66:268-73.
20. Frati AC, Iniestra F, Ariza CR. Acute effect of cigarette smoking on glucose tolerance and other cardiovascular risk factors. Diabetes Care 1996;19:112-8.
21. Celermajer DS, Sorensen KE, Georgakopoulos D, Bull C, Thomas O, Robinson J, *et al*. Cigarette smoking is associated with dose-related and potentially reversible impairment of endothelium-dependent dilation in healthy young adults. Circulation 1993;88:2149-55.
22. Schwartz GG, Il'yasova D, Ivanova A. Urinary cadmium, impaired fasting glucose, and diabetes in the NHANES III. Diabetes Care 2003;26:468-70.
23. Scemama O, Hamo-Tchatchouang E, Le Faou AL, Altman JJ. Difficulties of smoking cessation in diabetic inpatients benefiting from a systematic consultation to help them to give up smoking. Diabetes Metab 2006;32:435-41.
24. Hur NW, Kim HC, Nam CM, Jee SH, Lee HC, Suh I. Smoking cessation and risk of type 2 diabetes mellitus: Korea Medical Insurance Corporation Study. Eur J Cardiovasc Prev Rehabil 2007;14:244-9.
25. Al-Delaimy WK, Manson JE, Solomon CG, Kawachi I, Stampfer MJ, Willett WC, *et al*. Smoking and risk of coronary heart disease among women with type 2 diabetes mellitus. Arch Intern Med 2002;162:273-9.
26. Shaw NJ, McClure RJ, Kerr S, Lawton K, Smith CS. Smoking in diabetic teenagers. Diabet Med 1993;10:275-7.
27. Yeh HC, Duncan BB, Schmidt MI, Wang NY, Brancati FL. Smoking, smoking cessation, and risk for type 2 diabetes mellitus: a cohort study. Ann Intern Med 2010;152:10-7.
28. Clair C, Cornuz J. Diabetes: risk of diabetes mellitus: should smokers quit smoking? Nat Rev Endocrinol 2010;6:250-1.
29. Lethbridge-Cejku M, Schiller JS, Bernadel L. Summary Health Statistics for US Adults: National Health Interview Survey, 2002. Report no. 10. Hyattsville, MD: National Center for Health Statistics; 2004.
30. Ahmed AT, Karter AJ, Liu J. Alcohol consumption is inversely associated with adherence to diabetes self-care behaviours. Diabet Med 2006;23:795-802.
31. Li H, Wang G, Wang A, Tong W, Zhang Y. Alcohol Consumption and Risk of Type 2 Diabetes in Mongolian Population, Inner Mongolia, China. J Diabete Metab 2011;2:1.
32. Emanuele NV, Swade TF, Emanuele MA. Consequences of alcohol use in diabetics. Alcohol Health Res World 1998;22:211-9.
33. Katon WJ, Lin EH, Williams LH, Ciechanowski P, Heckbert SR, Ludman E, *et al*. Comorbid depression is associated with an increased risk of dementia diagnosis in patients with diabetes, a prospective cohort study. J Gen Intern Med 2010;25:423-9.
34. Egede LE, Nietert PJ, Zheng D. Depression and all-cause and coronary heart disease mortality among adults with and without diabetes. Diabetes Care 2005;28:1339-45.
35. Egede LE, Zheng D. Independent factors associated with major depressive disorder in a national sample of individuals with diabetes. Diabetes Care 2003;26:104-11.
36. Cassidy F, Ahearn E, Carroll BJ. Elevated frequency of diabetes mellitus in hospitalized manic-depressive patients. Am J Psychiatry 1999;156:1417-20.
37. Lin EH, Korff MV, Alonso J, Angermeyer MC, Anthony J, Bromet E, *et al*. Mental disorders among persons with diabetes—results from the World Mental Health Surveys. J Psychosom Res 2008;65:571-80.
38. de Groot M, Anderson R, Freedland KE, Clouse RE, Lustman PJ.

Association of depression and diabetes complications: a meta-analysis. Psychosom Med 2001;63:619-30.
39. Katon WJ, Rutter C, Simon G, Lin EH, Ludman E, Ciechanowski P, *et al*. The association of comorbid depression with mortality in patients with type 2 diabetes. Diabetes Care 2005;28:2668-72.
40. Egede LE, Zheng D, Simpson K. Comorbid depression is associated with increased health care use and expenditures in individuals with diabetes. Diabetes Care 2002;25:464-70.
41. Mezuk B, Eaton WW, Albrecht S, Golden SH. Depression and type 2 diabetes over the lifespan: a meta-analysis. Diabetes Care 2008;31:2383-90.
42. Campayo A, de Jonge P, Roy JF, Saz P, de la Cámara C, Quintanilla MA, *et al*. Depressive disorder and incident diabetes mellitus: the effect of characteristics of depression. Am J Psychiatry 2010;167: 580-8.
43. Pan A, Lucas M, Sun Q, van Dam RM, Franco OH, Manson JE, *et al*. Bidirectional association between depression and type 2 diabetes mellitus in women. Arch Intern Med 2010;170:1884-91.
44. Talbot F, Nouwen A. A review of the relationship between depression and diabetes in adults: is there a link? Diabetes Care 2000;23: 1556-62.
45. Andersohn F, Schade R, Suissa S, Garbe E. Long-term use of antidepressants for depressive disorders and the risk of diabetes mellitus. Am J Psychiatry 2009;166:591-8
46. Rubin RR, Ma Y, Marrero DG, Peyrot M, Barrett-Connor EL, Kahn SE, *et al*. Elevated depression symptoms, antidepressant medicine use, and risk of developing diabetes during the diabetes prevention program. Diabetes Care 2008;31:420-6.
47. Hiles BW. Hyperglycaemia and glucosuria following chlorpromazine therapy. JAMA 1956;162:1651.
48. Sernyak MJ, Leslie DL, Alarcon RD, Losonczy MF, Rosenheck R. Association of diabetes mellitus with use of atypical neuroleptics in the treatment of schizophrenia. Am J Psychiatry 2002;159:561-6.
49. American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity. Consensus development conference on antipsychotic drugs and obesity and diabetes. Diabetes Care 2004;27:596-601.
50. Huang CJ, Chiu HC, Lee MH, Wang SY. Prevalence and incidence of anxiety disorders in diabetic patients: a national population-based cohort study. Gen Hosp Psychiatry 2011;33:8-15.
51. Engum A. The role of depression and anxiety in onset of diabetes in a large population-based study. J Psychosom Res 2007;62:31-8.
52. Hermanns N, Kulzer B, Krichbaum M, Kubiak T, Haak T. Affective and anxiety disorders in a German sample of diabetic patients: prevalence, comorbidity and risk factors. Diabet Med 2005;22: 293-300.
53. Grigsby AB, Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. Prevalence of anxiety in adults with diabetes: a systematic review. J Psychosom Res 2002;53:1053-60.
54. Green L, Feher M, Catalan J. Fears and phobias in people with diabetes. Diabetes Metab Res Rev 2000;16:287-93.
55. Expert Group. 'Schizophrenia and Diabetes 2003'. Expert Consensus Meeting, Dublin 3-4 October 2003: consensus summary. Br J Psychiatry Suppl 2004;47:S112-4.
56. Lamberti J, Crilly J, Maharaj K. Prevalence of adult-onset diabetes among out-patients receiving anti-psychotic drugs. Schizophr Res 2003;60 (Suppl):S360
57. Vinogradova Y, Coupland C, Hippisley-Cox J, Whyte S, Penny C. Effects of severe mental illness on survival of people with diabetes. Br J Psychiatry 2010;197:272-7.
58. Holt RI, Bushe C, Citrome L. Diabetes and schizophrenia 2005: are we any closer to understanding the link? J Psychopharmacol 2005;19(6 Suppl):56-65.
59. Sridhar GR. Psychiatric co-morbidity and diabetes. Indian J Med Res 2007;125:311-20.
60. Sridhar GR, Madhu K, Veena S, Radha Madhavi P, Sangeetha B, Asha Rani S. Living with diabetes: Indian experience. Diab Met Syndr Clin Res Rev 2007;1:181-7.
61. Goldberg RW, Kreyenbuhl JA, Medoff DR, Dickerson FB, Wohlheiter K, Fang LJ, *et al*. Quality of diabetes care among adults with serious mental illness. Psychiatr Serv 2007;58:536-43.
62. Nelson LA, Graham MR, Lindsey CC, Rasu RS. Medication adherence and glycemic control in patients with psychotic disorders in the Veterans Affairs healthcare system. Pharm Pract (Internet) 2011;9:57-65.

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