

Diabetes Mellitus and Impaired Glucose Tolerance in Patients With Schizophrenia

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Objectives: This study aimed to establish the prevalence of diabetes mellitus (DM) and impaired glucose tolerance in patients with schizophrenia and to elucidate some of the factors associated with hyperglycemia.

Methods: We studied a sample of 194 patients with schizophrenia. We determined fasting blood glucose and insulin levels at the start of the testing period; patients were given an oral glucose tolerance test after an overnight fast.

Results: The overall prevalence of diabetes and impaired glucose tolerance in these patients was 16.0% and 30.9%, respectively. These rates were higher than those reported in the general population. Patients with disordered glucose homeostasis were significantly older ($P = 0.005$, Kruskal–Wallis test). There was no significant effect of sex or ethnicity on diabetes.

Conclusions: Our findings suggest that patients with schizophrenia are more vulnerable to developing DM. We caution clinicians to be mindful of the increased risk and to be vigilant for such a development.

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Clinical Implications

- This study highlights a high rate of diabetes mellitus (DM) among patients with schizophrenia.
- Clinicians should be vigilant for the early symptoms of DM and should consider regular glucose monitoring in those who have risk factors for developing DM.

Limitations

- This study's cross-sectional design did not allow us to consider the cumulative exposure to neuroleptics among our patients, which may be a more important factor than the daily dosage.
- Owing to the widespread practice of polypharmacy, we were unable to elucidate the differential effect of the various neuroleptics.
- We did not establish the presence of a family history of DM, low HDL, or high triglycerides, which are the other risk factors for DM.

Key Words: *schizophrenia, diabetes mellitus, glucose tolerance*

Compared with the general population, it has been shown that patients with schizophrenia have a higher risk of impaired glucose tolerance and diabetes mellitus (DM) (1). A study of 248 patients conducted in Japan reported a type 2 DM prevalence of 8.8%, compared with 5% in a control group matched for age and sex (2). Another study by Mukherjee and others reported an overall prevalence of 15.8% among schizophrenia patients in Italy (3), which is considerably higher than reports from population surveys in Italy. A recent study by

Dixon and others, using databases collected by the Schizophrenia Patient Outcomes Research Team (PORT), found that rates of diagnosed diabetes (14.9%) exceeded general population statistics well before the widespread use of the newer antipsychotic drugs (4).

Several factors may contribute to schizophrenia patients' increased susceptibility to developing DM. For example, poor health behaviours are likely to be an important contributing factor. Brown and others evaluated 102 schizophrenia

Table 1 Demographic and clinical characteristics of schizophrenia patients

Variables	Normal glucose (<i>n</i> = 103)	Impaired GT (<i>n</i> = 60)	Diabetes mellitus (<i>n</i> = 31)
	Mean (SD)	Mean (SD)	Mean (SD)
Age (years) ^a	53.1 (7.9)	57.8 (9.4)	57.3 (7.9)
Duration of illness (years)	30.0 (9.0)	33.9 (9.4)	32.4 (8.0)
Age of illness onset (years)	21.8 (6.3)	23.6 (9.2)	23 (4.9)
Daily chlorpromazine equivalents	509.5 (570.1)	401.8 (436.5)	441.0 (457.4)
Fasting insulin (mU/l) ^a	3.7 (2.3)	5.4 (3.9)	6.3 (4.9)
Weight (kg)	52.4 (8.5)	51.3 (10.6)	52 (11.6)
Body Mass Index (kg/M ²)	19.1 (2.8)	19.3 (3.0)	20 (4.1)

^aKruskal-Wallis < 0.005
GT = glucose tolerance

Table 2 Age-specific prevalence rates of diabetes mellitus (DM)

Age (years)	Prevalence rates of DM in schizophrenia patients (%)	Prevalence rates in general population of Singapore (%)
18–29	—	0.8
30–39	4.0	3.3
40–49	17.3	9.6
50–59	50.0	21.8
60–69	23.7	32.4
70–79	5.0	—

patients living in the community and found that they exercised less, smoked more, and had less healthy diets, compared with normal control subjects (5). Lindenmayer and others proposed an additive risk model to identify risk factors that increase the probability of schizophrenia patients’ developing DM (6). Ethnicity, family history of diabetes, history of glucose dysregulation, and preexisting hypertension were all suggested to increase the risk of type 2 DM.

Another putative factor may be psychotropic medications: it has been reported that chlorpromazine and lithium impair glucose tolerance (7). The mechanism of action of these drugs is much debated and includes increased peripheral resistance to insulin, which may be secondary to the weight gain in these patients. However, weight gain is not a prerequisite for the development of hyperglycemia and diabetes (8). The newer atypical drugs may contribute directly to hyperglycemia by inhibiting glucose uptake in different cell types. Recent evidence suggests that the antipsychotics may do so by binding to and blocking the glucose transporter protein (9).

This study aimed to establish the prevalence of DM and impaired glucose tolerance in a population of schizophrenia patients and to elucidate some of the factors associated with hyperglycemia.

Method

We surveyed 607 patients; residents of the long-stay wards in Woodbridge Hospital, Singapore. Two psychiatrists independently verified that all the patients fulfilled DSM-IV criteria for schizophrenia. The prevalence of DM (that is, those patients with a chart diagnosis of DM) was found to be 4.9% (*n* = 30). For this study, we recruited patients

who were able to give an informed, written consent and who had no documented chart diagnosis of diabetes, impaired glucose tolerance, significant physical illness, or history of drug or alcohol abuse. We subsequently included 194 patients in the study. None had received any atypical neuroleptics, either in the past or at the time of the study.

We reviewed the case records to obtain information on age, sex, illness-onset age, illness duration, and current medication status. We calculated body mass index (BMI) after using the same scale to record the weight and height of all patients. Patients were given an oral glucose tolerance test after an overnight fast. Fasting blood glucose and insulin levels were determined at the start of the testing period. We used the World Health Organization (WHO) diagnostic classification criterion for the Oral Glucose Tolerance Test (OGTT) to classify DM and impaired glucose tolerance (10).

Results

Of the 194 patients, 155 were men and 39 were women. Their mean (SD) age was 55.5 (8.7) years, with an age range of 33 to 83 years. The mean age at onset of schizophrenia was 22.6 years, and the mean duration of illness was 31.8 years.

The overall prevalence of diabetes was 16% (*n* = 31), and the overall prevalence of impaired glucose tolerance was 30.9% (*n* = 60). Of the 31 diabetes patients, 22 were men, and 9 were women. There was no significant effect of sex or ethnicity on diabetes ($\chi^2 = 1.9, P = 0.17$ and $\chi^2 = 0, P = 1.0$, respectively).

Table 1 shows the clinical characteristics of the 194 patients. Patients with DM and impaired glucose tolerance were significantly older than those with a normal glucose profile (*P* = 0.005, Kruskal–Wallis test). Fasting insulin levels were significantly higher in the patients with DM and in those with impaired glucose tolerance, compared with nondiabetic patients (*P* < 0.005, Kruskal–Wallis test). However, the 3 groups of patients did not differ significantly in other clinical variables. Overall, 12 patients had a BMI \geq 25; that is, 12 patients were overweight according to the WHO recommendations for BMI

(11). Analysis of age-specific prevalence revealed that the highest prevalence (50%) occurred in patients belonging to the group aged 50 to 59 years.

Discussion

According to the National Health Survey, the DM morbidity rate in the general population of Singapore was 9%, and the rate of impaired glucose tolerance was 15% (12). However, the prevalence rates of DM and impaired glucose tolerance in our study were much higher—16% and 30.9%, respectively. The mean age of patients in our study was 55.5 years; in the comparative population (that is, those aged 50 to 59 years), the prevalence of diabetes was 21.8%.

We found age to be associated with diabetes, but we found no association with sex, ethnicity, or daily neuroleptic dosage. Tan and others have reported the increased risk of DM with increased age in the Singapore general population (13). These authors report the highest prevalence of DM to be in Asian Indians, although a significant ethnic difference between Chinese subjects and the other 2 ethnic groups (that is, Malays and Indians) could be demonstrated only in women.

Obesity is another well-established risk factor that can lead to insulin insensitivity, glucose intolerance, and subsequently, DM. However, the weight and BMI of patients with disordered glucose homeostasis and of those without did not differ significantly. Almost all the patients had been institutionalized for long periods and within the same environment, and their similar diets and lifestyles could account for this lack of variance in weight and BMI. However, Mukherjee and others, reporting similar findings, suggest that individual biological differences in response to diet, rather than diet per se, may be more critical in determining the risk of DM in these patients (3).

Our study highlights a high rate of DM among patients with schizophrenia. This comorbidity is associated with an increased risk of hypertension and coronary heart disease,

which in turn may contribute to the higher mortality of patients with schizophrenia. Clinicians should be vigilant for the early symptoms of DM in this population, and regular glucose monitoring should be considered for those who have risk factors for developing DM.

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Résumé : Diabète sucré et intolérance au glucose chez les patients souffrant de schizophrénie

Objectifs : Cette étude visait à établir la prévalence du diabète sucré (DS) et de l'intolérance au glucose chez les patients souffrant de schizophrénie ainsi qu'à élucider certains des facteurs associés à l'hyperglycémie.

Méthodes : Nous avons étudié un échantillon de 194 patients souffrant de schizophrénie. Nous avons déterminé à jeun la glycémie et les niveaux d'insuline au début de la période de l'étude; et nous avons administré aux patients un test oral de tolérance au glucose, à jeun le matin.

Résultats : La prévalence globale du diabète et de l'intolérance au glucose chez ces patients était de 16,0 % et de 30,9 %, respectivement. Ces taux étaient plus élevés que ceux déclarés dans la population générale. Les patients ayant une homéostasie du glucose désordonnée étaient significativement plus âgés ($P = 0,005$, test de Kruskal–Wallis). Il n'y avait pas d'effet significatif selon le sexe ou l'origine ethnique sur le diabète.

Conclusions : Nos résultats indiquent que les patients souffrant de schizophrénie sont plus susceptibles de développer le DS. Nous prévenons les cliniciens de tenir compte du risque accru et d'être vigilants quant à ce développement.