

Diabetes and impaired fasting glucose in Sri Lankan patients with schizophrenia

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Background

Type 2 diabetes is commoner among South Asians than Europeans. The few studies of South Asian patients with schizophrenia have found increased prevalence of diabetes.

Aims

To determine prevalence of diabetes and impaired fasting glucose among patients with schizophrenia presenting to an acute psychiatry unit.

Methods

The sample consisted of all patients with ICD-10 diagnosis of schizophrenia admitted to an acute psychiatry unit during one year. Data was obtained by retrospective review of patients' records. Diabetes was diagnosed according to the American Diabetes Association criteria when fasting plasma glucose (FPG) was ≥ 7.0 mmol/l. Impaired fasting glucose (IFG) was diagnosed when FPG was ≥ 5.6 mmol/l but < 7.0 mmol/l.

Results

Of the 164 patient records reviewed 104 (63.4%) had a recorded FPG level. There was no significant difference in age, gender and treatment between patients tested and not tested. Of the sample 28 (26.9%) were antipsychotic naive and 76 (73.1%) had been treated previously. Mean age of the sample was 35.1 years (SD 12.7). Diabetes was diagnosed in 15 patients. Overall prevalence was 14.4% (females 11.4%, males 16.7%). Prevalence of IFG was 26%. Diabetes rates were highest (26.9%) among 30-39 year age group and IFG rates were highest (54.5%) among 50-59 year age group.

Conclusions

Prevalence of diabetes and IFG is higher compared to the general population of Sri Lanka (10.3% and 11.5%) but similar to that of Caucasian patients with schizophrenia. Due to the high risk of dysglycaemia FPG should be done in all patients with schizophrenia.

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Introduction

Second generation antipsychotics are associated with weight gain and other metabolic side effects (1). Among the atypical antipsychotics, treatment with olanzapine has been found to worsen the lipid profile (2). Atypical antipsychotics also increase the risk of developing metabolic syndrome (3, 4). The baseline prevalence of diabetes maybe two to three folds higher in patients with schizophrenia compared to the general population (5).

Type 2 diabetes is commoner among South Asians than Europeans. This pattern is seen both in the people living in Asia as well as those who have migrated to Europe and USA. There is an increase in the prevalence of diabetes among urban and rural populations in South Asia and the prevalence is increasing over time (6). The rate of ischemic heart disease is higher among South Asian men and they have a higher age standardized mortality rate from coronary heart disease (7). South Asians, Chinese, and Aboriginal people have similar distributions of glucose and lipid factors at significantly lower body mass index (BMI) values compared with Europeans. Thus normal ranges for obesity using BMI cut off points derived from European populations may be misleading when applied to these populations (8).

Most of the available data on diabetes in schizophrenia are from studies conducted on Caucasian patients.

The few studies done on South Asian populations have found increased prevalence of diabetes and metabolic syndrome. A study of patients with first episode schizophrenia in India found the prevalence of metabolic syndrome to be 10.1% and 18.2% as assessed by ATP IIIA (9) and International Diabetes Federation (IDF) criteria respectively (10). The prevalence of metabolic syndrome after 6 weeks of treatment with antipsychotics according to ATP IIIA and IDF criteria respectively were 20 and 25% for patients treated with olanzapine, 9% and 24% for risperidone and 0% and 3% for haloperidol (11). Overall prevalence of metabolic syndrome was five times as much as in the healthy control group.

In the same sample treatment-emergent diabetes by WHO definition was present in 11.4% of subjects in the olanzapine group, 9.1% of subjects in the risperidone group and 9.7% of subjects in the haloperidol group. Using the American Diabetic Association definition the prevalence was 2.9% of subjects in the olanzapine group, 3.2% of subjects in the haloperidol group and none in the risperidone group (12).

Because the prevalence of diabetes among the general population is higher among South Asians and treatment with antipsychotics is known to increase risk of diabetes we looked at the rates of diabetes and impaired fasting glucose in patients with schizophrenia in an acute psychiatry unit in Sri Lanka.

Methods

We did a retrospective review of all records of patients with ICD-10 diagnosis of schizophrenia admitted to the University Psychiatry Unit, Colombo over a one year period. One Hundred and sixty four patient records were reviewed of which 60 were excluded as they did not have a recorded FPG and 104 (63.4%) patient records were included in the study. Diabetes and impaired fasting glucose (IFG) were diagnosed according to the American Diabetes Association (ADA) criteria. FPG was measured on venous blood samples. Diabetes was diagnosed when FPG was ≥ 7.0 mmol/l. Impaired fasting glucose (IFG) was diagnosed when FPG was ≥ 5.6 mmol/l but ≤ 7.0 mmol/l. In patients with FPG ≥ 7.0 mmol/l at least two elevated FPG readings were required before diagnosing diabetes.

Statistical analysis

Chi square test was used to test the difference between groups for non parametric data and independent t test was used to identify the difference in mean duration of treatment between those with and without diabetes.

Results

The characteristics of the sample are given in table 1. Because only 63.4% of the records had a FPG level we compared characteristics of patients with a FPG record and those without. As shown in table 1 there was no statistically significant difference in gender, age distribution or antipsychotic treatment in patients with and without a FPG record. This shows that there is less likelihood that non availability of FPG in 36.6% would have created a systematic bias. Males and females were equally likely to be tested. Patients over 30 years of age were more likely to be tested but the difference was not statistically significant. Patients on second generation antipsychotics were more likely to be tested than patients on first generation antipsychotics or patients

who were transferred from first to second generation antipsychotics during the admission.

Only the 104 patients with a FPG record were analysed further. Of the 104 patients 57.7% were males. The mean age of the sample was 35.1 years (SD 12.7). Majority (61.5%) were aged 20-40 years. Twenty eight patients were antipsychotic naive on admission. First generation antipsychotics (haloperidol, trifluoperazine or chlorpromazine) were used in 7, second generation antipsychotics (risperidone, olanzapine or clozapine) in 78 and 11 were transferred from first to second generation during the admission.

Prevalence of diabetes and IFG according to age is given in table 2. The table also compares the prevalence in our study sample with those of the general population in Sri Lanka as reported in the Sri Lanka Diabetes and Cardiovascular study (13).

Fifteen patients were diagnosed with diabetes and 27 had impaired fasting glucose. The overall prevalence of diabetes among those over 16 years was 14.4% (95% CI 7.6-21.2) Prevalence of diabetes among females was 11.4% (95% CI 1.6-21.1) and in males 16.7% (95% CI 6.7-26.4). The prevalence of impaired fasting glucose was 26.0% (95% CI 17.4-34.5). Prevalence of IFG in females was 18.2% (95% CI 6.3-30.0) and males 31.7% (95% CI 19.7-43.8). Prevalence of diabetes was highest among 30-39 year age group (26.9%). Prevalence of impaired fasting glucose was highest among 60-69 year age group.

There was no statistically significant difference in rates of diabetes or IFG according to gender, educational level or smoking status.

Of the patients diagnosed with diabetes 5 (33.3%) were previously undiagnosed. The mean FPG level was 5.3mmol/l (SD 1.08) The mean duration of treatment with antipsychotics in patients diagnosed with diabetes

Table 1- Description of study population

Employment	FBS available frequency (%) n=104	FBS not available frequency (%) n=60	Significance
Gender			$\chi^2=0.503, p=0.48$
Male	60 (57.7)	38 (63.3)	
Female	44 (42.3)	22 (36.7)	
Age distribution			$\chi^2=8.63, p=0.13$
12-19 years	6 (5.8)	6 (10.0)	
20-29 years	38 (36.5)	31 (51.7)	
30-39 years	26 (25.0)	11 (18.3)	
40-49 years	19 (18.3)	10 (16.7)	
50-59 years	11 (10.6)	2 (3.3)	
60-69 years	4 (3.8)	0 (0)	
Medication			$\chi^2 =6.08, p=0.11$
First generation antipsychotics	7 (6.7)	5 (8.3)	
Second generation antipsychotics	78 (75.0)	41 (68.3)	
Transfer from first to second generation antipsychotics	11 (10.6)	13 (21.7)	
Not on antipsychotics	8 (7.7)	1 (1.7)	

Table 2- Prevalence of diabetes and IFG according to age

Age group	Diabetes prevalence (95%CI)	Diabetes Prevalence Katulanda et al (13) (95%CI)	IFG prevalence (95%CI)	Pre diabetes Katulanda et al (13) (95%CI)
16-19 years	0	No data	16.7(-26.2-59.5)	No data
20-29 years	5.3 (2.1-12.7)	1.3 (0.4–2.2)	13.2 (1.9-24.4)	5.4 (3.6–7.2)
30-39 years	26.9 (8.7-45.1)	6.4 (4.7–8.1)	15.4 (0.52-30.3)	10.6 (8.6–12.6)
40-49 years	15.8 (-2.3-33.9)	12.4 (10.4–14.4)	47.4 (22.6-72.1)	13.0 (10.9–15.1)
50-59 years	18.2 (-8.9-45.4)	17.4 (14.9–19.9)	54.5 (19.5-89.6)	15.5 (13.1–17.9)
60-69 years	25.0 (-54.6-104.6)	21.2 (17.7–24.7)	50.0 (-41.9-8-141.9)	16.0 (12.9–19.1)
>70 years	No data	23.5 (18.9–28.1)	No data	20.4 (16.1–24.7)

was 7.34 years (SD 11.53) and in patients without diabetes 6.54 years (SD 7.08). The difference was not statistically significant ($t = -0.33$, $df = 88$, $p = 0.741$).

Discussion

We compared rates of diabetes and IFG in our study with that of the general population of Sri Lanka as reported in the Sri Lanka Diabetes and Cardiovascular study, a cross sectional study which included a nationally representative sample of 5000 adults.

Our patients had a higher prevalence of diabetes compared to the general population of Sri Lanka (13). As diabetes rates vary according to age the overall prevalence in a population depends on the age distribution structure. When the age specific rates are considered the prevalence among the 30-39 year age group of 26.9% was more than four times that of the general population of 6.4% (13). There is a similar higher prevalence of diabetes amongst the 20-29 year age group (5.3%) compared to that of the general population (1.8%). Therefore it appears that prevalence of diabetes was several fold higher among younger patients with schizophrenia who had been treated with antipsychotics. Males were at a higher risk of developing diabetes. The prevalence of diabetes among patients with schizophrenia in our study is similar to that of American and European patients with schizophrenia. (1,5,14,15).

When compared with the general population IFG rates were higher among our patients in all age categories. In the 40-69 year age groups IFG rates were more than three times that of the general population (13).

The prevalence of IFG of 26.0% is higher than that reported in most studies of Caucasian patients with schizophrenia. This may be either due to the increased risk of dysglycaemia amongst South Asian populations or due to the longer treatment history in our sample. A higher prevalence of IFG has been reported when patients are treated for a longer duration (16, 17).

Despite evidence that South Asians in general have higher rates of diabetes, metabolic syndrome and cardiovascular disease, studies of diabetes and other metabolic complications among South Asian patients treated with antipsychotics are few (11, 12, 18). In a sample of drug naïve Indian patients with schizophrenia, prevalence rates of diabetes according to the ADA criteria after six weeks of treatment with antipsychotics were 2.9% for subjects in the olanzapine group and 3.2% for subjects in the haloperidol group (12). In this study males were at a higher risk of developing diabetes.

There are several limitations in the study. Because this is a retrospective review we were unable to establish that the increased rates of diabetes and IFG are caused by antipsychotic treatment. As some patients had been treated with more than one antipsychotic during the entire illness period we could not calculate prevalence of diabetes for individual antipsychotics. Because only 66% of the records had a FPG testing it is possible that patients at higher risk were more likely to be tested thus inflating prevalence of diabetes and IFG. We reported that there was no significant difference in age, gender and class of antipsychotics used amongst those tested and not tested. This indicates that the bias caused by non testing of 33% of patients is probably minimal.

Despite these limitations our study has important implications for clinical practice and future research. The high prevalence of diabetes and IFG underscores the importance of routine FPG monitoring of patients treated with antipsychotics. This study also provides preliminary data to justify a prospective study of diabetes and metabolic syndrome in patients treated with antipsychotics.

Declaration of interest

The authors have received educational grants from Sun Pharmaceutical Company.

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References

- Lindenmayer JP, Czobor P, Volavka J, Citrome L, Sheitman B, McEvoy JP, Cooper TB, Chakos M, Lieberman JA: Changes in glucose and cholesterol levels in patients with schizophrenia treated with typical or atypical antipsychotics. *Am J Psychiatry* 2003; 160:290-296.
- Perez-Iglesias R, Crespo-Facorro B, Amado JA, Garcia-Unzueta MT, Ramirez-Bonilla ML, Gonzalez-Blanch C, Martinez-Garcia O, Vazquez-Barquero JL: A 12-week randomized clinical trial to evaluate metabolic changes in drug-naive, first-episode psychosis patients treated with haloperidol, olanzapine, or risperidone. *J Clin Psychiatry* 2007; 68:1733-1740.
- Medved V, Kuzman MR, Jovanovic N, Grubisin J, Kuzman T: Metabolic syndrome in female patients with schizophrenia treated with second generation antipsychotics: a 3-month follow-up. *J Psychopharmacol* 2009; 8: 915-22.
- Kelly DL, Conley RR, Love RC, Morrison JA, McMahon RP: Metabolic risk with second-generation antipsychotic treatment: a double-blind randomized 8-week trial of risperidone and olanzapine. *Ann Clin Psychiatry* 2008; 20:71-8.
- Dixon L, Weiden P, Delahanty J, Goldberg R, Postrado L, Lucksted A, Lehman A: Prevalence and correlates of diabetes in national schizophrenia samples. *Schizophr Bull* 2000; 26:903-912.
- Ramachandran A, Snehalatha C, Baskar AD, Mary S, Kumar CK, Selvam S, Catherine S, Vijay V: Temporal changes in prevalence of diabetes and impaired glucose tolerance associated with lifestyle transition occurring in the rural population in India. *Diabetologia* 2004; 47(5):860-865.
- Barnett AH, Dixon AN, Bellary S, Hanif MW, O'Hare J P, Raymond NT, Kumar S: Type 2 diabetes and cardiovascular risk in the UK south Asian community. *Diabetologia* 2006; 49:2234-2246.
- Razak F, Anand SS, Shannon H, Vuksan V, Davis B, Jacobs R, Teo KK, McQueen M, Yusuf S: Defining obesity cut points in a multiethnic population. *Circulation* 2007; 115:2111-2118.
- Grundy SM, Cleeman JI, Merz CN, Brewer HB Jr, Clark LT, Hunninghake DB et al., Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation* 2004; 110: 227-239.
- IDF, 2005. The IDF Consensus Worldwide Definition of the Metabolic Syndrome. International Diabetes Federation, Brussels. Available at www.idf.org
- Saddichha S, Manjunatha N, Ameen S, Akhtar S: Metabolic syndrome in first episode schizophrenia - a randomized double-blind controlled, short-term prospective study. *Schizophr Res* 2008; 101:266-272.
- Saddichha S, Manjunatha N, Ameen S, Akhtar S: Diabetes and schizophrenia - effect of disease or drug? Results from a randomized, double-blind, controlled prospective study in first-episode schizophrenia. *Acta Psychiatr Scand* 2008; 117:342-347.
- Katulanda P, Constantine GR, Mahesh JG, Sheriff R, Seneviratne RD, Wijeratne S, Wijesuriya M, McCarthy MI, Adler AI, Matthews DR: Prevalence and projections of diabetes and pre-diabetes in adults in Sri Lanka--Sri Lanka Diabetes, Cardiovascular Study (SLDCS). *Diabet Med* 2008; 25:1062-1069.
- Ryan MC, Collins P, Thakore JH: Impaired fasting glucose tolerance in first-episode, drug-naive patients with schizophrenia. *Am J Psychiatry* 2003; 160:284-289.
- Mukherjee S, Decina P, Bocola V, Saraceni F, Scapicchio PL: Diabetes mellitus in schizophrenic patients. *Compr Psychiatry* 1996; 37:68-73.
- De Hert M, van Winkel R, Van Eyck D, Hanssens L, Wampers M, Scheen A, Peuskens J: Prevalence of diabetes, metabolic syndrome and metabolic abnormalities in schizophrenia over the course of the illness: a cross-sectional study. *Clin Pract Epidemiol Ment Health* 2006; 2:14.
- Srisurapanont M, Likhitsathian S, Boonyanaruthee V, Charnsilp C, Jarusuraisin N: Metabolic syndrome in Thai schizophrenic patients: a naturalistic one-year follow-up study. *BMC Psychiatry* 2007; 7:14.
- Saddichha S, Manjunatha N, Ameen S, Akhtar S: Effect of olanzapine, risperidone, and haloperidol treatment on weight and body mass index in first-episode schizophrenia patients in India: a randomized, double-blind, controlled, prospective study. *J Clin Psychiatry* 2007; 68:1793-1798.