

A Study on Association Between Blood Glucose Level and Schizophrenia



MEDICAL SCIENCE

KEYWORDS : Schizophrenia, Blood glucose, Drug naive

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ABSTRACT

OBJECTIVE: To determine whether drug-naive, first-episode patients with schizophrenia have a higher frequency of impaired fasting glucose tolerance or of type II diabetes mellitus than a healthy volunteer group matched for age.

This study examined the prevalence of impaired fasting glucose levels in first-episode, drug-naive patients with schizophrenia. METHOD: Fasting plasma glucose level is measured in forty patients with schizophrenia and age-matched healthy comparison subjects. **RESULTS:** Twenty Percent (20%) of the drug-naive, first-episode patients with Schizophrenia had impaired fasting glucose levels, compared to none of the healthy volunteers. Also the patients with Schizophrenia had significantly higher fasting plasma levels of glucose. (mean=93 mg/dl SD=12.1, for the healthy subjects versus mean=94mg/dl SD=6.9 for the patients). **CONCLUSIONS:** First-episode, drug-naive patients with schizophrenia have impaired fasting glucose levels than healthy comparison subjects.

INTRODUCTION:

Schizophrenia is a life-shortening illness, with mortality rates among schizophrenic patients twice as high as in the general population. In addition, patients with schizophrenia also appear to have higher rates of impaired fasting glucose levels, insulin resistance, and type II diabetes mellitus than the general population.

However, most of the evidence indicating that type II diabetes mellitus occurs more commonly in schizophrenia has come from studies in which patients were either receiving neuroleptics or had been exposed to neuroleptics in the past. It is difficult to determine whether schizophrenia per se has an independent role in the development of abnormal glucose metabolism, as both conventional and atypical neuroleptics have been implicated in the pathogenesis of type II diabetes mellitus and impaired glucose tolerance. Despite these reservations, support for the hypothesis that schizophrenia and diabetes may be linked independently of medication comes from the observation that the rate of type II diabetes mellitus in family members of schizophrenic patients is between 18% and 30%(1), which is far higher than the rate in the population at large 1.2%–6.3%(7). Therefore, patients with schizophrenia appear to be predisposed to developing type II diabetes mellitus.

Further support for the hypothesis that problems with abnormal glucose metabolism may occur in schizophrenia independently of antipsychotic exposure comes from a study by in 1989. In their study, Mukherjee S, Schnur DB and Reddy R found that 5.8% of the patients with schizophrenia were hyperglycemic (on the basis of two measurements of fasting plasma glucose levels), but those who were drug naïve had higher rates of hyperglycemia than those who were taking haloperidol. In addition, Mukherjee et al. showed that the prevalence of type II diabetes in patients with schizophrenia was age dependent, with rates of 0% in those below age 50 years, 12.9% in those aged 50–59 years, and 18.9% in those aged 60–69 years. This increase in rates mirrors that found in the general population, in which the rates of type II diabetes are approximately 1.2% in those aged 18–45 years and 6.3% in those aged 46–64 years

A study comparing baseline metabolic parameters in drug-naïve schizophrenia patients and healthy controls(n=26 in each group) reported that the patients had significantly higher fasting plasma

glucose and insulin levels and were more insulin resistant (Ryan MCM& Thakore JH, 2003). This was also the first study to note that the frequency of impaired fasting glucose tolerance was higher in patients (15.4%) compared to controls (0%). A second study by the same research group, using an independent sample, confirmed the previous report that drug-naïve schizophrenia patients had significantly higher frequency of impaired glucose tolerance (10.5%) compared to controls (0%) (Spelman LM, Walsh PI, Sharifi N, Collins P,&Thakore JH, 2007)

However, the second study (Spelman et al., 2007) reported that the levels of fasting plasma glucose were comparable between patients and healthy controls, contrary to the earlier report (Ryan et al., 2003). An independent study comparing fasting plasma glucose and insulin levels, in drug naïve First Episode Psychosis patients and healthy controls (n=50 in each group), did not find significant differences in these measures (Arranz B, Rosel P, Ramírez N, Dueñas R, Fernández P, Sanchez JM, Navarro MA & San L 2004).

Another independent study, conducted with a Chinese Han population, reported that there were no differences in fasting plasma levels of glucose, insulin between drug-naïve first-episode schizophrenia patients and healthy controls (46 patients and 38 controls in each group) (Zhang Z-J, Yao Z-J, Liu W, Fang Q & Reynolds GP, 2004).

MATERIALS AND METHODS:

40 subjects (25 men and 15 women; mean age=33.6 years, SD=13.5) who fulfilled ICD-10 criteria for schizophrenia were recruited in this cross-sectional study. Of these, 8 patients come under 20-29 yrs, 13 patients under 30-39 yrs, 10 patients under 40-49 yrs, 9 patients under 50-59 yrs. This study was approved by the Institutional ethical committee. All patients were experiencing their first episode of schizophrenia and were drug naïve. Their status was confirmed by collateral histories obtained from family members. The patients were assessed for independent risk factors for type II diabetes mellitus, i.e., family history of type II diabetes mellitus, generalized obesity as indicated by body mass index.

The normal comparison group, consisting of 40 subjects (25 men and 15 women; mean age=34.4 years, SD=1.9), were physically healthy and had no personal or family history of psychiatric ill-

ness. The comparison subjects were recruited from within the hospital. The patients and normal comparison subjects were matched in terms of age. The life-style factors of diet and exercise were rated. Weight (kg), height (m) measurements were taken for all subjects, and body mass index (kg/m²) were calculated for each subject.

Blood was withdrawn from an ante cubital vein for measurement of plasma levels of glucose. Serum glucose measures (mg/dl) were determined enzymatically by using the hexokinase method. Impaired fasting glucose tolerance was defined by using the American Diabetic Association criteria as a plasma glucose level ≥ 110 mg/dl and ≤ 125 mg/dl. Student's t tests (two-tailed), chi-square tests, and Pearson's product-moment correlation analyses were used, as appropriate, to compare results for the patients and the healthy subjects. All results are expressed as means and standard deviations.

Inclusion criteria:

Newly diagnosed patients of schizophrenia.(based on ICD10) Patients of either sex between 18–60years of age.

Exclusion criteria:

Patients with history of taking antipsychotics before study.
Patients who has no reliable informant.
Patients who are not willing for the study

Limitations .:

Short term study yields less degree of values

RESULTS:

From Table 1, we find that 20% of the patients with schizophrenia had impaired fasting glucose levels, compared to none of the matched healthy comparison subjects and three-fourth of the patients had normal fasting blood glucose levels. In this study, we found that the impaired glucose values were common among 30- 49 yrs which is evidenced from Table 2. Analysis of anthropometric showed no significant differences between the patient and comparison groups. In contrast, the frequency of impaired fasting glucose tolerance, as defined by the American Diabetic Association criteria (>110 mg/dl and <126 μ g/dl), was 20% (N=8) in the patient group and 0% in the comparison group. Compared with the healthy subjects, patients with schizophrenia had a significantly higher mean fasting plasma levels of glucose (mean=94 mg/dl, SD=6.9, versus mean=93 mg/dl for the comparison subjects, SD=12.1) [p=0.313]

In the patients with schizophrenia, fasting concentrations of plasma glucose correlated positively with, body mass index (p=0.53) and age (p=0.64).

DISCUSSION:

An association between schizophrenia and glucose intolerance might occur because diabetes and schizophrenia share some common risk factors and/or genetics. In patients with schizophrenia, fasting concentration of plasma glucose correlated positively with body mass index.

The 20% frequency of impaired fasting glucose tolerance observed in the patients in this study, who had a mean age of 34.3 years, is higher than the age-adjusted (35–64 years) frequencies of 11.8% in men and 5.2% in women in a recent study of the general population(1,9,12). From a prognostic perspective, earlier studies have suggested that one-third of those with impaired fasting glucose tolerance will eventually develop type II diabetes mellitus (10,15). Thus, schizophrenic patients with impaired fasting glucose tolerance may be predisposed to developing type II diabetes, and the high frequency of impaired fasting glucose tolerance in this group may explain in part the reduced life expect-

tancy of patients with schizophrenia.

One potential reason may be that patients did not fast before being tested. However, all subjects with schizophrenia in our study were fasting was strictly enforced for the 10–12 hours before plasma sampling.

Medication may induce hyperglycemia and hyperinsulinemia. This is an unlikely explanation for our findings, as the patients in this study were drug naive and were experiencing their first episode of schizophrenia; the latter was corroborated by collateral histories obtained from family members. Yet, the average age of the patients in our study was 34.3 years, and thus it is highly unlikely that their age was a factor in their high rates of impaired fasting glucose tolerance.

Leaving aside the issues of medication and age, factors such as smoking and diet habits may also play a crucial role in the development of type II diabetes. But both the schizophrenic patients and the comparison subjects were from the same homogeneous ethnic background.

Obesity is a well-recognized risk factor for the development of diabetes. However, both the patients and the comparison subjects in our study were matched in terms of body mass index, and were not obese. Increased visceral fat, with or without obesity, is associated with glucose intolerance, which is a precursor to type II diabetes. Yet, the patients with schizophrenia in our study had higher levels of plasma glucose than the comparison subjects, and neither group were obese, which raises the issue of whether patients with schizophrenia have higher rates of visceral obesity.

Although no comprehensive explanation has been put forward to account for the co-occurrence of this group of conditions, it would appear that dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis may play a role.(Altamura C,Guercetti G,&Percudani M:1989; Coryell W,& Tsuang D:1992). Schizophrenia is also associated with abnormalities of the HPA axis(Kane-ko M, Yokoyoma F, Hoshino Y, Takaghi K& Murata S:1992)

CONCLUSION:

In conclusion,20% of the drug-naive, first-episode patients with schizophrenia in our study had impaired fasting blood glucose levels, compared to none of the matched healthy subjects. The findings of this and other studies suggest that the illness of schizophrenia is associated with various aspects of the metabolic syndrome, which in turn may explain why patients with this illness die prematurely. Screening for metabolic syndrome in all drugnaive schizophrenic patients will help in prevention and early intervention for diabetes.

TABLE:1 Fasting blood glucose values of the patients and controls with reference to gender

Fasting blood glucose level	Schizophrenics (n=40)		Controls(n=40)	
	Male	Female	Male	Female
Normal	20	12	20	20
Impaired	5	3	-	-

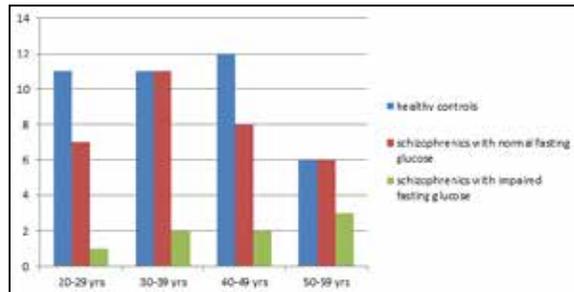
TABLE:2Fasting blood glucose values corresponding with age of the patients and healthy subjects

Age in years	Schizophrenics		Healthy Controls
	Normal (n=32)	Impaired (n=8)	
20 -29	7	1	11
30 -39	11	2	11
40 -49	8	2	12
50 – 59	6	3	6

TABLE:3 Comparison of characteristics between first episode schizophrenia patients and controls

Characteristics	Schizophrenics	Controls	P value
Age in years (mean)	34.3	34.8	p=0.64
BMI(s .d.)	24.5 (2.9)	23.9 (3.5)	p=0.53
Males/ Females	25/15	20/20	p=0.16
Fasting glucose levels (mg/dl)	94 (6.9)	93 (12.1)	p=0.313

CHART 1: COMPARISON OF SCHIZOPHRENICS AND CONTROLS



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