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Fasting Plasma Glucose and Lipid Profile of Patients with Schizophrenia and Bipolar Disorder in Abakaliki, Ebonyi State Nigeria: A Controlled Study

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Abstract: Patients with schizophrenia and bipolar disorder have a reduced life expectancy of 10 to 25 years compared to the general population. Cardio-metabolic disorders are to a large extent responsible for premature mortality among patients with severe mental illness. Major risk factors of cardiovascular disease include hyperglycemia, obesity, dyslipidemia and hypertension. This study measured the plasma glucose and lipid profile in a sample of patients with severe mental illness and assessed the risk of cardio-metabolic disorders among them. Eighty patients with schizophrenia, 40 patients with bipolar disorder and 50 control subjects were recruited for the study from the Department of Psychiatry, Alex Ekwueme Federal University Teaching Hospital, Abakaliki. Form each consenting participant, 5mls of fasting blood samples was drawn using venipuncture. Enzymatic techniques were employed in the assay of fasting plasma glucose (FPG) and lipid profile The findings showed that the FPG of patients with schizophrenia (6.45±3.74mmol/l) was significantly higher (p=0.026) when compared to the FPG of the control subjects (5.14±1.55mmol/l) but there was no significant difference when the FPG value of the subjects with bipolar disorder was compared to either that of the control or the subjects with schizophrenia. The plasma total cholesterol (5.34±1.29mmol/l) and triglycerides (1.45±0.78mmol/l) of patients with schizophrenia were statistically higher (p=0.000 and 0.001) respectively when compared with that of the control group 4.67±1.15mmol/l and 0.99±0.44mmol/l respectively. In Conclusion: Subjects with schizophrenia are at increased risk of developing cardio-metabolic abnormalities. Their metabolic profile should be monitored closely during the course of their management to enable early intervention in event of any cardio-metabolic disorders.

Key words: Lipid Profile · Fasting Plasma Glucose · Schizophrenia · Bipolar Disorder · Cardio-Metabolic Risks

INTRODUCTION

The rate of mortality and morbidity in patients with severe mental illnesses including schizophrenia and bipolar disorder is two to three times higher than the general population [1-3]. This reduces their life expectancy by 10 to 25 years compared to the general population. Physical illnesses and cardiovascular risk factors are responsible for the high rate (about 60%) premature mortality and increased morbidity in patients with severe mental illness [4-6]. Poor management and under-diagnosis of physical illnesses and cardiovascular disease in this class of patients further contribute to reduced life expectancy [7, 8].

People suffering from severe mental illnesses are at more risk of developing cardiovascular disease compared to the general population [9]. Major risk factors for cardiovascular disease include hyperglycemia, abdominal obesity or an increase in body mass index, hypertension and dyslipidemia, defined as a low serum concentration of

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high density lipoprotein cholesterol (HDL-C) and increased serum concentration of low density lipoprotein cholesterol (LDL-C), triglycerides and total cholesterol. Other risk factors include sedentary life style, poor dietary habits consisting of low fiber and high saturated sugar, age, male gender and family history of cardiovascular disease [10]. Although also present in the general population, these cardio-metabolic risks are more prevalent in patients with schizophrenia and bipolar disorder [11, 12].

Antipsychotic medications especially atypical antipsychotics used commonly in the management of psychotic patients further poise a risk of developing cardiovascular disease by interfering with metabolism in these patients [13]. Obesity, a common side effect of antipsychotic medication is a common denominator in the etiology of metabolic syndrome and also a major risk for cardiovascular disorders [14].

Metabolic syndrome, described as a cluster of cardio-metabolic risk factors associated with insulin resistance including abdominal obesity, dyslipidemia, hyperglycemia and hypertension, is common in patients with schizophrenia and bipolar disorder. Its estimated prevalence in patients with severe mental illness ranges from 30 to 60%, a rate higher compared to the general population [15].

In order to improve the life expectancy of patients with schizophrenia and bipolar disorder, it is paramount to monitor early signs of cardio-metabolic risks. Therefore, this study investigated the fasting plasma glucose (FPG), total cholesterol, low density lipoprotein cholesterol (LDL-C), triglycerides and high density lipoprotein cholesterol (HDL-C) in patients with schizophrenia and bipolar disorder compared with the general population and also assessed the risk of cardio-metabolic disorder in this sample of patients.

MATERIALS AND METHODS

Study Setting: The study is a cross sectional case-control study carried out in Alex Ekwueme Federal University Teaching Hospital, Abakaliki Ebonyi State Nigeria. The hospital came into existence in 2011 following the merger of Ebonyi State University Teaching Hospital and Federal Medical Centre Abakaliki by the Federal Government of Nigeria. The Teaching Hospital is planned as a 1000-bed capacity tertiary health facility offering specialist services in several medical and surgical subspecialties [16].

Study Subjects: One hundred and twenty patients with severe mental illness of which 80 were diagnosed with schizophrenia and 40 diagnosed with bipolar disorder were randomly selected from both out-patient and in-patient sections of the Department of Psychiatry. Consenting patients who met inclusion criteria were recruited if diagnosed by consultant psychiatrists using the International Classification of Diseases-10 to have either schizophrenia or bipolar disorder. Patients who were between 15 to 65 years of age were recruited. Patients were excluded if they had co-morbid HIV, epilepsy or history of substance use. For the control group, 50 healthy subjects with no history of medical and psychiatric conditions after examination by consultant psychiatrists were recruited from among staff and students of the hospital.

Ethical Issues: Ethical approval for the study was obtained from the Ethical Committee of Alex Ekwueme Federal University Teaching Hospital, Abakaliki. Informed consent from the patients and/or care givers was obtained. Patients were educated on the details of the study and assured of confidentiality of information. Only subjects who consented were enrolled in to study.

Procedure: Fasting blood samples were obtained by venipuncture from each consenting participant and analyzed for FPG, total cholesterol, triglyceride, LDL-C and HDL-C. Measurements of anthropometric variables which included, BMI (height and weight), waist circumference, systolic and diastolic blood pressure were obtained.

Enzymatic method according to Tinder [17], was employed in the estimation of glucose. For the estimation of total cholesterol and HDL-C, the method of Allan *et al.* [18] was employed while the method of Bucolo and David [19], was used in the estimation of triglyceride.

LDL-C was calculated using Friedewald equation [20]:
LDL-C = TC - TG/2.2 - HDL-C

Dyslipidemia was defined as elevated total cholesterol ($\geq$5.0mmol/l), elevated LDL-C ($\geq$3.4mmol/l), elevated triglyceride ($\geq$1.6mmol/l) and a low HDL-C ($\leq$1.04mmol/l). Hyperglycemia was defined as fasting blood glucose $\geq$6.2mmol/l. Elevated BP was defined when BP was more than 130/85mmHg, abdominal obesity was defined with waist circumference >80cm for women and 102cm for men.

All laboratory analysis was carried out in the Laboratory Department, Alex Ekwueme University Teaching Hospital. The performance of the parameters was evaluated using commercially purchased control sera and the routine quality control procedures were maintained.

Data Analysis: The results were analyzed using statistical package for social science version 20. Descriptive variables were described in mean ± standard deviation while qualitative variables were expressed in percentage. Students t-test one-way ANOVA was used to compare variables. P value was considered significant when $P< 0.05$.

Limitation of the Study: The limitations of the study include a small sample size and short period of research.

None consideration of treatment regimen of the patients also limits the findings of this research. We recommend further studies with a large sample size and with specific interest in the different antipsychotics and mood stabilizers used in the management of the psychiatric conditions.

RESULTS

The socio-demographic characteristics of the study participants is shown in Table 1. This study assessed 80 subjects with schizophrenia, 45% male and 55% female, 40 subjects with bipolar disorder of which 42.5% were male and 57.5% were female and 50 control subjects, 46.0% males and 54.0% females. The mean age was 37.09±10.14years, 28.20±6.84year and 31.44±10.77years for subjects with schizophrenia, bipolar disorder and control, respectively.

The treatment characteristics of the study participants are shown in Table 2. The table shows that treatment naïve patients were 22.5% while 11.25, 38.75 and 27.5% had been on treatment for 1 to 6 months, 6 to 12 months and more than 12 months respectively. Also, 40 subjects with bipolar disorder, 42.5% male, 57.5% female, 45.0% treatment naïve, 20.0, 25.0 and 10.0% treated for 1 to 6 months, 6 to 12 months and more than 12 months respectively with mean age 28.20±6.84 years and 50 apparently healthy control subjects with mean age 31.44±10.77 years were included in the study.

Table 1: Socio-demographic characteristics of the study groups

Variables	Schizophrenia N=80(%)	Bipolar disorder N=40(%)	Control N=50(%)
Sex			
Male	36(45.0%)	17(42.5%)	23(46.0%)
Female	44(55.0%)	23(57.5%)	27(54.0%)
Marital status			
Single	52(65.0%)	26(65.0%)	34(68.0%)
Married	28(35.0%)	14(35.0%)	16(32.0%)
Age range			
16-25years	9(11.25%)	16(40.0%)	17(34.0%)
26-35years	35(43.75%)	18(45.0%)	19(38.0%)
36-45years	21(26.25%)	6(15.0%)	9(18.0%)
46-55years	9(11.25%)	0(0.0%)	2(4.0%)
56-65years	6(7.50%)	0(0.0%)	3(6.0%)

Table 2: Treatment characteristics of the study groups

Variables	Schizophrenia N=80(%)	Bipolar Disorder N=40(%)
Duration of treatment		
Naïve	18(22.5%)	18(45.0%)
1-6months	9(11.3%)	8(20.0%)
6-12months	31(38.7%)	10(25.0%)
>12months	22(27.5%)	4(10.0%)
Class of antipsychotic		
Not on antipsychotic	18(22.5%)	18(45.0%)
Atypical	37(46.2%)	11(27.5%)
Typical	25(31.3%)	11(27.5%)

Table 3: Comparison of the metabolic indices among the study groups

Variables	SCZ N=80	BD N=40	Control N=50	F-stat	P-value	SCZ vs. BD	SCZ vs. Control	BD vs. Control
BMI (kg/m^2)	24.78±4.61	22.99±3.66	23.57±5.07	2.390	0.095	0.129	0.431	1.000
WC (cm)	90.75±14.62	80.89±5.59	81.58±6.11	15.923	<0.001*	<0.001**	<0.001*	1.000
SBP (mmHg)	123.24±21.68	116.35±11.256	128.48±12.241	5.525	0.005*	0.121	0.279	0.003*
DBP (mmHg)	80.23±12.280	76.20±10.311	82.22±10.243	3.249	0.041*	0.201	0.982	0.038*
FPG (mmol/L)	6.45±3.74	5.23±0.79	5.14±1.55	4.563	0.012*	0.069	0.026*	1.000
T.chol (mmol/l)	5.34±1.29	4.45±1.02	4.67±1.15	9.240	<0.001**	<0.001**	0.006*	1.000
TG (mmol/l)	1.45±0.78	1.26±0.64	0.99±0.44	7.083	0.001*	0.446	0.001*	0.188
LDL-C (mmol/L)	2.82±1.28	2.07±0.97	2.49±1.20	5.300	0.006**	0.004**	0.408	0.284
HDL-C (mmol/L)	1.91±0.96	1.82±0.82	1.68±0.61	1.158	0.317	1.000	0.390	1.000

*values differ significantly from control (p<0.05). **values differ significantly between Schizophrenia and Bipolar disorder (p< 0.05). BMI = Body mass index WC = waist circumference, SBP = systolic blood pressure, DBP = diastolic blood pressure, FPG = fasting plasma glucose, T. chol = total cholesterol, TG = triglycerides LDL-C = low density lipoprotein cholesterol, HDL-C = high density lipoprotein cholesterol, SCZ = Schizophrenia, BD = Bipolar Disorder

Table 4: Relationship between metabolic indices and age of the study groups

	Age Group						
Variables	----------						
FPG (mmol/l)	16-25	26-35	36-45	46-55	56-65	F-stat	P-value
Schizophrenia	5.11±0.65	5.26±0.96	5.59±1.03	10.10±2.88	12.92±10.32	12.930	<0.001
Bipolar disorder	5.18±0.88	5.29±0.81	5.18±0.57	??	??	0.095	0.909
Control	5.09±1.23	5.31±2.12	5.06±1.12	4.95±0.64	4.67±0.49	0.134	0.969
T.Chol (mmol/l)							
SCZ	5.51±1.35	4.88±1.23	5.40±0.67	5.57±1.48	7.22±1.49	5.300	0.001
BD	3.94±1.12	4.60±0.81	5.33±0.43	??	??	5.563	0.008
Control	4.82±1.36	4.23±1.08	5.17±0.66	4.15±0.49	5.47±0.99	1.737	0.158
TG (mmol/l)							
SCZ	1.43±1.01	1.26±0.67	1.47±0.62	1.70±1.22	2.08±0.46	1.791	0.140
BD	1.38±0.54	1.27±0.75	0.90±0.51	??	??	1.224	0.306
Control	0.90±0.37	1.08±0.54	0.99±0.40	0.85±0.49	1.07±0.40	0.440	0.779
LDL-C (mmol/l)							
SCZ	3.19±1.20	2.22±1.35	3.22±0.93	3.24±1.27	3.68±0.77	4.094	0.005
BD	1.89±1.07	1.97±0.77	2.85±1.04	??	??	2.468	0.099
Control	2.71±1.29	2.08±1.25	2.73±0.75	2.00±1.13	3.50±1.06	1.427	0.241
HDL-C (mmol/l)							
SCZ	1.70±1.03	2.17±0.77	1.50±0.66	1.58±0.91	2.60±1.94	3.049	0.022
BD	1.36±0.43	2.09±1.02	2.20±0.42	??	??	4.801	0.014
Control	1.70±0.58	1.56±0.58	1.89±0.83	1.80±0.85	1.57±0.06	0.464	0.762

FPG= fasting plasma glucose, T.chol= total cholesterol, TG= triglycerides, LDL-C= low density lipoprotein cholesterol, HDL-C= high density lipoprotein cholesterol, SCZ=Schizophrenia, BD=Bipolar Disorder

Comparison of the metabolic indices among the study groups is as shown in Table 3. The fasting plasma glucose of patients with schizophrenia (6.45±3.74mmol/l) was significantly higher (p=0.01) when compared with values for the control subjects (5.14±1.55mmol/l). The values of total cholesterol (5.34±1.29mmol/l) and triglycerides (1.45±0.78mmol/l) of patients with schizophrenia were significantly higher (p=0.00) and (p=0.00) respectively when compared with the values of the control group, 4.67±1.15mmo/l and 0.99±0.44mmol/m respectively. Also, serum total cholesterol (5.34±1.29mmol/l) and low density lipoprotein cholesterol (2.82±1.28mmol/l) were significantly higher (p=0.00) in patients with schizophrenia compared to patients with bipolar disorder.

The relationship between metabolic variables and the age is shown in Table 4. The mean values for fasting plasma glucose are significantly higher in the older patients with schizophrenia (p=0.00). All clinical parameters studied in the subjects with schizophrenia show significant increase (p<0.05) in the older age group compared to the younger age group except for TG which showed no significant difference (p>0.05).

Subjects with bipolar disorder recruited were between 16 to 45 years. In these subjects, there was no significant age related difference in the mean values of fasting plasma glucose (p>0.05). Total cholesterol shows significant difference (p<0.05) among the older age group compared to the younger group. HDL-C and LDL-C are significantly higher (p<0.05) between groups.

DISCUSSION

In this study, we aimed at evaluating the risk of cardio-metabolic disorders in a sample of patients with schizophrenia and bipolar disorder by assessing their fasting plasma glucose, total cholesterol, triglyceride, LDL-C, HDL-C levels.

Schizophrenia and bipolar disorders are life threatening and shortening illnesses due to the disease itself or due to physical illnesses especially, cardiovascular disorders [9]. Metabolic syndrome, a cluster of hypertension, dyslipidemia, hyperglycemia and obesity, is a modifiable risk factor for cardiovascular death [21]. The etiology of this excess cardiovascular disease is multi-factorial and likely includes genetic factors and lifestyle factors as well as disease specific and treatment effects [2]. Early detection and management is important in preventing death due to medical problems in patients with severe mental illnesses, including schizophrenia and bipolar disorder. In the present study, we ascertained the risk of cardiovascular diseases in patients with schizophrenia by studying their fasting glucose level, lipid profile as well as obesity and blood pressure.

Results of this study shows a statistical significant higher blood glucose in patients with schizophrenia compared to the control but no significant difference between patients with bipolar disorder and the control group. This is consistent with reports of earlier studies which reported a higher prevalence diabetes mellitus in patients with severe mental illness compared to the general population [5, 22]. Also, in similar demographic region, higher prevalence of diabetes mellitus was reported in patients with schizophrenia compared to the other psychiatric illness [23]. This study also reports hyperglycemia significantly higher in patients with schizophrenia between 46 to 65years compared to the younger age group. This report is in tandem with earlier studies which reported an association between age and diabetes mellitus/hyperglycemia in patients with schizophrenia [23, 24]. A higher prevalence of diabetes mellitus among patients with schizophrenia with mean age of 55years has been reported by previous studies [24]. Long term use of antipsychotics and unhealthy lifestyle practiced by these patients may further increase risk of developing hyperglycemia. Although the effect of antipsychotic treatment was not taken into consideration in the present study, majority of the subjects with schizophrenia 37(46.2%) who were enrolled in the study were on atypical antipsychotics, a known risk of developing disorders in glucose metabolism. Our result on the glycemic state of patients with bipolar disease showed no statistical significant difference when compared with that of the control group and patients with schizophrenia, differs from reports from previous study [25]. Increased rate of glucose dysregulation was reported in patients with bipolar disorder, particularly in women above 40 years of age compared to the general population [25]. Medications used in the treatment of bipolar disorder further increased their risk of developing hyperglycemia and diabetes mellitus [26]. The difference in report may be because majority (45%) of subjects with bipolar disorder recruited was treatment naïve. Also, our subjects were mostly younger in age.

The presence of hyperglycemia in schizophrenia may present as an independent entity or may be complicated by the psychiatric condition. Schizophrenia however has been found to act as a significant independent risk factor for development of hyperglycemia and diabetes [27]. Increased circulating concentrations of cortisol and catecholamines and immunological alterations, such as altered cytokine expression, has been recorded in schizophrenia and may provide a putative mechanism by which psychiatric disease itself contributes to the pathogenesis of diabetes as well cardiovascular disease [28]. Knowledge of associated risk factors can help identify and manage at-risk patients promptly.

Epidemiological studies have shown that dyslipidemia is a powerful risk factor for coronary heart disease. Dyslipidemia has been associated with schizophrenia in previous studies [29-32]. This is in keeping with results of the present study. From the present study we observed that total cholesterol and triglyceride were significantly higher in subjects with schizophrenia compared to the control subjects. The serum LDL-C of patients with schizophrenia though higher than LDL-C of the control subject did not show a statistical significant difference. From our result, we observed that schizophrenia is associated with abdominal obesity, evident by waist circumference which is significantly higher than the waist circumference of the control subjects, an observation in keeping with previous reports [33]. Patients with schizophrenia are prone to obesity due positive and negative symptoms of the disease as well as negative life style habits such as physical inactivity and increased calorie intake [33]. Obesity and sedentary lifestyle are known predictors of dyslipidemia and cardiovascular disease.

Dyslipidemias occur in schizophrenia with or without antipsychotic medication though the condition may be worsened by medication and progresses with treatment

[30]. Although we did not look at the effect of different antipsychotic medications on the lipid profile of the patients, a greater percentage (46.2%) of subjects with schizophrenia enrolled were on atypical antipsychotic medication which is known to increase the risk of dyslipidemia [30, 34].

From our results, we observed that there is no significant difference between the lipid parameters of subjects with bipolar disorder and control subjects. This result may be explained by the fact that the enrolled subjects with bipolar disorder were majorly young and treatment naïve. There was no statistical significant difference between the waist circumference of patients with bipolar disorder and the control subjects.

On comparing the metabolic parameters of schizophrenia with bipolar disorder, we observed that the subjects with schizophrenia are more at risk of developing cardio-metabolic disorders. Explainable by the fact that the patients with bipolar disorder recruited for the study were younger compared to those with schizophrenia. According to reports, bipolar disorder is diagnosed more in adolescents [35]. The results of this study suggests that the adult population with schizophrenia are more likely to develop metabolic abnormalities as significant hyperglycemia and dyslipidemia is observed among this sample of subjects. This is not very surprising since hyperglycemia, dyslipidemia and obesity are associated with increase in age.

CONCLUSIONS

Patients with severe mental illness especially schizophrenia are exposed to risk of cardio-metabolic disorders due to the presence of hyperglycemia and dyslipidemia commonly associated with this condition. One major finding of the present study is that increase in age to a large extent influences abnormalities in metabolism among the studied patients. This risk may be increased further the use of atypical antipsychotic medication. Management of these patients should include strict monitoring of their metabolic profile especially as they advance in age.

What Is Known about the Topic?: The prevalent rate of dyslipidemia, obesity and hyperglycemia among patients with schizophrenia and bipolar disorder is high compared to the general population. This increases the risk of mortality among these of patients by about 60%. Variable factors including antipsychotic medication used in the management of the patients are contributory to the increased risk.

What this Study Adds:

- The prevalence of cardiometabolic risk especially hyperglycemia and dyslipidemia is high among patients with severe mental illness especially those with schizophrenia compared to the general population.
- The use of typical antipsychotic medication may contribute the development of cardio-metabolic disorders among patients with schizophrenia.
- Increase in age is a major risk factor of hyperglycemia among patients with schizophrenia.

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