Original Research Article

Weight gain and obesity among out-patients with schizophrenia on antipsychotic medications in Uyo, South-South Nigeria.

ASTRACT

Background: Treatment of schizophrenia with antipsychotic medications is often associated with increased risks for weight gain, overweight and obesity but the associated risk factors in these patients are not fully known.

Objective: The aim of our study is to determine the prevalence of overweight and obesity in patients with schizophrenia on antipsychotic medications and the risk factors associated with it.

Methods: This was a cross-sectional study. One hundred and six subjects diagnosed with schizophrenia were recruited for the study. Demographic and anthropometric variables, fasting glucose profile and treatment variables were obtained and results analysed using SPSS version 20. Significance was set at *P=.05*.

Result: Study participants had a mean age of 34.67±8.8 years, 55.8% was male, and had a weight gain of 11.92±6.2 and mean BMI of 27.22±3.5. The prevalence of overweight and obesity was 62.3% and 20.8% respectively. The risk of weight gain and obesity in the study population was increased for all class of antipsychotic medication (typical or atypical) and was more likely with increased duration of antipsychotic medication use. There was no association of weight gain with age, sex, degree of weight gain and duration of illness.

Conclusion: Treatment with antipsychotic medications was associated with a significantly increased risk for weight gain and obesity. There is the need for routine weight monitoring during treatment with antipsychotic medications.

Key words: *Schizophrenia, Antipsychotic medications, overweight, obesity, Nigeria*

1. INTRODUCTION

Schizophrenia is a severe and debilitating major mental disorder characterized by a chronic progressive nature and significant impairment in family, social and occupational functioning [1]

Schizophrenic patients typically have 20% shorter lifespan compared to the general population due in part to a high prevalence of diabetes, coronary artery disease, hypertension, and other chronic medical conditions in this patient population. The unhealthy lifestyle habits of many schizophrenic patients, which include poor diet, smoking, excessive alcohol consumption, and use of illegal substances, are believed to contribute to their higher mortality [2,3].

Antipsychotic medications are typically used to treat nearly all forms of psychosis, including schizophrenia, schizoaffective disorder, affective disorder with psychosis, and psychosis associated with organic mental disorders. These drugs have been classified into classical (also referred to as typical or conventional) antipsychotics and atypical antipsychotics group [4]. Weight gain is a well-known side effect of treatment with psychotropic drugs [5,6]. The rates of obesity and diabetes in patients with schizophrenia are higher than the general population [7]. According to a study, when obesity is defined as a body mass index (BMI) of or greater than 27 kg/m^2, 42% of schizophrenic patients are considered obese as compared to 27% of the general population [8].

Obesity has been associated with a number of co-morbid conditions, such as hypertension, type 2 diabetes, coronary heart disease, stroke, osteoarthritis, obstructive sleep apnea, and various cancers, decreased quality of life, non-compliance with antipsychotic medications, a lowered self-esteem, social withdrawal and increased stigmatization [9-13]. Additionally, Patients with schizophrenia are known to have unhealthy diets and inadequate physical activity due to lower socioeconomic status, lower educational level, and sub-optimal living situations [14].

It is widely believed that antipsychotic drugs contribute to weight gain via effects mediated by binding to serotonin (5-HT_2), noradenaline, dopamine, and/or histamine receptors. Serotonin activity at receptor sites is a potent satiety signal, with the most implicated receptors being 5-HT_{1A} and 5-HT_{2C}. Stimulation of 5-HT_{1A} is associated with an increase in food intake whereas stimulation of 5-HT_{2C} is related to a decrease in food intake. Antagonism of the 5-HT_{2C} receptor can, in turn, lead to an increase in food intake, with most SGAs possessing 5-HT_{2C} antagonist activity.[15,16]

In Nigeria studies on antipsychotic associated weight gain are scanty and few. The present study was designed to determine the prevalence of overweight and obesity and factor associated with it.

2. MATERIALS AND METHODS

2.1 Location of the study

This study was conducted at University of Uyo Teaching Hospital from November 2017 to February 2018. The hospital is located in Uyo, the capital city of Akwa Ibom State, Nigeria. The hospital is a 450 bed capacity tertiary healthcare centre that offers secondary and tertiary care. It receives referral from primary and secondary healthcare facilities in the state as well as from the neighbouring states. All diagnoses made in the institution were according to the tenth edition of the International Classification of Diseases and health-related disorders (ICD -10) criteria. [17] Clinically generated data for each subject enrolled were matched to the ICD -10 criteria.

2.2 Subjects. The sample size was calculated using a public domain software available on-line **(**www.statpages.org**)** [18] using a prevalence of obesity as determined from previous Nigerian studies (12.4%).[19] The sample consisted of one hundred and ten participants but only one hundred and six (n=106) subjects with schizophrenia were included in the analysis because 4 subjects had incomplete data. A subject is enrolled if he/she met the following inclusion criteria: a diagnosis of schizophrenia as confirmed by a consultant psychiatrist using the ICD 10 criteria, who has been receiving anti-psychotic medications for at least one year prior to study entry, adults above the age of 18years, and who granted consent. The exclusion criteria were: refusal to participate in study and florid psychopathology that could impair response to question.

2.3 Procedure. Approval for the study was obtained from the Research and Ethical Committee of the University of Uyo teaching Hospital. Informed consent was obtained from patients or their accompanying family members. Patients who met the inclusion criteria were consecutively recruited into the study after a comprehensive psychiatric evaluation and diagnosis by resident doctors in psychiatry. The Mini International Neuropsychiatric Interview (MINI) English Version 5.0.0 (20) was further used to confirm the diagnosis of schizophrenia in the participants. The MINI was designed as a brief structured interview for the major Axis 1diagnosis in the Diagnostic and Statistical Manual (DSM-IV) and ICD-10.

2.4 Measures

2.4.1 Socio-demographic characteristics.

A socio-demographic questionnaire designed by the authors was used to obtain information Measures evaluated includes socio-demographic details (age of the patient and family member, gender, educational status, marital status, religion) illness related variables (total duration of illness)

and medication related variables (type of medication, doses and the chlorpromazine equivalence of the antipsychotic medications)

2.4.2 Medication profile

The medication profile of each individual patient was obtained through chart review of the medication record files domiciled in the hospital. Data recorded include: The number of antipsychotic medicines on the patients' current treatment regimen. Exposure to antipsychotic medication was measured as 1.class of antipsychotics used 2, duration of antipsychotic use 3, doses of medication used. All the antipsychotics used by the test subjects were converted to their chlorpromazine equivalent doses.

2.4.3 Data Analysis:

Descriptive statistics such as frequencies, mean and standard deviation were computed for socio-demographic and clinical characteristics of the participants and other variables as appropriate. Relevant inferential statistics such as chi-square, t-test, ANOVA, Pearson's correlation were used as appropriate. The statistical package for social sciences (SPSS) version 20 was used for analysis. Significance was computed at $P < .05$.

3. RESULT

One hundred and six participants were included in the study. The mean age of the participants was 34.52 ± 8.9 years (range 20-60 years). More than half of them were females (58.5%). The majority (79.2%) was never married and about 72.1% of them had formal education to at least secondary school level and 72.6% of them were unemployed.

Table 1 Socio-demographic and Clinical characteristics of the participants

Variables	N (%)
Age in years (mean ±SD)	34.52±8.9
Age	
>40 years	72(67.9)
≤40 years	34(32.1)
Sex	
Male	44(41.5)
Female	62(58.5)
Marital status	
Single/separated	84(79.2)
Married	22(20.8)
Educational level	
Primary	6(5.7)
Secondary	68(64.2)
Tertiary	32(30.2)

Employment status	
Employed	29(27.4)
Unemployed	77(72.6)
Duration of illness	
≤10 years	76(71.7)
>10 years	30(28.3)
Mean duration of Antipsychotic use (years)	5.71 ±2.4
Duration of antipsychotic use	
≤5 years	37(34.1)
>5 years	69(65.1)
Class of antipsychotic medication	
Conventional	12(11.3)
Atypical	28(26.4)
Combination	66(62.3)
Body Mass Index (BMI)	
Normal	31(29.2)
Overweight	53(50.0)
Obese	22(20.8)

The mean duration of illness was 6.96±6.2 years and the mean duration of use of antipsychotic drugs 5.71±2.4 years. Mean weight gain of participants was 12.32±6.4

3.1 Distribution of the antipsychotic-related variables

About 27.5% of subjects were on conventional antipsychotics and the three most commonly prescribed first generation antipsychotics were: haloperidol (48.6%) stelazine (22.3%) chlorpromazine (15.5%). The remaining 13.6% were on thioridazine, long acting injectables like Fluphenazine decanoate or Flupenthixol decanoate.

40.5% of the subjects were on atypical antipsychotics. The most commonly prescribed serotonin dopamine antagonists (SDAs) were olanzapine (36.8%), risperidone (55.6%). The remaining 7.6% of subjects were on clozapine (2.5%), quatiepine (3.8%) aripiprazole (1.3%). Over 56.0% of the subjects were on polytherapy and the most common combinations were: any class of antipsychotics like combination of two conventional antipsychotics or conventional antipsychotics and atypical and any class of antipsychotics and long acting injectables. The dosing frequency of 45% of the subjects was at least twice per day and 28% were on once daily dose regimen.

The mean daily dosage per day in milligram for subjects on chlorpromazine was 320 mg/day. The subjects on haloperidol had 15.45 mg/day mean value while those prescribed stelazine 12.85 mg/day. The mean chlorpromazine equivalent dosage was 512.82. and 256.0mg for those on haloperidol and stelazine respectively.

The mean daily dosage for olanzepine was 18.40±2.5. mg/day. Subjects on risperidone received a mean daily dosage of 3.85±1.3 mg/day The chlorpromazine equivalent dosage for patients on olanzapine and risperidone was 368.0mg and 385mg respectively.

3.2 Antipsychotic Usage and weight gain

The mean weight gain of the subjects on antipsychotic medication was 11.92±6.17 kg over a mean 5 year period of antipsychotic medication use. The mean weight of subjects before commencement of antipsychotic medications was 62.13±11.74kg. At one year of antipsychotic medication use, the mean weight was 68.25±8.9kg. After a mean 5 years period of antipsychotic medications mean weight of subjects was 73.00±10.53kg (*ANOVA (F)=13.05, P=<.001*). This implies that 56.3% of the weight gain of subjects occurred within the first year of antipsychotic medication use.

Table 2. Demographic and clinical characteristics by body mass index classification

Variables value	Normal or low Weight n(%)	Overweight n(%)	Obesity n(%)	Statistics	P-value
Sex					
Male	12(27.9)	25(58.1)	6(14.0)	x^2=6.89	**.04**
Female	6(9.5)	41(65.1)	16(25.4)	df 2	
Age					
≤40 years	11(20.0)	31(56.4)	13(23.6)	x^2=1.7	.43
>40 years	7(13.8)	35(68.6)	9(17.6)	df=2	
Marital status					
Married	1(4.5)	16(72.7)	5(22.7)	x^2=3.07	.22
Single	17(20.2)	50(59.5)	17(20.2)	df=2	
Employment					
Employed	6(20.7)	18(62.1)	5(17.2)	x^2=0.56	.76
Unemployed	12(15.6)	48(62.3)	17(22.1)	df=2	
Duration of Antipsychotic use					
≤5years	11(29.7)	18(48.6)	8(21.6)	x^2=6.89	**.03**
>5years	7(10.1)	48(69.6)	14(20.3)	df=2	
BMI before Treatment					
Normal	15(19.5)	51(66.2)	11(14.3)	x^2=11.23	**.02**
Overweight	2(7.7)	15(57.7)	9(34.6)	df=4	
Obesity	1(33.3)	0(0)	2(66.7)		
Class of Antipsychotics					
Conventional	2(16.7)	5(41.7)	5(41.7)	x^2=5.63	.26
Atypical	3(9.7)	18(64.3)	7(25.3)	df=4	
Combination	13(20.6)	43(68.3)	43(68.3)		

Duration of illness					
≤10 years	13(17.1)	46(60.5)	17(22.4)	x^2=1.67	.43
>10 years	5(16.7)	20(66.7)	5(16.7)	df=2	
Hyperglycaemia					
No	14(17.3)	51(67.9)	12(14.8)	x^2=7.6	
.03					
Yes	4(16.0)	11(44.0)	10(40.0)	df=2	

There was correlation between period of antipsychotic use and weight gain (*r=0.23, P=.03*). There was no association found between mean weight gain of subjects (determined as the difference between weight at first presentation before commencement of antipsychotic medications and weight at study entry) and sex, age, duration of illness, class of antipsychotic medication. The mean weight gain in kg four individual antipsychotic medications after mean 5 year duration of antipsychotic medication use was stelazine 9.89±3.5kg, haloperidol 11.62±6.8kg, risperidone 11.74±5.5kg and olanzepine 14.34±6.9kg There was no significant difference among the individual medications on their propensity to cause weight gain among participants (*ANOVA (F)=1.76,P=.14)*

Patient characteristics and body mass index

For subjects, antipsychotics naïve, at presentation at the treatment facility, the prevalence rates of normal weight, overweight and obesity were 72.6%, 24.5% and 2.8% respectively. At study entry, after a mean 5 year period of antipsychotic medication use, the prevalence of overweight and obesity were 62.3% and 20.8% respectively showing significant differences from values before commencement of antipsychotic medication (x^2*=11.23, P=.02*). Gender was a factor in the propensity to gain weight. Relative to men, women were more likely to become overweight and obese following antipsychotic use (*p=.03*). Increasing duration of antipsychotic use was associated with increased tendency for overweight and obesity among study participants (*P=.03*). There was no association found between BMI values and age of participants, employment status, and class of antipsychotic medication.

Body mass index and glycaemic status

According to the American Diabetes Association (ADA) any individuals with fasting glucose level of 100-125mg/dl (5.6-6.9 mmol/l) or glucose level of 140-199mg/dl (7.8-11 mmol/l) two hours after 75-g oral glucose tolerance test or hemoglobin A(1c) 5.7%-6.4% be classified as prediabetic, indicating increased risk for the emergence of diabetes [21]. In this study, when a subject had pre-diabetes

(fasting plasma glucose 100–125 mg/dl) or diabetes (fasting plasma glucose ≥126 mg/dl), he/she was considered to have hyperglycaemia. The prevalence of hyperglycaemia was 17%. The glycaemic status of subject in this study showed significant association with the degree of overweight and obesity (*P=.03*).

4. DISCUSSION

In this study, the prevalence of overweight and obesity among patients with schizophrenia on antipsychotic medications were 50% and 20.8% respectively. These rates are relatively high compared to rates reported in a previous Nigerian study which found obesity rate of 7.3% [19]. In our sample, the prevalence of overweight is high compared to the findings reported in the general Nigerian adult population in which overweight rate of 8.1-22.2% was obtained. The obesity rate in our study approximate to the figure of 8.1-22.2% reported among the general population in Nigeria [22]. For patient who never received antipsychotic medications, the prevalence rate of overweight and obesity at first presentation to our treatment facility, were 24.5% and 2.8% respectively. At study entry, after mean five year duration of treatment with various antipsychotic medications, the prevalence of obesity in our sample (20.8%) differs from findings from other developing countries such as Ghana and Indonesia [23,24]. This difference may be attributed to patients' characteristics in our sample. A high proportion of our participants are unemployed and this may translate to a more sedentary life style which has the potential to promote more weight gain.

Worldwide, the prevalence rate of obesity in the present study is in agreement with several studies from high income countries which have reported similar prevalence [25,26]. Increasingly, more patients in our setting now receive newer atypical antipsychotic medications as first line medications as reflected in the high proportion (about 55%) of patients on newer second generation antipsychotics either as monotherapy or in combination with conventional antipsychotics in this study. This may partly explain the proximity of the obesity rate found in this study to figures reported from some advanced industrialised nations.

The atypical antipsychotic medications have been reported to contribute more to drug-induced weight gain compared to the conventional antipsychotics. Weight gain is a well-established side-effects of both first and second generation antipsychotic medications [8] and has been cited as an important reason for medication non-adherence [13,27,28]. The mean weight gain of our sample in kg

193 significantly increased by 56.3% from the mean weight at onset of treatment to a period of one year
194 after antipsychotic medication use. This represents a 10% increase on the initial body weight at
195 presentation to our treatment facility. This is consistent with a study by Hummer et al [29] who
196 reported that after 1 year of treatment, 36% of patients treated with clozapine had gained more than
197 10% of their initial body weight. Other studies have reported remarkable contributions by both classes
198 of antipsychotic medications, especially the newer atypical antipsychotic medications, to the
199 prevalence of obesity in the medicated schizophrenic population, with current estimates ranging from
200 40 to 60% versus 30% of the general adult population [30,31]

201 The role of demographic factors in promoting weight gain and obesity following use of antipsychotic
202 medication was explored in the study. Social-demographic variables like age, marital status and
203 employment status have not been consistently predictive of weight gain and obesity in this population
204 of patients and our study is generally in support of studies which did report significant association with
205 these variables. In the current study, women were significantly more likely to be overweight and obese
206 compared to the male subjects. This is in agreement with previous studies which have reported
207 similar findings [19,32]. The gender differences in the prevalence of overweight and obesity between
208 male and female participants on antipsychotic medications have partly been attributed to events such
209 as pregnancy, oral contraceptives therapy and menopause [33,34].
210 The impact of treatment duration on the propensity for weight gain and obesity for patients on
211 antipsychotic medications have been reported in some studies [29,35,36]. In this study, weight gain
212 and obesity was significantly related to the duration of antipsychotic medication use. Treatment with
213 atypical antipsychotics had more remarkable impact on weight of participants than the conventional
214 medications. However, the class of medication was not a statistical predictor of weight gain and
215 obesity in this study and therefore in agreement with studies which reported such findings [19, 31].

216 We found a significant statistical association between treatment the degree of weight gain and the risk
217 of developing hyperglycaemia. The impact of antipsychotic medications on the glycaemic status of
218 patients with schizophrenia on antipsychotic medications has long been recognised. Several studies
219 have reported that this tendency for antipsychotic medication to cause hyperglycaemia and type 2
220 diabetes mellitus is related in part to their ability to cause weight and obesity [37,38]. Both typical and
221 atypical antipsychotics have been associated with increased risk of weight gain diabetes mellitus in

patients with schizophrenia. Recent reports suggest that newer (atypical) antipsychotic medications contribute more to clinically significant hyperglycemia than the conventional antipsychotics [39]

5. CONCLUSION:

Patients on antipsychotic medication for schizophrenia or other illnesses should be considered a high-risk group for significant increases in weight gain and obesity. There in the need for regular and routine monitoring of all patients on antipsychotic medication for necessary intervention to prevent excessive weight gain during treatment.

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