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Research Article

# Sexual Dysfunction among Psychiatric Patients on Antipsychotic Medications

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## ABSTRACT

The aim of this study was to determine the relationship between use of antipsychotics and the occurrence of sexual dysfunction and hyperprolactinemia among patients. From a sample of 70 patients (43 males and 27 females) taking antipsychotics for at least 3 months and an equal number of psychotropic naïve controls matched for sex and age (±5 years), demographic, clinical, and medication information were collected. Sexual function was assessed using the International Index of Erectile Function and Female Sexual Function Index among male and female respondents, respectively. Serum prolactin level was also assayed. The mean daily dose of antipsychotics was 303.81 mg; mean prolactin level was 24.50 ng/ml and 12.66 ng/ml among the subjects and controls, respectively. The prevalence of hyperprolactinemia was 38.6% among the subjects and 1.4% among the controls ($\chi^2$ = 0.637, df = 1, p = 0.000). The prevalence of sexual dysfunction was higher among the subjects (67.2%) than the controls (40%) ($\chi^2$ = 0.173, df = 1, p = 0.796). The presence of hyperprolactinemia ($\chi^2$ = 12.904, df = 1, p = 0.000), use of antipsychotic combination ($\chi^2$ = 6.656, df = 1, p = 0.013), and daily dose of antipsychotics (*t*= -3.986, df = 65.229, p = 0.000) were found to be significantly associated with sexual dysfunction. Hyperprolactinemia was the strongest predictor of sexual dysfunction (Wald = 6.30, df = 1, OR = 1.131, 95% CI = 1.027 to 1.245, p = 0.016). Sexual dysfunction and hyperprolactinemia were more prevalent among subjects than controls. These findings should guide psychiatrists in antipsychotics prescription.

**Keywords:** Sexual dysfunction, psychiatric patients, antipsychotics.

## INTRODUCTION

Sexual dysfunction can occur during any phase of the sexual response cycle**.** It is an important cause of medication nonadherence in psychiatric practice. It consists of ways in which an individual is unable to participate in a sexual relationship as the person would wish. There may be lack of interest, enjoyment, or failure of the physiological responses necessary for sexual interaction (penile erection, vaginal lubrication) or inability to experience orgasm (anorgasmia, delayed orgasm, premature ejaculation) [1].

Antipsychotics are medications used to manage psychosis and sometimes used in the management of nonpsychotic disorders [2]. Hyperprolactinemia describes plasma prolactin level above upper limit of normal [3]. The normal plasma level varies with age and gender. Normal plasma range is 2.1–17.7 ng/ml for males and 2.8–29.2 ng/ml for nongravid premenopausal females [4, 5]. It is the most common pituitary hormone abnormality clinically [6]. Sexual dysfunction is one of the recognized adverse effects that could arise during antipsychotic treatment and may predate treatment with an antipsychotic [7–9]. Aizenberg and Kockott, in two separate studies, reported that prevalence of sexual dysfunction is higher in patients on antipsychotic medication than in unmedicated patients [10, 11].

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Additionally, sexual dysfunction is a major source of worry to patients taking antipsychotic medications [12, 13]. This finding is supported by report of a survey conducted by The National Schizophrenia Fellowship [14]. Furthermore, complaints about sexual dysfunction are not given as much attention by clinicians as its prevalence from available data was daunting and at best only vague reassurances are given [15]. This may lead to medication nonadherence and hence lower quality of life [13, 16]. Sexual dysfunction is sensitive; hence, patients may not initiate discussion with caregivers [17]. Although the causes of sexual dysfunction in patients on antipsychotics are numerous, one factor in particular stands out which is hyperprolactinemia. Studies have established a correlation between hyperprolactinemia and the presence of sexual dysfunction in patients taking antipsychotic with prevalence rate for hyperprolactinemia from 38% to 71% depending on study design [18].

The present study is important because despite high prevalence of sexual dysfunction among patients taking antipsychotics, it is still underresearched [19, 20]. A survey had psychiatrists reporting 28% and 40% rates of sexual dysfunction in female and male patients, respectively, whereas the corresponding figures reported by the patients themselves were 40% and 60% [21]. Moreover, in Nigeria, most of the studies on sexual dysfunction were either done in a general psychiatric population or restricted to male patients with schizophrenia or those taking first-generation antipsychotics only. These tend to make the generalization of their findings difficult. In addition, other studies did not look at prolactin level of patients to determine true association between hyperprolactinemia and sexual dysfunction. Hence, they excluded an important marker and guide to the management of sexual dysfunction in these patients. This aim of this study is to determine relationship between use of antipsychotics, sexual dysfunction, and hyperprolactinemia among outpatients attending Federal Neuropsychiatric Hospital, Calabar. Specifically, we intend to determine the sociodemographic correlates of sexual dysfunction among subjects and controls, prevalence of sexual dysfunction in patients on antipsychotic medications and in controls not on antipsychotic medication, relationship between illness severity and sexual dysfunction, relationship between sexual dysfunction and hyperprolactinemia in the subjects and controls as well as the relationship between type of antipsychotic and sexual dysfunction

## MATERIALS AND METHODS

### Study location

Study was carried out at the outpatient clinic of the Federal Neuropsychiatric Hospital, Calabar, Cross River State, Nigeria.

### Study population

The study population consisted of consecutive attendees to the outpatient clinic of the Federal Neuropsychiatric Hospital, Calabar, who were receiving antipsychotic medication during the period of the study and gave informed consent to take part in the study.

### Study design

It was a comparative cross-sectional design.

### Inclusion criteria

Patients should be between 18 and 60 years of age, had been on the same antipsychotic medication for up to 3 months, gave informed consent, were stable enough to complete the study questionnaires and could read and write English or Efik language. Each patient's age (±5 years) and sex were matched to a control.

Controls should be between 18 and 60 years of age who accompany patient to the hospital, had never taken antipsychotic medication, gave informed consent, and who could read and write English or Efik language.

### Exclusion criteria

This includes patients who had depression as a diagnosis or were taking antidepressants, patients and controls who were taking medications known to interfere with sexual function such as antihypertensives, patients who had comorbid medical condition that could interfere with sexual function, and female patients or controls who were pregnant or breast feeding at the time of the study.

### Sample size determination

The sample size for the study was calculated using the computer software for comparative study.

The software gave a value of 62 for each of the study and control groups. Using an attrition rate of 10%, the total became 68.2 for each group. This figure was rounded off to 70 for each group which gave a total sample size of 140 for the study.

### Instruments

1. Questionnaire for collecting information on sociodemographics (medication and illness) factors.
2. Brief psychiatric rating scale (BPRS). This was used to rate the current severity of each participant's illness: The Brief Psychiatric Rating Scale is a psychometric instrument developed by J.E. Overall and D.R. Gorham in 1962. It is a widely used instrument for assessing the positive, negative, and affective symptoms of individuals who have psychotic disorders. It has proven particularly valuable for monitoring response to treatment in patients who have moderate to severe disease [11]. There are 3 versions available, the 16 (the original version), 18 (introduced in 1976), and 24 (introduced in 1986) item versions. The 18-item version was used in this study.
3. International index of erectile function questionnaire (IIEF): This was used to assess the male participants for the presence of sexual dysfunction. There are 2 versions of the instrument, the 15-item questionnaire (the original version) and an abridged 5-item version. The 15-item version was used in this study.
4. Female sexual function index (FSFI): It is used to assess female participants for sexual dysfunction. The Female Sexual Function Index is a 19-item questionnaire, which was developed as a brief, multidimensional self-administered instrument for assessing the fundamental dimensions of sexual function in women in the previous 4 weeks. It was developed on a female sample of normal controls and age-

matched subjects who met Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) criteria for female sexual arousal disorder. It provides scores on a 5-point Likert scale in six domains of sexual function (desire, arousal, lubrication, orgasm, satisfaction, and pain) and also gives a total score.

### Procedure

Data collection took place from June to September 2019. Consecutive attendees to the outpatient clinic were screened for eligibility into the study. Each patient's age (±5 years) and sex were matched to a control that met the eligibility criteria stated earlier. Explanation was provided to the eligible participant about the purpose of the study, and informed consent was sought from them. The eligible participants who gave consent were recruited into the study and were given copies of the self-administered questionnaires (International Index of Erectile Function, Female Sexual Function Index, and questionnaire for sociodemographic and medical information) to fill. Then, the researcher administered the BPRS to the patients. A single venous blood sample (5 ml) was taken for prolactin assay from both patients and controls.

Other information like psychiatric diagnosis, name of antipsychotic, dose, duration of use, and number of episodes of psychiatric illness was taken from patients' case notes.

### Statistical analysis

The Statistical Package for Social Sciences (SPSS) version 22 was used for data analysis. The association between two nonparametric variables was analyzed using the Chi-square test, while association between nonparametric and parametric variables was tested using independent student t-tests and ANOVA. The association between two continuous variables was tested with bivariate correlation. Multiple linear and binary logistic regression analyses were used to test for the predictor(s) of continuous and categorical dependent variables, respectively. All tests were two tailed, and level of significance was set at <0.05.

### Ethical issues

Permission was sought and received from the Health Research Ethics Committee (HREC) of the Federal Neuropsychiatric Hospital, Calabar. Informed consent was sought from all participants before their inclusion in this study. The costs of the prolactin assessment as well as other costs incurred in this study were borne entirely by the researchers.

## RESULTS

### Sociodemographic characteristics of subjects and controls

A total of 70 subjects and 70 controls took part in this study. In both study populations, there were 43 males and 27 females representing 61.4% and 38.6%, respectively (Table 1).

### Sociodemographic correlates of sexual dysfunction among subjects and controls

This study did not find a significant gender difference in sexual function among the subjects ($\chi^2$ = 1.239, df = 1, p = 0.304). The mean age of the subjects who had sexual dysfunction was 34.17 years (SD = ±7.15), and there was no significant relationship between sexual dysfunction and age among the subjects ($t$ = 0.931, df = 68, p = 0.355). The mean age of the controls who had sexual dysfunction was 38.61 years (SD = ±9.07), and it had significant relationship with sexual dysfunction among the controls ($t$ = -3.450, df = 68, p = 0.001)

This study did not find association between marital status and sexual dysfunction among the subjects ($\chi^2$ = 0.227, df = 1, p = 0.746). There was no association between level of education and sexual dysfunction among the subjects ($\chi^2$ = 0.091, df = 1, p = 0.792). There was no association between occupational status and sexual dysfunction among the subjects ($\chi^2$ = 1.706, df = 1, p = 0.210).

### Prevalence of sexual dysfunction among subjects and controls

Among the subjects, the prevalence of sexual dysfunction was 67.2% (n = 47), while it was 40% (n = 28) among the controls. There was no significant difference between the sexual dysfunction among the subjects and controls ($\chi^2$ = 0.173, df = 1, p = 0.796).

Sixteen (59.3%) of the female subjects had sexual dysfunction, but it was not significantly higher than that of the controls ($\chi^2$ = 2.440, df = 1, p = 0.517).

Among the male participants, sexual dysfunction was higher among the subjects (n = 31, 72.1%), but it was not significantly different compared to the controls ($\chi^2$ = 0.497, df = 1, p = 0.224). All the FSFI and IIEF scores (total and domains) of the subjects were significantly lower than that of the controls except in the pain domain of FSFI which did not show a significant difference among the subjects and controls ($t$ = -1.221, df = 26, p = 0.233).

### Relationship between illness severity and sexual dysfunction

Forty-three subjects had diagnosis of schizophrenia, 7 had a diagnosis of schizoaffective disorder, and 4 had a diagnosis of acute psychosis (i.e. a total of 54, 77.1% with an F2 diagnosis), while 16 subjects had bipolar affective disorder (F3 diagnosis). The mean age of onset of illness was 24.4 years (SD = ±7.19), and the mean number of episodes of psychotic illness was 4.56 (SD = ±3.96). The mean BPRS scores was 26.84 (SD = ±9.40).

This study did not find a significant association between psychiatric diagnosis and sexual dysfunction among subjects ($\chi^2$ = 0.024, df = 1, p = 1.000). This study did not find relationship between age of onset of illness and sexual dysfunction among subjects ($t$ = 0.021, df = 68, p = 0.977).

There was no statistically significant relationship between number of episodes of illness and sexual dysfunction among the subjects ($t$ = -0.076, df = 68, p = 0.940).

### Relationship between sexual dysfunction and hyperprolactinemia

The prevalence of hyperprolactinemia was 38.6% (n = 27) among the subjects. Seven (25.9%) of the female subjects and 20 (46.5%) of the male subjects had hyperprolactinemia. None of the male controls had hyperprolactinemia (Table 2).

**Table 1:** Sociodemographic characteristics of subjects and controls.

| Variable | Frequency | | Statistic | p value |
|---|---|---|---|---|
| | Subject | Control | | |
| | n (%) | n (%) | | |
| **Gender** | | | $\chi 2 = 0.000$ | 1.000 |
| Male | 43 (61.4) | 43 (61.4) | | |
| Female | 27 (38.6) | 27 (38.6) | | |
| **Age group** | | | | |
| 18–27 | 9 (12.9) | 17 (24.3) | | |
| 28–37 | 42 (60.0) | 29 (41.4) | | |
| 38–47 | 12 (17.1) | 16 (22.9) | | |
| 48–57 | 7 (10.0) | 8 (11.4) | | |
| **Mean age (SD)** | 34.79 (±7.90) | 34.39 (±9.00) | t = 1.225 | 0.225 |
| Marital status | | | $\chi 2 = 0.591$ | 0.541 |
| Unmarried | 57 (81.4) | 39 (55.7) | | |
| Married | 13 (18.6) | 31 (44.3) | | |
| **Education** | | | $\chi 2 = 3.838$ | 0.074 |
| ≤Secondary | 47 (67.1) | 37 (52.9) | | |
| ≥Tertiary | 23 (32.9) | 33 (47.1) | | |
| **Occupation** | | | $\chi 2 = 7.488$ | 0.010** |
| Unemployed | 41 (58.6) | 3 (18.6) | | |
| Employed | 29 (41.4) | 57 (81.4) | | |
| **Ethnicity** | | | $\chi 2 = 3.870$* | 0.863 |
| Efik | 14 (20.0) | 19 (27.1) | | |
| Igbo | 3 (4.3) | 4 (5.8) | | |
| Yoruba | 0 (0.0) | 1 (1.4) | | |
| Others | 53 (75.7) | 46 (65.7) | | |

Key:
*Fisher's Exact Test
**p is significant (<0.05)

**Table 2:** Hyperprolactinemia and prolactin level among subjects and controls.

| Variable | HP | | Mean Prolactin (SD) | | t-test | p value |
|---|---|---|---|---|---|---|
| | n (%) | | ng/ml | | | |
| | subjects | controls | subjects | controls | | |
| **Overall** | 27 (38.6) | 1 (1.4) | 24.50 (±21.24) | 12.66 (±6.26) | 4.851 | 0.000* |
| **Females** | 7 (25.9) | 1 (3.7) | 28.14 (±24.00) | 16.63 (±7.22) | 2.404 | 0.024* |
| **Males** | 20 (46.5) | 0 (0.0) | 22.21 (±19.26) | 10.16 (±3.95) | 4.547 | 0.000* |

KEY:
HP = Hyperprolactinemia (prolactin level >17.7 ng/ml among males and >29.2 ng/ml among females)
* p is significant (<0.05)

**Table 3:** Binary logistic regression analysis for sexual dysfunction among subjects.

| Variables in the equation | | | | | | |
|---|---|---|---|---|---|---|
| | Wald | df | Odds Ratio | 95% CI | | p value |
| | | | | Lower | Upper | |
| OVERALL | | | | | | |
| HP | 5.769 | 1 | 1.137 | 0.027 | 0.694 | 0.016* |
| Dose | 2001 | 1 | 1.004 | 0.999 | 1.009 | 0.157 |
| Combination(1) | 0.448 | 1 | 0.430 | 0.036 | 5.090 | 0.503 |
| Constant | 1.459 | 1 | 7.530 | 0.227 | | |

**KEY:**
*p is significant (<0.05)
Dose = Daily dose of antipsychotics in chlorpromazine equivalence
Combination (1) = Not using antipsychotic combination therapy

The mean prolactin level for the subjects was 24.50 ng/ml (SD = ±21.24), and it was significantly different from the mean prolactin level of the controls ($t$ = 4.851, df = 69, p = 0.000) (Table 2). The mean prolactin level for the female subjects, 28.14 ng/ml (SD = ±24.00), was statistically different from the mean prolactin level of the female controls ($t$ = 2.404, df = 26, p = 0.024) (Table 2).

There was a statistically significant difference in the mean prolactin level of the male subjects, 22.21 ng/ml (SD=±19.26), compared to the controls ($t$ = 4.547, df = 42, p = 0.000).There was no significant gender difference in the mean prolactin level among the subjects of this study ($t$ = 1.140, df = 68, p = 0.258), but a significant gender difference was seen in the mean prolactin level among the controls ($t$ = 4.275, df = 35.883, p = 0.000).

Two (8.7%) of the subjects with normal sexual function had hyperprolactinemia, while 25 (53.2%) of the subjects with sexual dysfunction had hyperprolactinemia. There was a statistically significant association between sexual dysfunction and hyperprolactinemia among the subjects in this study ($\chi^2$ = 12.904, df = 1, p = 0.000).

One (2.4%) of the controls who had normal sexual function had hyperprolactinemia, while none of the controls who had sexual dysfunction had hyperprolactinemia. There was no significant association between hyperprolactinemia and sexual dysfunction among controls in this study ($\chi^2$ = 0.676, df = 1, p = 1.000).

### Relationship between type of antipsychotic and sexual dysfunction

Thirty-six (51.4%) of the subjects were taking first-generation antipsychotics, while 16 (22.9%) were taking more than one antipsychotic medication. The most prescribed antipsychotic, olanzapine, was taken by 21 (30.0%) of the subjects, while the mean daily dosage of antipsychotic, reported in chlorpromazine equivalence, was 303.81 mg (SD = ±250.83). In this study, the mean duration of use of current antipsychotic was 9.14 months (SD = ±8.60).Twenty-six (72.2%) of the subjects taking first-generation antipsychotics had sexual dysfunction, while 21 (61.8%) subjects taking second-generation antipsychotics had sexual dysfunction. This difference was not statistically significant ($\chi^2$ = 0.867, df = 1, p = 0.447).

This study found a statistically significant association between use of antipsychotic combination and sexual dysfunction among the subjects ($\chi^2$ = 6.656, df = 1, p = 0.013).

There was a statistically significant relationship between the daily dose of antipsychotic and sexual dysfunction among the subjects ($t$ = -3.986, df = 65.229, p = 0.000).

There was no association between the type of antipsychotic/s used and sexual dysfunction among the subjects ($\chi^2$ = 16.827, df = 15, p = 0.216).

### Predictor(s) of sexual dysfunction

A binary logistic regression analysis was done to determine the predictor(s) of sexual dysfunction among the subjects. Prolactin level was found to be the only independent predictor of sexual dysfunction among the subjects (Wald = 6.307, df = 1, OR = 1.131, 95% CI = 1.027 to 1.245, p < 0.05) (Table 3).

## DISCUSSION

Whereas existing local studies have failed to look at the relationship between use of antipsychotics, hyperprolactinemia, and sexual dysfunction among psychiatric patients taking antipsychotic medications (irrespective of the class), this descriptive cross-sectional study has addressed these lapses. We have also studied the sociodemographic correlates of sexual dysfunction using a naturalistic setting.

### Sociodemographic characteristics of subjects and controls

All participants had formal education, while over half had at least a secondary education. Subjects in this study were significantly less likely to be employed than the controls because schizophrenia has been significantly associated with higher rate of unemployment than the general population [21].

### Sociodemographic correlates of sexual dysfunction among subjects and controls

There was no significant gender difference in the prevalence of sexual dysfunction in this study, although it was higher among the male subjects than the female subjects. This is similar to the

findings in the studies by Liu-Seifert *et al.* and Howes among male and female subjects [22, 23]. This is different from the findings from a Scottish study titled Nithsdale Schizophrenia Surveys: Sexual Dysfunction: Case–control study by MacDonald *et al.* [24]. The Scottish study found a much higher prevalence of sexual dysfunction among the subjects than in this present study. They also found a higher prevalence of sexual dysfunction among female subjects than male subjects. The likely reason for these differences might be because they used a self-administered sexual function questionnaire prepared by the authors but was not validated in any study prior to use, a fact that was admitted by the authors of the study as one of their limitations. In addition, they also included subjects not taking antipsychotics. The prevalence of sexual dysfunction is known to differ among subjects with psychosis who were taking antipsychotics and those who were antipsychotic naïve [10, 11]. Furthermore, their study included patients who were using tobacco, whereas these subjects were excluded from this present study. They found that men who smoked had lower prevalence of sexual dysfunction than those who did not smoke. This, they explained that this could be due to the tendency for tobacco to induce metabolism of antipsychotics which results in lower plasma level. This assertion is supported by findings from other studies [22, 25].

This study found no association between sexual dysfunction and age among the subjects. Similarly, Montejo *et al.* found no association [26]. However, Oyekanmi *et al.* found an association between age and occupational status of male patients and sexual dysfunction [7]. The mean age of the patients in their study was 39.5 years, while the greater proportion (about two-thirds) of the patients in this present study is below that age. Older age has been associated with a higher risk of sexual dysfunction by some studies [27–29]. The fact that this present study found an association between age and sexual function among the controls but not among the subjects might suggest that the effect of age on sexual function among patients taking antipsychotic medication might not be as significant as it is in the general population.

This study did not find a significant association between marital status and level of education and the presence of sexual dysfunction among the subjects. This is similar to findings from a study by Montejo *et al.* [26]. This is quite different from the findings by Oju *et al.* [30]. Their study found a significantly higher prevalence of sexual dysfunction among the male and female subjects who were not married and less educated than among those who were married and more educated. However, their study was done among general psychiatric outpatients, while this present study was done among patients taking antipsychotic medications only. There might be factors that could affect sexual function of the married or unmarried patients among the general psychiatric outpatients which might differ from a population taking antipsychotic medications alone. One of such factors is the fact that some studies have shown that marriage requires certain social abilities which a patient with schizophrenia might lack and that Schizophrenia is associated with cognitive impairment which might put them at an educational disadvantage [31, 32]. However, the most severe cases, which might not have been married and less educated, were excluded from this study to select those who were stable and could fill in the study questionnaires. This could have been responsible for the difference in outcome from the two studies.

This study did not find an association between sexual dysfunction and the occupational status among the subjects. This is similar to findings from a study [26] by Montejo *et al.* However, Oyekanmi *et al.* found an association between occupational status and sexual dysfunction [7]. While this study only categorized patients as either employed or unemployed without stating how patients who were students were grouped. A difference in categorization between the two studies may explain the contrast in outcomes.

This study did not find any association between diagnosis and sexual dysfunction among subjects. A similar result was reported by Kandrakonda *et al.* [33]. A study by Smith *et al.* found depression to be associated with sexual dysfunction [34]. This present study excluded patients with diagnosis of depression. Furthermore, our study only included subjects who had been receiving treatment and were stable enough to fill the study questionnaire. Mosaku and Ukpong suggested that this might lead to selection of patients with only few active psychopathologies which might have affected the outcome when the diagnoses are considered [27].

This study found no association between age of onset of illness and number of episodes of illness and presence of sexual dysfunction among subjects. The age of onset of some psychotic illnesses or the number of episodes might be an indication of severity of the illness. For example, schizophrenia with earlier age of onset and frequent relapse is associated with a poorer outcome [35, 36]. Similarly, a poor prognosis bipolar affective disorder might be expected to have an earlier age of onset [37]. Since this study excluded patients who were not stable enough to fill the study questionnaires, the most severe cases might have been excluded.

### Prevalence of sexual dysfunction among subjects and controls

Prevalence of sexual dysfunction among subjects was higher than among controls in this study. The prevalence rate is similar to what was reported in a Nigerian study by Olisah *et al.* among subjects attending outpatient clinic in a psychiatric hospital in Northern Nigeria [38]. However, Üçok *et al.* found a much lower rate among subjects taking antipsychotic medication from a study involving multiple centers in Turkey [39]. The study in Turkey was done among 847 patients between 18 and 45 years of age, with diagnosis of schizophrenia and had received adequate doses of antipsychotics for at least 3 months with a daily haloperidol equivalent dose of between 5 mg and 15 mg. Certain factors, notable in their study, might have been responsible for the lower rate of sexual dysfunction. One of these being the maximum age limit of 45 years adopted in the study. It has been shown by other studies that sexual function worsens with age [7, 34]. Therefore, excluding the older age group, who are more likely to have sexual dysfunction, could be a reason for the lowered prevalence of sexual dysfunction they reported. Another possible explanation for the lower rate of sexual dysfunction in their study could be the limitation of the maximum antipsychotic dose to 15 mg in haloperidol equivalence (500 mg chlorpromazine equivalence) compared to a maximum antipsychotic dose of 1250 mg chlorpromazine equivalence used in my study. The use of high-dose antipsychotic has been found in some studies to be associated with the presence of sexual dysfunction [7, 34].

### Relationship between illness severity and sexual dysfunction

This study found no association between the severity of psychopathology and sexual dysfunction. An American study by Olfson *et al.* among patients with schizophrenia taking antipsychotics had similar findings [16]. This contrasts with the finding from a study by Üçok *et al.* which found a significant association between clinical severity of illness and sexual dysfunction [39]. The study differs from present study in the instrument used to assess the severity of illness. According to the authors of the Turkish study, "clinical severity of the disease was evaluated using the" Clinical Global Impressions (CGI) scale unlike the present study that used BPRS to assess severity of the illness. The CGI scale unlike the BPRS measures average severity of symptoms over preceding seven days [40]. The differences between these two instruments might be responsible for the difference in outcomes of the two studies.

### Relationship between sexual dysfunction and hyperprolactinemia

In this study, hyperprolactinemia was significantly associated with sexual dysfunction among the subjects. Knegtering *et al.* found an association between sexual dysfunction and prolactin level [41]. This contrasts with the report by Ghadirian *et al.* which did not show association between prolactin level and sexual function among female subjects [42]. The difference in outcome between their study and present study may be because the sexual function instrument used in their study was not validated, which may affect finding [43].

Furthermore, Liu-Seifert *et al.* found no association between prolactin levels of subjects taking antipsychotics and presence of sexual dysfunction [22]. Difference between the outcome of the American study and present study might be because their study included subjects who were taking psychoactive substances such as alcohol and tobacco that have been associated with sexual dysfunction, whereas these subjects were excluded from this present study [38]. Moreover, the American study found tobacco smoking, a known inducer of antipsychotic metabolism, to be associated with good sexual function among the subjects [25]. It may reduce bioavailability of antipsychotics in American study and therefore affect prolactin level. This may explain the reported lack of association.

### Relationship between type of antipsychotic and sexual dysfunction

This study found no significant difference between the prevalence of sexual dysfunction among subjects taking first- and second-generation antipsychotics. A similar outcome was reported by Liu-Seifert *et al.* [22]. However, Aizenberg *et al.* studying subjects taking clozapine and typical antipsychotics [44] found a significant difference between the prevalence of sexual dysfunction among subjects who were taking first-generation antipsychotics and those taking clozapine. This might be because it is not usually associated with prolactin increase which may cause sexual dysfunction among patients taking antipsychotics. This may be due to clozapine's selectivity for the mesolimbic dopaminergic pathway [45–47].Present study found no association between the types of antipsychotics and sexual dysfunction. Kockott and Pfeiffer found similar outcome in their study on sexual disorders among psychiatric subjects taking antipsychotics [11]. Nevertheless, Oyekanmi *et al.* found haloperidol to be associated with sexual dysfunction [7]. However, their study included subjects taking first-generation antipsychotics unlike our study that included subjects taking first- and second-generation antipsychotics.

This study found association between the dose of antipsychotics and sexual dysfunction similar to reported by Oyekanmi *et al.* [7]. However, Liu-Seifert *et al.* did not find a significant association overall between dose of antipsychotics and sexual dysfunction [22]. Noteworthy is that subjects in American study used tobacco which may induce antipsychotic metabolism [25]. Therefore, the bioavailability of the antipsychotics used in the American study will be significantly reduced compared to the bioavailability of the antipsychotics used by the subjects in this present study since none of them were using tobacco.

This study found a significant association between the use of antipsychotic combination therapy and the presence of sexual dysfunction. Antipsychotic combination has been associated with high dose prescription [48].

### Predictors of sexual dysfunction

This study did not find any significant association between the different types of antipsychotics, use of antipsychotic combination therapy, and the daily dose of antipsychotics included in the study and having sexual dysfunction alone. Oyekanmi *et al.* found the dose of antipsychotics and use of haloperidol to be predictive of sexual dysfunction but did not assess the prolactin level [7].

## CONCLUSION

This study showed that sexual dysfunction and hyperprolactinemia are higher among patients taking antipsychotics than a control group not taking antipsychotics. The first-generation antipsychotics were not more associated with hyperprolactinemia or sexual dysfunction than the second-generation antipsychotics. This study also showed that hyperprolactinemia is predictive of sexual dysfunction.

The clinical implication of the findings from this study is that psychiatrists should be aware of the relationship between use of antipsychotics, hyperprolactinemia, and sexual dysfunction. Furthermore, the knowledge that these side effects do not depend on the class of antipsychotics rather on the individual antipsychotic. Also, psychiatrists need to understand the likely impact the presence of these side effects might have on the patient's quality of life and treatment adherence.

## LIMITATIONS

This is a cross-sectional study and as such cannot determine causality of sexual dysfunction or hyperprolactinemia by antipsychotics unlike a prospective study where serial assessments will be done. However, the peculiarities of the individual who is acutely psychotic present an interesting challenge in reliably assessing the sexual function.

Although the sample size for this study was correctly calculated, the relatively small sample size used limits generalization of the findings from this study. Nevertheless, some other studies have used even smaller sample sizes. Despite this, findings from this study may serve as an important baseline for future studies.

## FUTURE RESEARCH DIRECTION

Large-scale, multicenter, longitudinal studies that controls for important confounders of sexual dysfunction among patients taking antipsychotic medications are encouraged to be able to elucidate the true nature of the relationship between antipsychotics, hyperprolactinemia, and sexual dysfunction.

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