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# Comparative prescription patterns of antipsychotics among schizophrenic patients attending two public health facilities in North-Eastern and North-Central Nigeria: a cross-sectional study

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**Abstract**
In the care of patients, assessment of the use of drugs is very imperative as it shows the quality of care delivered to patients by the caregivers. The study aimed to compare the prescription patterns of antipsychotics in two public healthcare facilities in Nigeria using a standardized World Health Organization instrument. The studies were conducted at the General Hospital, Offa (GHO), Kwara State, and the Federal Neuropsychiatric Hospital, Maiduguri (FNPHMM), Borno State. Ethical approvals were obtained from the studied facilities. A total of 625 prescriptions in each of the facilities were selected by random sampling. Frequency distributions and student t-test were used. The average number of drugs prescribed per encounter was 3.9 in the GHO, while 1.2 was recorded in the FNPHMM. Injections were prescribed in 14.4% and 18.7% of encounters in the GHO and the FNPHMM, respectively. One hundred percent (100.0%) of the drugs were prescribed by generic name in the GHO and 98.2% in the FNPHMM. The percentage of drugs from the National Essential Drug List was 72% in the FNPHMM and 100% in the GHO. The prescribing indicators assessed were found to be below standard in the FNPHMM while the GHO showed polytherapy.

*Keywords*: Antipsychotic drugs, prescribing patterns, World Health Organization drug indicators, Nigeria.

## INTRODUCTION

Schizophrenia is a chronic debilitating illness of the mind with consequences on occupational social and interpersonal functioning among the affected patients. It significantly contributes to the world's burden of disease [1]. Antipsychotic agents are the main treatment as they improve positive symptoms with less efficacy on negative and cognitive symptoms. One third of patients with schizophrenia achieve better improvement with antipsychotic monotherapy [1]. The World Health Organization (WHO) drug use indicators had assisted greatly in identifying deficiencies in the writing of drug prescription patterns [2]. Many factors are related to the antipsychotic prescribing behavior of healthcare practitioners in different settings.

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These include healthcare policies, availability and cost of drugs, psychiatric training, preferred treatment modalities, health status, gender, income, weight, age, education, patient adherence, and multiple drug usage [3]. Periodical revisions of antipsychotic drug use are also essential as the drugs are associated with various adverse effects including withdrawal symptoms, drug interactions, and toxicities [4]. Without prior information on drug prescription patterns, recommending appropriate measures in improving the quality of life, therapeutic outcome and prescribing habits of the prescribers can be challenging [5]. According to a previous study in India, about 2.20 was the average number of drugs per prescription in schizophrenia patients [6]. Also, there was an earlier report that polypharmacy was common with typical and atypical antipsychotic prescription patterns majorly utilized in Spain [7]. Other researchers in China discovered that there is no upward trend in the rate of second-generation antipsychotic usage among outpatients [8].

The study on antipsychotic pattern of prescription in Nigeria is dearth as merely 3% of publications on health are on psychiatry [1]. Thus, identification of areas of need in making decisions on policy directions and monitoring its progress could be challenging [9]. This study aimed to compare the antipsychotic prescription pattern in two public healthcare hospitals in Nigeria using WHO indicators to encourage a rational antipsychotic drug prescription among mental healthcare givers.

## EXPERIMENTAL METHODS

**Description of study areas.** The two study sites included were; the Federal Neuropsychiatric Hospital Maiduguri (FNPHM), North-Eastern Nigeria, and the General Hospital Offa (GHO), North-Central Nigeria. The FNPHM is a tertiary health institution that was established by the Federal Government of Nigeria for the North-East zone to carry out research, training, treatment, and prevention in the areas of Neuroscience and Mental Health [10]. It serves other neighbouring states (Yobe, Bauchi, Taraba, and Gombe) and countries (Niger Republic, Chad and Cameroon). The GHO is a secondary healthcare facility owned by the Kwara State Ministry of Health. The facility is a 50-bed hospital and provides in- and out-patient healthcare including mental health services [11]. The choice of these facilities was to evaluate the pattern of antipsychotic prescriptions in two geo-political zones of Nigeria for WHO prescribing indicators' compliance.

**Sample population and sample size.** A total of 625 patients' prescriptions were reviewed during the study period from each of the two facilities. World Health Organization (WHO) recommended that a minimum of 600 patient records should be evaluated retrospectively for drug prescribing study in health facilities [5]. To increase the power of this study, 5% was added resulting in a total of 625 prescriptions.

**Study design.** A retrospective cross-sectional, hospital-based study was conducted at the Outpatient Unit of the FNPHM and the Behavioural Unit of the GHO. The study was carried out over two years, between February 2018 and January 2020. The prescription patterns of antipsychotic drugs and WHO prescribing indicators were used. Those prescriptions included were; prescriptions of schizophrenic patients between the age of 20 and 70 years, prescriptions of patients diagnosed to have schizophrenia by psychiatrists, and schizophrenic patients whose medical folders were available in record sections of the Federal Neuropsychiatric Hospital Maiduguri and Behavioural Unit of the General Hospital, Offa.

**Study instruments:**

**Socio-demographic form.** The form was designed by the researchers and contained four questions. The questions were about the patients' age, gender, marital status,

educational qualifications and monthly income.

**Health and antipsychotic medication form.** This proforma contained nine questions on patients' treatment variables.

**Patients' medical files.** These files were used to fill the research instruments.

**Data collection.** Systematic random sampling was employed to select patients' prescriptions for the study. One prescription was chosen for every five prescriptions. Six hundred and twenty-five prescriptions of schizophrenic patients from each of the facilities were examined and analyzed for prescription patterns using WHO and other drug indicators. The other indicators were shown on the next page. Patient case notes without interviews were used to extract information on socio-demographic variables (age, gender, marital status and monthly income), and treatment variables (duration of treatment, name of each medication: generic or branded and the number of oral medications on prescription (per encounter).

**The WHO prescribing drug indicators were as follows:**

1. The average number of drugs per encounter: This was obtained by dividing the total number of drugs prescribed, by the number of encounters studied.
2. Percentage of drugs prescribed by generic name: The calculation was achieved by dividing the number of drugs prescribed by generic name, by the total number of drugs prescribed, and multiplied by 100.
3. Percentage of encounters with an injection prescribed: This was found by dividing the number of encounters in which an injection was prescribed, by the total number of encounters assessed, and multiplied by 100.
4. Percentage of drugs prescribed from Essential Drugs List (EDL) or formulary-This was obtained by dividing the number of drugs prescribed from the EDL or formulary, by the total number of drugs prescribed, and multiplied by 100.

**Other indicators used were:**

1. Percentage of fixed dose combinations prescribed.
2. Percentage of patients receiving more than one antipsychotic.
3. Percentage of polypharmacy (prescribing 4 or more drugs).

**Antipsychotic drug combination.** The antipsychotic drug combination is the use of more than one antipsychotic drug at the same time for the same individual. Studies on antipsychotic drug combinations are steadily increasing. The types of combinations differ and include:

i. Two Second Generation Antipsychotic drugs.
ii. One Second-Generation Antipsychotic drug plus one First Generation Antipsychotics.
iii. Two First Generation Antipsychotics.
iv. Other combinations involving two or more Second Generation Antipsychotics or First-Generation Antipsychotics.

**Data analysis.** Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) for Windows Version 23.0 (SPSS Inc; Chicago, IL, USA). Frequency distribution tables were produced from the analysis. Comparisons of results were made with WHO prescribing indicators using student t-test. Statistical significance was set at $p < 0.05$.

**Ethical consideration.** Ethical clearance to conduct the research was obtained from the Research and Ethics Committee of the Federal Neuropsychiatric Hospital Maiduguri with a reference number FNSH/112019/REC036. In the General Hospital Offa, approval was sought from the Department of Research and Protocol, Ministry of Health, Ilorin, Kwara State with an approved reference number of MOH/KS/EU/777/235.

## RESULTS

**Sociodemographic characteristics of patients on antipsychotic drugs at the General Hospital, Offa (GHO), and Federal Neuropsychiatric Hospital, Maiduguri (FNPHM).** Out of 625 patients' prescriptions studied in each of the two health facilities, the females were 64.8% and 55.7%, in the General Hospital Offa and the Federal Neuropsychiatric Hospital, Maiduguri, respectively (Table 1). The mean age of the

patients at GHO was 36.51±149 years and 30.55±126 years for FNPHM. In this study, 578(92.5%) of the patients were unemployed in GHO and 559 (89.4%) in FNPHM. Three hundred and sixty-five patients (58.4%) in GHO and 306 (49.0%) were married.in FNPHM. Also, the majority of 359 (57.5%) in GHO and 397 (63.5%) in FNPHM had no formal education. However, those with tertiary education in GHO 97 (15.5%) doubled the patients in FNPHM 46 (7.4%).

**Treatment variables of the patients on antipsychotic drugs at the General Hospital, Offa, and Federal Neuropsychiatric Hospital, Maiduguri. Nigeria.** Haloperidol 174 (27.8%) in FNPHM and chlorpromazine 449 (71.8%) in GHO were the most commonly prescribed First-Generation Antipsychotic Agents (FGAs) in both facilities followed by Trifluoperazine 73 (11.6%) in GHO and 93 (14.9%) in FNPHM as oral medications. Injectable Fluphenazine 126 (20.2%) in the GHO and 36 (5.8%) in FNPHM was commonly used in both hospitals as First-Generation Antipsychotic Agent. Olanzapine 6(1.0%) in GHO, 126 (20.2%) for FNPHM. Also, risperidone 3 (0.5%) in GHO and 67 (10.7%) in FNPHM were less prescribed Second-Generation Antipsychotic Agents in both facilities. However, these oral medications were widely used in Maiduguri. Clozapine 2 (0.3%) was the least prescribed Second-Generation Antipsychotic Agent (SGA) in Maiduguri but was not recommended for any patients in Offa. Overall, in GHO only a few 9 (1.4%) patients were on second generation antipsychotic agents as compared with 195 (32.2%) in FNPHM with a statistically significant difference at a p-value of 0.043. This was contrary with first generation agents 616 (98.6%) in GHO and 430 (68.8%), though no statistically significant difference was observed (at p-value > 0.916). Most patients in General Hospital, Offa were on antipsychotic agents for a duration of four to five years 381 (61.0%) whereas, in Maiduguri, the majority 259 (41.4%) were between three and four years as shown in Table 2.

**Antipsychotics combination prevalence at General Hospital, Offa, and Federal Neuropsychiatric Hospital, Maiduguri. Nigeria.** Despite the prescribed WHO treatment guideline and numerous studies that encouraged antipsychotic monotherapy use, about 20% of the prescriptions were polytherapy in the Federal Neuropsychiatric Hospital Maiduguri. However, in the General Hospital Offa, the prevalence of antipsychotic polytherapy was 100.0% (Table 3).

**Comparison of prescription patterns of antipsychotics in Federal Neuropsychiatric Hospital, Maiduguri and General Hospital, Offa.** There was a statistically significant difference ($p = 0.042$) in the average injectables prescribed in the two facilities studied (FNPHM with 18.7% and GHO, 14.4%). The average percentage of drugs prescribed by generic names in this study was 98.2% in the FNPHM and 100.0% in the GHO. Hence, there was no statistically significant difference ($p = 0.570$) observed. A statistically significant difference at a p-value of 0.001 in the average number of drugs per prescription (1.2) in FNPHM and (3.9) in General Hospital, Offa was noted. All the drugs used in General Hospital were (100.0%) and were obtained from National Essential Drug List and only 72.0% from EDL in Maiduguri with a statistically significant difference of ($p = 0.026$) (Table 4).

**Table 1:** Sociodemographic characteristics of patients on antipsychotic drugs at the General Hospital, Offa (GHO), and Federal Neuropsychiatric Hospital, Maiduguri (FNPHM)

| Sociodemographic characteristics | | GHO N= 625 (%) | FNPHM N= 625 (%) |
|---|---|---|---|
| Gender | Male | 219 (35.2) | 277 (44.3) |
| | Female | 406 (64.8) | 348 (55.7) |
| Age (years) | 20 | 149 (23.8) | 138 (22.1) |
| | 21-30 | 245 (39.2 .) | 246 (39.4) |
| | 31-40 | 112 (17.9) | 125(20.0) |
| | 41-50 | 53 (8.5) | 77(12.3) |
| | 51-60 | 40 (6.4) | 21(3.4) |
| | 61-70 | 26 (4.2) | 18 (2.8) |
| Mean age and standard deviation | | 36.51 ± 14.9 | 30.55 ±12.62 |
| Level of Education | No formal education | 359 (57.5) | 397 (63.5) |
| | Primary education | 132 (21.1) | 58 (9.3) |
| | Secondary education | 37 (5.9) | 124 (19.8) |
| | Tertiary education | 97 (15.5) | 46 (7.4) |
| Marital Status | Single | 149 (23.8) | 250 (40.0) |
| | Married | 365 (58.4) | 306 (49.0) |
| | Divorced | 65(10.4) | 33 (5.3) |
| | Widowed | 46 (7.4) | 36 (5.7) |
| Employment Status | Employed | 47 (7.5) | 66 (10.6) |
| | Unemployed | 578 (92.5) | 559 (89.4) |

**Table 2:** Treatment variables of the patients on antipsychotic drugs at the General Hospital, Offa, and Federal Neuropsychiatric Hospital, Maiduguri. Nigeria

| | Facility | GHO N= 625 (%) | FNPHM N= 625 (%) | p-value |
|---|---|---|---|---|
| Duration on antipsychotic drugs (years) | 2-3 | 102 (16.3) | 74 (11.8) | |
| | 3-4 | 53 (8.5) | 259 (41.4) | |
| | 4-5 | 381 (61.0) | 213 (34.1) | |
| | > 5 | 89 (14.2) | 79 (12.7) | |
| 1st line antipsychotic drugs | Flupentixol | - | 5 (0.8) | |
| | Chlorpromazine | 449 (71.8) | 32 (5.12) | |
| | Trifluoperazine | 73 (11.6) | 93 (14.9) | |
| | Haloperidol | 58 (9.3) | 174 (27.8) | |
| | Fluphenazine | 36 (5.8) | 126 (20.2) | |
| | Percentage of First-line agents used by each facility | 616 (98.6) | 430 (68.8) | 0.916 |
| 2nd line antipsychotic agents | Risperidone | 6 (1.0) | 126 (20.2) | |
| | Olanzapine | 3 (0.5) | 67 (10.7) | |
| | Clozapine | - | 2 (0.3) | |
| | Percentage of Second-line agents used by each facility | 9 (1.4) | 195 (31.2) | 0.043* |

* Statistically significant at $P < 0.05$.

**Table 3:** Antipsychotics combination and the prevalence at General Hospital, Offa, and Federal Neuropsychiatric Hospital, Maiduguri. Nigeria

| | | GHO N= 625 (%) | FNPHMM N= 625 (%) |
|---|---|---|---|
| No of drugs | 1 | 0 (0.0) | 526 (84.2) |
| | 2 | 74 (11.9) | 95 (15.2) |
| | 3 | 548 (87.7) | 4 (0.6) |
| | 4 | 3 (0.4) | 0 (0.0) |
| Percentage of Combination Therapy | Monotherapy | 0 (0.0) | 526 (84.2) |
| | Polytherapy | 625 (100.0) | 99 (15.8) |

**Table 4:** Comparison of prescription patterns of antipsychotics in Federal Neuropsychiatric Hospital, Maiduguri and General Hospital, Offa

| WHO Prescribing Indicators | Study values at GHO | Study values FNPHM | WHO values | P-value |
|---|---|---|---|---|
| The average number of drugs per prescription | 3.9 | 1.2 | 1.6-1.8 | 0.001* |
| Percentage of drugs prescribed in generic | 100% | 98.2 % | 100.0 % | 0.570 |
| Percentage of injectable prescribed | 14.4% | 18.7 % | <10.0 % | 0.042* |
| Percentage of drugs prescribed from the Essential Drug List | 100 % | 72.0 % | 100.0% | 0.026* |

* Statistically significant at $P < 0.05$.

## DISCUSSION

The choice and pattern of antipsychotics utilization in patients with schizophrenia is essential to the understanding and determination of those crucial factors in drug treatment that mitigate or aggravate patients' suffering and positively or negatively affect the outcome of the disease [3]. The age and sex of the respondents in this study were comparable to those reported by similar studies [12, 13]. The mean age of the patients was 33 years in the two facilities studied. However, a recent study has reported that the commonest age group among these patients was below 30 years [14]. Five hundred and sixty-eight (90.9%) of the patients were unemployed in the studied facilities. Similar studies reported that the majority of them were unemployed [15]. Employment rates among patients with schizophrenia are low, with an estimate from a European study ranging from 8 to 35% [16]. Individual factors (such as job histories), illness-related factors (such as illness severity) and societal conditions (such as discrimination and social welfare policy) are all potential contributors to variations in employment rates [17]. Though the employment of a patient does not attest to their capability to afford medications, some unemployed patients get adequate family and other caregivers' support for their treatment [18].

Haloperidol and chlorpromazine were the most 623 (99.68%) commonly prescribed First-Generation Antipsychotic Agents (FGAs) in both facilities. Olanzapine and risperidone were the prescribed Second-Generation Antipsychotic Agents, especially in FNPHM. Clozapine was the least 3(0.5%) prescribed Second-Generation Antipsychotic Agent as observed in the current studies. The basis could be that olanzapine and clozapine were used to treat difficult-to-manage schizophrenic cases. Other probable reasons include the non-affordability of the drugs by the patients, the physicians' conservative method of avoiding various adverse effects, and routine examinations associated with this drug utilization [19]. Contrarily, recent researchers reported that SGAs have better tolerability and superior efficacy compared with FGAs and that SGAs were more favorably exploited than FGAs. The FGAs being affordable are prescribed in treating unresponsive patients and those intolerant to newer medications [20]. However, previous studies reported that there was no clear

evidence that FGAs are less effective or tolerated than SGAs. Leppien et al (2019) concluded that FGAs were preferred drugs during the initiation of treatment of schizophrenia, except the patient experienced intolerable side effects. In developing countries like Nigeria, due to relatively expensive SGAs, FGAs were consistently prescribed with a decline in transition to SGAs [21]. The findings of this study were in upkeeping with an earlier study in Nigeria that found haloperidol and other old-generation antipsychotics were the most commonly prescribed at the initiation of treatment [3]. This therefore clearly affirmed persistent prescriptions of relatively cheaper drugs like haloperidol and chlorpromazine at initiation phase in the two facilities of study. The efficacy of FGAs in reducing positive symptoms is not in doubt but their action is quite limited in other outcomes, notably, their effect on negative symptoms [22]. The side effects of haloperidol and other FGAs constitute a major problem in the pharmacotherapy of schizophrenia. This has largely contributed to the search and emergence of SGAs, these drugs have been increasingly preferred over FGAs. Furthermore, there are treatment guidelines in some countries which recommend SGAs over FGAs [15]. The rationale for the preference of SGAs over FGAs could be that side effects were a major problem associated with the use of FGAs [23]. Side effects themselves may cause or worsen schizophrenia symptoms, including negative, positive and cognitive symptoms. In addition, they may increase the risk for other medical disorders and can affect the patients' quality of life and willingness to take the medication [4]. In addition, another report has noted that there is no clear evidence that SGAs are more effective or better tolerated than FGAs [21]. Those authors concluded that FGAs should be used in the initial treatment of an episode of schizophrenia unless the patient has not previously responded to these drugs or have unacceptable extrapyramidal side effects [21]. The choice of which drug to prescribe is generally influenced by several factors, such as cost of the drug, side effects, actual or perceived efficacy, familiarity with the drug, safety, patient's socioeconomic status, efficacy, formulary status, patients' tolerability, clinical symptoms and prescription restrictions [24]. Furthermore, prescription choices are determined by a complex interaction of multiple factors, considerations and circumstances [25].

The average number of drugs prescribed per encounter was (1.2) in Federal Neuropsychiatric Hospital, Maiduguri (FNPHMM), which is lower than the majority of values obtained in previous studies: Yemen 1.5, Uganda 1.9, Sudan 1.4, Tanzania 2.3, and 1.44 in Bangladesh [26], but the value obtained at General Hospital, Offa (GHO) (3.9) was higher than the earlier studies [ 27]. However, the findings obtained from previous researchers reported that (4.4) and (4.8) were comparable with the results found in GHO [28, 19]. Thus, the lower value in FNPHM is a pointer to the low level of polypharmacy practice which in turn improves the therapeutic outcome in patients and reduces the negative effects associated with poly pharmacy. The effects of polypharmacy include increased incidences of side effects, drug-drug interactions, confusion where aged patients are involved and non-adherence by patients to the drug regimen as a result of the large number of drugs to be taken at a time and for prolonged periods in most cases [29]. This is contrary to the findings in GHO where polypharmacy prescription pattern was found. In this study, the average injection prescribing pattern in the facilities studied was higher (18.7% in FNPHM and 14.4% in GHO) than the standard value of less than 10%. These values were similar to the findings in Ethiopia with 18.3% but lower when compared with results from previous studies in other countries such as Iran at 58% [30]. However, these results were

higher than the value of 3.9% obtained in Nigeria [31]. Writing prescriptions using a generic name is an important drug-use quality to avoid undesirable drug interactions, adverse drug reactions, medication errors and save cost [29]. The average percentage of drugs prescribed by generic name in this study was 98.2%, in FNPHM and 100.0% in GHO which exhibited the acceptable values in terms of the WHO criteria about prescribing by generic names (100%). This compliance with WHO criteria could probably be because branded drugs are very costly to be afforded by the patients that were dependent on families and friends. Prescription of drugs in their generic names leads to patient adherence and less financial burden contrary to the use of brand names. Similar results showed that a high level of generic prescriptions found could probably be attributed to the fact that the study was conducted in governmental health centers, where the procurement of generic drugs is the prevailing practice [27]. The study also found that most of the drugs prescribed were from the National Essential Drug list in GHO and FNPHM. These figures comply with WHO standard values but are lower than the study in Ethiopia [32].

Antipsychotic medications are the first line for the treatment of patients with schizophrenia. Although monotherapy is supported, antipsychotic combination therapy in schizophrenia is common in clinical practices [33]. Despite recommendations by guidelines to avoid combinations of antipsychotics, unless after multiple trials of antipsychotic monotherapy, it is a common practice to use combinations that have no clinical benefits or economic drawbacks [34]. This practice leads to unnecessary expenses and exposes the patient to severe adverse drug effects. Despite the treatment guideline and several studies that encouraged the use of antipsychotic monotherapy, in the studied facilities, the number of antipsychotic drugs combination among patients in FNPHM was 15.8%. This value was similar to the findings of (14.9%) in India but lower than earlier studies in other countries such as; Canada; (25.7%), South Africa; (28.4%) and Ethiopia; (28.2%) [35-38]. However, in GHO, the prevalence of antipsychotic combination therapy was 100.0%. This value was similar to previous studies conducted in Nigeria, (92.0%) [39] and (92.0%), [40]. The discrepancies in the prevalence of antipsychotic drug combinations observed in the two facilities could probably be related to the educational qualifications of the prescribers. Contrarily, further research work on antipsychotic polypharmacy reported that higher rates of antipsychotic combination therapy are beneficial in the treatment of resistance, management of acute exacerbation of psychosis, use of high-dose monotherapy and arrested medication switch [41].

**Conclusion.** Based on WHO prescribing indicators, some of the prescribing practices observed in this study fell short of standard requirements. The prevalence of polypharmacy remained high in one of the facilities. Hence, the need arises to watch out for drug-drug interaction. Also, there is a need to reduce injection used to prevent injection-related hazards and infections. Compliance with the Essential Drug List as observed in the study is quite commendable.

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