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## MEDICATION ADHERENCE IN SCHIZOPHRENIA: THE ROLE OF FAMILY SUPERVISION, DOSAGE FREQUENCY AND MEDICATION KNOWLEDGE

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### ABSTRACT

**BACKGROUND:** Non adherence to antipsychotic medications in patients with schizophrenia leads to frequent relapses, poor treatment outcome, reduced quality of life and significant increases in healthcare cost in a resource poor country and a healthcare system already overburdened by infectious illnesses and other diseases. This study verified the adherence of people with schizophrenia and compared among adherent and non-adherent patients the impact of supervised treatment, regimen complexity and patients' understanding of medication regimen.

**Objectives:** The aim of this study was to assess the prevalence of poor treatment adherence to anti-psychotic medications and to explore its association with these potentially modifiable factors.

**Method:** This study is a cross sectional study of outpatients with schizophrenia in a tertiary healthcare facility in southeast Nigeria (n=150). The participants were aged 18 years and above, with illness duration of at least one year who have been on oral antipsychotic medications were selected using systematic sampling. They were assessed for socio-demographic details, dosage frequency, understanding of treatment regimen and availability of treatment supervision.

**Results:** The prevalence of treatment non-adherence was 52%. The factor most significantly associated with adherence was availability of treatment supervision (OR 0.055, 95%CI= 0.021-0.142 p-value <0.001). Other significant variables on univariate analysis include marital status ( $\chi^2=5.035, df=1, p=0.03$ ), number of tablets

taken per day ( $\chi^2=10.667, df=1, p=0.01$ ) and patients' living arrangement ( $\chi^2=4.287, df=1, p=0.03$ ). The non-adherent patients were more likely to be living alone, less likely to be married, less likely to have supervised treatment and also less likely to be employed.

**Conclusion:** Adherence to antipsychotic medications among patients with schizophrenia is suboptimal. Active intervention strategies should take these factors into consideration while implementing programmes to improve adherence behaviour among out-patients with schizophrenia.

**Key words:** schizophrenia, antipsychotics, adherence.

### INTRODUCTION

When patients with schizophrenia do not adhere to their drug prescriptions, the efficacy of the medications declines.<sup>28</sup> Schizophrenia is a chronic mental illness characterised by psychosis, negative symptoms, cognitive impairments and affects approximately one percent of the world population.<sup>1</sup> Currently, antipsychotic medication is the primary treatment modality for the management of acute psychosis as well as for relapse prevention in long term maintenance treatment.<sup>2</sup> They are highly effective in attenuating symptoms and preventing acute episode relapse. Adherence with medication describes the extent to which a patient's medication intake matches the recommendations from a health care provider.<sup>9</sup> Non-adherence in chronic disease has been described as taking less than 80% of the prescribed treatment.<sup>8</sup>

Non-adherence to medication has been and continues to be a major problem the world over across many medical disciplines.

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Studies on this subject show that adherence is about 50% for medication in chronic diseases.<sup>8</sup> It is recognised as a common problem with many chronic illnesses.<sup>3</sup> It has been shown that the overall compliance rate for patients with chronic mental disorder was lower than those with physical disorders.<sup>10</sup> Adherence increases the likelihood of positive outcomes in all aspects of a patient's life including better symptom control,<sup>4</sup> reduced risk of relapse and rehospitalisation,<sup>5</sup> and improvement in quality of life, social and occupational functioning.<sup>5</sup> Conversely, poor adherence results in persistence of symptoms and predisposes the patient to relapse which can contribute to a poorer long term prognosis.<sup>6</sup> Several studies have been carried out to identify risk factors for treatment non-adherence. Four types of factors affecting adherence have been identified: factors due to medication (side effects, dosing schedule, efficacy), factors linked to patients (level of education, age, marital status, delusions, lack of insight) factors depending on the therapeutic relation with the clinician, social/environmental/economic factors (living arrangement, supervision, family support, stigmas, cost, access to treatment facility).<sup>7</sup>

Recent studies have generated varied results of factors associated with treatment non-adherence in chronic illnesses. A number of patient and medicine related factors which have been cited in some studies include: poor patients knowledge about the disease and the reason medication is needed,<sup>11</sup> degree of psychopathology<sup>18</sup> frequency of dosing and pill burden/complex drug regimen,<sup>13,14</sup> side effects burden of medications,<sup>15,16</sup> availability of supervision, family and social support<sup>7</sup> as positively associated with medication adherence. It is also well known that a person's knowledge and understanding of medications regimen, motivation, and attitudes towards medication significantly influences treatment adherence.<sup>12</sup>

Most of the studies on this subject have been

carried out in developed countries setting leaving a gap in knowledge as to which risk factors for non-adherence are more relevant in a resource poor setting like ours. This study, designed to make some contributions in this regard has the following aims. To determine the prevalence of self reported treatment non-adherence among patients with schizophrenia and to assess its association with availability of medication supervision, dosage frequency and patients' understanding of medication regimen.

## MATERIALS AND METHODS

**Location of the study:** Patients for this study were obtained from Federal Neuropsychiatric Hospital, Enugu. Patients with schizophrenia attending the out-patients clinic of the hospital were recruited for the study. Federal Neuropsychiatric Hospital, Enugu is a tertiary health institution, which provides specialist health service to about five states in the southeast region of Nigeria. Patients with duration of illness of less than one year, who were less than 18 years of age and who were taking parenteral forms of medicines were excluded from the study.

All cases had been diagnosed as having schizophrenia based on the ICD-10 criteria which is used for the classification of diagnoses by the institution. A random selection of the patients based on their case file number was made, giving a total number of one hundred and fifty participants.

**Data Collection:** This was a cross sectional study with quantitative methods of data collection. The study protocol was approved by the ethics committee of the Federal Neuropsychiatric Hospital, Enugu, Nigeria. Written informed consents were obtained from the participants after explaining the aims and objectives of the study. Structured questionnaires were used to obtain information on patient's demographic characteristics and some risk factors for non-adherence to antipsychotic treatments. Measures evaluated included socio-demographic details (age, gender, years of formal education, marital status, and

employment status). Living arrangements was also assessed as living independently, living with family members, or being homeless. The degree of available medication supervision was assessed as either independently responsible for the administration of his medication or all aspect of medication are managed by a third party.

Non-adherence was assessed using patients self report of how they had been taking their medications in the one week preceding the interview. They were asked to recall if they missed any doses of medication on day by day bases over a period of one week. A review of patient's medical records yielded information on the doses actually prescribed. Recent compliance was calculated as a percentage of doses taken over the total number of medication doses prescribed.

Patient's medication knowledge was assessed using a validated interviewer administered medication knowledge assessment questionnaire. The questionnaire consists of three questions and two columns named as 'actual' and 'patient' for each question. The actual column contains the current actual list of medications taken by the patient as recorded in the patient's case record. An interview was conducted for each patient to assess parameters like the ability of the patient to recall the names of his/her medications, dosage and dosage frequency and the responses were rated on five point (1-5) likert scale. A score of 1-3 was classified poor while 4-5 was regarded as good.

**Data Analysis:** Descriptive statistics were used for general description of study participants and to obtain the prevalence of treatment adherence to antipsychotic medication. Univariate analysis was done between the various independent variables and treatment adherence. Chi square analysis was used to assess the association between treatment adherence and various sociodemographic, medication, patient, illness and socioeconomic variables.

Independent variables with p-values <0.05 were selected for multivariate analysis using Logistic regression. The Statistical package for the social sciences 16 (SPSS Inc., Chicago, IL, USA) program was used for statistical analysis.

## RESULTS

The average age of the participants was  $36 \pm 10.8$  years and more than half of them were females (56.0%). The majority of the participants were single 105 (70%) and more than half of them 85 (56.6%) has secondary education as the highest level of education attained. Most of the participants were Christian (93.3%, n=140) and about 60 (40.0%) were employed. The mean duration with schizophrenia was  $10 \pm 7.6$  years. About 112 (74.7%) of participants lived in an urban setting. Those that lived in the same house/home environment with at least someone were 132 (88%) while those who had some form of supervision during medication intake were 62 (41.3%).

The mean number of tablets taken by participants was 2.91 (SD 1.269). About 21 (14.0%) took their tablets once daily while about 129 (86.0%) took their medications more once a day. When more than three tablets were taken in a day, 77% of respondents showed good adherence to treatment. When less than three tablets were taken in a day, more of the subjects (55.6%) were non adherent to medication. The socio-demographic and clinical characteristics of the participants are summarised in table 1.

Factors found to show significant differences between the adherent and the non-adherent participants on univariate analysis were marital status (p-value 0.03), living arrangements of the participants (p-value 0.04), employment status (p-value 0.03), and treatment supervision ((p-value <0.001). Other variables including dosage frequency (p-value 0.09), medication prescription knowledge (p=0.06) and educational level (p-value=0.37) did not show statistically significant differences between both groups of participants (See table 2)

Table 1: Socio-demographic and clinical characteristics of respondents

Characteristics	Participants N(%)
Mean age	36±10.8
Age in years	
<=40years	82(66.7)
Sex (male)	65(43.3)
Marital status	
Single	96(64.0)
Married	40(26.7)
Widowed	8(5.3)
Divorced	3(2)
Educational status	
Primary	16(10.7)
Secondary	69(40.0)
Tertiary	65(43.3)
Employment status (employed)	60(40.0)
Living arrangement (with someone)	132(88)
Treatment supervision (not supervised)	88(58.7)
Duration of illness in years	
<=10years	112(74.7)
Tablets taken per day	
<=3tablets	117(74.7)
Dosage frequency (more than once per day)	58(64.2)
Rating scales	
Adherence (optimal adherence)	65(52.8)
Understanding drug regimen (good)	53(35.8)

The point prevalence of treatment non-adherence among the respondents was 49.3% (n=74). The treatment adherent participants were more likely to be married, more likely to be employed, more likely to have their treatment supervised and were

more likely to be better informed about prescribed medications. Age, sex, place of residence, education level, duration of illness did not show significant differences between the adherent and the non-adherent groups of participants.

Table 2: Associations between socio-demographic, clinical variables and adherence

Variables	optimal Adherence (n%)	suboptimal adherence (n%)	statistics X <sup>2</sup>	p-value
Age (<=40years)	51(50.0%)	51(50.0%)	0.057	0.81
Sex(male)	36(55.4%)	29(44.6%)	1.021	0.31
Marital status (married)	28(65.1%)	15(34.9%)	5.053	0.03
Educational level				
<=6years	19(57.6%)	14(42.4%)	0.808	0.37
Employment (employed)	37(61.7%)	23(38.3%)	4.841	0.03
Tablets taken per day				
<=3tablets	52(43.7%)	67(56.3%)	11.189	0.01
Dosage frequency				
(more than once daily)	62(49.6%)	63(50.4%)	0.341	0.09
Living arrangement				
(with someone)	71(53.8%)	61(46.2%)	4.287	0.04
Duration of illness				
<=10 years	55(49.1%)	57(50.9%)	20.18	0.51
Supervision				
(supervised)	54(87.1%)	8(12.9%)	56.112	<0.001
Understanding drug				
Regimen (good)	32(60.4%)	21(39.6%)	3.557	0.06

The significant variables were then entered into regression analysis to determine predictors of treatment adherence. The

compliance with medication for patients with schizophrenia and in disagreement with this study. Our findings are consistent

Table 3 Predictors of adherence by logistic regression analysis

<u>Variables</u>	OR	95% C.I	p-value
Marital status	0.886	0.327-2.399	0.81
Tablets taken per day	0.534	0.156-1-831	0.31
Supervision	0.055	0-021-0-142	<0.001
Living arrangement	1.162	0-325-4.158	0.81
Employment	0.458	0.190-1.103	0.08

result of regression analysis (Table 3) shows that the most significant predictor of adherence is supervision of treatment.

## DISCUSSION

The prevalence of treatment non-adherence in this study was 48% indicating that about one in two patients were non-compliant with their medications. Other studies<sup>19,20</sup> had reported higher rates of over 60% non

with the non-compliance rate reported by other researchers.<sup>22,31</sup> The level of adherence found in our study is clearly suboptimal but may still represent an overestimation of the true prevalence of adherence in the population because self reports that were used to assess non-adherence in this study usually overestimate their adherence<sup>8</sup> This level of

non adherence is bound to lead to increased morbidity, relapses and rehospitalisation and increased cost burden of management. This result also implies that healthcare providers must intervene actively to address this challenge.

In this study, socio-demographic variables of the participants had varying impact on treatment adherence. Some subjects' characteristics were found to influence treatment adherence more than others. This study revealed that subjects were more likely to be adherent to medication if they were married ( $p=0.025$ ). The participants that were adherent to medications were more likely to be employed ( $p=0.03$ ) compared to the non adherent participants. However, the employment status of the participants was not found to be a predictor of adherence behaviour on multivariate analysis. This is in disagreement with a study<sup>30</sup> which found such association. However, the significant difference in the employment status between the adherent and non-adherent participants on univariate analysis suggests that non-adherence could have been attributed to their possible financial constraints, as they might find it difficult to afford visiting their healthcare facility on a regular basis and thus, might not have regular availability/supply of medications. This implies that financial constraints is a factor for non compliance with medications in a resource poor setting like ours where payment for treatment is mainly from out of pocket expenditures in the absence of a universal and a comprehensive health insurance scheme.

A large number of participants (88%) reported that they reside with members of their family. Those that resided with someone were significantly more likely to adhere to medications than those who were not ( $p=0.04$ ) however it did not predict non adherence on multivariate analysis. This finding is supported by several studies<sup>23,24</sup> which have reported that social support is consistently associated with outpatient adherence. This may be partly due to the fact that family members will ensure

patients keep follow up appointments, have the finances to buy drugs especially when the subjects are not working. It can also be argued that some peculiar features of mental illness such as lack of insight,<sup>7</sup> the degree of psychopathology,<sup>18</sup> cognitive impairments that promote forgetfulness, and self stigma<sup>29</sup> by themselves constitute major risk factors for treatment non-adherence hence the role of caregivers and relatives in ensuring good adherence behaviour cannot be overemphasized. Supervision of treatment by care givers becomes very important to increase adherence behaviour.

This study found supervised treatment to be a strong predictive factor for treatment adherence. This is in agreement with a study<sup>7</sup> which reported that supportive behaviour provided by caregivers may reinforce medication usage and that higher medication usage may elicit supportive behaviour from caregivers and this create a therapeutic chain of events. However, the compliance enhancing effect of supervised treatment was not supported by other study<sup>25</sup> carried out in Northern Nigeria which investigated family member's involvement in the treatment of the mentally ill and reported that social support of family members in treatment did not increase adherence behaviour. Lack of supervised treatment and family support may be a reflection of cultural belief and attitude towards mental illness in believing that a spiritual solution is required to resolve their mental health problems and therefore treatment with western medicine becomes futile<sup>22</sup>

Our study found that the number of tablets taken per day was significantly different between the participants that were adherent to medications and those who were not. A number of studies<sup>26,27</sup> have evaluated the impact of the number of tablets taken in a day and treatment adherence. An interesting finding of this study is that adherence behaviour correlated negatively with number of tablets taken in a day. This is at variance with a number of studies

which have reported significant association between number of tablets prescribed and adherence behaviour.<sup>26,27</sup> In their study, they opined that reducing the number of tablets ultimately reduces the likelihood of treatment default and improves treatment adherence. This seems to be related to the convenience associated with reduced frequency and comfort from reduced side-effects burden.<sup>1</sup> however, our study has highlighted the fact that the mentally ill will need social support for optimum medication adherence regardless of how few the number of tablets taken in a day. This reinforces the need for more active involvement of members of the family in the treatment of the mentally ill. Other medication variables including dosage frequency and a good knowledge of the names of medications (generic/brand) did not show significant differences between both groups. Although medication knowledge was not a significant statistical predictor of adherence, it is observed that a higher percentage (60.4%) of adherent subjects compared to (39.4%) of non-adherent subjects knew the names of prescribed medication. This seems to suggest it may be a contributor to non-adherence especially in a resource poor environment like ours where poorly regulated drug environment allows for easy over the counter purchase of medications.

A limitation of this study was that self reports were utilized in the assessment and measurement of medication adherence; this may occasionally be unreliable and biased. This is due to self reported measures being subject to recall bias and recall difficulties and forgetfulness partly from cognitive impairments,<sup>21</sup> seen in the mentally ill. Thus, this may result in an unreliable ascertainment of medication adherence status. It has been reported that self report measures usually overestimate their adherence.<sup>8</sup>

In conclusion, we have shown that the level of adherence to treatment is suboptimal among out-patients with schizophrenia in our setting and that strategies that encourage family member's participation in patient's

management will significantly improve treatment adherence.

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