Medication Related Factors of Adherence and Attitude to Medication among Outpatients with Bipolar Disorder in Uyo, South-South Nigeria

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Authors' contributions

This work was carried out in collaboration between both authors. Author JHE designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author AUI managed the analyses of the study and the literature searches. Both authors read and approved the final manuscript.

Original Research Article	

ABSTRACT

A high level of medication adherence is required for effective treatment of bipolar disorder due to the chronic progressive nature of the illness requiring maintenance treatment.
Aims: This study was conducted to determine the prevalence of medication non-adherence of people with bipolar affective disorder and explore the roles of attitude to medication and medication related factors in promoting treatment adherence.
Materials and Methods: This was a cross-sectional descriptive study conducted on a sample of one hundred and twenty six out-patients with bipolar affective disorder. Adherence to medication was assessed on the basis of patients' self report. Socio-demographic parameters, attitude to medication and medication related variables were collected and compared between adherent and non-adherent participants. Logistic regression analysis model was used to determine predictors of treatment non-adherence.

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Results: The mean age of participants was 34.4±9.84 and 69.0% were males. Prevalence of medication non-adherence was 56.7%. Factor that significantly associated with medication non-adherence were high cost of medication ($x^2=25.8, P<.001$). By multiple regression analysis, factors that independently predicted non-adherence to treatment were: a lack supportive marital union (*OR=7.42,P=.009*), poor attitude to medication (*OR=0.06 P<.001*), high dosing frequency of medication (*OR=0.18,P=.05*) and high side effects burden of medication (*OR=19.52,P=.04*).
Conclusion: A high prevalence of treatment non-adherence was found in a sample of outpatients with bipolar disorder in a mental health service in Nigeria. Psycho-educational Interventions and measures that reduce treatment cost are required to improve medication adherence.

1. INTRODUCTION

Bipolar affective disorder is a severe mental disorder characterized by chronicity, multiple recurrent episodes, heterogeneity and significant impairment in family, social and occupational functioning. Symptoms usually first appear in late adolescence or early adulthood. It affects about 1.6% of the population [1]. It is associated with a high rate of co-morbidity, suicide and functional impairment that causes high economic and social burden [2,3]. It is the sixth leading cause of disability worldwide among people 15–44 years of age. It is associated with a greater degree of disability than several prominent chronic medical conditions, including osteoarthritis, HIV infection, diabetes, and asthma [4] Non-adherence to medication among patients with bipolar are common often resulting in worsening symptoms, reduction in the quality of life, more hospital admissions and increased suicide behaviour [5,6].

The World Health Organization (2003) defined adherence as "the extent to which a person's behaviour–taking medication, following a diet and/or executing life style changes, corresponds with agreed recommendations from a health care provider" [7].

Several pharmacological treatment strategies have been proposed for relapse prevention in patients with bipolar disorder such as mood stabilizers and, according to more recent guidelines, second-generation antipsychotics either as monotherapy or in combination with lithium or anticonvulsants have been recommended [8,9,10].

Recent studies have shown that the overall compliance rate for medications in bipolar disorder is low. A large scale study by Montoya et al found that 40% of individuals with bipolar mania were partially or totally non-adherent with prescribed medication treatments [11]. Other studies have reported rates ranging from 20% - 70% [12,13,14].

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 and factor related to the social/environmental/economic factors (living arrangement, supervision, family support, stigmas, cost, access to treatment facility) [15,16,17].

There have been many efforts to predict non-adherence in bipolar disorder with only limited success. For example, demographic features such as race, age, and gender have not been consistently associated with non-adherence [17,18]. Commonly encountered reasons for non-adherence in bipolar patients include negative attitudes toward the illness, poor insight, psychotic symptoms, manic symptoms, severity of depression, substance use [2,19,20,21].

Many of these studies have been conducted in developed societies. Data on predictors of non adherence among patients with bipolar disorder from a developing country like Nigeria is scarce. Information in this regard will help in the design of effective interventions to enhance adherence behaviour in bipolar patients in a resource poor setting existing in many developing countries.

Aim of the study was to assess the prevalence of treatment non-adherence in patients with bipolar disorder and explore the role of attitude to medication and medication-related variables in promoting adherence.

2. MATERIALS AND METHODS

2.1 Location of the Study

This study was conducted at University of Uyo Teaching Hospital from July 2014 to November 2014. The hospital is located in Uyo, the capital city of Akwa Ibom State, Nigeria. The hospital is a 500 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 of Cross River, Abia and Rivers. 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 [22]. Clinically generated data for each subject enrolled were matched to the ICD -10 criteria. This was a cross sectional descriptive study.

2.2 Subjects

The minimum sample size was computed using a public domain software available on-line (www.statpages.org) [23] using a prevalence of treatment non adherence as determined from a previous nigerian studies (54.7%) [24]. Data was collected from 130 participants within a period of four months, July to October 2017 by random sampling. However, 126 respondents with complete data were analysed.

A subject was randomly selected and enrolled into the study if the following eligibility criteria were met: a diagnosis of bipolar disorder according to the International Classification of Diseases (ICD-10) diagnostic criteria, had been on medications for at least a year prior to study entry, adults above the age of 18years, and who granted consent. The exclusion criteria were: presence of florid psychopathology capable of impairing response, and co morbid psychoactive substance use or physical disorders.

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 and 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 [25] was further used to confirm the diagnosis of bipolar in the participants. The MINI was designed as a brief structured interview for the major Axis 1 diagnosis in the Diagnostic and Statistical Manual (DSM-IV) [26] and ICD-10.

2.4 Measures

2.4.1 Semi-structured socio-demographic questionnaire

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, monthly family income, place of stay, occupation), duration of illness, attitude towards medication, and medication related variables (number of tablets taken per day, dosing frequency, monthly cost of medication. The medication side effects profile of each individual patient was obtained from subjects' clinical records. Sample questions include, What is the duration of your illness (in Months), How much do you spend in a month to buy your medications (In Naira) etc.

2.4.2 Morisky Medication Adherence Scale (MMAS)

The compliance level of patients was defined by the application of the MMAS-8. The MMAS is a reliable and validated 8 items; self reported measure of medication use patterns. Each item on the MMAS measures a specific medication-taking behaviour. Each of the items is presented in a "yes or no" format. These involve asking the patient about their extent and tendency to forget to take their medication and their discontinuance of medication treatment upon feeling that their condition has improved or alternatively worsened. Answers were scored as 0 or 1, with score 1 corresponding to positive answers. The item scores obtained from the MMAS are summed to indicate an overall level of medication adherence. The MMAS scores range from zero to eight and have been stratified into three levels to classify adherence levels: high adherence-MMAS score of 8, moderate adherence-MMAS scores of 5>7 and low adherence-MMAS score of less than or equal to 4 [27].

2.4.3 Drug Attitude Inventory (DAI 10)

Drug Attitude inventory (DAI-10) is self report instrument of false-true statement is used to

assess the nature of patient's experience with taking psychotropic medication, patients feeling about medication and their attitudes and beliefs about medication. It consist of true-false statements about the perceived effects and benefits of medication with which the patients can agree or disagree. Each item ticked 'yes' is rated +1 and items ticked 'no' is rated as -1 [28]. Respondents with score less than six was considered to be having negative attitude towards treatment [29].

All the questionnaires were translated into Ibibio language separately by two bilingual translators. The two versions were combined and revised and then back translated into English by another bilingual translator. The translation was refined after back translation until agreement was obtained among the four people involved in the translations.

2.5 Data Analysis

Descriptive statistics such as frequencies, median, 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 was used to determine the relationship between outcome and independent variables. Significant variables were entered into a logistic regression analysis model to determine predictors of attitude to medication and treatment adherence. Significance was computed at $p < 0.05$.

The Statistical package for the social sciences 16 (SPSS Inc., Chicago, IL, USA) program was used for statistical analysis.

3. RESULTS

A total of 126 respondents were recruited from the population attending the outpatient Clinic. The mean age of the participants was 34.44±9.84 years and more than half of them were males (59.0%). The majority of the participants (66.7%) were less than 40 years. 33.3% of the subjects were married and more than half of them 81(64.3%) had secondary education. The mean duration with bipolar disorder was 6.86±2.63 years. 73.0% of participants lived in an urban setting (Table 1).

Table 1. Socio-demographic characteristics of participants

Characteristics	Participants N (%)
Age (Mean=34.44±9.84, Range=20-60)	
≤40 years	84(66.7)
>40 years	42(33.3)
Gender	
Male	87(69.0)
Female	39(31.0)
Marital status	
Single	84(66.7)
Married	42(33.3)
Educational status	
Primary	22(17.5)
Secondary	59(46.8)
Tertiary	45(35.7)
Employment status	
Employed	72(57.1)
Unemployed	54(42.9)
Residential area	
Urban	92(73.0)
Rural	34(27.0)

Table 2. Distribution of clinical variables in the subjects

Variables	Participants N (%)
Duration of illness (Mean=6.86±2.63, Range=2-12)	
≤10 years	100(57.1)
>10 years	26(20.6)

Class of medication	
Conventional	42(33.3)
Atypical	50(39.7)
Combined conventional/atypical	28(22.2)
Anticonvulsants	45(35.7)
Antidepressants	10(7.9)
Dosing frequency	
Once per day	55(43.7)
More than once per day	71(56.3)
Medication cost ($=#360)	
≤#3000 per month	34(27.0)
>#3000 per month	92(73.0)
Medication side effects	
Extrapyramidal side effects	18(14.3)
Sedation	10(7.9)
Weight gain	31(24.6)
Hyperprolactin	5(4.0)
Anticholinergic	15(11.9)
Sexual problems	7(5.6)
No side effects	27(21.4)
Treatment adherence	
High	55(43.7)
Medium	26(20.6)
Medium	45(35.7)
Attitude to medication	
Positive	72(57.1)
Negative	54(42.9)
Drug combination	
Monotherapy	50(39.7)
Polytherapy	76(60.3)

3.1 Medication Related Variables

The mean number of tablets taken by respondents was 6.86±2.63. Among the respondents, 43.7% had a dosing frequency of once per day and 56.3% had a dosing frequency of more than once per day. 33% of subjects were on conventional antipsychotics and the three most commonly prescribed first generation antipsychotics were: haloperidol (48.6%), chlorpromazine (34.6%) and trifluperazine (20.2%). Atypical antipsychotics were prescribed for 39.7% of subjects and 22.2% were on combined conventional and atypical medications. The commonly prescribed atypical antipsychotics were olanzapine (52.4%) risperidone (40.6%). The anticonvulsants prescribed included carbamazepine (85.5%) sodium valproate (15.5%). About 73.0% of subjects spend more than #3000 ($=#360 equivalent) on medication monthly. A high dosing frequency (*P=.02*)

polytherapy (P=.001) and high cost of medication (*P=.001*) impacted negatively on medication adherence.

3.2 Attitude to Medication

Attitude to medication was significantly correlated with treatment adherence (*r=0.64,P<.001*). 57.1% of the respondents were categorised as having a positive attitude to medication. Subjects with positive attitude were significantly more like to adhere to treatment prescription than those with negative attitude (*P=<.001*). Factors significantly associated with a positive attitude were low medication dosing frequency with those taking medication once daily having a more positive attitude towards medication compared to those taking medication more than once per day (x^2=25.81,P=<.001) , availability of active social support (x^2=16.27,P=<.001), the absence of medication side effects (x^2=18.71,P=.001).

3.3 Prevalence of Treatment Non-adherence

The point prevalence of non adherence was 56.3% using an MMAS cut-off score of ≤7 adapted for this study. 35.7% of the subjects were categorized as having low adherence, while 20.6% were categorized as having medium adherence and 43.7% were classified as having high adherence. The variables that are significantly associated with non adherence to medication include being unmarried (x^2=25.8, P=<.001), high cost of medication (x^2=10.90, P=.001), high dosing frequency (x^2=13.1, P=.001), presence of side effects of medication (x^2=16.3, P <.001), negative attitude to medication (x^2=72.3, P<.001). The years of formal education, duration of illness, age of participants did not show a significant association with medication adherence in this study.

3.4 Predictors of Treatment Non Adherence

The variables were fitted into logistic regression model for multivariate analysis. The predictors of treatment non adherence among bipolar subjects were a negative attitude to medication (P< 0.001), absence of active social support in a marital union (P =.009), high dosing frequency of medication (P=.05) and experience of side effects (P=.04).

4. DISCUSSION

This study explored the role of attitude to medication and medication related factors in treatment adherence. The prevalence of treatment non-adherence in this study was 56.3% implying that about one in two patients were non-adherent to medications. This finding is consistent with rates reported in previous studies by Ibrahim et al [26] in north-east nigeria and Hibdye et al [29] in Ethiopia. Worldwide, the prevalence of medication non-adherence in the present study is in agreement with studies [30,31] which have reported similar prevalence and in disagreement with other studies which have either reported lower prevalence [32,33] or much higher prevalence [34,35]. Differences in study population characteristics and design may account for these differences. The high prevalence of treatment non-adherence in the current study may be related in part lack of sustained psycho-educational interventions and poor quality of social support evidenced by lack of treatment supervision in a high proportion of the respondents [36,37].

Table 3. Associations between socio-demographic variables and adherence to medication

Variables	Adherent (n%)	Non Adherent (n%)	Statistics X^2	P-value
Age				
≤40 years	41(48.8)	43(48.8)	2.7	**.09**
>40 years	14(33.3)	28(66.7)		
Gender				
Male	39(44.8)	48(55.2)	0.16	.69
Female	16(41.0)	23(59.1)		
Marital status				
Married	37(88.1)	5(11.9)	25.8	**<.001**
Single	50(59.5)	34(40.5)		
Educational level				
≤12 years	33(40.7)	48(59.3)	0.78	.38
>12 years	22(48.9)	23(51.1)		
Employment				
Employed	35(48.6)	37(51.4)	1.68	.20
Not employed	20(37.7)	34(63.0)		
Duration of illness				
≤10 years	42(42.0)	58(58.0)	0.53	.46
>10 years	13(50.0)	13(50.0)		
Medication cost ($=#360)				
≤#3000 per month	23(67.6)	11(32.4)	10.90	**.001**
>#3000 per month	32(34.8)	60(65.2)		

Table 4. Association of clinical variables and treatment adherence

Variables	Adherent N(%)	Non Adherent N(%)	Statistics x^2	P-value
Attitude to medication				
Positive	47(87.0)	7(13.0)	72.3	**<.001**
Negative	8(11.1)	64(88.9)		
Experience of side effects				
Yes	34(34.3)	65(65.7)	16.3	**< .001**
No	21(77.8)	6(25.6)		
Drug combination				
Monotherapy	29(70.7)	12(29.3)	5.11	**.02**
Polytherapy	43(50.6)	42(49.4)		
Dosing frequency				
Once per day	38(76.0)	12(24.0)	13.1	**.001**
≥Twice per day	43(56.6)	33(43.4)		

Table 5. Predictors of adherence by logistic regression analysis

Variables	OR	95% C.I		P-value
		Lower	**Upper**	
Marital status	7.42	1.64 -	33.63	**.009**
Drug combinations (polytherapy)	0.37	0.08 -	1.63	.19
Experience of side effects	19.52	1.13 -	33.59	**.04**
Cost of medication	0.59	0.093 -	0.59	.58
Attitude to medication	0.06	0.015 -	0.24	**<.001**
Dosing frequency	0.18	0.03 -	1.05	**.05**

Demographic variables have not been consistently associated with medication non-adherence in patients with bipolar disorder. The absence of a significant relationship between age, gender and educational status of respondents and treatment adherence is supported in this study. The marital status of respondents in this study predicted treatment adherence. This is consistent with previous studies [2,14] which have reported significant association between being married and greater treatment adherence. It is however, in disagreement with other studies [9,38] which reported no such links. The positive impact of supportive marital union on adherence in this study may be due in part to the fact that active social support from spouses and relations has the potential to promote medication adherence and reduce the risk of discontinuation of treatment. The link of marital status to the risk of medication non-adherence may also be related to the fact that major part of the care for an illness is done at home and inside the family [39]. In this study, all the participants reported that they reside with members of their family. Previous study had reported that the more the social support received from spouse and other family members, the more serious the patient would be in terms of adherence to medication and self-care activities [36].

Concerning attitude to medication, we found a higher proportion of respondents with a positive attitude to medication. The subjects with positive attitude to medication were significantly more likely to adhere to medication compared to the subjects with negative attitude. Positive attitude towards medication was therefore a significant statistical predictor of adherence to medication. This finding is consistent with previous studies [12,14,20,40] which have reported that patients' compliance was predicted by attitude towards medication. Attitude to medication has been described as an indirect measure of medication adherence [41]. To achieve a change in patient's attitude, it is essential to include psychoeducation in the treatment program, to teach patient about their illness, medication and adverse effects and relapse prevention [40].

The impact of medication related variables on adherence were explored in this study. The independent medication-related predictors of non adherence were; high cost of the medications,

polypharmacy, high dosing frequency and the high burden of side effects of medications. Concerning the impact of side effects on adherence, our finding is in agreement with studies that have found a significant relationship between medication side-effects [42,43,44] and treatment non-adherence and in disagreement with other studies that found no such relationship [45]. The side effects burden has been reported as an important reason for treatment non compliance. Previous studies had noted that for many patients, extra pyramidal side-effects (EPS), weight gain, and sexual dysfunction are especially likely to decrease adherence [42,44]. In terms of the cost of the medications, high cost of the medications per day and a high dosing frequency were significantly associated with treatment non-adherence. It is observed in this study that a high proportion of participants (57.1%) were unemployed and majority (64.3%) has 12 years or less of formal education implying that most patients with bipolar disorder are from a low socioeconomic background. This translates to low economic placement and greater healthcare financing burden. In Nigeria, the setting in which this study was conducted has one of the highest poverty rates in the world with over 70% of the inhabitants living below the $1 per day benchmark (United Nations Development Programme, 2013) [45]. There is the need to reduce the cost burden of medications to patients through increased prescription of drugs in their generic names and rational drug prescription without reducing treatment efficacy [46]. According to Morris in his study [47], he reports that 'Probably the simplest and single most important action that healthcare providers can take to improve adherence is to select medications that permit the lowest daily dosing frequency'.

Our study has some limitations. First being a cross-sectional study and cannot confirm associations between the factors studied, the value must be limited to the descriptive and its exploratory nature. Also, treatment adherence was measured using indirect scale. Patient self reports that are used to estimate adherence may overestimate their adherence [39]. There was no objective measure of side effects profile using a validated instrument.

5. CONCLUSION

This study found a high prevalence of treatment non-adherence among out-patients with bipolar disorder in a tertiary healthcare facility. In a resource poor setting that is prevalent in many developing countries like Nigeria where this study was conducted, socioeconomic factors are important variables to be taken into consideration in patients' management. Psycho-educational interventions are important to improve adherence to medication.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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