

DOI: 10.21767/1791-809X.1000520

Prevalence of Antipsychotic Drug Non Adherence and Associated Factors Among Patients with Schizophrenia Attending at Amanuel Mental Specialized Hospital, Addis Ababa, Ethiopia: Institutional Based Cross Sectional Study

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Received date: 12 August 2017; Accepted date: 20 August 2017; Published date: 28 August 2017

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Citation: Girma S, Abdisa E, Fikadu T (2017) Prevalence of Antipsychotic Drug Non Adherence and Associated Factors among Patients with Schizophrenia Attending at Amanuel Mental Specialized Hospital, Addis Ababa, Ethiopia: Institutional Based Cross Sectional Study. Health Sci J. Vol. 11 No. 4: 521.

Abstract

Background: Drug non adherence is a problem in all areas of medicine, and psychiatry is no exception. Mental health institutions are widely over burdened by mental ill patient who sought frequent treatment as a result of drug non adherence. Although patients suffering from psychiatric disorders are the most likely not to adhere to treatment than any other physical illness; there was no study done to determine the prevalence and associated factors of antipsychotic drug non adherence among schizophrenia patients in Ethiopia. So this study was aimed to assess the prevalence and associated factors of antipsychotic drug non-adherence among patients with schizophrenia attending at Amanuel mental specialized hospital.

Methods: An institution based cross-sectional study was conducted on 403 schizophrenia patients attending outpatient department of AMSH from March 26 to April 6, 2013. Morisky Medication Rating Scale and Drug Inventory Attitude were used to collect data. Three trained data collectors and one supervisor were involved in the data collection process. Ethical clearance was obtained from institutional review board of University of Gondar and Amanuel mental specialized hospital. Written informed consent was obtained from the respondents.

Result: The study had response rate of 95.3%. A total of 268(66.5%) male were participated in this study. The mean age of participants was 32.7(SD+9.59 years) and age ranged from 18 to 57. Prevalence of antipsychotic drug non adherence was found to be 48.4%. The factors having co-morbid mental illness AOR=2.23, 95%CI (1.12, 4.45), Extra pyramidal side effect AOR=2.66, 95%CI (1.44, 4.91), Poly therapy AOR=2.37, 95%CI (1.21, 4.65), Negative attitude towards treatment AOR=3.79, 95%CI (1.56, 9.23) and alcohol use AOR=4.72, 95%CI (1.79, 12.46) were

found to be significantly associated with antipsychotic drug non adherence.

Conclusion: About half of patients were found to be non-adherent. The factors substance use, extra pyramidal side effects, co-morbid depression, attitude towards treatment and lack family encouragement were found to be significantly associated with drug non adherence. At last self-reported method used in this study tends to under estimate non adherence conducting further study by combining certain methods is of paramount importance.

Keywords: Schizophrenia; Non adherence; Antipsychotic drugs

Abbreviations: AMSH: Amanuel Mental Specialized Hospital; AOR: Adjusted Odds Ratio; CI: Confidence Interval; DIA: Drug Inventory Attitude; EPS: Extra Pyramidal Side Effect; MMARS: Morisky Medication Adherence Rating Scale

Introduction

Background

Non communicable diseases, mental health disorders, HIV/AIDS and tuberculosis combined represented 54% of the burden of all illness worldwide [1] and predicted to rise to 65% of the global burden of disease in 2020 [2].

Schizophrenia is one of the serious mental health problem characterized by clinical syndrome of variable, but profoundly disruptive, psychopathology that involves cognition, emotion, perception, and other aspects of behavior. The classic course of schizophrenia is one of exacerbations and remissions and patient usually relapse [3]. Antipsychotic medications are the mainstay of the treatment for schizophrenia and have reduced

the number of recurrent psychotic episodes among persons with schizophrenia [4].

Advancements in the treatment of psychiatric disorders are limited by non-adherence, which steal power from even the most beneficial medications [5]. WHO defined non adherence as "a case in which a person's behavior in taking medication does not corresponds with agreed recommendations from a health care provider". Medication non adherence, either willful or inadvertent and can include: Failing to initially fill or refill a prescription, discontinuing a medication before the course of therapy is complete, taking more or less of a medication than prescribed and taking a dose at the wrong time [1].

Patients with psychiatric disorders show a greater degree of non-adherence to treatment than those with physical disorders. The adherence rates range from 40 to 70% to 60-92% in the respective disorders [6]. Among different psychiatric illnesses patients suffering from psychotic disorders are the most likely not to adhere to treatment followed by those suffering from depressive disorders and bipolar disorder [5].

Study done in Kenya on 100 psychiatric outpatients discharged from mental hospital to estimate the treatment compliance or adherence after 3 months; patients were interviewed to assess treatment adherence and 55 percent of them fail to adhere to their treatment for certain reason [7]. Similar studies were done in different part of Africa to determine magnitude of antipsychotic drug non adherence on schizophrenia patients. Study done in Nigeria on 313 schizophrenia patients to examine medication adherence among outpatients in relation to their subjective quality of life and other socio demographic, clinical and service related factors indicated that 40.3% of the respondents were medication non adherent [8]. Related study done on 217 schizophrenia patients to assess factors associated with relapse in Johannesburg; South Africa indicates that more than one third of patients (35.8%) were non adherent to their treatment [9].

Factors influencing non-adherence may be broadly categorised into factors related to the treatment, patient-related factors, health care, and socio-economic circumstances [10]. There are certain studies which were undertaken by scholars regarding factors associated with antipsychotic drug non adherence. Study done in Pakistan came across the following common self-reported personal factors of the patients as cause of non-adherence: 'I forgot to take medication'(36%) and 'I thought I am better now and do not need to take medication' (32%) [5].

Pilot study done in Uganda indicated that non adherence was correlated significantly and negatively with need for treatment and insight. In the same study no demographic factors were correlated with non-adherence [11]. Study done in India to assess reason for drug non adherence showed that 35% of patients were non adherent because they were not able to come for medicine due to long distance that was inconvenient. Additionally 28% patients due to improvement

in symptoms, 41% because of financial problem, 16% because of side effects and 15% because of lack of care givers discontinued their treatment [12].

Failure to adhere to antipsychotic regimens is associated with exacerbation of psychotic symptoms, increased aggression against self and others, worse prognosis, increased use of inpatient and acute outpatient services and increased costs. Importantly, non-adherence to medication has been suggested to be the most important modifiable factor contributing to psychotic relapse [13] which leads to re-hospitalization [14].

Data regarding the prevalence and associated factors of non-adherence among psychiatric patient particularly schizophrenia from developing countries, especially Ethiopia is scarce. To the knowledge of the present researcher although certain study was done on non-adherence of chronic medical illness there is no study done on this regard in Ethiopia. This study attempts to bridge the gap and information in this regard and helps to design effective interventions and therapeutic techniques for enhancing adherence behavior among schizophrenia patients.

Methods

Study design and subject

Over a month period, we performed institutional based cross-sectional study on 403 schizophrenia patient at Amanuel mental specialized hospital. Amanuel mental specialized hospital is the only mental hospital in the country which engaged in giving core mental clinical services, conducting research and trainings of professionals. There were about 41,583 schizophrenia patient who had regular follow in the year 2012 at outpatient; the majority are male (24,154). The hospital has 300 beds in 11 case teams (wards) which serves patient from the whole country. Eligible patients were age 18 and above, had given informed consent and had DSM-IV diagnosis of schizophrenia. However patients who were acutely agitated and cannot be able to communicate with data collectors were excluded from study.

Measurements

Structured, pre tested and pre coded questionnaire was used to collect socio-demographic characteristics and non-adherence related factors by face to face interview of the participants. Data regarding the type of schizophrenia, the type of drug/s, frequency of drug taken, drug regimen and presence of co-morbid depression were reviewed from patient document. Drug non-adherence was assessed using the 4-item version of self-reporting questionnaire of Morisky Medication Adherence Rating Scale (MMARS) [15], patient attitude towards treatment was assessed by 10-item Drug Inventory Attitude (DIA) [16].

Statistical analysis

Data were entered and cleaned using EPI Info version 2002 and exported to SPSS version 20 for analysis. Descriptive statistics were used to summarize the data. Multiple logistic regressions were used to identify associated factors of drug non adherence with several independent variables. Odds ratio, 95% confidence interval and p-value were used to identify associated factors. A p-value of <0.05 was considered to indicate statistical significance association and p-value of Hosmer and Lemeshow test was found to be 0.394. Ethical clearance was obtained from university of Gonder ethical review board and AMSH. Informed consent was obtained from Participants and Participation was on voluntary bases and had full right to withdraw at time of need during the interview process.

Results

Patient characteristics

Four hundred three respondents were participated in the study with the response rate of 95.3%. 268(66.5%) male were participated in this study. The mean age of participants was 32.7(SD+9.59 years) and age ranged from 18 to 57. 250(62.0%), 313(77.7%) and 226(56.1%) participants were Orthodox Christians, never married and jobless respectively. As to income, 270(67%) by participants earn less than 30 USD (Table 1).

Table 1 Distribution of patients by socio-demographic factors attending at AMSH; March, 2013 (n=403).

| Variables | Categories | Number | Percent |
|--------------------|------------------------|--------|---------|
| Sex | Male | 268 | 66.5 |
| | Female | 135 | 33.5 |
| Age | 18-27 | 142 | 35.2 |
| | 28-37 | 138 | 34.2 |
| | >38 | 123 | 30.5 |
| Marital Status | Never married | 313 | 77.7 |
| | Ever married | 90 | 22.3 |
| Religion | Orthodox | 250 | 62 |
| | Muslim | 94 | 23.3 |
| | Protestant | 59 | 14.6 |
| Ethnicity | Amhara | 168 | 41.7 |
| | Oromo | 91 | 22.6 |
| | Gurage | 87 | 21.6 |
| | Tigrae | 57 | 14.1 |
| Educational Status | Above Secondary School | 151 | 37.5 |
| | Secondary School | 147 | 36.5 |

| | | | |
|----------------|---------------------|-----|------|
| | Primary School | 92 | 22.8 |
| | No Formal Education | 13 | 3.2 |
| Occupation | Jobless | 226 | 56.1 |
| | With job | 177 | 43.9 |
| Monthly Income | < 570 | 270 | 67 |
| | > 570 | 133 | 33 |

Regarding treatment related factors of participants 375(93.0%) were on conventional antipsychotic drug, 269(66.7%) were on mono therapy, 210(52.1%) took their medication on daily bases (Table 2). 109(27.0%), 45(11.2%) and 29(7.2%) of the participants reported extra pyramidal, psychic and anti-cholinergic side effects respectively (Table 2).

Table 2 Distribution of patients by treatment related factors attending at AMSH; March, 2013 (n=403).

| Variables | Categories | Number | Percent |
|--------------------------------|---------------------|--------|---------|
| Type of schizophrenia | Paranoid | 226 | 56.1 |
| | Disorganized | 62 | 15.4 |
| | undifferentiated | 85 | 21.1 |
| | Catatonic | 30 | 7.4 |
| Type of drug | Low potency | 250 | 62 |
| | High potency | 125 | 31 |
| | Atypical | 28 | 7 |
| Drug regimen | Mono therapy | 269 | 66.7 |
| | Poly therapy | 113 | 33.3 |
| Frequency of drug | Once every day | 210 | 52.1 |
| | Twice daily | 193 | 47.9 |
| Duration of being on treatment | < 6 months | 115 | 28.5 |
| | 6 months to 2 years | 166 | 41.2 |
| | > 2 years | 122 | 30.3 |
| Experienced side effects | Yes | 181 | 44.9 |
| | No | 222 | 55.1 |

Of the respondents, 370(91.8%) had free access to drugs and 51(12.7%) had no family encouragement (Table 3). Concerning substance, 108(26.8%) used alcohol and 41(10.2%) were used khat/chat use since initiation of treatment. As measured by MMARS, the overall prevalence of antipsychotic drug non adherence in the study population was found to be 48.4%.

Factors associated with drug non adherence

During bivariate analysis of antipsychotic drug non adherence in relation to each explanatory variable: sex, monthly income, Type of drug taken, duration of treatment,

co-morbid depression, drug regimen, extra pyramidal side effects, perceived stigma, having family encouragement, attitude towards drug, alcohol use, khat/chat use and cannabis use were variables that fulfilled the minimum requirement (0.2 level of significance in this study) and were further analyzed by multivariate logistic analysis.

Table 3 Distribution of patients by health care and patient related factors; March, 2013 (n=403).

| Variable | Categories | Number | percent |
|-------------------------------------|------------|--------|---------|
| Time taken to reach hospital | < 2 hours | 235 | 58.3 |
| | > 2 hours | 168 | 41.7 |
| Psychiatric co-morbidity | Yes | 110 | 27.3 |
| | No | 293 | 72.7 |
| Insight during treatment initiation | Yes | 158 | 39.2 |
| | No | 245 | 60.8 |
| Perceived stigma | Yes | 199 | 49.4 |
| | No | 204 | 50.6 |
| Family encouragement | Yes | 352 | 87.3 |
| | No | 51 | 12.7 |
| Substance use | Yes | 256 | 63.5 |
| | No | 147 | 36.5 |
| Health information | Yes | 317 | 78.7 |
| | No | 86 | 21.3 |
| Attitude towards drug | Positive | 355 | 88.1 |
| | Negative | 48 | 11.9 |

On the other hand age, marital status, religion, ethnicity, educational status, occupation, type of schizophrenia, anti-cholinergic side effect, psychic side effect, frequency of drug taken, time taken to reach hospital and cigarette use were not fulfilled the minimum requirement i.e., 0.2 level of significance and were excluded from further analysis.

During the multivariate analysis, co-morbid depression, drug regimen, extra pyramidal side effects, perceived stigma, alcohol use, khat/chat use, family encouragement and attitude towards treatment were found to be statistically significant.

Patients who had co-morbid depression were about two times more likely to be non-adherent as compared with patients who had no co-morbid depression (AOR=2.23, 95%CI (1.12, 4.45)). As to drug regimen patients who were on poly therapy were about twice more likely to be non-adherent as compared to patients who were on mono therapy (AOR=2.37, 95%CI (1.21, 4.65)).

Regarding antipsychotic drug side effects among study participants, patients who had EPS were about three times more likely to be non-adherent to their antipsychotic drug when compared to patients who had no EPS (AOR=2.66, 95%CI (1.44, 4.91)). Similarly study participants who had felt

stigmatized were about three times more likely to be non-adherent to their drug as compared to patients who hadn't felt stigmatized (AOR=3.35, 95%CI (1.94, 5.81)).

Concerning substance use patients who were using khat/chat, cannabis and alcohol after treatment initiation were found to be two times, about four times and about five times more likely non adherent than patients who had no history of those substance use with (AOR=2.01, 95%CI (1.11, 3.65)), (AOR=4.46, 95%CI (1.64, 12.12) and (AOR=4.72, 95%CI (1.79, 12.46) respectively.

Absence of family encouragement (AOR=2.99, 95%CI (1.31, 6.86)), negative attitude towards treatment (AOR=3.79, 95%CI (1.56, 9.23)), were factors remained to be statistically significant. On the other hand sex, monthly income, duration of treatment and type of drug found to have no statistically significance association with antipsychotic drug non adherence (Table 4).

Table 4 Factors associated with antipsychotic drug non adherence among patients attending at AMSH; March, 2013 (n=403).

| Explanatory variables | Drug adherence | | COR(95% CI) | AOR(95% CI) |
|-------------------------------------|----------------|-----|-------------------|--------------------|
| | Yes | No | | |
| Sex | | | | |
| Male | 141 | 127 | 1 | 1 |
| Female | 54 | 81 | 0.60 (0.39,0.91) | 0.79(0.44, 1.41) |
| Monthly income | | | | |
| Less than 570 | 139 | 131 | 1 | 1 |
| > 570 | 56 | 77 | 0.69 (0.45,1.04) | 0.82(0.46, 1.47) |
| Type of drug taken | | | | |
| Low potency | 120 | 130 | 1 | 1 |
| High potency | 69 | 56 | 1.34 (0.87,2.05) | 1.96(1.09,3.52) |
| Atypical | 6 | 22 | 0.29 (0.12, 0.75) | 1.03(0.34, 3.16) |
| Co-morbid depression | | | | |
| Yes | 83 | 27 | 3.75 (2.28,6.18) | 2.23(1.12, 4.45)** |
| No | 112 | 181 | 1 | 1 |
| Drug regimen | | | | |
| Mono therapy | 102 | 167 | 1 | 1 |
| Poly therapy | 93 | 41 | 2.38 (1.52,3.73) | 2.37(1.21, 4.65)** |
| Extra pyramidal side effects | | | | |

| | | | | |
|------------------------------|-----|---------|----------------------|--------------------|
| Yes | 75 | 34 | 3.19 (2.01, 5.10) | 2.66(1.44, 4.91)** |
| No | 120 | 17 4 | 1 | 1 |
| Duration of treatment | | | | |
| < 6 months | 46 | 69 | 1 | 1 |
| 6 months to 2 years | 85 | 81 | 0.60 (0.36, 1.01) | 1.69(0.87, 3.28) |
| > 2 years | 64 | 58 | 0.95 (0.59, 1.52) | 1.72(0.66, 4.47) |
| Perceived stigma | | | | |
| Yes | 123 | 76 | 2.97 (1.98, 4.45) | 3.35(1.94, 5.81)** |
| No | 72 | 13 2 | 1 | 1 |
| Family encouragement | | | | |
| Yes | 156 | 19 6 | 1 | 1 |
| No | 39 | 12 | 4.08 (2.07, 8.06) | 2.99(1.31, 6.86)** |
| Attitude towards drug | | | | |
| Positive | 159 | 19 6 | 1 | 1 |
| Negative | 36 | 12 | 3.69 (1.86, 7.34) | 3.79(1.56, 9.23)** |
| Khat use | | | | |
| Yes | 66 | 42 | 2.02 (1.29, 3.17) | 2.01(1.11, 3.65)** |
| No | 129 | 16 6 | 1 | 1 |
| Alcohol use | | | | |
| Yes | 31 | 10 | 3.74 (1.78, 7.86) | 4.7(1.79,12.46)** |
| No | 164 | 19 8 | 1 | 1 |
| Cannabis use | | | | |
| Yes | 32 | 9 | 4.34 (2.01, 9.36) | 4.5(1.64,12.12)** |
| No | 163 | 19 9 | 1 | 1 |

Discussion

The overall prevalence of antipsychotic drug non adherence in the current study area was found to be slightly higher than study done in Nigeria and India which were 40.3% [8] and 35.5% [17] respectively. Meta-analysis of published literature indicated that the prevalence of antipsychotic drug non adherence in schizophrenia ranged from 40% to 50% [18]. The possible reason for the difference in the magnitude of

prevalence can be due to the socio cultural difference in the study population and clinical related factors. Almost all (93%) of study subjects in the current study area were taking conventional antipsychotic. The other possible factors that cause higher non adherence in this study area might be the higher substance uses and the difference in the sample size and inclusion criteria.

During bivariate analysis no socio-demographic factors were found to be statistically associated with drug non adherence. This finding was consistent with many previous studies [19,20]. Type of antipsychotic drugs was not found to have statistical significance. Contrary to this study done in France indicated that Individuals prescribed atypical antipsychotic drugs were more likely to be adherent than those prescribed typical antipsychotics [21]. The possible reason can be since participant in the current study area had less availability of atypical antipsychotic over typical antipsychotics which resulting in taking their medication unless they developed extra pyramidal side effects which is difficult for patient to tolerate side effects. Additionally small numbers of participant were on atypical antipsychotic in the current study area.

Regarding the drug regimen, study participants who were on poly therapy were about two times more likely to be non-adherent than those on mono therapy which is in line with study done in Nigeria in which participants who took significantly fewer number of medications were independently and negatively associated with antipsychotic drug non adherence [8].

Study done by Hamburg indicated that patients presenting with side effect compared with patients without side effect had a significantly more negative general attitude toward antipsychotics and were less likely to be encouraged to take such a medication in case of need [22]. Similarly another study indicated patient having extra pyramidal and psychic side effects and sedation were found to be statistically significantly associated with non-adherence [23]. Current study also found out that side effect is highly associated with non-adherence. Patient experiencing EPS has to about three fold risk of being non adherent; while this study didn't appreciate anti cholinergic side effects and psychic side effect as a reason of non-adherence.

Alcohol use, cannabis use and khat/chat use were independently and significantly associated with non-adherence. Participants who used alcohol and cannabis were four to five times more likely to be non-adherent than those who didn't used. This finding coincides with study done in France which reported non adherence was associated in patients with substance use [24]. Possible reasons includes the specified substance use can have negative impacts on a person's internal state causing increased cognitive anomalies and unpleasant withdrawal symptoms. In addition to the physical consequences there are a number of long term social and clinical consequences associated with drug and alcohol use. Substance users also tend to report greater extra pyramidal symptoms than abstinent patients and are at greater risk of tardive dyskinesia. Other consequences of those substances are increased risk of social exclusion and

ultimately, homelessness or lack of family support which can end up with medication non-adherence.

Current study also found out perceived stigma and attitude towards treatment were the other factors which were identified to have statistical significance; which coincides with study done in Nigeria and Uganda [11,25].

The present study has some limitations: In this study drug non adherence was measured using self-report which tends to underestimate drug non adherence and also raises the question of patients' ability to recall events. Additionally the study did not consider the degree/ severity of drug non adherence.

Conclusion

In the current study area about half of study participants were non-adherent to their drug. In the final adjusted multivariate analysis drug regimen, co-morbid depression, attitude towards treatment, extra pyramidal side effect, alcohol use and khat use were found to have statistical significance with antipsychotic drug non adherence.

Factors such as duration of being on treatment, income and gender in the final adjusted model were not shown any significant relationship with antipsychotic drug non adherence in this study. Concerned body should consider the accessibility of drugs having lower extra pyramidal side effects. Furthermore investigations that combine self-report with other methods should be conducted.

Competing Interests

There is no financial and non-financial competing interest.

Authors' Contributions

All authors contributed to the design of the study. S G. participated in the design of the study, performed the statistical analysis, and drafted the manuscript EA Participated in the design of the study, statistical analysis, and helped to draft the manuscript, TF participated in the design and statistical analysis. All authors have reviewed and approved the manuscript.

Acknowledgements

This study was supported by university of Gondar and Amanuel Mental Specialized hospital, Addis Ababa, Ethiopia. We would like to express our appreciation to all the participants who agreed to be interviewed. We also thank those who provide technical support, and the physicians and nurses for their assistance and efforts.

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