Antipsychotic Medications Switch and Contributing Factors among Ambulatory Patients with Schizophrenia at Amanuel Specialized Mental Hospital, Addis Ababa, Ethiopia

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This is to certify that the thesis prepared by Getachew Asfaw entitled "Antipsychotic medication switches and contributing factors among ambulatory patients with schizophrenia at Amanuel Specialized Mental Hospital" and submitted in partial fulfillment of the requirements for the degree of Master of Pharmacy in Pharmacy Practice complies with the regulations of the university and meets the accepted standard with respect to originality and quality.

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Abstract

Antipsychotic medications switch and contributing factors among ambulatory patients with schizophrenia at Amanuel Specialized Mental Hospital, Addis Ababa, Ethiopia

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Antipsychotic medications are the cornerstone of treatment for schizophrenia. Antipsychotic switching is a common practice in the treatment of schizophrenia. As there is limited current data on antipsychotics medication switch among patient with schizophrenia in Ethiopia; this study aimed to generate information on antipsychotics medication switch among patient with schizophrenia. Using a systematic random sampling a cross sectional patient interview and retrospective chart review of the same patients was conducted from 1 to 30, November 2016. A total of 411 study participants were included in the study. Three Focus Group Discussion was also conducted with 24 health care professionals from different departments. Descriptive and inferential statistics were computed for the quantitative part of the study and a thematic analysis was taken for the qualitative study. The result showed that, there has been medication switch in 42.8% of the study participants and in 64% of the participants the switch was shown to be within the same class of First Generation Antipsychotics. For more than half of the patients (55.68%) who had a medication switch, the reasons for initial antipsychotic medication switch were not documented. Side effects, relapse, admission history, high and very high dose of antipsychotic were significantly associated with antipsychotic medication switches. The Focus Group Discussion revealed that interrupted supply of antipsychotic medication was raised as the major reason for the switch. The practice of antipsychotic medications switch in the setting is within the range in terms of prevalence worldwide and reasons for medications switch were not recorded for majority of the patients. Clear and complete recording of the reasons should be maintained by clinicians whenever switching is considered.

***Key words**: Antipsychotic medications, Antipsychotic switch, Schizophrenia*

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Abbreviations / Acronyms

ASMH Amanuel Specialized Mental Hospital

APA American Psychiatrist Association

CI Confidence Interval

DSM IV-TR Diagnostic and Statistical Manual for Mental Disorder 4th edition Text Revision

COR Crude Odds Ratio

CPZeq Chlorpromazine Equivalent Dose

FGA First Generation Antipsychotic

FGD Focus Group Discussion

IPAP International Psych pharmacotherapy Algorithm Project

NICE National Institute for Health and Clinical Excellence

PORT Patient Outcome Research Team

SD Standard Deviation

SGA Second Generation Antipsychotic

SPSS Statistical Package Software for Social Studies

TMAP Texas Medication Algorithm Project

WHO World Health Organization

1. Introduction

1.1. Background

Schizophrenia is a psychotic disorder or a group of disorders marked by severely impaired thinking, emotions, and behaviors (Dipiro *et al*., 2014; Kasper *et al*., 2015). It is believed that the risk of schizophrenia is related to genetic and environmental factors. However, the exact etiology of the schizophrenia is unknown (Mueser & McGurk, 2004; Maziade & Rouleau, 2009; WHO, 1998).

Schizophrenia is a disorder with relatively low prevalence (1-3% projected life time risk) (WFMH, 2014). It is ranked 12th globally in terms of years lived with disability (YLD) and acute schizophrenia ranked first as the most disabling disease state of all Global Burden Disease (WFMH, 2014; WHO, 2017). In Ethiopia, the lifetime prevalence of schizophrenia was around 0.5% (Kebede *et al*., 2003; Teferra *et al*., 2012) and it is also the number one diagnosis for admission to the only mental hospital in the country (Fekadu *et al*., 2007). According to Abdullahi *et al*. (2001), schizophrenia accounts for 11% in terms of burden of diseases among non-communicable diseases in Ethiopia.

Schizophrenia is diagnosed based on criteria in either the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, version DSM-IV-TR (APA, 2000), or the World Health Organization's International Statistical Classification of Diseases and Related Health Problems, the ICD-10 (WHO, 1993). The diagnosis rests on the combination of the occurrence of typical clinical features and longitudinal observation. Based on the clinical features, three symptoms of schizophrenia are identified: positive, negative, and cognitive dysfunction (Andreasen *et al.*, 1995; Stover *et al.*, 2007).

Positive symptom of the disorder includes delusions, disorganized speech, hallucination, behavior disturbance and illusions while negative symptom includes alogia, avolition, flat affect, anhedonia and social isolation. Cognitive dysfunction includes impairments of attention, working memory and executive function. In order to confirm the diagnosis of schizophrenia, a patient must have at least two of these symptoms for one month and continuous symptoms for at least six months (APA, 2000 ; DiPiro *et al*., 2014; Kasper *et al*., 2015).

The treatment of schizophrenia involves both psychosocial support and antipsychotic medications use with the goal of therapy: to alleviate or even eradicate symptoms, to optimize quality of life, social functioning and to promote and maintain recovery and prevent relapse (Davies *et al.,* 1992). Antipsychotic medications are the cornerstone of treatment for schizophrenia and effective in the treatment of hallucinations, delusions, and thought disorders. There are two types of antipsychotics: typical or conventional or First generation antipsychotics and atypical or Second generation antipsychotics. Typical antipsychotics act by blocking the dopamine D2 receptors and atypical antipsychotics act on dopamine, serotonin, and other neurotransmitter systems (DiPiro *et al*., 2014; Kasper *et al.*, 2015).

Several clinical practice guidelines: The Expert consensus guide line (Mc Evoy et al.,1999); Practice guideline for the treatment of patient with schizophrenia (APA, 2010) ; Texas medication algorithm project : schizophrenia treatment guide line (Moore TA, 2008) ; The International Psychopharmacology Algorithm (IPAP, 2009) have been developed on the use of antipsychotic for the treatment of schizophrenia.

Antipsychotic medication switching should only be considered only after evaluation of tolerability, efficacy and safety. As much as possible a patient should have received an adequate trial of antipsychotics. Patient need at least four weeks of therapeutic dosage of antipsychotic (excluding clozapine) before they can be considered for antipsychotic medication switches (Argo RT *et al.,* 2008) and in clinical practice, switching from one to another antipsychotic may be seen as an overall expression of unsatisfactory response to treatment, including both treatment failure and unacceptable adverse effects (Weiden *et al*., 1997).

The switching strategy should always consider the efficacy-to-safety benefit and be tailored to the individual patient (Winans, 2003). However so far, there was no published study done showing the prevalence of antipsychotic medication switch among patient with schizophrenia in Ethiopia.

1.2. Statement of the Problem

Schizophrenia is one of the most disabling and challenging psychotic disorders associated with substantial morbidity and burden at great cost to a patient, family, community and country. In addition to this, despite progress in treatment of schizophrenia, both in pharmacotherapy and psychosocial interventions, there was a worsening of the gap in mortality between the patients and the general population over the past several decades (Saha *et al*., 2007; Mueser & Mc Gurk, 2004; Shibre *et al*., 2003).

In the treatment of schizophrenia many patients are often switched between antipsychotic therapies. Mahmud *et al.* (2004) showed that patients may receive up to 7 different antipsychotics within a 1-year period due to frequent switching from one drug to another and many patients were on polypharmacy without justifications (Sernayk *et al*., 2004). Faries *et al*.(2009), showed that patient who switched antipsychotics experienced a significantly higher risk of acute-care services, including hospitalization and crisis services also used acute-care services significantly sooner and accrued an additional $3,000 (a 25% increase) in annual total health care costs per patient, most of which was due to acute-care expenditures.

Essock *et al* (2002) showed the higher presence of medication discontinuation rate among patient who had were undergone antipsychotic medication switch compared with those who were not switched from their base line antipsychotic. In addition to this, many of the predictable problems that can occur when switching between antipsychotic could be resulted in the symptoms like psychosis, agitation, parkinsonism /akithisia and anxiety. This might be due to receptor antagonism which might be inherently related to the new antipsychotic or may be rebound symptom related to withdrawal from the previous drug (Casey *et al*., 2003; Ganguli *et al*, 2002)

In Ethiopia, where mental health service is poor compared to other African countries (WHO-AIMS, 2006), and only few number of patients attend mental health service (Alem, 2004; Lund et al, 2012). In addition to these, the supplies of antipsychotic are a challenge for primary mental health care (Ayano, 2016), so antipsychotic medication switches could have additional enormous negative impact on treatment outcome of patients with schizophrenia. As a result, this study was conducted to assess the prevalence of antipsychotic medication switches and factors associated with antipsychotic medication switch in the management of patients with schizophrenia who were on follow up.

1.3. Literature Review

1.3.1. Prevalence of antipsychotic medication switches

Different studies carried out in developed countries showed that the prevalence of antipsychotic medications switch ranges from 25% to 74%. According to the cohort study carried out in Connecticut's public mental health system, USA, the rate of antipsychotic medication switch at least once among patient with schizophrenia spectrum was 42% and survival analyses indicated that the rate of medication switch was 21% within 6 months, 33 % within 1 year, and 45 % within 2 years. Among those who had changed antipsychotic medications at least once, 41% changed antipsychotic medication a second time within 2 years (Covell *et al* .,2002) but another study done in the USA found a 25 % annual rate of antipsychotic medication switch among outpatients with schizophrenia (Williams *et al.*,1999) and A cohort study that followed 21,873 patients with schizophrenia and who had stable 3-month prescription of any antipsychotic medication reported that 25% had their medication switched during the next year (Leslie & Rosenheck, 2002). Another randomized, open-label, one-year, multicenter, cost-effectiveness study of antipsychotics in the treatment of schizophrenia done in different states of USA showed about one-third of patients (29.5%, 191/648) switched antipsychotics before the end of the one-year study (Faries et al., 2009; Nyhuis et al.,2010).

A retrospective case control study carried out within three psychiatric hospitals of the Netherlands which have recently merged to a large center for mental health care showed that among admitted patients who started treatment with an oral antipsychotics, 48.5% switched their treatment with another oral antipsychotic during the first admission (Hugenholtz *et al*., 2004).

The open label, multi center, randomized study done in Asia Pacific among patient with schizophrenia which defined a successful switch as completing 6 weeks of therapy without worsening of symptoms or extrapyramidal side effects found that the rates of successful switching from previous typical antipsychotic into olanzapine direct switch was 74.1% and start-taper switch, 67.9% (Lee Chien Te *et al*., 2002) but another study done with chronic schizophrenia who were treated with conventional antipsychotics at two psychiatric hospitals in Japan during the period June 2001–February 2003 with fifty patients showed switching to monotherapy was achieved in 34 patients (68%) (Nakanishi *et al*., 2006).

1.3.2. Reasons for Antipsychotic medication switch

A retrospective cohort study conducted at 21 sites in 15 states of USA indicated that among medication switchers, the reasons for the switching were noted as patient's decision (34.6%), lack of medication efficacy (27.7%), adverse event (22.5%), and other or unknown reasons (15.2%) (Nyhuis *et al*., 2010). Another study carried out in different states of USA showed that 28.2% reasons as not recorded, 26.3% as per patients' request, 23.1% as lack of efficacy and 22.4%, as due to adverse events (Faries *et al.,* 2009)

''A retrospective survey carried out among 60 patients with schizophrenia identified some of the main reasons underlying medication switching. Insufficient compliance was the cause in 26.7% of the cases, lack of efficacy in 66.7%, and complexity of treatment in 10% of cases. Patient and family choice may also play a part in medication switch in schizophrenia, particularly if these individuals are informed of new treatment options. In addition there are several factors that contribute to the rationale for switching from one to an alternative antipsychotic drug, including a partial or total lack of efficacy for the treatment of positive or negative symptoms or the occurrence of adverse effects such as movement disorders, weight gain, somnolence, endocrine side effects, sexual side effects, or metabolic dysfunction (Burns *et al.*, 2002)''.

1.3.3. Factors associated with antipsychotic medications switch

The six variables identified as the best predictors of antipsychotic switching are lack of antipsychotic use in the prior year, pre-existing depression, female gender, lack of substance use disorder, worsening of akithisia and worsening of symptoms of depression or anxiety during the first two weeks of antipsychotic therapy (Nyhius *et al.,* 2010)

The study done in the Netherlands showed that previously treated with typical antipsychotic being initially treated with short acting parenteral antipsychotic and having an involuntary admission or restrictive measures were predictors of antipsychotic switches (Hugenholtz *et al.,* 2004)

According to clinical guide lines factors that favors switching antipsychotic from one to another antipsychotic are: persistent extrapyramidal symptoms, disturbing side effects , risk of tardive dyskinesia , persistent positive or negative symptoms, relapse despite adherence to treatment , to improve level of functioning, patient or family preference, persistent cognitive problems , persistent agitations , persistent severe mood symptoms, history of suicide risk , taking high dosage of first antipsychotic(Argo RT *et al.*,2008; Mc Evoy *et al.*, 1999)

Since there is no published study done in Ethiopia which determines antipsychotic switch practice in the public health institution like ASMH. The current study aimed to determine the antipsychotic switch practice in patients with schizophrenia at Amanuel specialized mental hospital.

2. Objectives

2.1 General objective

- To assess antipsychotic medications switch and contributing factors among ambulatory patients with schizophrenia at Amanuel Specialized Mental Hospital, Addis Ababa

2.2 Specific objectives

- To determine the prevalence of antipsychotic medications switch
- To assess the reason for antipsychotic medications switch
- To explore the reasons for antipsychotics medications switch from health care professionals' perception

3. Methods

3.1 Study setting and period

The study was conducted at Amanuel Specialized Mental Hospital which is one of the public hospitals under Ethiopian Federal Ministry of Health. Amanuel specialized mental hospital is located in the Addis Ketema sub city of Addis Ababa, Ethiopia. The hospital gives service on average for 500 patients per day who come from different parts of the country. The hospital also plays a vital role as a training institute for psychiatry professionals to expand the service to all levels of health care delivery system in the country. The study was conducted from 1 November to 30, December, 2016

3.2. Study design

A cross sectional study design was conducted at outpatient psychiatric departments of ASMH which includes quantitative and qualitative data collection techniques. Initially, patient interview was conducted by structured Amharic translated version of questionnaire and then retrospective chart review was done for the same patient. Furthermore an FGD was conducted with health care professionals from different departments as Phenomenological qualitative method.

3.3. Sample size and sampling procedures

The minimum number of participants required for quantitative study was determined by using single population proportion formula considering the following assumptions:

$$n = \frac{(Z\ a/2)2\ p\ (1-p)}{d2}$$

Where

n= minimum sample size required for the study

Z= standard normal distribution (Z=1.96) with confidence interval of 95% and *a* =0.05

P= the prevalence of antipsychotic switch among patient with schizophrenia which is unknown in Ethiopia; hence, P= 50 %(0.5) was used.

d= Absolute precision or tolerable margin of error (d) =5%=0.05

$$n = \frac{(Za/2)2\ p\ (1-p)}{d2} = \frac{(1.96)2\ 0.5\ (1-0.5)}{(0.05)2} = 384$$

Then adding 10% contingency (384 x 0.1 = 38.4 ≈39) of non-respondent, the final sample size for this study was 384+39= 423

Systematic random sampling technique was used to recruit the study participants. The average number of patients with schizophrenia who were on follow-up according to the hospital data a month prior data collection was 5334. The sampling fraction (k) was calculated to be 5334/423 ≈13. A starting point was selected randomly from numbers 1 to 13. Then, every 13th patient was interviewed and medical record was reviewed following the interview the same day.

For qualitative study, health care professionals were selected purposively and 24 participants participated in three Focus Group Discussion. Three focus group discussion was conducted with the first group consists of 10 professionals, second group consists of 7 professionals and the third group also consist of 7 professionals

3.4. Study Subjects

3.4.1. Source population

For quantitative study, all patients with schizophrenia who were diagnosed at Amanuel specialized mental hospital by DSM-IVTR were in the sampling frame. For qualitative study, participants were selected from health care professionals who were prescribers and pharmacists.

3.4.2. Study Population

All patients with schizophrenia who were on follow up at outpatient department of ASMH and fulfill inclusion criteria during the study period were the study population. For qualitative study, selected prescribers and pharmacists who volunteered to participate.

3.5. Inclusion and Exclusion Criteria

3.5.1. Inclusion Criteria

Quantitative study

- Patients with schizophrenia who would volunteer to participate in the study
- Patients with schizophrenia who were 18 years and above
- Patients with schizophrenia who had a minimum of 1 year history of treatment at ASMH.

- Qualitative study: Prescribers and pharmacists, who were purposefully selected and worked at least for 1 year at ASMH

3.5.2. Exclusion Criteria

Quantitative study

- Patients with schizophrenia who were acutely disturbed during the study period.
- Patients with schizophrenia who were lost from follow up within the last 1 year.
- Patients whose card was incomplete.

Qualitative study: Prescribers and pharmacists who wouldn't volunteer to participate in the study.

3.6. Data collection and management

3.6.1. Data collection instrument

For quantitative study, data were collected using a structured and semi structured questionnaire (Annex I) interview from the patient prospectively after it was translated to Amharic version (Annex II) and back translated into English to check the consistency of the questionnaire. The questionnaire for interview contained socio demographic characteristics, Morisky Medication Adherence predictor scale and medication related questions. At the same time the patient's chart was reviewed retrospectively by data extraction format. The data extraction format was employed to collect clinical factors, medication related factors and reason for medication switch.

For qualitative study, the topic guide included questions about when antipsychotic medication switches is indicated, what factors contribute to antipsychotic medication switch, why were reasons for antipsychotic medication switch not recorded were raised and recorded with aid of tape recorder and the group discussions lasts within a range of 1-1:30 hour (Annex III)

Morisky Medication Adherence Scale-8

Morisky Medication Adherence Scale-8 is a patient self-reported and medication taking behavior scale. It contains eight individual questions in focusing on past medication use patterns with a scoring scheme of "Yes" = 1 and "No" = 0 for the first seven items except item number five in which the values of "Yes" and "No" were reversed and question number

8, is a Likert response with options “never”=0, “once in a while”=0.25, “sometimes”=0.5, “usually”=0.75, and “always”=1. The total score was finally computed by adding all and sub-divided to give a range of scores from low adherence (score=>2), Medium Adherence (score 0.25-2) and high adherence (score=0) (Annex-I). The instrument has been validated for different types of chronic illnesses and it is widely validated for hypertension patients in different countries and set up. It was also validated for psychiatric patients in Spain (Cuevas and Penate, 2015).

Chlorpromazine Dose Equivalencies (CPZeq)

The Chlorpromazine Dose Equivalencies (CPZeq) is a measure of the relative antipsychotic potencies of antipsychotics. It is generally expressed as a ratio, relative to the arbitrary value of 1, which corresponds to the antipsychotic effects of chlorpromazine. The daily dose of antipsychotic medications prescribed to each patient was converted to milligram equivalents of chlorpromazine according to conversion factors derived from the literature (Woods, 2003; Vijay & Ganesan, 2013; Schooler & Levine, 1976). Total CPZeq was constructed by calculating a total daily dose of each antipsychotic listed in the medical file. Then each converted antipsychotic specific CPZeq amount is added to arrive at a total daily dose. A maintenance dose of CPZeq less than 300 mg is sub therapeutic, the range of 300–600 mg is optimum 600-1000mg high and greater than 1000mg are considered as very high dose (Kreyenbuhl *et al.,* 2010).

Data extraction format

The patient’s chart was reviewed retrospectively by data extraction format (Annex I: part 2). The data extraction form contained diagnosis, duration of illness, relapse and, other co-morbid illness, antipsychotic switch and reason for switches.

3.6.2. Data collectors

For quantitative study, nine psychiatry nurses were recruited to collect the data. They were trained for one day on the use of questionnaire and the ethical principles of confidentiality and data management prior to their involvement in data collection. The data were collected for one month. For qualitative study, the principal investigators collected the data.

3.6.3. Data Quality Control

For quantitative study, the data collection instrument which included the questionnaire and the data extraction form was assessed by a psychiatrist and other health professionals for clarity and comprehensiveness of contents. Pre-test was performed on 5% (22 patients) of the sample size before conducting the study. Then, the final tool was developed with some modifications after reviewing the results of the pre-test. Patients who participated in the pretest were excluded from the final analysis. The questionnaires were reviewed and checked every day for completeness and the necessary feedbacks were provided to the data collectors by the principal investigator daily throughout the data collection period. The quality of data was checked at data entry, analysis, and interpretation. The principal investigator leaded the discussion, took notes and recorded with the aid of tape recorder. In cases of ambiguity clarifies the issues raised instantaneously.

3.6.4. Data Analysis and Interpretation

For quantitative analysis, coded data was entered into Epi Info v-7 then transported to and analyzed using SPSS v-20. Descriptive statistics including: frequency, mean, standard deviation and range were used to summarize patients' socio-demographic data and evaluate distribution of responses. Univariable binary logistic regression analysis was performed to calculate crude odds ratio (COR) for each variable and those variables with $p < 0.2$ were selected for multivariable binary logistic regression analysis and the result was expressed as adjusted odds ratio (AOR). 95% confidence level was used to determine factors associated with Antipsychotics switch. A p-value of 5% or less was considered statistically significant. For qualitative study, all focus group discussions were analyzed manually.

3.7. Study variables

3.7.1. Dependent variable

- Antipsychotic medication switch

3.7.2. Independent variables

- Socio-demographic variables**:** age, gender, marital status, educational status, employment status, place of residence, source of medication fee, family income, living arrangement

- Treatment/ medication related variables**:** Current/switched drug used, Class of drugs, Dose of drugs
- Clinical variables**:** Clinical diagnosis, Co-morbid condition, Duration of mental illness**,**
- Medication Adherence,
- Substance use: khat chewing , smoking cigarette, alcohol and cannabis use

3.8 Ethical consideration

Ethical approval was obtained from Ethical Review Board of School of Pharmacy, College of Health Science Addis Ababa University and ASMH research and development department. For the document review part and patient information sheet contains patient identifiers. The data was collected by the trained psychiatry nurses recruited from the same department in order to ensure the confidentiality of the patient information. Since they are working in the same department there is no risk of disclosing the patient data to the third party. A participant of the study was asked for informed written consent before participating in the study. During the consent process, they were provided with information regarding the purpose of the study, why and how they are selected to be involved in the study, what is expected of them and that they can withdraw from the study at any time.

3.9. Operational definitions

Antipsychotic medication switch: 1) stop the old antipsychotic abruptly and immediately start the new antipsychotic, 2) cross-titration—gradually reduce the dose of the first antipsychotic while gradually increasing the dose of the new antipsychotic, 3) overlap and taper—don't reduce the dose of the old antipsychotic until the new antipsychotic is at a full therapeutic dose (Mc Evoy et al., 1999).

Relapse is broadly recognized as the reemergence or the worsening of symptoms. It includes: aggravation of symptoms, hospital admission, and more intensive case management and/or a change in medication in the past 6 months (Almond et al, 2004; Kazadi et al., 2008).

Prescribers: includes psychiatrists, psychiatry residents, psychiatry professionals, public health officers.

Polypharmacy: More than one antipsychotic medication prescribed concurrently, excluding oral and parenteral preparation of the same medication.

Substance use history: refers to using khat, cigarette and tobacco within 3 months.

Chlorpromazine dose Equivalence: The equivalent dose of antipsychotics for 100 mg of chlorpromazine as indicated in Annex v.

Sub-therapeutic dose: Total daily chlorpromazine equivalent dose less than 300 mg

Optimum daily dose: Total daily chlorpromazine equivalent dose in a range of 300-600 mg

High daily dose: Total daily chlorpromazine equivalent dose in a range of 600-1000 mg

Very high daily dose: Total daily chlorpromazine equivalent dose in a range of above 1000 mg

High adherence: Morisky medication adherence scale-8 score of "0"

Medium adherence: Morisky medication adherence scale-8 score of "0.25-2"

Low adherence: Morisky medication adherence scale-8 score greater than 2

Interrupted supply of antipsychotics: refers to unavailability of antipsychotics in the institution during patient's appointment.

4. Results

4.1. Quantitative Results

Socio-demographic and behavioral characteristics of the participants

A total of 411 study participants were involved for quantitative data analysis. Of these participants 250 (60.8%) males and the mean age (± standard deviation) of the participants was $36.3. \pm 11$ years (range, 18–79 years). One-third of the participants (34.1%) have completed secondary education and greater than two third of them (71.5%) were from urban area. About three-fifth of the study participants (59.6%) were single and over the three quarter of the participants (77.4%) were unemployed. The substance use appeared to be 7.8%, 16.8%, 18.2% of the respondents take alcohol, smoke cigarette and chew khat, respectively as shown in Table 1.

Table 1 : Socio-demographic and behavioral characteristics of ambulatory patients with schizophrenia on follow up at Amanuel Specialized Mental Hospital

Variables	Frequency(N=411)	Percent
Age		
<= 24	41	10
25-34	146	35.5
35-44	138	33.6
45-54	51	12.4
55and above	35	8.5
Sex		
Male	250	60.8
Female	161	39.2
Level of education		
Not literate	66	16.1
Primary	128	31.1
Secondary	140	34.1
Tertiary	77	18.7
Residence		
Urban	294	71.5
Rural	117	28.5
Marital status		
Single	245	59.6
Married	113	27.5
Divorced	39	9.5
Widowed	14	3.4
Family income		
Very low(<585)	160	38.9
Low (586-3145)	207	50.4
Average (3146-7758)	33	8.0
Above average **(**>= 7759)	11	2.7
Employment status		
Unemployed	318	77.4
Employed	93	22.6
Living arrangement		
Alone	39	9.5
With family	368	89.5
In charity	4	1.0
Cigarette Smoking		
Yes	69	16.8
No	342	83.2
Alcohol use		
Yes	32	7.8
No	379	92.2
Khat use		
Yes	75	18.2
No	336	81.8

Illness Characteristics of the Study Participants

As indicated in Table 2, more than seventy percent of the participants had illness duration of ranging 1 -10 years. Fifty seven participants (13.9%) had a relapse but only forty one of the participants had hospital admission history in the last one year.

Table 2: Illness characteristics of ambulatory patients with schizophrenia on follow up at Amanuel Specialized Mental Hospital

Variables	Frequency (N=411)	Percent
Duration of mental illness (years)		
1-10	295	71.8
11-20	80	19.5
21-30	33	8.0
31-40	3	0.7
Co-morbid psychiatric illness *		
No	319	78
Yes	92	22
Co -morbid medical illness*		
No	382	92.9
Yes	29	7.1
Relapse history in the last 1 year		
No	354	86.1
Yes	57	13.9
Psychiatry admission history in the last 1 year	370	90.1
No	41	9.9
Yes		

Co-morbid psychiatry illness*: Depression, Bipolar disorder, Anxiety, substance use disorder

Co-morbid medical illness*: Diabetes, hypertension, chronic kidney disease, obesity, chronic Heart Failure

Medication related factors

As shown in Table 3, more than one-quarter of the study participants (28%) experienced side effects and over forty percent of the participants (44.5%) reported as having high adherence to their medication.

Table 3: Medication and follow up pattern of ambulatory patients with schizophrenia at Amanuel Specialized Mental Hospital, November, 2016

Variables	Frequency (N=411)	Percent
Source of medication		
Free	299	72.7
Payment	112	27.3
Presence of Side effects		
No	296	72
Yes	115	28
Follow-up interval		
Monthly	93	22.6
Two month	89	31.7
Three month	113	27.5
Four month or above	116	28.3
Medication adherence level		
High	183	44.5
Medium	122	29.7
Low	106	25.8

Antipsychotic medication use pattern of the Study Participants

Medication use pattern before switch almost three-fourth (72.3%) of the participants were on FGA while only around one –fifth of the respondents were on SGA as shown in figure 1. Regarding polypharmacy pattern, during the last one year, ninety percent of the participants had monotherapy pattern before switch and two-third (68.1%) of the participants were on sub therapeutic dose before the switch as shown in Table 4.

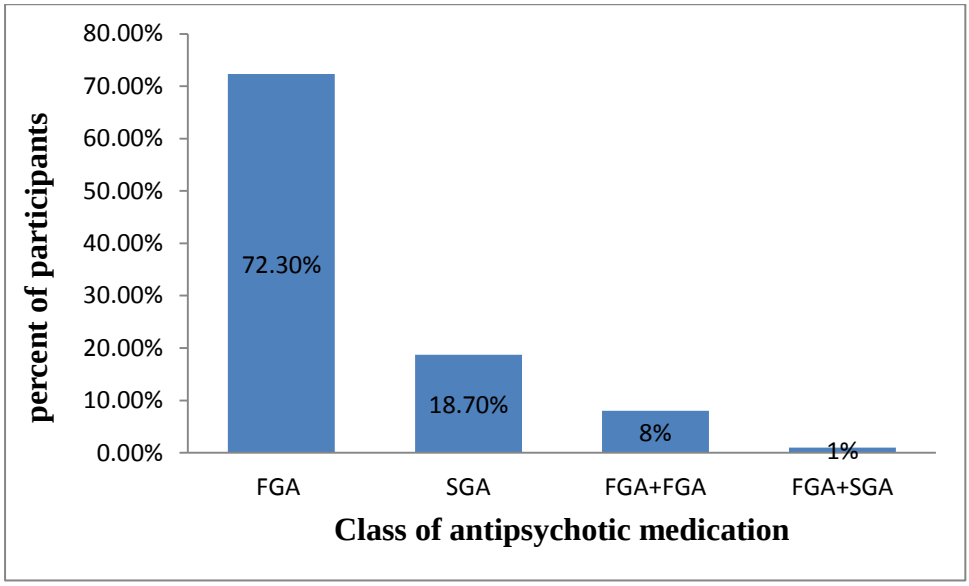

Figure 1: Class of Antipsychotic medication used by ambulatory patients with schizophrenia on follow up at Amanuel Specialized Mental Hospital

Table 2: Past and Current Antipsychotic medication use pattern of the ambulatory patients with schizophrenia on follow up at Amanuel Specialized Mental Hospital

Medication use	Frequency (N=411)	Percent
Medication use before switches		
Chlorpromazine	209	50.9
Fluphenazine decaonate	70	17
Haloperidol	56	13.6
Thiordazine	25	6.1
Trifluoperazine	6	1.5
Risperidone	56	13.6
Olanzapine	25	6.1
Poly pharmacy before switches in the last 1 year		
No	374	91
Yes	37	9
Maintenance dose before switch (CPZeq dose)		
Sub therapeutic	280	68.1
Optimum	80	19.5
High	26	6.3
Very high	25	6.1
Anticholinergic medication current use		
No	394	95.9
Yes	17	4.1
Adjuvant medication		
No	302	73.5
Yes	109	26.5

Antipsychotic medication switch pattern of patients with schizophrenia

As depicted in figure 2, antipsychotic medication switches (at least one switch); during one year, was practiced in greater than two-fifth (42.8%) of the study participants. Only ten patients had at least two medication switch pattern.

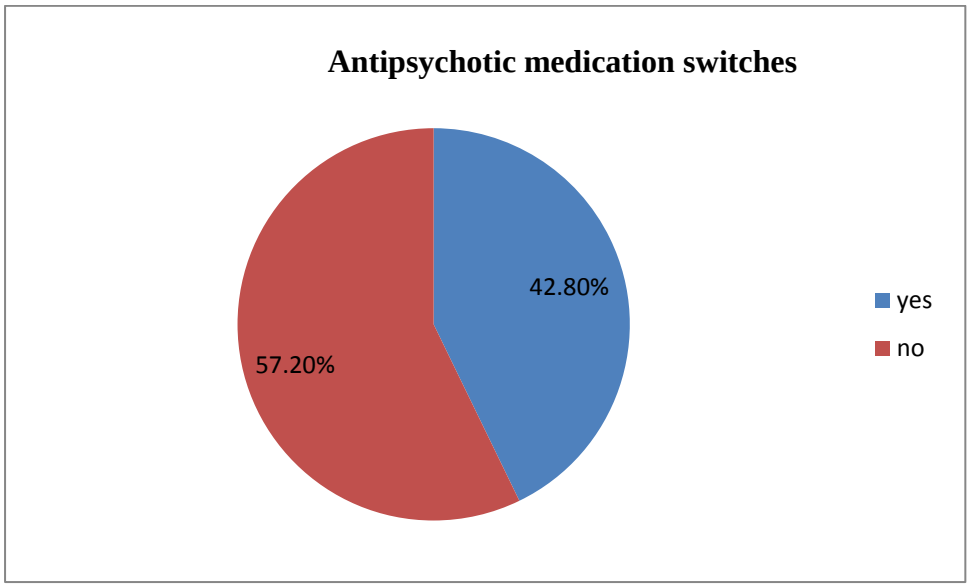

Figure 2: Prevalence of Antipsychotic medication switches among ambulatory patient with schizophrenia at Amanuel Specialized Mental Hospital, November, 2016

Concerning the average time prior to medication switch, the average duration on treatment was 159.41 days. Over half (54.5%) of the participants were on FGA after medication switch as shown in figure 3.

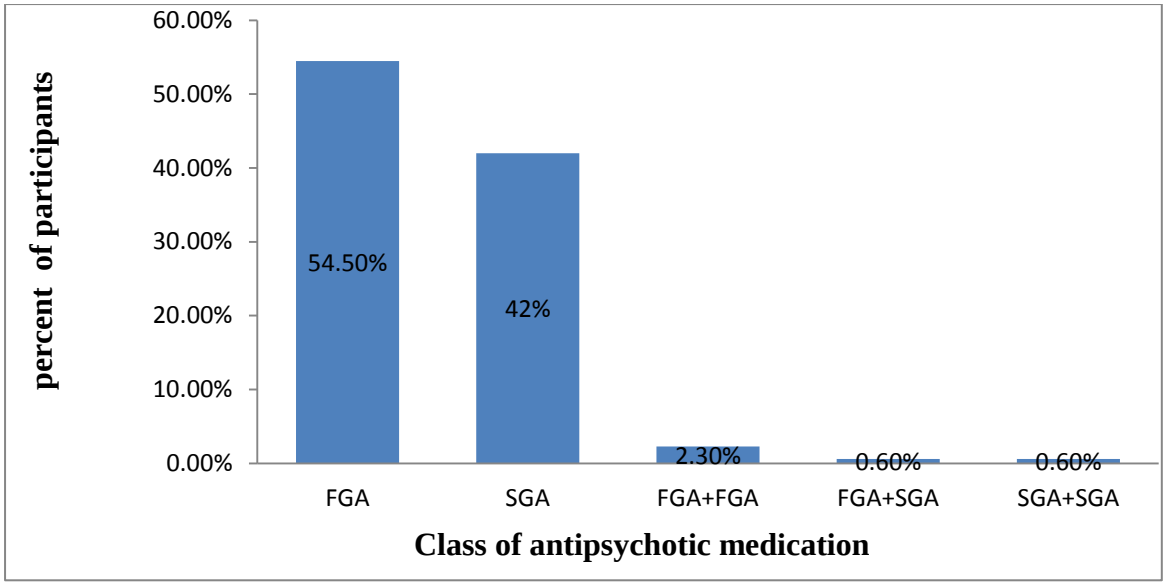

Figure 3: Class of antipsychotics medication use after switch among ambulatory patients with schizophrenia at Amanuel Specialized Mental Hospital

Reasons for Antipsychotic Medication Switches

More than half (55.68%) of the reasons for the first time antipsychotic medication switches was unrecorded as shown in table 5 and similarly greater than half (60%) of the reasons for second time antipsychotic medication switch were also unrecorded on patient charts.

Table 5: Reasons for antipsychotic medication switches among ambulatory patients with schizophrenia at Amanuel Specialized Mental Hospital

Reason for 1st time antipsychotic medication switch	Frequency (N=176)	Percent
Reason unrecorded	98	55.68
Unavailability of medication	42	23.86
Inadequate response or partial response	14	7.95
Non adherence to medication	12	6.81
Presence of side effects	8	4.54
Others*	2	1.13

*patient preferences, previous diagnosis changed

Factors associated with Antipsychotic medication switches

In multivariate logistic regression analysis it was noticed that side effects experienced history, relapse, psychiatry admission and high or very high maintenance dose were found to have significant association with antipsychotic medication switches as shown in Table 7.

The odds of antipsychotic medication switches was nearly eight (AOR=7.5, CI 95%, 4.8-12) compared to those who did not have side effects. The odds of antipsychotic medication switch also greater than 12 (AOR=12.4, CI 95%, 5.8-19) in patients who had a relapse history compared to those who didn't in the last 1 year.

The odds of antipsychotic medication switches was almost six (AOR=5.8, CI 95%, 2.8-12) in patients who had admission history in the last one year compared to those who had no admission history. The odds of antipsychotic medication switches was almost twice in patients who were taking high dose of antipsychotic compared to those who were on sub -therapeutic dose and it was three times in patients who were taking very high dose of antipsychotic compared to those patient who were on sub -therapeutic dose.

Table 6: Multivariate logistic regression analysis results of factors associated with Antipsychotics Medication switch among ambulatory patients with schizophrenia at Amanuel Specialized Mental Hospital

Variables	Medication Switch		COR (95 %CI)	AOR(95% CI)
	No (%)	**Yes (%)**		
medication obtained				
Freely	162(69.8)	137(73.7)	1.00	1.00
Payment	70(30.2)	42(26.3)	0.70 (0.5, 2.2)	1.38 (0.88,2.2)
Khat Chewing				
No	196(84.5)	140(78.2)	1.00	1.00
Yes	36(15.5)	39(21.8)	1.5 (0.4, 1.9)	0.72 (0.43,1.2)
Psychiatric Admission				
No	216(93.1)	154(86)	1.00	1.00
Yes	16(6.9)	25(14)	2.2 (2. 1, 8.8)	5.7 (2.8,12)**
Side effects experienced				
No	175(75.4)	121(67.6)	1.00	1.00
Yes	57 (24.6)	58 (32.4)	1.5 (1.4 ,10.5)	7.5 (4.8 ,12)**
Relapse				
No	209(90)	145(81)	1.00	1.00
Yes	23(10)	34(19)	2.13(2.2, 18.3)	12.4 (5.8,19)**
Medication dose used				
Sub therapeutic	163(70.1)	117(65.4)	1.00	1.00
Optimum	39(16.8)	41(22.9)	1.52 (0.64,3.65)	1.92(0.77,4.77)
High	13(5.7)	13(7.3)	1.4(1.37,5.76)	2.37 (1.89,6.29)**
Very high	17(7.3)	8(4.6)	0.65(0.58-6.64)	2.61(1.18, 8.48)**

** ($p<0.05$)

4.2. Qualitative Findings

Focus group discussion was employed to generate information on perspective of health care professionals on antipsychotic medication switch for ambulatory patients with schizophrenia at ASMH. Among participants 5 of them were female. Regarding participants' compositions: 6 Psychiatrists, 4 Psychiatry Residents, 8 senior psychiatry officers, 3 Pharmacist and 3 health officers participated. The average age of participants was 31 years with a minimum of 25 years and a maximum of 46 years. All of the participants had greater than 1 year work experiences.

4.2.1 Antipsychotic medication switches Indicators

All participants (n=24) in the discussion agreed on the importance of antipsychotic medication switch for patient with schizophrenia on follow up when there is relapse despite of taking optimum dose, with optimum duration of treatment and adherence to the medication.

One of the discussant groups stated antipsychotic medication switch indications as follows

> *".....Antipsychotic Medication switch is indicated when a patient with schizophrenia takes a medication of adequate dose, for adequate duration on regular basis, and with appropriately made diagnosis but when there is no response; it is mandatory to switch antipsychotic medication (APS 001)."*

Another discussant group describes points to be considered to switch antipsychotic medication by prescribers.

> *"...in order to switch antipsychotic medication a prescriber has to evaluate whether the patient has taken the right medication with the recommended optimum dose with the optimum duration of time and right diagnosis set but no symptom improvement without intolerable side effects (APS 007)."*

Factors contributing to antipsychotic medication switches among patient with schizophrenia

Repeatedly raised factors that affect antipsychotic medication switch were the following *"interrupted supply of medication, intolerable side effects, co-morbid medical problem and family chronic medical illness history, patient adherence to the medication, misdiagnosis, age of the patient, prescriber preferences, lack of a single prescriber for a given patient (poor communication between prescribers), cost of the medication… are major reasons for antipsychotic medication switch."*

One of the discussant groups stated that

> *"Prescribers might switched the medication from conventional antipsychotic into atypical antipsychotic earlier and patient progress was good but when the patient comes another day for fill, all atypical antipsychotics will be stocked out, so the prescriber will be forced to put the patient on conventional antipsychotic which causes suffering to the patient when the changed drug is not agreeable (APS 013)"*

Another theme that came in the discussion was

> *"Lack of communication among attending prescribers as one of the factors for medication switch. Currently there are different psychiatrist and other paramedical professionals (psychiatry professional and health officers) with different knowledge about the condition and diagnosis of the patient. Sometimes it is difficult to reach consensus on the diagnosis of the case and assessment for a particular patient, so they prescribe different medication for the different assessment found in particular a patient (APS 016)."*

On the top of the above one psychiatry professional discussant stated about interrupted supply of medication

> *"…I fear to put my patients on atypical antipsychotic even though he /she deserved to take it based on clinical conditions because of their uninterrupted availability in the hospital (APS 022)."*

Reasons not to document antipsychotic medication switch on patient's medical chart

> *All participants (n=24) in the discussion agreed that poor documentation is the main problem for all clinical service in the hospital but not only for the reason of antipsychotic medication switch , but for other necessary information that need to be documented as well.. The probable reasons for not recording reason of antipsychotic medication switched were : lack of confidence for the reason of medication switch, lack of mentoring from the seniors, focusing on the treating a patient rather than documenting, absence or low understanding of usefulness of proper documentation, lack of knowledge how to document information in the patient chart, negligence of the professionals, don't considering documentation as ethical practice, being incompetents and patient load .*

5. Discussion

The clinical practice of managing schizophrenia appears to differ in different countries depending on the available expertise and resources. In clinical practice, switching from one to another antipsychotic can be considered as overall expression of unsatisfactory response to treatment, including both treatment failure and unacceptable adverse effects (Weiden *et al*., 1997) and switching strategy should always consider the efficacy-to-safety benefit to the individual patient (Winans, 2003).

The present study therefore attempted to assess antipsychotic medication switches among patient with schizophrenia at ASMH. The prevalence of antipsychotic medication switches among patients with schizophrenia on follow up in this study was 42.8% and among these, ten participants had undergone a second times antipsychotic medication switches within 1 year. The prevalence of the antipsychotic medication switch in this study is with the range of previous reports from other studies. Our finding was higher than that of studies conducted in different states of USA, 29.5% (Nyhuis *et al.,* 2010; Faries *et al.,* 2009), 33% (Covell *et al*., 2002), 25% (Leslie and Rosenhec, 2002); 25% (Williams *et al.,* 1999). It was however lower than the finding from the study conducted in the Netherland, 48.5% (Hugenholtz *et al*., 2004) and other Asian countries studies; Japan 68% (Nikashi *et al.,* 2006), Pacific Asia 74.1% or 67.9 % (Lee *et al.,* 2002). The discrepancy might be due to our study focused only on outpatients while the previous studies both inpatient and outpatient and sample sizes differences compared to the current study.

In this study, the reason for majority of antipsychotic medication switch was not recorded on the patients' chart which was in line with the study conducted in different states of USA (Faries *et al.,* 2009) and the probable reason for this as described by focus group members was lack of confidence by health professionals' to put a reason for antipsychotic medication switch and not seeing the importance of it which lead them to focusing on only treating the patients rather than documenting and patient load was also one other reason for not doing proper documentation.

In those charts that had some documentation, interrupted supply of antipsychotic medication was recorded as a major reason for antipsychotic medication switch which was supported by focus group discussion and this is in line with the study conducted in Ethiopia that showed interrupted supply of drugs as a challenge for primary mental health care service (Ayano, 2016). Supply of antipsychotic medications for public health institutions like ASMH is only from government owned Pharmaceuticals Supply and Fund Agency, so that when there is a problem of supply of pharmaceuticals in the organization there is no way of getting these medications from another private suppliers in the country. Another reason might be in Low and Middle Income Countries (LMIC), psychiatric services are poorly developed and there is a large treatment gap (Murray *et al*, 2013). Hence, suppliers would not be interested to import enough quantity when there is not great demand and that in turn affects availability of adequate essential antipsychotic medication in the country.

In this study, inadequate response or partial response to a drug was also recorded as a reason for antipsychotic medication switch and this finding supported previous studies (Mc Evoy *et al.,* 1999; Nyhius *et al.,* 2010; Burns *et al.,* 2002); Non adherence which is one of the reasons recorded in this study also is consistent with another studies (Mc Evoy *et al.,* 1999; Burns *et al.,* 2002) and the same is true with side effects, one of the documented reasons in this study (Nyhius *et al.,* 2010).

The literature and Guidelines put second generation antipsychotic as first line choice of treatment and the importance of switching from FGA to SGA which has showed the benefit in terms of improvements of positive and negative symptoms, general psychopathology, global functioning, increase insight, lower risk of relapse and improved adherence (Masand SP, 2005; Mc Evoy *et al.,* 1999; Argo RT *et al.,* 2008). But in this study, 64% of switch were done from one FGA into another FGA which has similarity with the study done in Netherlands (Hugenholtz *et al.,* 2004). In our case this happens because of limited availability of second generation antipsychotic medication (only risperidone and olanzapine available in the country while this study was undergoing). Even the two antipsychotic medications are not dependably on regular supply in the country. Higher cost of SGAs might also lead to switch within the same class of antipsychotics. Leslie and Rosenhec, 2002 stated that the use of atypical antipsychotic medication has been a concern for mental health systems because, in constrained budgets, these medications cost as much as twenty times more than conventional antipsychotics.

The average duration on treatment prior to antipsychotic medication switch in this study was about one hundred sixty days which is longer than the average duration stated by Faries et al., 2009 which was hundred days. The difference might be due to long interval between patient follow-up visits to refill their medication in our study which leads to more time lapse. However, this our finding is in line with the study which recommends medications should not be switched from a one that is successfully maintaining recovery from a psychotic state for 3 to 6 months unless they are experiencing side effects that are of clinical concern (Ganguli, 2002). Most of schizophrenia treatment guidelines recommend that patients in schizophrenia should be treated with antipsychotic medications with adequate titration for adequate period of time before switching antipsychotics (Mc Evoy *et al.,* 1999; Argo RT *et al.,* 2008).

Those who experienced side effects, relapse, admission history, high dose of antipsychotics and very high dose of antipsychotics had significant association with antipsychotic medication switch in this study. The odds of a medication switch for patients who had experienced side effects was about eight times that of patients who had no side effects history in the last one year which is justifiable. In this study majority of the patients were on conventional antipsychotics before antipsychotic medication switch were considered and 28% of the participants reported having had side effects in the last one year, so being on these medications is likely to expose patients for side effects such as extrapyramidal side effects and or risk of tardive dyskinesia which leads to medication switch (Mc Evoy *et al.,* 1999).

The odds of antipsychotic medication switches were almost six times in patients who had psychiatry admission compared to those patients who had no admission. This could be patient admitted to the hospital when there are no improvements of symptoms, relapse, presence of side effects, treatment non adherence and other factors which might contribute for antipsychotic medication switches.

Re-emergence or the worsening of symptoms, aggravation of symptoms and more intensive case management and/or a change in medication clinical deterioration associated with each subsequent relapse poses significant burden for both patients and families (APA, 2010; Almond *et al,* 2004; Mc Evoy *et al.,* 1999; kazadi *et al.,* 2008). Relapse rate varies from 50% to 92% in a six month period for schizophrenia globally (Kazadi et. al, 2008). Patients with schizophrenia have progressive brain tissue loss after onset and extended relapse duration and treatment intensity associated with relapse intensify the decrease in both general and regional

brain measures (Andreasen *et.al,* 2013) in addition to these, repeated relapse episodes are also risk factors for development of treatment resistance (Shives, 2007; Christy LM HUI, 2011; Dammak, 2013), so in this study the odds of antipsychotic medication for patients who had relapse were about twelve times that of patients who had no relapse.

The odds of antipsychotic medication switches for patients who had been on high dose of antipsychotics were about twice of patients who were on sub therapeutic dose of antipsychotic medication and the odds of antipsychotic medication switches for patients who had been on very high dose were about three times of patients who were on sub therapeutic dose of antipsychotic medication in this study. According to consensus guide line a patient taking high dosage of antipsychotics could contributed for high risk of side effects without therapeutically benefit that might be contributed for antipsychotic medications switch (Mc Evoy *et al.,* 1999). However, The study done in Japan showed that a patient who was on excessive dose (greater than or equal to chlorpromazine equivalents of 1000mg /day) was failed in switching antipsychotic (Nakanishi *et al.,* 2006). This might be due to small sample size and switch into only risperidone.

6. Limitation of the Study

The study design of this study is cross sectional so it did not allow drawing any definite conclusion concerning causality between antipsychotic medication switch and predicting variables. Most variables in this study retrieved from patients 'medical charts which are subject to errors in that there might be some missing data. The study was done among patients on follow up only and hence attention should be taken in extrapolating the results. The medication adherence level was assessed based from patient self-reporting so it could contribute for over estimation of the result. There was a limitation of literature review related to the present study to discuss the findings with the low and middle income country. The chlorpromazine equivalent dose has a limitation for second generation antipsychotic so direct conversion of them had a limitation. Despite these limitations, the study was able to give some insight on antipsychotic medication switches among patients with schizophrenia.

7. Conclusion

Antipsychotic medication switches among ambulatory patients with schizophrenia on follow up was practiced among 42.8% of the study participants. Greater than two-third of the participants were using FGA before antipsychotic medication switching was considered and 64% percent of them switched from FGA into FGA for most of the patient who had a medication switch. The reason for antipsychotic medication switch wasn't recorded for most of the patients who had a medication switch on patient chart but focus group discussion revealed interrupted supply of antipsychotics was the main reason for antipsychotic medication switches. Relapse, side effects, psychiatry admission and high dose or very high dose of antipsychotics were significantly associated with antipsychotics medication switches.

8. Recommendations

Antipsychotic medication switches among ambulatory patients with schizophrenia on follow up was found to be common in this study. Based on this result of the following points would be recommended.

- Prescriber should be clearly and completely record reasons for antipsychotic medication switch on the patients chart.
- The hospital should work with different stake holders to strength the supply of antipsychotic medications.
- Pharmaceutical Fund and Supply Agency, Federal Ministry of Health and Amanuel Specialized Mental Hospital should work together to avail different types of second generation antipsychotics other than Olanzapine and Risperidone .
- Treatment guideline should be developed for the hospital about antipsychotic medication switch
- Further longitudinal researches should be done with different study designs.

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Annexes

Annex –I: Consent Form (English)

Hello, my name is _____, I am part of a team of people who are conducting a research on antipsychotic medication switch and contributing factors among patients with schizophrenia on ambulatory at Amanuel specialized mental hospital. I would like to ask you to participate in a research study. Involvement in the study is voluntary and you are selected randomly, so you may choose to participate or not to participate. I am now going to explain to you the aim of the study. Please feel free to ask any questions that you may have about the research; I will be glad to explain anything in greater detail.

You will be asked to answer questions regarding the medications you currently are taking and the questions related to your treatment. This will take approximately 20 min of your time. All information will be kept anonymous and confidential. There will be no information that will identify you in particular. The findings of the study will be general for the study community and will not reflect anything particular to individual persons. The questionnaire will be coded to conceal identity.

The benefit of this research is that you will be helping us to understand the prevalence of antipsychotic medication switches and contributing factors among patient with schizophrenia at Amanuel specialized mental hospital. There is no risk imposed on you by participating in this study. If you do not wish to continue, you have the right to withdraw from the study, without penalty, at any time. If there are any questions or enquires any time about the study or the procedures, please contact: 0911759971or getachewasfaw2005@gmail.com

Are you willing to participate? ☐ Yes ☐ No

Sign. Of the patient_____ Sign. of data collector_____

1. Socio-Demographic Characteristics	
1.1	Age (in years) _____
1.2	Gender : ☐ Male ☐ Female
1.3	Education : ☐ No formal Education ☐ Primary School ☐ Secondary School ☐ College / University
1.4	Work status : ☐ Private business ☐ Government employee ☐ Student ☐ Merchant ☐ Farmer ☐ House wife ☐ Un employed ☐ Others (specify)……..
1.5	Place of residence ☐ Urban ☐ Rural
1.6	Ethnicity : ☐ Oromo ☐ Amhara ☐ Gurage ☐ Tigree ☐ Others
1.7	Religion : ☐ Orthodox ☐ Muslim ☐ Protestant ☐ Catholic ☐ Others…….

1.8	Marital status: ☐ Single ☐ Married ☐ Divorced ☐ Widowed
1.9	Family monthly income approximately (in birr)_____
1.10	Living arrangements ☐ Alone ☐ With family or relatives ☐ In charity organization
	2. Disease Related Factors
2.1	What is your frequency of follow up at the hospital?_____
2.2	Have you admitted to the hospital within the last year?(I mean in 2008 E.C) ☐ Yes, I have ☐ No ,I have not
2.3	If your answer is yes to question 2.2, how many times you were admitted to the hospital? ☐ Once ☐ Twice ☐ Three times ☐ Four times ☐ Five times ☐ Others (specify)
	3. Substance Use History
3.1	Do you smoke cigarette? ☐ Yes ☐ No

3.2	Do you drink alcohol? ☐ Yes ☐ No		
3.3	Do you chew khat? ☐ Yes ☐ No		
3.4	Do you use cannabis? ☐ Yes ☐ No		
	4. Medication Related Factors		
4.1	How do you get your medication? ☐ Free of charge ☐ By sponsorship ☐ Self sponsored		
4.2	Have you ever experienced any side effects from your medication? ☐ Yes, I have ☐ No, I have not		
4.3	If your answer to question no# 4.2 is yes, which side effects you have experienced? _____		
	5**. Adherence**	YES	NO
5.1	Do you sometimes forget to take your pills?		
5.2	People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your medicine?		

5.3	Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it?		
5.4	When you travel or leave home, do you sometimes forget to bring along your medicine?		
5.5	Did you take all your medicine yesterday?		
5.6	When you feel like your symptoms are under control, do you sometimes stop taking your medicine?		
5.7	Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?		
5.8	How often do you have difficulty remembering to take all your medicine? a. Never/rarely b. Once in a while c. Sometimes d. Usually e. All the time		

Part Two: Data Extraction form from Patients' Chart

I. History of schizophrenia and other chronic Illnesses

1. Current working diagnosis _____

2. How long has it been since diagnosed with schizophrenia? (Duration of mental illness?)_____

3. Is there other co morbid mental illness?

- ☐ Yes
- ☐ No

4. If the answer to question number 3 is yes, what is the other co morbid mental condition:

- ☐ Bipolar Disorder
- ☐ Major Depressive Disorder
- ☐ Brief Psychotic Disorder
- ☐ Schizoaffective Disorder
- ☐ Anxiety Disorder
- ☐ Substance use disorder
- ☐ Others (specify)_____

5. Is there other co morbid chronic medical illness?

- ☐ Yes
- ☐ No

6. If the answer to question number 5 is yes, what is other Co morbid chronic medical illness :

- ☐ Hypertension
- ☐ Diabetes
- ☐ Chronic kidney disease
- ☐ Hyperlipidemia
- ☐ Obesity
- ☐ Chronic heart Failure
- ☐ Others (specify)……

7. Was there relapse in the last 1 year?

☐

☐ Yes

☐ No

8. If the answer to #7 is yes, how many times relapse occurred?_____

9. Was there psychiatry admission history in the last 1 year?_____

Yes ☐

No ☐

10. how many times admitted?_____

2. Medication Related Questions

2.1 Was there antipsychotic medication switch in the last 1year?

☐ Yes

☐ No

2.2 If the answer to question 2.1 is yes, How many times have antipsychotic medication switch occurred in the last 1 year

☐ Once

☐ Twice

☐ Three times

☐ Four times

☐ Others (specify)_____

2.3 If the answer to question # 2.2 is once, for how long did the patient take the antipsychotic before the switch

_____(days)

2.4 If the answer to question no 2.2 is twice ,

I. How long did the patient take the antipsychotic before the first antipsychotic switch? _____(days)

II. How long did the patient take the antipsychotic after first switch to second switch?

_____(days)

2.5 . If the answer to question no 2.2 is three times ,

I. How long did the patient take the antipsychotic before the first antipsychotic switch? _____(days)

II. How long did the patient take the antipsychotic after first switch to second switch?
_____(days)

III. How long did the patient take the antipsychotic after second switch to third switch?
_____(days)

2.6 . If the answer to question no 2.2 is four times ,

I. How long did the patient take the antipsychotic before the first antipsychotic switch? _____(days)

II. How long did the patient take the antipsychotic after first switch to second switch?
_____(days)

III. How long did the patient take the antipsychotic after second switch to third switch?
_____(days)

IV. How long did the patient take the antipsychotic after third switch to fourth switch? _____(days)

2.7 If the answer to question no 2.2 is others (specify)

_____

_____

_____

_____

2.8. Antipsychotic Medication switch Related Questions							
First Generation Antipsychotic	Before switch	1st switch	2nd switch	3rd switch	4th switch	5th switch	
Chlorpromazine							
Haloperidol							
Fluphenazine							
Thiordazine							
Trifluoroperazine							
Pimozide							
Others							
Second Generation Antipsychotic							
Risperidone							
Olanzapine							
Clozapine							
Others							
Anticholinergic current use							
Benzhexol							
Others							
Benzodiazepiens current use							
Diazepam							

Bromazepam							
Clonazepam							
What was /were the possible reason for medication switch? (Use the listed reason and put the number under each column.)							

3. Possible Reason/s for medication switch/es**?**

1. Presence of side effects
2. Inadequate response or partial response
3. Frequent relapse
4. Non -Adherent to treatment
5. Unavailability of medication
6. Patient preference
7. Prescriber preference
8. Family preference/care giver preferences
9. Cost of medication
10. Resistant to the existing medication
11. Previous diagnosis has changed
12. Presence of psychiatry co morbidity
13. Presence of medical co morbidity
14. Unrecorded reason for medication switch

15. Others (if any)_____

4. Medication for Co Morbid (Mental and Chronic medical) Disorder

Co Morbid Disorder	Name of the medication	Dose and frequency

Annex II: Focus Group Discussion Questionnaire

1. *When do you think that antipsychotics medication switch is /are indicated for the patient with schizophrenia?*

   _____

   _____

   _____

2. *What is /are the reason /s for antipsychotic medication switch for the patient with schizophrenia?*

   _____

   _____

   _____

3. *What do you think that a reason/s for antipsychotic medication switch is/are not recorded on the patient's chart?*

   _____

   _____

   _____

Annex III: Amharic version of Questionnaire

የአማርኛ መጠይቅ ቅፅ

የጥናቱ መረጃ ቅጽ ቀን፡-_____

ውድ የቃለ መጠይቅ ተሳታፊ፤ እንደምን አደሩ/ዋሉ?

<u>የጥናቱ መግቢያ</u>

ስሜ_____ ይባላል። “በአማኑኤል የአእምሮ ስፔሻላይዝድ ሆስፒታል “ስኪዞፍሪኒያ” በሽታ ታካሚዎች ዙርያ የ“ስኪዞፍሪኒያ” መድሃኒቶች በተመለከተ በታዘዘው መሰረት በአግባቡ የአወሳሰድና እና ሰለ “ስኪዞፍሪኒያ”መድሀኒቶች መለዋወጥ የተሰኘ የድህረ ምረቃ ጥናት አባል ነኝ።

<u>የጥናቱ አላማ</u>

የዚህ ጥናት ዋና አላማው የ””ስኪዞፍሪኒያ”መድኃኒቶች እንዴት እንደሚጠቀሙት፣ በታዘዘው መሰረት በአግባቡ እንዴት መድኃኒትዎን እንደሚወሰዱት እና ለምን እንደምቀየር በማወቅ፤ የመፍትሄ ሀሳቦችን ማቅረብ ነው።

<u>ከጥናቱ የሚጠበቁ ውጤቶች</u>

በዚህ ጥናት ላይ የእርስዎ የ“ስኪዞፍሪኒያ”መድኃኒቶች በታዘዘው መሰረት በአግባቡ የአወሳሰድና የአጠቃቀም እንዲሁም ለምን እንደምቀየር ለማወቅ ይጠናሉ። በመሆኑም ዋና ዋና ክፍተቶችን ከጥናቱ በሚገኙ ግኝቶች የ“ ስኪዞፍሪኒያ” ህክም ዉጤትን በተወሰነ መልኩ ለማሻሻል እንደሚቻል በመገመት፤ እርስዎ የጥቅሙ ተካፋይ ይሆናሉ ብለን እናምናለን። ስለዚህ የእርስዎ ቅንና ሐቀኛ መረጃ ለጥናቱ እጅግ በጣም ወሳኝ ነው።

የተከበረ ጊዜዎ ስለሰጡን እጅግ በጣም እናመሰግንዎታለን።

በቃለ መጠይቅ ለመሳተፍ የፈቃደኝነት ቃል መቀቢያ ቅጽ

በዚህ ጥናት የእርስዎ መረጃ ሙሉ በሙሉ በሚስጥር የተጠበቀና ለምርምሩ አላማ ብቻ የሚዉል ነው። በተጨማሪም የእርስዎ ተሳታፊነት በፈቃደኝነት የተመሠረተ ነው። የጥናቱ አላምውን ተረድተውና ጊዜዎን ሰውተው፤ ከ 20-25 ደቂቃዎች ለሚፈጅ ቃለ-መጠይቅ እውተኛው መረጃ ለመስጠት ፍቃደኛ በመሆንዎ በቅድሚያ አመሰግናለሁ።

በየትኛው ጊዜ ጥያቄ ካለዎት ጌታቸዉ አስፋዉ ብለው በ ስ.ቁ. (+251) -911-75 - 99- 71 ወይም

በ ኢ-ሜይል፡ getmed2005@gmail.com ይጠይቁን።

_____ _____

የቃለ መጠይቅ የቀረበለት ሰው ፊርማ የቃለ መጠይቅ አቅራቢ ፊርማ

ቃለ- መጠይቅ ከታካሚው

ክፍል ፣፡ አጠቃላይ መገለጫዎች

		ካርድ ቁጥር_____
1.	ዕድሜ:_____	
2.	ፆታ: ወንድ☐ ሴት ☐	
3.	የት/ርት ደረጃ: ያልተማረ/ች ☐1ኛ ደረጃ ☐ ሁለተኛ ደረጃ☐ ቴክኒክና ሙያ/ኮሌጅ/ዩኒቨርሲቲ ☐	
4.	የመኖሪያ አድራሻ: ከተማ ☐ ገጠር ☐	
5.	ብሄር: አማራ ☐ ኦሮሞ ☐ ትግሬ ☐ ጉራጌ ☐ ሌላ ካለ ይጠቀስ ____	
6.	ሀይማኖት: ኦርቶዶክስ ☐ እስልምና☐ ፕሮቴስታንት☐ ሌላ ካለ ይጠቀስ_____	
7.	የጋብቻ ሁኔታ: ያላገባ/ች☐ ያገባ/ች ☐ የፈታ/ች ☐ የሞተች/የሞተባት ☐	
8.	ቤተሰብ ወርሃዊ ገቢ (በብር): ……	
9.	የስራ ሁኔታ: የቤት እመቤት ☐ ተማ ሪ ☐ የግል ስራ ☐ ገበሬ ☐ የቀን ሰራተኛ ☐ የመንግስት ሰራተኛ ☐ ሥራ እጥ ☐ ሌላ ካለ ይጠቀስ ----------	
10.	የኑሮ ሁኔታ: 1. ብቻውን/ብቻዋን የምትኖር ☐ 2. ከቤተሰብ/ከረዳት ጋር ☐3.በበጎአድራጎት ድርጅት ስር ☐	

11.	የሚከተሉትን ይጠቀማሉ?	**አዎ**	**አልጠቀምም**	
	ሲጋራ			
	አልኮል			

ጫት			
ካናቢስ			

12.መድሀኒቶን እንዴት ነዎ የምያገኙት?

◯በነጻ

◯በበጎ አድራጎት ድርጅት በኩል

◯በራሴ ገዝቼ

13. መድሀኒቶዎን በወሰዱባቸዉ ጊዝያት የጎንዮሽ ጉዳት አጋጥሞት ያዉቃል ?

◯አዎ አጋጥሞኛል

◯አይ አላጋጠመኝም

14. ለጥያቄ 13 መልሰዎ፣ አዎ አጋጥሞኛል ከሆነ የትኛዉ የጎንየዎሽ ጉዳት አጋጥሞት ያዉቃል

---

15. በየስንት ጊዜ ነዉ ለክትትል ወደ አማኑኤል ሆስፒታል የምመጡት ?

---

16. ባለፈዉ 1 አመት ዉስጥ ተኝቶ ታክመዎ ያዉቃሉ ?

◯አዎ

◯አይ

17. ለጥያቄ 16 መልሰዎ አዎ፣ ከሆነ ስንት ጊዜ ነዉ ተኝቶ የታከሙት

◯አንዴ ◯ ሁለቴ

◯ሶስቴ◯አራቴ ◯አምስቴ

◯ሌላ ካለ.....

ክፍል 2፡ ሞሪስኪ” መድኃኒትን በታዘዘው መሰረት በአግባቡ ስለመውሰድ” መለኪያ- 8

ተ.ቁ	ጥያቄዎች	አዎ	አይደለም
18	አንዳንድ ጊዜ መድኃኒትዎን ረስተው ሳይወስዱ ቀርተው ያውቃሉ?		
19	ሰዎች አንዳንድ ጊዜ ከመርሳት ውጪ ባሉት የተለያዩ ምክንያቶች መድኃኒታቸውን ሳይወስዱ ይቀራሉ፡፡ ባለፉት ሁለት ሳምንታት፣ መድኃኒትዎን ሳይወስዱ የቀሩበት ቀናቶች ነበሩ’?		
20	ሐኪምዎን ሳይነግሩ፣ መድኃኒትዎን እየወሰዱ ህመምዎ ሲባባስ፣ መድኃኒትዎን አቋርጠው ያውቃሉ?		
21	በጉዞ ምክንያት ወይም ከቤትዎ አርቀው ሲጓዙ፣ አንዳንድ ጊዜ መድኃኒትዎን (ወደጉዞው) ረስተውት ሳይወስዱት ያውቃሉ?		
22	በትላንትናው ዕለት ሁሉንም መድኃኒትዎን ወስደውታል?		
23	ህመምዎ ሲሻልዎት (የህመምዎ ስሜቶች ሲጠፉ) አንዳንድ ጊዜ መድኃኒትዎን አቋርጠው ያውቃሉ?		
24	በየቀኑ መድኃኒት መውሰድ፣ ለአንድ አንድሰዎች ምቾት አይሰጣቸውም፡፡ እርስዎ በየቀኑ፣ እንድሁም አንድም ሰዓት ሳያዛንፉ መድኃኒትዎን መውሰድዎ፣ የመሰላቸት ስሜት ተሰምቶት ያውቃል?		
25	መድኃኒትዎን አስታውሰው ለመውሰድ ምን ያክል ይቸገራሉ? ◯ጭራሽ አይቸግረኝም ◯ከዕለታት አንድ ጊዜ ይቸግረኛል ◯አንዳንድ ጊዜ ይቸግረኛል ◯አብዛኛው ጊዜ ይቸግረኛል ◯ ሁል ጊዜ ይቸግረኛል		

Annex IV: Chlorpromazine Dose Equivalencies (CPZeq) of Antipsychotics

S.N	Generic Name	Equivalent dose for 100 mg Chlorpromazine
1	Haloperidol*	2 mg per day
2	Risperidone (oral)*	2 mg per day
3	Trifluoperazine*	2 mg per day
4	Olanzapine*	5 mg per day
5	Chlorpromazine*	100 mg per day
6	Thioridazine*	100 mg per day
7	Fluphenazine (depot)*	2.5 mg per 21 days

* Drugs currently available in Ethiopia

For fluphenazine depot the manufacturers' recommended equivalent for the depot to oral conversion is used for the same drug and then converted to oral chlorpromazine equivalents. For fluphenazine the manufacturer recommends 12.5 mg depot/3 weeks as equivalent to 10 mg/d orally. This estimate is supported by a dose comparison study (12.5 mg depot/3 week equivalent to approximately 9 mg/d orally) (Schooler & Levine, 1976)