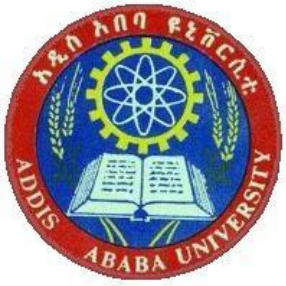

Prevalence of antipsychotic induced movement disorders among schizophrenia patients at Amanuel Mental Specialized Hospital, Addis Ababa, Ethiopia.

A Research thesis submitted to the department of psychiatry, school of medicine, Addis Ababa University, in partial fulfillment of the requirement for the specialty program in Psychiatry.

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Acronyms:

AA	Addis Ababa
AAU	Addis Ababa University
AIMS	Abnormal Involuntary Movement Scale
AMSH	Amanuel Mental Specialized Hospital
AIMD	Antipsychotic medications induced movement disorder
BAS	Barnes Akathisia Scale
DIMD	Drug Induced Movement disorder
DRA	Dopamine Receptor Antagonist
EPS	Extrapyramidal Side Effect
FGAs	First Generation Antipsychotics
NIA	Neuroleptic Induced Parkinsonism
PANSS	Positive and Negative Syndrome Scale
SANS	Scales for Negative Symptoms
SAS	Simpson Angus rating Scale
SDA	Serotonin and Dopamine Antagonists
SGAs	Second Generation Antipsychotics
SOM	School of medicine
TD	Tardive Dyskinesia
WHO	World Health Organization

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Abstract:

Introduction: Despite an increasing number of studies identifying the prevalence of antipsychotic induced movement disorders among schizophrenia patients in high income countries, limited reports on prevalence of this disorder who were visited health facilities has been published in Ethiopia among patients who were treated with antipsychotics and all studies were focused on first generation antipsychotics.

Objective: To determine the prevalence of antipsychotic induced movement disorders, and associated factors among schizophrenia outpatients at Amanuel Mental Specialized Hospital.

Methods: Data was obtained from the baseline assessment of the clinical trial placebo-controlled trial of folate with B12 in schizophrenia patients with residual symptoms conducted from 2014 to 2017 at Amanuel Mental Specialized Hospital. A total of 200 outpatients who were taking antipsychotics for at least six months or stable at least for six weeks were recruited in the study. Rating scales were used including Abnormal Involuntary Movement Scale (AIMS) for Tardive dyskinesia (TD), the Simpson-Angus Rating Scale (SAS) for Antipsychotic-Induced Parkinsonism and Barnes Rating Scale (BAS) for Akathisia. The minimum threshold value for the diagnosis of TD was a score of ≥2 on AIMS; for Parkinsonism, SAS mean global score of ≥0.65 and for Akathisia a BAS total score of ≥2. Positive and negative syndrome scale (PANSS) and scale for assessment of negative symptoms (SANS) were used to measure symptom severity of schizophrenia as mildly ill 58, moderate 75, marked 95 and severe 116 and at least moderate one is taken.

Data analysis was conducted using SPSS version 24.0. Frequency and percentage were used to summarize the data, tables and graphs were used to present the data. Binary logistic regression was done to see the association between the outcome variable and explanatory variables. The 95% confidence interval was used and significance value $P<0.05$, odds ratio reference of 1 was estimated to see the association between outcome variable and explanatory variables.

Results: The overall prevalence of antipsychotic induced movement disorders was 39%. Prevalence of antipsychotic induced Parkinsonism, tardive dyskinesia, and antipsychotic induced Akathisia were found to be 28.5%, 19%, and 8% respectively. SANS score of 31-46 [Odds

ratio=3.409, 95%CI=1.044-11.129] and SANS score ≥ 47 [Odds ratio=5.714, 95%CI= 1.488-21.948] were associated with TD which shows markedly and severely ill; whereas, being female was found to be protective [Odds ratio= 0.346; 95%CI= 0.144-0.832]. Participants who had not been working or jobless [Odds ratio=2.585, 95%CI= 1.079-6.193] and having a SANS score of ≥ 47 [Odds ratio=3.000, 95%CI=1.020-8.825] were factors associated with the presence of antipsychotic induced parkinsonism which shows the association between being severely ill and presence of antipsychotic induce parkinsonism. PANSS score between 95 and 115 and SANS score between 31 and 46 had [odds ratio=5.444 and 9.854] were factors associated with the presence of antipsychotic inducedakathisia.

Conclusions: Thisstudy shows that,aconsiderable number of patients with schizophrenia are suffering from antipsychotic induced movement disorders. Those who had severe psychotic symptoms measured by PANSS, SANS, and those who were not working or jobless were found to be significantly affected by antipsychotic-induced movement disorders.

Recommendation: Screening of patients who are on antipsychotics, early detection and possible intervention, psycho-education for patients and their family about the side effects, designing treatment guideline, increasing availability of drugs with minimal side effects are recommended to reduce these disorders.

Introduction:

One out of hundred people are diagnosed with schizophrenia worldwide. Even though it is not a common mental illness, it can be serious and chronic in nature. (Sadock , et al., 2017) Schizophrenia affects about 0.3 to 0.7% people in the world in the life time, but there is report variation by race, gender, between countries, place of origin from immigrants and their children. Longer duration of schizophrenia associated with poor outcome that shows high prevalence for males. Patients with more symptoms and brief presentation associated with better outcome show equivalent risks for both sexes. (Jeste,, et al., 2013)

As reported in the study done in Butajira, Ethiopia, three out of four schizophrenia cases recruited in the study had reduced functioning for at least two years and 15-30% for at least six years. Physical and social functioning were found the most prevalent reduced functioning. (Kebede, et al., 2019)

In one study reported in Ethiopia, schizophrenia found to be episodic course in the majority of patients while some of the patients had continuous psychotic illness but only few patients were continuously in full remission following a single episode. Males were more likely to have an episodic course pattern with inter-episode residual or negative symptoms. The number of relapses per person ranged from one to ten, with a mean number of relapses of 1.55. Overall there were 225 psychotic relapses during the follow-up period, with 152 relapses occurring from a state of full remission and 144 relapses from a state of partial remission or sub-threshold state from the total 358 patients participated in the study. (Shibre, et al., 2015)

Chlorpromazine, the first antipsychotic medication in clinical practice to treat schizophrenia and other conditions since 1952. Eventually several phenothiazines were synthesized and appeared equally effective in the treatment of schizophrenia. The efficacy is well established for the treatment of acute symptoms and relapse prevention. But associated with side effects, the most prominent of which is the development of different movement disorders. In the later years second generation antipsychotics (SGAs) also became available in clinical practice like risperidone, olanzapine and clozapine. (Sadock , et al., 2017)

The pharmacologic property of all neuroleptics with antipsychotic properties was their ability to block dopamine D2 receptors. The therapeutic actions of conventional or first-generation antipsychotic medications (FGAS) are due to blockade of D2 receptors specifically in the mesolimbic dopamine pathway. (Stahl, 2013) Relative property of antipsychotic medications for inducing movement disorders was originally the primary factor behind typical (first generation) or atypical (second generation) classification. All antipsychotic medications introduced since 1990 are classified as second generation, but clozapine and olanzapine introduced in 1959 and 1971 respectively. (Taylor, et al., 2018)

The pathophysiology of drug induced Parkinsonism (DIP) is related to antipsychotic medication induced changes in basal ganglia secondary to blockade in dopaminergic pathway. When dopamine D2 receptors in the striatum is blocked, the gamma aminobutyric acid and encephalin containing striatal neurons are diminished, ultimately leading to a relative decrease in activity in thalamocortical circuitry.A number of neurotransmitter systems disruptions and damage in oxidative have been proposed as potential pathways underlying TD. Dopamine receptor hypersensitivity, altered amino acid metabolism and GABA-containing neuron activity, and NMDA receptor excitotoxicity are included as pathophysiology. Genetics are associated with TD susceptibility similar to DIP. (Citrome, 2018)

Drug induced movement disorders can be induced by all drugs used to treat schizophrenia. These medications characterized as neuroleptics by DSM-5. It can be categorized as first-generation antipsychotics (FGAs) and second-generation antipsychotics (SGAs). One potential differentiation is being their propensity to produce movement disorders.

Neuroleptic induced Parkinsonism (NIP) is antipsychotic induced movement disorder in which tremor, muscular rigidity, bradykinesia or akathisia developing within a few weeks of starting, increasing or discontinuing the dose of antipsychotic medications or after reducing a medication used to treat EPS.**Medication induced acute dystopia** is abnormal positioning or spasm of muscles of the head, neck, limb or trunk developing within a few days of starting or raising the dose or after reducing a medication used to treat EPS.**Medication induced acute akathisia (NIA)** is subjective complaints of restlessness accompanied by observed movements develop within a few weeks of starting or increasing the dose of antipsychotic medications or

after reducing medications used to treat EPS.**Tardive dyskinesia (TD)** can occur during starting, reducing the dose or discontinuing the medication and manifested as involuntary movement of parts of the body which occur after in the course of treatment and persists for months to year. (Sadock, et al., 2017)

Higher total PANSS positive, negative and anxiety/depression sub scores seen in patients with DIMD. PANSS total, positive and anxiety/depression factor scores were higher in patients with DIMD, like akathisia and Parkinsonism, but not in those with TD. PANSS negative scores were also higher in patients with DIMD and Parkinsonism, but not akathisia and TD. A higher PANSS negative score was associated with Parkinsonism, whereas a higher PANSS total score was associated with akathisia. Patients with more severe anxious and depressive symptoms were more likely to have more severe DIMD, akathisia and Parkinsonism, but not TD. It is worth noting that the presence of TD was not correlated with higher PANSS scores.(Chouinard, 2006).

There are a number of studies done on the prevalence of drug induced movement disorders (DIMDs) in schizophrenia patients for both FGAs and SGAs in different high-income countries and eastern Africa (Kenya). In one study conducted in India there was no significant difference between FGAs and SGAs with regard to the risk of developing tardive dyskinesia (TD). (Achalia, et al., 2014)

In Ethiopia, even if some studies done on DIMDs all of them are focused on FGAs, so in order to include the prevalence of SGAs specially risperidone and olanzapine which is commonly prescribed in our country, and knowing the prevalence of movement disorders is essential for early detection of movement disorders and to intervene early before the problem become worse. It can also save extra cost to treat movement disorders and improve antipsychotic medication adherence.

Literature Review:

There are many studies done on drug induced movement disorders on schizophrenia patients treated with antipsychotic medications in different countries including Ethiopia at Amanuel Mental Specialized Hospital.

The most common drug induced movement disorders are discussed as follows. Dystonia are involuntary movements presented by intermittent or sustained muscle action or spasm. Vary from fleeting disturbance to maintained abnormal postures. May occur in 25 to 40% of patients who are receiving FGAs. The muscle stiffness and postural distortion are both painful and disturb patient's comfort and can make patients agitated and frightened. TD is a more severely disabling antipsychotic medication side effect, and symptoms are more sustained compared to the acute form. The prevalence of TD is about 1.5 to 4%. The motor presentations are similar to symptoms seen in acute dystonia but differ by its long duration. NIP symptoms develop gradually within days of starting antipsychotic treatment. The development of symptoms is dose dependent and emerges in about 20 to 40% of patients. With continuation of medication, the Parkinsonian symptoms may gradually decrease and may be tolerated. Akathisia presented by motor restlessness accompanied by subjective feelings of inner tension and discomfort, mostly seen in the limbs. It may coexist with Parkinsonian symptoms, but may be more common, and symptoms can be distressing and cause poor adherence to treatment. (M, et al., 2005)

American journal of psychiatry reported in 2004, the prevalence of DIMDs was 61.6% in Estonian patients with schizophrenia who took antipsychotic medications [31.3% neuroleptic induced akathisia (NIA), 23.2% neuroleptic induced Parkinsonism (NIP) and 32.3% tardive dyskinesia (TD)]. The prevalence of DIMDs in patients receiving clozapine was significantly lower than in patients on FGAs (35% vs. 68.8%). FGA medication use by schizophrenia patients in Estonia increased from 32% in 2004 to 61% in 2009. From 72 patients studied male were 33 and female 39. Mean age was 55.3 year and followed for 20 years on continuous treatment and both low and high potency drugs was used. Combination of two of any antipsychotic medications found the risk of development of TD by six-fold in 2009. 13 patients had switched from FGAs to SGAs. In 2001, 3 of them had NIA, 2 NIP and 1 had TD. There was no report

NIA or NIP and 4 had TD when evaluated in 2009. 15.3% did not show any movement disorder in 2001 or 2009.(Janno, et al., 2004)

The study done in Indian on 706 patients those on at least one antipsychotic medication, 46 movement disorders was reported during the study period, the most common movement disorders were Parkinsonism 36 patients, Akathisia 6 patients and TD 4 patients. (Desai, et al., 2017)

Another study which was done in India on 160 patients, 56.3% of patients took SGAs, 43.8% SGAs only and never exposed to FGAs were 46.3% and FGAs only and never exposed to SGAs were 41.3%. Among patients on SGAs Risperidone was the most common antipsychotic medication (55.6%) received followed by Olanzapine (26.7%) and Clozapine 13.3%. Among patients on FGAs, chlorpromazine 32.9% and combination with injection fluphenazine 31.4% were the most common FGAs received followed by injection fluphenazine 22.9% and haloperidol 8.6%. Patients on FGAs were older 39. 78 - 11.65 years compared to patients on SGAs 32.90 - 10.19 years and higher dose was received compared to non-TD patients. Patients on FGAs were having longer duration of illness 131. 14 - 49 months compared to those on SGAs 86.50 - 47.22 months and received longer duration than on SGAs from this 26.4% met criteria for TD. A significant difference is seen between who took different classes of (SGAs 20%) and (FGAs 34.3%), as well as between patients on SGAs only and never exposed to FGAs 16.2% and FGAs only and never exposed to SGAs 33.3%. After dose adjustment analysis there was no difference between the FGAs and SGAs in the development of TD. (Achalia, et al., 2014)

A study by Ye from China in 2014, compared 243 patients on FGA group with 341 patients on clozapine group and overall prevalence of TD found to be 44.5%. There was significant difference in the adjustment of covariant of age, dose of antipsychotic medications, duration of taking medications and education. (Ye, et al., 2014)

Another study done in china, in 2003, on tardive dyskinesia in 225 (160 male and 65 female) chronic schizophrenia patientswith mean age of 41.7 years, mean age of onset of illness of 21 years (range = 10–49), mean duration of contact with psychiatric services of 20 years (range = 5–40). The mean current dose of antipsychotic medication was 812 chlorpromazine equivalent dose mg/day. The most frequently prescribed medications were FGAs and least likely SGAs was

prescribed and those on FGAs develop side effects. Older age and not being currently on antiparkinsonian medication were associated with the presence of TD. (kau & Leung, 2003)

In the study done in UK, in 2013, on patients taking antipsychotic medications and concomitantly using substance including Alcohol, Tobacco, cannabis,other hallucinogens, stimulants and opiates.There was also no correlation between smoking and acute dystonia, akathisia, Parkinsonian symptoms and tardive dyskinesia. No association was found between suicidality and any acute dystonia, akathisia, Parkinsonian symptoms and tardive dyskinesia or substance abuse. (Hansen, et al., 2013)

The study in Finland, 2008, from the total patients who was participated in the study more than 95% of Neuroleptic induced Akathisia and Parkinson patients showed rhythmical activity. Patients who had movement disorder and particularly NIP, TD and NIA patients had higher frequencies in rhythmical activity than other patients. (Janno, et al., 2008)

A study done by N. Getere from Nairobi, Kenya, in 2002, two hundred two schizophrenia patients (108 male and 94 female) with the mean age of 35.59 years ranging from 16-68 years. Age 60 and above found the highest prevalence for TD and out of these age groups 3 patients had TD from the 6 patients. The lowest prevalence of TD 6.3% was seen between 40 and 49 years. Out of 202 patients 24 patents had TD with the prevalence of 11.9% and there was no significant gender difference (M: F=12:11.7). (N. Gatere, 2002)

The study done in Ethiopia at Amanuel mental specialized hospital (AMSH), by Habtamu Taye, in 2014, of 377 patients 80.6% had schizophrenia. 58.4% had less than five years with their illness and family history of primary movement disorders was 9%. 41.4% of patients took high potent antipsychotics of Chlorpromazine equivalent dose ranges from more than 400 mg daily were 32% and 15.38% participants were taking combination of antipsychotic drugs. Of these 13.3% of them were taking fluphenazine and chlorpromazine combination treatment. Prevalence of FGAs DIMD was 56%, NIP 46.4%, akathisia 28.6% and TD 11.9% respectively as measured by Barnes rating scale for akathisia, Simpson-angus rating scale for DIP and AIMS for TD. During analysis of NIP in relation to all explanatory variables, being on chlorpromazine equivalent dose range of 100 to less than 400 mg daily as well as being FGAs were factors remained to be statistically significant. Regarding TD age greater than 45 years, jobless, alcohol

use and chlorpromazine equivalent dose range of more than 400 mg daily were the most contributing to statistically significant. (taye, et al., 2014)

Another study done in Ethiopia at AMSH, by Wubshet in 2019, 300 patients were participated in the study with the mean age of 33.7 ±10.2 years (ranges from 18 to 67 years). Male were 65% which accounts the majority, 55.3% which accounts more than half of participants were urban residents. Nearly one third completed primary education, 38% are jobless, 20.3% were cigarette smokers. The mean duration of the disorder was 3.4 years ranging from 6 months to 10 years. 35.3% participants had the disorder for more than five years. 10.7% had another co morbid illness. The most commonly prescribed FGAs were chlorpromazine 38% followed by haloperidol 17.7%. The majority 69.3% were on monotherapy. Chlorpromazine and fluphenazine decanoate combination were most commonly used regimen (18.3%). Majority of patients were taking less than 300 mg chlorpromazine equivalent dose (56.3%), 38% received therapeutic dose 300-600mg of chlorpromazine equivalent dose. 5.7% were taking supratherapeutic 600-1000mg chlorpromazine equivalent dose of FGA, 88.3% had adequate remission of illness after initiation. Most of participants 97.7% were developed FGA related side effects. The most common type of FGAs related side effects were cardiovascular side effects (56.3%), sedation and CNS side effects (49.6%) and EPS (38%) as measured by Glasgow antipsychotic side effects scale and Nariño adverse drug reaction probability scale. There is significant association between occurrence of side effect of FGAS and duration of the illness. In this study age, gender, substance use, total daily dose of antipsychotic medications, presence of co morbid illness and number of antipsychotic medications are not significantly associated with the occurrence of side effects. (Wubshet, et al., 2019)

Significance (the rationale) of the study:

Understanding the prevalence of AIMDs among schizophrenia patients in Ethiopia may contribute to early detection of the movement disorders due to both FGAs and SGAs specially risperidone and olanzapine which are most commonly prescribed medications and can be managed accordingly. On the other hand, determining and aware of the side effects may also help to prevent poor adherence to antipsychotic medications among schizophrenia patients. Even though researches done on FGAs, there is no study done that includes SGAs in Ethiopia and knowing the prevalence of both antipsychotics can help us to compare with previous studies done only on first generation antipsychotic medications.

Research questions:

1. What is the prevalence of antipsychotic induced movement disorders among schizophrenia out patients at Amanuel mental specialized hospital?
2. What are the factors associated with antipsychotic induced movement disorders among schizophrenia out patients at Amanuel mental specialized hospital?

Objectives of the study:

General objective

To determine the prevalence of antipsychotic induced movement disorders and associated factors among people with schizophrenia out patients at Amanuel Mental Specialized Hospital.

Specific objectives

1. To determine the prevalence of drug induced movement disorders among schizophrenia patients.
2. To identify and describe the sociodemographic and clinical factors associated with antipsychotic induced movement disorders.

Methods:

Study setting

This study was done from secondary data collected from AMSH, the hospital which the primary research was conducted. Amanuel mental specialized hospital is the first psychiatric hospital in Ethiopia, which is located in Addis Ababa, capital city of Ethiopia. Staffed with psychiatrists, general practitioners, MSC and BSC psychiatry professionals, clinical nurses and clinical psychologists. The hospital gives the service in different case teams including outpatient, inpatients and 24 hours emergency psychiatry service. One of the case teams is the psychosis case team, which is led by psychiatrist and staffed with psychiatrist, rotating residents, nurses and clinical psychologists.

Study design

This study is a secondary data analysis, facility based cross-sectional quantitative research from a primary research done on folate and B12 trial in Ethiopia at Amanuel mental specialized hospital.

Study period

The data cleaning and analysis was conducted from July to September, 2017.

Study population

The study used participants who were treated with antipsychotic medications for at least six months at optimal does or stable dose for at least six weeks who recruited in the primary study a placebo-controlled trial of folate with B12 in patients with schizophrenia with residual symptoms in Ethiopia.

Sample size

The study was conducted on participants who were treated with antipsychotic medications for at least six months at optimal does or stable dose for at least six weeks who recruited in the primary

study a placebo-controlled trial of folate with B12 in patients with schizophrenia with residual symptoms in Ethiopia. A total number of 200 subjects filled the Barnes Akathisia rating scale for assessment of Akathisia, the Simpson-angus rating scale for assessment of pseudo Parkinsonism side effect, AIMS for TD and other measurements as base line at outpatient department.

Inclusion and Exclusion criteria:

Inclusion criteria

- Participants who had a diagnosis of schizophrenia.
- Both genders.
- Age 18-65 years.
- Treatment with antipsychotic medications for at least for six months at optimal dose or stable dose for at least six weeks and
- PANSS total score of at least 60, with at least a 3 (moderate) on one negative symptom item or on positive symptom item.

Exclusion criteria

- Those patients who are unstable to provide informed consent or do not have guardian to consent.
- Those patients who had unstable physical or psychiatric illness who is unable to communicate.

Instruments and measures:

1. **The Barnes Akathisia Rating scale** assesses Akathisia which is designed by Barnes, in 1989. Directed to look for the characteristic motor phenomena as well as systematically probe the subjective aspects of akathisia, including the amount of discomfort and distress that might be reasonably attributed to the condition. The scale is administered by physician to assess the severity of drug induced akathisia and includes objective and subjective items such as the level of the patient's restlessness. Patient should be observed while they are seated, and then standing while engaged in neutral conversation for a minimum of two minutes in each position. Symptoms observed in other situations, for example while engaged in activity on the ward and should be rated. Subsequently, the

subjective phenomena should be elicited by direct questioning. It is the most commonly used scale in clinical trials. A four-item scale that scores patients' akathisia based on (i) brief observation by the clinician (ranked 0 to 3); (ii) patient report of awareness of restlessness (ranked 0 to 3); (iii) patient report of distress related to restlessness (ranked 0 to 3), which produces (iv) a global clinical assessment of akathisia. **(TR, 2003)**

2. **The Simpson-Angus EPS scale**was developed in the 1960s by Simpson GM to identify neuroleptic-induced parkinsonism. It contains 10 items: one measuring gait, six measuring rigidity, and three measuring glabella tap, tremor, and salivation. Each item is scored on a five-point scale from 0 (complete absence) to 4 (extreme), and a total score is obtained by adding all item scores and dividing by 10 (the total number of items). Scores of up to 0.3 were considered to be within the normal range; however, it has recently been suggested that the upper limit of normal be raised to 0.65. Used in both clinical practice and research settings.(Hawley, et al., 2003)

3. **Abnormal Involuntary Movement Scale (AIMS)** was originally developed by the National Institute of Mental Health for research purposes in 1970s, used to measure involuntary movements called TD. Can be done either before or after completing the psychiatric interview observe the patient unobtrusively, at rest. The chair to be used in this examination should be a hard, firm one without arms. It includes a total of 12 items. The first 7 items are used to measure the severity of abnormal movements in the orofacial region. Except for the items related to dentition, items are scored on a five-point scale; none (0), normal (1), minimal (2), mild (3), moderate (4), or severe (5). Because of the simplicity of this scale, it is generally agreed that the AIMS can be easily administered in both research and clinical settings. (Kane, et al., 2018)

4. **Positive and Negative syndrome scale (PANSS)** was developed in 1987 by Stanley Kay, et al. A medical scale used for measuring symptom severity of patients with Schizophrenia. It is widely used in the study of antipsychotic therapy. The scale is known as the "golden standard" that all assessments of antipsychotic behavioral disorders should follow. To assess a patient using PANSS, an approximately 45-minute clinical interview is conducted. The patient is rated from 1 to 7 on different symptoms based on the interview as well as reports of family members or primary care hospital workers. Includes positive symptoms, negative symptoms and general psychopathologyIt provides a

complete definition of each item as well as detailed anchoring criteria for each of seven rating points: 1 = absent, 2 = minimal, 3 = mild, 4 = moderate, 5 = moderate–severe, 6 = severe, 7 = extreme. In the 30-item scale, seven items related to positive symptoms, seven items to negative symptoms, and 16 items to general psychopathology. Finally, a composite scale may be derived by subtracting the negative score from the positive score.(Kay SR, 1987) Severity scored as mildly ill=58, moderately ill=75, markedly ill= 95 and severely ill=116. (Leucht, 2005)

5. **The scale for assessment of negative symptoms (SANS)** was the first instrument developed in 1982-3 in order to provide for comprehensive assessment of negative symptoms in schizophrenia. Consists five scales that evaluate five different aspects of negative symptoms alogia, affective blunting, avolition- apathy, anhedonia and attentional impairment. Scoring of the severity is the same as PANSS score (Andreasen, 2018)

Data management and analysis:

Statistical package for social sciences (SPSS) version 24 was used for data management. Data was cleaned and analyzed using same computer package. Abnormal Involuntary Movement Scale (AIMS) for Tardive dyskinesia (TD) to assess movement disorders, the Simpson-Angus Rating Scale (SAS) for Antipsychotic-Induced Parkinsonism and Barnes Rating Scale (BAS) for Akathisia were used. The threshold value for the diagnosis of TD, a minimum global rating of "mild" (i.e. 2 or more on AIMS); for Parkinsonism, the threshold value was a SAS mean global score of 0.65 or more and Akathisia was a BAS total score of 2 or more, was used. Positive and negative syndrome scale (PANSS) and scale for assessment of negative symptoms (SANS) were used to measure symptom severity of schizophrenia as mildly ill 58, moderate 75, marked 95 and severe 116 and at least the moderate one has been used to assess severity of symptoms.

For analysis, variables were coded after cleaned on SPSS version 24.0 window software program and categorized based on the national category and clinical basis. Frequency and percentage were used to summarize the data. Tables and graphs were used to present the data. Binary logistic regression was done after the dependent variable is dichotomized for effect estimation of

factors to see the associations between the outcome and the independent variables. The 95% confidence interval was used and significance value P<0.05, odds ratio reference, 1 was estimated to see the association between outcome variable and explanatory variables.
Descriptive statistics has been done to see the frequency after computed for sociodemographic, clinical and substance use profiles of participants.

Variables and outcome measures:

Dependent variable: Which is the primary variable used to measure antipsychotic induced movement disorders in schizophrenia out patients.

Independent variables: variable used to measure the Socio-demographic characteristics such as age, gender, marital status, educational level, occupation and living arrangement; clinical variables such as medication profile, PANSS score, SANS score, and substance use.

Ethical considerations:

This study was conducted from the primary data with the permission of the principal investigator of the primary study. It had obtained all the required ethical clearance from the regulatory bodies.

Dissemination and utilization of results:

The results of this study will be submitted to the department of psychiatry, SOM, AAU as part of postgraduate thesis and it will also be submitted to AMSH. The study is expected to generate evidence on the prevalence of drug induced movement disorders among schizophrenia outpatients in Ethiopia and will provide the basis for designing appropriate interventions.

Results:

1. Sociodemographic characteristics of participants:

A total of 200 participants were included in the study. Higher number of participants 129 (64.5%) were males. The mean age is 38.8 years with a standard deviation (SD) of ±9.8. Majority of participants, 176(88%) were between ages 25-54 years. More than three-fourth of responders, 155(77.5%) were jobless, the majority of them, 92(46%) were within grade 9-12 educational levels and 83% were under grade 12, majority of responders, 172(86%) were not in marital relationship [single 159 (79.5%), divorced 9(4.5%), separated 2(1%) and widowed 2(1%)] and 160(80%) were living with parental family. (Table 1).

Table 1: Sociodemographic characteristics of participants among outpatients with schizophrenia at Amanuel mental specialized hospital.

Sociodemographic Characteristics	Number (N=200)	Percent
Gender		
Male	129	64.5
Female	71	35.5
Age* **		
≤24 year	11	5.5
25-54 year	176	88
≥ 55 year	13	6.5
Marital status		
In marital relation	28	14
Not in marital relation**	172	86
Occupational status		
With job	45	22.5
Jobless	155	77.5
Living arrangement		
Living with marital family	25	12.5
Living with parental family	160	80
Others *	15	7.5
Educational status		
≤grade 8	74	37
Grade 9-12	92	46
Above grade 12	34	17

Others* Live alone, live with friends or live with other relative.

** single 159, divorced 9, separated 2 and widowed 2

*** Age categorized based on Ethiopia age structure demographics.

2. Clinical characteristics of study participants:

The mean duration of schizophrenia being 14.82 years, standard deviation of 8.78. Majority of study participants, 142(71%), suffered from schizophrenia for the duration of between five years. Out of the total study participants, 147(73.5%), were on monotherapy. Three fourth of participants, 154(77%) were taking first generation antipsychotics, of which 85(42.5%) of participants were taking the low potent antipsychotic medications and chlorpromazine was the most antipsychotic used by 80(40%) of participants. Majority of participants, 67.5% were taking medications about two to three years. Greater number of patients, 161(80.5%) were taking <300mg Chlorpromazine equivalent dose which is below the recommended standard dose. Those participants taking only FGAs were 147(73.5), SGAs only were 41(20.5%) and the overall combination was 12(6%), of which 8(4%) was FGA and SGA, 4 (2%) participants were taking combination of FGAs. The most combined antipsychotic medications were the first-generation antipsychotics, Fluphenazine decanoate and Chlorpromazine, 33(62.3%), followed by Fluphenazine decanoate and Risperidone, 9(17%). One fourth of participants, 26(49.1%) were on high potent antipsychotic combinations. Out of patients who were taking combination of medications, 49(92.5%) were taking <300mg Chlorpromazine equivalent dose. Majority of participants, 32(61.5%) were taking combination of antipsychotic medications for less than five years. (Table 2)

Out of 200 participants 41(20.5%) were taking second generation antipsychotics and 8(4%) were taking combination of second-generation antipsychotics.

Majority of participants, 73(36.5%) were reported moderately ill due to schizophrenia symptoms with the positive and negative symptoms (PANSS score) of 60-74%. On the assessment of negative symptoms, 75 (37.5%) of participants found to have a SANS score between 16 and 30. (Table 2a)

Table 2: Antipsychotic medications being used by participants among Schizophrenia outpatients at Amanuel mental specialized hospital.

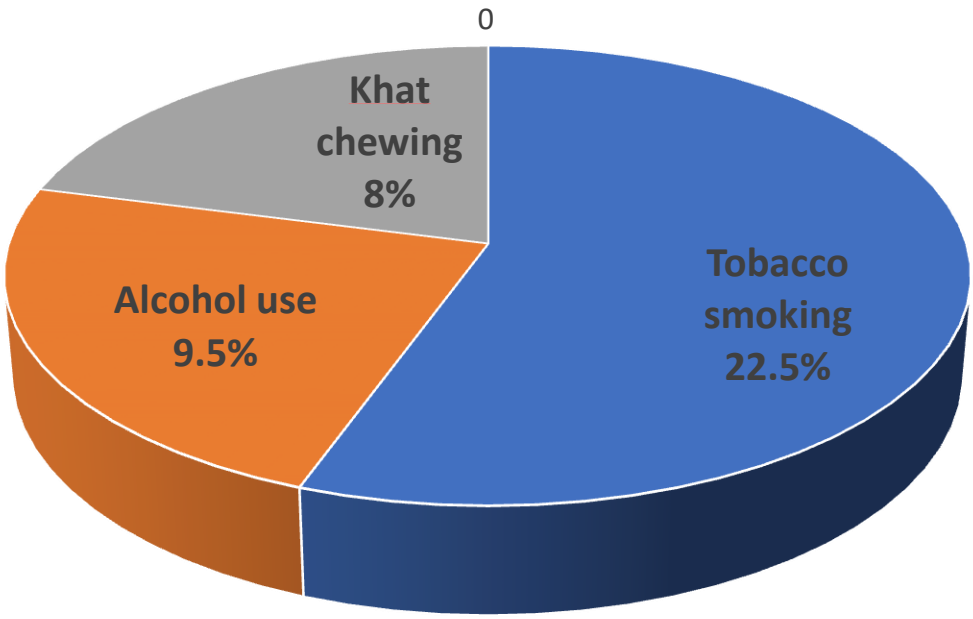
Clinical Characteristics	Number(N=200)	Percent
List of antipsychotic medications		
Chlorpromazine	80	40
Fluphenazine decanoate	43	21.5
Haloperidol	22	11
Risperidone	33	16.5
Olanzapine	13	6.5
Thioridazine	5	2.5
Trifluoperazine	4	2
Generation of antipsychotic medications		
First generation antipsychotics	154	77
Second generation antipsychotics	46	23
Potency of antipsychotic medications		
High potent antipsychotics	69	34.5
Low potent antipsychotics	85	42.5
Chlorpromazine equivalent dose		
Chlorpromazine $\geq$ 300 mg	39	19.5
Chlorpromazine < 300 mg	161	80.5
Duration of treatment		
< 24 months	80	40
24-59 months	68	34
$\geq$ 60months	52	26
Combination of antipsychotics		
Combined antipsychotics	53	26.5
Only one antipsychotic	147	73.5
Type of combined antipsychotic medications		
Fluphenazine decanoate and Chlorpromazine	33	62.3
Fluphenazine decanoate and Risperidone	9	17

Table 3: Positive and Negative syndrome scale (PANSS) score and the scale for assessment of Negative symptom (SANS) scores.

PANSS and SANS category	Number (N=200)	Percent
PANSS score category		
60-74	73	36.5
75-94	72	36
95-115	37	18.5
≥116	18	9
SANS score category		
0-15	44	22
16-30	75	37.5
31-46	59	29.5
≥47	22	11

Out of the total 200 participants, seventy-one (40.5%) were using substances, of which the majority of participants, 45(22.5%), were smoking tobacco, 19(9.5%) participants were using Alcohol, and 17(8.5%) participants were chewing Khat.(Figure 1)

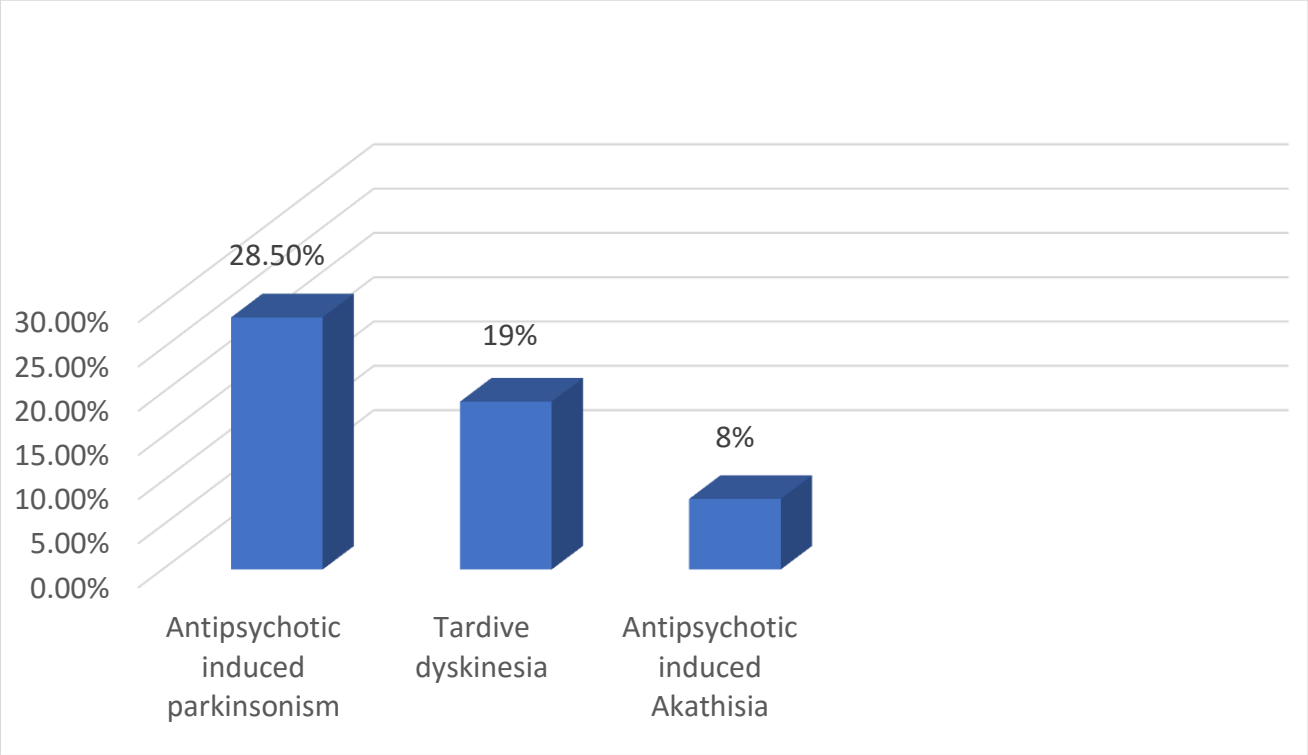
Figure 1: Substance use by participants among schizophrenia outpatients at Amanuel mental specialized hospital.



Prevalence of antipsychotic induced movement disorders:

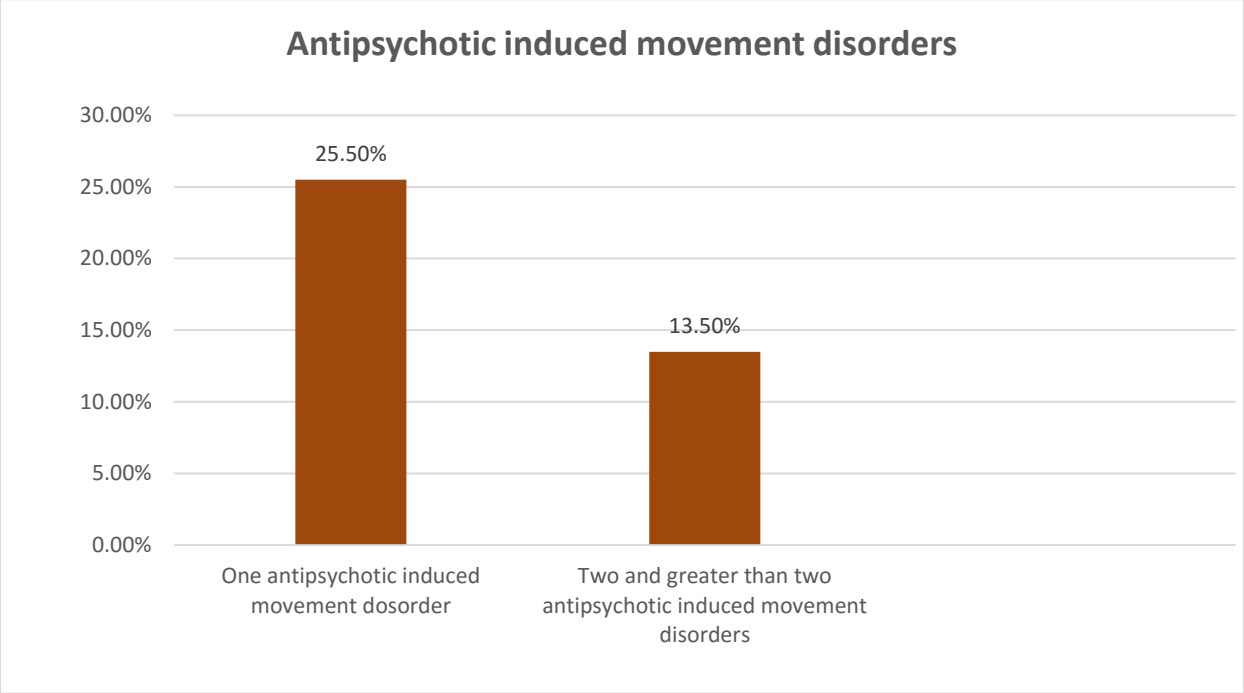
The overall prevalence of antipsychotic medication induced movement disorders among schizophrenia out patients participated in the study found to be (39%). Antipsychotic induced Parkinson 57(28.5%),Tardive dyskinesia 38(19%)and antipsychotic induced akathisia 16(8%). (Figure 2)

Figure 2: Prevalence of antipsychotic induced movement disorders in the participants among Schizophrenia outpatients at Amanuel mental specialized hospital.



Out of the total 200 participants, one fourth 51(25.5%) had only one antipsychotic induced movement disorder, 27(13.5%) had two or more antipsychotic induced movement disorders. (Figure 3)

Figure 3: Prevalence of antipsychotic induced movement disorders in participants among schizophrenia outpatients at Amanuel mental specialized hospital.



During the bivariable analysis of antipsychotic induced parkinsonism in relation to all explanatory variables, those participants who were not working or jobless [odds ratio of 2.585, 95% CI=1.079-6.193] and SANS score of 47 and above or severely ill due to negative symptoms of schizophrenia with [odds ratio =3.000, 95% CI=1.020-8.825] were factors remained to be statistically significant and more likely associated with antipsychotic induced movement disorders. The majority of participants scored a SANS score between 31 and 46. In general; the ages between 25 and 54, those who are not in marital relationship and living with their parents, those who had no work and were not working, educational status below grade 12, who were taking high potent antipsychotics for more than two years had more pseudo parkinsonism than other groups.(Table 4)

Table 4: Factors (sociodemographic)associated with antipsychotic induced parkinsonism (a bi-variable analysis) among participants with schizophrenia, at Amanuel mental specialized hospital.

Explanatory variables	Pseudo parkinsonism		Significance	Odds Ratio	95% confidence interval	
	Yes	No			Lower	Upper
Gender						
Male	33	96		1.00		
Female	24	47	0.219	1.485	0.790	2.792
Age						
≤24 years	2	9		1.00		
25-54 years	51	125	0.447	1.836	0.383	8.793
≥55 years	4	9	0.482	2.000	0.290	13.814
Marital status						
In marital relationship	4	24		1.00		
Not in marital relationship**	53	119	0.082	2.672	0.883	8.083
Living arrangement						
Live with marital family	4	21		1.00		
Live with parental family	48	112	0.20	2.250	0.733	6.906
Others*	5	10	0.212	2.625	0.577	11.944
Occupational status						
With job	7	38		1.00		
Jobless	50	105	**0.033**	2.585	1.079	6.193
Educational status						
≤grade 8	20	54	0.383	0.679	0.284	1.622
Grade 9-12	25	67	0.376	0.684	0.295	1.585
>Grade 12	12	22		1.00		

Others* Live alone, live with friends or live with other relative. ** single, divorced, separated and widowed.

Table 5: Factors (clinical)associated with antipsychotic induced parkinsonism (a bi-variable analysis) among participants with schizophrenia, at Amanuel mental specialized hospital.

Sociodemographic characteristics	Tardive dyskinesia		Significance	Odds ratio	95% Confidence interval	
	Yes	No			Lower	upper
Type of medication						
First generation antipsychotics	40	114	0.150	0.599	0.298	1.204
Second generation antipsychotics	17	29		1.00		
Potency of first generations						
High potency	21	48	0.257	1.521	0.737	3.133
Low potency	19	66		1.00		
Chlorpromazine Equivalent Dose						
Chlorpromazine ≥300 mg	10	29	0.606	0.838	0.378	1.852
Chlorpromazine <300 mg	47	114		1.00		
Duration of treatment						
≤24 months	6	15		1.00		
25-59 months	40	95	0.921	1.053	0.381	2.908
≥60 months	11	33	0.759	0.833	0.259	2.677
Combinations of antipsychotics						
No	43	104		1.00		
Yes	14	39	0.695	1.152	0.568	2.335
Substance use						
Alcohol use No	51	130		1.00		
Yes	6	13	0.755	1.176	0.424	3.3263
Tobacco smoking No	45	110		1.00		
Yes	12	33	0.757	0.889	0.421	1.875
Khat chewing No	52	131		1.00		
Yes	5	12	0.931	1.050	0.352	3.127

Table 6: Symptom severity measures associated with antipsychotic induced parkinsonism (a bi-variable analysis) among participants with schizophrenia, at Amanuel mental specialized hospital.

Symptom severity characteristics	Tardive dyskinesia		Significance	Odds ratio	95% confidence interval	
	Yes	No			Lower	upper
PANSS score						
60-74	22	51		1.00		
75-94	19	53	0.617	0.831	0.403	1.715
95-115	12	25	0.806	1.113	0.475	2.605
≥116	4	14	0.508	0.662	0.196	2.240
SANS score category						
0-15	11	33		1.00		
16-30	15	60	0.525	0.750	0.309	1.820
31-46	20	39	0.332	1.538	0.645	3.671
≥47	11	11	**0.046**	3.000	1.020	8.825

During the bivariable analysis of antipsychotic induced tardive dyskinesia (TD) in relation to all the independent variables or explanatory variables, the odds of having tardive dyskinesia among those participants who were scored a SANS score of 31-46 with [odds ratio=3.409, 95% CI=1.044-11.129] and SANS scores of 47 and above, [odds ratio=5.71495%CI=1.514-21.948] were factors remained to be statistically significant and had association with TD. Females have been [odds of 0.35, 95% CI=0.144-0.832], Of the total study participants, 31 males and 7 females had antipsychotic induced tardive dyskinesia. Although the result shows females are more association to develop TD, it shows females are protected but epidemiologically it inlineold females are more developing TD than males. This result shows that ages between 25 and 54 found to have relatively more tardive dyskinesia than other age groups. Out of 53 participants who were taking combination of Fluphenazine decanoate and Chlorpromazine, 11 participants found to have tardive dyskinesia. 44 participants were in the range of SANS score 31-46, 14 participants found in the score of 47 and above. The ages between 25 and 54 years, those who are not in marital relationship, those participants living with their parents, who had no job or working, those participants under grade 12, participants who were taking high potent antipsychoticsfor more than two years had more tardive dyskinesia in comparison to other groups. During the analysis of substance use; Alcohol use, tobacco smoking and khat chewing, there was no association for the development of tardive dyskinesia than not using substances. Those participants, with a Positive and negative syndrome scale who have moderate illness have more TD than lower sore. (Table 3)

Table 7: Sociodemographicfactors associated with antipsychotic induced Tardive Dyskinesia (TD) (a bi-variable analysis) among participants with schizophrenia, at Amanuel mental specialized hospital.

Explanatory variables	Tardive dyskinesia		Significance	Odds Ratio	95% confidence interval	
	YES	No			Lower	Upper
Gender						
Male	31	98		1.00		
Female	7	64	**0.018**	0.346	0.144	0.832
Age						
≤ 24 year	2	9		1.00		
25-54 years	34	142	0.926	1.077	0.223	5.216
≥ 55 years	2	11	0.855	0.818	0.095	7.016
Marital status						
In marital relationship	1	135		1.00		
Not in marital relationship**	37	27	0.053	7.400	0.973	56.276
Living arrangement						
Live with marital family	1	24		1.00		
Live with parental family	34	126	0.072	6.476	0.846	49.603
Others*	3	12	0.138	6.000	0.563	63.984
Occupational status						
With job	8	30		1.00		
Jobless	37	125	0.812	1.110	0.469	2.628
Educational status						
≤ grade 8	16	58	0.903	1.064	0.392	2.889
Grade 9-12	15	77	0.575	0.751	0.277	2.039
> Grade 12	7	27		1.00		

Others* Live alone, live with friends or live with other relative.

** single, divorced, separated and widowed.

Table 8: Factors (clinical) associated with antipsychotic induced Tardive Dyskinesia (TD) (a bi-variable analysis) among participants with schizophrenia, at Amanuel mental specialized hospital

Clinical characteristics	Tardive Dyskinesia		Significance	Odds ratio	95% confidence interval	
	Yes	No			lower	upper
Type of medication						
First generation antipsychotics	31	123	0.458	1.404	0.573	3.439
Second generation antipsychotics	7	39		1.00		
Potency of first generations						
High potency	17	52	0.211	1.658	0.750	3.663
Low potency	14	71		1.00		
Chlorpromazine Equivalent Dose						
Chlorpromazine ≥300 mg	7	32	0.852	0.917	0.370	2.272
Chlorpromazine <300 mg	31	130		1.00		
Duration of treatment						
≤ 24 months	5	16		1.00		
25-59 months	24	111	0.510	0.692	0.231	2.072
≥60 months	9	35	0.759	0.823	0.237	2.852
Combinations of antipsychotics						
No	27	120		1.00		
Yes	11	42	0.704	1.164	0.531	2.550
Substance use						
Alcohol use No	34	147		1.00		
Yes	4	15	0.811	1.153	0.360	3.694
Tobacco smoking No	27	128		1.00		
Yes	11	34	0.293	0.534	0.692	3.402
Khat chewing No	33	150		1.00		
Yes	5	12	0.259	1.894	0.625	5.743

Table 9: Symptom severity measures associated with antipsychotic induced Tardive Dyskinesia (TD) (a bi-variable analysis) among participants with schizophrenia, at Amanuel mental specialized hospital

Symptom severity characteristics	Tardive dyskinesia		Significance	Crude Odds ratio	95% confidence interval	
	Yes	No			Lower	Upper
PANSS score						
60-74	13	60		1.00		
75-94	14	58	0.800	1.114	0.483	2.572
95-115	9	28	0.421	1.484	0.567	3.878
≥116	2	16	0.497	0.577	0.118	2.822
SANS score						
0-15	4	40		1.00		
16-30	11	64	0.381	1.719	0.512	5.767
31-46	15	44	**0.042**	3.409	1.044	11.129
≥47	8	14	**0.011**	5.714	1.488	21.948

During the bivariable analysis of antipsychotic induced Akathisia in relation to all explanatory variables, those participants who were markedly ill with a PANSS score of 95-115, [odds ratio of 5.444, 95% CI=1.318-22.491] and a SANS score of 31-46, [odds ratio =9.854, 95% CI=1.221-79.517]were factors remained to be statistically significant and more likely associated with antipsychotic induced akathisia. Those participants who were not in marital relationship, who were living with their parents, who had no job or those participants currently not working, those who attended school below grade 12, participants who were taking high potent antipsychotics for longer than two years had more akathisia. (Table 5)

Table 10: Factors (sociodemographic) associated with antipsychotic induced Akathisia (a bi-variable analysis) among participants with schizophrenia, at Amanuel mental specialized hospital.

Explanatory variables	Akathisia		Significance	Odds Ratio	95% confidence interval	
	Yes	No			Lower	Upper
Gender						
Male	13	116		1.00		
Female	3	68	0.157	0.394	0.108	1.431
Marital status						
In marital relation	1	25	0.41	2.580	0.327	20.341
Not in marital relation**	15	157		1.00		
Living conditions						
Live with marital family	1	24		1.00		
Live with parental family	13	147	0.478	2.122	0.265	16.975
Others*	2	13	0.305	3.692	0.305	44.692
Occupational status						
With job	3	42		1.00		
Jobless	13	142	0.709	0.780	0.212	2.868
Educational level						
≤ Grade 8	7	67	0.713	0.784	0.213	2.880
Grade 9-12	5	87	0.232	0.431	0.109	1.711
>Grade 12	4	30		1.00		

Others* Live alone, live with friends or live with other relative.

** single, divorced, separated and widowed.

Table 11: Clinicalfactors associated with antipsychotic induced **Akathisia** (a bi-variable analysis) among participants with schizophrenia, at Amanuel mental specialized hospital.

Sociodemographic characteristics	Tardive dyskinesia		Significance	Odds ratio	95% confidence interval	
	Yes	No			Lower	Upper
Type of medication						
First generation	11	143	0.417	0.631	0.207	1.919
Second generation	5	41		1.00		
Potency of first generations						
High potency	58	82	0.964	1.029	0.300	3.525
Low potency	31	29		1.00		
Chlorpromazine Equivalent Dose						
Chlorpromazine ≥300 mg	4	35	0.56	1.419	0.432	4.664
Chlorpromazine<300 mg	12	149		1.00		
Duration of treatment						
≤24 months	2	19		1.00		
25 – 59 months	10	125	0.736	0.760	0.155	3.738
≥60 months	4	40	0.955	0.950	0.160	5.651
Combinations of antipsychotics						
No	11	136	0.654	0.776	0.257	2.349
Yes	5	48		1.00		

Table 12: Symptom severity measures associated with antipsychotic induced Akathisia (a bi-variable analysis) among participants with schizophrenia, at Amanuel mental specialized hospital.

Symptom severity characteristics	Akathisia		Significance	Crude Odds ratio	95% confidence interval	
	Yes	No			lower	upper
PANSS score						
60-74	3	70		1.00		
75-94	3	69	0.986	1.014	0.198	5.201
95-115	7	30	**0.019**	5.444	1.318	22.491
≥116	3	15	0.075	4.667	0.857	25.410
SANS score						
0-15	1	43		1.00		
16-30	1	74	0.704	0.581	0.035	9.529
31-46	11	48	**0.032**	9.854	1.221	79.517
≥47	3	19	0.107	6.789	0.663	69.551

Discussion:

The overall prevalence of antipsychotic induced movement disorders in this study was found to be 39%; the most common movement disorder seen was antipsychotic induced Parkinsonism 57(28.5%), followed by Tardive dyskinesia 38(19%), and antipsychotic induced akathisia 16(8%) measured by using clinical rating scales the Simpson Angus scale (SAS), Abnormal involuntary movement scale (AIMS), and Barnes akathisia scale(BAS) respectively. Schizophrenia symptom severity measures using Scale for Assessment of Negative Symptoms (SANS) was associated with the presence of antipsychotic induced movement disorder. Female gender was found to be protective for TD.

The overall prevalence of antipsychotic induced movement disorders is almost similar or consistent with the previous study done at the same setting by Wubshet, et al., in 2019 who reported an overall prevalence of extrapyramidal side effect of 38%, but they didn't report the movement disorders by sub-type and use different instruments that differs the instruments used in this study. Another study done in 2014 by Taye et al. reported prevalence rates of 46.4%, 28.6% and 11.9% for neuroleptic induced parkinsonism, akathisia and tardive dyskinesia respectively. The prevalence rate for tardive dyskinesia in our study is higher than what was reported from Mathari psychiatric hospital in Kenya, which reported a prevalence rate of 11.9% in a study done in 2000 involving 202 inpatients (Gatere, Othino and Kathuku, 2000).

But the findings from our study were lower than the report from Estonia in a report involving 99 institutionalized patients with chronic schizophrenia (Janno et al, 2004).

During the bivariable analysis of antipsychotic induced parkinsonism in relation to all explanatory variables, those who had no job and scale for assessment of negative symptoms (SANS) score of ≥47 had 2.585 and 3.00 times more chance of inducing antipsychotic induced parkinsonism than who had job (working) and lesser scores of scale for assessment of negative symptoms (SANS). The above result was not consistent with previous studies. Taye et, al, 2014, N. Getere,2002. The absence of association between gender and antipsychotic induced Parkinsonism was consistent with other study done in same setting. Taye et.al, 2014.

During the bivariable analysis of tardive dyskinesia (TD) in relation to all explanatory variables, being female had odds ratio of 0.346 that shows females are protective even though epidemiologically old females are more likely to develop antipsychotic induced tardive dyskinesia. Scale for assessment of negative symptoms, symptom severity of severely ill with a SANS score between 31 and 46 and a SANS score 47 and above had 3.409- and 5.714-times chance of association with TD respectively in this study. This result is not consistent with previous studies done in Ethiopia at same setting or abroad for many possible reasons. Taye et, al, 2014, N., Getere,2002, S., et al., 2004.

During the bivariable analysis of antipsychotic induced akathisia in relation to explanatory variables, the positive and negative syndrome scale (PANSS) score between 95 and 115 and a scale for assessment of negative symptoms (SANS) a score between 31 and 46 had 5.444 and 9.854 times more likelihood of inducing antipsychotic induced akathisia than lesser scores of SANS.

For all out come variables; pseudo parkinsonism,tardive dyskinesia and antipsychotic induced akathisia; the age between25 and 54, those participants who were not in marital relationship and living with their parental families, those who had no job and attended school below grade 12, those who were taking high potent antipsychotics for more than two years and high score of positive and negative syndrome scale and the scale for assessment of negative symptoms had high level of antipsychotic induced movement disorders.

In general, the overall prevalence of antipsychotic induced movement disorders as compared to the previous study done in the same setting by Taye et. al, 2014 is low in this study, the possible reasons might be most of participants were taking <300 mg chlorpromazine equivalent dose which is below standard recommended doses, one fourth of participants were taking second generation antipsychotics that has low risk of developing antipsychotic induced movement disorders, clarity of data being high quality of data; collected by high level of psychiatry professionals (MSCs) and close follow up and monitoringby the principal investigator during the collection of data might be the reasons for relatively low prevalence in this study.

Limitations:

The study was conducted from secondary data and fixed sample size**,** Co-occurrence of spontaneous movement disorders, commonly detected in schizophrenic patients, could not be excluded.Bias towards more chronically unwell schizophrenia patients those who are more vulnerable to develop movement disorders and bias towards people who are able to seek care from a tertiary care center which is associated with severity of the illness and towards people who are eligible to be included in the trial. substance use is by nature a sensitive issue especially in our culture.

Conclusions and Recommendations:

Conclusions:

In this study, we found high prevalence of antipsychotic induced movement disorders among patients with chronic schizophrenia which were seen as burdening both the patient and the care giver or the family and potentially resulting in stigma to the patient. Severity of illness, as measured by SANS, was found to be associated with the presence of antipsychotic induced movement disorders.

Recommendations:

For the clinician: Designing treatment guideline to optimize doses of antipsychotic medications to decrease the development of antipsychotic induced movement disorders, increasing availability of drugs with minimal side effects like atypical antipsychotics, early detection of side effects and adherence, planning frequent scheduled follow up visits, screening the adherence and common movement disorders in each visit and psycho-education on the possible and common side effects and emergence of antipsychotic induced movement disorders is essential specially for females, elderly, those patients who are taking high potency antipsychotics who are taking for long duration and assessing the schizophrenia symptoms might decrease the development of antipsychotic induced movement disorders. .

For the institution (hospital): focus on antipsychotic medications with lesser side effect profile and regular organized refreshment onsite training for the staff those who are responsible to prescribe antipsychotic medications and update the possible side effects as well as the temporal development or occurrence of the acute and chronic. medication induced movement disorders.

For researchers: strong design organized training for the data collectors and participate those more experienced and high-level psychiatry professionals and further study is essential.

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Appendix:

Positive and Negative Syndrome Scale (PANSS)

Instructions: *circle the term for each symptoms which best describes the patient's condition over the last week not relevant to any other time*

Note: refer to symptoms definitions located in the Rating Scales Procedure Manual

Positive Scale (P)

Symptom		Description						
		Absent	Minimal	Mild	Moderate	Moderate Severe	Severe	Extreme
P1.	Delusions	1	2	3	4	5	6	7
P2.	Conceptual Disorganizations	1	2	3	4	5	6	7
P3.	Hallucinatory Behavior	1	2	3	4	5	6	7
P4.	Excitement	1	2	3	4	5	6	7
P5.	Grandiosity	1	2	3	4	5	6	7
P6.	Suspiciousness/ Persecution	1	2	3	4	5	6	7
P7.	Hostility	1	2	3	4	5	6	7

Negative Scale

(N)

Symptom		Description						
		Absent	Minimal	Mild	Moderate	Moderate Severe	Severe	Extreme
N1.	Blunted Affect	1	2	3	4	5	6	7
N2.	Emotional Withdrawal	1	2	3	4	5	6	7
N3.	Poor Rapport	1	2	3	4	5	6	7
N4.	Passive/Apathetic Social Withdrawal	1	2	3	4	5	6	7
N5.	Difficulty in Abstract Thinking	1	2	3	4	5	6	7
N6.	Lack of Spontaneity and Flow of Conversation	1	2	3	4	5	6	7
N7.	Stereotyped Thinking	1	2	3	4	5	6	7

Abnormal Involuntary Movement Scale

Either before or after completing the Examination Procedure observe the patient unobtrusively, at rest (e.g., in v
The chair to be used in this examination should be a hard, firm one without arms.

I. Facial and Oral Movements: | **III. Trunk Movements:**

1.	Muscle of facial expression - e.g., movements of forehead, eyebrows, periorbital area, cheeks; including frowning, blinking, smiling, grimacing	0 1 2 3 4	None Minimal Mild Moderate Severe

2.	Lips and perioral area - e.g., puckering, pouting, smacking	0 1 2 3 4	None Minimal Mild Moderate Severe

3.	Jaw - e.g., biting, clenching, chewing, mouth opening, lateral movement	0 1 2 3 4	None Minimal Mild Moderate Severe

4.	Tongue - Rate only increase in movement both in and out of mouth, NOT inability to sustain movement	0 1 2 3 4	None Minimal Mild Moderate Severe

II. Extremity Movements:

1.	Upper (*arms, wrists, hands, fingers*) - Include choreic movements (e.g., rapid, objectively purposeless,	0 1 2	None Minimal Mild

1.	Neck, shoulders, hips - e.g., rocking, twisting, squirming, pelvic gyrations	0 1 2 3 4	No Mi Mi Mo Se

IV. Global Judgments:

1.	Severity of abnormal movements	0 1 2 3 4	No Mi Mi Mo Se

2.	Incapacitation due to abnormal movements	0 1 2 3 4	No Mi Mi Mo Se

3.	Patient's awareness of abnormal movements - Rate only patient's report	0 1 2 3 4	No Av Di Av Di Av Di Av Di

	irregular, spontaneous), athetoid movements (e.g., slow, irregular, complex, serpentine). DO NOT include tremor (e.g., repetitive, regular, rhythmic)	3 4	Moderate Severe

2.	Lower (*legs, knees, ankles, toes*) - e.g., lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot	0 1 2 3 4	None Minimal Mild Moderate Severe

V. Dental Status:

1.	Current problems with teeth and/or dentures	0 1	No Ye

2.	Does patient usually wear dentures?	0 1	No Ye

Barnes Akathisia Rating Scale

Instructions: Patient should be observed while they are seated, and then standing while engaged in neutral conversation (for a minimum of two minutes in each position). Symptoms observed in other situations, for example while engaged in activity on the ward, may also be rated. Subsequently, the subjective phenomena should be elicited by direct questioning.

1. Objective

0 = Normal, occasional fidgety movements of the limbs

1 = Presence of characteristic restless movements: shuffling or tramping movements of the legs/feet, or swinging of one leg while sitting, and/or rocking from foot to foot or "walking on the spot" when standing, but movements present for less than half the time observed

2 = Observed phenomena, as described in (1) above, which are present for at least half the observation period

3 = Patient is constantly engaged in characteristic restless movements, and/or has the inability to remain seated or standing without walking or pacing, during the time observed

2. Subjective - Awareness of restlessness

0 = Absence of inner restlessness

1 = Non-specific sense of inner restlessness

2 = The patient is aware of an inability to keep the legs still, or a desire to move the legs, and/or complains of inner restlessness aggravated specifically by being required to stand still

3 = Awareness of intense compulsion to move most of the time and/or reports strong desire to walk or pace most of the time

3. Subjective - Distress related to restlessness

0 = No distress

1 = Mild

2 = Moderate

3 = Severe

4. Global Clinical Assessment of Akathisia

0 = Absent. No evidence of awareness of restlessness. Observation of characteristic movements of akathisia in the absence of a subjective report of inner restlessness or compulsive desire to move the legs should be classified as pseudoakathisia

1 = Questionable. Non-specific inner tension and fidgety movements

2 = Mild akathisia. Awareness of restlessness in the legs and/or inner restlessness worse when required to stand still. Fidgety movements present, but characteristic restless movements of akathisia not necessarily observed. Condition causes little or no distress.

3 = Moderate akathisia. Awareness of restlessness as described for mild akathisia above, combined with characteristic restless movements such as rocking from foot to foot when standing. Patient finds the condition distressing

4 = Marked akathisia. Subjective experience of restlessness includes a compulsive desire to walk or pace. However, the patient is able to remain seated for at least five minutes. The condition is obviously distressing.

5 = Severe akathisia. The patient reports a strong compulsion to pace up and down most of the time. Unable to sit or lie down for more than a few minutes. Constant restlessness which is associated with intense distress and insomnia.

Simpson-Angus Rating Scale (SAS)

1. GAIT
0 Normal 1 Diminution in swing while patient is walking 2 Marked diminution in swing with obvious rigidity in the arm 3 Stiff gait with arms held rigidly before the abdomen 4 Stooped shuffling gait with propulsion and retropulsion

2. ARM DROPPING
0 Normal; free fall with loud slap and rebound 1 Fall slowed slightly with less audible contact and little rebound 2 Fall slowed, no rebound 3 Marked slowing, no slap at all 4 Arms fall as though against resistance; as though through glue

7. HEAD ROTATING
0 Normal 1 Slight stiffness and resistance 2 Moderate stiffness and resistance 3 Marked rigidity with difficulty in passive movement 4 Extreme stiffness and rigidity with almost a frozen neck

8. GLABELLA TAP
0 0-5 blinks 1 6-10 blinks

3. SHOULDER SHAKING
0 Normal 1 Slight stiffness and resistance 2 Moderate stiffness and resistance 3 Marked rigidity with difficulty in passive movement 4 Extreme stiffness and rigidity with almost a frozen shoulder

4. ELBOW RIGIDITY
0 Normal 1 Slight stiffness and resistance 2 Moderate stiffness and resistance 3 Marked rigidity with difficulty in passive movement 4 Extreme stiffness and rigidity with almost a frozen elbow

5. FIXATION OF POSITION or WRIST RIGIDITY
0 Normal

2 11-15 blinks 3 16-20 blinks 4 21 and more blinks

9. TREMOR
0 Normal 1 Mild finger tremor, obvious to sight and touch 2 Tremor of hand or arm occurring spasmodically 3 Persistent tremor of one or more limbs 4 Whole body tremor

10. SALIVATION
0 Normal

1 Slight stiffness and resistance

2 Moderate stiffness and resistance
3 Marked rigidity with difficulty in passive movement
4 Extreme stiffness and rigidity with almost a frozen wrist

6. LEG PENDULOUSNESS

0 The legs swing freely
1 Slight diminution in the swing of the legs
2 Moderate resistance to swing
3 Marked resistance and damping of swing

4 Complete absense of swing

1 Excess salivation to the extent that pooling
takes place if the mouth is open and the
tongue
raised
2 Excess salivation is present and might

occasionally result in difficulty in speaking
3 Speaking with difficulty because of excess
4 Frank drooling

TOTAL SCORE:

_____

1. **Current Psychotropic Medication:** **Yes** ☐ **No** ☐

Medication Name	Dose	Frequency	Indication	Start Date	Continui