PSYCHOTROPIC MEDICATIONS INDUCED MOVEMENT DISORDERS ANDASSOCIATED FACTORS AMONG PATIENTS WITH MENTAL ILLNESS ATTENDING FOLLOWUP TREATMENT AT JIMMA UNIVERSITY MEDICAL CENTER, PSYCHIATRY CLINIC, JIMMA, SOUTHWEST, ETHIOPIA, 2019

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A RESEARCH THESIS TO BE SUBMITTED TO JIMMA UNIVERSITY, INSTITUTE OF HEALTH, FACULTY OF MEDICINE, DEPARTMENT OF PSYCHIATRY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE IN INTEGRATED CLINICAL AND COMMUNITY MENTAL HEALTH

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JIMMA, ETHIOPIA

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Abstract

Background

Drug induced movement disorders remain a significant burden especially among patient populations taking psychotropic medications. They are associated with adverse effects that can lead to subjective suffering, stigma, poor compliance to medication and poor quality of life. However, they are unrecognized and overlooked in clinical settings.

Objectives: *To assess psychotropic medications induced movement disorders & associated factors among mentally ill patients attending follow up treatment at Jimma University Medical Center psychiatry clinic, Jimma, Southwest Ethiopia, 2019.*

Methods: *Institution based cross-sectional study design was conducted. A total of 420 participants were selected by systematic random sampling techniques. Data was collected by semi structured interviewer administered questionnaire and document was reviewed to obtain patient profile. Psychotropic medications induced movement disorders was assessed by using Extra Symptom Rating Scale after informed consent was obtained from respondents. Data entry was done by Epi data version 3.1 and analysis was done by SPSS 22.0statistical software. Binary Logistic regression was used for comparison of the subjects with and without drug-induced movement disorders and multivariate logistic regression were used to identify independent factors. The p-value of <0.05 will be considered as statistically Significant.*

Results: *The overall prevalence of psychotropic medication induced movement disorder was 40.7% (CI 95%: 36.1, 45.6):- drug induced Parkinsonism 14.4% (CI 95%: 11.0, 18.3), drug induced akathisia 12.4% (CI 95%: 9.3, 15.4), drug induced tardive dyskinesia 15.4% (CI 95%: 12.0, 19.3) and tardive dystonia 2.2% (CI 95%: 1.7, 3.7) respectively.*

Conclusions and Recommendation: *The prevalence of psychotropic medications induced movement disorder in this study was high. Khat was positively associated with drug induced akathisia and smoking was negatively associated with tar dive dyskinesia. Sex and age were positively associated with most of drug induced movement disorders. Routine psycho-education for the patients and families, designing treatment guideline and providing drugs with minimal side effects is important to reduce these stigmatizing side effects.*

Keywords: *Antipsychotics, movement disorders, psychotropic medications, and Psychotropic drugs induced Akathisia, drug induced Parkinsonism, Tardive dyskinesia and tardive dystonia.*

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Acronyms and abbreviations

AIMS	Abnormal Involuntary Movement Disorder Scale
AMSH	Amanuel Mental Specialized Hospital
BARS	Barnes Akathisia Rating Scale
DDD	Defined Daily Dose
DIA	Drug-Induced Akathisia
DIMD	Drug Induced Movement Disorders
DIP	Drug-Induced Parkinsonism
DITD	Drug-Induced Tar dive Dyskinesia
DRA	Dopamine receptor antagonists
DSM	Diagnostic and Statistical Manual of American Psychiatric Association
DSRA	Dopamine serotonin receptor antagonists
EPS	Extra pyramidal symptoms
ESRS	Extra pyramidal symptom rating scale
FDA	Food and Drug Administration
FGAs	First-Generation Antipsychotics
JUMC	Jimma University Medical Center
MMAS	Mo risky Medication Adherence Scale
NIP	Neuroleptic Induced Parkinsonism
SGAs	Second-Generation Antipsychotics
TD	Tar dive Dyskinesia
UPDRS	Unified Parkinson Disease Rating Scale
USA	United State of America
WHO	World Health Organization

Chapter 1: Introduction

1.1. Backgroundof the study

Drug induced movement disorders are neurological motor disturbances that most frequently associated with drugs that block dopamine (D2) receptors(1). Drug-induced movement disorders are the potential adverse effects of psychotropic medications most commonly antipsychotic use that often expose the patient to stigma and can impair patient's ability to complete activities of daily living(2).

Drug-induced movement disorders can be caused by different kinds of agents and almost all kinds of movement disorders can happen as a result of medication side effect.

The major groups of drugs that causes drug-induced movement disorders include antipsychotic drugs, antidepressant medications, calcium channel blockers, antiepileptic drugs, gastrointestinal drugs, mood stabilizer medications, antimicrobial medications, anti-arrhythmic medications and chemotherapeutic agents among others(3). They are most commonly related to antipsychotic use and the common ones include: drug-induced akathisia, Parkinsonism, dystonia and tardive dyskinesia(4). Following the introduction of antipsychotic medications in 1952, drug-induced movement disorders emerged as a complication of treatment. To date, drug-induced movement disorders remain a major concern in treatment with antipsychotic medication because these Movement disorders are associated with social stigmatization, physical disabilities, poorer quality of life and noncompliance which results in psychotic relapse(5).

The most frequently used antipsychotic medications are classified into two (2) classes: The older dopamine receptor antagonists (DRA) and the newer Dopamine serotonin receptor antagonist (DSRA). Typical antipsychotics causes different types of side effects including antipsychotic induced movement disorders, sedation, sexual dysfunction, Anticholinergic side effects, cardiovascular side effects,gastrointestinal side effects(6). Second generation antipsychotics are commonly associated with weight gain and metabolic side syndrome but less likely to produce drug induced movement disorders and are more expensive than conventional antipsychotics(7).

Drug Induced Movement Disorders are still common in the treatment of psychotic disorders despite the increasing amount of atypical antipsychotics availability because:Globally, many patients continue to use conventional antipsychotics rather than Atypical Antipsychotics; Even atypical antipsychotics may cause extra pyramidal symptoms and Clinicians have a poor ability to identify Neuroleptic Induced Movement Disorders, which vary between 10% and 59%(8). Drug-induced movement disorders can be classified based on the onset of symptoms as acute which appear within hours to days, sub-acute (which occur after days to weeks) after starting antipsychotic or increasing the dosage. The examples of these include: Dystonia, Parkinsonism and akathisia(9). Chronic (tardive syndromes) which occurs after months spent in exposure to the offending drug.Examples of these are tardive dystonia and Tardive dyskinesia (TD). The risk factors which lead to TD are: old age, females sex, brain damage, increased dose of antipsychotics, long duration of exposure, presence of drug induced parkinsonism in the early phase of neuroleptic, use of anticholinergic drugs &anti parkinsonism drugs, Electroconvulsive treatment, intermittent neuroleptic treatment, diabetes mellitus, total daily drug dosage, primary Psychiatric diagnosis of affective disorder and substance including alcohol.

The risk factors for development of drug induced Parkinsonism include: high dose, high potent drug use, elderly, female sex and AIDS. The risk factors for DIA are: advanced age, female sex, high dose, high potent medication, affective disorders, rapid dose escalation and risk factors for dystonia also includes: male sex, young age, high potent neuroleptic and ECT treatment(10).

In general, this study focuses on this topic because Drug-induced movement disorders are common and severe but most of the times, under recognized/overlooked. They result in severe subjective distress, functional impairment, medication discontinuation which ends in the relapse of the illness and re-hospitalization. Especially, stigma is a big problem in the treatment of mental illness and on the top of that, drug-induced movement disorders worsens the stigma which results in poor medication adherence.

1.2. Statement of the problem

Drug Induced Movement Disorders are a worldwide problem in the treatment of different psychiatric conditions, and have been of major limitation in the use of typical antipsychotics since their discovery in the early 1950s(11).These movement disorders are a serious burden on the patients, family, community, health care system and economy(12).

The burden ofdrug-induced movement disorder according to DSM-iv criteria was 61.6%(13).

As many as 10million people worldwide and 1million Americans' suffer from Drug-Induced Parkinsonism. Among drug-induced movement disorders, drug-induced Parkinsonism is one of the most frequent neurological diseases encountered in primary care globally, including Africa. Overall, the frequency of drug-induced Parkinsonism encountered in specialist care was 66.7% (4^{th} in Southeast Asia) and 18.8 % (6^{th} in Africa)(14). Some studies also indicate that up to 50% of all patients treated with some antipsychotic medications for mental illness will develop drug-induced tardive dyskinesia(12). In Ethiopia also, the magnitude of psychotropic medications-induced movement disorders was 56% which was very large(15).

The risk factors which have been associated with Drug Induced Parkinsonism development include: older age, female gender, History of EPS, family history of PD, cognitive impairment, HIV infection, and higher potency and longer duration antipsychotic use(16). For drug-induced akathisia, the risk factors include increasing age, female sex, negative symptoms, iron deficiency, prior history of akathisia, Hyperthyroidism and mood disorders(17).

The risk factors for TD mainly include older age and increased antipsychotic medication exposure (particularly typical antipsychotics), but also to some degree female sex, preexisting mood disorder, cognitive disturbance, alcohol or substance abuse, use of lithium or anti-parkinsonism agents, early occurrence of Drug-Induced Parkinsonism, diabetes and HIV(5).The risk factors for dystonia includes: male sex, young age, high potent neuroleptics and ECT treatment(10).

As it already discussed above drug-induced movement disorders are more prevalent and broadly distributed all over the world, Even SGAs have not completely fulfilled the expectation of being EPS-free antipsychotic drugs. Recent studies showed that SGAs do not significantly differ from FGAs in terms of efficacy (with the exception of clozapine for treatment-resistant patients)(18).

The negative social reaction because of having a serious mental illness and the socially undesirable side effects associated with drug induced movement disorders may combine to worsen stigma associated with treatment for mental illness(19).

In general, the consequences of DIMDs are that Patients with these disorders have difficulty with social functioning, motor-task performance, interpersonal communication, and activities of daily living. They are also less likely to adhere to their medication regimen, making disease relapse and re-hospitalization more likely. Even, care givers also sometimes prefer traditional treatment modalities than the modern ones because of fear of side effects. In our country also mental health strategies are included in national health policy. But, no adequate study had done on the prevalence of drug induced movement disorder including the study area.

Previously, it was done on psychotic patients taking typical antipsychotic medications so this study is aimed to determine the prevalence of psychotropic medications-induced movement disorders and associated factors among:

All mentally ill patients attending follow up treatment at JUMC, psychiatry clinic who had been on both typical & atypical antipsychotic medications and also on other psychotropic medications and this will help the clinicians to be aware of these disorders and to make clinical judgment.

It addressed some variables not addressed by another study.

It will also help for researchers as a base line for further study.

Chapter 2: Literature

2.1. The overall prevalence of drug-induced movement disorders

According to retrospective study done in Canada in 2004, the range of patients affected by psychotropic medications induced movement disorders who were on convectional antipsychotic medications has varied from 2%-90%(20). The study from different 11 countries including Australia, Canada, France, Israel, South Africa and the USA, which included 535 individuals shows that; 30.4% (n= 111)had signs of Drug-induced movement disorders with an ESRS item with a score of 3 or 4 (moderate to moderately severe)(21).A study conducted on the prevalence of neuroleptic-induced tardive movement sub-syndromes among schizophrenic patients residing in southern region of Israel have shown that between 29 - 74% of all patients those on neuroleptic will experience one form of movement disorder(22).A study done in France on pharmaco-vigilance Evaluation by using a case–non case analysis using spontaneous reports from the World Health Organization (WHO) Global Individual Case Safety Report (ICSR) database in 2016; Compared with second-generation Antipsychotics, first-generation Antipsychotic were found to be significantly more associated with the report of antipsychotic-induced movement disorders in 16 917 (5.8%) patients(23).

A 4 year prospective naturalistic study done in Netherland, 2011 in order to determine the frequency of tardive dyskinesia, parkinsonism, akathisia and tardive dystonia in 209 patients with chronic severe mental illness using AIMS, UPDRS, BARS and Fahn-Marsden scale respectively shows that 68% of participants had at least one type of persistent movement disorder; 43.3% had a single type of persistent movement disorder, and 24.7% had at least 2 types of persistent movement disorder(24). According to study done in central Estonia, Finland to assess DIMDs in a naturalistic schizophrenia population that uses conventional neuroleptics, the total prevalence of DIMDs according to the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV)was 61.6%,and 22.2% had more than one DIMD (8).According to cohort study done in Filipino in which a total of 227 inpatients fulfilling the DSM-IV TR criteria for schizophrenia patients participated using the Abnormal Involuntary Movement Scale (AIMS) and Simpson Angus Rating Scale (SARS) shows that, 53% of patients had significant extrapyramidal features(25).

A prospective cross sectional study done in University of Port Harcourt Teaching Hospital, Nigeria between Jan 2008- 2011including a total of both inpatient and outpatient 2057 cases for 3 years, the overall prevalence of DIMDs using involuntary movement disorder schedule criteria was 5%(26).A cross-sectional survey done in Kenya (Nairobi),Mathari Hospital, the main psychiatric referral hospital among164 adult outpatient psychiatric patients in 2014 reveals that the prevalence of extra pyramidal side effect was 78.05%(27). According to a cross sectional study done in Ethiopia in 2014including 377 psychotic outpatients using Barnes akathisia rating scale, SAS and AIMS the overall prevalence of antipsychotic medications induced movement was 56%(15).

2.1.1. Factors associated with drug-induced movement disorders

Risk factors of Drug induced movement disorders can vary with individual patient vulnerabilities: socio-demographic factors, clinical factors, substance related factors, treatment duration, dosage, and drug class (conventional/first-generation antipsychotics [FGAs] or atypical/second-generation antipsychotics [SGAs]). Hence, the relationship between DIMD and different factors has been explored in different studies.

2.2. Drug induced akathesia

According to Prospective Study done in Netherland in 2011,on 209patients with severe mental illness using Barnes Akathesia Rating Scale reveals that the prevalence of Antipsychotic-Induced akathesia was 4.6%(24).The study conducted in California reported that from the total 125 patients, who developed movement disorders, the prevalence of akathesia was 7%(10). A systematic review of the prevalence and management of antipsychotic adverse effects done in United Kingdom on 225 psychiatric patients found that 1.3% was antipsychotic-induced akathisia(29). According to cross sectional study which consisted 261 subjects done in Poland on Clinical assessment of antipsychotic-induced extrapyramidal symptoms & risk factors in nursing home residents with schizophrenia using the Barnes Akathisia Rating Scale indicates that the prevalence of antipsychotic-induced akathisia was 24.52%(30).

A study done in France on pharmaco-vigilance Evaluation by using a case–non case analysis using spontaneous reports from the World Health Organization (WHO) Global Individual Case Safety Report (ICSR) database in 2016; Compared with second-generation Antipsychotics, first-generation Antipsychoticwere found to be significantly more associated with the reporting of movement disorders in general and antipsychotic-induced akathisia accounts 3368(1.2%)(23).
According to study done in Serbia on schizophrenic patients treated with FGAs, the Prevalence of antipsychotic-induced akathisia has been reported to be 25%(18).According to study done in central Estonia to assess neuroleptic-induced movement disorders in a naturalistic schizophrenia population that uses conventional neuroleptics, the prevalence of antipsychotic-induced akathisiaaccording to the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) was 31.3%(8).According to the prospective study done in University of Port Harcourt Teaching Hospital, Nigeria on a total of 2057 cases for 3 years, the prevalence of drug induced akathisia was (14.6%)(26).According to a cross sectional study done in Ethiopia in 2014, the prevalence of antipsychotic medications induced Akathisiawas 108(28.6%)(15).

2.2.1. Factors associated with Drug-induced Akathisia

According to the study done in Israel in 2010 a remarkably high rate of akathisia (about 15–25%) was reported in patients treated with the partial dopamine agonist aripiprazole, leading the manufacturer to refer to akathisia as one of aripiprazole's most frequent and trouble- some side-effects(31).According to The European Mania in Bipolar Longitudinal Evaluation of Medication observational study reported the effectiveness and tolerability of olanzapine monotherapy and olanzapine combination therapy with other antipsychotics, anticonvulsants,&/or lithium in the treatment of mania, the incidence of Akathisia was 3% in the olanzapine monotherapy group compared with 6% in the olanzapine combination group, a statistically significant difference(32).
According to study done in Poland on Clinical assessment of antipsychotic-induced extrapyramidal symptoms & risk factors in nursing home residents with schizophrenia in 2016, among concomitant diseases; Epilepsy significantly increased the risk of some extrapyramidal antipsychotic- induced motor symptoms, such asakathisia(23)**.**According to a prospective study done in University of Port Harcourt Teaching Hospital, Nigeria for 3 years, the risk of developing drug induced akathisia was 1:1with male to female ratio(26).

A cross-sectional study done in Ethiopia on conventional antipsychotic-induced movement disorders indicates that Khat use was factors remained to be significantly associated with the presence of neuroleptic induced akathisia and being on chlorpromazine equivalent dose range of > = 400mg /day was associated with neuroleptic induced akathisia(15)

2.3. Drug-induced Parkinsonism

The study conducted in California reported that from the total 125 patients, who developed movement disorders, 30% had antipsychotic-induced Parkinsonism(10). According to a 4year Prospective Study done in Netherland in 2011, on 209 patients with chronic severe mental illness to determine the frequency of drug-induced parkinsonism using UPDRS reveals that the prevalence of Antipsychotic-Induced Parkinsonism was 56.2%(24).A systematic review of the prevalence and management of antipsychotic adverse effects done in United Kingdom on 225 psychiatric patients found that the prevalence of antipsychotic-induced Parkinsonism was 26%(29). According to cross sectional study which consisted 261 subjects done in Poland on Clinical assessment of antipsychotic-induced extra pyramidal symptoms & risk factors in nursing home residents with schizophrenia using the SAS indicates that DIP was (22.99%)(30).

A study done in France on pharmaco-vigilance Evaluation by using a case–non case analysis using spontaneous reports from the World Health Organization (WHO) Global Individual Case Safety Report (ICSR) database in 2016; Compared with second-generation Antipsychotics, first-generation Antipsychotic were found to be significantly more associated with the reporting of movement disorders in general and antipsychotic-induced parkinsonism was 3829(1.3%)(23).According to study done in central Estonia to assess DIMDs in a naturalistic schizophrenia population that uses conventional neuroleptics, the prevalence of DIP according to the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) was 23.2%(8). According to a retrospective cross-sectional study done among 151 psychotic patients treated with conventional antipsychotic drugs in 4 hospitals in Saudi Arabia, the prevalence of neuroleptic-induced Parkinsonism was 6.8%(33).

According to the prospective study done in University of Port Harcourt Teaching Hospital, Nigeria on a total of 2057 cases for 3 years, the prevalence of drug induced Parkinsonism was (27.2%)(26).According to a cross sectional study done in Ethiopia in 2014, the prevalence of antipsychotic medications induced- induced Parkinsonism was 175(46.4%)(15).

2.3.1. Factors associated with Drug-induced Parkinsonism

A 4-year prospective naturalistic study done in 209 patients with chronic mental illness in order to assess risk factors for incident TD, Parkinsonism, akathisia, and tardive dystonia in long-stay patients on long-term antipsychotics treatment in general psychiatric hospital,Netherlands2011, Parkinsonism was positively associated with age and the total antipsychotic defined daily dose (DDD)(24). A retrospective descriptive study done in Saudi Arabia to determine the prevalence and risk factors among psychotic patients treated with conventional antipsychotics shows that 6.8% had neuroleptic induced Parkinson disorder(33).According to a prospective study done in University of Port Harcourt Teaching Hospital of Nigeria in 2016, for consecutive 3 years, the risk/ratio of developing antipsychotic- induced Parkinsonism with male to female ratio was 2:1 and among patients those had developed NIP: (66.9%) patients were on high potency typical antipsychotic both depot injection and oral medication (e.g. fluphenazine and haloperidol) and (26.2%) were on low potency typical antipsychotic medications (e.g. chlorpromazine) while (6.8%) were on atypical drugs(26).A cross-sectional study done in Ethiopia indicates that being on chlorpromazine equivalent dose range of > = 400mg /day and being on high potent conventional antipsychotics were associated with neuroleptic induced Parkinsonism(15).

2.4. Drug Induced Tardive Dyskinesia

According to retrospective study done in Canada in 2004 among patients who were on conventional antipsychotic medications, the prevalence of drug induced tardive dyskinesia accounts approximately 25%(20). According to Prospective Study done in Netherland in 2011, on 209 patients with chronic severe mental illness to determine the frequency of drug-induced tardive dyskinesia using AIMS reveals that the prevalence of Antipsychotic-Induced tardive dyskinesia was 28.4%(24).The study conducted in California reported that from the total 125 patients, who developed movement disorders, tardive dyskinesia was accounting 63%(10). According to cross sectional study which consisted 261 subjects done in Poland on Clinical assessment of antipsychotic-induced extrapyramidal symptoms & risk factors in nursing home residents with schizophrenia using AIMS indicates that the prevalence of antipsychotic-induced Tardive dyskinesia was 11.9%(30).

A study done in France on pharmaco-vigilance Evaluation by using a case–non case analysis using spontaneous reports from the World Health Organization (WHO) Global Individual Case Safety Report (ICSR) database in 2016; Compared with second-generation Antipsychotics, first-generation Antipsychotic were found to be significantly more associated with the reporting of movement disorders in general and tardive dyskinesia was 3955(1.4%)(23).Based on a Cross-sectional study done in 160 Indian patient's full filling the DSM-IV TR criteria for schizophrenia and who received antipsychotics, the frequency of probable Tardive dyskinesia in the total samplewas26.4%(34). A study done in Serbia on schizophrenic patients shows that the Prevalence of drug induced Tardive Dyskinesia has been reported to be 0.5% to 70% of patients receiving First Generation Antipsychotics, with the average rate being between 24% and 30%(18).According to study done in central Estonia to assess DIMDs in a naturalistic schizophrenia population that uses conventional neuroleptics, the prevalence of drug induced Tardive Dyskinesia according to the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) was 32.3%(8).

According to a retrospective descriptive study done among 151 psychotic patients treated with conventional antipsychotic drugs in 4 hospitals in Saudi Arabia in 2007,the prevalence of neuroleptic-induced tardive dyskinesia was 5.9%(35).

A study done in South Africa on 102 subjects who had been exposed to typical antipsychotic drugs for at least 6 months and were screened for abnormal movements using the Abnormal Involuntary Movement rating Scale (AIMS), 29 patients (28.4%) met criteria for a positive AIMS(36). According to the prospective study done in University of Port Harcourt Teaching Hospital, Nigeria on a total of 2057 cases for 3 years between 2008- 2011, the prevalence of drug induced tardive dyskinesia was(5.8%)(26). A study done in Kenya among 164 psychiatric outpatients at Mathari Hospital indicates that the prevalence of drug induced tardive dyskinesia was 11.9%(37). A cross sectional study done on 377 psychotic patients in Ethiopia, 2014,reveals that the prevalence of psychotropic medications induced tardive dyskinesia using AIMS was 45(11.9%)(15).

2.4.1. Factors associated with Drug-induced Tardive dyskinesia

According to a meta-analysis done in Italy including > 11,000 subjects from 41 studies mostly (77%) diagnosed with schizophrenia spectrum and other psychotic disorders confirmed that the TD prevalence was significantly higher in current 1st generation antipsychotic users than current 2nd generation antipsychotic users. The prevalence of probable Tardive Dyskinesia was 30.0% in 1st generation antipsychotic-treated subjects and 20.7% in 2nd GA-treated adults. Intermittent drug treatment("drug holidays") and intermittent non adherence have been shown to increase risk of TD up to 3-fold(38). Based on a systematic search of the BIOSIS, Cochrane Central Register of Controlled Trials, EMBASE, MEDLINE, and PsycINFO databases conducted for English-language papers and abstracts in the UK, risperidone was most likely and quetiapine least likely to be associated with EPS. In the analysis of ant cholinergic medication use, risperidone was most likely and aripiprazole least likely to be associated with the use of ant cholinergic medication(39). The study conducted in California in 2007 reported that high dose neuroleptics use and longerduration of treatment are associated with increased risk of developing TD(10). According to a study done in India on schizophrenic patients indicates that**:** long-term antipsychotic treatment, older age of patient, intermittent antipsychotic treatment/non-compliance, a high total cumulative antipsychotic dose was associated with high risk of developing TD. But, there is no significant difference between 2nd generation antipsychotics with regards to the risk of causing TD as compared to 1st generation antipsychotics(30).

According to study done in central Estonia to assess neuroleptic-induced movement disorders in a naturalistic schizophrenia population, the prevalence of tardive dyskinesia in the patients receiving clozapine was significantly lower than in those receiving conventional antipsychotics (35.0% versus 68.4%)(8).A retrospective descriptive study done in Saudi Arabia to determine the prevalence and risk factors among psychotic patients treated with conventional antipsychotics shows that 5.9%had neuroleptic induced Tardive Dyskinesia(10). A study done in South Africa consisting 102 subjects who had been exposed to typical antipsychotic drugs for at least 6 months and currently on an antipsychotic were screened for abnormal movements using the Abnormal Involuntary Movement Scale (AIMS) rating scale; Years of treatment and total cumulative antipsychotic dose were significant predictors of TD.

It was less prevalent in smokers, but this difference did not reach statistical significance. Age, sex, and psychiatric diagnosis did not predict the presence of TD(36).

According to a prospective study done in University of Port Harcourt Teaching Hospital, Nigeria for 3 years, the risk of developing drug induced tardive dyskinesia was 1:2 with male to female ratio(16). A cross-sectional study done in Ethiopia on conventional antipsychotic induced movement disorders and associated factors indicates that Alcohol use was factors remained to be significantly associated with TD and being on chlorpromazine equivalent dose range of

> = 400mg /day was associated with neuroleptic induced TD(15).

2.5. Drug Induced Dystonia

A prospective study done in Netherland in 2011, to determine the frequency of persistent drug-induced movement disorders consisting 209 patients with psychotic disorders indicated that the prevalence of drug-induced tardive dystonia using Fahn-Marsden scalewas 5.7%(24). A 1year retrospective patient medical card review at medical center in southern Taiwan shows that the prevalence of tardive dystonia was 21.1%(40). The risk factors for tardive dystonia include; male sex, young age, high potent antipsychotic medication use and ECT treatment(10).

2.5.Conceptualframework

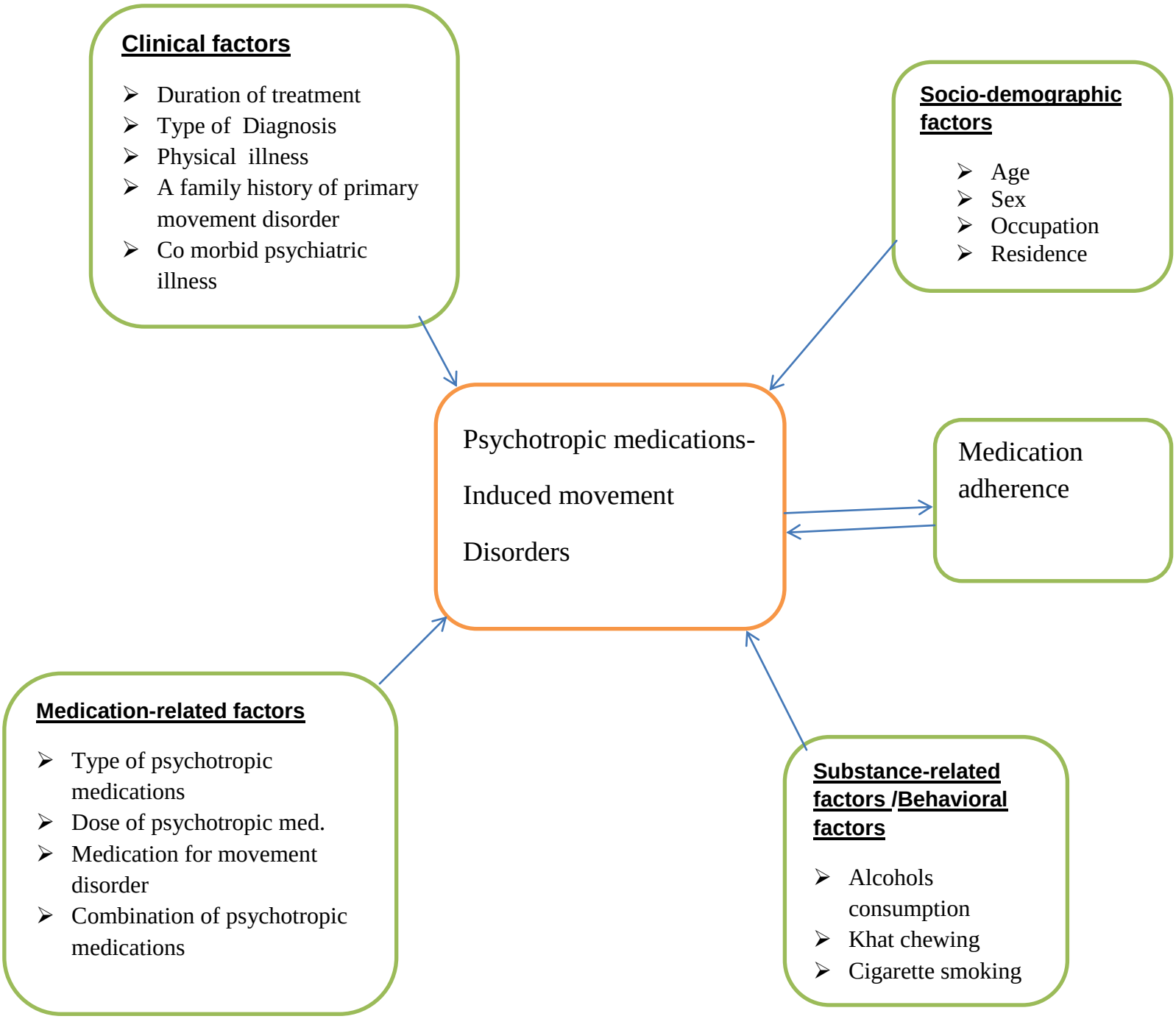

Figure1: conceptual frame work of factors associated with Psychotropic medications induced movement disorders

2.6. Significance of the study

Drug-induced movement disorders are disabling and distressing problems which results in behavioral disturbances (violence and aggression), non-adherence, stigma and exacerbation of psychosis and impair the patient's daily activities of living. There is high prevalence of drug-induced movement disorders among patients receiving psychotropic medications as indicated by different literatures. However, these patients are not carefully assessed ratheroverlooked. Drug induced movement disorders have become relevant in the fact that they determine to a large extent the patient's adherence to medication and also the prognosis of the primary disorder. In addition, the psychosocial burdens of the complications of treatment impact on both patients and relatives will make this study very important.Thus, this study is aimed to assess psychotropic medications-induced movement disorders and associated factors among mentally ill patients attending follow up treatment at Jimma University Medical Center, psychiatric clinic which will help the clinicians:

In increasing their awareness to regularly evaluate patients for drug-induced movement disorders which are very stigmatizing to prevent their emergence and progression.

It helps in making clinical decisions.

It will also use to address some variables not addressed by other study done in our country. The previous study was on conventional antipsychotics-induced movement disorders & associated factors among psychotic patients. But this study will include mentally ill patients taking both conventional & atypical antipsychotic and other psychotropic medications.

It will also try to address the association of non-compliance with drug-induced movement disorders which is not addressed in other study.

It will also serve as a baseline study for further study

Chapter 3: Objectives

3.1. General objective

- To assess the prevalence of psychotropic medications-induced movement disorders and associated factors among mentally ill patients attending follow up treatment at JUMC psychiatric clinic, Jimma, Southwest Ethiopia 2019.

3.2. Specific objectives

- To determine the prevalence of psychotropic medications-induced movement disorders among mentally ill patients attending follow up treatment at JUMC, 2019.
- To identify factors associated with psychotropic medications-induced movement disorders among mentally ill patients attending follow up treatment at JUMC, 2019.

Chapter 4: Methods and Materials

4.1. Study area and period

The study was conducted in Jimma University Medical Center (JUMC) psychiatry clinic from April 01 to June 05. Jimma University Medical Center (JUMC) is found in Jimma town, Oromiaregional state, which is 352 km far apart from Addis Ababa to southwest of Ethiopia. Jimma University Medical Center is one of the oldest governmental hospitals, which was established in 1937 during Italian occupation for the service of their soldiers. After the withdrawal of the colonial conquerors, it has been running as public hospital under the Ministry of Health by different names at different times and currently named as "Jimma University Medical Center". It renders service including inpatient and outpatients for about 15 million populations in southwest Ethiopia. Psychiatric clinic of JUMC was established in 1996 next to Amanuel mental health specialized hospital and currently there are around 1000 psychiatric patients who were taking antipsychotic medications and attending follow up treatment at OPD monthly and on average around 50 patients were visiting daily. Psychiatric clinic has 40 beds for inpatient services and 5 OPD.

4.2. Study design

Hospital based cross-sectional study design was conducted.

4.3. Population

4.3.1. Source population

- All mentally ill patients attending follow up treatment at JUMC psychiatric clinic in 2019.

4.3.2. Study population

- All mentally ill patients attending follow up at treatment JUMC psychiatric clinic during the study period.

4.4. Inclusion and Exclusion criteria

4.4.1. Inclusion criteria

- All mentally ill Patients attending follow up at the psychiatric outpatient department and who had been on antipsychotic medications.

4.4.2. Exclusion criteria

- Mentally ill Patients who were unstable and unable to give the required information
- Patients who had history of primary movement disorders

4.5. Sample size and sampling techniques

4.5.1. Sample size determination

The minimum number of sample size required for this study was determined by using the formula to estimate single population proportion and the following assumption was considered. Minimum sample size for this study was calculated for specific subtypes of movement disorder and the largest sample size was considered for this study. The following assumptions were considered in the study: p= 46.4% for parkinsonism, p= 28.6% for akathesia, p= 11.9% and P= 56% for overall drug induced movement disorders which was taken from the study conducted in Amanuel Specialized Mental Hospital (15) and with 95% confidence level and 5% margin of error.

$$n = \frac{(\frac{z\alpha}{2})^2 p(1-p)}{d^2}$$

Where,

n= minimum sample size required for the study

Z= the reliability coefficient corresponding to 95% confidence level (Z=1.96)

P= patients who were taking conventional antipsychotic medications from the study done at AMSH andd= Absolute precision or tolerable margin of error (d) =5%=0.05

It was also calculated for each subtypes of drug induced movement disorder i.e. Parkinsonism, akathisia, tardive dyskinesia and the maximum sample size was used in this study.

The minimum sample size obtained is depicted in table below (Table 1).

Table 1: Sample size calculation for dependent variables

Variable	Assumption	Minimum sample size obtained(n)
Overall DIMD	P=56%, d=5%, z=1.96,	417
Akathesia	P=28.6%, d=5%, z=1.96,	374
Parkinsonism	P=46.4%, d=5%, z=1.96,	420
TD	P=11.9%, d=5%, z=1.96,	181

The maximum sample size calculated by using certain outcome variables in this study was **420**and it was used for this study.

4.5.2. Sampling techniques

A systematic random sampling technique was used to select the sample participants. The average number of mentally ill patients attending follow up treatment at JUMC psychiatric clinic and who had been on antipsychotic medications per a month was around 1000. The sample size required for this study was 420 as calculated using single population proportion.

So, sampling fraction was; k=N/n=1000/420=2.38~ 2. Therefore, Participants was selected from the patients every 2 intervals and the first participant was selected by lottery method, and then continued every 2.Card of the patients were coded to address repetition of the cases

4.6. Study variables

4.6.1. Dependent variables

Psychotropic medications-induced movement disorders

4.6.2. Independent variables

Socio-demographic factors

Age

Sex

Educational level

Marital status

Residence

Occupation

Clinical factors

Diagnosis of patient

Duration of treatment

Co morbid psychiatric diagnosis

Chronic medical illness

The family history of primary movement disorders

Medication-related factors

Type of psychotropic medication

Dose of psychotropic medications

Combination of psychotropic medications

Medication for movement disorders

Medication non-adherence

Substance-related factors/behavioral factors

Alcohol consumption

Khat chewing

Cigarette smoking

4.7. Data collection procedure and instrument

4.7.1. Data collection Instrument

Data was collected using semi-structured interviewer administered questionnaire which has six sections: a socio-demographic questionnaire to assess the patients' background information, Medication-related factors and clinical factors were assessedbyyes/noanswersofrespondentsand by using chartreview. Medication non-adherence was measured by the Mo risky medication adherence scale-4(41).Substance related factors were assessed by using some factors adopted from ASSIST WHO,V3.1(42)**.**Extra pyramidal symptom rating scale (ESRS) was used to assess the presence of drug-induced movement disorders(4). The Extra Pyramidal Symptom Rating Scale was developed to assess four types of Drug-induced movement disorders: DIA, DIP, Drug-induced dystonia and Drug-induced tardive dyskinesia.

It consists of four subscales and four CGI-S scales: -

I) Questionnaire for DIMDs: For subjective examination and rated on 4-oint scale

(0=Absent, 1=Mild, 2=Moderate, 3=Severe)

II) An examination of Parkinsonism and akathesia: The Parkinsonism score, ranging from 0-96(16items), and the 2 factors; hypokinesia (0-42) and hyperkinesia (0-49).The score for akathisia (0–6) is based on the combined score of subjective akathisia (item 6 of the questionnaire) and objective akathisia (item 7 of the Parkinsonism/Akathisia objective examination).

III) Examination of Dystonia: The score for Dystonia ranges from 0-60 (10 items), and is formed by including both acute and chronic dystonia which scored on 7-point scale (0=absent, 6=most severe), based on the dystonia examination. When establishing presence versus absence of dystonia, a score of 3 or greater on at least one item, or a score of 2 on 2 items is required to indicate presence of dystonia.

IV) Examination of tardive dyskinesia: The score for TDwhich ranges from 0-42 is based on the sum of all 7-items in TD objective examination. When scoring presence versus absence of TD, a score of 3 or greater on at least one item or a score of 2 on 2 items is required to indicate presence of TD.

V) to VIII) Clinical Global Impression Severity (CGI-S)scales for tardive dyskinesia, akathisia, Parkinsonism and dystonia: Theseare rated according to results of the subjective questionnaire, examination subscales, and the evaluator's clinical experience by applying an 8 point rating (0:=absent; 1= borderline; 2:=very mild; 3= mild; 4:=moderate; 5=moderately severe; 6= marked; 7= severe; 8= extremely severe). The 4 CGI-S's are analyzed as separate items.

Studies found high inter-rater reliability correlations and for inter rater reliability of raters > or =80% of items ratings of the complete scale should be +/-1 point of expert ratings and > or= 70% of ratings on individual items of each ESRS subscale should be +/-1 point of expert ratings. During a cross scale comparison, AIMS and ESRS were found to have a 96% agreement between TD defined cases by DSM-IV TD criteria. In this study also the Cronbach's alpha was found to be 78.9%.

4.7.2. Data collection procedure

Data was collected using face to face interview by using semi structured & pre-tested interviewer administered questionnaires, medical chart review and examination of the patient. Data was collected by 4 BSc psychiatric nurses and was supervised by MSc psychiatry professional and the training was given for both data collectors& supervisors regarding how to use the tool. The Study participants were identified by data collectors by reviewing patient record. Then, data was collected from selected study participants after informed consent was obtained.

4.8. Operational definitions

- **Drug-induced movement disorders:-** defined as if the patient has at least one movement disorders among these four(4) DIMDs: DIA, DIP,Drug induced Dystonia and Drug induced Tardive Dyskinesia(4).
- Score of 3 or more on one item or scores of 2 on 2 items is required to determine the presence versus absence of drug-induced akathesia, drug-induced Parkinsonism, dystonia and tardive dyskinesia.
- **Mentally ill**:- any person who received any psychiatric diagnosis by mental health professional.
- **Current substance use:** using at least one of a specific substance for nonmedical purpose within the last 3 months
- **Ever use of substance**: using at least one of any specific substance for the nonmedical purpose at least once in a lifetime(42).
- **Medication non-adherence**: a patients on psychotropic medications scored >1 or more on MMAS-4 were considered as having poor adherence to medications(41).
- **Combination of psychotropic medications:** is the use of two or more psychotropic drugs
- **Presence of chronic medical illness:** when subjects have at least 1 or more ofany diagnosed other medical disease like Hypertension, Diabetes mellitus,
  Cardiac disease, HIV/AIDS made by clinician as reviewed from the card.

4.9. DataQualityControl

A semi-structured interviewer administered questionnaire containing six sections was translated into Amharic/Afan Oromo by speakers of both languages then translated back to English to check for consistency and understandability of the tool. Training was given for data collectors and supervisors on the data collection tool & sampling methods. The questionnaire was pretested prior to the actual data collection on 5% of sample size at shenen Gibe general Hospital and the questionnaire was checked for its clarity, simplicity, and understandability.

During data collection, the questionnaire was checked for its completeness on daily basis by data collectors, supervisors and then by the investigator.

4.10. Data processing and Analysis

The data was edited, cleaned, coded and entered into Epi-data 3.1 version and analyzed by using SPSS 22 version. Binary Logistic regression was used for comparison of the subjects with and without psychotropic medications induced movement disorders. Bivariate results less than 0.25 were candidate for multivariate and collinearity were checked by variance inflation factor (VIF). MultivariateLogistic regression analysis was used to identify the associated factors. The p-value less than 0.05 were considered as statistically significant. The strength of the association was presented by odds ratio with 95% C.I and Hosmer-lemeshow goodness was used to check model fits. Results were presented in the form of table, figures & chart using frequency & summary statistics such as mean, & percentage to describe the study population in relation to different variables.

4.11. Ethical consideration

Ethical clearance was obtained from the Ethical review board of Jimma University Institute of health, school of post graduate studies. The data collectors were clearly explaining the aims of the study for study participants. Information was collected after obtaining written informed consent from each study participants. The right was given to the study participants to refuse or discontinue participation at any time they want and the chance to ask any thing about the study. Privacy and confidentiality of information given by each respondent was kept by data collectors. Data collectors were put their signature at the end. Those study participants who suffer from side effects were getting a better management at outpatient department.

4.12. Dissemination plan

The results of the study will be submitted to Jimma University Faculty of Medicine, Institute of Health and the copies of paper also submitted to hospital administration of JUMC department of psychiatry and to JUMC administrative office psychiatry clinic. The research paper will be presented in health professional organizations‟ annual meetings and professional conferences. Finally, the results will be published in national and international journal to disseminate the results of the study.

Chapter 5: Results

5.1. General description of participants

A total of 410 patients responded to the questionnaire, which gives a response rate of 97.3%. The mean age of the respondents was 33.3years with SD ± 8.55years. About 263(64.1%) of the study participants were male. About 213(52%) of the study participants were single. Majority 237(58.7%) of the study participants were Oromo, 222(54.1%) were Muslim, 218(53.2%) were jobless and 206(50.2%) were residing in Urban areas respectively (Table 2).

Table 2: Socio-demographic characteristic distributions of mental ill patients attending follow up treatment at JUMC psychiatry clinic, 2019.

Variables	Categories	Frequency(N=410)	Percentage(%)
Age(year)	15-29years	145	35.4
	30-44years	201	49.0
	>45years	64	15.6
Sex	Male	263	64.1
	Female	147	35.9
Marital status	Married	168	41
	Single	213	52
	Divorced	28	6.8
	Widowed	1	0.2
Religion	Muslim	222	54.1
	Orthodox	120	29.3
	Protestant	67	16.3
	Others	1	0.2
Ethnicity	Oromo	237	57.8
	Amhara	107	26.1
	Tigre	12	2.9
	Dawuro	39	9.5
	Others	15	3.6
Residence	Rural	204	49.8
	Urban	206	50.2
Educational status	Can't read & write	90	22.0
	1-4grade	126	30.7
	5-8grade	109	26.6
	9-12grade	52	12.7
	College & above	33	8.0
Occupational status	With job	192	46.8
	Jobless	218	53.2

Other religion; catholic, wakefata, **other ethnicity**; silte, wolayta, yem

5.2. Clinical characteristics of study participants

Most of the study participants 223(54.4%) had the diagnosis of schizophrenia. Majority of the study participants 246(60.0%) had received treatment within the range of 1-5years with the mean length of 4.8years (SD=3.9) and 38(9.3%) had history of physical illness.

Table3: Distribution of clinical characteristics of mentally ill patients attending follow-up treatment at JUMC psychiatry clinic, 2019.

Characteristics	Frequency(N=410)	Percent(%)	DIMD	
			Yes	No
Diagnosis of patients				
Schizophrenia	223	54.4	91	132
Major depressive disorder	99	24.1	30	69
Bipolar I disorder	74	18.0	45	29
Other schizophrenia spectrum disorder	14	3.4	2	12
Duration of treatment				
<1years	37	9.0	10	27
1-5yyears	246		85	161
>5years	127	31.0	72	55
Co morbid psychiatric diagnosis				
Yes	3	0.7	3	
No	407	99.3	164	243
Physical illness				
Yes	38	9.3	35	3
No	372	90.7	167	205

Other schizophrenia spectrum disorders: brief psychotic disorder, schizophreniform disorder, delusional disorder, substance induced psychotic disorder, psychotic disorder due to other medical condition

5.3. Medication related characteristics of the study participants

Of the study participants, 240(58.5%) patients were receiving typical antipsychotic medications, 95(23.2%) were receiving atypical and 75(18.3%) were receiving both typical and atypical antipsychotic medications. The mean daily chlorpromazine equivalent dose was 425mg (SD=245). 75(18.3%) of patients received mood stabilizers, 66(16.1%) received antidepressants, 28(6.8%) received benzodiazepines and 187(45.6%) patients received anti cholinergicdrugs in combination with antipsychotic medications. Among patients who had drugs induced Parkinsonism 32(54.2%) were using typical antipsychotics, 18(30.5%) were using atypical antipsychotics, 13(22%) were taking mood stabilizers and 9(15.2%) were taking antidepressants. Of those developed akathesia 27(52.9%) were taking typical antipsychotics, 13(25.5%) were taking atypical antipsychotics, 27(52.9%) were using mood stabilizers and 41(80.4%) were using anti-cholinergic medications. Of Tardive dyskinesia patients 33(52.4%) were using typical antipsychotics, 10(15.9%) received benzodiazepines and 7(11.1%) were taking antidepressants. (Table 4)

Table 4: Distribution of medication related characteristics of patients with mental illness attending follow up treatment at JUMC psychiatry clinic, 2019

Characteristics	frequency	Percent (%)	DIP		DIA		TD	
			Yes	No	Yes	No	Yes	No
Types of antipsychotics								
Typical	240	58.5	32	208	27	213	33	207
Atypical	95	23.2	18	77	13	82	8	87
Both	75	18.3	9	66	11	64	22	53
Dose of antipsychotics								
<200	143	34.9	15	128	6	337	11	132
200-600	263	64.1	42	221	45	218	50	213
>600	4	1.0	2	2		4	4	
Mood stabilizers	75	18.3	13	52	27	48	7	68
Antidepressants	66	15.6	9	55	7	59	24	42
Benzodiazepines	28	6.8	5	23		28	10	18
Anticholinergic medications use								
Yes	187	45.6	48	139	41	146	136	51
No	223	54.4	11	212	10	213	31	192
Medication adherence								
Yes	373	91.1	53	320	43	330	44	329
No	37	9.0	6	31	8	29	19	18

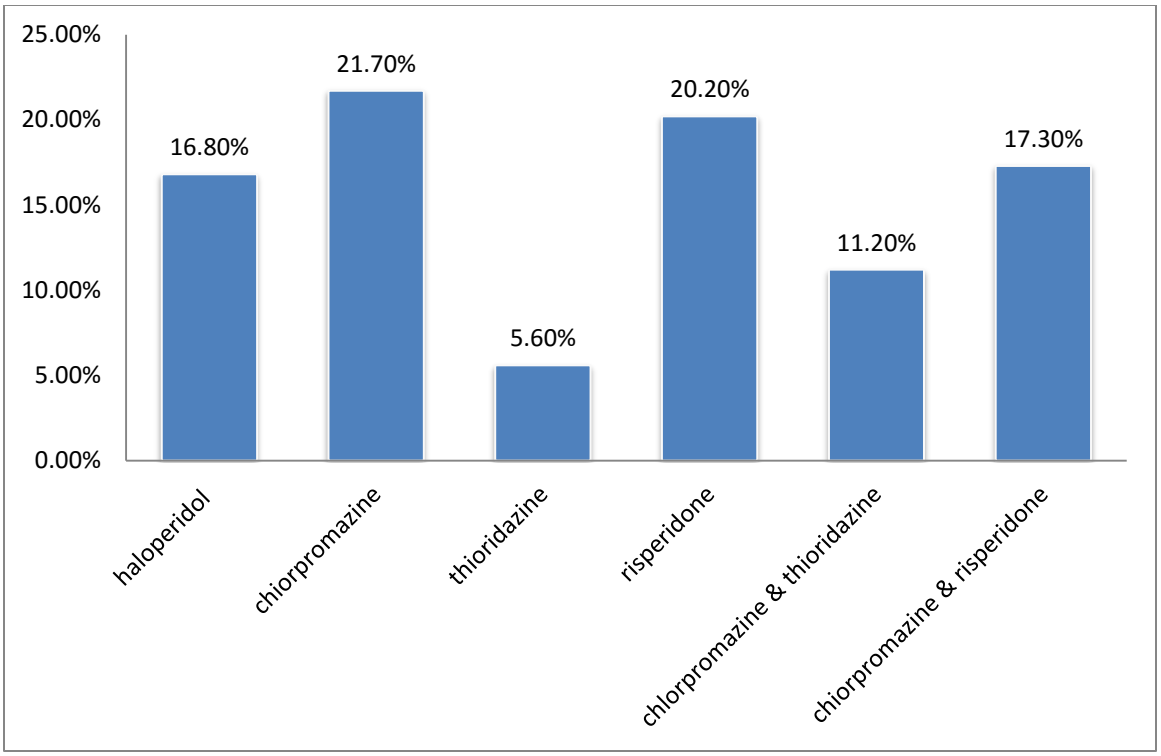

Figure2: Distribution of type of antipsychotic medications received by patients with mental illness attending follow up treatment at JUMC, 2019.

5.4 Substance related characteristics of study participants

From the study participants 164 (39.9%) had used substances at least once in their life time and 99 (24.1%) were using substances in the last three months before the study period (figure3).

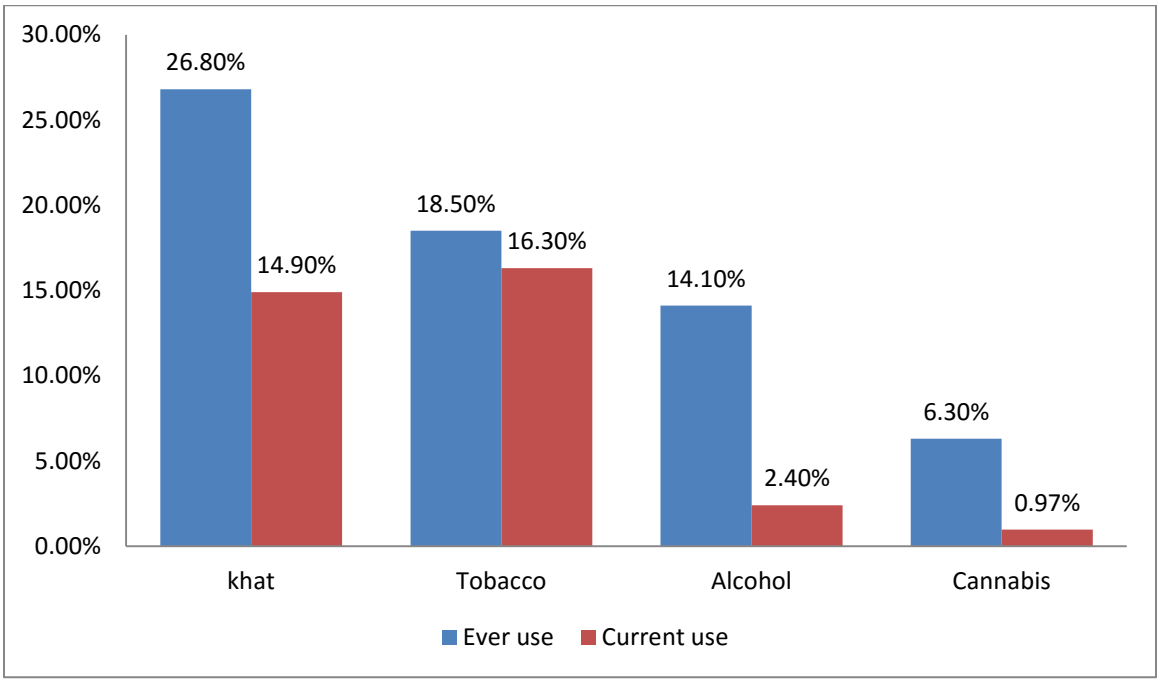

Figure3: Distribution of type of substances used by mentally ill patients who were taking antipsychotic medications and attending follow up treatment at JUMC, 2019.

- 373(91%) of study participants were adherent to their medication.

5.5. Prevalence of psychotropic medications induced movement disorders

The overall prevalence of psychotropic medications induced movement disorder was 40.9% (95% CI: 36.1, 45.6):- Drug induced Parkinsonism 59(14.4% 95% CI: 11.0, 18.3), drug induced akathisia 51(12.4%, 95% CI: 9.3, 15.8), drug induced tardive dyskinesia 63(15.4%, 95% CI: 12.0, 19.3) and drug induced tardive dystonia 9(2.2%, 95% CI: 1.7, 3.4) respectively.

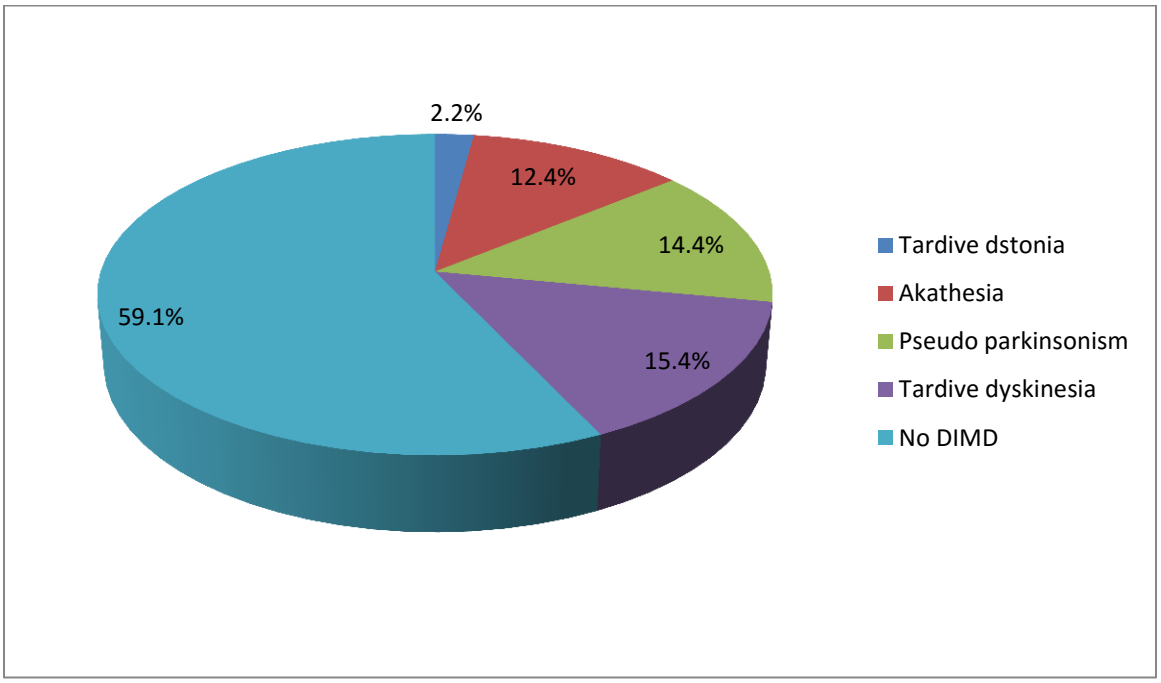

Figure4: Prevalence of psychotropic medications induced movement disorders among mentally ill patients attending follow up treatment at JUMC, 2019.

Clinical global impression of severity of psychotropic medications induced movement disorders

Table 5: Severity of extra pyramidal signs related to psychotropic exposure among mentally ill patients attending follow up treatment at JUMC, 2019.

	Drug Induced Movement Disorders			
	DIP	Akathisia	TD	Tardive Dystonia
Mild	32(7.8%)	34(8%)	29(7.1%)	6(1.5%)
Moderate	25(6.4%)	18(4.2%)	31(7.2%)	2(0.5%)
Severe	1(0.2%)	1(0.2%)	5(1.1%)	1(0.2%)

Among patients having drug induced akathesia, 8% (n=34) of patients had CGIS score of mild; 7.8% (n=32) of patients having Parkinsonism had mild score and 7.1% (n=29) of patients having TD had mild score. 6.4% (n=25) of patients having DIP had moderate score and 7.2% (n=31) of patients having TD had moderate score.

Table 6: Distribution of signs and symptoms and body parts affected by psychotropic medications- induced movement disorder among mentally ill patients attending follow up treatment at JUMC Psychiatry clinic, 2019

Items	Frequency (yes)	Percent (%)
Questionnaire(subjective)		
The impression of slowness or weakness, difficulty in carrying out routine tasks	37	9.0
Difficulty walking or with balance	33	8.0
Stiffness, stiff posture	7	1.7
Restless, nervous, unable to keep still	52	12.7
Tremors, shaking	70	17.1
Oculogyric crisis, abnormal sustained posture	1	0.2
Abnormal involuntary movements	67	16.3
Examination: Parkinsonism		
Tremor	80	19.5
Bradykinesia	35	8.5
Gait and posture	56	13.7
Postural stability	1	0.2
Rigidity	6	1.5
Expressive automatic movements (facial mask/speech)	51	12.4
Examination: Dystonia		
Acute torsion, and non-acute or chronic or tardive dystonia head and jaw and Lingual and Jaw movements		
a. Right upper limb	7	1.7
b. Left lower limb	7	1.7
c. Right lower limb	2	.5
d. Left lower limb	2	.5
e. Head	0	.0
f. Tongue	3	.7
g. Eyes	0	.0
h. Jaw/chin	3	.7
i. Lips	1	.2
j. Trunk	3	.7
Examination: Dyskinesia movement		
Lingual movements	46	11.2
Jaw movements	66	16.1
Bucco-labial movements	2	.5
Truncal movements	5	1.2
Upper extremities	52	12.7
Lower extremities	2	.5
Other involuntary movements	6	1.5

The most commonly reported subjective items were restlessness 52(12.7%) and tremor of the hand 70(17.1%). On examination, the most prevalent signs of Parkinsonism were tremor 80(19.5%) and gait and posture disturbance 56(13.7%). Jaw movement 66(16.1%) and upper extremities movement 52(12.7%) were the most prevalent signs of tardive dyskinesia.

5.6. Factors associated with drug induced movement disorders

During bivariate analysis of drug induced Parkinsonism in relation to each explanatory variable: sex, age, duration of treatment, type of antipsychotics, dose of antipsychotics, physical illness and medication for movement disorders were the variables that fulfilled the minimum requirement (in this study 0.25 level of significance) and entered into multivariate analysis for further analysis.

During bivariate analysis of psychotropic drug induced akathisia in relation to each explanatory variable: sex, age, diagnosis of the patient, job, dose of antipsychotics, other psychotropic medications used other than antipsychotics, medication for movement disorder and khat use were fulfilled the requirement (0.25 level of significance) and entered into multivariate for further analysis.

Bivariate analysis of psychotropic medications induced tardive dyskinesia in relation to different explanatory variables shows that: sex, age, educational level, diagnosis, type and dose of antipsychotics, medication for movement disorder, medication adherence, khat and tobacco use were fulfilling the requirement and entered into multivariate analysis for further analysis.

Table 7: Factors associated with psychotropic medication induced Parkinsonism (Bivariate analyses and multivariate analysis) among patients taking antipsychotics and attending follow up treatment at JUMC, 2019.

Explanatory variables	**Pseudo parkinsonism (N=410)**		**COR (95% CI)**	**AOR (95% CI)**	**P-value**
	Yes	**No**			
Age					
15-29	15	130	1.00	1.00	
30-44	22	179	1.52(0.87, 2.65)	1.51(1.17, 3.12) **	**0.004**
≥45	22	42	2.46(1.34, 4.52) *	2.9(2.5, 8.4) *	**0.011**
Sex					
Male	38	225	1.00	1.00	
Female	21	126	3.42(2.2, 5.4) *	2.3(1.06, 5.07) *	**0.035**
Duration of Rx					
<1year	10	27	1.00	1.00	
1-5year	23	222	1.52(0.87, 2.65)	1.55(0.17, 3.12)	0.482
≥5year	26	102	2.41(1.52, 5.57) *	2.8(0.78, 4.61)	0.079
Type of antipsychotics					
Typical	32	208	3.49(1.96, 4.2) *	2.92(1.34, 4.71) **	**0.003**
Atypical	18	77	1.00	1.00	
Both	11	64	1.15(1.12, 2.48)	1.42(1.24, 3.14) *	**0.013**
Anticholinergic use					
Yes	48	139	0.15(0.08, 0.29)	0.12(0.049, 0.29)**	**0.004**
No	11	212	1.00	1.00	
Physical illness					
Yes	24	14	2.12(1.28, 3.50) *	4(2.2, 8.2) ***	**0.002**
No	35	337	1.00	1.00	

*****Statistically significant at p value <0.05, ****** at p value <0.01, *** at p value <0.001Hosmer and lemeshow test= **0.65**

The result of multivariate analysis shows that drug induced Parkinsonism was significantly associated with: sex, age, type of antipsychotics, physical illness, and anticholinergic medication use.The odds of developing drug induced Parkinsonism among female patients were 2.3times (AOR=2.31, 95% CI: 1.29, 7.23) higher as compared to male patients. Patients with age ≥45years were 4.3times (AOR=4.31, 95% CI: 1.6, 11.6) more likely to develop antipsychotic induced Parkinsonism compared to those patients age between 15-29years. Those patients who have physical illness were 4times (AOR=4.19, 95% CI: 2.2, 8.2) more likely to develop drug induced Parkinsonism compared to those who have no physical illness.Taking anti-cholinergic medication use was 88% (AOR=0.119, 95% CI: 0.05, 0.29) from developing drug induced Parkinsonism as compared to those not using anti-cholinergic medication. Those patients who received typical antipsychotics were 2.92times (AOR=2.9, 95% CI: 1.34, 4.71) and those taking both typical and atypical were 1.4times (AOR= 1.42, 95% CI: 1.24, 3.13) more likely to develop DIP as compared to those patients who were taking atypical antipsychotic medications.

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Table8: Factors associated with psychotropic drugs induced Akathisia (Bivariate and multivariate analysis) among mentally ill patients attending follow up treatment at JUMC, 2019.

Explanatory variables	**Akathisia** (N=410)		**COR (95% CI)**	**AOR (95% CI)**	**P-value**
	Yes	**No**			
Sex					
Male	25	237	1.00	1.00	
Female	25	122	1.9(1.53, 3.37) *	3.9(2.6, 9.5) **	**0.003**
Diagnosis					
Schizophrenia	15	208	1.00	1.00	
MDD	7	92	2.97(1.3,2.46) *	4.76(2.65,7.22) *	**0.014**
BID	29	45	3.11(1.05,7.2) *	2.3(0.071, 3.4)	0.063
Other schizophrenia spectrum disorders	2	12	1.2(0.30, 7.16)	1.7(0.23, 6.34)	0.925
Chlorpromazine equivalent dose					
<200	6	137	1.00	1.00	
200-600	45	218	1.19(0.08, 1.48)	1.36(1.17,3.7) **	**0.008**
>600	1	3	2.2(0.6, 4.9)	3.19(0.13, 9.06)	
Other psychotropic medications than antipsychotics					
Sodium valproate	15	212	2.14(0.4,11.4)	1.88(1.3, 11.8) *	**0.023**
Amitriptyline	7		3.06(1.1,8.4)*	1.26(0.09, 2.88)	
Sodium & carbamazepine	10	14	7.3(3.28,12.5)*	1.9(1.3, 4.8) *	**0.010**
Not taking other medications	17	337	1.00	1.00	
Anticholinergic use					
Yes	41	146	1.7(0.08, 3.3)	2.1(1.09, 4.9)**	**0.009**
No	10	213	1.00	1.00	
Khat					
Yes	13	97	2.6(1.19,5.69)*	4.9(1.9,12.7)***	**0.000**
No	51	249	1.00	1.00	

*statistically significant at p value <0.05, **at p value <0.01, ***at p value <0.001 Hosmer and lemeshow test=**0.39**

The multivariate analysis of psychotropic medications induced akathesia in relation to explanatory variables shows that: Sex, diagnosis of the patient, dose of antipsychotics, use of other psychotropic medications i.e. mood stabilizers, antidepressants, use of anticholinergic medication and khat use were significantly associated with drug induced akathisia. The odds of developing drug induced akathisia among females was 3.9times (AOR=3.9, 95% CI: 2.6, 9.5) as compared to male patients. Those patients who treated with 200-600mg doses of antipsychotics were 1.36times (AOR= 1.36, 95% CI: 1.17, 3.7) and those with >600mg 3.19times (AOR=3.19, 95% CI: 1.13, 9.06) more likely to develop drug induced akathisia as compared to those who were taking <200mg equivalent doses of chlorpromazine.

The odds of developing DIA among patients taking anti-cholinergic medications increased by 2.1times (AOR=2.1, 95% CI: 1.09, 4.9) compared to those who did not take anti-cholinergic medications. Those patients using khat were 4.9times (AOR=4.9, 95% CI: 1.9, 12.7) more likely to develop drug induced akathisia as compared to those who didn't use khat.

Those patients treated with other psychotropic medications in addition to antipsychotic medications were i.e. Sodium valproate 1.88times (AOR=1.88, 95% CI: 1.3, 11.8) more likely to develop drug induced akathisia as compared those who only treated with antipsychotics.

Patients diagnosed with Major depressive disorder were 4.76times (AOR=4.76. 95% CI: 2.65, 7.22) more likely to develop drug induced akathisia as compared to those diagnosed as schizophrenia.

Table9: Factors associated with tardive dyskinesia (bivariate and multivariate analysis) among patients taking antipsychotics and attending follow up treatment at JUMC, 2019.

Explanatory variables	Tardive dyskinesia(N=410)		COR 95% CI	AOR 95% CI	P-value
	Yes	No			
Age					
15-29	14	131	1.00	1.00	
30-44	38	163	1.45(0.24,2.88)	1.41(1.12, 3.36) *	**0.039**
≥45	11	53	2.4(1.2, 5.0) *	2.51(1.79, 5.42) **	**0.005**
Sex					
Male	54	209	1.00	1.00	
Female	11	136	3.96(1.89, 8.28) *	3.74(1.56,8.9) *	**0.028**
Diagnosis					
Schizophrenia	49	187	1.00	1.00	
MDD	10	91	2.14(1.18,5.3) *	2.3(1.21, 9.3) **	**0.006**
BID	6	67	2.9(1.22, 7.34) *	1.74(0.16, 6.3)	0.206
Duration					
<1year	3	34	1.00	1.00	
1-5year	29	216	1.3(1.9, 2.04) *	1.67(0.42, 5.4)	0.406
>5year	33	95	1.27(1.02, 3.57) *	1.37(1.16, 2.86) *	**0.015**
Chlorpromazine equivalent dose					
<200	11	136	1.00	1.00	
200-600	50	204	2.26(1.79,5.37) *	2.3(0.37, 6.8)	0.481
>600	4	5	3.2(1.84,10.8) **	1.89(1.72, 4.3) *	**0.032**
Ant cholinergic medication use					
Yes	54	133	6.5(4.6,10.19) **	4.05(3.12,8.70) ***	**0.000**
No	9	214	1.00	1.00	
Smoking					
Yes	24	11	0.53(0.24,0.93) *	0.26(0.093,0.75) ***	**0.000**
No	39	336	1.00	1.00	

*=statistically significant at p value <0.05, ****** at p value <0.01, *** at p value < 0.001, Hosmer and lemeshow test= **0.29**

During multivariate analysis of antipsychotic medications induced tardive dyskinesia in relation to explanatory variables: sex, age, duration of treatment, dose of antipsychotic, major depressive disorders, medication for movement disorders (anti cholinergic medication use) and tobacco use were significantly with drug induced TD.

Female patients were 3.7times (AOR=3.74, 95% CI: 1.56, 8.9) more likely to develop psychotropic drug induced tardive dyskinesia than male patients. The odds of developing drug induced TD among patients age range between 30-44yearswere 1.4(AOR=1.41, 95% CI: 1.12, 3.36) and ≥45years were 2.5times (AOR=2.51, 95% CI: 1.79, 5.42) higher as compared to those age range 15-29years. Patients diagnosed with major depressive disorder were 2.3times (AOR=2.3, 94%CI: 1.21, 9.3) more likely to develop drug induced TD as compared to schizophrenic patients. Those patients taking chlorpromazine equivalent dose >600mg were 1.89times (AOR=1.89, 95% CI: 1.97, 4.3) more likely to develop TD as compared to those taking <200mg. Patients taking anti cholinergic medications were 4times (AOR= 4.05, 95% CI: 3.12, 8.70) more likely to develop psychotropic medications induced tardive dyskinesia than those not using anti cholinergic medications. Smoking cigarette was 73.6% (AOR=0.264, 95% CI: 0.093, 0.75) protective from developing tardive dyskinesiaas compared to non-smokers.

Chapter 6: Discussion

6.1. Prevalence of psychotropic medications induced movement disorders

The overall prevalence of psychotropic DIMD in this study was 40.7% (95% CI: 36.1, 45.6) which was higher than study done in 11 countries including Australia, Canada, France, Israel, South Africa and the USA, 30.4%(21). The difference may be due to use of mono therapy and low mean daily dose of psychotropic medications taken by the patient in the previous study. It was also higher than the study done in Nigeria 5%(26)and the variation might be due to the difference in clinical rating scale and difference in type of antipsychotic availability.

It was lower than study done in Netherland 68%(24), Estonia 61.6%(8), Filipino 53%(25), 78.05%(25)and Ethiopia 56%(15). The possible reasons for the difference might be due to the difference in: - study setting which was both inpatient and outpatient in some of the previous studies, type of psychotropic medication exposed, daily drug dosage and difference in clinical rating scale (tool).

The prevalence of drug-induced akathisia was 12.4% (95% CI: 9.3, 15.4) which was higher than study done in Netherland 4.6 %(43), California 7 %(10), United Kingdom 1.3%(29) and France 1.2%(23) in which the variation might be due to difference in study population, sample size and types of psychotropic medications used. But it was lower than study done in Poland 24.52%(30), Serbia 25%(18), Estonia 31.3%(8) and Ethiopia 28.6%(15) which might be due to difference in rating scale used. It was in line with study done in Nigeria 14.6%(26).

The prevalence of drug-induced Parkinsonism was 14.4% (95% CI:11.0, 18.0) which was lower than studies done in California 30%(10), Netherland 56.2%(24) ,United kingdom 26%(29), Poland 22.99%(30), Estonia 23.2%(8),Nigeria 27.2%(26) and Ethiopia 46.4%(15). The discrepancy may be due to difference in tools used and relatively high daily drug dosage usage in the previous studies. But it was higher than study done in France 1.3%(23) and Saudi Arabia 6.8%(33) and it may be due to exposure to low dosage and short duration of psychotropic medications in the previous studies.

The prevalence of drug-induced tardive dyskinesia was 15.4(95% CI: 12.0, 19.0) which was lower than study done in Canada 25%(20), Netherland 28.4%(24), California 63%(10), Indian 26.4%(34), Estonia 32.3%(8) and south Africa 28.4%(36) and it may be due difference in clinical rating scale and exposure to only typical antipsychotics in the previous studies. But it was in line with study done in Poland 11.9%(30), Kenya 11.9%(37) and Ethiopia 11.9%(15). The prevalence of drug induced tardive dystonia in this study was 2.2% (95% CI: 0.7, 3.4) which was relatively in line with study done in Netherland 5.7%(24). But it was lower than study done in southern Taiwan 21.1%(40) and this difference might be due to the difference in sex and mean age of population.

6.2. Factors associated with psychotropic medication induced movement disorders

During analysis of drug induced Parkinsonism in relation to explanatory variables: female patients were significantly associated with DIP as compared with male patients(AOR=2.3, 95% CI: 1.06, 5.06).This might be due to that striatal dopaminergic and cholinergic systems are under regulatory control by estrogen and in females the balance between these two neurotransmitter systems in the striatum may be shifted towards higher cholinergic activity, a condition which favors the development of movement disorders in females. This was supported by other studies done in Netherland(33).

Patients with age range between 30-44years were 1.51times and ≥ 45years 2.9times (AOR=2.9, 95% CI: 2.5, 8.4) more likely to develop drug induced Parkinsonism as compared to those patients age range between 15-29years. This was supported by study done in India and Netherland(30,33). Those patients taking typical antipsychotics were 2.92times (AOR=2.92, 95% CI: 1.34, 4.71) more likely to develop drug induced Parkinsonism. This was supported by study done in Saudi Arabia(33) and Nigeria(26). Those having physical illness were 4times (AOR=4.01, 95% CI:2.2, 8.2) more likely to develop drug induced Parkinsonism than those who did not have physical illness.This was supported by study done in Poland(23) but in contrary to study done in south Africa(36). Anti-cholinergic medications use was88%(AOR=0.12, 95% CI: 0.049, 0.29) protective as compared to those who did not take anti- cholinergic medications.

During analysis of drug induced akathisia in relation to explanatory variables: Being female was significantly associated with drug induced akathisia as compared to male patients (AOR=3.9, 95% CI: 2.6, 9.5). This was in contrary to study done in Nigeria in which the ratio was 1:1(26).

Those who treated with chlorpromazine equivalent doses of 200-600mg were 1.36times (AOR=1.36, 95% CI: 1.17, 3.71) and >600mg were 3.19times (AOR=3.19, 95% CI: 1.13, 9.06) more likely to develop drug induced akathisia than those treated with <200mg doses. This was consistent with the study done in Ethiopia(15).Those patients receiving sodium valproate were 1.88times more likely to develop akathisia as compared to receiving only antipsychotics.

Khat was also significantly associated with drug induced akathisia (AOR=4.9, 95% CI: 1.9, 12.7). This could be due that some withdrawal symptoms of khat mimics the symptoms of akathisia and this was consistent with the study done in our country(15). The odds of developing drug induced akathisia among patients diagnosed as major depressive disorder were 4.76times (AOR=4.76, 95% CI: 2.65, 7.22) as compared to schizophrenia patients. The possible reason could be results from the fact that the rates of movement disorders would increase when some antidepressants combined with antipsychotics. This was supported by study done in Poland(23) and Philippines(25). Drug induced akathisia was 2.1times more common among patients who were receiving anti cholinergic medications than those who didn't take anti cholinergic drugs. The reason might be anti-cholinergic medications given after the side effect developed.

During analysis of drug induced tardive dyskinesia in relation to explanatory variables: Those aged ≥45years were 2.5times more likely to develop TD compared to those aged between15-29years. This was consistent with the study done in India(30).Being female patients were significantly associated with drug induced TD compared to male patients (AOR=3.74, 95% CI: 1.56, 8.9). This was supported by study done in Nigeria(26).The odds of developing TD among patients diagnosed with major depressive disorders were 2.3times more likely as compared to those diagnosed with schizophrenia.Those treated for ≥5years were 2.43times (AOR=2.43, 95% CI: 1.2,7.12) more likely to develop drug induced TD as compared to those who treated for <1year.This was supported by other study done previously(10,30). Smoking cigarette was 73.6% (AOR=0.26, 95% CI: 0.093, 0.75) protective from developing TD as compared to non-smokers. The reason might be due to that smoking is an enzyme inducer and this was supported by study done in South Africa(36). The odds of developing drug induced TD among patients taking anti cholinergic medications were 4times (AOR=4.05, 95% CI: 3.12,8.70) as compared to those who did not use anti cholinergic medications. The reason could be anti-cholinergic medications might prescribed after the onset of tardive dyskinesia and this was supported the study done in United Kingdom(44).

Those patients receiving chlorpromazine equivalent dose >600mg were 1.89times more likely to develop to TD as compared to those receiving doses <200mg. This was supported by other studies done(15,30,36).

Limitations of the study

ESRS was not validated in our country.

Recall bias might occur because of that some reports are about past history.

It was difficult to differentiate tardive dystonia symptoms from that of tardive dyskinesia.

Physical illness and psychiatric diagnosis were reviewed from card.

Presence of medical condition used for analysis rather than type of medical illness.

Chapter7: Conclusion and Recommendation

7.1. Conclusion

The prevalence of psychotropic medications induced movement disorder was high in this study. Sex and age were found to be associated with drug induced Parkinsonism and TD. Dose of mediation was positively associated with Akathisia and TD. Major depressive disorder and taking sodium valproate were positively associated with akathisia. Physical illness was associated with Parkinsonism. Khat was positively associated with drug induced akathisia and smoking was associated with tardive dyskinesia.

7.2. Recommendation

To Jimma University Medical Center

- It is better if treatment guideline regarding the use of psychotropic medications, i.e. antipsychotics is designed for psychiatry case team.
- It is better if drugs with minimal side effects are available

To Health Professionals

- It is better to start with low dose of psychotropic medications and maintain on lowest possible dose.
- It is better to consider patients sex and age during prescribing psychotropic medications
- It is better if standard tools are used for early diagnosis, routine evaluation and treatment of drug induced movement disorders
- It is better if psycho education is given regularly on khat use which is indigenous to the study area.
- It is better to look for physical illness and manage accordingly during psychiatric assessment.

To researchers

- It is better to consider the longitudinal study to establish cause and effect relationship

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Appendices

Annex I: Information sheet

Dear Participants: Code No: _____

My name is_____; I am hereby on behalf of AssefaKumsa who is a student undertaking a **Master's Degree in Integrated clinical & community Mental Health** at Jimma University. The research is one of the requirements for the degree and this letter serves to ask consent from you to take part in this research. The purpose of this study is to assess the **prevalence of psychotropic medications-induced movement disorders and associated factors among mentally ill patients attending follow up treatment at JUMC psychiatry clinic, Jimma, southwest Ethiopia in 2019** which are common among mentally ill patients being treated with psychotropic medications and resulted in poor outcome as a result of treatment non-adherence, hospitalization, stigma, suicide and increase psychotic relapse. This will be an important input for the clinicians and institutions involved in care and support of patients with mental illness. Your participation in this research is voluntary. Your participation in this study is very important for the achievement of the study and there is no any risk that will come to you because of your participation in this study. If you decide not to participate there will be no negative consequences for you and you have full right to withdraw at any time in-betweens from the interview if you don't wish. All the responses given by you and results obtained will be kept confidential. Without your and other legal body's permission, any information will not be disclosed to the third person. You are not expected to give your name or phone number.

The interview period will take about 20-30minutes. If you are willing to participate in this study, you need to understand and sign the agreement form, and then you will be asked to give your responses to data collectors.

Name of investigator: **AssefaKumsa** **Phone: +251922392567**

E-mail: getassefa67@gmail.com

Annex II: Informed consent form

Are you voluntary to participate in the study? Yes ☐ No ☐

I hereby confirm that I understand the contents of this document and the nature of the research project, and I consent to participate voluntarily in the research project. I understand that I am autonomous to withdraw from the project at any time.

Signature of participant Date

_____ _____

Name and signature of data collector_____ Date_____

Name and signature of supervisor_____ Date_____

Informed assent form

I confirm that I read the content of this document and the nature of the research project and I agree my child to participate in the research project. I understand I can make him/her withdraw from the project at any time.

Signature of parent/s (legal guardian)…… Date……

I understand what I must do in this study and I want to take part in this study.

Name and signature of supervisor……. Date……

Name and signature of data collector…… Date……

Annex III: Questionnaire English version

Code No. _____

Questionnaire on: prevalence of drug-induced movement disorder and associated factors among patients attending follow up treatment at JUMC, psychiatry clinic, Jimma, Southwest, Ethiopia, 2019.

INSTRUCTION: The questionnaire has six parts. It will take about 25 minutes to complete the examination and interview. Thank you very much for your patience.

SECTION I: Socio-demographic information

S.No	*Questionnaires*	*Alternative response*	*Coding*
Q-101	*How old are you?*	*Age in years----------*	
Q-102	*Sex*	1. *Male* 2. *Female*	
Q-103	*What is your religion?*	1. *Muslim* 2. *Orthodox* 3. *Protestant* 4. *Others----------*	
Q-104	*What is your marital status?*	1. *Married* 2. *Single* 3. *Divorced* 4. *Widowed*	
Q-105	*What is your ethnicity?*	1. *Oromo* *6.others……* 2. *Amhara* 3. *Tigre* 4. *Kaffa(dawuro)* 5. *Silte*	
Q-106	*Residence*	1. *Rural.* 2. *Urban*	
Q-107	*What is your educational level?*	1. *Can't write and read* 2. *1-4 grade* 3. *5-8 grade* 4. *9-10 grade* 5. *College and above*	
Q-108	*What is your job?*	1. *Farmer* 2. *Merchant* 3. *Government employee*	

		4. *Student* 5. *Daily laborer* 6. *Housewife* 7. *jobless* 8. *other Specify _____*	
Q-109	*How much in average do you think your Monthly Income?(ETB)*	_____	

Section 2: Question to assess clinical factors

No.	*Question*	*Answers*	*Coding*
202	*Diagnosis of patient*	*……..*	
202	*Duration of treatment in a year*	*……..*	
203	*Co morbid psychiatric diagnosis*	*……* *……..*	
204	*Chronic medical illness (physical illness)*	1. *Diabetes* 2. *HTN* 3. *Heart disease* 4. *HIV.* 5. *Tuberculosis* 6. *Asthma* 7. *Cancer* 8. *Others specify…..*	
205	*The family history of primary movement disorder*	1. *Yes* 2. *No*	

Section 3: Questions to assess medication-related factors

301.	*Type of antipsychotic medications*	1. *Typical* 2. *Atypical* 3. *Both*	
302.	*Name of antipsychotictaken, route, dose, and frequency*	*…….*	

303.	*Others psychotropic medications that patient takes*	*……*	
304	*Medication for movement Disorder*	1. *Anticholinergic* 2. *propranolol* 3. *benzodiazepine* 4. *Others specify…*	

Section 4: Question for medication adherence

Mo risky 4-item medication adherence scale		*Yes(0)*	*No(1)*
401	*Do you sometimes forget to take your pills?*		
402	*Do you ever have problems remembering to take your medication?*		
403	*When you feel better, do you sometimes stop taking your medicine?*		
404	*Sometimes if you feel worse when you take your medicine, do you stop taking it?*		

Section5. Question to assess Substance-related and behavioral factors

501	*In your lifetime, have you ever used any of following the substances?*	1. *Yes* 2. *No*
	If your answer is Yes, which substance do you use?	1. *Alcohol (beer, wine, arake, teji, tella)* 2. *Khat* 3. *Tobacco product* 4. *Others specify*
502	*In the past 3 months, have you used any of the following substances?*	1. *Yes* 2. *No*
	If your answer is Yes, which substance do you use?	1. *Alcohol* 2. *Khat* 3. *Tobacco product* 4. *Others specify*

Section6: Questions to assess psychotropic medications-induced movement disorders

Extrapyramidal Symptom Rating Scale (ESRS)

In case of doubt score the **lesser severity**.

I. Questionnaire (Subjective): Parkinsonism, Akathisia, Dystonia, and Dyskinesia.

In this questionnaire, take into account the verbal report of the patient on the following:

1) The duration of the symptom during the day
2) The number of days where the symptom was present during the last week; and,
3) The evaluation of the intensity of the symptom by the patient.

Enquire into the status of each symptom and rate accordingly

		Absent	Mild	Moderate	severe
601.	The impression of slowness or weakness, difficulty in carrying out routine tasks	0	1	2	3
602.	Difficulty walking or with balance	0	1	2	3
603.	Stiffness, stiff posture	0	1	2	3
604.	Restless, nervous, unable to keep still	0	1	2	3
605.	Tremors, shaking	0	1	2	3
606.	Oculogyric crisis, abnormal sustained posture	0	1	2	3
607.	Abnormal involuntary movements(dyskinesia) of the tongue, jaw, lips, face, extremities or trunk	0	1	2	3

II. EXAMINATION: PARKINSONISM AND AKATHISIA
Items based on physical examinations for Parkinsonism

	Score	Explanation
608. Tremor a. Right upper limb b. Left upper limb c. Right lower limb d. Left lower limb e. Head f. Tongue g. Jaw/chin h. lip		0= None 1= Borderline 2= Small amplitude 3= Moderate amplitude 4= Large amplitude
609. Bradykinesia		0: normal 1: global impression of slowness in movements 2: definite slowness in movements 3: very mild difficulty in initiating movements 4: mild to moderate difficulty initiating movements 5: difficulty in starting or stopping any movement, or freezing on initiating a voluntary act 6: rare voluntary movement, almost completely immobile
610. Gait & posture		0: normal 1: mild decrease of pendular arm movement 2: moderate decrease of pendular arm movement, normal steps 3: no pendular arm movement, head flexed, steps more or less normal 4: stiff posture (neck, back) small step (shuffling gait) 5: more marked, festination or freezing on turning 6: triple flexion, barely able to walk

611. Postural stability		0: normal 1: hesitation when pushed but no retropulsion 2: Retropulsion but recovers unaided 3: exaggerated retropulsion without falling 4: absence of a postural response would fall if not caught by the examiner 5: unstable while standing, even without pushing 6: unable to stand without assistance
		0: normal muscle tone 1: very mild, barely perceptible 2: mild (some resistance to passive movements) 3: moderate (definite difficulty to move the limb) 4: moderately severe (moderate resistance but still easy to move limb) 5: severe (marked resistance with definite difficulty to move the limb) 6: extremely severe (limb nearly frozen)

Items based on overall observation during an examination for Parkinsonism

613. Expressive automatic movements (Facial mask/speech)		0: normal 1: very mild decrease in facial expressiveness 2: mild decrease in facial expressiveness 3: rare spontaneous smile, decrease blinking, voice slightly monotonous 4: no spontaneous smile, staring gaze, low monotonous speech, mumbling 5: marked facial mask, unable to frown, slurred speech 6: extremely severe facial mask with unintelligible speech
614. Akathisia		0: absent 1: looks restless, nervous, impatient, uncomfortable 2: needs to move at least one extremity

		3: often needs to move one extremity or to change position 4: moves one extremity almost constantly if sitting, or stamps feet while standing 5: unable to sit down for more than a short period of time 6: moves or walks constantly

III. EXAMINATION: DYSTONIA
Based on examination and observation

615.Acute torsion, and non-acute or chronic or tardive dystonia	**Score**	**Explanation**
a. Right upper limb b. Left upper limb c. Right lower limb d. Left lower limb e. Head f. Tongue g. Eyes h. Jaw/Chin i. Lips j. Trunk		0: absent 1: very mild 2: Mild 3: moderate 4: moderately severe 5: severe 6: extremely severe

IV. EXAMINATION: DYSKINETIC MOVEMENT
Based on examination and observation

	Score	**Explanation**
616. Lingual movements (slow lateral or torsion movement of the tongue)		0: none 1: borderline 2: clearly present, within the oral cavity 3: with an occasional partial protrusion 4: with a complete protrusion
617. Jaw movements (lateral movement, chewing, biting clenching)		0:none: 1: borderline 3: clearly present, small amplitude

		4: moderate amplitude: but without mouth opening 5: large amplitude: with mouth opening
618. Bucco-labial movements (puckering, pouting, Smacking, etc.)		0: none 1: borderline 2: clearly present, small amplitude 3: moderate amplitude, forward movement of lips 4: large amplitude 5: marked, noisy smacking of lips
619. Truncal movements (involuntary rocking, twisting, pelvic gyrations)		0: none 1: borderline 2: clearly present, small amplitude 3: moderate amplitude 4: greater amplitude
620. Upper extremities (choreoathetoid movements only: arms, wrists, hands, fingers)		0: none 1: borderline 2: clearly present, small amplitude, movement of one limb 3: moderate amplitude, movement of one limb or movement of small amplitude involving two limbs 4: greater amplitude, a movement involving two limbs
621. Lower extremities (choreoathetoid movements only: legs, knees, ankles, toes)		0: none 1: borderline 2: clearly present, small amplitude, movement of one limb 3: moderate amplitude, movement of one limb or movement of small amplitude involving two limbs 4: greater amplitude, a movement involving two limbs
622. Other involuntary movements (swallowing, irregular Respiration, frowning, blinking, Grimacing, sighing, etc.)		0: none 1: borderline 2: clearly present, small amplitude 3: moderate amplitude 4: greater amplitude

CLINICAL GLOBAL IMPRESSION OF SEVERITY (CGI-S)

V. CLINICAL GLOBAL IMPRESSION OF SEVERITY OF DYSKINESIA

Considering your clinical experience, how severe is the dyskinesia at this time?

0: absent	3: Mild	6: marked
1: borderline	4: moderate	7: severe
2: very mild	5: moderately severe	8: extremely severe

VI. CLINICAL GLOBAL IMPRESSION OF SEVERITY OF PARKINSONISM

Considering your clinical experience, how severe is the Parkinsonism at this time?

0: absent	3: Mild	6: marked
1: borderline	4: moderate	7: severe
2: very mild	5: moderately severe	8: extremely severe

VII. CLINICAL GLOBAL IMPRESSION OF SEVERITY OF DYSTONIA

Considering your clinical experience, how severe is the dystonia at this time?

0: absent	3: Mild	6: marked
1: borderline	4: moderate	7: severe
2: very mild	5: moderately severe	8: extremely severe

VIII. CLINICAL GLOBAL IMPRESSION OF SEVERITY OF AKATHISIA

Considering your clinical experience, how severe is the akathisia at this time?

0: absent	3: Mild	6: marked
1: borderline	4: moderate	7: severe
2: very mild	5: moderately severe	8: extremely severe

Amharic version consent form

የ ስ ምምማ ት ዉል

እ ኔ አ ቶ_____እ ባ ላ ለ ሁ፡

አ ቶ አ ሳ ፋ ኩ ምሣ በ ጅ ማ ጁ ኒ ቨ ር ሲ ቲ በ ሚ ሰ ጡ ዉያ ሁ ለ ተ ኛ ዲ ግ ሪ ፕ ሮ ግ ራ ም ዋ ስ ነ አ እ ምሮ ህ ክ ም ና ት ም ህ ር ታ ቸ ዉ ን በ ማ ከ ታ ተ ል ላ ይ ይ ገ ኛ ሉ፡ ። ስ ለ ሆ ነ ም ዋ ማ ሚ ቂ ያ ፅ ሁ ፋ ቸ ዉ ን ለ አ እ ምሮ ህ ማ ም ዋ ሚ ሰ ጡ ማ ሀ ኒ ቶ ች የ ሚ ያ ስ ከ ት ሉ የ እ ን ቅ ስ ቃ ሴ ማ ዛ ባ ት ም ን ያ ክ ል እ ን ደ ሆ ነ ና እ ን ዲ ሁ ም ት ያ ያ ዝ ነ ት ያ ላ ቸ ዉ ን ገ ሮ ች በ ሜ ል ር ዕ ስ ዙ ሪ ያ ጥ ና ት እ ያ ካ ሄ ዱ ይ ገ ኛ ሉ፡ ። ከ ዚ ህ በ ፊ ት የ ተ ሰ ሩ ጥ ና ቶ ች እ ን ደ ሚ ያ ማ ላ ክ ቱ ት ለ አ እ ምሮ ህ ማ ም ዋ ሚ ሰ ጡ ማ ሀ ኒ ቶ ች የ ሚ ያ ስ ከ ት ሉ የ እ ን ቅ ስ ቃ ሴ ማ ዛ ባ ት እ ን ደ ሚ ዛ ያ ሳ ያ ል፡ ። ይ ህ ደ ግ ሞ ታ ካ ሚ ዎ ች ማ ዴ ሀ ኒ ታ ቸ ዉ ን እ ን ዲ ያ ቆ ር ጠ ም ን ያ ት ሊ ሆ ን ይ ች ላ ል ፤ ህ መ ም ቹ ን ያ ባ ብ ሳ ል ፤ እ ን ዲ ሁ ም ም ር ታ ማ ታ ቸ ዉ ን እ ን ዲ ቀ ን ስ ያ ደ ር ጋ ል፡ ። ይ ህ ጥ ና ት ወ ደ ፊ ት ለ አ ዕ ም ሮ ህ መ ሞ ቸ የ ሚ ሰ ጡ ማ ሀ ኒ ቶ ች የ ሚ ያ ስ ከ ት ሉ የ እ ን ቅ ስ ቃ ሴ ማ ዛ ባ ት ጥ ን ቃ ቄ እ ን ዲ ደ ረ ግ ና ህ ክ ም ና ዉ ን ያ ጠ ና ክ ራ ል ተ ብ ሎ ይ ታ ሰ ባ ል፡ ። በ ዚ ህ ም ር ም ር ዉ ስ ጥ ያ ለ ዎ ት ተ ሳ ት ፎ በ ፈ ቃ ደ ኝ ነ ት ላ ይ የ ተ መ ሰ ረ ተ ነ ው ። ይ ህ ደ ብ ዳ ቤ በ ዚ ህ ጥ ና ት ላ ይ ለ ማ ካ ፈ ል ዎ ፍ ቃ ድ ለ ማ ከ የ ቅ ያ ገ ለ ግ ላ ል፡ ። ለ ማ ሳ ተ ፍ ፈ ቃ ደ ኛ ካ ል ሆ ኑ በ እ ር ስ ዎ ላ ይ ም ን ም አ ይ ነ ት ች ግ ሪ አ ይ ደ ሪ ስ ባ ች ዉ ም ። በ ማ ሳ ተ ፍ ዎ የ ሚ ሰ ጡ ት ማ ን ኛ ዉ ም ሚ ጃ በ ሚ ጥ ር ይ ያ ዛ ል፡ ። የ እ ር ስ ዎ ን ስ ም ወ ይ ም ስ ል ክ ቁ ጥ ር ማ ስ ጠ ት አ ይ ጠ በ ቅ ብ ዎ ት ም ። ቃ ለ-ማ ጪ ይ ቁ ቢ በ ዛ 30 ደ ቂ ቃ ይ ወ ስ ዳ ል፡ ።

ለ ማ ሳ ተ ፍ ፈ ቃ ደ ኛ ከ ሆ ኑ ሚ ዳ ት ና የ ስ ምምማ ት ቅ ፅ ላ ይ ሜ ፈ ረ ም አ ለ ብ ዎ ት፡ ።

ጥ ና ቱ ን የ ሚ ያ ካ ሄ ድ ስ ም ……. ስ ል ክ +251 922392567

በ ቃ ለ-ማ ጪ ይ ቁ ላ ይ ለ ማ ሳ ተ ፍ ፈ ቃ ደ ኛ ነ ዎ? አ ዎ ☐ አ ይ ደ ለ ሁ ም ☐

ፊ ር ማ---------- ቀ ን ----------

እ ር ስ ዎ የ ዚ ህ ጥ ና ት ተ ሳ ታ ፊ በ ሚ ሆ ነ ዎ በ ጣ ም እ ና ማ ስ ግ ና ለ ን፡ ።

Amharic version assent form

እድሜያቸዉከ18አመትበታችለሆኑተሳታፊዎች

የሰነዱንይዘትየተረዳሁሲሆንየምርምርፕሮጀክቱንምአላማዝረድችያለሁ፡ ፡ በዚህምርምርፕሮጄክትላይ እንዲሳተፍፍቃደኛሆኛለሁ፡ ፡ በማንኛውምሳአትምክጥናቱእራሴንለማገለልመብትእንዳለኝአዉቃለሁ፡ ፡

የወላጅ (ህጋዊአሳዳጊ) ፊርማ……ቀን .....

የሚጃሰብሳቢስምና ፊርማ……..ቀን ……

የሱፐርቫይዘርስምና ፊርማ……ቀን ……..

Amharic version questionnaire

የአሚኛማከይቅ

01. የማከይቁተሳታፊዎችማላያቁጥር ……

ክፍል-1-የማህበራዊአኗኗርሚጃዎች

ተ.ቁ	ጥያቄዎች	አማራጮችልሶች
101	ዕድሜዎስንትነዉ?	_____በአመት
102	ጾታ	1.ሴት 2.ወንድ
103	የጋብቻሁኔታ	1.ያላገባ 2.ያገባ 3.የፈታ/የፈታች 4.የሞተበት/የሞተባት
104	የምንሀየማመንተከታይኖዎት?	1. ማህሊም 2.አርቶዶክስ 3.ፕሮቴስታንት 4.ካቶሊክ 5.ሌላከሆነ ይጥቀሱ
105	ብሄርዎትምንድነዉ?	1.አሮሞ 2.አማራ 3.ትግሬ 4.ጉራጌ 5.ሌላከሆነ ይጥቀሱ
106	የሞሪያቦታ	1.ገጠር 2.ከተማ

107	የ ትምህ ር ትደ ረ ጃ	1.ማን በ ብና ማጉፍ የ ሚይችል 2.የ መጃ ሚ ያ ደ ረ ጃ 3.ሁለ ተ ኛ ደ ረ ጃ 4.ኮ ሌጅድግሪ ና ከ ዚ ያ በ ላ ይ
108	ምን ድን ዉ ያ ሚሰ ሩ ት?	1.ተ ሚ 2.ገ በ ሬ 3.ተ ቀ ጥሮ የ ሚሰ ራ 4.የ ራ ሱስ ራ 5. የ ቀ ን ሰ ራ ተ ኛ 6. የ ቤ ት እ ማ ቤ ት 7.ስ ራ የ ሌ ለ ዉ 7.ሌ ላ ካ ለ ይ ግ ለ ጡ
109.	በአ ማ ካ ኝ በ ወ ር ስ ን ት ገ ቢ ያ ገ ኛ ሉ?	

ክ ፍ ል 2፡ ህ ክ ም ና ን የ ሚ ሞ ላ ከ ቱ ሚ ጃ ዎ ች

ተ.ቁ	ጥ ያ ቄ	አ ሚ ራ ጭ ሜ ል ሶ ች
201	የ ህ ሙ ማ ይ ነ ት	……
202	ህ ሙ ማ ገ ር ሽ ቶ ቦ ዎ ት ያ ዉ ቃ ል	አ ዎ የ ለ ም ስ ን ት ግ ዜ …….
203	ህ ክ ም ና ከ ጀ ሙ ስ ን ት ግ ዜ ሆ ነ	……
204	ሌ ላ የ ታ ወ ቀ የ አ እ ምሮ ህ ሙ ማ ካ ለ ይ ጥ ቀ ሱ	……

205	የ ታወቀአ ካላ ዊህ ሞም	ስ ኪር በ ሽ ታ ደ ምብዛ ት የ ል ብህ ሞም ኤ.አ ይ ቪ.ኤ ድስ ካ ን ሰ ር ሌላ ካ ለ ይጥቀ ሱ.....
206	በ ቤተ ሰ ብዉስ ጥየ እ ን ቅስ ቃሴ ማዛ ባ ትያ ለ በ ትኣ ለ ?	አ ዎ የ ለ ም

ክ ፍል 3፡ ከ ሞድሃ ኒ ት ጋ ር ተዛ ማጅ የ ሆኑ ሚ ጃ ዎች (ከ ካ ር ድየ ማ ሟ ሉ)

ተ.ቁ	ጥያ ቄ	አ ማራጭ ሜል ሶ ች	ኮ ድ
301	የ አ ን ቲ ሳ ይኮ ቲ ክ ሞድሃ ኒ ት ስ ም፡ ማ ከን ና ስ ን ትግ ዜ በ ቀ ን እ ን ደ ሚ ዉሰ ድ ይ ጥቀ ሱ	.....	
302	ሌ ሎ ች የ ሚ ዉስ ዱ ት ን የ ሞድሃ ኒ ት አ ይነ ት ይ ግ ለ ፁ	.....	
303	ለ እ ን ቅስ ቃሴ ማዛ ባ ት የ ሚ ሰ ጡ ሞድሃ ኒ ት ወስ ደ ዉያ ዉቃ ሉ?	አ ዎ የ ለ ም አ ይነ ቱ ን ይ ግ ለ ፁ.....	

ክ ፍል 4፡ በ ሀ ኪ ምት ዛ ዝ ማ ከ ረ ት የ ሞድሃ ኒ ት አ ጠቃ ቀ ም ማ ላ ክ ያ ሚ ስ ኪ ባ ለ አ ራ ት ማ ከ ይ ቅ

401.	ሞድሃ ኒ ት ን ሚ ዉሰ ድ ረ ስ ተ ዉያ ዉቃ ሉ?	አ ዎ አ ላ ዉቅ ም	
402.	አ ን ዳ ን ድ ግ ዜ ሞድሃ ኒ ት ለ ሚ ዉሰ ድ ችል ተ ኛ ይ ሆ ና ሉ?	አ ዎ አ ላ ዉቅ ም	
403.	በ ሚ ሸ ሎ ት ወቅ ት አ ን ዳ ን ድ ግ ዜ ሞድሃ ኒ ት ሚ ዉሰ ድ ያ ቆ ማ ሉ?	አ ዎ አ ላ ዉቅ ም	
404.	ሞድሀ ኒ ት በ ሚ ዉስ ዱ በ ት ግ ዜ ካ ሚ ሞ ት ሞድሃ ኒ ት ሚ ዉሰ ድ ያ ቆ ማ ሉ	አ ዎ አ ላ ዉቅ ም	

ክ ፍል 5፡ እ ፅ ማ ከ ቀ ምን በ ተ ማ ላ ከ ተ

501.	በ ህ ይ ወ ት ዎ ከዚህበ ታ ች ከ ተ ዘ ረ ዘ ሩ ት የ ት ኞ ቹ ን ተ ጠቅ መዋ ል ? /በ ህ ክ ምና ያ ል ታ ዘ ዙ ብ ቻ /	የ ቶ ባ ኮ ዉ ዉ ጤ ቶ ች (ሲ ጋ ራ እ ና የ መ ሳ ሰ ሉ ት ን) አ ል ኮ ል መ ጠ ጦ ች /ቢ ራ ፤ ወ ይ ን ፤ ጠ ላ ፤ ዐ ረ ቄ) ጫ ት ሌ ላ ካ ለ ይ ጥ ቀ ሱ
502.	ባ ለ ፉ ት ሶ ስ ት ወ ራ ት ከዚህበ ታ ች ከ ተ ዘ ረ ዘ ሩ ት የ ት ኞ ቹ ን ተ ጠቅ መዋ ል ?/በ ህ ክ ምና ያ ል ታ ዘ ዙ ብ ቻ /	የ ቶ ባ ኮ ዉ ጤ ቶ ች (ሲ ጋ ራ እ ና የ መ ሳ ሰ ሉ ት ን አ ል ኮ ል መ ጠ ጦ ች /ቢ ራ ፤ ወ ይ ን ፤ ጠ ላ ፤ ዐ ረ ቄ) ጫ ት ሌ ላ ካ ለ ይ ጥ ቀ ሱ .....

ክ ፍ ል 6፡ የ እ ን ቅ ስ ቃ ሴ ማ ዛ ባ ት የ ሚ ም ላ ከ ቱ ሚ ጃ ዎ ች

በ ታ ም ሟ ቿ የ ሚ ም ላ ሱ የ ፓ ር ኪ ን ሰ ኒ ዝ ም ፡ አ ካ ቴ ዥ ያ ፣ ዲ ስ ቶ ኒ ያ እ ና ታ ር ዲ ቭ ዲ ስ ካ ኔ ዥ ያ ማ ከ የ ቅ

ከ ዚ ህ በ ታ ች ባ ለ ዉ ማ ኪ ይ ቅ በ ታ ም ሟ ቿ የ ሚ ም ላ ሱ ሲ ሆ ኑ የ ሚ ከ ተ ሊ ት ን ማ ን ዘ ብ ያ ስ ፈ ል ጋ ል

ም ል ክ ቶ ቹ በ ቀ ን ለ ም ን ያ ህ ል ግ ዜ እ ን ደ ሚ ቆ ይ

ም ል ክ ቶ ቹ በ ሳ ምን ት ዉ ስ ጥ ለ ም ን ያ ህ ል ቀ ን እ ን ደ ሚ ቆ ዩ

ታ ም ሟ ቿ ለ ም ል ክ ቶ ቹ የ ሚ ጎ ጠ ዉ ክ ብ ደ ት

የ ህ ሙ ማ ም ል ክ ት ክ ብ ደ ት የ ሚ ሊ ካ ዉ በ ባ ለ ፈ ዉ ሰ ባ ት ቀ ና ት ዉ ስ ጥ የ ነ በ ረ ዉ ን ይ ሆ ና ል

		የ ለ ም	አ ነ ስ ተ ኛ	ጫ ከ ለ ኛ	ከ ፍ ተ ኛ
601	ዝ ግ ተ ኝ ነ ት፣ ድ ካ ም፡ የ እ ለ ት ተ ለ ት ተ ግ ባ ር ማ ከ ና ወ ን አ ለ ማ ቻ ል				
602.	ሚ ራ ሚ ድ አ ለ ማ ቻ ል ወ ይ ም ባ ድ ጋ ፍ ማ ቀ ሳ ቀ ስ				
603.	ግ ት ር ነ ት;፣ ግ ት ር ያ ለ አ ቾ ም				
604.	ጫ ቁ ነ ጥ ነ ጥ፣ ሜ ጨ ሄ ቅ;፣ ሚ ረ ፍ አ ለ ማ ቻ ል				
605.	ማ ቀ ጥ ቀ ጥ፣ ማ ወ ዘ ወ ዝ				
606.	የ አ ይ ን ወ ደ ተ ለ ያ የ አ ቅ ጣ ጭ ሟ ር ፣ ት ክ ክ ል ያ ል ሆ ነ አ ቾ ም				
607.	ት ክ ክ ል ያ ል ሆ ነ ና ከ ቁ ጥ ጥ ር ዉ ጪ የ ሆ ነ የ ም ክ ል ፣ አ ገ ጭ ፣ ከ ን ፈ ር ፣ ፊ ት ፣ እ ጅ ና እ ግ ር ላ ይ የ ሚ ታ ይ እ ን ቅ ስ ቃ ሴ				

Declaration

I, the undersigned, MSc student in integrated clinical and community mental health declares that this thesis is my original work in partial fulfillment of the requirement for Master of Science degree in integrated clinical and community mental health.

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Date of submission ———————————————

This research thesis has been submitted for examination with my/our approval as University advisor(s)

Advisor(s) **Signature**

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