PREVALENCE AND RISK FACTORS FOR METABOLIC AND MOVEMENT DISORDERS IN PATIENTS WITH BIPOLAR DISORDER IN KENYATTA NATIONAL HOSPITAL AND MATHARE REFERRAL HOSPITAL

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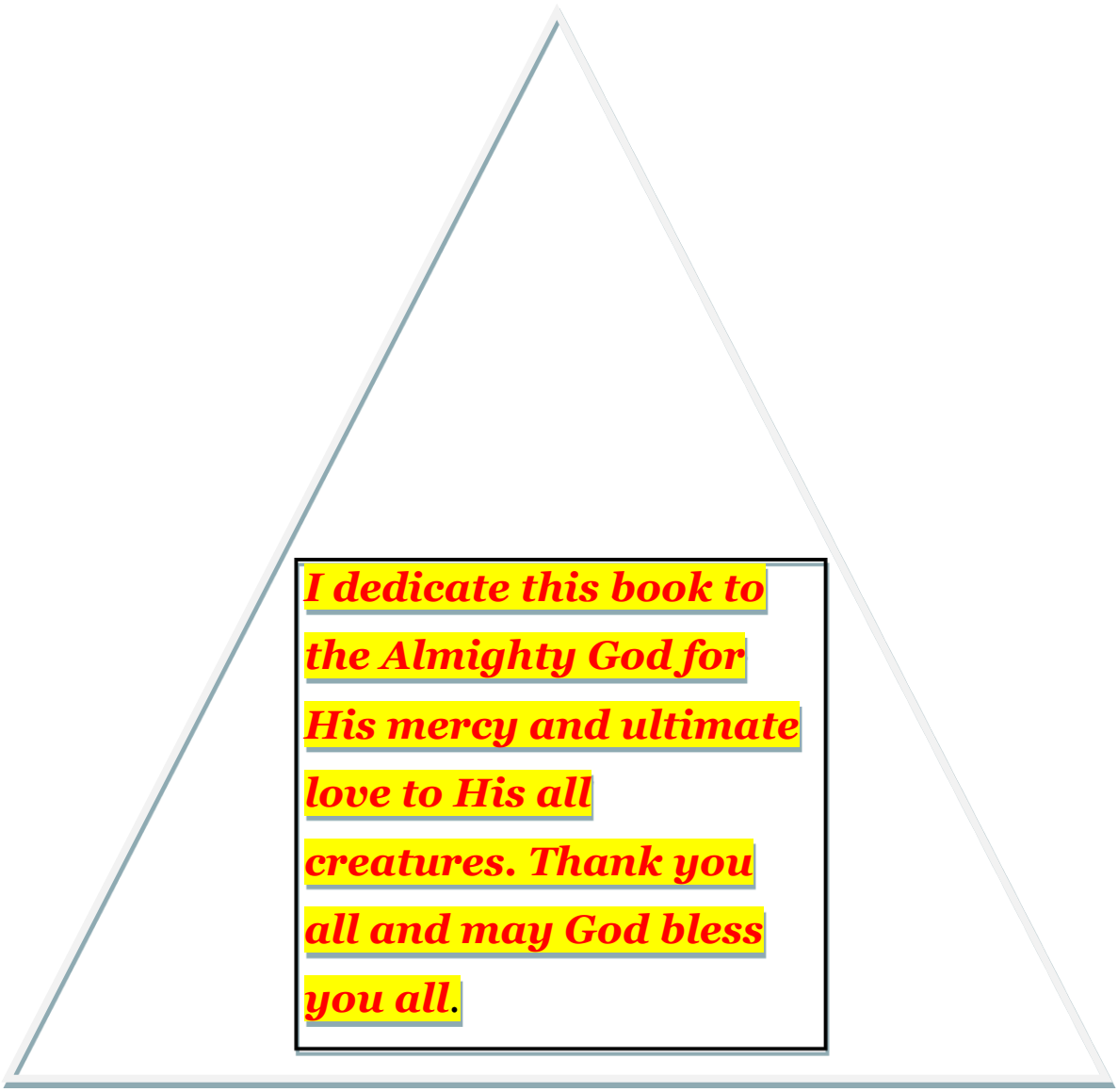
DEDICATION


I dedicate this book to the Almighty God for His mercy and ultimate love to His all creatures. Thank you all and may God bless you all.

ABSTRACT

Background:

Bipolar disorder is one of the most widely investigated psychiatric disorders. Only few patients get minimally adequate treatment, due to social stigma, lack of funds and education. The Pharmacological treatment of bipolar syndromes causes an increase in weight, lipid and glucose metabolism alterations. This increases the risk of cardiovascular syndromes leading to increased mortality and shortens the life expectancy. Movement disorders are also most common among people who take antidepressants, neuroleptics, antipsychotics and mood stabilizer drugs.

Study objective: The purpose of this study is to measure the prevalence and risk factors for movement and metabolic disorders among patients on treatment for bipolar disorders at Kenyatta National Hospital and at Mathari Referral Hospital.

Methods: The study was a hospital based ambi-directional cross sectional study involving 189 out and in-patients on treatment for bipolar disorders in Kenyatta National Hospital and at Mathari Referral Hospital. All data was collected anonymously and kept confidentially. Descriptive and inferential data analyses have been used to summarize data. Raw data was collected using study tools and entered into a password protected Epi -Info version 7(2007 to 2010) database then exported to STATA version 14 for analysis. The logistic regression used to determine the risk factors.

Results: The results found 189 patients with bipolar disorders, males were 107 (57.7%) and females were 82 (42.3%). The prevalence for metabolic disorders was 65.6% included hypertension 83 (43.9%); diabetes 53 (28.03%); obesity 9 (4.8%); overweight 19 (10.1%) and underweight 59.8% (113). The prevalence of movement disorders was: parkinsonism 102 (54%), masked faces 101 (53.4%); reduced arm swing 62 (32.8%); slowed initiation of activities 140 (74.1%); speech 131 (69.3%); abnormal posture 89 (47.1%); rigidity of neck 92 (48. 7%); tremor at rest 145 (76. 7%); tremor on action 105 (55%); focal perioral tremor 35 (18.5%); abnormal gait 74 (39.2%); and hypersalivation 130 (68.8%);

The risk factors for movement disorders in Kenyatta National Hospital and Mathari Referral Hospital were as follows: residence; bromazepam; zolpiderm, nifedipine and residence.

Conclusion:

There was a high prevalence for metabolic and movement disorders in bipolar patients attending and admitted in Kenyatta National Hospital and Mathari Referral Hospital. However there was an association between the metabolic, movement disorders and bipolar disorder.

ABBREVIATIONS AND ACRONYMS LIST.

ADA	American Diabetes Association
bTSH	Blood levels of thyroid stimulating hormone
DIMD	Drug induced movement disorder
EPS	Extra Pyramidal Side Effects
GPs	General practitioners
GCP	Good Clinical Practice
HR	Hazard Ratio
HDL	High density Lipoprotein
INCID	Incidence
KNH	Kenyatta National Hospital
LDL	Low density Lipoprotein
MRH	Mathari Referral Hospital
MFPG	Multifamily Psychoeducation Groups
OGC	Oculogyric crisis
PSP	Advanced Supranuclear Palsy
SCID	Structured Clinical Interview for Diagnostic and Statistics Manual
SSRIS	Selective serotonin reuptake inhibitors
UFMG	*Universidad Federal de Minas Gerais*
UMSARS	Unified Multiple System Degenerate Assessment Measure
UON	University of Nairobi
USCRS	*Universidad Federal Minas Gerais Sydenham's Chorea Assessment*

OPERATION DEFINITION:

Acute Parkinsonism is an acute neuroleptic induced movement disorders or side effect of dopamine blocking agents. Also are an immediately clinical symptoms characterized by slow movement, muscle inflexibility, trembling of extremities while resting, missing balance on standing.

Akathisia is a movement disorder characterized by feeling of inner restlessness and a compelling need to be in constant motion, as well as by actions such as rocking while standing or sitting, lifting the feet as if matching on the spot and crossing and uncrossing the legs while sitting.

Akinesia is an absence of movement. It is an opposite of hyperkinetic movement and progressive of supernuclear palsy. Akinesia includes bradykinesia and rigidity which has no movement and is crucially and basically progress to fatigue. Other features are dull movements in fingers or foot tapping and gait icing.

Catatonia is a life-threatening group complaint characterized by lethargy, motionlessness, mutism, gesture, emptiness and nervousness.

Dystonia is an abnormal distinctive attitudes and movements, produced by slow sustained muscle contraction, which misrepresent limbs, trunk neck, face or mouth. It is a twisting motion or abnormal posture (combination) that may manifest as acute or late involuntary movements, facial grimacing, cervical dystonia, oculogyric crisis, rhythmic tongue protrusion, jaw opening or closing, spasmodic dysphonia and rarely, stridor and dyspnea.

Tardive dyskinesia is the unintentional movement of the extremities, tongue, jaws, face and chest as a result of long term antipsychotics treatment.

CHAPTER ONE: INTRODUCTION

1.1 Background

Bipolar disorder, also called manic depression, is a complicated and troublesome psychiatric illness which includes maniac and depressive symptoms. Alteration in mood is a central feature of an affective disorder characterized by low mood or depression; and sometimes elevated mood known as mania (Walker *et al*., 2007).

Bipolar disorders occur when a patient develops one or more severe episodes of mood disorders including mania. There are several types of this condition. Bipolar I, involving periods of severe mood episodes is characterized by overexcited or else varied incidents. Bipolar II, a milder form of mood elevation, is characterized by sad or low moods occurrences.

These mood disorders and other symptoms if not treated can lead to suicide, destruction of valued items, violence and hazardous situations and strained relationships with neighbors, relatives and friends.

Apart from taking medicines, precaution attention must be paid to any changes in the patients who consuming drugs; otherwise adverse effects may occur like metabolic and movement disorders. These disorders may be caused by use of antipsychotics, antidepressants and mood stabilizer drugs (Mclntyres *et al*., 2012).

Optimization of therapy of mentally ill patients must be achieved and rationalized. Proper diagnosis must be done and cooperative teamwork must be established in patient management. Medicines to counteract the adverse effects must be available at affordable costs, because most of the patients are totally financially dependent on others' income.

The risk factors for bipolar disorders are genetic predisposition; biochemical and neurotransmitter changes; endocrine disorders; environmental factors; physical illness and side effects of drugs. Viral illness and other infections can also cause bipolar disorders (Walker *et al*., 2007).

1.2 Statement of the Research Problem

Bipolar disorder is a serious psychiatric condition with alternating manic and depressive states. It is characterized by changes in mood, sleep and eating patterns, ability to think well and energy levels. This affects the progression of patients, their ability to perform their daily activities as well as their relationship with their colleagues, friends and family members. The disorder can cause harm to themselves or others (Mclntyre *et al*., 2012; Fountoulakis *et al*., 2017). There was no previous study done in this patient population.

Drugs used for the management of bipolar disorder like antidepressants, mood stabilizers and antipsychotic are known to have side effects that increase appetite and induce obesity hence the high prevalence of prediabetes and other are metabolic and movement disorders in these patients (Gradidge *et al*., 2016; Bai *et al*., 2016; Burke, 2017).

Due to the large numbers of patients seen in Kenyan hospitals, many psychiatrists may not pay attention to occurrence to the metabolic and movement disorders. Therefore, patients with bipolar diseases may suffer from these drug induced complications and fail to receive appropriate early medical interventions. Patients with bipolar disease particularly are at risk because they are put on neuroleptics or antidepressants and mood stabilizer with the multiple drugs increasing the risk of the noted adverse events.

Though the studies on the prevalence of movement disorders have been conducted in Kenya, there still remains a gap with regard to their link to specifically bipolar disorder management. This study therefore, seeks to measure the prevalence and risk factors for metabolic and movement disorders. The finding of this study may draw the attention of health care personnel on the need to optimally diagnose and manage these conditions in patients with bipolar disorder.

1.3. Study Justification and Rationale

Metabolic disorders tend to have a high prevalence in patients taking antipsychotics due to medication induced increase in appetite which leading to obesity and subsequently hyperlipidemia and hypertension (Gradidge *et al*., 2016; Bai *et al*., 2016; Burke, 2017). In additions medications inhibit the activity of dopamine in the basal ganglia, mesolimbic

system and substantial nigra. This leads to a range of movement disorders. These are not routinely diagnosed and managed in a typical psychiatric clinic.

There is no study that has been conducted on the prevalence of metabolic and movement disorders in patients with bipolar disorder in Kenya. The study filled the knowledge gap that needs attention, due to large number of bipolar patients.

Kenyatta National Hospital and Mathari Referral Hospital attended and managed bipolar patients as either inpatients or outpatients. Finding on prevalence and risk factors for metabolic disorders such as diabetes, obesity and hypertension, and for movement disorders were making a case for more integrative approach management of patients with bipolar disorders; that entails collaboration with other specialists such as neurologists, endocrinologists and general physicians in the management of psychiatric illness. This will potentially reduce morbidity and mortality among patients on treatment for bipolar disorders.

1.4 Purpose of the study

The primary aim of this study is to find out about the relationship between metabolic and movement disorders and medicines use against the bipolar disorders. The study was additionally endeavored to determine the prevalence of risk factors on the bipolar disorders management for patients at Kenyatta National Hospital and Mathari Referral Hospital.

1.5 Research Questions

1. What are the treatment modalities for bipolar disorders at Kenyatta National Hospital and Mathari Referral Hospital?
2. What is the prevalence of movement and metabolic disorders in patients with bipolar diseases at Kenyatta National Hospital and Mathari Referral Hospital?
3. What are the risk factors for the movement disorder in patients with bipolar disorder's management?
4. What are the risk factors for the metabolic disorder in patients with bipolar disorder's management?

1.6 Objectives

1.6.1 Main Objective

To measure prevalence and the risk factors for movement and metabolic disorders in patients on treatment for bipolar disorders at Kenyatta National Hospital and Mathari Referral Hospital.

1.6.2 Specific Objectives

The specific objectives are to:

1. Determine prevalence of movement disorder in patients with bipolar diseases at Kenyatta National Hospital and Mathari Referral Hospital.
2. Determine the prevalence of metabolic (pre-diabetes, diabetes and obesity) disorder in in-outpatients. On treatment for bipolar disorders at KNH and Mathari Referral Hospital.
3. Determine risk factors for movement disorder in outpatients on treatment for bipolar disorders at Kenyatta National Hospital and Mathari Referral Hospital outpatients and inpatients.
4. Determine risk factors for metabolic disorder (pre-diabetes, diabetes and obesity) amongst in-outpatients on treatment for bipolar disorder at Kenyatta National Hospital and Mathari Referral Hospital.

1.8 Conceptual Framework

Bipolar disorders' management can cause metabolic and movement disorders. This bipolar management can be classified into two groups. Thus medicines for mania which lead antagonize the dopamine and cause the movement disorders. The other one is the medications for major depression which is reciprocally susceptibility to diabetes or hypertension. The rest of bipolar treatments lead to increased appetite, as result eating disorders. This also can cause obesity, diabetes or hypertension. See the conceptual framework in figure 1.

Conceptual Framework figure

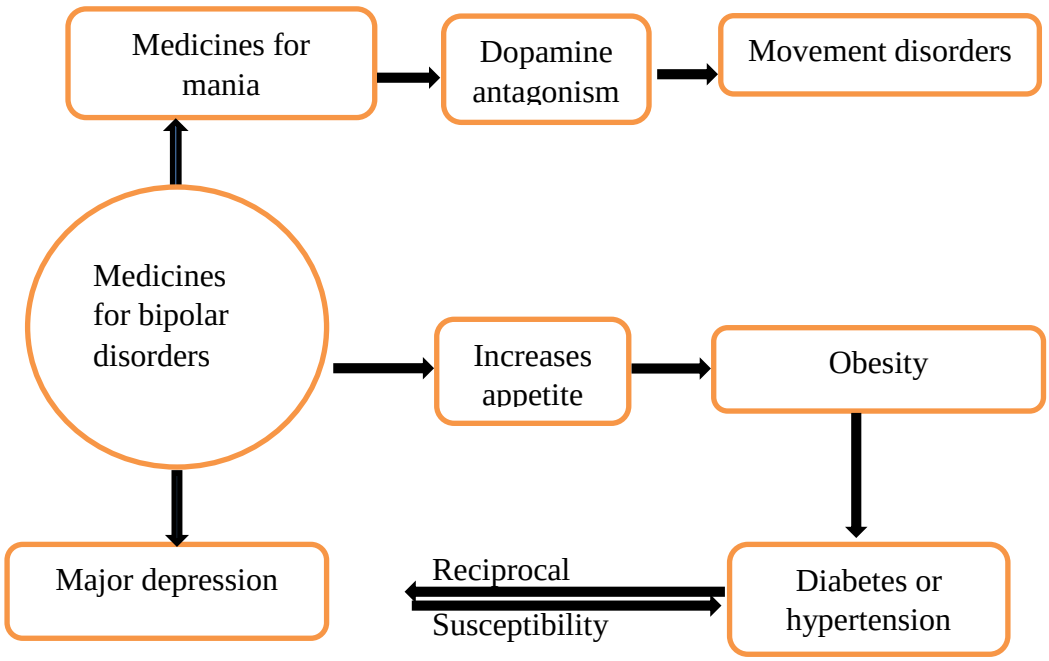


Figure1. The conceptual Framework for movement and metabolic disorders in patients with bipolar disorder management

CHAPTER TWO: LITERATURE REVIEW

2.1 TYPES OF BIPOLAR DISORDERS

Bipolar disorder is a chronic disease that needs lifetime management (Muneer, 2016). The disorder is usually managed by professionals like psychologists and psychiatrists. Management comprises a mixture of treatments which includes supportive management and medicines.

Bipolar disorder comprises sudden changes in attitude from either depression or mania. Mania is when a patient is overexcited and has many ideas. In addition, the patient is easily irritated and talks fast and for long periods of time. Also the patient may practice risky behavior, such as spending excessive amounts of money or engaging in unsafe sex (Merikangas *et al.,* 2012).

Depression is a low mood where the patient experiences sadness, unhappiness, despair, misery and hopelessness. There is chronic depression in bipolar disorder (ElMallakh *et al*., 2006). When symptoms are controlled, the medication should continue for a life time for prevention and reducing relapsing events of either mania or depression.

The Diagnostic and Statistical Manual of Mental Disorders 5 enumerated six types of bipolar disorders as: bipolar I and bipolar II, bipolar and related disorders as a result of another medical condition, substance or medication induced bipolar and related disorder, cyclothymic as well as unspecified bipolar and related disorders (Kochman, 2005; Tohen *et al*., 2014; Fountoulakis *et al*., 2017).

Bipolar I disorder refers to illness where one has one manic episode in the life of the patient (Suppes *et al*., 2017; Bhandari, 2017; Purse *et al*., 2017).

Bipolar II disorder is when the mood cycles between high and low frequently but the elevated moods never reach complete mania. The less-intense elevated mood disorder is termed hypomania. Patients with bipolar II live normal typical life (Benazzi, 2007; Fountoulakis *et al*., 2017).

Cyclothymic disorder is characterized by a very short period between hypomania and depression such that it is often difficult to determine if patient is in a manic state or is in a depressive state (Moore *et al*., 2004; Kochman, 2005).

Substance or medication induced bipolar and related disorders are drug-induced depression or mania. It occurs in individuals who have a high risk for bipolar disorders or dysthymia. Among the main risk factors for such patients is a family or personal history of mood or substance disorder (Chandragir *et al*., 2016).

Bipolar disorder and other related disorders which may result from another medical condition, applies only when there is a clinical significant presentations of symptoms. Such a condition may not meet the full criteria of any disorder (Regier *et al*., 2017).

Unspecified bipolar and related disorder is the diagnosis used when the clinician not suggest the causes, also not encountered exactly the types of bipolar. It has incomplete diagnosis (Moore *et al*., 2001; Tohen *et al*., 2014).

2.2 PREVALENCE OF BIPOLAR SPECTRUM DISORDERS

Bipolar syndromes affects about 60 million people worldwide (NCCMH, 2006; Leboyer *et al*., 2010). About 2.4% of the global population has been diagnosed to have suffered at some point in their life. The highest prevalence is in United States with the prevalence rate at 4.4%. India has the lowest prevalence at 0.1%, followed by Japan at 0.7% and Columbia at 2.6% (Leboyer *et al*., 2010; Gardner 2011). One year occurrence of bipolar-I disorder is 0.4%, bipolar II disorder is 0.3%, sub threshold bipolar disorder is 0.8%, and bipolar disorder spectrum is 1.5% (WHO, 2012).

In 2005, a survey was conducted in Ethiopia that involved 295 individuals. The prevalence of the bipolar I disorder in men was 0.6% while that of women was 0.3% (Negash *et al*., 2005). Bipolar I disorder affected mainly people aged 29.5 years, and there was no sex difference in its distribution.

The mean age for the first illness is 22.0 years. For the male gender it is estimated to be 22.3 years while for female it is estimated to be 21.2 years. In addition the mean age where the depressive phase sets in is 23.4 years (24.1 for men and 22.5 for women) (Fountoulakis *et al*., 2016).

A study had shown that the onset of the manic and the depressive disorder phases exhibits no significant sex difference. Further with regard to the prevalence of the bipolar disorders it is observed that for the 22.7% of the identified cases of bipolar I illness, the onset is mainly characterized by a depressive episode while for 77.3% identified cases, the onset is mainly characterized by a manic episode.

A study established that 8.1% of the males and 5.4% of the females attempted to commit suicide (Negash *et al*., 2005).

The lifetime prevalence estimate is 0.1 and 1.83% in Nigeria and Ethiopia respectively. About 60 % of patients with bipolar disorder have at- least one comorbidity (Esan *et al*., 2016; Fountoulakis *et al*., 2016).

2.2.1 Risk factors for bipolar disorder

Several risk factors have been shown to contribute to genesis of the bipolar disorders have been implicated in the disease. A variety of genes are responsible for coding the serotonin transporter protein. Twin and adoption studies indicate genetic vulnerability and familial inheritance as the etiology of bipolar disorder (Nambi, 2004; Craddock *et al*., 2006; Escamilla *et al.,* 2008).

Environmental factors can trigger mania or depression (Aldinger *et al*., 2017). In addition other risk factors linked to bipolar disease are stressful life events, low social support and self-esteem (Belova *et al*., 2014; Muneer, 2015).

Biochemical factors are involved when some parts of brain have a shortage of neurotransmitter amines (Walter *et al*., 2011).

Endocrine factors such as hormones from the hypothalamic pituitary adrenal axis and the hypothalamic pituitary thyroid axis can cause development of affective disorders (Barden, 2004; Muneer, 2015).

Some drugs may trigger mania or depression due to their side effects. Such drugs include analgesics, antidepressants, antihypertensive and anticonvulsants. Other side effects may be caused by withdrawal of some dugs like opiates, amphetamine and benzodiazepine. It is concluded that antipsychotics such as haloperidol can lead to depressive condition due to dopamine 2 receptors disturbances. Drugs like benzodiazepines resulting into manic or depressive events. Also drugs like benzodiazepine, antiparkinsonism medicines, steroids, oral contraceptives and drug abuse can cause addiction, dependence and bipolar disorders (Diaper, 2014).

Additionally, central nervous system disorders like brain tumour may lead to cognition dysfunction and reduced memory capacity as well as dementia in the late stage. Stroke due to deficiency of oxygen nutrients to brain and neurotransmitters defect can cause bipolar disorders as well as subdural hematoma and neurohormonal dysfunction.

Others causes include multiple sclerosis and head injury which can lead to mental disturbances as well as neuroleptic events (Shahripour, 2014).

Physical illness like carcinoma can lead to depression and confusion in the patient if not well counseled or does not understand the advices given. Diabetes, especially at late stage, with a lot of complications such as limb amputations may also lead to mental disorders (Meyer *et al*., 2012).

Nutritional deficiency of essential amino acids such as L Tryptophan and fatty acids may cause metabolic disorders like hyperlipidemia as it results of poor transmission of neurotransmitters. Since in homeostasis amino acid play a vital role, many systems will be disturbed, mainly the brain part that can lead to either mania or depression (Garbazza *et al*., 2016; Kelly *et al*., 2017).

2.2.2 Etiology of bipolar disorders or theories of bipolar disorders

Membrane and cation theories involving irregular neuronal calcium, sodium movement and homeostasis that can cause neurotransmitters dysregulation are implicated in the etiology of bipolar disorders (Zapata *et al*., 2003; Powell *et al*., 2016).

Neurotransmitter or neuroendocrine or neurohormonal theories state that dysregulation between excitatory and inhibitory neurotransmitters leads to bipolar disorders (Belousov *et al*., 2001; Muneer, 2017).

Cholinergic hypothesis states that acetylcholine deficiency causes imbalance in cholinergic adrenergic activity. Thus leads to mania while increased central acetylcholine levels lead to depression. Noradrenaline, adrenaline and dopamine imbalances cause the manic or depressive events (Belousov *et al*., 2001; Enkhuizen *et al* 2015).

Secondary messenger system dysregulation entails abnormal G protein functioning, dysregulated adenyl cyclase activity and phosphoinositide responses can cause either mania or depressive episodes. Also other secondary messenger like Na+/K+/Ca2+ exchange and phospholipases, lead to bipolar disorders (Deane *et al*., 2008).

Changes in sleep wake cycle or dark light cycle which are precipitated by psychosocial or physical stressful life events precede manic episodes and can prolong time to recovery and also cause recurrent episodes (Germain *et al*., 2008; Jung *et al*., 2014).

2.2.3 Clinical presentation of bipolar disorder

The clinical presentations are usually diagnosed between ages of 18 and 24 years and include psychosis where the patient has a lot suspicion and social withdrawal. Depression in a patient may present crying spontaneously, too much sleeping than usual, and either weight gain or weight loss, staying at bed for days, feeling of tiredness and isolating from hobbies or an earlier interested activities. Mania such as delusions has the patient either filled with energy or able to do anything, also has little sleep, substance abuse and never minds about financial situations. Hypomania is when the patient shows his or her confidence never minds about any serious problems as if nothing can let him or her down and has increased creativity (Macdonald *et al*., 2009; Miniati *et al*., 2010).

2.2.4 Diagnosis of bipolar disorders

Diagnostic methods for bipolar disorders include the Diagnostic and Statistical Manual of Mental Disorders IV & Diagnostic and Statistical Manual of Mental Disorders V. Rating scales and dexamethasone suppression test are also used. Experienced clinicians can examine patient without blood tests or brain scans. Only questions about mood, sleeping patterns, patient's energy, behavior, medical problems in family such as alcohol and depression are used (NICE, 2013; Turner, 2014).

2.2.5 Prognostic indicators of treatment outcomes in bipolar disorder

Prognostic factors comprise quality of family life as well as social support as it is important to have collaboration of patient and family. Substance use can cause commencement of dangerous events which can lead to be incapability of patient to participate in any productivity activities. Indicators such as suicidal thoughts, history for earlier attempts, recent exposure or family history and presence of personality disorder such as antisocial, theatrical, limitations and selfishness may be significant in treatment outcomes. Other prognostic factors include of severity history of prior episodes and age of onset (Macdonald *et al*., 2009; Kim *et al*., 2017).

2.3 PHARMACOLOGICAL MANAGEMENT OF BIPOLAR DISORDER

There is no cure for bipolar disorder but medicines only control symptoms and signs. Management includes pharmacotherapy and non-pharmacotherapy means (Li *et al*., 2012; Nierenberg *et al*., 2014).

2.3.1 Role of anticonvulsants

Anticonvulsants are the primarily used medicines to treat bipolar disorders apart from epilepsy. Anticonvulsants are as good as lithium. Anticonvulsant drugs are supplementary in the management of bipolar disorder. Lithium is not appropriate for long term management.

Anticonvulsants comprise for example of carbamazepine, lamotrigine, topiramate, valproic acid and gabapentin. These drugs stabilize nerve membranes and prevent the release of some neurotransmitters, which helps patients with bipolar disorder (Antosik *et al*., 2015). Below is the table 1 summarizes the anticonvulsants for bipolar disorder with their side effects.

Table 1: Medications summary in bipolar disorder worldwide with their side effects and contraindications:

Drugs	Side effects	Doses per day	Contraindications
Lithium carbonate	Tiredness, tranquility, trembling, weightiness advance, overt hypothyroidism (occurs in 5-10% of patients), bed wetting.	300-600 mg per oral thrice daily or every six hours. Monitor the blood level concentration is recommended	Hypothyroidism, diabetes insipidus, polyuria, polydipsia
Valproic acid Sodium	Agitation, weightiness increase, alopecia, liver disease, platelet dysfunction.	15-60 mg/kg/d Dose monitoring blood concentration level. Titrate up on twice or thrice a day. (Croft 2017).	Raised liver enzymes or liver illness Bone core invasion
Carbamazepine	Drowsiness, liver toxicity (rarely dizziness, rashes, Suppressed White Blood Serum.	200 mg twice a day per oral. Blood plasma level should be controlled.	Bone marrow defect, Drug-Drug interactions
Gabapentin	Ataxia,fatigue,headache, weight gain sedation, dizziness,	Not recognized	
Lamotrigine	Ataxia, benign rash, diplopia, nausea or emesis, dizziness, sleep disruption, Sedation, headache.	Not recognized	Stevens-Johnson disorder
Topiramate	psychomotor, Nephrolithiasis Somnolence slowing.	Not well-known	Reduction dosages renal or in liver impairment
Felbamate	Headache, Liver disease, photosensitivity, somnolence	Not well-known	Aplastic anaemia
Vigabatrin investigational drug	Agitation, insomnia, Weight gain	Not well-known	Unidentified

(Malhi, 2015; Grohol, 2016; Atkin *et al*., 2017; Croft, 2017).

2.3.2 Use of antidepressants in bipolar disorders

Antidepressants treat depression by facilitating the increase of neurotransmitters in the brain. They uplift an individual's mood, and help in reducing the feeling of depression. The

use of antidepressants for bipolar illness is controversial because they stimulate manic incidents in a minor proportion of individuals with bipolar disorder. Many studies show antidepressants are not primarily used for bipolar disorder is as stated by the International Society for Bipolar Disorder (Barden, 2004; Yatham *et al*., 2013). In more than 173 studies reviewed it was found that antidepressants could not conclusively be recommended to treat bipolar disorders may tend to increase risk for death (Cassels, 2013). The antidepressants are not effective for hospitalized patients and may have side effects and therefore their use requires to be monitored (Dodd *et al*., 2017; Ekeri *et al*., 2017).

In addition, the bipolar patients on the antidepressant venlafaxine and are in need of anxiety control, have a higher chance of hospital readmission. Patients who are suffering from comorbid anxiety disorders have a higher chance of being readmitted to the hospital irrespective of the antidepressant that is utilized. Clinicians should take care when they are using antidepressants to treat the bipolar depression and they should remain watchful of the effectiveness of the antidepressant (Antosik *et al*., 2015; Keks *et al*., 2016).

Sometimes a doctor will prescribe a mood stabilizer and antidepressant together, which reduces the risk of manic episodes and to control the moods. Antidepressants are mostly prescribed with other medications, such as a mood stabilizer or antipsychotic or calcium channel blockers (Antosik et al., 2015). Another useful group of antidepressants include selective serotonin reuptake inhibitors, such as fluoxetine, which are useful in major depression, obsessive compulsive disorders, panic disorder and bulimia (Shorter, 2018).

2.3.3 Use of Antipsychotics for management of Bipolar disorders

Antipsychotics are drugs with great benefit for managing of bipolar sickness as well as psychiatric illness in general. There are older (typical) antipsychotics such as haloperidol, and newer (atypical) antipsychotics such as clozapine and risperidone (Watt, 2012; Katayi *et al*., 2015).The older antipsychotics can cause many undesirable side effects while the newer ones cause fewer side effects. Third generation antipsychotics such as aripiprazole useful in managing bipolar disorder but also causes undesirable effects (Shireen, 2016). The most dangerous side effect is neuroleptic malignant syndrome characterized by hypertension and difficulty in breathing. Antipsychotic treatment may also cause increased white blood cells,

rigidity of the muscles, confusion and fever among others (Lambert *et al*., 2011; Einsenberg, 2013; Grande *et al*., 2014). Parkinsonism disease symptoms may occur that includes: trembling, rigidity, and slow talking and movement. Other side effects include tardive dyskinesia, acute dystonic reactions, akathisia, increased appetite, weight gain, seizures and heart abnormalities (Katayi *et al*., 2014; Jeon *et al*., 2017).

Antipsychotics can control the manic episodes and in addition they are useful in the treatment of the hallucinations (Lambert *et al*., 2011; Soroya, 2012).

2.3.5 Role of Benzodiazepines in bipolar disorder

Benzodiazepines are useful drugs in the treatment of anxiety and lack of sleep in individuals who are suffering from the bipolar disorder (Lambert *et al*., 2011; Soreff *et al*., 2017). The drugs are very addictive and their use is only limited for relief of symptoms. The drugs should not be used by individuals who take alcohol or any other substance which may inhibit the central nervous system (Soreff *et al*., 2017). They treat insomnia, racing thoughts, abnormal talkativeness, abnormal activity and agitation, which are some of the aspects of the manic and hypomanic episodes (Soreff *et al*., 2017).

Benzodiazepines affect the neurotransmitter gamma-aminobutyric acid (GABA). Through the increase of the activity of GABA, the drugs relax the brain which helps in relieving the anxiety. The drugs help in the slowing down of the nervous system which has the benefit of reducing the anxiety (Lambert *et al*., 2011; Lytle *et al*., 2017).

The drugs are prescribed for use for a short duration especially to the patients who are suffering from provoked anger, unusual stress and anxiety. Their effects are felt immediately and they are recommended for routine use. The only side effect of these drugs is that their long-term use may lead to tolerance or dependence (Soreff *et al*., 2017). The age group that may experience these side effects is 65 years and above. Use in pregnancy is not recommended as it is teratogenic and may cause the cleft palate. The drugs may also cause sleepiness, aggression and amnesia. Benzodiazepines include: alprazolam, chlordiazepoxide, diazepam and lorazepam (Lambert *et al*., 2011; Lytle *et al*., 2017).

2.3.6 Role of Lithium in Bipolar Disorder

Lithium stabilizes the mood, and is the most effective drug for treatment of bipolar disorder (Machadovieira *et al*., 2009; Won *et al*., 2017). It prevents recurrence of manic and depressive symptoms. Its use needs to be controlled by a doctor or professional practitioners to avoid side effects (Geddes, 2015). The patients who may be affected by side effects are those suffering from kidney, thyroid diseases and expectant mothers, or women who have the intention of getting pregnant (Wellington, 2007; Parminder *et al*., 2015). High doses may be hazardous to the patient (Devaki *et al*., 2006).

The side effects may include diarrhea, disorientation, nausea, drowsiness, lack of mental coordination, and inability to concentrate. Other effects may include kidney damage and dysfunction of the thyroid. These side effects may be reduced through therapeutic monitoring (Devaki *et al*., 2006).

For expectant mothers lithium use may lead to reduced heart rate, abnormal kidney functioning of the newborn and muscle weakness among others (NCCMH, 2006). Nursing mothers may also transfer lithium during breastfeeding to the newborn. Other side effects of excessive lithium levels may include loss of mother's hair, increased weight, memory loss, acne, and polyuria. These conditions can only be managed through the monitoring of the dosage being given (Wellington, 2007). Lithium can be used alone or with other bipolar drugs such as the anticonvulsants or antipsychotics. These combinations are effective for the manic and depressive phases of the bipolar disorder (NCCMH, 2006; Sreevan *et al*. 2011).

2.3.7 Alternative Treatments for Bipolar Disorder

Alternative treatments include regular multivitamins and fish oil tablets. Some are useful. They used for major depression. There is a relationship between mood swings and deficiencies of nutrients (NCCMH, 2006**).**

Supplements interact with standard bipolar medications in numerous ways. Depending on the supplement and how it interacts with the body, some supplements worsen depression or manic symptoms (Wong, 2011). Others include Light therapy and electro-convulsive therapy (ECT) also constitutes alternative therapy (Kerner *et al.*, 2014; Lin *et al*., 2017). The

Repeated transcranial magnetic stimulation (r-TMS), circadian rhythm and melatonin theory (Meyer *et al*., 2012; Turner, 2014).

2.3.8 Psychotherapy for Bipolar Disorder

Psychotherapy includes types of psycho-education, family interventions and multifamily and psycho-education groups (MFPG). Others are cognitive-behavioral therapy (CBT), rainbow program, interpersonal and social rhythm therapy (IPSRT) and schema-focused therapy. Group therapy mainly focuses on prevention of relapse, getting the knowledge on causes of disorder and behavior treatment. Therapies which are meant for families include training on problem solving and communication training. The aim of the psycho-education is to address issues to do with fear, guilt and shame. As a result is the ability to deal with difficult situations which is greatly enhanced (NCCMH, 2006).

2.3.9 Impact of bipolar disorders

If bipolar disorders are not treated there are different events might happen, which might include suicide. It is estimated that 15-20% of patients commit suicide if they do not seek medical attention. In a study undertaken with regard to bipolar I disorder it was revealed that of patients more than 50% attempted to commit suicide. Among children with bipolar disorders is 25% are seriously suicidal (Macdonald *et al*., 2009).

Bipolar disorders are a major blow to an economy, and can cost a country up to $ 45 billion. This is inclusive of direct as well as indirect costs (Macdonald *et al*., 2009).

Additionally it becomes very difficult for the family members as well as those who caregivers for those with bipolar disorders to live with them, because they unexpectedly cause chaos. Most of the times family members feel not very well socially integrated due to having a person who is mentally ill (Macdonald *et al*., 2009).

For the individuals living with bipolar disorder, the habit of smoking cigarette is prevalent and in particular among those who have regular psychotic symptoms. The use of nicotine is speculated by some experts to be a form of self-medication, especially for those who suffer

schizophrenia as it has some effects on the brain. Almost 60% of patients suffering bipolar disorder take other drugs in some point (Macdonald *et al*., 2009).

Bipolar patients tend to suffer memory loss, the speed of how information is processed in the brain might slow down; and they may experience mental inflexibility (Macdonald *et al*., 2009).

2.4 THE PREVALENCE OF METABOLIC DISORDERS

2.4.1 Definition and prevalence of metabolic syndromes

Metabolic syndrome is defined as a group of disorders which promote the risk of stroke, heart diseases and all causes of death in the overall population. Metabolic disorders comprise lipid abnormalities, hypertension, diabetes, obesity and renal failure. Mainly metabolic syndromes are caused by sedentary life, medicines, eating disorders, stresses, genetic factors and life style. They can also be caused by endocrine disorders and dysfunction of the sympathetic nervous systemic (Raikou *et al*., 2017; Elamin *et al*., 2017; Jadhay *et al*., 2017).

The metabolic prevalence related to bipolar disorders due to thyroid disease is 2.4% of the general population with high rates of relapse (Amann *et al*., 2017; Elamin *et al*., 2017; Jadhay *et al*., 2017).

In most of the countries, patients living with bipolar disorder are highly susceptible to metabolic syndrome as indicated by a large prevalence from 16.7 to 67% (Bai *et al*., 2016; Amann *et al.*, 2017).

The impact of these physical and psychiatric comorbidities on outcomes in bipolar disorder is unknown. Nearly 55% of patients have at least a one physical comorbidity and 23.2% have at least the one psychiatric comorbidity. The prevalence of various comorbidities in bipolar disorders due to metabolic are (22.0%) cardiovascular; (18.8%) thyroid; (18.8) neurological; (7.6%) neurotic, stress-related, and somatoform disorders; (15.5%) personality disorders; (12.0%) nicotine dependence; (52.9%) osteoporosis and pneumonia (Burke, 2017; Amann *et al*., 2017). All these comorbidities do not increase the risk of relapse except in thyroid disease. Thyroid disease is linked with an increased risk of manic relapse in bipolar

disorder-I even when controlling for the presence of medications or alcohol use disorders (Amann *et al*., 2017; Fountoulakis *et al*., 2017).

2.4.2 Risk factors with metabolic disorders management

Patients on antipsychotic treatment are more likely to exhibit the metabolic syndrome with variation noted between those on typical antipsychotics, mood stabilizers and those on atypical antipsychotics. Other risk factors include age, smoking status, sex, bipolar disorder subtype (I or II), as well as psychiatric medication (Abbaaji, 2017; Freyberg et al., 2017).

Other factors are biological markers such as C reactive protein levels more than 5mg/l, hyperhomocysteinaemia, high interleukin 6, the diagnostic marker of metabolic syndromes (Grover *et al*., 2012).

2.4.3 Pre-diabetes

Prediabetes is defined by a blood sugar level that surpasses the normal level, but is not high enough to be considered as type 2 diabetes. Individuals experiencing pre-diabetes can only be protected from type 2 diabetes through lifestyle changes. In the long-term, pre-diabetes leads to heart damage, blood vessels and kidneys failure ((Mansour *et al*.,2016; Gladidge *et al*., 2016; Han *et al*., 2016; Vilanova *et al*., 2017). Normally, there may be no symptoms or signs existing in patients with prediabetes. The only sign might be some parts of the body becoming darkened for instance knuckles, knees, armpits, neck, as well as elbows (Bai *et al*., 2016).

There is however several blood tests can be used in the diagnosis for prediabetes. These include glycated hemoglobin (A1C) test, fasting blood sugar test and oral glucose tolerance test. Other tests may include triglycerides, high density lipoprotein and low-density lipoprotein (LDL) as well as total cholesterol level determinations.

The general global prevalence of prediabetes is 33.2 and 21.7 % for female and males, respectively (WHO, 2017; Jalloh *et al*., 2016; Ferrari *et al*., 2013).

2.5 PREVALENCE OF MOVEMENT DISORDERS

Movement disorders are clinical conditions with either an insufficiency movement, or spontaneous movements, unrelated to dullness or spasticity. Movement disorders are signs of basal or extra pyramidal illnesses. These illnesses are predictably classified as; hyperkinetic and hypokinetic. Hyperkinetic state is an excessive muscular movement such as spasmodic torticollis, dyskinesia and choreas. Hypokinetic is an abnormal slowness in motion, such as Parkinsonism disorders and striatonigral degradation (Peluso *et al*., 2012; Chen, 2012; Crump *et al*., 2013; Mitchell, 2015; Flemming *et al*., 2015; Mishal *et al*., 2016).

Treatment of movement disorders depends on the underlying causes, which are often associated with a variety of autoimmune diseases (BaizabalCarvallo et al., 2012)

Parkinsonism is a progressive illness of the central nervous system that largely affects the autonomic nervous system. Normally, the symptoms develop slowly over a period of time. The obvious early signs of the disease include tremors, slowdown in movement, inflexibility, as well as walking difficulties.

Problems of thinking as well as behaviour may also occur. At the advanced stage, dementia becomes a common symptom (Meyer *et al*., 2012; Sveinbjornsdottir, 2016). Parkinsonism may also lead to sleep disturbances, sensual and relationship problems.

In 2015, the worldwide deaths among 6.2 million people suffering from Parkinsonism were 117,400. This illness is common in individuals above the age of 60 years. With women less affected than men. Parkinsonism that occurs earlier than the age of 50 years is known as young-onset Parkinsonism. Its duration is around 7 to 14 years (Antosik *et al*., 2015; Rickards, 2005).

2.5. 1 Drug movement disorder induced by antipsychotics

The different types of movement disorders due to drugs include acute or tardive spontaneous movement, parkinsonism, dystonia and akathisia. They are commonly known as extrapyramidal disorders (Stewart *et al*., 2009).

Mainly drug induced movement disorders (DIMD) are caused by the drug and dose, also the age of the inhabitants. Few may be due to idiosyncratic conditions inductive genetic factors. The true occurrences and frequencies of DIMDs are not well recognized due to variation in clinical presentations, wrong diagnosis or masking of effects by other drugs used (Stewart *et al*., 2009).

The prevalence for those patients on atypical and typical antipsychotics is 19% and 42% respectively (Stewart *et al*., 2009).

2.5.2 Pathophysiology of drug induced movement disorders by antipsychotics

The pathophysiology of drug induced movement disorders by antipsychotics is not well understood several theories have been proposed.

Postsynaptic dopamine receptor hypersensitivity theory states that; inhibition of presynaptic dopamine receptors causes the glutamatergic neurotransmitters to be in excitatory state. This increases the extracellular glutamate levels and release in neurotoxic stress in the striatum that causes dopaminergic hypersensitivity. About 80% of dopamine 2 receptors found in patients taking neuroleptics drugs have the drug induced movement disorders (Stewart *et al*., 2009; Shireen, 2016).

Dopamine GABA hypothesis assumes that there are chemical reactions between GABA and dopamine because dopamine has both excitatory and inhibitory effects on the GABA neurons in the brain, which leads to toxicity (Stewart *et al*., 2009; Shireen, 2016).

Neurotoxicity theory states that by increasing the turnover of neurotransmitters due to dopamine receptor blocking drugs in the basal ganglia leads to membrane lipid peroxidation caused by free radical derivatives of catecholamines (Mathew et al., 2005; Elkouzi *et al*., 2017). Figure 2 below brief describes the pathophysiology mechanisms of how the drug induced movement disorders may occur

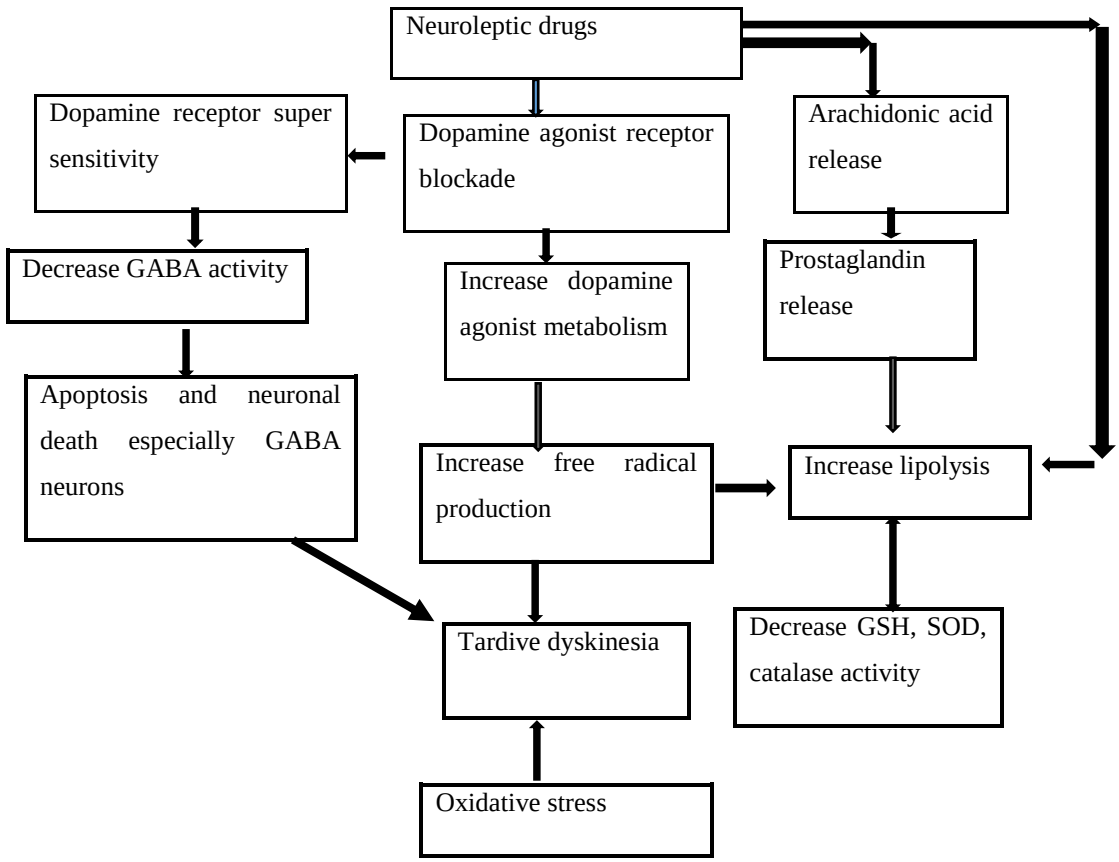


Figure 2: Pathophysiological mechanisms of antipsychotic induced tardive dyskinesia (Shireen, 2016).

GABA Gamma amino butyric acid; GSH Glutathione; SOD Superoxide dismutase.

2.5.3 The signs and symptoms of movement disorders induced by antipsychotics drugs

Disorders commonly experienced after antipsychotic use include parkinsonism, tardive dyskinesia, akathisia and dystonia. The sign of parkinsonism are postural instability, bradykinesia where the patient has slow movement, cannot walk properly and sometimes has difficulties in doing simple tasks. Rigidity and pain may occur due to stiffness of the muscles. While resting the tremors of extremities of arms and legs occurs. There will be changes in speaking which is accompanied by fear before talking, or slurring of speech and sometimes either soft speech or quick speech. Other signs of Parkinsonism can be noted in the hand writing which becomes too small (Stomski *et al*., 2016; Selfani *et al*., 2017).

Tardive dyskinesia usually develops after taking antipsychotics for one month, and has the following signs and symptoms: chewing, speaking and swallowing difficulties. The patient

may also have wounds in the mouth, dental problems and orofacial dyskinesia. This may lead to stigmatization and isolation (Elkouzi *et al*., 2017).

Akathisia due to antipsychotics have the symptoms which can occur and disappear for a while and be exhibited inform of suicidal ideas, anger and aggregation (Stewart *et al*., 2009; Selfani *et al*., 2017).

Dystonia due to antipsychotics presents as vision impairment, breathing problems and respiratory stridor, protruding tongue and laryngeal painful contraction. The patient also develops the oculogyrisis signs thus eyes move in either direction laterally or upwards (Peluso *et al*., 2012; Mishal, 2016; Zagaria, 2018).

2.5.4 Management of drug induced movement disorders by antipsychotics

The management of drug induced movement disorders by antipsychotics involves stopping the drug or reducing the dosage. Changes of medications from one pharmaceutical group to another to manage the disorders can control the situation if started at early stages. Using serotonin and adjuvant antioxidants such as vitamin E, curcumin and red rice bran oil, will assist to avoid further injury and control the behavioral disorders (Shireen, 2016).

Using some antimuscarinic such as diphenhydramine or benztropine or benzhexol can reduce this disorder to some extent. Benzodiazepines, clonidine, amantadine and cyproheptadine can be used to control the drug induced movement disorders by antipsychotics (Mishal, 2016).

Education of the patient or caregiver on life style, food eating and exercise routine is necessary. Continuous counseling and monitoring of outcomes by comprehensive evaluations at least every four months is required. Advising patients to report when they feel different from their normal condition to their doctors or health personnel are encouraged (Stewart *et al*., 2009). Examples of drugs that causes drug induced movement disorders are briefly outlined in table 2.

Table 2 Drugs that Cause Movement Disorder

Drug category	Examples	Movement disorder	Incidence
Antidepressant			
Tricyclic	Imipramine, Desipramine, Amitriptyline Amoxapine	Tremor, gait ataxia	+
		Parkinsonism, TD, NMS	+++
SSRIS	Citalopram, Escitalopram, Fluoxetine, Fluvoxamine, Paroxetine, Sertraline	Akathisia, tremor, serotonin syndrome	+
Antiemetics	Metoclopramide, Droperidol Prochlorperazine	Akathisia, acute dystonia, parkinsonism, TD, NMS	+++
Antipsychotics			
Typical	Chlorpromazine, Fluphenazine Haloperidol, Loxapine, Molindone, Perphenazine, Pimozide, Thioridazine Thiothixine, Trifluoperazine Zuclopenthixol	Akathisia, acute dystonia, parkinsonism, TD, NMS	+++
Atypical	Aripiprazole, Clozapine Olanzapine, Paliperidone, Quetiapine, Risperidone Ziprasidone	Akathisia, acute dystonia, parkinsonism, TD, NMS	+ ++
Adrenergic agents (sympathomimetics)	Psychostimulants: amphetamine, methamphetamine, methylphenidate, cocaine		
	Decongestants: pseudoephedrine, phenylephrine	Tremor	++
	Antiglaucoma agents: Demecarium, echothiophate		
	Corticosteroids		
Amiodarone		Tremor, parkinsonism	++
Dopamine depletors	Reserpine, tetrabenazine	Parkinsonism, akathisia	+++
Antiepileptic agents	Phenytoin	Chorea with toxicity	++
	Lamotrigine	Tremor, chorea	+
	Valproate	Tremor, parkinsonism	+++
	Carbamazepine		++
Lithium		Tremor, parkinsonism	+++
			+

SSRI Selective serotonin reuptake inhibitors; TD Tardive dyskinesia; NMS Neuroleptic malignant syndromes

2.5.5 Tools used in diagnosis of movement disorders induced by antipsychotics

There are many tools used for assessment of movement disorder due to neuroleptic medication (Stomski *et al*., 2016).

Tools used to detect the Akathisia

Abnormal involuntary movement scales (AIMS) has been used from 1970s for measuring the tardive dyskinesia. It has twelve items for rating spontaneous movement of different parts of body of the patient (Guy, 1976; Munez *et al*., 1988; Rush, 2000; Stomski *et al*., 2016). The AIMS tool is often applied by Clinical personnel but sometimes it can be administered by to non-clinical personnel. Appendix F section A.

It is recommended for use after every quarter to half a year for monitoring the progression of tardive dyskinesia. For geriatric it can be used monthly. It takes a short time to administer. It measures the severity of patients over a duration time (Blacker *et al*., 2009). Appendix F section C.

AIMS tool has of the following disadvantages: has unknown responsiveness; low reliability due to insufficient sample size assessment and unknown internal consistency (Stomski *et al*., 2016).

The Simpson Angus Scale (SAS) is used to detect neuroleptic induced Parkinsonism (NIP). This tool is valid and reliable. It is a ten item rating scale. Six items assess rigidity; one item is for gait measurement; and 3 items for assessing salivation, trembling and glabella tap each. Each item rates in a 5 point scale; 0 to 4. The overall rating is mean score obtained by the summation of the items and divided by the total items (Janno *et al*., 2005; Simpson, 2013; Kaijsers *et al*., 2015).

SAS tool is also used in assessing the neuroleptic induced akathisia and tardive dyskinesia; Clinical population neuroleptic induced Parkinsonism for patients from healthy controls and lessening phase without themselves overlapping (Janno *et al*., 2005; Simpson, 2013; Kaijsers *et al*., 2015).

Apart from its usefulness there are also shortcomings such as: insufficiently statistical studied; unclear definitions and instructions; too much emphasis on the rigidity item; and

many items unreliable in old patients. These short-coming have been addressed in a modified version (Janno *et al.*, 2005; Simpson, 2013; Kaijsers *et al*., 2015).

Barnes Akathisia Rating Scales (BARS) is used for measuring for drug induced akathisia which integrates diagnostic criteria for false akathisia, mild; moderate; and severe akathisia. It is useful for rating global severity, restless movements, the observable; the subjective awareness of restlessness and any distress associated with akathisia. It is intended for observer rated and constructs validity (Perminder, 1994; Barnes, 1989; Stomsik *et al*., 2016). The purpose of this tool is to assess subjective aspects and characteristic motor occurrences. Patient is assessed while sitting, standing and not talking for a very short time in each position. It contains one objective and one subjective which has 4 item rated scale 0 to 3 each. Also includes one global clinical assessment which has six item rated scale 0 to 5; describes about the severity, marked, moderate, mild, absent and questionable movement (Perminder, 1994; Barnes, 1989; Stomsik *et al*., 2016).

The Hillside akathisia rating scale has been in use since 1989. It contains two parts, such as subjective and objective. Appendix F section B (Fleischhacker *et al*., 1989); Also Extrapyramidal Symptom Rating Scale (ESRS) and Prince Henry Hospital akathisia scale are used in assessing the tardive dyskinesia (Brock *et al*., 2007). As indicated in Appendix E and Appendix F section B.

Parkinsonism tools used to detect the disorder

Chouinard's extrapyramidal rating scale is used for assessing extrapyramidal symptoms. It has four scales to examine Parkinsonism, akathisia, dystonia and dyskinesia. It has been used since the 1980s. It is also known as extrapyramidal rating scale. It has insufficiently validity. Has confirmed predefined hypotheses and associated with other measures. Appendix E.

Simpson and Angus Scale (ESES) are also used since 1970s to assess extrapyramidal symptoms as well as the Parkinsonism. It is similar as in SAS / ESRS tools in almost all aspects. Intended for use by observer its validity is insufficient (Janno *et al.*, 2005; Simpson, 2013; Kaijsers *et al*., 2015).

Targeting abnormal kinetic effects (TAKE), Neurological rating scale for extrapyramidal side effects (Simpson Angus Scale) and The Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS) are the tools used for extrapyramidal symptoms (Morrison *et al*., 2000; Lambert *et al*., 2003). They are interrelated with each other tool because one tool can be used for assessing more than two types of movement disorder.

Tardive dyskinesia tools used to detect the disorder

The 12 item abnormal involuntary movement scale (AIMS) it is sometimes known as SMARTS (Haddad *et al*., 2014b). It has 12 items assessed independently. It is intended for self-rating. It has insufficient validity (Janno *et al*., 2005; Simpson, 2013; Kaijsers *et al*., 2015; Stomsik *et al*., 2016). It is similar to LUNSERS (Day *et al*., 1995). Appendix F section A.

Others include: Tardive dyskinesia rating scale (TDRS) and Extrapyramidal rating scale. All the description is as above. Sometimes known as MPRC, (Cassady *et al*., 1997).Its aim is to assess extrapyramidal symptoms. Examining parkinsonism and dyskinesia, (Stomsik *et al*., 2016). Also are used for assessing parkinsonism, tardive dyskinesia, akathisia and dystonia. UMSARS, USCRS and UFMG tools are used for quick motor assessment and autonomic assessment. Appendix D. In this study only part of this tool is used (Wenning *et al*., 2004; Teixera *et al*., 2005).

3.0 RESEARCH METHODS

3.1 Study Design and Area

The design was a descriptive, ambi-directional cross sectional study. The study was conducted in the psychiatric outpatient and inpatients clinics of Kenyatta National Hospital and Mathari Referral Hospital.

Kenyatta National Hospital is the teaching Hospital of university of Nairobi and referral hospital that receives patients from Eastern and Central Africa. It is located in Upper Hill along Hospital road around 3 to 4 kilometers from Nairobi Central Business District. It has a 2000 bed capacity with 50 wards and 22 outpatient clinics. Among them is an adult psychiatric clinic is conducted once a week on Wednesdays. Services provided at the hospital are based on the medical care model which does not include services such as occupational and rehabilitation therapy.

Mathari Referral Hospital is a referral and teaching psychiatric hospital. It is located in Nairobi County about 7 kilometres from the central business district off the Thika Super Highway and has a capacity of 700 beds, with around 280 staff; comprising 243 are nurses, 7 psychiatrists, 2 pharmacists and other support staff. The hospital serves both outpatients and inpatients**.**

3.2 Study Population

The study population included adult patients who attended the outpatients and inpatients psychiatric clinics and had bipolar disorder and were seen in Kenyatta National Hospital and Mathari Referral Hospital during the study period.

3.3 Inclusion and exclusion criteria

The inclusion criteria included patients who:

1. Had a written diagnosis of bipolar disorder and had been on treatment for at least six months.
2. Were outpatients and attended clinic or were inpatient during the study period.
3. Adults 18 to 70 years consenting to study

4. In case of being too depressed or in a manic state, proxy consent has been obtained from the care giver to participate in the study. Participants were included after the care giver provided the proxy consent.
5. In absence of a care giver, the attending clinician gave reprobate assent on behalf of the patient.

Patients who did not meet any of the inclusion criteria were excluded. In addition the participant was excluded when:

1. They were too violent.
2. They were incoherent to communicate sufficiently.
3. They were too depressed to communicate.
4. They have had any other condition that may be judged to make them unfit to participate.

3.4 Sample Size Determination

Given that the study design is cross sectional, the Cochran formula, presented in Equation 1, was used for sample size determination.

Equation One: **The Cochran Formula for computation of sample size for surveys**

$$N=Z^2 \text{ X } P(1- P) / d^2$$

Where; N = Sample size

P= estimated prevalence of movement/ metabolic disorder.

Z= critical value of 1.96 corresponding to two tailed level of significance of 0.05.

d= desired degree of accuracy for the study of 0.05.

The prevalence of either metabolic or movement disorders was assumed to be 78.05%. This prevalence was obtained from a study conducted by Katayi *et al*., (2015) who conducted a study on patients with any psychiatric illness at Mathari Hospital in Kenya.

The margin of error was set at $\pm$5% and the level of significance at 5%.

$1.96^2 \text{ X } 0.78(1–0.78)/ 0.05^2 = 264$

Given that the study was conducted in small outpatient of about 500 per year, the Cochran formula for correction of a finite population was applied (Equation 2).

Equation Two: Cochran Formula for correction for a finite population

$$n_1 = n_0 / (1 + n_0/N)$$

Where,

n_1= adjusted sample size

n_0= calculated sample size

N= estimated population of patients with bipolar disorder.

n_1= 264/ (1+264/500) = 264/ 1.528 = 173

The calculated figure was inflated by 10% to cater for non-response. Therefore the minimum sample size for the study was 189 participants.

3.5 Sampling Method and Recruitment of Participants

Convenient sampling was done whereby all bipolar patients who met the inclusion criteria were and consented were recruited until the desired sample size was achieved. The participants were recruited in the psychiatric clinic outpatients and inpatients at Kenyatta National Hospital and Mathari Referral Hospital wards.

Participant recruitment was conducted in a private room on Wednesdays in clinic 24 at Kenyatta National Hospital where the adult psychiatric clinic is usually held. At Mathari Referral Hospital recruitment was conducted from Monday, Tuesday, Thursday and Friday in the wards.

In the morning of the clinic day the files of the patients listed for the day's clinic, were screened to determine if they have had bipolar disorder for at least six months. The eligibility check list in (Appendix A) was used to screen for eligibility. The potentially eligible patients and their care givers were then approached in a waiting room and informed about the study. Patients who gave consent and/ or their care givers gave proxy assent were recruited. The informed consent forms were presented as in Appendix B. Recruitment was done by the principal investigator, trained nurses and students allocated to the clinic units and wards. The study procedures had been explained to the care giver. Recruitment procedures were done before the potential participants were seen by the psychiatrists.

3.6 Data Collection

Data collection included clinical procedures and questionnaires (Appendix C). Data collection instrument was divided into four parts: abstraction of information from patient's files; physical examination; and researcher administered questionnaires.

Participants were also screened for metabolic and movement disorders by the principal investigator or research assistants and findings recorded in Form E before participants were seen by the clinicians.

3.6.1 Abstraction of participants' files

The following information was abstracted from the patient medical records files; socio-demographic information; type of bipolar disorder the participant had any other comorbidities, history of movement or metabolic disorders medications taken and their classification in the last six months. Blood pressure records were also noted. This information was captured and summarized in Appendix C.

3.6.2 Interview of consenting participants

Data collection by interview was only carried out with the consenting participants. Structured questionnaires were used to collect information from patients and caregivers on types of side effects that they experienced. Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS) was used for this purpose (Day *et al*., 1995). The tool was developed in Liverpool University and has51 items. The tool was selected because it is simple and can be filled by the patient. It was designed to collect information on a wide spectrum of antipsychotic related effects. It is useful for investigation of neuroleptic side effects. It was easy for the patient to complete in less than 20 minutes. It was easy to know if the patient was not telling the truth because it has 10 items used for validation. For each question there are 5 scales for answering the questions; the responses are scored from 0 to 4. A score of 0 means the patient was not affected at all, a score 4 means the patient was very much affected.

The principal investigator and the research assistants briefly explained to the participant on how to use the tool. The participant was been encouraged to complete the tool by themselves. Those who could not comprehend or were not able to complete the tool for any other reason were assisted to complete the questionnaire.

3.6.3 Physical assessment

Participants were referred to a research assistant who was a Clinical Officer or Clinical Pharmacist who took the blood pressure, body weight and height. The blood pressure was measured by using both the digital and sphygmomanometer machine. The data was recorded using the form in Appendix D.

The Clinical officer and Clinical Pharmacist had received prior training by a neurologist on how to conduct the quick motor assessment used Appendix E, a tool that developed by Burn *et al* (2003), the tool was used to guide the quick motor assessment by the clinical officer and the clinical pharmacist.

Only Part II of the original questionnaire was used because it was tailored to assess for signs of Parkinsonism which include: a masked facial expression, tremor, rigidity, abnormal gait and posture. The assessment was done by the two; one took notes while the other gave the participant instructions and conducted the examination.

3.6.4 Neurological assessment for akathisia using the Hillside akathisia scale

Akathisia was also assessed by the clinical officer or clinical pharmacist using the Hillside akathisia scale (Fleischhacker *et al* 1989; Perminder, 1994). This scale comprises of two parts; the subjective and objective scales. The subjective part involved asking the patient two questions on if she or he feels restless. The objective scale is an assessment of the patient's actions which is clearly seen by moving legs, hands, arms, or the trunk or head restlessly. The tool has seven items. In the sixth item, the severity of akathisia was rated on a scale ranging from 0 to 7. The last question the tool was not addressed in the study because it was an assessment of improvement since the patient began treatment on akathisia.

In the study we modified the Hillside akathisia questionnaire by adding two questions that are borrowed from the Barnes Rating Scale for drug induced akathisia. These two questions assess whether the patient was aware that they were restless and if the problem causes distress to the patient.

3.6.5 Neurological assessment for tardive dyskinesia

Tardive dyskinesia was assessed using the Abnormal Involuntary Movement scale (AIMS) (Stomski *et al*., 2016). The scale required the clinical officer or the clinical pharmacist to conduct a physical examination that was guided using twelve instructions. The physical examination required the patient to stretch out their hands and their limbs and also to walk a few steps. The severity of an abnormal movement was rated on a scale of 0 to 4. The questionnaire is presented in appendix F section B. All study procedure is summarized in Figure 3.

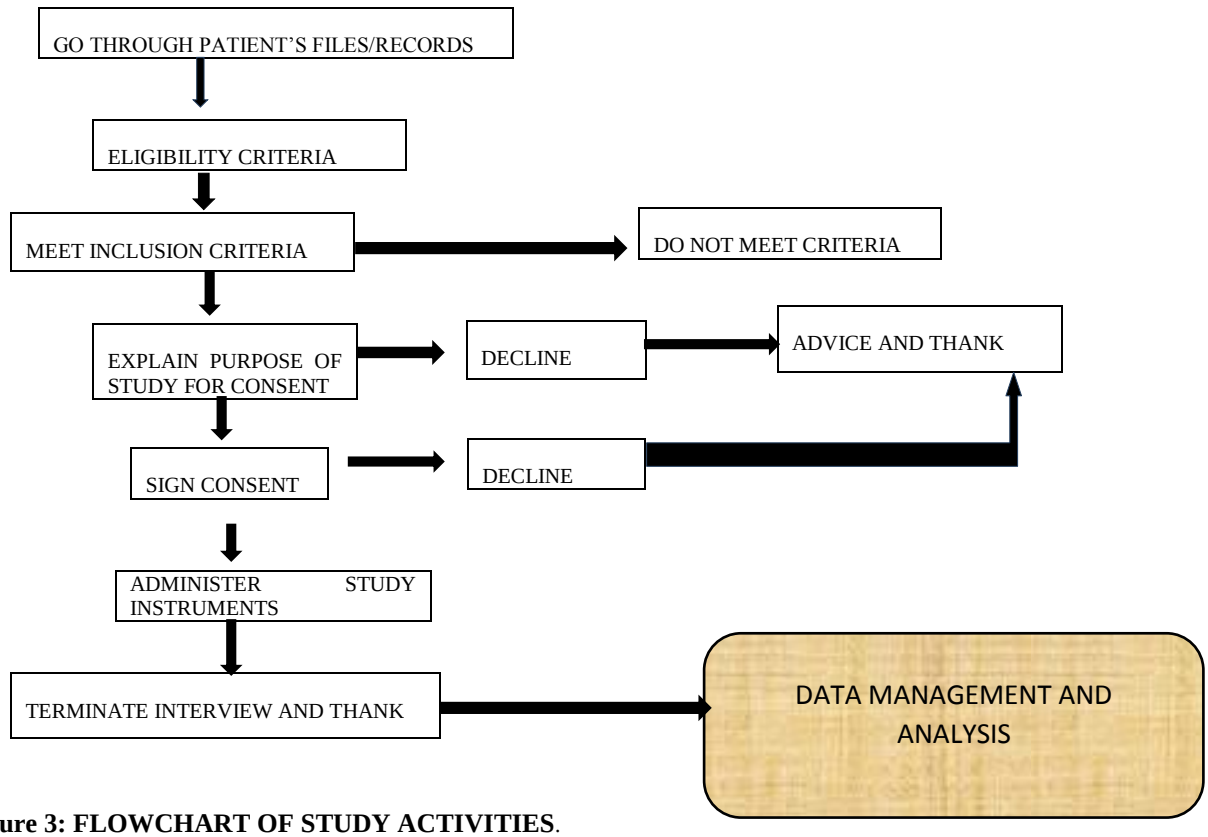


Figure 3: FLOWCHART OF STUDY ACTIVITIES.

3.7 Quality Assurance

Medical students were recruited and used as research assistants. They were trained on filling research tools, organizing and handling research tools and health records. In addition, all the research personnel were trained by a neurologist on how to conduct a quick assessment for movement disorders. All the instruments that were used had been piloted and calibrated beforehand. All the completed data collection forms were checked daily for any inconsistences.

3.8 Data Management

Raw data was collected using study tools and entered into a password protected Epi Info version 7(2007 to 2010) database then exported to Stata version 14 for analysis. Before and after analysis, the filled questionnaires were stored in a lockable cabinet in the investigator's office. It was only then moved to a lockable cabinet in the statistician's office during data entry and analysis. Upon completion of data entry, hard copy forms were compared with the entered data to identify errors and corrections made appropriately. The data collected forms were archived for 5 years after completion of the study or after publication of data, whichever comes earlier.

3.9 Case Definition

Blood pressure: though two blood pressure readings are required for a patient to be declared hypertensive, in this study only the blood pressure at the time the patient was recruited was be considered. The American Heart Association System for classification of hypertension was used. The four categories of blood pressure were as presented in the Table 3.

Table 3: Four categories of blood pressure

AHA system	BPA system	WHO	Systolic mmHg	Diastolic
Normal	Normal	Normal	Less than 120	Less than 80
Elevated	Prehypertension	Stage1	120-129	Less than 80
Hypertension stage 1	Stage1, 140-159/ 90-99	Stage2	130-139	80-89
Hypertension stage 2	Stage2,more than 160/100 or more	Stage3	140 or more	90 or more
Hypertensive crisis		Stage 4	More than 180	More than 120

(Goodman, 2017). AHA: American Heart Association. BPA: British Pressure Association. WHO: World Health Organization

Obesity is excess body weight. Body mass index was computed using the patient's weight in kg divided by the square of height in metre (kg/m^2). A patient was considered obese if their BMI is greater than 30. A BMI of below 18.5 is underweight; where 18.5 to 25 is normal body weight. A range of 25 to 29.9 is overweight; 30 or more is obese. Obesity was further classified as follows as presented in Table 4.

Table 4 Classification of Obesity according to Body Mass Index.

Types	BMI (Kg/m^2)
Class1	30 - ≤ 35
Class2	35 - ≤ 40
Class3	≥ 40

(WHO, 2018; MacMillan, 2**0**18).

Hyperlipidemia defined as one of the following:

1. Low Density Lipoprotein (LDL) in excess of100mg/dL or 5mmol/L.
2. High Density Lipoprotein (HDL) male less than 1.03 mmol/L or 40mg/dL and female less than 1.30mmol/L or 50mg/dL.
3. Triglycerides more than 1.7mmol/L or 150mg/Dl.
4. Very low density Lipoprotein (VLDL)
5. Cholesterol above 200mg/dL

Pre diabetes defined by: fasting blood glucose of 100 to 125mg/dl and HbAIc 5.7 to 6.4% (WHO, 2014; Bahijiri *et al*., 2016). Not performed.

Diabetes is when the blood glucose rises from normal ranges due to either not utilized by body cells or not produced by insulin hormone. Also diabetes can be defined as glucose levels after meal ≥ to 200mg/dL and as fasting blood glucose more ≥ to 126mg/dL (Coutts *et al*., 2012; Bahijiri *et al*., 2016; Vilanova *et al*., 2017). Not performed.

Acute Parkinsonism is an acute neuroleptic induced movement disorders or side effect of dopamine blocking agents. Also are an immediately clinical symptoms characterized by slow movement, muscle inflexibility, trembling of extremities while resting, missing balance on standing. It is assessed by Barnes tool and AIMS.

Akathisia is a movement disorder characterized by feeling of inner restlessness and a compelling need to be in constant motion, as well as by actions such as rocking while standing or sitting, lifting the feet as if matching on the spot and crossing and uncrossing the legs while sitting. It is assessed by HAS.

Akinesia is an absence of movement. It is an opposite of hyperkinetic movement and progressive of supernuclear palsy. Akinesia includes bradykinesia and rigidity which has no movement and is crucially and basically progress to fatigue. Other features are dull movements in fingers or foot tapping and gait icing. It is assessed by abnormal movement.

Catatonia is a life-threatening group complaint characterized by lethargy, motionlessness, mutism, gesture, emptiness and nervousness. It is assessed by using quick motor tool.

Dystonia is an abnormal distinctive attitudes and movements, produced by slow sustained muscle contraction, which misrepresent limbs, trunk neck, face or mouth. It is a twisting motion or abnormal posture (combination) that may manifest as acute or late involuntary movements, facial grimacing, cervical dystonia, oculogyric crisis, rhythmic tongue protrusion, jaw opening or closing, spasmodic dysphonia and rarely, stridor and dyspnea.

Tardive dyskinesia is the unintentional movement of the extremities, tongue, jaws, face and chest as a result of long term antipsychotics treatment.

3.10 Study Variables

The variables which were used to assess metabolic disorders were hypertension, stroke, and records of elevated random blood sugar levels, lipid levels and obesity.

The variables that were used to indicate movement disorders were any record of Parkinsonism, akathisia or tardive dyskinesia.

The independent variables were: the demographic information of the patients, the types of bipolar disorder and the presence of other comorbidities. Other independent variables were medications and family history of metabolic and movement disorders.

3.10.1 Data Analysis

Summarization of descriptive statistics was carried out, with discrete variables summarized as frequencies and percentages. Continuous variables were summarized using measures of central tendency and dispersion such as mean, median, mode, standard deviation and interquartile ranges. The prevalence of metabolic and movement disorders were estimated using frequencies and percentages.

Exploratory data analysis was conducted by comparing the prevalence of selected metabolic and movement disorders across the factors of discrete variables such as different types of drugs and their side effects, respectively. Comparison of data sets was done using inferential tests like Analysis of Variance (ANOVA), unpaired Student test or Chi square test. Odds ratios were computed to measure any association between variables.

The prevalence of movement or metabolic disorder were calculated and presented as a percentage with 95% confidence interval and percentages. Risk factors associated with bipolar disorders were also identified by using logistic regression using a forward stepwise model building approach. Multivariable analysis was done to control for confounding. The level of significance was set at 5% ($p<0.05$).

Presentation of findings was done using tables and graphs based on the Dummy tables are presented in appendix G. Dummy Table1 was a summary of socio-demographic characteristics of the study participants. Dummy Table2 was a summary of clinical characteristics of the study

participants including the bipolar related characteristics as well as comorbidities. Dummy Table 3 was a summary of profile of prescribed medications; Table 4 was a summary of presence of metabolic and movement disorders in the participants and Table 5 a Logistic regression analysis for risk factors for the presence of metabolic or movement disorders.

3.10.2 Dissemination of the Results

The results will be communicated as follows; the final report will be sent to the Psychiatry Department at Kenyatta National Hospital and Mathari Referral Hospital, Clinical Health Services Library: At the Department of Pharmaceutics and Pharmacy Practice the results will be work then be complex published into a health related journal project dissertation for examination. Also be presented at Scientific Conferences of workshops.

3.10.3 Limitations of the study

The study was a cross-sectional study which determines the association of dependent and self-determining variables once in a study period which could not be the case other times. It also relied on participant's responses which were subject to recall bias. Some of the groups of participants were too small to carry out statistical tests. Another limitation is the relatively small sample size which may not extrapolated to all bipolar disorders patients in the country. Patients aged below 18 and over 70 years old (geriatric) were not considered. The LUNSER Scale gave the results of dystonia movement disorder.

3.10.4 Delimitations

The study was limited to outpatients at Kenyatta National Hospital and Mathari Referral Hospital, adults and youth (18 years to 70 years) with bipolar disease.

3.11 Ethical Consideration

The study started upon approval from the KNH/UoN Research and Ethics Committee and Permission (P130/03/2018 dated May 09, 2018) from KNH and Mathari Referral Hospital psychiatric clinics. All the participants were informed about the study and their rights. Participants and caregivers were informed about the study objectives, the benefits and risks. They were also informed about the procedures of selection and study. Participants were free to

ask any questions and seek any clarification. For those patients who were not competent to give consent, care givers were asked to give proxy consent. In cases where the participant was unaccompanied, the psychiatrist gave reprobate assent on their behalf.

Participants were not be coerced to sign the informed consent form before participation. Only consenting patients were recruited, after patients freely signing consent forms. Where participants were unable to consent the care giver of the participant were required to give proxy consent after appropriate explanation. (Appendix B subsections C).

Names of participant were not recorded anywhere on the study tool, instead codes were used. There was no link to the identification of the participant. Interviews were conducted in a private room and consent forms were kept under lock and key. Patients were assured of privacy and their identity was not appearing anywhere.

The study involved asking questions, and the participants were allowed to respond in their own language.

One of the benefits might be early identification and referral of patients with hypertension and or any movement disorders for patients who may have not been diagnosed already. This had the potential of reducing future morbidity or mortality. No monetary benefits or other compensation were given to participants for agreeing voluntarily to use their time for the study.

Some of psychosocial risks that could arise as a result of stress upon the patient discovering that they had other comorbidities like hypertension, diabetes or obesity. Such stress was mitigated by first informing the clinician and the psychologists working in the clinic or wards so that they could break then news gently to the participant.

CHAPTER FOUR: RESULTS

This chapter presents the findings of the investigations involving a total of 189 study participants with bipolar disorder attending the Mental Health Department at Kenyatta National Hospital (KNH) as well as In and Out-patient departments at Mathari Referral Hospital (MRH), Nairobi.

4.1 SCREENING AND RECRUITMENT

This study was conducted in the months of May and June, 2018. A total of 630 files were screened, out of which the 230 participants had bipolar disorder. Twenty-two of these had missing the information, 15 had been on treatments for less than six months, and 5 patients were under 18 and above 70 years in age which were all exclusion criteria. The patients from KNH comprised 13.2% (n=25) of total participants investigated with the rest, more than six times KNH figures (86.8% (n=164) were from MRH. The screening and recruitment procedures are schematically summarized in the flow chart Figure 4.

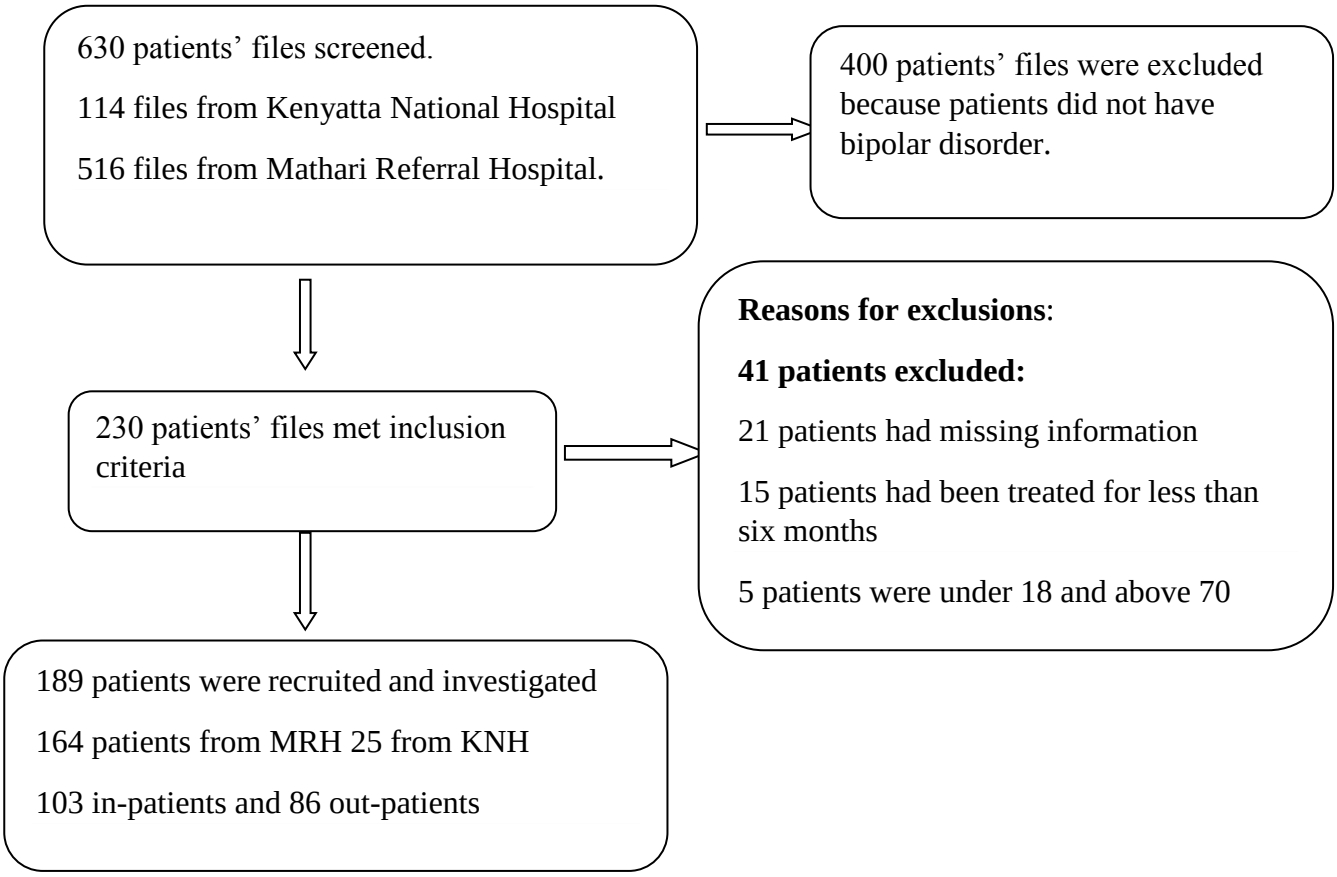


Figure 4: Flow chart on participant's screening and recruit.

4.2 SOCIO-DEMOGRAPHIC CHARACTERISTICS

The socio-demographic characteristics of bipolar participants recruited from the two sites -KNH and MRH- forming 3 categories of participants are presented in Table 4.1.

Table 4.1: Socio-Demographic Characteristics of Participants

VARIABLE	KNH OUT-PATIENT	MRH OUT-PATIENT	MRH IN-PATIENT	TOTAL	P-Value
Age median [IQR]	39 [32, 55]	33 [27, 44]	38 [30, 47]	36 [29, 48]	**0.023**
Gender					
Female	13 (52%)	32 (52.5%)	35 (34%)	80(42.3%)	
Male	12 (48%)	29 (47.5%)	68 (66%)	109(57.7%)	**0.040**
Marital status					
Married	17 (68%)	27 (44.3%)	29 (28.2%)	73(38.6%)	
Single	8 (32%)	33 (54.1%)	60 (58.3%)	101(53.4%)	**< 0.001**
Divorced	0	1 (1.6%)	14 (13.6%)	15(7.9%)	
Residence					
Rural	18 (72%)	37(60.7%)	60(58.3%)	115(60.9%)	
Urban	7 (28%)	17(27.9%)	30(29.1%)	54(28.6%)	0.178
Rural then urban	0	7(11.5%)	7(6.8%)	14(7.4%)	
Urban then rural	0	0	6(5.8%)	6(3.2%)	
Education level					
Primary	4 (16%)	17(27.9%)	34(33%)	55(29.1%)	
Secondary	7 (28%)	24(39.3%)	27(26.2%)	58(30.7%)	0.091
Tertiary	6 (24%)	15(24.6%)	21(20.4%)	42(22.2%)	
None	8 (32%)	5(8.2%)	21(20.4%)	34(18%)	
Employment status					
Employed	23(92%)	53(86.9%)	97(94.2%)	173(91.5%)	0.268
Not employed	2(8%)	8(13.1%)	6(5.8%)	16(8.5%)	
Substance abuse					
Not abusing	22(88%)	43(70.5%)	57(55.3%)	122(64.5%)	**0.005**
Abusing	3(12%)	18(29.5%)	46(44.7%)	67(35.5%)	
Alcohol consumption					
Not taking alcohol	22(88%)	42(68.9%)	55(53.4%)	119(63%)	**0.003**
Takes alcohol	3(12%)	19(31.1%)	48(46.6%)	70(37%)	

The overall median age was 36[29, 48, IQR] showing a statistically significantly difference in the age distribution across the three categories of participants (p= 0.023). The age range was 18 and 70, respectively.

Out of the 189 participants, 57.7% (n=109) were male and 42.3% (n=80) were female. There was a statistically significant difference in the gender distribution across the two facilities. Most of the inpatients at MRH were males (66%). There was an equal gender distribution among the outpatients in KNH and MRH. Most of the participants were single (n=101, 53.4%), very few

divorced (n=15, 7.9%) and nearly all the divorces were in-patients at MRH. There were no statically significant differences across the two arms with regard to education levels (p=0.091) and employment status (p=0.268). Over 90% of the participants were unemployed (p= 0.268). The differences in the proportions of married or unmarried participants differed across the 3 arms.

The prevalence of substance use was highest among inpatients in MRH with nearly a third (35.5%) having a history of substance use (Table 4.1). The out-patients at KNH had the lowest prevalence of substance use. The differences in patterns of substance use across the participant categories was statistically significant (p=0.003). It was noted that most respondents did not report alcohol use (n=119, 63%), but 70, (37%) were actually taking alcohol with the highest prevalence at 46.6% for MRH inpatients and the least prevalence was 12% at KNH. There were statistically significance differences in the patterns of alcohol consumption (p=0.003).

4.3: CLINICAL CHARACTERISTICS OF STUDY PARTICIPANTS

The most prevalent psychiatric diagnosis was type 1 bipolar disorder, accounting for 121 cases (64%); followed by type 2 bipolar disorder (43, 22.8%). Table 4.2 presents the psychiatric diagnosis and comorbidities. Type 3 and 4 bipolar disorders were only diagnosed in MRH (Table 4.2). There was no statistically significant difference between the two hospitals with regard to the distribution of the various types of bipolar disorder (P=0.291). The median duration of treatment at KNH out-patient department was 7 years [IQR 3, 13] while at MRH 5 years [IQR 2, 13]. There was a statistically significant difference in the median duration of treatment with the out-patients having been on treatment for the shortest duration.

The patients' co-morbidities were obtained from file records and are summarized in Table 4.2 The co-morbidities differed across facilities with the prevalence of hypertension highest amongst KNH out-patients (36%) as compared to 4.9%. for MRH. A similar pattern was noted for diabetes.

The other co-morbidities included spinal injury, skin dermatitis, itching, HIV infection, convulsions and mutism.

Table 4.2: Distribution of types of bipolar disorders and comorbidities by patients

VARIABLE	KNH OUT-PATIENT	MRH OUT-PATIENT	MRH IN-PATIENT	TOTAL	P-Value
Types of bipolar disorder					
Type 1	15 (60%)	35 (57.4%)	71 (68.9%)	121 (64%)	
Type 2	9 (36%)	14 (23%)	20 (19.4%)	43 (22.8%)	0.291
Type 3	1 (4%)	4 (6.6%)	2 (1.9%)	7 (3.7%)	
Type 4	0	4 (6.6%)	7 (6.8%)	11 (5.8%)	
Not indicated	0	4 (6.6%)	3 (2.9%)	7 (3.7%)	
Treatment duration median [IQR] (years	7 [3, 13]	5 [2, 13]	6 [3, 12]		**0.024**
Other documented co-morbidities with bipolar disorder					
Hypertension	9 (36%)	7 (11.5%)	5 (4.9%)	21 (11.1%)	**< 0.001**
Diabetes	2 (8%)	2 (3.3%)	6 (5.8%)	10 (5.3%)	0.632
Anxiety disorders	9 (36%)	12 (19.7%)	25 (24.3%)	46 (24.3%)	0.277
Thyroid problem	1 (4%)	1 (1.6%)	1 (1%)	3 (1.6%)	0.553
Other comorbidities	13 (52%)	22 (36.1%)	64 (62.1%)	99 (52.4%)	**0.005**
Family History of metabolic and movement disorders					
Blood pressure	8 (32%)	0	7 (6.8%)	15 (7.9%)	**< 0.001**
Acute parkinsonism	1(4%)	0	0	1(0.5%)	
Chronic parkinsonism	0	0	1(1%)	1(0.5%)	0.115
Diabetes	2(8%)	0	4(3.9%)	6(3.2%)	0.131
Any systemic disorder	5(20%)	0	3(2.9%)	8(4.2%)	**< 0.001**
History any problems	10(40%)	0	10(9.7%)	20(10.6%)	**< 0.001**

4.4 COMPARATIVE USE OF MEDICATIONS IN KNH AND MRH

4.4.1. Prevalence Use of Antipsychotics Tablets and Injectable at MRH &KNH

The cumulative use of antipsychotic drugs was greater than that of antidepressants (95.8%, 29.1%, respectively). Nearly 37% (n=69) were only on one antipsychotic drug. There were 112 (59.6%) participants taking 2 or more antipsychotic drugs (Table 4.3).

Most in-patients in MRH were on at least 2 antipsychotics (58.8%) as compared to 32% of out-patients. In KNH, 42% of the out-patients sampled were on 2 or more antipsychotics. There were 5 in-patients in MRH on 5 or 6 antipsychotics**.** The most frequently used antipsychotic drug was haloperidol (51%). The differences in pattern of use of this drug was statistically significant different across the three arms, (p=0.002). Olanzapine was the third most widely used antipsychotic agent with no statistically significant difference in the prevalence of its use across

the 3 arms (P=0.569). Only one participant was on clozapine, 7 on aripiprazole and 19 on risperidone.

Table 4.3 Prevalence Use of Antipsychotics

VARIABLE	KNH OUT-PATIENT	MATHARI OUT-PATIENT	MATHARI IN-PATIENT	TOTAL	P-Value
Number of Antipsychotics tablets taken per patient per prescription					
One drug type taken	11(44%)	31(50.8%)	27(26.2%)	69(36.5%)	
Two drugs taken	4(16%)	16(26.2%)	40(38.8%)	60(31.8%)	
Three drugs taken	3(12%)	11(18%)	20(19.4%)	34(18%)	**0.012**
Four drugs taken	2(8%)	2(3.3%)	9(8.7%)	13(6.9%)	
Five drugs taken	1(4%)	0	3(2.9%)	4(2.1%)	
Six drugs taken	0	0	1(1%)	1(0.5%)	
Types of Antipsychotics injectable per patient per prescription					
One	5(20%)	31(50.8%)	42(40.8%)	78(41.3%)	
Two	0	5(8.2%)	30(29.1%)	35(18.5%)	
Three	0	0	10(9.7%)	10(5.3%)	< **0.001**
Four	0	0	1(1%)	1(1%)	
Antipsychotic tablets					
Haloperidol 5mg	6(24%)	28(45.9%)	63(61.2%)	97(51.3%)	**0.002**
Olanzapine	10(40%)	27(44.3%)	37(35.9%)	74(39.2%)	0.569
Chlorpromazine	3(12%)	8(13.1%)	35(34%)	46(24.3%)	**0.003**
Quetiapine	7(28%)	6(13.6%)	14(13.6%)	27(14.3%)	0.088
Risperidone	3(12%)	8(13.1%)	8(7.8%)	19(10.1%)	0.514
Aripiprazole	2(8%)	1(1.6%)	4(3.9%)	7(3.7%)	0.362
Clozapine	0	1(1.6%)	0	1(0.5%)	0.348
Antipsychotics injectable					
Fluphenazine	0	22(36.1%)	63(61.2%)	85(45%)	< **0.001**
Flupenthixol	5(20%)	16(26.2%)	39(37.9%)	60(31.8%)	0.121
Chlorpromazine	0	2(3.3%)	27(26.2%)	29(15.3%)	< **0.001**
Haloperidol	0	1(1.6%)	4(3.9%)	5(2.7%)	0.465
Risperidone	0	0	4(3.9%)	4(2.1%)	0.182
Antispasmodic drug					
Benzhexol 5mg	9 (36%)	25 (41%)	62 (60.2%)	96 (50.8%)	**0.017**

The most widely used injectable was fluphenazine (45%) followed by flupenthixol (31.8%). Only 5 (20%) of the out-patients in KNH were not on an injectable antipsychotic (flupenthixol). The most commonly used injectable antipsychotic among the out-patient in MRH was fluphenazine (36%) (Table 4.3).

Benzhexol was a most widely agent with about 50% of participants on it. Out-patients in KNH were least likely to be on benzhexol with a prevalent of use of 36%. Nearly two thirds of the in-patients were on benzhexol and there was a statistically significant difference in the prevalence of its use the 3 sets of patients (p=0.017).

4.4.2 Antidepressants

The cumulative frequency of use of antidepressants was 29.1 %. About a fifth (20.6%) was on at least one drug (Table 4.4). Sixteen patients (8.5%) were on 2 or more antidepressants drugs. The frequency of multiple uses of anti-depressants was highest amongst KNH patients (36% of patients seen in this facility). The use of anti-depressants was also very high in MRH –inpatients (8.5% of all patients). There were statistically significant differences in use of individual anti-depressants especially with regard the use of mirtazapine (p<0.001), sertraline (p<0.001) and desvenlafaxine (p=0.037).

Table 4.4: Prevalence of antidepressants use

VARIABLE	KNH OUT-PATIENT	MRH OUT-PATIENT	MRH IN-PATIENT	TOTAL	P-Value
Number of drugs per patient					
One drug type	6 (24%)	10 (16.4%)	23 (22.3%)	39 (20.6%)	**<0.001**
Two drugs	4 (16%)	0	6 (5.8%)	10 (5.3%)	
Three drugs	5 (20%)	0	1 (1%)	6 (3.2%)	
Drugs taken					
Amitriptyline	4 (16%)	4 (6.6%)	19 (18.5%)	27 (14.3%)	0.106
Mirtazapine	6 (24%)	0	3 (2.9%)	9 (4.8%)	**< 0.001**
Imipramine	1 (4%)	0	0	1 (0.5%)	**0.037**
Venlafaxine	6 (24%)	0	0	6 (3.2%)	**< 0.001**
Sertraline	2 (8%)	1 (1.6%)	2 (1.9%)	5 (2.7%)	0.200
Fluoxetine	7 (28%)	6 (9.8%)	12 (11.7%)	25 (13.2%)	0.061
Citalopram	1 (4%)	0	1 (1%)	2 (1.1%)	0.256
Escitalopram	1 (4%)	0	1 (1%)	2 (1.1%)	0.256
Desvenlafaxine	1 (4%)	0	0	1 (0.5%)	**0.037**

The most frequently used anti-depressant across all patients was amitriptyline (14.7%). Its use was highest in MRH especially among in-patients. Fluoxetine was the next widely used antidepressant with 28% prevalence in KNH and 11.7% amongst inpatients and 9.8% amongst out-patients at MRH. The use of newer and more expensive antidepressants was more predominant in KNH. Drugs like desvenlafaxine and venlafaxine were only used in KNH (Table 4.4).

4.4.3 Uses of Mood Stabilizers and Benzodiazepines

About 91% of participants were on a mood stabilizer. The most widely used mood stabilizer was carbamazepine followed by divalproex. There were no statistically differences in the prevalence use of mood stabilizes across the groups with the exception of lamotrigine (Table 4.5) which was only prescribed in KNH.

Table 4.5 Prevalence Use of Mood Stabilizers and Benzodiazepines

VARIABLE	KNH OUT-PATIENT	MATHARI OUT-PATIENT	MATHARI IN-PATIENT	TOTAL	P-Value
Number of Mood depressants per participant					
One drug taken	17(68%)	48(78.7%)	88(85.4%)	153(81%)	0.268
Two drugs taken	3(12%)	7(11.5%)	7(6.8%)	17(9%)	
Three drugs taken	1(4%)	0	3(2.9%)	4(2.1%)	
Number of Benzodiazepines per participant					
One drug taken	7(28%)	2(3.3%)	12(11.8%)	21(11.2%)	
Two drugs taken	2(8%)	0	3(2.9%)	5(2.7%)	**0.001**
Three drugs taken	1(4%)	0	0	1(0.5%)	
Number of Anticonvulsants per participant					
One drug taken	0	0	1(1%).	1(0.5%)	0.491
Two drugs taken	0	0	3(2.9%)	3(1.6%)	
Mood depressants					
Carbamazepine	15(60%)	49(80.3%)	85(82.5%)	149(78.8%)	0.108
Divalproex	4(16%)	6(9.8%)	12(11.7%)	22(11.6%)	0.721
Valproic acid	5(20%)	7(11.5%	9(8.7%)	21(11.1%)	0.273
Pregabalin	3(12%)	0	0	3 (1.6%)	**<0.001**
Gabapentine	0	0	1(1%)	1(0.5%)	0.657
Topiramate	0	0	1(1%)	1(0.5%)	0.657
Lamotrigine	0	0	1(1%)	1(1%)	0.657
Lithium	0	0	1(1%)	1(1%)	0.657
Benzodiazepines					
Bromazepine	2(8%)	0	1(1%)	3(1.6%)	**0.020**
Diazepam	4(16%)	1(1.6%)	8(7.8%)	13(6.9%)	**0.050**
Diazepam injection.	0	1(1.6%)	7(6.8%)	8(4.2%)	0.151
Alprazolam	5(20%)	0	1 (1.1%)	6 (3.2%)	**< 0.001**
Zolpiderm	2(8%)	0	1(1%)	3 (1.1)	**0.020**
Lorazepam	1(4%)	0		2(1.1%)	0.256
Anticonvulsants					
Phenobarbitone	0	0	4(3.9%)	4(2.1%)	0.182
Phenytoin	0	0	3(2.9%)	3(1.6%)	0.280

Cumulatively 14.4% of the participants were on benzodiazepines. There were statistically significant differences in the types of benzodiazepines used across the two facilities. The most widely used benzodiazepine was diazepam (6.9%). Out-patients in MRH had the lowest

prevalence of benzodiazepines use (3.3%) compared to in-patients at 14.4% and 40 % amongst the out-patients in KNH.

4.4.4 Prevalence of Use of Other Drugs

Slightly over 11 % of participants (21, 11.3%) were on anti-hypertension medicines (Table 4.6.). The most widely used drugs were ACE inhibitors (n=18, 11.3%) followed by calcium channel blockers (4.7%). Only one patient (from KNH) was on clopidogrel (antiplatelet drug) and lipid lowering agents (atorvastatin). About 11 patients were on anti-diabetic medications with 4 (3.9%) on glibenclamide and 5 on metformin. Two (1.9%) were on mixtard insulin and were inpatients at MRH (Table 4.6).

Individually the most prescribed drug was Neurobion forte ® (vitamin B complex) at 7.4% high, followed by folic acid at 4.8%. There was a statistically significant difference in the prevalence of use of folic acid and vitamin B complex across the facilities ($p < 0.001$). These vitamins were mainly prescribed in KNH. The least prescribed drug was monteleukast, a leukotriene receptor antagonist used to prevent and manage asthma symptoms and to relieve the symptoms of seasonal allergies (Table 4.6).

Table 4.6 Prevalence use of Other Drugs

VARIABLE	KNH OUT-PATIENT	MATHARI OUT-PATIENT	MATHARI IN- PATIENT	TOTAL	P-Value
Calcium channel blockers					
Sildenafil	0	0	1(1%)	1(0.5%)	0.657
Nifedipine	2(8%)	2(3.3%)	4(3.9%)	8(4.2%)	0.594
Amlodipine	3(12%)	1(1%)	1(1%)	5(2.7%)	**0.007**
ARBs					
Losartan H	4(16%)	0	1(1%)	5(2.7%)	**< 0.001**
Losartan	2(8%)	1(1%)	0	3(1.6%)	**0.016**
ACE inhibitors					
Enalapril	0	2(3.3%)	0	2(1.1%)	0.120
Ramipril	2(8%)	0	1(1%)	3(1.6%)	**0.020**
Other antihypertensive drugs					
Methyldopa	0	0	1(1%)	1(0.5%)	0.657
Hydrochlorthiazide	3(12%)	3(4.9%)	1(1%)	7(3.7%)	**0.027**
Nebilolol	1(4%)	0	0	1(0.5%)	**0.037**
Number of Antihypertensive per participant					
One drug	5(20%)	1(1.7%)	5(4.9%)	11(5.9%)	
Two drugs	3(12%)	1(1.7%)	1(1%)	5(2.7%)	**< 0.001**

Three drugs	2(8%)	2(3.3%)	1(1%)	5(2.7%)	
Antiplatelet /anti- lipids					
Clopidogrel	1(4%)	0	0	1(0.5%)	**0.001**
Atorvastatin	1(4%)	0	0	1(0.5%)	
Antidiabetes drugs					
Glibenclamide	0	0	4(3.9%)	4(3.9%)	0.182
Metformin	0	0	5(4.9%)	5(2.7%)	0.117
Mixtard insulin	0	0	2(1.9%)	2(1.1%)	0.430
Number of Antidiabetics per patient					
One drug	0	0	1(1%)	1(0.5%)	
Two drugs	0	0	2(1.9%)	2(1.1%)	0.638
Three drugs	0	0	2(1.9%)	2(1.1%)	
Other groups of drugs					
Multivitamin/pabrine	0	1 (1.6%)	5 (4.9%)	5 (3.2%)	0.327
Folic acid	6 (24%)	1 (1.6%)	2 (1.9%)	9 (4.8%)	**<0.001**
Vitamin E	2(8%)	0	0	2 (1.1%)	**0.001**
Vitamin B complex	9(36%)	1(1.6%)	4(3.9%)	14(7.4%)	**<0.001**
Monteleukast	0	0	1 (1%)	1 (0.5%)	0.657
Chlorpheniramine	1 (4%)	0	2 (2.9%)	3 (2.1%)	0.357

4.5 PREVALENCE AND RISK FACTORS FOR METABOLIC

4.5.1 Prevalence and Risk Factors for Obesity

The body mass index, a risk factor for metabolic syndrome, was obtained from measured weight and height of the participants. Nearly five percent (5.3%) were obese, 9.5 % overweight and 59.8 % underweight (Table 4.7).

Table 4.7 Prevalence and Risk Factors of Obesity

VARIABLE	KNH OUT-PATIENT	MATHARI OUT-PATIENT	MATHARI IN-PATIENT	TOTAL	P-Value
Weight in (kg) [IQR]	74.5 [64, 77]	60 [55, 62]	60 [55, 68]	60 [56, 68]	**< 0.001**
Height(m) [IQR]	166 [161, 169]	169 [161, 172]	168 [160, 172]	168 [161, 172]	**0.047**
Body mass index Median [IQR]	26 [24, 28.3]	26 [20.1, 22.3]	22 [20, 23.9]	22 [20.3,23.9]	**< 0.001**
Body mass index, grouping					
Underweight16-20	9(36%)	44(72.1%)	60 (58.2%)	113 (59.8%)	**< 0.001**
Normal 21-25	1(4%)	17(27.9%)	30 (29.1%)	48 (25.4%)	
Overweight 26-30	12(48%)	0	6 (5.8%)	18 (9.5%)	
above 30 Obese	3(12%)	0	7 (6.8%)	10 (5.3%)	

The median weight in all participants was [IQR] 60 [56, 68] while for KNH participants was 74.5 [64, 77]. There were high statistically significant differences in weight across the two facilities by $p< 0.001$.

Participants in KNH out-patient unit had the highest body mass index with median [IQR] of 26 [24, 28]. The MRH in-patients had the lowest body mass index. The highest prevalence of obesity was among the KNH out-patient with prevalence of 12% as opposed to the participants in MRH with prevalence ranges from 5.3% to 6.8%.

The prevalence of participants categorized as underweight was noted to be higher amongst participants seen in MRH with about 60% recorded as opposed to KNH with an underweight prevalence far less than 36%. On all these participants there were no records of lipid profile (Table 4.2 and 4.7) evaluation having been done during their care.

Table 4.8: Linear Regression Analysis of Body Mass Index against Socio-Demographic and Clinical Characteristics.

VARIABLE	B crude	95%CI	p-value
Study site	3.081	1.283-7.402	**0.012**
In-outpatient vs. out-patient	1.151	0.641-2.066	0.638
Gender	0.848	0.471-1.526	0.583
Age	1.005	0.983-1.026	0.670
Marital status	1.028	0.671-1.742	0.748
Residence	0.92	0.627-1.35	0.669
Education	1.186	0.903-1.556	0.220
Employment status	0.653	0.217-1.961	0.448
Substance abuse	1.006	0.548-1.847	0.986
Alcohol consumption	0.986	0.54-1.801	0.964
Duration of illness	0.974	0.939-1.011	0.172
Types of bipolar disorder	0.971	0.735-1.284	0.838
Has diabetes mellitus	2.336	0.636-8.573	0.201
Has blood pressure	3.419	1.309-8.929	**0.012**
Has anxiety disorder	1.062	0.540-2.087	0.862
Has thyroid disease	0.74	0.066-8.308	0.807
Other co-morbidity records	2.084	1.149-3.78	**0.016**
Has a Family History of (metabolic and movement disorders)			
Has blood pressure	2.396	0.816-7.034	0.112
Parkinsonism history	0.835	0.128-5.453	0.851
Has diabetes	7.887	0.903-68.909	0.062
Other disease	11.362	1.368-94.345	**0.024**
Family history any disorder	4.027	1.472-11.015	**0.007**

As seen in the comparison of body mass index across facilities a study site had a positive association with body mass index. The difference in body mass index across facilities was 3 units. As presented in Table 4.8 there was also a positive correlation between history of hypertension and body mass index. A participant with a history of hypertension had higher body mass index of 3.42 units (95%CI 1.393-8.93) compared to those with a family history of hypertension. It was noted that participants who had family history of any disorder such as diabetes or hypertension tended to have higher body mass index. However, there was no statistically significant association between body mass index and potential predictors such as medications.

There was a positive association with body mass index across rash. The difference in body mass index across rash was 1.4 units (95%CI 1.031-1.878). Also there was a positive correlation between reduced sex drive and body mass index. The participant had 1.3 units of reduced sex drive for every increase of body mass index. There was a positive association with body mass index against difficult to climax. The difference in body mass index against difficult to climax was 1.5 units. For every increase in body mass index there was 1.6 unit times' chances of the period to be less frequent for the participant. There was increase of body mass index by 2 units for movement rate tongue obtained. There were 2 units for the association between the body mass index and lower extremities movement disorders (Table 4. 9).

Table 4.9 Logistic Regression of Body Mass Index against LUNSERS results

VARIABLE	**OR**	**95%CI**	**P-Value**
Rash	1.392	1.031-1.878	**0.031**
Reduced sex drive	1.297	1.029-1.635	**0.027**
Difficult climax	1.445	1.008-2.072	**0.045**
Period less frequent	1.599	1.000-2.557	**0.050**
Rate tongue movement	2.121	1.060-4.244	**0.034**
Upper extremities movement	1.329	0.951-1.857	0.096
Lower extremities movement	1.947	1.066-3.556	**0.030**

4.5.2 Evaluation of Systolic Hypertension as a Measure of Metabolic Disorder

The median systolic blood pressure of patients seen at KNH was generally higher than that of patients at MRH. The overall prevalence of systolic hypertension was 34.4%. (n=65). There was a statistically significant difference in the distribution of hypertensive patients across the sites.

The median [IQR] systolic hypertension was 120 [111, 136] as shown in Table 4.10. About 56% of patients in KNH had systolic hypertension compared to 27.9% of out-patients in MRH and 33% of in-patients (Table 4.10).

Table 4.10 Prevalence of Systolic and Diastolic Hypertension from Measurement

VARIABLE	KNH OUT-PATIENT	MATHARI OUT-PATIENT	MATHARI IN-PATIENT	TOTAL	P-Value
Median[IQR] systolic blood pressure	137[118,150]	120[111,131]	120[111,131]	120[111, 136]	**0.048**
Median[IQR]diastolic blood pressure	78[75, 85]	75[70, 84]	78[71, 85]	78[70, 85]	0.337
Hypertension	14(56%)	17(27.9%)	34(33%)	65 (34.4%)	**0.041**
Hypotension	1(4%)	9(14.8%)	16(15.5%)	26(13.8%)	0.312

The isolated hypertension is the definition of systolic hypertension according to JNC 8 and Smith et al., 2013. The cut off for elevated systolic blood pressure was above 130mmHg. The normal blood pressure was 120-130mmHg as per JNC 8 and outlined in Table 4.11.

Table 4.11 Measurement of systolic blood pressure

WHO	Systolic mmHg	Frequency	Percentage %
Optimal	Less than 120	85	44.97
Normal	120-129	39	20.64
High normal	130-139	34	16.4
Grade 1 hypertension	140 -159	26	14.29
Grade 2 hypertension	160-179	7	3.7
Grade 3 hypertension	≥180	0	0
Isolated hypertension	≥140	33	18

The most prevalent state was the optimal pressure with 45% followed by normal at 21% and the least grade 2 hypertension at 3.7%.

To assess any associations between the risk factors for systolic hypertension, logistic analysis was carried out and the he results are presented in Table 4.12. An evidence of positive association of systolic hypertension across study sites was noted with a difference across facilities was 2.3 units.

Table 4.12 Logistic Regression Analysis for Risk Factors for Systolic Hypertension

VARIABLE	B crude	95%CI	P-Value
Socio-demographic characteristics			
Gender	1.1571	(0.6286-2.1299)	0.639
Age	1.043	(1.0193-1.0674)	**<0.001**
Weight	1.0410	(1.0130-1.0699)	**0.004**
Facility-hospitals	2.333	(0.9965-5.4633)	**0.051**
In-patient vs. out-patients	0.7238	(0.3963-1.322)	0.293
Marital	0.4135	(0.24136- 0.70852)	**0.001**
Residence	0.90736	(0.6086-1.3527)	0.633
Education	1.2798	(0.9657-1.6958)	**0.086**
Employment	2.035	(0.7265-5.7003)	0.176
Substance abuse	0.9957	(0.5316-1.8649)	0.989
Alcohol	1.0972	(0.9176-0.9883)	0.769
Clinical and history of bipolar disorder			
Treatment duration	1.0517	(1.0139-1.0909)	**0.007**
Type of bipolar disorder	1.1414	(0.8642-1.5075)	0.351
Blood pressure	4.5882	(1.7479-12.0438)	**0.002**
Diabetic mellitus	4.8678	(1.2146-19.5094)	**0.025**
Anxiety	3.9048	(0.5090-2.0565)	0.949
Thyroid	3.9048	(0.3474-43.8942)	0.270
Other morbidity	2.3734	(1.2719- 4.4284)	**0.007**
Medications			
Sertraline	2.951	(0.4806-18.1283)	0.243
Aripiprazole	5.0833	(0.9582-26.9682)	0**.056**
Quetiapine	0.3549	(0.1594-0.7904)	**0.005**
Haloperidol	0.3700	(0.1986-0.6894)	**0.002**
Haloperidol duration	2.5277	(1.4224-4.4917)	**0.002**
Desvenlafaxine	3.1944	(1.2849-7.9426)	**0.012**
Desvenlafaxine duration	0.4410	(0.2029-0.9585)	**0.039**
Benzodiazepines group	1.8200	(0.9826-3.3715)	0.057
Family history and others variables			
Historical group problems	2.6029	(1.0183-6.6527)	**0.046**
Body mass index	1.0920	(1.0164-1.1732)	**0.016**
Ocular-motor dysfunction	2.7320	(1.4111-5.2891)	**0.003**

There was also strong association across age increase and systolic hypertension by 1.043 units. The male gender was 1.2 as likely as female to get a systolic hypertension. There were 1.041 units for the association between weight and systolic hypertension. There were 1.3 units increases in education for getting systolic hypertension (Table 4.12). There was strong positive association between the systolic hypertension and treatment duration. A participant with diabetes mellitus had 5 times higher chance of having systolic hypertension. There was positive correlation between the use of quetiapine and systolic blood pressure. Participants who used aripiprazole had had higher chance of having systolic hypertension of 5.1 units (95% CI 0.958-26.968) compared to participants took quetiapine. There was positive association between systolic hypertension and desvenlafaxine by 3.2 units.

4.5. 3 Evaluation of Diastolic Hypertension as a Measure of Metabolic Disorder

The cut off for elevated diastolic blood pressure was above 90 mmHg. The most prevalence was normal 72% and only 1.6% was grade 3 hypertension as outlined in Table 4.13. The median [IQR] diastolic hypertension was 78 [70, 85] (Table 4.10).

Table 4.13 Diastolic evaluation as by JNC 8

WHO	Diastolic mmHg	Frequency	Percentage %
Optimal	Less than 80	105	55.6
Normal	80-84	31	16.4
High normal	85-89	25	13.2
Grade 1 hypertension	90-99	16	8.5
Grade 2 hypertension	100-109	9	4.7
Grade 3 hypertension	≥110	3	1.6
Isolated hypertension	≥90	28	14.8

The logistic regression was done to identify risk factors for diastolic hypertension (Table 4.14). It was found that the use of many of the drugs was not statistically significantly associated with diastolic blood pressure (amitriptyline, p=0.225; mirtazapine p=0.526; venlafaxine p=0.215) (Table 4.14). Some drugs showed significant association such as quetiapine (p=0.024) and nifedipine (p=0.011) (Table 4.14).

Diastolic hypertension was related significantly statistically across other outcome measures such as weight (p=0.052); height (p=0.029); systolic hypertension (p= <0.001) and heart rate (p=0.043) (Table 4.14). Also there were strong associations among socio-demographic against diastolic hypertension such as age (p= 0.002), marital status (0.034), residence (0.018), treatment duration (p=0.001), hypertension records (< 0.001), diabetes records (p= 0.004), thyroid records (0.043) and other comorbidities (p=0.002). There was strong positive association with quetiapine (p= 0.024) and quetiapine duration use (p= 0.040). But was not significant with body mass index measured (p=0.437); body mass index group (p= 0.153); and co-morbidities history records such as hypertension (p=0.506); and diabetes (p=0.897) (Table 4.14).

Table 4.14 Logistic Regression for Risk Factors for Diastolic Hypertension

VARIABLE	B CRUDE	95%CI	P-Value
Socio-demographic characteristics			
Age	1.048	(1.018-1.078)	**0.002**
Facility- hospitals	1.533	(0.523-4.488)	0.436
In –patient vs out-patient	0.809	(0.362-1.806)	0.605
Gender	1.159	(0.510-2.632)	0.724
Weight	1.031	(0.999-1.062)	0.052
Marital status	0.458	(0.222-0.942)	**0.034**
Residence	1.741	(1.101-2.754)	**0.018**
Education	1.376	(0.947-2.000)	0.094
Employment	1.366	(0.363-5.140)	0.644
Substance abuse	1.014	(0.439-2.343)	0.975
Alcohol	1.119	(0.491-2.549)	0.790
Medical history			
Treatment duration	1.071	(1.027-1.116)	**0.001**
Type of bipolar disorder	0.863	(0.563-1.3230)	0.499
Hypertension records	5.882	(2.191-15.787)	< **0.001**
Diabetic records	6.783	(1.822-25.254)	**0.004**
Anxiety	1.295	(0.528-3.175)	0.572
Thyroid records	12.308	(1.077-140.639)	**0.043**
Other co-morbidities	5.145	(1.864-14.202)	**0.002**
Quetiapine	2.9894	(1.157-7.726)	**0.024**
Duration of quetiapine use	0.3909	(0.159-0.959)	**0.040**
Risperidone	1.6222	(0.496-5.303)	0.423
Chlorpromazine	1.9290	(0.819-4.546)	0.133
Duration of chlorpromazine use	0.542	(0.255-1.152)	0.111
Haloperidol	0.564	(0.249-1.280)	0.171
Duration of haloperidol use	1.861	(0.871-3.974)	0.109
Family diabetes records	1.156	(0.130-10.279)	0.897
Family other co-morbidity records	0.815	(0.096-6.890)	0.851
Body mass index measured	1.034	(0.951-1.124)	0.437
Body mass index category	1.360	0.892-2.072)	0.153
Systolic hypertension	1.123	(1.080-1.167)	< **0.001**
Heart rate	2.412	(1.029-5.654)	**0.043**

4.6 THE PREVALENCE AND RISK FACTORS FOR MOVEMENT DISORDERS

A movement disorder is the second major desired outcome in this study. Different predictors were used to describe the risk factors and these included: the socio-demographic characteristics and the clinical characteristics of the participants. Five tools were used to assess the disorders. The following five major disorders were observed among the participants as follows parkinsonism (54%), akathisia (89.9%), dystonia (46%), dyskinesia (78.8%), neuromuscular syndrome (68.3%) and catatonia (82.5%) as shown in Table 4.15, 4.16, 4.17

4.6.1 Comparison of Quick Motor Assessment Part I.

Several quick motor variables were assessed and the results were shown in Table 4.15. Out of all patients assessed, a high percentage (41.3%) exerted hypomania, could be normal (poker) facial expression with majority being MRH in-patients. However, there was no statistical significant difference in facial expression between the facilities. Most patients at MRH in-patient were mildly slow, slurred and dysphonic in speech (50.5%) constituting 49.2% of total study participants. High prevalence in moderately slow speech was exhibited by KNH participants (20%), while more severely slow speech was exhibited by MRH in-patient (4.9%). There was no statistical difference across the two facilities as regards speech (p= 0.606) (Table 4.15).

Nearly 60% of participants showed slight and infrequently present tremor at rest. Over 76% reported no increased sex drive but around 3.2% reported very much increased, mostly across KNH and MRH in-patient, 4% and 3.9%, respectively. Nearly 60% of participants reported mildly impaired finger tap task and about 1% hardly could perform the task with majority being out-patients.

There was a statistically significant differences between the two sites with regard to ocular motor dysfunction (p=0.024) the most prevalent being abnormal ocular motor sign showed by 20% at KNH and 11.1% across all participants. There was high prevalence of slight action tremor of small amplitude (A) that did not interfere with finger pointing (B) at MRH in-patients(51.5%) and 42.3% of all participants. This finding was statistically significance across the sites (p= 0.033) and one participant at MRH in-patient exhibited severe amplitude (A) with finger pointing impossible (B).

Regarding leg agility, there was statistically significance differences across sites (p=0.003). The most prevalent was the mildly impaired leg agility at 24.9% for all constituting 32% of KNH out-patients and a 1.1% of MRH in-patient who could hardly perform the task. There was a normal heel knee shin test by 85.7% of participants with the majority MRH in-patients. Mildly and severely dysmetric and ataxic were at 17.5% and 1%, respectively. The KNH out-patients (16%) were only found moderately dysmetric and ataxic. This gave a statistical significant difference across the sites (p=0.002).

Table 4.15: Quick Motor Assessment Part I results

VARIABLE	KNH OUT-PATIENT	MATHARI OUT-PATIENT	MATHARI IN-PATIENT	TOTAL	P-Value
Facial Expression					
Minimal hypomimia, could be normal (poker face)	7(28%)	23(37.7%)	48(46.6%)	78(41.3%)	
Slight but definitely abnormal diminution of facial expression.	2(8%)	5(8.2%)	12(11.7%	19(10%	
Moderate hypomimia; lips parted some of the time.	0	1(1.6%)	2(1.9%)	3(1.6%)	0.509
Masked or fixed faces with severe or complete loss of facial expression, lips parted inch or more.	0	0	1(1%)	1(0.5%)	
Speech					
Mildly slow, slurred, and/ or dysphonic. No need to repeat statements	11(44%)	30(49.2%)	52(50.5%)	93(49.2%)	
Moderately slow, slurred, and/ or dysphonic. Sometimes asked to repeat statements.	5(20%)	7(11.5%)	16(15.5%)	28(14.8%)	
Severely slow, slurred, and/ or dysphonic, frequently asked to repeat statements.	1(4%)	1(1.6%)	5(4.9%)	7(3.7%)	0.606
Unintelligible	0	0	3(2.9%)	3(1.6%)	
Ocular Motor dysfunction					
One abnormal ocular motor sign.	5(20%)	4(6.6%)	12(11.7%)	21(11.1%)	
Two abnormal ocular motor signs.	3(12%)	0	4(3.9%)	7(3.7%)	**0.024**
Tremor at rest					
Slight and infrequently present.	9(36%)	45(73.8%)	59(57.3%)	113(59.8%)	
Mild in amplitude and persistent. Or moderate in amplitude, but only intermittently present.	3(12%)	4(6.6%)	13(12.6%)	20(10.6%)	
Moderate in amplitude and present most of the time.	1(4%)	3(4.9%)	5(4.9%)	9(4.8%)	0.073
Marked in amplitude and present most of the time.	1(1%)	0	2(1.9%)	3(1.6%)	
Action Tremor					
Slight tremor of small amplitude (A). No interference with finger pointing (B).	7(28%)	20(32.8%)	53(51.5%)	80(42.3%)	
Moderate amplitude (A). Some interference with finger pointing (B).	2(8%)	3(4.9%)	11(10.7%)	16(8.5%)	
Marked amplitude (A). Marked interference with finger pointing (B).	0	2(3.3%)	5(4.9%)	7(3.7%)	**0.033**
Severe amplitude (A). Finger pointing impossible (B).	0	0	1(1%)	1(0.5%)	
Increased Tone					
Slight or detectable only when activated by mirror or other movements.	9(36%)	20(32.8%)	42(40.8%)	71(37.6%)	
Mild to moderate.	1(4%)	2(3.3%)	13(12.6%)	16(8.5%)	
Marked, but full range of motion easily achieved.	0	1(1.6%)	5(4.9%)	6(3.2%)	0.090

Severe, range of motion achieved with difficulty.	1(4%)	2(3.3%)	0	3(1.6%)	
Rapid alternating movements of hands					
Mildly impaired	7(28%)	16(26.2%)	48(46.6%)	71(37.6%)	
Moderately impaired.	0	0	1(1.9%)	2(1.1%)	0.064
Severely impaired.	0	1(1.6%)	3(2.9%)	4(2.1%)	
Leg agility					
Mildly impaired.	8(32%)	9(14.8%)	30(29.1%)	47(24.9%)	
Moderately impaired	5(20%)	1(1.6%)	4(3.9%)	10(5.3%)	**0.003**
Severely impaired.	0	0	1(1.9%)	2(1.1%)	
Can barely perform the task.	0	0	2(1.9%)	2(1.1%)	
Finger taps					
Mildly impaired.	13(52%)	40(65.6%)	59(57.3%)	112(59.3%)	
Moderately impaired	2(8%)	8(13.1%)	16(15.5%)	26(13.8%)	0.319
Severely impaired.	0	2(3.3%)	5(4.9%)	7(3.7%)	
Can barely perform the task.	1(4%)	1(1.6%)	0	2(1.1%)	
Heel knee shin test					
Normal	19(76%)	60(98.4%)	83(80.6%)	162(85.7%)	
Mildly dysmetric and ataxic	4(16%)	1(1.6%)	18(17.5%)	23(12.2%)	
Moderately dysmetric and ataxic.	2(8%)	0	0	2 (1.1%)	**0.002**
Severely dysmetric and ataxic.	0	0	1 (1%)	1 (0.5%)	
Can barely perform the task.	0	0	1 (1%)	1 (0.5%)	
Arising from chair					
Normal.	11 (44%)	17 (27.9%)	30 (29.1%)	58 (30.7%)	
Clumsy, or may need more than one attempt.	12 (48%)	38 (62.3%)	59 (57.3%)	109 (57.7%)	
Pushes self-up from arms of seat.	2 (8%)	5 (8.2%)	11 (10.7%)	18 (9.5%)	0.782
Tends to fall back and may have to try more than once but can get up without help.	0	1 (1.6%)	1 (1%)	2 (1.1%)	
Unable to arise without help.	0	0	2 (1.9%)	2 (1.1%)	
Posture					
Normal.	17(68%)	36(59%)	47(45.6%)	100(52.9%)	
Not quite erect slightly stooped posture; could be normal for older person.	7(28%)	20(32.8%)	47(45.6%)	74(39.2%)	
Moderately stooped posture, definitely abnormal; can be slightly leaning to one side.	1(4%)	4(6.6%)	8(7.8%)	13(6.9%)	0.427
Severely stooped posture with kyphosis; can be moderately leaning to one side.	0	1 (1.6%)	1 (1%)	2 (1.1%)	

Body sway					
Normal.	20 (80%)	55 (90.2%)	82 (79.6%)	157 (83.1%)	
Slight body sway and/or retropulsion with unaided recovery.	4 (16%)	4 (6.6%)	18 (17.5%)	26 (13.8%)	
Moderate body sway and/or deficient postural response; might fall if not caught by examiner.	1 (4%)	2 (3.3%)	2 (1.9%)	5 (2.7%)	0.510
Severe body sway. Very unstable. Tends to lose balance spontaneously.	0	0	1(1%)	1(0.5%)	
Gait					
Normal.	21(84%)	48(78.7%)	46(44.7%)	115(60.9%)	
Mildly impaired.	4(16%)	11(18%)	50(48.5%)	65(34.4%)	
Moderately impaired. Walks with difficulty, but requires little or no assistance.	0	2(3.3%)	6(4.2%)	8(4.2%)	**< 0.001**
Severely impaired. Requires assistance.	0	0	1 (1%)	1 (0.5%)	

Almost 61%, of participants showed a normal gait while the most prevalent abnormality at 34.4% of participants, being mildly impaired gait comprising 48.5% of MRH in-patients. Only 0.5% (mostly from MRH) was severely impaired and required assistance showing a statistically significant difference across the sites (p=< 0.001).

Upon pooling each participant's score of the various variables in the tool, the total aggregate scores were categorized into either normal (8-14 score) or abnormal (0-7 score). The results are summarized in Table 4.16. The most frequent total score was 5 (11.1%), closely followed by 6 (10%). These are in abnormal category. There was no statistically significant difference of association across two hospitals (p=0.299).

Table 4.16 Participants aggregate scores of Quick Motor Assessment Part I

Aggregate Score per participant	KNH OUT-PATIENT	MRH OUT-PATIENT	MRH IN-PATIENT	TOTAL	P-value
1	0	0	4 (3.9%)	4(2.1%)	
2	2(8%)	2(3.3%)	10(9.7%)	14(7.4%)	
3	1(4%)	2(3.3%)	11(10.7%)	14(7.4%)	
4	1(4%)	5(8.2%)	4(3.9%)	10(5.3%)	
5	2(8%)	6(9.8%)	13(12.6%)	21(11.1%)	
6	1(4%	6(9.8%)	12(11.7%)	19(10%)	0.299
7	3(1)2%)	7(11.5%)	6(5.8%)	16(8.5%)	
8	2(8%)	1(1.6%)	6(5.8%)	9(4.8%)	
9	1(4%)	4(6.6%)	6(5.8%)	11(5.8%)	
10	3(12%)	8(13.1%)	8(7.8%)	19(10%)	
11	2(8%)	6(9.8%)	5(4.9%)	13(6.9%)	
12	2(8%)	10(16.4%)	6(5.8%)	18(9.5%)	

13	1(4%)	3(4.9%)	1(1%)	5(2.7%)	
14	3(12%)	1(1.6%)	8(7.8%)	12(6.4%)	
Overall abnormality score from the quick motor assessment I					
Normal (8-14);	14(56%)	33(54.1%)	40(38.8%)	87(46%)	0.093
Abnormal (0-7)	11(44%)	28(45.9%)	63(61.2%)	102(54%)	

4.6.2. Assessment by Quick Motor Assessment Part II test

This part of quick motor test consisted of assessing four motor activity items including dysarthria, chorea, tongue protrusion and muscle tone. It is an assessment often used to determine the neuroleptic syndrome and dystonia. The results are summarized in Table 4.17.

Table 4.17: Results of Quick Motor Assessment Part II

VARIABLE	KNH OUT-PATIENT	MATHARI OUT-PATIENT	MATHARI IN-PATIENT	TOTAL	P-Value
Dysarthria					
Minimal (present but completely comprehensible, or speech easily understood).					
	7(28%)	11(18%)	27(26.2%)	45(23.8%)	
Mild (< than 25% of the speech is incomprehensible, or some difficulty in understanding speech).					
	2(8%)	2(3.3%)	6(5.8%)	10(5.3%)	
Moderate (25–50% of the speech is incomprehensible, or marked difficulty in understanding speech).					
	0	0	1 (1%)	1 (0.5%)	0.669
Severe (more than 50% of speech is incomprehensible).					
	0	0	2 (1.9%)	2 (1.1%)	
Chorea					
Minimal (action chorea, or intermittent rest chorea).					
	5(20%)	6(9.8%)	20(19.4%)	31(16.4%)	
Mild (continuous rest chorea, but without functional impairment).					
	0	2(3.3%)	4(3.9%)	6(3.2%)	
Moderate (continuous rest chorea with partial functional impairment)					
	0	0	1(1%)	1(0.5%)	
Severe (continuous rest chorea with complete functional impairment.)					
	0	0	3(2.9%)	3(1.6%)	
Tongue protrusion					
Can hold tongue protruded for more than 1 minute					
	15(60%)	4(6.6%)	26(25.2%)	45(23.8%)	
Can hold tongue protruded for more than 30 seconds					
	5(20%)	0	26(25.2%)	9(4.8%)	
Can hold tongue protruded for more than 10 seconds					
	0	2(3.3%)	2(1.9%)	4(2.1%)	
Can hold tongue protruded for less than 10 seconds					**< 0.001**
	0	2(1.9%)	5(4.9%)	5(2.7%)	
Cannot protrude tongue	5(20%)	55(90.2%)	66(64.1%)	126(66.7%)	
Muscle tone					
Minimal decrease (not apparent when the contralateral limb is simultaneously moved)					

	8(32%)	23(37.7%)	46(44.7%)	77(40.7%)	
Mild decrease (apparent even when the contralateral limb is simultaneously moved, but without functional impairment)					
	2(8%)	5(8.2%)	7(6.8%)	14(7.4%)	
Moderate decrease (apparent even when the contralateral limb is simultaneously moved and with functional impairment)					0.443
	0	0	2(1.9%)	2(1.1%)	
Severe decrease (loss of postural tone)					
	0	0	4(3.9%)	4(2.1%)	

The most common category exhibited in dysarthria was the minimal presentation (present but completely comprehensible, or speech easily understood) at 28% among KNH out-patients and 23.8% of all participants seen. In mild category there was 8% at KNH out-patient and 5.3% of total. Only MRH in-patients presented moderate and severe condition of dysarthria at 0.5% and 1.1%, respectively although this was not statistically significantly (p-value= 0.669). A large proportion of total participants could not protrude their tongue (66.7%) with 90.2% of MRH out-patients exhibiting this trait giving a statistically significant difference across the 3 sites. Considering the quick motor severity index, there were 29.1% of participants that could be categorized to be in severe quick motor abnormality category**.** This obtained through multinomial logistic regression analysis achieved by STATA version.

The distribution of motor severity is presented in Figure 6. This histogram obtained by analyzing the summary of total quick motor in detail, there was difference in mean and median percentile, we draw a normal histogram which show us cut off point should lay between10-20. But by analyising the total quick motor in detail gave the upper limit 16 which was used to determine the severity. Due to abnormal distribution there was calculated by 100/16 of the normal value.

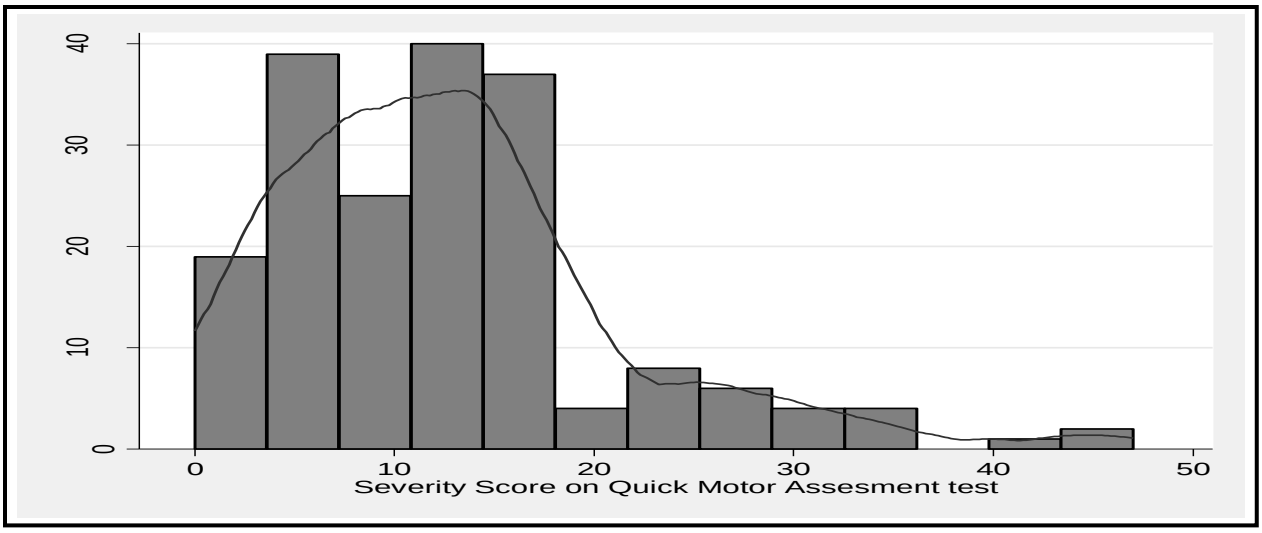


Figure 5 Histogram of severity in quick motor assessment test part I and part II results.

4.6.3 Logistic Regression for risk factors for Quick Motor Assessment

The logistic regression analysis was done to identify the risk factors for quick motor assessment results obtained. The results are displayed in Table 4.18.

A statistically significance difference (p=0.004) across the sites (in-patient versus out-patient) with the quick motor assessment was noted. In-patients were three times more likely as out-patients to get problems associated with the quick motor assessment. In addition, there was positive association with regard gender with males twice as likely as females to have the quick motor movement disorders assessed. There were several other risk factors identified for movement disorders according to the quick motor assessment, some with positive association. These include age (OR 1.03; 95% CI 1.007-1.054; p=0.011), employment status (OR 0.925; 95%CI 1.139-12.424; p=0.030) and the type of medication the participant was taking. Some of the first generation antipsychotic medications identified are risperidone (OR 0.119; 95%CI0.016-0.917; p=0.041), chlorpromazine tablets (OR 2.092; 95%CI 1.041-4.203; p=0.038), chlorpromazine injection (OR 2.282; 95%CI 1.013-5.142; p=0.046), haloperidol tablets (OR 2.032; 95%CI 1.065-3.877; p= 0.031) and generally antipsychotic drugs as a group (OR 1.419; 95%CI 1.073-1.875; p= 0.014). Presence of low blood pressure was also shown to be a possible risk factor (OR 2.392; 1.026-5.574; p=0.043).

Table 4.18 Logistic Regression for risk factors for Quick Motor scores

VARIABLE	OR	95%CI	p-value
In-patient vs. outpatient	2.666	(1.36-5.23)	**0.004**
Gender	1.983	(1.02-3.86)	**0.044**
Age	1.030	(1.007-1.054)	**0.011**
Weight	1.006	(0.979-1.033)	0.46
Marital status	0.925	(0.552-1.551)	0.768
Residence	0.749	(0.479-1.172)	0.206
Education	0.978	(0.729-1.311)	0.881
Employment status	3.763	(1.139-12.424)	**0.030**
Substance abuse	1.318	(0.690-2.520)	0.403
Alcohol takes	1.330	(0.700-2.530)	0.384
Medications			
Amitriptyline	0.971	(0.356-2.650)	0.955
Aripiprazole	3.424	(0.740-15.840)	0.115
Risperidone	0.119	(0.016-0.917)	**0.041**
Chlorpromazine	2.092	(1.041-4.203)	**0.038**
Haloperidol	2.032	(1.065-3.877)	**0.031**
Benzodiazepine	1.880	(0.990-3.570)	0.054
Antipsychotics	1.419	(1.073-1.875)	**0.014**
Chlorpromazine inject	2.282	(1.013-5.142)	**0.046**
Fluphenazine injection	1.724	(0.916-3.245)	0.092
Mood stabilizer group	1.833	(0.981-3.424)	0.057
Glibenclamide	7.673	(0.780-75.450)	0.081
Low blood pressure	2.392	(1.026-5.574)	**0.043**

4.6.4 LUNSERS Self-Administered tool assessment.

The LUNSER tool, which is self- administered by the patient is mostly useful to detect medication side effects and adverse effects. The assessment is based on medications effect on five aspects including those leading to dermatological /systemic skin (8 items), hormonal imbalance (5 items), central nervous system (9 items), medical conditions (6 items); movement disorders(21 items) as outlined in Tables 4.19 -4.22.

4.6.4.1 Comparison for Effect on Dermatological conditions (Skin and Systemic)

The largest number (27.5%) of participants reported very little itch skin. Only 4.8% reported very much itching and these were MRH out-patients. There was a statistically significant difference between the two facilities (p=0.044) (Table 4.19) with regards to itchy skin. Also there were significant differences with flushing of face (p= <0.001).

The majority of participants (30.2%) reporting itching effects reported very little itching most notable being amongst of MRH out- patients (42.6%).

Table 4.19: Dermatological effects (Systemic, Skin)

VARIABLE	KNH OUT-PATIENT	MATHARI OUT-PATIIENT	MATHARI IN-PATIENT	TOTAL	P-Value
Itchy skin:					
Not at all	12(48%)	10(16.4%)	18(17.5%)	40(21.2%)	
Very little	5(20%)	19(31.2%)	28(27.2%)	52(27.5%)	
A little	3(12%)	17(27.9%)	27(26.2%)	47(24.9%)	
Quite a lot	3(12%)	14(23%)	24(23.3%)	41(21.7%)	
Very much	2(8%)	1(1.6%)	6(5.8%)	9(4.8%)	**0.044**
Sensitivity to sun:					
Not at all	21(84%)	33(54.1%)	69(67%)	123(65.1%)	
Very little	2(8%)	16(26.2%)	18(17.5%)	36(19.1%)	0.156
A little	1(4%)	7(11.5%)	8(7.8%)	16(8.5%)	
Quite a lot	0	5(8.2%)	7(6.8%)	12(6.4%)	
Very much	1(4%)	0	1(1%)	2(1.1%)	
Flushing of face					
Not at all	11(44%)	25(41%)	71(68.9%)	107(56.6%)	
Very little	8(32%)	26(42.6%)	23(22.3%)	57(30.2%)	< **0.001**
A little	3(12%)	9(8.7%)	9(8.7%)	21(11.1%)	
Quite a lot	3(12%)	1(1.6%)	0	4(2.1%)	
Greasy skin:					
Not at all	2(8%)	5(8.2%)	14(13.6%)	21(11.1%)	
Very little	0	4(6.6%)	7(6.8%)	11(5.8%)	
A little	8(32%)	7(11.5%)	14(13.6%)	29(15.3%)	0.111
Quite a lot	13(52%)	42(68.9%)	67(65.1%)	122(64.6%)	
Very much	2(8%)	3(4.9%)	1(1%)	6(3.2%)	
New or unusual skin marks:					
Not at all	17(68%)	60(98.4%)	84(81.6%)	161(85.2%)	
Very little	5(20%)	1(1.6%)	11(10.7%)	17(9%)	
A little	1(4%)	0	1(1%)	2(1.1%)	**0.033**
Quite a lot	1(4%)	0	3(2.9%)	4(2.1%)	
Very much	1(4%)	0	4(3.9%)	5(2.7%)	
Dry mouth:					
Not at all	14(56%)	15(24.6%)	47(45.6%)	76(40.2%)	
Very little	5(20%)	22(36.1%)	18(17.5%)	45(23.8%)	
A little	3(12%)	12(19.7%)	17(16.5%)	32(16.9%)	**0.044**
Quite a lot	3(12%)	6(9.8%)	15(14.6%)	24(12.7%)	
Very much	0	6(9.8%)	6(5.8%)	12(6.4%)	
Chilblains:					
(Not at all	24(96%)	53(86.9%)	89(86.4%)	166(87.8%)	**0.009**
Very little	1(4%)	7(11.5%)	12(11.7%)	20(10.6%)	
A little	0	1(1.6%)	2(1.9%)	3(1.6%)	
Rash:					
Not at all	14(56%)	21(34.4%)	34(33%)	69(36.5%)	0.127
Very little	8(32%)	30(49.2%)	37(35.9%)	75(39.7%)	
A little	2(8%)	8(13.1%)	20(19.4%)	30(15.9%)	
Quite a lot	0	2(3.3%)	8(7.8%)	10(5.3%)	
Very much	1(4%)	0	4(3.9%)	5(2.7%)	

Nearly 65% of participants reported quite a lot of greasy skin with no statistical difference across the sites (p=0.11). There was 'very much new or unusual skin marks' at KNH (4%) and at MRH in-patients (3.9%). Over 40% reported no dry mouth effects whilst 'very much dry mouth' effects (6.4%) were reported by MRH out-patients.

4.6.4.2 Comparison for Effects leading to Hormonal Imbalance

The effects assessed that could arise from hormonal imbalance were reported and these included

Table 4.20: Comparative Hormonal Imbalance effects

VARIABLE	KNH OUT-PATIENT	MATHARI OUT-PATIENT	MATHARI IN-PATIENT	TOTAL	P-Value
Increased sex drive:					
(Not at all	15(60%)	47(77.1%)	82(79.6%)	144(76.2%)	
Very little	3(12%)	8(13.1%)	8(7.8%)	19(10%)	0.349
A little	5(20%)	5(8.2%)	8(7.8%)	18(9.5%)	
Quite a lot	1(4%)	0	1(1%)	2(1.1%)	
Very much	1(4%)	1(1.6%)	4(3.9%)	6(3.2%)	
Reduced sex drive:					
Not at all	12(48%)	23(37.7%)	69(67%)	104(55%)	
Very little	4(16%)	8(13.1%)	19(18.5%)	31(16.4%)	
A little	4(16%)	11(18%)	11(10.7%)	26(13.8%)	**< 0.001**
Quite a lot	4(16%)	10(16.4%)	2(1.9%)	16(8.5%)	
Very much	1(4%)	9(14.8%)	2(1.9%)	12(6.4%)	
Difficulty in achieving climax					
Not at all	14(56%)	56(91.8%)	80(77.7%)	150(79.4%)	
Very little	1(4%)	3(4.9%)	10(9.7%)	14(7.4%)	
A little	8(32%)	1(1.6%)	12(11.7%)	21(11.1%)	
Quite a lot	0	0	1(1%)	1(0.5%)	**< 0.001**
Very much	2(8%)	1(1.6%)	0	3(1.6%)	
Periods less frequent					
Not at all	19(76%)	44(72.1%)	95(92.2%)	158(83.6%)	
Very little	4(16%)	9(14.8%)	8(7.8%)	21(11.1%)	
A little	2(8%)	3(4.9%)	0	5(2.7%)	**0.006**
Quite a lot	0	4(6.6%)	0	4(2.1%)	
Very much	0	1(1.6%)	0	1(0.5%)	
Period problem in female					
Not at all	18(72%)	46(75.4%)	93(90.3%)	157(83.1%)	
Very little	7(28%)	10(16.4%)	7(6.8%)	24(12.7%)	
A little	0	4(6.6%)	2(1.9%)	6(3.2%)	**0.036**
Quite a lot	0	1(1.6%)	1(1%)	2(1.1%)	
Lack of emotions:					
Not at all	5(20%)	4(6.6%)	13(12.6%)	22(11.6%)	
Very little	5(20%)	2(3.3%)	10(9.7%)	17(9%)	
A little	3(12%)	6(9.8%)	12(11.7%)	21(11.1%)	**< 0.001**
Quite a lot	9(36%)	7(11.5%)	7(6.8%)	23(12.2%)	
Very much	3(12%)	42(68.9%)	61(59.2%)	106(56.1%)	

increased sex drive, reduced sex drive, difficulty in achieving climax, less frequency of periods and lack of emotions. These are outlined in Table 4.20.

Over 76% reported no increased sex drive but around 3.2% reported much increase mostly those from KNH and MRH in-patients. About 55% was reported to have no reduced sex drive but 6.4% reported very much reduced sex drive. There was a statistically significant difference across the sites reporting ($p< 0.001$). About 79.4% participants reported no difficulty in achieving climax, but only 0.5% reported quite a lot difficulty in achieving climax.

Around 84% reported no less frequent periods but only 0.5% reported quite a lot less periods frequency and this was found to show a statistically significant difference across the two facilities($p=0.006$). Over 83% reported no effects on periods with a statistically significant difference across facilities ($p=0.036$).

About 56.1% of participants reported very much lack of emotions with statistically significant difference across the facilities $p<0.001$(Table 4.20).

4.6.4.3 Comparison for Effects on the Central Nervous System

This part deals with medication effects on central nervous system including increased dreaming, difficulty in concentrating, getting to sleep, remembering things and staying awake during the day as well as sleeping too much, tension, depression and restlessness (Table 4.21). Around 51% of participants reported a little increased dreaming which was statistically insignificant across facilities $p=0.330$. Over 52% reported a little difficulty in concentrating with a statistically significant difference between the facilities ($p= 0.026$). A significant statistical difference across the patient categories was with 'very much difficulty in getting sleep' (Over 60%, $p=0.020$). Almost 53% reported a little difficulty in remembering things, but 8% reported very much difficulty in remembering things mostly affecting KNH out-patients and there was no statistically significance difference across the two facilities ($p=0.437$). About 50% reported no difficulty staying awake during the day. Over 61% reported no sleeping too much but a 3.9% at MRH out-patient reported 'too much' sleeping.

About 36% of all participants reported very much tension; KNH out-patient mostly reported a little tension (40%) while 41% MRH out-patients experienced very much tension. Over 73%

reported being very much depressed and this cut across all categories of patients (p=0.278). Similarly, over 62% reported very much restlessness which was similar across all classes.

Table 4.21: Effect on Central Nervous System

VARIABLE	KNH OUT-PATIENT	MATHARI OUTPATIENT	MATHARI IN-PATIENT	TOTAL	P-Value
Increased dreaming					
Not at all	4(16%)	5(8.2%)	9(8.7%)	18(9.5%)	0.330
Very little	4(16%)	6(9.8%)	24(23.3%)	34(18%)	
A little	12(48%)	33(54.1%)	51(49.5%)	96(50.8%)	
Quite a lot	3(12%)	14(23%)	12(11.7%)	29(15.3%)	
Very much	2(8%)	3(4.9%)	7(6.8%)	12(6.4%)	
Difficulty in concentrating					
Not at all	1(4%)	3(4.9%)	14(13.6%)	18(9.5%)	
Very little	7(28%)	2(3.3%)	10(9.7%)	19(10.1%)	
A little	10(40%)	37(60.7%)	52(50.5%)	99(52.4%)	**0.026**
Quite a lot	6(24%)	18(29.5%)	24(23.3%)	48(25.4%)	
Very much	1(4%)	1(1.6%)	3(2.9%)	5(2.7%)	
Difficulty in getting to sleep:					
Not at all	1(4%)	3(4.9%)	10(9.7%)	14(7.4%)	
Very little	2(8%)	5(8.2%)	12(11.7%)	19(10.1%)	
A little	3(12%)	7(11.5%)	12(11.5%)	22(11.6%)	**0.020**
Quite a lot	8(32%)	2(3.3%)	11(10.7%)	21(11.1%)	
Very much	11(44%)	44(72.1%)	58(56.3%)	113(59.8%)	
Difficulty in remembering things:					
Not at all	2(8%)	2(3.3%)	10(9.7%)	14(7.4%)	
Very little	4(16%)	9(14.8%)	11(10.7%)	24(12.7%)	
A little	13(52%)	33(54.1%)	54(52.4%)	100(52.9%)	0.437
Quite a lot	4(16%)	17(27.9%)	23(22.3%)	44(23.3%)	
Very much	2(8%)	0	5(4.9%)	7(3.7%)	
Difficulty staying awake during the day:					
Not at all	14(56%)	20(32.8%)	61(59.2%)	95(50.3%)	
Very little	6(24%)	20(32.8%)	22(21.4%)	48(25.4%)	
A little	2(8%)	13(21.3%)	12(11.7%)	27(14.3%)	0.082
Quite a lot	1(4%)	6(9.8%)	5(4.9%)	12(6.4%)	
Very much	2(8%)	2(3.3%)	3(2.9%)	7(3.7%)	
Sleeping too much					
Not at all	18(72%)	24(39.3%)	74(71.8%	116(61.4%)	
Very little	2(8%)	17(27.9%)	15(14.6%)	34(18%)	
A little	3(12%)	10(16.4%)	7(6.8%)	20(10.6%)	
Quite a lot	2(8%)	7(6.8%)	7(6.8%)	16(8.5%)	**0.003**
Very much	0	3(4.9%)	0	3(1.6%)	
Tension:					
Not at all	3(12%)	2(3.3%)	9(7.4%	14(7.4%)	
Very little	3(12%)	2(3.3%)	8(7.8%)	13(6.9%)	
A little	10(40%)	11(18%)	16(15.5%)	37(19.6%)	0.056
Quite a lot	4(16%)	21(34.4%)	33(32%)	58(30.7%)	

Very much	5(20%)	25(41%)	37(35.9%)	67(35.5%)	
Depression:					
Not at all	2(8%)	1(1.6%)	3(2.9%)	6(3.2%)	
Very little	4(16%)	4(6.6%)	12(11.6%)	20(10.6%)	
A little	1(4%)	3(4.9%)	13(12.6%)	17(9%)	0.278
Quite a lot	2(8%)	2(3.3%)	4(3.9%)	8(4.2%)	
Very much	16(64%)	51(83.6%)	71(68.9%)	138(73%)	
Restlessness:					
Not at all	4(16%)	2(3.3%)	7(6.8%)	13(6.9%)	
Very little	3(12%)	1(1.6%)	9(8.7%)	13(6.9%)	
A little	3(12%)	4(6.6%)	8(7.8%)	15(7.9%)	0.174
Quite a lot	4(16%)	9(14.8%)	17(16.5%)	30(15.9%)	
Very much	11(44%)	45(73.8%)	62(60.2%)	118(62.4%)	

4.6.4.4 Comparison for Effects on movement and related Medical Conditions

The comparison across the two facilities showed statistically significant differences in some effects across the sites like shakiness ($p < 0.001$); slowing of movement ($p= 0.002$); part of the body moving on its own ($p < 0.001$) and over wet or drooling mouth ($p= 0.015$) (Table 4.22).

Table 4.22: Effects on movement and related Conditions

VARIABLE	KNH OUT-PATIENT	MATHARI OUT-PATIENT	MATHARI IN-PATIENT	TOTAL	P-Value
Shakiness:					
Not at all	8(32%)	3(12%)	24(23.3%)	35(18.5%)	
Very little	7(28%)	8(13.1%)	34(33%)	49(25.9%)	
A little	6(24%)	27(44.3%)	29(28.2%)	62(32.8%)	
Quite a lot	2(8%)	19%)	11(10.7%)	32(16.9%)	**< 0.001**
Very much	2(8%)	4(6.6%)	5(4.9%)	11(5.8%)	
Slowing of movement:					
Not at all	14(56%)	9(14.8%)	26(25.2%)	49(25.9%)	
Very little	3(12%)	7(11.5%)	21(20.4%)	31(16.4%)	
A little	4(16%)	23(37.7%)	32(31.1%)	59(31.2%)	
Quite a lot	3(12%)	20(32.8%)	16(15.5%)	39(20.6%)	**0.002**
Very much	1(4%)	2(3.3%)	8(7.8%)	11(5.8%)	
Part of the body moving on their own accord. E.g. foot moving up and down					
Not at all	10(40%)	3(4.9%)	34(33%)	47(24.9%)	
Very little	5(20%)	31(50.8%)	52(50.5%)	88(46.6%)	
A little	6(24%)	23(37.7%)	13(12.6%)	42(22.2%)	
Quite a lot	1(4%)	4(6.6%)	0	5(2.7%)	**< 0.001**
Very much	3(12%)	0	4(3.9%)	7(3.7%)	
Muscle spasms:					
Not at all	10(40%)	37(60.7%)	66(64.1%)	113(59.8%)	
Very little	8(32%)	17(27.9%)	32(31.1%)	57(30.2%)	
A little	4(16%)	4(6.6%)	4(3.9%)	12(6.4%)	0.067
Quite a lot	1(4%)	1(1.6%)	1(1%)	3(1.6%)	
Very much	2(8%)	2(3.3%)	0	4(2.1%)	
Over wet or drooling mouth:					
Not at all	9(36%)	18(29.5%)	32(31.1%)	59(31.2%)	
Very little	8(32%)	18(29.5%)	19(18.5%)	45(23.8%)	**0.015**
A little	6(24%)	12(19.7%)	10(9.7%)	28(14.8%)	
Quite a lot	0	4(6.6%)	5(4.9%)	9(4.8%)	

Very much	2(8%)	9(14.8%)	37(35.9%)	48(25.4%)	
Muscle stiffness:					
Not at all	16(64%)	32(52.5%)	49(47.6%)	97(51.3%)	
Very little	7(28%)	24(39.3%)	39(37.9%)	70(37%)	
A little	194%)	2(3.3%)	12(11.7%)	15(7.9%)	
Quite a lot	0	1(1.6%)	0	1(0.5%)	0.447
Very much	1(4%)	2(3.3%)	3(2.9%)	6(3.2%)	

Over 33% reported a little shakiness led by MRH out-patient (44.3%). About 25.9% reported no slowing of movement, 31.2% a little slowing movement and only 5.8% reported very much slowing movement led by MRH in-patients (7.8%.). Over 47% reported very little part of the body moving on their own while 12% KNH out-patient reported very much of such movement. Over 31.2% reported no over wet or drooling mouth but 25.4% reported very much over wet or drooling mouth led by 35.9% of MRH in-patients (Table 4.22).

Over 60% reported no muscle spasm while 51.3% reported no muscle stiffness. There was statistically no significant difference in muscle spasms (p=0.067, 0.447. respectively) across the categories of participants.

4.6.4.5. Comparison of Effects of medications LUNSERS of the participants

This part included risk factors predictors for signs and symptoms of the participants who took bipolar disorder medications. Table 4.23 described in detail.

Over 37% reported very little increased sweating led by 50.8% of MRH out-patient and was statistically significance difference across facilities (p=0.001). About 2.7% reported very much hair loss with statistically significant difference across the facilities. Over 5.8% reported very much headache.

Almost 56.6% reported very little diarrhea led by MRH (out and in-patients), giving a statistical significance difference across the facilities (p<0.001). Over 50% reported very little difficulty in passing water that had a statistically significant difference across the two facilities. There was a little dizziness was reported in 33.9% of participants. Over 41% reported a little pins and needles feeling and 4.2% very much pins and needles led by 24% of KNH out-patients (p<0.001).

There was either very little weight loss (15.9%) or very little putting on weight (14.3%). Only 2.1% reported very much putting on weight led by 8 % exhibited in KNH out-patients. About

4.8% reported very much feeling sick led by 16% at KNH out-patient giving a statistically significant difference across facilities (p<0.001).

Table 4.23: Effects of medications from LUNSERS

VARIABLE	KNH OUT-PATIENT	MATHARI OUT-PATIENT	MATHARI IN-PATIENT	TOTAL	P-Value
Runny Nose:					
Not at all	19(76%)	27(44.3%)	59(57.3%)	105(55.6%)	
Very little	4(16%)	24(39.3%)	29(28.2%)	57(30.2%)	
A little	1(4%)	8(13.1%)	11(10.7%)	20(10.6%)	
Quite a lot	1(4%)	0	2(1.9%)	3(1.6%)	0.194
Very much	0	2(3.3%)	2(1.9%)	4(2.1%)	
Increased sweating:					
Not at all	6(24%)	3(4.9%)	24(23.3%)	33(17.5%)	
Very little	13(52%)	17(27.9%)	40(38.8%)	70(37%)	
A little	4(16%)	31(50.8%)	26(25.2%)	61(32.3%)	
Quite a lot	1(4%)	10(16.4%)	9(8.7%)	20(10.6%)	**0.001**
Very much	1(4%)	0	4(3.9%)	5(2.7%)	
Hair loss:					
Not at all	21(84%)	44(72.1%)	85(82.5%)	150(79.4%)	
Very little	3(12%)	8(6.8%)	7(6.8%)	18(9.5%)	
A little	1(4%)	7(11.5%)	7(6.8%)	15(7.9%)	
Quite a lot	0	0	1(1%)	1(0.5%)	0.689
Very much	0	2(3.3%)	3(3.3%)	5(2.7%)	
Headaches:					
Not at all	4(16%)	4(16%)	19(18.5%)	27(14.3%)	
Very little	4(16%)	4(16%)	24(23.3%)	40(21.2%)	0.391
A little	10(40%)	10(40%)	44(42.7%)	86(45.5%)	
Quite a lot	4(16%)	4(16%)	11(10.7%)	25(13.2%)	
Very much	3(12%)	3(12%)	5(4.9%)	11(5.8%)	
Diarrhea:					
Not at all	14(56%)	2(3.3%)	30(29.1%)	46(24.3%)	< **0.001**
Very little	9(36%)	46(75.4%)	52(50.5%)	107(56.6%)	
A little	1(4%)	7(11.5%)	14(13.6%)	22(11.6%)	
Quite a lot	1(4%)	4(6.6%)	3(2.9%)	8(4.2%)	
Very much	0	2(3.3%)	4(3.9)	6(3.2%)	
Difficulty passing water:					
Not at all	10(40%)	8(13.1%)	42(40.8%)	60(31.8%)	**0.009**
Very little	9(36%)	37(60.7%)	48(46.6%)	94(50%)	
A little	4(16%)	13(21.3%)	9(8.7%)	26(13.8%)	
Quite a lot	1(4%)	1(1.6%)	0	2(1.1%)	
Very much	1(4%)	2(3.3%)	4(3.9%)	7(3.7%)	
Dizziness:					
Not at all	3(12%)	3(12%)	22(21.4%)	28(14.8%)	
Very little	12(48%)	12(48%)	29(28.2%)	55(29.1%)	**0.004**
A little	8(32%)	8(32%)	35(34%)	64(33.9%)	
Quite a lot	1(4%)	1(4%)	15(14.6%)	36(19.1%)	

Very much	1(4%)	1(4%)	2(1.9%)	6(3.2%)	
Swollen or tender chest:					
Not at all	18(72%)	40(65.6%)	75(72.8%)	133(70.4%)	0.094
Very little	3(12%)	15(24.6%)	22(21.4%)	40(21.2%)	
A little	4(16%)	5(8.2%)	2(1.9%)	11(5.8%)	
Quite a lot	0	1(1.6%)	4(3.9%)	5(2.7%)	
Constipation:					
Not at all	18(72%)	58(95.1%)	93(90.3%)	169(89.4%)	0.136
Very little	4(16%)	2(3.3%)	6(5.8%)	12(6.35%)	
A little	2(8%)	1(1.6%)	2(1.9%)	5(2.7%)	
Quite a lot	1(4%)	0	1(1%)	2(1.1%)	
very much	0	0	1(1%)	1(0.5%)	
Urine darker than usual:					
Not at all	9(36%)	34(55.7%)	57(55.3%)	100(52.9%)	0.387
Very little	15(60%)	25(41%)	45(43.7%)	85(45%)	
A little	1(4%)	1(1.6%)	1(1%)	3(1.6%)	
Quite a lot	0	1(1.6%)	0	1(0.5%)	
Painful joints:					
Not at all	13(52%))	8(13.1%)	37(35.9%)	58(30.7%)	**0.02**
Very little	4(16%)	22(36.1%)	31(30.1)	57(30.2%)	
A little	5(20%)	19(31.2%)	24(23.3%)	48(25.4%)	
Quite a lot	3(12%)	9(14.1%)	7(6.8%)	19(10.1)	
Very much	0	3(4.9%)	4(3.9%)	7(3.7%)	
Passing a lot of water:					
Not at all	16(64%)	27(44.3)	56(54.4%)	99(52.4%)	
Very little	6(24%)	24(39.3)	33(32%)	63(33.3%)	
A little	1(4%)	9(14.8%)	10(9.7%)	20(10.6%)	0.424
Quite a lot	2(8%)	1(1.6%)	3(2.9%)	6(3.2%)	
Very much	0	0	1(1%)	1(0.5%)	
Pins and needles:					
Not at all	5(20%)	10(16.4%)	22(21.4%)	37(19.6%)	< **0.001**
Very little	5(20%)	15(24.6%)	29(28.2%)	49(25.9%)	
A little	6(24%)	29(47.5%)	42(40.8%)	77(40.7%)	
Quite a lot	3(12%)	6(9.8%)	9(8.7%)	18(9.5%)	
Very much	6(24%)	1(1.6%)	1(1%)	8(4.2%)	
Losing weight:					
Not at all	18(72%)	29(47.5%)	75(72.8%)	122(64.6%)	0.062
Very little	5(20%)	15(24.6%)	10(9.7%)	30(15.9%)	
A little	1(4%)	11(18%)	13(12.6%)	25(13.2%)	
Quite a lot	0	3(4.9%)	3(2.9%)	7(3.7%)	
Very much		3(4.9%)	2(1.9%)	5(2.7%)	
Putting on weight					
Not at all	13(52%)	39(63.9%)	74(71.8%)	126(66.7%)	0.245
Very little	4(16%)	9(14.8%)	14(13.6%)	27(14.3%)	
A little	2(8%)	8(13.1%)	8(7.8%)	18(9.5%)	
Quite a lot	4(16%)	4(6.6%)	6(5.8%)	14(7.4%)	
Very much	2(8%)	1(1.6%)	1(1%)	4(2.1%)	
Tiredness:					
Not at all	1(4%)	5(8.2%)	15(14.6%)	21(11.1%)	0.192
Very little	12(48%)	25(41%)	34(33%)	71(37.6%)	
A little	3(12%)	18(29.5%)	35(34%)	56(29.6%)	
Quite a lot	5(20%)	7(11.5%)	13(12.6%)	25(13.2%)	

Very much	4(16%)	6(9.8%)	6(5.8%)	16(8.5%)	
Neck muscles aching:					
Not at all	19(76%)	56(91.8%)	79(76.7%)	154(81.5%)	0.174
Very little	2(8%)	3(4.9%)	11(10.7%)	16(8.5%)	
A little	4(16%)	2(3.3%)	10(9.7%)	16(8.5%)	
Quite a lot	0	0	3(2.9%)	3(1.6%)	
Very much	0	0	0	0	
Feeling sick					
Not at all	4(16%)	51(83.6%)	36(35%)	91(48.2%)	
Very little	2(8%)	2(3.3%)	23(22.3%)	27(14.3%)	
A little	11(44%)	5(8.2%)	27(26.2%)	43(22.8%)	**< 0.001**
Quite a lot	4(16%)	23.3%)	13(12.6%)	19(10.1%)	
Very much	4(16%)	1(1.6%)	4(3.9%)	9(4.8%)	
Blurred vision:					
Not at all	6(24%)	13(21.3%)	27(26.2%)	46(24.3%)	
Very little	6(24%)	22(36.1%)	39(37.9%)	67(35.5%)	**0.015**
A little	6(24%)	23(37.7%)	32(31.1%)	61(32.3%)	
Quite a lot	6(24%)	3(4.9%)	3(2.9%)	12(6.4%)	
Very much	1(4%)	0	2(1.9%)	3(1.6%)	
Weak fingernails:					
Not at all	13(52%)	12(19.7%)	45(43.7%)	70(37%)	
Very little	6(24%)	28(45.9%)	45(43.7%)	79(41.8%)	
A little	4(16%)	14(23%)	10(9.7%)	28(14.8%)	
Quite a lot	2(8%)	5(8.2%)	3(2.9%)	10(5.3%)	**0.007**
Very much	0	2(3.3%)	0	2(1.1%)	
Palpitations:					
Not at all	3(12%)	3(4.9%)	17(16.5%)	23(12.2%)	
Very little	10(40%)	7(11.5%)	6(5.8%)	23(12.2%)	**< 0.001**
A little	4(16%)	3(4.9%)	10(9.7%)	17(9%)	
Quite a lot	5(20%)	24(39.3%)	37(35.9%)	66(34.9%)	
Very much	3(12%)	24(39.3%)	33(32%)	60(31.8%)	

Similarly, there was statistically significance differences across the two facilities as regards blurred vision (p=0.015), weak fingernails (p=0.007) and palpitation (p<0.001).

4.7 ASSESSMENT OF NEUROLEPTIC SIDE EFFECTS

The LUNSERS neuroleptic-side effect rating scale measured the side effects of neuroleptic drugs obtained by participants' self-evaluation. The assessment gives the general overview of the participant's experience and reporting of the side effects. It has a 0-4 rating scale as shown in the Table 4.24.

Table 4.24 Guide Range of LUNSERS Scores Obtained from Previous Work

LUNSERS score	Percentile	Grade of side effects	Rating scale
Class one 0-7	0-5%	Very low	0
Class two 8-27	6-25%	Low	1
Class three 28-58	26-74%	Average	2
Class four 59-80	75-94%	High	3
Class five >80	95-100%	Very high	4

4.7.1 Prevalence and Severity Score of Each LUNSERS Scale

The LUNSERS side effects scores are further grouped into extrapyramidal, anticholinergic, autonomic, allergic reactions, hormonal and psychic side effects as shown in the summarized in Table 4.25.

Table 4.25 Classification of Neuroleptic Side Effects According to LUNSERS scores

Extrapyramidal (range 0-28 score)	Anticholinergic(range 0-20 score)	Autonomic (range 0-28score)
Muscle stiffness	Dry mouth	Dizziness
Slowing movement	Constipation	Feeling sick
Muscle spasm	Difficulty passing water	Palpitations
Restlessness	Blurred vision	Increased sweating
Shakiness	Passing a lot of water	Diarrhea
Parts of body moving of their own		
Over-wet or drooling mouth		

Allergic(range 0-16)	Psychic (range 0-40)	Hormonal (range 0-24)
Rash	Tension	Swollen or tender chest
Sensitivity to sun	Increased dreaming	Period problems (women)
New or unusual marks	Difficulty in concentrating	Increased sex drive
Itchy skin	Difficulty staying awake during the day	Difficulty in achieving climax
	Tiredness	Reduced sex drive
	Difficulty in remembering things	Periods less frequent (women)
	Lack of emotions	
	Depressions	
	Sleeping too much	
	Difficulty getting to sleep	

The analysis shows that the extrapyramidal side effects had the highest score of 93.1% being in the class 4 (75-94%) score 3.The possible score was 0-28 range (Table 4.26).

4.26 Prevalence for Extrapyramidal side- effects of the Participants

VARIABLE	FREQUENCY	PERCENTILE (%)
Shakiness	154	81.5
Slow movement	140	74.1
Moving body parts	142	75.1
Muscle spasm	76	40.2

Over-wet or drooling	130	68.8
Muscle stiffness	92	48.7
Restlessness	176	93.1

Percentage is the number of score over hundred. The percentile obtained from the hundred percent over the upper limit range 28 through STATA version analysis. The severity score for extrapyramidal side-effects was as presented in Table 4.27.

Table 4.27 severity score for extrapyramidal side-effects

SCORE	FREQUENCY	PERCENTILE %
1	5	2.65
2	43	22.40
3	141	74.60

The anticholinergic side-effects had higher chances of more than 59-80. The anticholinergic severity score results were as: 'not at all' -10.6%, 'mildly'- 60.9% and 'average'- 28.6% with a possible range of 0-20. The highest prevalence was 75.6 % (Table 4.28).

Table 4.28 Prevalence for Anticholinergic Side-Effects of the Participants

VARIABLE	FREQUENCY	PERCENTILE (%)
Dry mouth	113	59.8
Constipation	20	10.6
Difficulty passing water	129	68.3
Blurred vision	143	75.6
Passing a lot of water	90	47.6

The autonomic side-effects severity score had the highest score 3. The possible range was 0-20 score. The highest prevalence was 56.6% (Table 4.29).

Table 4.29 Prevalence for Autonomic Side-Effects of the Participants

VARIABLE	FREQUENCY	PERCENTILE (%)
Dizziness	64	33.9
Feeling sick	43	22.8
Palpitation	66	34.9
Increasing sweating	70	37
Diarrhoea	107	56.6

The highest allergic side-effects score result was 3 for 'not at all' response with a prevalence of 85.2% for new or unusual marks, and a possible range score of 0-16 (Table 4.30).

Table 4.30 Prevalence for Allergic Side-Effects of the Participants

VARIABLE	FREQUENCY	PERCENTILE (%)
Rash	75	39.7
Sensitivity to sun	123	65
Itchy	52	27.5
New or unusual marks	161	85.2

The hormonal side-effects severity score prevalence was 45.5% score 2 (mildly). The possible range was 0-24. Table 4.31 described in detail the severity percentile score for hormonal side-effects. The contents included into this part are all hormonal side-effects as described in Table 4.26 above.

Table 4.31 Distribution of severity Score for Hormonal Side-Effects

SCORE	FREQUENCY	PERCENTILE (%)
1	58	30.7
2	86	45.5
3	45	23.8

The psychic side-effects severity score gave a prevalence of 73.5% (Table 4.32) with a severity score of 2. The possible range was 0-40. These contents were described in Table 4.26. On logistic regression cancelled almost all risk factor predictors.

Table 4.32 Psychic Side-Effects Severity Score of the Participants.

SCORE	FREQUENCY	PERCENTILE (%)
1	48	25.4
2	139	73.5
3	2	1.06

4.7.2 Validation According To LUNSERS Scale of the Participants

From LUNSER Scale previous study there was two classes for validation of neuroleptic side-effects, these were red herring and miscellaneously groups. Table 4.33 summarizes the validation assessment data for neuroleptic side effects. These data were just picked from the different prevalence's Tables with the components. The reference used from LUNSERS validation. The validation and results as described in Table 4.33. Still there were challenges if the patient felt and some are really the side effects of other drugs the non-antipsychotics, however, this is not final

say because of their really clinical and general conditions they had. These were just self-feeling of the participants for one previous month before study performed.

Table 4.33: Validation Assessment of Neuroleptic Side-Effects.

VARIABLE	FREQUENCY	PERCENTAGE (%)
Runny nose	85	45
Chilblains	23	12.2
Dark urine than usual	89	47.1
Painful joints	131	69.3
Neck aching	35	18.5
Finger nails weakness	119	63
Flushing face	82	43.4
Greasy skin	168	88.9
Mouth ulcers	98	51.9
Hair loss	39	20.6
Possible range 0-40		
Miscellaneous		
Headaches		
Losing weight		
Putting on weight		
Pins and needles		

The neuroleptic drugs have proven effectiveness for reducing psychotic symptoms but may be associated with many side effects such as movement disorder and metabolic disorders. The LUNSERS tool has used by different studies and its scales validated relative to the self-evaluation reports.

4.7.3 Logistic Regression for Neuroleptic Side-Effects

The logistic regression analysis of the relationship between the different types of side effects and the various risk factors was carried to explore any association between the two.

4.7.3.1 The Association between the LUNSERS scores and Extrapyramidal Side-Effects

The logistic regression between the extrapyramidal side-, as obtained from participant's LUNSERS tool responses and the various risk factors is presented in Table 4.34.The analysis covers the demographic and clinical characteristics as well as those aspects related to the assessment of the movement and metabolic disorders.

Almost all socio-demographic variables were not statistically significantly associated as risk factors, except residence of the participant. Most of the clinical characteristics were statistically

insignificantly associated risk factors except the use of bromazepam, nifedipine and Zolpidem showed a positive association with extrapyramidal side-effects. Across other groups only few risk factors had related positive association with extrapyramidal side-effects. The other variables with a positive association are difficulty in remembering things, tension, depression, tiredness, severity of akathisia and subjective distress related to restlessness.

Table 4.34: Logistic Regression for Extrapyramidal Side-Effects of the Participants.

VARIABLE	OR	95%CI	p-value
Marital status	0.181	(0.026-1.241)	0.082
Residence	0.297	(0.101-0.874)	**0.027**
Bromazepam	0.022	(0.001-0.349)	**0.007**
Zolpiderm	0.022	(0.001-0.349)	**0.007**
Nifedipine	0.078	(0.006-0.969)	**0.047**
Lack of emotions	1.909	(0.895-4.071)	0.094
Difficulty getting sleep	2.172	(0.972-4.855)	0.059
Difficulty in remembering	9.063	(1.460-56.253)	**0.018**
Tension	2.851	(1.091-7.452)	**0.033**
Depression	2.695	(1.122-6.475)	**0.027**
Tiredness	9.167	(1.037-81.075)	**0.002**
Palpitation	2.261	(0.913-5.599)	0.078
Subjective items for HAS	1.507	(0.976-2.328)	0.068
Severity of Akathisia	77.839	(5.835-1038.38)	**0.001**
Subjective awareness of restlessness BAS	2.310	(0.897-5.956)	0.083
Subjective distress related to restlessness	5.950	(1.549-22.861)	**0.009**

4.7.3.2 The Association between the LUNSERS scores and Autonomic Side-Effects

The logistic regression result for autonomic side effects is shown in Table 4.35. All socio-demographic variables were statistically insignificant associated with autonomic side-effects. Also the clinical variables were statistically insignificant associated with autonomic side-effects only few medications were statistically significantly associated with list medications hereutonomic side-effects. The respective drugs involved are citalopram, hydrochlorothiazide, losartan and amlodipine. The other associated risk factors are greasy skin, depression, tension, difficulty in getting sleep, increase dreaming and subjective distress.

A positive association was noted with a seven times chance of increased dreaming for those with autonomic side-effects. There was a six times subjective distress association with autonomic side-effects.

Table 4.35: Logistic Regression for Autonomic Side-Effects of the Participants.

VARIABLE	OR	95%CI	p-value
Citalopram	0.011	(0.001-0.241)	**0.004**
Hydrochlorothiazide	0.067	(0.005-0.840)	**0.036**
Losartan	0.022	(0.001-0.349)	**0.007**
Amlodipine	0.044	(0.003-0.590)	**0.018**
Greasy skin	3.300	(1.129-9.643)	**0.029**
Restlessness	1.982	(0.960-4.092)	0.064
Depression	5.010	(1.203-20.868)	**0.027**
Tension	2.851	(1.091-7.452)	**0.033**
Difficulty in remembering things	3.175	(0.947-10.645)	0.061
Difficulty getting sleep	3.431	(1.096-10.748)	**0.034**
Increase dreaming	7.119	(1.240-53.952)	**0.029**
Lack of emotions	4.234	(0.893-20.076)	0.069
Subjective distress	5.950	(1.549-22.861)	**0.009**

4.7.3.3 The Association between the LUNSERS scores and Hormonal side-effects.

The logistic regression analysis between hormonal side-effects and other risk factors are presented (Table 4.36). There was a statistically insignificantly association with most of the risk factors.

T**able 4.36 Logistic Regression for Hormonal Side-Effects of the Participants**

VARIABLE	OR	95%CI	p-value
Desvalproate	0.195	(0.043-0.883)	**0.034**
Dry mouth	2.390	(0.889-6.416)	0.084
Greasy skin	2.264	(1.294-3.961)	**0.004**
Posture	5.871	(0.760-45.364)	0.090
Pins	2.406	(1.048-5.525)	**0.038**
Dark urine than usual	6.405	(0.784-52.320)	0.083
Headache	2.177	(1.024-4.631)	**0.043**
Tension	1.872	(1.109-3.161)	**0.019**
Difficulty in remembering things	1.892	(0.903-3.962)	0.091
Clinical impression of akathisia	3.772	(0.821-17.329)	0.088
Severity of akathisia	5.428	(0.802-36.748)	0.083
Muscle stiffness	0.468	(0.273-0.801)	**0.006**
shakiness	3.675	(1.386-9.745)	**0.009**
Palpitation	1.872	(1.125-3.114)	**0.016**
Blurred vision	4.300	(1.324-13.964)	**0.015**

Only few listed variables were statistically significantly associated with hormonal side effects. Table 4.36 described. E.g. use of desvalproate (OR 0.195; 95%CI 0.043-0.883; p=0.034), a greasy skin (OR 2.264; 95%CI 1.294-3.961; p= 0.004), feeling of pins and needles (2.406; 95%CI 1.048-5.525; p= 0.038), headache (OR 2.177; 95%CI 1.024-4.631; p= 0.043), tension (OR 1.872; 95%CI 1.109-3.161;p=0.019), muscle stiffness (OR 0.468; 95%CI 0.273-0.801;

p=0.006) and experience of shakiness (OR 3.675; 95%CI 1.386-9.745; p=0.009), palpitations (OR 1.872; 95%CI 1.125-3.114; p=0.016) and blurred vision (OR 4.3; 95%CI 1.324-13.963; p=0.015).

4.7.3.4 The Association between the LUNSERS and Allergic Reactions

The result of logistic regression for allergic reactions against various variables is presented in this section. There was statistically significant strong positive association with most variables (Table 4.37).

Table 4.37: Logistic Regression for Allergic Reactions of the Participants.

VARIABLE	OR	95%CI	p-value
Identity	1.026	1.013	**<0.001**
Site facility	0.24	(0.086-0.673)	**0.007**
Chlorpromazine	7.317	(0.954-56.115)	0.056
Haloperidol	2.308	(0.887-6.007)	0.087
Benzhexol	3.782	(1.325-10.797)	**0.013**
Antipsychotics	1.793	(1.072-2.300)	**0.026**
Flupenthixol injection	3.081	(0.871-10.898)	0.081
Antipsychotic injections	1.784	(0.966-3.296)	0.065
Bromazepine	0.057	(0.005-0.657)	**0.022**
Nifedipine	0.184	(0.041-0.835)	**0.028**
Neurobion	0.125	(0.038-0.408)	**0.001**
Other drugs	0.336	(0.155-0.728)	**0.006**
Blood pressure	0.203	(0.066-0.666)	**0.009**
Weight	0.951	(0.921-0.983)	**0.003**
Body mass index	0.895	(0.824-0.972)	**0.009**
Tremor at rest	2.488	(1.170-5.291)	**0.018**
Action tremor	2.237	(1.028-4.870)	**0.042**
Finger taps	2.012	(0.986-4.107)	0.055
Posture	2.440	(0.996-5.976)	0.051
Tongue protrusion	2.121	(1.551-2.901)	**<0.001**
Muscle tone	1.951	(0.902-4.220)	0.090
Greasy skin	1.62	(1.119-2.346)	**0.011**
Dry mouth	2.273	(1.266-4.081)	**0.006**
Mouth ulcers	7.445	(1.918-28.909)	**0.004**
Lack emotions	1.721	(1.283-2.310)	**<0.001**
Difficulty in concentration	1.548	(0.969-2.472)	0.068
Difficulty getting sleep	1.377	(1.016-1.865)	**0.039**
Difficulty in remembering things	1.973	(1.202-3.237)	**0.007**
Difficulty staying awake during day	1.778	(0.984-3.214)	0.057
Tension	1.618	(1.145-2.286)	**0.006**
Restlessness	1.522	(1.121-2.067)	**0.007**
Runny	2.662	(1.095-6.472)	**0.031**
Increase sweating	2.922	(1.581-5.402)	**0.001**
Headache	1.484	(0.944-2.332)	0.087
Diarrhea	22.78	(6.362-81.563)	**<0.001**
Difficulty passing water	2.043	(1.025-4.073)	**0.042**
Dizziness	2.150	(1.300-3.557)	**0.003**
Weight off	1.989	(0.945-4.186)	0.070

Tiredness	1.552	(0.968-2.489)	0.068
Finger nails weak	3.493	(1.536-7.945)	**0.003**
Palpitation	1.840	(1.324-2.555)	**<0.001**
Shakiness	2.150	(1.321-3.501)	**0.002**
Slowing movement	2.730	(1.624-4.589)	**<0.001**
Moving body part	6.135	(2.542-14.804)	**<0.001**
Over wet or drooling	2.135	(1.314-3.469)	**0.002**
Global improvement akathisia	2.206	(1.368-3.557)	**0.001**

The strongest positive associations were against involuntary body part movements (six times), slowing movement (three times), finger nails (3.5 times) and diarrhea (twenty three times).

4.7.3.5 The Association between the LUNSERS scores and Anticholinergic Side-effects

Table 4.38: Logistic Regression for Anticholinergic Side-Effects

VARIABLE	OR	95%CI	p-value
Identification of participant	1.020	(1.006-1.035)	**0.006**
Chlorpromazine	0.329	(0.092-1.174)	0.087
Diazepam injection	0.175	(0.031-0.982)	**0.048**
Parkinsonism	0.114	(0.012-1.051)	0.055
Speech	6.230	(1.762-22.014)	**0.005**
Tremor at rest	6.56	(1.982-21.709)	**0.002**
Action tremor	3.557	(1.044-12.119)	**0.042**
Increase tone	3.001	(0.913-9.857)	0.070
Arising chair	3.316	(1.112-9.885)	**0.032**
Posture	4.391	(1.006-19.166)	**0.049**
Gait	7.032	(0.924-53.513)	0.060
Tongue protrusion	2.233	(1.423-3.505)	**< 0.001**
Itchy	2.257	(1.181-4.315)	**0.014**
Greasy skin	2.213	(1.389-3.525)	**0.001**
Mouth ulcers	4.136	(1.121-15.265)	**0.033**
Rash	4.517	(1.368-14.923)	**0.013**
Lack of emotions	1.723	(1.186-2.503)	**0.004**
Difficulty in concentration	1.649	(0.915-2.974)	0.096
Difficulty in getting sleep	1.809	(1.227-2.669)	**0.003**
Difficulty in remembering things	2.361	(1.263-4.410)	**0.007**
Difficulty in staying awake during the day	3.846	(1.037-14.267)	**0.044**
Depression	1.544	(1.036-2.300)	**0.032**
Restlessness	1.694	(1.161-2.470)	**0.006**
Headache	2.478	(1.297-4.734)	**0.006**
Severity of akathisia	2.463	(0.895-6.783)	0.081
Subjective distress	3.568	(1.980-6.430)	**<0.001**
Global improvement	1.830	(1.030-3.250)	**0.039**
Subjective awareness	1.558	(0.980-2.477)	**0.061**
Clinical impression	9.129	(2.603-32.018)	**0.001**
Over-wet or drooling	2.591	(1.205-5.573)	**0.015**
Palpitation	1.867	(1.225-2.843)	**0.004**
Shakiness	2.510	(1.282-4.917)	**0.007**
Slowing movement	1.901	(1.081-3.341)	**0.026**
Moving of body parts	2.547	(1.060-6.119)	**0.037**

The results of logistic regression for anticholinergic side-effects against investigated risk factors studied are presented (Table 4.38). Strong positive associations have been observed between the possible risk factors and the anticholinergic side-effects.
The strongest positive associations were clinical akathisia impression at a nine times chance, gait seven times, tremor at rest seven times, speech six times, rash 4.5 times, posture and difficulty staying awake during the day four times.

There was strong positive association between the risk factor predictors and the different tools to give approval for the presence of metabolic and movement disorders. Table 4.39. These were included: LUNSERS across risk factors predictors, out of fifty-one variables fifteen were shown highly relationship association: thus in sensitivity to sun (OR 1.47; 95%CI 1.038-1.935; p=0.028), unusual skin marks (OR 1.787; 95%CI 1.203-2.654; p=0.004), dry mouth (OR 1.330; 1.042-1.697; p=0.022), rash (OR 1.765; 95%CI 1.276-2.443; p=0.001), reduced sex drive (OR 0.733; 95%CI 0.551-0.976; p= 0.033), lack of emotions (OR 1.445; 95%CI 1.109-1.881; p=0.006), runny nose (OR 1.404; 95%CI 1.033-1.909; p= 0.030), diarrhea (OR 1.483; 95%CI 1.055-2.086; p= 0.023), difficulty passing water (OR 1.451; 95%CI 1.036-2.032; p=0.030), pins and needle feelings (OR 1.360; 95%CI 1.000-1.850; p= 0.050), neck aching (OR 1.924; 95%CI 1.245-2.971; p= 0.003), feeling sick (OR 1.408; 95%CI 1.096-1.810; p= 0.007), slowing movement (OR 1.612; 95%CI 1.223-2.125; p= 0.001), over wet or drooling (OR 1.820; 95%CI 1.457-2.273; p< 0.001) and muscle stiffness (OR 1.928; 95%CI 1.329-2.798; p= 0.001).

The HAS and Barnes tools were shown strong positive associations in subjective akathisia (OR 1.155; 95%CI 1.068-1.249; p< 0.001), objective akathisia (OR 1.239; 95%CI 1.107-1.387; p < 0.001), clinical impression (OR 7.044; 95%CI 2.611- 19.003; p < 0.001) and severe akathisia (OR 6.105; 95%CI 2.679- 13.910; p < 0.001).

The AIMS tool out of twelve variables, half of them gave the strongest positive associations in: muscle expression (OR 2.107; 95%CI 1.463-3.035; p < 0.001), lips (OR 5.723; 95%CI 2.756-11.886; p < 0.001), rate tongue movement (OR 3.761; 95%CI 1.697-8.334; p=0.001), upper extremities movement (OR 3.693; 95%CI 2.378-5.734; p < 0.001), lower extremities movement (OR 3.157; 95%CI 1.610- 6.196; p= 0.001) and neck (OR 6.381; 95%CI 2.844-14.320; p < 0.001).

Table 4.39 Logistic regression for risk factors across side effects and adverse events of other tools LUNSERS, Hilside Akathisia Scale [HAS], Abnormal Involuntary Movement Scale [AIMS]

VARIABLE	OR	95% CI	p-value
LUNSERS TOOL			
Itchy skin	1.256	(0.960-1.650)	0.097
Sensitivity to sun	1.417	(1.038-1.935)	**0.028**
Greasy skin	1.350	(0.960-1.900)	0.085
Unusual skin marks	1.787	(1.203-2.654)	0.004
Dry mouth	1.330	(1.042-1.697)	**0.022**
Rash	1.765	(1.276-2.443)	**0.001**
Reduced sex drive	0.733	(0.551-0.976)	**0.033**
Lack of emotions	1.445	(1.109-1.881)	**0.006**
Tension	1.281	(0.967-1.700)	0.086
Runny nose	1.404	(1.033-1.909)	**0.030**
Hair loss	1.383	(0.983-1.947)	0.063
Diarrhea	1.483	(1.055-2.086)	**0.023**
Difficulty passing water	1.451	(1.036-2.032)	**0.030**
Swollen chest	1.421	(0.940-2.151)	0.096
Pain joints	1.300	(0.981-1.720)	0.068
Pins	1.360	(1.000-1.850)	**0.050**
Neck aching	1.924	(1.245-2.971)	**0.003**
Feeling sick	1.408	(1.096-1.810)	**0.007**
Palpitation	1.250	(0.973-1.600)	0.081
Slowing movement	1.612	(1.223-2.125)	**0.001**
Moving body parts	1.375	(0.992-1.906)	0.056
Over wet or drooling	1.820	(1.457-2.273)	< **0.001**
Muscle stiffness	1.928	(1.329-2.798)	**0.001**
HAS TOOL			
Subjective akathisia	1.155	(1.068-1.249)	< **0.001**
Objective akathisia	1.239	(1.107-1.387)	< **0.001**
Clinical impression	7.044	(2.611-19.003)	< **0.001**
Severe akathisia	6.105	(2.679-13.910)	< **0.001**
AIMS TOOL			
Muscle expression	2.107	(1.463-3.035)	< **0.001**
Lips	5.723	(2.756-11.886)	< **0.001**
Jaw	3.830	(1.898-7.730)	< **0.001**
Rate tongue	3.761	(1.697-8.334)	**0.001**
Upper extremities	3.693	(2.378-5.734)	< **0.001**
Lower extremities	3.157	(1.610-6.196)	**0.001**
Neck	6.381	(2.844-14.320)	< **0.001**
Severe abnormality	2.008	(1.470-2.744)	< **0.001**
Incapacitation	4.537	(2.192-9.391)	< **0.001**
Patient awareness	1.717	(1.255-2.347)	**0.001**
Teeth	0.378	(0.125-1.151)	0.087
Group participants	2.025	(1.213-3.378)	**0.007**

CHAPTER FIVE DISCUSSION

Bipolar disorder is a complicated and chronic illness which requires continuous medical care as well as routine monitoring of the prevalence of risk factors for metabolic and movement disorders arising from medications used.

This study was conducted in government teaching hospitals- KNH and MRH which are within Nairobi city. The prevalence and risk factors for metabolic and movement disorders of bipolar disorder management were determined. Through logistic regression analysis, statistical relationship between medications used and the study outcomes were determined. The strength of such relationships through associations among the metabolic and movement disorders was determined.

This study attempts to prove that individuals with bipolar disorder have a higher prevalence of movement and metabolic disorders arising from the type of antipsychotic medicines used. This study has been ascribed by Quick motor assessment tool, Hilside Akathisia Scale [HAS], Abnormal Involuntary Movements Scale [AIMS], LUNSERS and Autonomic Scale by Physical examinations.

5.2 Differences in the socio-demographic characteristics of patients with bipolar disorders across facilities

There was male predominance at 57.7% as also been revealed by previous studies on mental illness (Katayi *et al*., 2016; Jalloh *et al*., 2016; Wageck *et al*., 2018) but in contrast to other studies that showed female predominance (Manson *et al*., 1990; Mathew *et al*., 2005; Bebbington *et al*., 2011, Silarova *et al*., 2015). There more males with bipolar disorders due to their psychological nature, aggressive behavior and social lifestyle. Majority were single (53.4%) more than half of the participants because of social pressure, escaping family responsibilities and psychiatric illness (Katayi *et al*. 2016; Jalloh *et al* 2016; Wageck *et al*., 2018). Unlike our study, a stud done by Fiedorowicz *et al*., (2008), found that most participants were married.

The median and interquartile age of the study participants was 36 [28, 48] years, meaning more than 84% were young adults in their productive age. The high prevalence of bipolar disorder amongst the young meant that they could not perform their social obligations well. Our study

had a mixture of in and out-patients, a study done by Ndetei *et al*., (2008), found that out-patients present with less severe illness compared to in-patients. This could explain why the in-patients in MRH tended to be divorcees and to report substance abuse.

Almost 92% of the participants were not employed. The in-patients stated that lack of the employment caused excessive worry and they used abusing drugs and an alcohol as are coping mechanisms. The overall prevalence of substance abuse and alcohol consumption was 35.5 and 37% respectively. Other studies have reported a high prevalence of drug abused among psychiatric patients (Jalloh *et al*, 2016, Raikou *et al*, 2017, Jadhay *et al*., 2017, Elamin *et al*., 2017). Lack of regular income may contribute to mental illnesses. Improved in economic status may improve situation.

Patients in KNH had higher level of education and therefore are respected to have a better understanding of their disease conditions and interventions as have been demonstrated by a study done by Silarova *et al*., (2015).

There was a statistically significantly difference in the age, marital status and gender distribution across the two hospitals. Nearly all the divorced participants were in-patients at Mathari. The prevalence of substance use was highest among in-patients of Mathari with nearly a third (35.5%) having a history of substance use. The out-patients at KNH had the lowest prevalence substance use. The previous supported study done by (Pettoruso *et al*., 2014) Most of the patients at MRH are the referral cases from KNH; given that males tend to have more severe disease and more likely to abuse substances, this could have accounted for a differences in socio-demographic characteristics in the two facilities.

Type 3 and 4 bipolar disorders were only diagnosed in MRH (Table 4.2). These types are less severe and do not require hospitalization. The previous supported studies done by (Busby *et al*., 2010, Slomkaa *et al*., 2012, Rao et al., 2016). This stated by previous supported study done by Busby *et al*., (2010) that type I and type II bipolar disorders were more prone to be hospitalized by having pre-mature mortality because of suicidal and comorbid illnesses.

5.3 Patterns of medication use amongst patients with bipolar disorder

The cumulative use of antipsychotic drugs was greater than that of antidepressants (95.8%, 29.1%, respectively). There were 112 (59.6%) participants taking 2 or more antipsychotic drugs

(Table 4.3). Most in-patients in MRH were on at least 2 antipsychotics (58.8%) as compared to 32% of out-patients.

There were 5 in-patients in MRH on 5 or 6 antipsychotics**.** The most frequently used antipsychotic drug was haloperidol (51%). The differences in pattern of use of this drug was statistically significant different across the three arms, (p=0.002). Olanzapine was the third most widely used antipsychotic agent with no statistically significant difference in the prevalence of its use across the two facilities.

Haloperidol is the first generation, in advanced countries it has been replaced by newer antipsychotics correctively known as atypical agents. Haloperidol has its major side effects of extrapyramidal symptoms and tardive dyskinesia. In Kenya the use of first generation antipsychotics seems to be declined because previous studies show that chlorpromazine and olanzapine were widely used. The previous supported studies done by (Hildrum *et al*., 2007, Fiedorowicz *et al*., 2009, Brown *et al.*, 2013, Kelbrick *et al*., 2014, Silaronova *et al*., 2015, Bond *et al*., 2017, Wageck *et al*., 2018).

Hazard associated with antipsychotics increase adverse effects especially extrapyramidal symptoms and elevated prolactine levels particularly with resperidone; it also increases metallic taste and prevalence of cardiovascular disease and metabolic syndromes.

Polypharmacy was more prevalence at MRH. This is supported by the previous study done by Jeon et al., 2017.

5.4 Prevalence and risk factors of Metabolic Disorders among the Participants

5.4.1 Obesity

Overall 14.8% cumulatively were overweight or obese. Majority of the patients were underweight with body mass index of less than twenty percentages, the prevalence were 59.8%. This prevalence is important because many studies place emphasis on obesity in psychiatric patients in this context wasting is more prevalence. Previous study done by Suguwala *et al*., (2015) ’17 studies have 6.2% prevalence; and one of the studies had 17% underweight. The other previous supported studies done by (Hildrum *et al*., 2007, Fiedorowicz *et al*., 2009, Slomkaa *et al.*, 2012, Brown *et al*., 2013, Kelbrick *et al*., 2014, Silaronova *et al*., 2015, Bond *et al*., 2017, Wageck *et al*., 2018).

The prevalence of underweight was much higher than those reported the highest was 17%. This observation may be attributed to the fact that seen in MRH is from low social economics status where malnutrition is prevalence. A study done by Fiedorowicz *at al*., (2008) found a higher number of underweight participants in patients with bipolar disorder attributed this to tardive dyskinesia which compromised the tendency to eat. This means that underweight patients probably should be investigated thoroughly for tendencies of tardive dyskinesia. The previous supported studies done by (Hildrum *et al*., 2007, Fiedorowicz *et al*., 2009, Slomkaa *et al*., 2012, Brown et al., 2013, Kelbrick *et al*., 2014, Silaronova *et al*., 2015, Bond *et al*., 2017, Wageck *et al*., 2018).

The prevalence of weight increase was much lower than that reported by Katayi et al., 2016. The study done by Katayi reported prevalence of 54.4% and this study conducted in general psychiatric at MRH. The differences in the prevalence could be attributed to the differences profile of patients studied. It has been reported with patients with depression tend to have low weights. The previous supported studies done by (Hildrum *et al*., 2007, Fiedorowicz *et al*., 2009, Brown *et al*., 2013, Kelbrick *et al*., 2014, Silaronova *et al*., 2015, Bond *et al*., 2017,Wageck *et al*., 2018).

In our study we find no clear positive association between body mass index and medications used. However, the most prominent risk factors for body mass index were clinical site where patients in KNH had higher body mass index compare to those seen in MRH. Given that patients seen at KNH were more educated and more likely to use atypical antipsychotics. Obesity in this group of patients may be attributed to better nutritions or atypical antipsychotic drugs. More studies may be required for determinants of body mass index in the two referral hospitals.

5.4.2 Hypertension

From the patients records 21 patients out of 189 (11.1%) had pre-existing diagnosis of hypertension. So the prevalence of hypertension differ in these sites, the prevalence was highest among patients seen at KNH (36%), the prevalence was lowest at MRH (4.9%).

On measuring the blood pressure 34.4% patients had systolic hypertension with highest prevalence been in KNH (56%). The prevalence of isolated hypertension was 18%.

On logistic regression the most important risk factors was age, weight, type of facility, treatment duration and diabetes mellitus. These are known risk factors for hypertension and renal failure. With regard to the medications there was positive association between systolic hypertension with use of atypical agents' aripiprazole with strong odds ratio of 5.083 similary positive association between desvenlafaxine and benzodiazepines. This has been reported in previous studies (Gaebel *et al*., 2010, Ibrahim *et al*., 2011, Slomka *et al*., 2012, Smith *et al*., 2013, Stomski *et al*., 2016, Raikou *et al*., 2017). We noted negative association between use of quetiapine and haloperidol. We did not adjust for confounding. However, these associations may be have been confounded by the clinical sites as most of the atypical agents used by KNH. This study suggests there is differential propensity for difference antipsychotic agents to cause hypertension.

So, the prevalence of isolated diastolic hypertension was 14%. The risk factors were age, marital status, history of hypertension, diabetes, thyroid disease and other commorbities. This is supported by previous study done by (Grover *et al*., 2012). There were some tendencies of genetic inheritance playing a role as shown from family histories of the participant's relatives. There was highly relationship for ocular-motor dysfunction to develop the cardiovascular disease. This supported previous study done by (Silarova *et al*, 2015, Kesebir *et al*., 2016). With regard to the drugs, there was positive association between quetiapine and hypetension, as well as chlorpromazine and risperidone and hypertension. Atypical antipsychotics had been noted to cause hypertension soon after commencement of therapy. This is particularly increase if the drug is co-administered with serotonin sustained release inhibitors as reported by Dr David Coulter case study in 2003. Some guidelines state that intensive monitoring for blood pressure should be done for patients initiated on atypical agents. It is generally assumed that atypical agents have a better safety profile and therefore, they are preferred over first line drugs. There is need to educate prescribers about the possible increase risk of cardiovascular complications associated with this drug.

5.4.3 Diabetes

At inception of the study 10 patients (5.3%) have confirmed diagnosis of diabetes. This is supported by previous studies done by Fiedorowicz *et al*., 2008, Kesebir *et al*., 2016, Wageck *et al*., 2018). The highest prevalence was at KNH (8%).

5.5 Prevalence and risk factors of Movement Disorders among the Participants

The prevalent of parkinsonism was 54%. The risk factors were reduced masked faces, arm swing, slowed initiation of activities, speech, posture, and rigidity of neck. Also tremor at resting, tremor on action, focal perioral tremor, gait, over wet or hyper salivation and greasy skin. Similar previous studies done by (Mathew *et al*., 2005, El-Malakh *et al*., 2006, Carroff *et al*., 2011, Mishal *et al.*, 2016, Selfani *et al.*, 2017, Zagaria *et al*., 2018). This study had less prevalence compare with previous similar studies as stated by Mishal *et al* (2016) had 90% bipolar patients with parkinsonism. This can be reduced by stopping or switching the drug indicated, to dopamine agonist levodopa, anticholinergic drugs - trihexphenydyl, benztropine and amantadine. Also surgery is applicable especially if medications are ineffective, have deep brain stimulation effective in treating as the primary motor features of parkinsonism disease. Similar previous studies done by (Mathew *et al*., 2005, El-Malakh *et al*., 2006, Carroff *et al*., 2011, Mishal *et al.*, 2016, Selfani *et al.*, 2017, Zagaria *et al*., 2018).

The prevalence of dystonia was 46%. The risk factors were muscle spasm, muscle stiffness, head, neck, eyes, dental trauma, jaw opening, tongue protrusion, dysarthria, dysphagia, lower limbs, upper limbs, increased sex drive and reduced sex drive. This proved by previous studies done (Mathew *et al*., 2005, El-Malakh *et al*., 2006, Mishal *et al*., 2016, Caroff *et al*., 2017). This study had less prevalence as compared to the previous studies done in different places. As Caroff *et al*., (2011) reported 95% bipolar patients had dystonia; Mashal *et al*., (2016) reported (77.8%) (Above 30 years old had 91.7%) bipolar patients had dystonia.This disorder can be treated by physical therapy, speech therapy, and stretching or massage therapy. Also some medications can be used such as carbidopa-levodopa, trihexyphenidyl, benztropine, tetrabenazine, clonazepam, diazepam, and baclofen reduces neurotransmission, side-effects and drowsiness and are skeletal muscle relaxants. This supported by previuos studies done by (Mathew *et al*., 2005, El-Malakh *et al.*, 2006, Mishal *et al*., 2016).

The prevalence of dyskinesia was 78.8%. The supported previous study done by Mathew *et al*., (2005) reported there were 87% bipolar patients with dyskinesia. The risk factors were underweight, speaking, low heart rate, high heart rate, orofacial or lingual musculature, chewing or jaw or protrusion, twisting of the tongue, chorea, alcohol, substance abuse, and eye blink frequently. This supported by study done (Mathew *et al*., 2005, El-Malakh *et al*., 2006, Mishal *et*

al., 2016). This can be minimized by using the newer classes of antipsychotics, anticholinergic drugs.

The prevalence of catatonia was 82.5%. As previous supported study done by Caroff *et al*., (2011) reported 2-4% of parkinsonism in bipolar patients who had catatonia. So the prevalence of catatonia in parkinsonism was 1.2% in this study. Majority of type I and type II bipolar disorder were compromised with catatonia disorder. This study was corroborated by previous study done by Mathew *et al*., 2005. The risk factors were tremor at rest, tremor on action, anxiety, depression, difficulty in concentration, difficulty in staying awake during the day, shakiness, palpitations, moving of the body parts, and hyperactivity in mania, speech, consciousness and mutism. The previous supported study done by (Mathew *et al*., 2005, Caroff et al., 2011, Mishal *et al*., 2016). Due to the higher prevalence, further studies should do.

The prevalence of neuroleptic malignant syndrome was 0.02% of all patients taking antipsychotics. The risk factors were potentially lethal form of extrapyramidal effect, difficult passing water, increasing sweating, benzodiazepines, serious medical conditions and rapid heart rate. The previous supported studies done by (Mathew *et al*., 2005, El-Malakh *et al*., 2006, Caroff *et al*., 2011). This can be reduced or corrected by stopping the offending drugs, starting other medications but remembering to taper the dosage on withdrawing the previous medication. Dantrolene can be used to minimize the neuroleptic malignant syndrome.

The prevalence of akathisia was 89.9%. As the previous supported study done by Caroff *et al*., (2011) reported that there were 90-96% bipolar patients with akathisia. The risk factors were restlessness, age, anxiety, urge to move, sleep, sensation, tapping, shifting of weight, violence, suicide and stress. Similar study done by (Mathew *et al*., 2005, El-Malakh *et al*., 2006, Caroff *et al*., 2011, Jalloh *et al*., 2016, Mishal *et al*., 2016). This disorder can be decreased by diphenhydramine, trazodone, benztropine, mirtrazapine and beta- blockers.

5.6 Patterns of co-morbidities of psychiatric disorders among participants

Apart from metabolic and movement disorders there were other co-morbidities such as convulsion, spinal injury, schizophrenia, anxiety, stress, suicidal ideation, infections (HIV and TB), dermatological and haematological. The results found were similar with other previous

study done by (Wamukhoma 2011, Ng'ang'a 2014, O'Leary 2014, Fagilioni *et al*., 2015, Mitchell 2015, Jalloh *et al*., 2016, Ortizprado *et al*, 2017, Torok *et al*., 2017, Ruesch 2017).

5.7 The Association Risk Factors for Metabolic and Movement Disorders of the Participants.

The most positive association risk factors for metabolic and movement disorders were the in-patient against out-patients, gender, age, and employment status. This implied that most serious cases, chronic illness and relapsed bipolar disorders required hospital management. The society should support the poor families by not abandoning them in different social and financial situation. The societies and communities should recognize the presence of these participants in their home places and hospitals, each should play a role on their treatment requirements. Previous studies that supported this study activities (Manson *et al*., 1990, Mishal *et al*., 2016, Ruesch 2017, Wageck *et al*., 2018).

The identified positive risk factors association between the body mass index and metabolic disorders were study site, blood pressure diagnosis and other co-morbidities in records. Further strong positive association were observed with family history; other diseases of family history including diabetes. This implied that there was a high possibility of role of genetic traits interplay. The supported previous studies were (Manson *et al*., 1990, Fiedorowicz *et al*., 2008, Raikou *et al*., 2017, Jadhay *et al*., 2017, AHA, 2018).

There were strong positive relationship association between the body mass index and self-interviewed questionnaires by LUNSERS, the risk factors included were reduced sex drive, difficulty in climax, rash, period less frequent in women, rate tongue and twice lower movement extremities. Previous studies in agreement include those by: (Fierodowicz *et al*., 2008, Wageck *et al*., 2018). These risk factors were obesity, overweight and underweight observed in this study. Thisis similarly observed by previous studies done by Fiedorowicz *et al*., 2008, Grover *et al*., 2012, Bai *et al*., 2016, Amann *et al*., 2017, Elamin *et al*., 2017, Abaji *et al*., 2017). Observation of overweight condition could be as a result of using lithium, valproate and atypical antipsychotics. The use is also associated with dyslipidemia, diabetes mellitus and insulin resistance.

This is supported by a study done by (Fiedorowicz *et al*, 2008, Silaronova *et al*., 2015) which found that the use of lithium, valproic acid, olanzapine, clozapine contributed to obesity and metabolic syndrome in the bipolar disorder group, mainly due to the effects on appetite and glucose and lipid metabolism. This could be because of increased appetite which leads to overeating and the weight gain as observed by (Grover *et al*., 2012, Freyberg *et al*., 2017). There was also a report of cardiovascular effects such as tachycardia, bradycardia and arrhythmias amongst the participants. A previous study stated that there were factors associated with a positive coronary calcium store in patients with bipolar type1 in Brazilian Psychiatric Association, (Wageck *et al*., 2018).

There were strong positive associations between the systolic blood pressure and the in the increase in weight and age as supported by a previous study done by (Manson *et al*., 1990, " weight gain associated with clozapine, risperidone, olanzapine or quetiapine had 67% metabolic syndrome in bipolar disorder "(Fiedorowicz *et al*., 2008, Grover *et al*., 2012,). "Systolic blood pressure and diastolic blood pressure were considered significant, blood pressure increased with age" (Hildrum *et al*., 2005).

Many neurological drugs had the largest number of the impact to the participants through their inhibitory effect on the dopamine 2 receptors as earlier reported (Mishal *et al*., 2016, Jalloh *et al*., 2016). Both first and second antipsychotic generations including haloperidol, chlorpromazine and clozapine, had positive impact association in causing the extrapyramidal side effects to the patients but with the second generation having lesser side effects than first antipsychotic generation (Katayi *et al*., 2016, Anderson *et al*., 2017, Ruesch *et al*., 2017).

The management of extrapyramidal side effects also can cause other problems such as worsening psychotic symptoms, due to the drug-induced blockade of dopamine receptors leading to dopamine deficiencies induced in the corpus striatum without affinity balanced by blocking the muscarinic cholinergic receptors. Most of long acting antipsychotic injectable can cause such effects to the participants. The previous supported study done by (Mathew *et al*., 2005).

The examples of neuroleptics used to manage the bipolar disease blocking the dopamine D2 receptors include olanzapine, risperidone, pimozide, haloperidol, fluphenazine, chlorpromazine and perphenazine (Jalloh *et al*., 2016, Katayi *et al*., 2016, Shireen, 2016).

Even serotonergic drugs had been reported to induce acute dystonic reactions and tremor. Drugs such as tricyclic antidepressants and selective serotonin reuptake inhibitors, and other anti-depressants like trazodone and mirtazapine. Also tremor can be caused by lithium, cocaine and alcohol; beta-agonists, theophylline and valproic acid (Mishal *et al*., 2016, Al-Melh M A.2016) Nifedipine, tricyclic antidepressants, selective serotonin reuptake inhibitors, lithium, phenytoin, valproic acid, carbamazepine, gabapentin, lamotrigine, vigabatrin, buspirone and alcohol can produce drug-induced myoclonus (Al-Melh MA 2016). Lamotrigine can cause tics a spasmodic contraction of the muscles, most often in the face. This always indicated by twitch, spasm, convulsions, contraction, tremor and jerk. A previous study as evidenced done by (Al-Melhel, 2016).

5.8 The Implications of the Findings

The study shall facilitate to know the causes of the metabolic and movement disorders in bipolar disorder. The management of the condition and the medicines side effects, the progression of the bipolar disorder, determination of the previous goals successful or failures and detecting the gap between for future patient health-care plan. Because the problems are still there so therapeutic drug monitoring of both medications (antipsychotics, antidepressants, mood stabilizers and others) to bipolar disorder patients should be taken. Drug is a toxic substance which has its potential and risk benefits so, attention on prescribing, dispensing, counseling, good instructions and make follow-up; will help to alleviate difficulties to our kings 'patients'.

5.9 Study Limitations

The ambi-directional cross section study design was allowed information to be collected within the frame time and did not allow to make follow up of participants. Due to this condition, the results may have been over-reported or under- reported by participants although some details were obtained from the files. The study included both bipolar patients out-patients and in-patients although no inpatients from KNH were interviewed. In KNH, only patients with other medical conditions were admitted in the wards for a while before being referred to Mathari Referral Hospital for further management. The questionnaires were too long which could lead to fatigue inpatients. The measurement of fasting blood sugar and lipid profile tests would have

been desirable as good markers of metabolic conditions. These were however not performed due to financial constraints.

5.10 Conclusions

The findings showed that there was a high prevalence for metabolic and movement disorders in bipolar patients attending in Kenyatta National Hospital and Mathari Referral Hospital.

5.11 Recommendations

There being high prevalence of metabolic and movement disorders due to medications in bipolar disorder management the following should be achieved:

- Better patient management approaches should be used. More effort should be done to improve the patients' conditions by counter checking their risk factors at least every 3 to 6 months. If possible a clinical pharmacist should be involved to review the patient medications and the impact at least twice a week in every ward. Treatment changes should be instituted for those affected or liable to be affected by their current medication.
- Routine monitoring for pre-diabetes, blood sugar and lipid profile should be performed to forestall development of medication induced metabolic disorders.
- The government should review the essential drugs list to include the atypical drugs to minimize on adverse effects.
- Further research should be done to identify appropriate biochemical markers for rapid and sensitive assessment for metabolic and movement disorders in patients on treatment for bipolar disorders.

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7.0 APPENDICES:

APPENDIX A: ELIGIBILITY CHECK LIST

Code_____ **Date**_____

Title: Prevalence and risk factors for metabolic and movement disorders in patients with bipolar disorders in Kenyatta national hospital and Mathare Referral Hospital.

INCLUSION CRITERIA

Question	**YES**	**NO**
Has bipolar diagnosis in file	☐	☐
Attending psychiatric clinic and admitted in the wards	☐	☐
Aged between 18 to 70 years	☐	☐
Patient give an assent	☐	☐
Care giver give proxy assent	☐	☐
Clinician give probate assent	☐	☐

EXCLUSION CRITERIA

Question	**YES**	**NO**
Violent patient	☐	☐
Incoherent patient	☐	☐
Too depressed patient	☐	☐
Unfit to communicate	☐	☐
Others	☐	☐

APPENDIX B: **INFORMED CONSENT FORMS (English Version)**

A. CONSENT EXPLANATION

Informed consent form for participants in the research titled.

'Prevalence and risk factors for metabolic and movement disorders in patients with bipolar disorders in Kenyatta National Hospital **and Mathare Referral Hospital'**.

Principal Investigator and Institutional affiliation:

Mumello Maria Benedicta OSB. University of Nairobi.School of Pharmacy. Department of Pharmaceutics and Pharmacy Practice.

Supervisors:

1. Prof Okalebo F A. Associate Prof. Department of Pharmacology and Pharmacognosy, University Of Nairobi.
2. Dr Amugune B, Senior Lecturer. Department of Pharmaceutical Chemistry. University of Nairobi.
3. Dr Kigamwa P. Senior Lecturer. School of Medicine. Department of Psychiatry. University of Nairobi.

Title of the study: Prevalence and risk factors for metabolic and movement disorders in patients with bipolar disorders in Kenyatta National Hospital and Mathare Referral Hospital.

This informed consent form has two parts:

1. Information sheet (to share information about the study about you).
2. Certificate of consent (for signatures if you agree to participate).

You will be given a copy of the full Informed Consent Form.

Part 1: Information Sheet

Introduction

I Dr. Mumello, a post-graduate Clinical Pharmacy Student, at the University of Nairobi, Kenyatta National Hospital. I am conducting a study on bipolar patients with the risk factors of metabolic and movement disorders at Kenyatta National Hospital **and Mathare Referral**

Hospital . Bipolar disorder is a mood disorder. If not treated can lead to hazardous events. The drugs used to manage bipolar disorder can affect a patient blood sugar levels, weight and blood pressure. They can also affect the body movements. I am going to give you information and invite you to be part of this research. In this study there will be questionnaires, some quick motor assessment and measurements of blood pressure, waist circumference, body weight and height.

Purpose of the research

The objective of this study was to determine the prevalence and the risk factors for movement and metabolic disorders in patients on treatment for bipolar disorders at Kenyatta National Hospital and Mathare Referral Hospital.

Also this research was been helped for academic degree dissertation award in Clinical Pharmacy master.

Type of Research Intervention

Was the questionnaire with structured questions administered to a study participant. In this case was either the patient or caregiver depending on the condition of the patients' agreement. Also some quick motor assessment and measurement of blood pressure, body weight, height, waist circumference and body mass index were performed.

Participant selection

You were being invited to take part in this research because you were a bipolar patient, also your input was extremely valuable as the information you gave, will be used to determine prevalence and risk factors of the metabolic or movement disorders with the bipolar disorder management.

Voluntary participation or withdrawal from study

The purpose of this consent form was to give you the information. You were needed to help you to decide whether or not to participate in the study. Patient was free to ask any questions or doubt about the study which was not clear to him or her. Your choice were not interrupted your daily services from the clinic. Once you understand and agree to be part of the study, I requested you to sign your name on this form. You should understand the general principles which applied to all participants in a medical research: 1) Your decision to participate is entirely voluntary. 2) You

may withdraw from the study at any time without necessarily giving a reason for your withdrawal. 3) Refusal to participate in the research was not affected the services you were supposed to in this hospital clinic or other facilities. It was your rights as a participant to terminate the consent at any time with any dire awareness.

Study procedure: I measured your blood pressure, weight and height. You were also fill a questionnaire about your condition and treatment you were receiving. We were also assessed your muscle movement. I needed to know which drugs you are taking. I was obtaining this information from your medical file.

Benefits: You were all tests free of charge. You were got back your results. You could raised issues regarding your treatment which we could discuss free of charge. One of the benefits might be early identification and referral of patients with hypertension and /or diabetes for patients who may have had not been diagnosed already. The results we obtained were shared with your physician and any necessary referrals for disorder problems were done. The study was giving us information about your conditions and how it was managed in Kenyatta National Hospital and Mathare Referral Hospital.

Risks: no risk is expected but you were stayed for at least one hour. Your daily clinic routine was not interfered. My assistants and I were tried to make you comfortable during the interview and examination.

Reimbursements

There were no incentives, payments or gifts as a result of participating in the study**.**

Assurance of confidentiality

All the information you gave me were treated confidentially and was only be used for the purpose of the study. Your name was not used and any information about you was a code. Only the researchers knew your number and were kept the information secured and confidential. The results of this study were used to improve knowledge on how to overcome those metabolic and

movement disorders while taking medications for bipolar disorder management. The research has been approved by the KNH UON ERC by the number P 130/03/2018.

Sharing of Research Findings

During the research findings were not shared except with the primary care physician in cases of patients who were requiring further management of metabolic or movement disorders to prevent morbidity and mortality from bipolar disorder management. This was done in respecting humanity and maintaining confidentiality so as to benefit the patient. After completing the research, findings was shared through publication in a journal and in conferences so that the study findings could benefit people interested in such information.

Contact information:

In case you have any questions related to this study and regarding your right as a research volunteer, you can contact the following:

1. Mumello Maria Benedicta OSB. University of Nairobi. School of Pharmacy. Department of Pharmaceutics and Pharmacy Practice. P o Box 19676-00202.Telephone number 0736924161. mumellob@yahoo.com
2. Prof Okalebo F A. Associate Prof. University Of Nairobi. Department of Pharmacology and Pharmacognosy, Telephone number 0737 434 204. okalebof@yahoo.com
3. Dr Amugune B, Senior Lecturer. University of Nairobi. Department of Pharmaceutical Chemistry. Telephone number 0722 802 074. beatrice.amugune@uonbi.co.ke'
4. Dr Kigamwa P. Senior Lecturer. University of Nairobi. School of Medicine. Department of Psychiatry. Telephone number 0722 521 261. pkigamwa@africaonline.co.ke
5. Prof. Chindia, secretary Kenyatta National Hospital / University Of Nairobi ERC. Telephone number. Email: uon_knh erc@uonbi.ac.ke, P o Box 20723 00202 Nairobi. Tel. 2726300 Ext. 44102.

B. PARTICIPANT INFORMED CONSENT FORM (English version)

Part 2: certificate of Consent

Study title: Prevalence and risk factors for metabolic and movement disorders in patients with bipolar disorders in Kenyatta National Hospital and Mathari Referral Hospital.

Institution: Department of Pharmaceutics and Pharmacy Practice, School of Pharmacy, University of Nairobi. P. o BOX 30197-00400, Nairobi**.**

Investigator: Mumello Maria Benedicta OSB. Mobile number: 0736924161

Supervisors:

1. Prof Okalebo F A. Associate Prof. University Of Nairobi. Department of Pharmacology and Pharmacognosy, Telephone number 0737 434 204.
2. Dr Amugune B, Senior Lecturer. University of Nairobi. Department of Pharmaceutical Chemistry. Telephone number 0722 802 074.
3. Dr Kigamwa P. Senior Lecturer. University of Nairobi. School of Medicine. Department of Psychiatry. Telephone number 0722 521 261.

Ethical Approval Board:

Kenyatta National Hospital/ University of Nairobi Ethical and Research Committee, P o Box 20723 00202 Nairobi. Telephone number: 2726300 Ext. 44102.

Certificate of Consent

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with the study investigator. I have had questions answered in a language I understand. The benefits and risks have been explained to me. I understand that my participation in this study is voluntary and that it is my rights as a participant to terminate the consent at any time with any dire awareness. I freely agree to participate in this research study. I understand that all efforts will be made to keep information regarding my personal identity confidential. By signing this consent form, I have not given up any of the legal rights that I have in a research study.

I agree to participate in this research study: Yes ☐ No ☐

I agree to participate in the study of movement/metabolic disorders in bipolar diseases. I understand that I will be required to come for measurement of blood pressure, weight and waist circumference.

Yes ☐ No ☐

I agree to provide my contact information for follow up: Yes ☐ No ☐

Participant Printed Name: _____

Participant Signature _____ Date …….

If illiterate

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness_____

___

Signature of witness _____

And

Thumb stamp of participant

Date_____

A copy of this Informed Consent Form will be provided to the participant/ carer giver _____

Print the name of researcher/ person taking the consent_____

An Informed Assent Form will……..OR will not …….be completed.

Researcher's statement:

I have explained information in the consent document to the participant and encourage them to ask questions which I took time to answer. I am satisfied that the participant has adequately understood explanation regarded study purpose, procedures, benefits and risks.

Researcher's Name: _____ Date: _____

Signature _____

Role in the study: _____ [*i.e. study staff who explained informed consent form]*

For more information contact_____ at_____

From_____ to _____

Witness Printed Name (*if witness is necessary. A witness is a person mutually acceptable to both the researcher and participant)*

Name: _____ **Contact information** _____

Signature: _____ **Date**: _____

MAELEZO YA MAKUBALIANO YA KUSHIRIKI KUFANYIWA UTAFITI

Consent information Form (Swahili version)

Fomu ya habari kwa ajili ya kushiriki kwenye utafiti

Hii ni fomu ni ya wale watakaoweza kushiriki kwa utafiti wetu. Utafiti wetu unachunguza jinsi mwili unavyofanya mabadiliko ninapokunywa dawa za ugonjwa wangu wa kuwa na huzuni pia uchangamfu uliokithiri katika Hospitali ya Taifa Kenyatta na Mathare Hospitali ya Rufaa.

Mtafiti Mkuu: Mumello Maria Benedicta OSB. Chuo Kikuu Nairobi. Shule ya Famasia. Idara ya dawa na tiba ya vitendo.

Wasimamizi wangu:

1. Prof Okalebo F A. Kaimu Prof. Chuo Kikuu Nairobi. Idara ya Famakolojia na Famakognosia.
2. Dr Amugune B, Mhadhiri. Chuo Kikuu Nairobi. Idara ya Madawa na Kemia.
3. Dr Kigamwa P. Mhadhiri. Chuo Kikuu Nairobi. Shule ya Udaktari. Idara ya Ugonjwa wa Akili.

Utafiti: uchunguzi wa ukuaji na visababishi vya kufanya mabadiliko mwilini ninapokunywa dawa za ugonjwa wa kuwa na huzuni pia uchangamfu unaokithiri katika Hospitali ya Taifa ya Kenyatta**.**

Hii Fomu ina sehemu mbili

1. Fomu ya maelezo
2. Hati ya makubaliano/ mkataba au idhini

Unapewa Fomu moja ya mkataba au idhini baada ya kuijaza.

Sehemu ya kwanza: Dibaji(Maelezo/ utangulizi)

Ninaitwa Mumello Maria Benedicta OSB. Mwanafunzi wa shahada ya udhamiri katika Chuo Kikuu cha Nairobi. Ninafanya utafiti juu ya uchunguzi wa ukuaji na visababishi vya kufanya mabadiliko mwilini ninapokunywa dawa za ugonjwa wa kuwa na huzuni pia uchangamfu unaokithiri. Ugonjwa huu ni mabadiliko ya hulka (tabia) ya mwanadamu. Usipotibu kwa kutumia dawa husababisha madhara makubwa. Pia dawa zinazotumika kuutibu ugonjwa huu

huweza kusababisha sukari kupanda, uzito kuongezeka na hata kupata shinikizo la damu. Pia huleta mabadiliko katika mfumo wa kutembea.

Katika utafiti huu tutauliza maswali mbalimabali yatakayohusiana kabisa na ugonjwa huu pamoja na tiba yako bila kusahau visababishi vya mabadiliko mwilini. Pia tutawafanyia tathimini kwa weredi kuona jinsi gani mmefanikiwa au mmeanza kupata mabadiliko katika mwili yatakayoweza kuwa hatari mbeleni kwa afya zenu.

Tutafanya hivyo pale tu mkitoa idhini, ruhusa baada ya kuelewa somo na kufikia muafaka wa uamuzi bila kushurutishwa kuweka sahihi ya kushiriki utafiti huu.

Uko huru kuuliza maswali juu ya utafiti au kama sijaeleweka katika maelezo niliyoyatoa. Pia unaruhusiwa kumuona mtalaam yeyote au kuuliza maswali juu ya utafiti huu kabla hujatia sahihi ya kushiriki utafiti huu.

Lengo la utafiti: kwa nini tunaafanya utafiti huu?

Lengo ni kutathimini hasa ukuaji au kuongezeka kwa shida nyingine zamabadiliko ya mifumo ya mwili na mwendo hata kushindwa kutembea au kujimudu kuafanya kazi, na kutaka kujua nini zaidi kinasababisha ninapokunywa dawa za ugonjwa wa kuwa na huzuni pia uchangamfu unaokithiri katika Hospitali ya Taifa ya Kenyatta**.**Utafiti huu utasaidia kupunguza shida za kushindwa kutembea, kuongezeka sukari mwilini au mafuta, shinikizo la damu na kuzuia kuongezeka uzito wa mwili kwa haraka.

Sifa za kujiunga na utafiti:

Ni wale wanaoumwa ugonjwa wa mabadiliko ya hulka au tabia yaani kuwa na huzuni au uchungu au fikra nzito sana na papo hapo kuwa na furaha sana au nguvu nyingi sana au hasira sana, na ambao tayari wametumia dawa zaidi ya miezi sita katika Hospitali ya Taifa ya Kenyatta na Mathare Hospitali ya Rufaa. Kwa wale wanaokuja kuhudhuria kliniki na kurudi nyumbani bila kulazwa.

Je ni lazima kujiunga na utafiti huu?

La hasha**.** Hushurutishwi hata kidogo. Uamuzi wa kujiunga ni wa hiari na tutaupa heshima na taadhima. Hata ukijiunga bado una nafasi ya kubadili mawazo yako bila kudaiwa au kubughudhiwa na yeyote.

Namna gani utafiti utafanyika?

Baada ya kukubaliana kuwa utashiriki katika utafiti. Tutakupa maswali na tutaomba uyajibu, na kama utakuwa na tatizo lolote la kusoma au kuandika tutakusaidia, na kwa wale wanaoshindwa kabisa kuongea ndugu au daktari wako atasaidia kujibu ili mradi uwe umeridhia kwa moyo kushiriki utafiti huo.

Pamoja na kumfanyia tathimini mgonjwa kwa baadhi ya vipimo kama shinikizo la damu, namna ya kutembea, kuongea na kupimwa uzito na mzunguko wa kiuno. Huu utafiti ni wa zaidi ya saa moja, na ni mara moja tu.

Madhara gani yatatokea kwa atakayeshiriki?

Hakuna madhara yoyote atakayopata mshiriki utafiti. Labda kukaa kwa ya saa moja. Lakini tutajitahidi kufanya haraka, kwa ustadi na kwa uangalifu mkubwa bila kukudhuru kwa aina yoyote.

Faida gani itapatikana kutokana na utafiti?

Utafiti huu utaweza kuwa na manufaa pale ambapo mgonjwa akiwa na aina zote za mabadiliko ya mwili na mwendo bila mwenyewe kujua, kwani ataanzishiwa dawa za kuzuia mwendelezo wa mabadiliko pia atapewa wataalam kadiri ya tatizo lilojulikana. Atapewa ushauri wa namna ya kuendelea kunywa dawa, mazoezi na hatalipa hata hela kwa huduma hizo zote. Katika utafiti huu huduma ni bure, kuuliza maswali na kujibiwa bure.

Pia utafiti huu utasaidia wagonjwa wengine wa baadaye, kwani kutokana na ushiriki wako mzuri na kutoa taarifa sahihi, zitasaidia watalaam, wanasayansi na madaktari wengine kuboresha matibabu mazuri yenye tija.

Je!kuna msaada wowote au malipo kutokana na utafiti huu?

Ni kutoa shukrani zetu kwa kukubali kwako kushiriki utafiti huu**.** Tunatambua mchango wako mkubwa katika ushiriki wako wa utafiti huu, kwani utakuwa umesaidia wengi wasio na idadi hapa Kenya na hata penginepo. Nawe pia ni mtaaluma katika utafiti huo. Juu ya pesa au chochote zaidi ya huduma hakitakuweko.

Je! Sitaanikwa nje habari zangu?

Hata kidogo hatutatoa nje utafiti huu, yale yote utakayosema au kuandika itabaki ni siri yetu. Kwani hata maelezo yote yatatunzwa kwa usiri mkubwa kwa kufungiwa kabatini, ili mimi na msaidizi wangu tuweze kutumia kwa ajili ya taaluma tu. Baada ya kutathimini huo utafiti, fomu zote zitachomwa ili kuzuia watu wengine wasisome.

Je! kuna fidia yoyote nikiumizwa?

Katika utafiti huu, hatuzamii kuwe na maumivu yoyote au mambo mabaya wakati tukifanya huo utafiti. Ikitokea bahati mbaya umezidiwa utashughulikiwa na madaktari na wauguzi wa hospitali. Tunaomba Mwenyezi Mungu apishe mbali baa lolote tufanikishe salama utafiti hadi mwisho.

Je! Nitashirikishwa matokeo ya utafiti?

Hutashirikishwa moja kwa moja matokeo, bali kama kuna hitajika usaidizi wa ziada au pekee tutamwambia daktari wako ambaye ataona jinsi gani akusaidie. Sisi tutaandika ripoti ambayo itasaidia madaktari na wanasayansi kuweza kuboresha matibabu ya ugonjwa wa huzuni sana na furaha iliyokithiri. Pia hiyo ripoti itaweza kusomwa na yeyote anayetaka wala usiwe na mashaka majina yako hayataandikwa humo kwenye ripoti.

Je ! ninaweza kukataa kujiunga na utafiti?

Unaweza kabisa na uko huru kukataa au kukubali kujiunga na utafiti. Hakuna mabadiliko yoyote katika matibabu yako hata kama utakataa kujiunga au kutoka katikati.

Naweza kuuliza maswali kwa nani?

Unaweza kuuliza kwangu, au kwa yeyote utakayemchagua; daktari, muuguzi au mhudumu**.** Kama umepata tatizo juu ya utafiti au unataka maelezo zaidi wasiliana na hawa wafuatao:

1. Mtafiti: Mumello Maria Benedicta OSB. Chuo Kikuu Nairobi. Shule ya Famasia. Idara ya dawa na tiba ya vitendo. SLP 19676-00202.
2. Prof Okalebo F A. Kaimu Prof. Chuo Kikuu Nairobi. Idara ya Famakolojia na Famakognosia. Nairobi.
3. Dr Amugune B, Mhadhiri. Chuo Kikuu Nairobi. Idara ya Madawa na Kemia. Nairobi.

4. Dr Kigamwa P. Mhadhiri. Chuo Kikuu Nairobi. Shule ya Udaktari. Idara ya Akili. Nairobi.
5. Prof. Chindia Hospitali ya Taifa Kenyatta / Chuo Kikuu Nairobi ERC. Nairobi.

Ukijiunga na utafiti utapewa fomu moja.

Je! Una swali lolote ungependa kuuliza au kujua zaidi?

Consent certificate (Swahili version)

Sehemu ya pili: Cheti cha makubaliano ya kuomba idhini.

Jina la utafiti: uchunguzi wa ukuaji na visababishi vya kufanya mabadiliko mwilini ninapokunywa dawa za ugonjwa wa kuwa na huzuni pia uchangamfu unaokithiri katika Hospitali ya Taifa ya Kenyatta na Mathare Hospitali ya Rufaa**.**

Mtafiti Mkuu: Mumello Maria Benedicta OSB.

Bodi ya maadili na utafiti: kamati ya maadili na utafiti ya Kenyatta Hospitali ya Taifa / Chuo Kikuu Cha Nairobi.

Watafiti wenzangu/ wasimamizi:

1. Prof Okalebo F A. Kaimu Prof. Chuo Kikuu Nairobi.
2. Dr Amugune B, Mhadhiri. Chuo Kikuu Nairobi.
3. Dr Kigamwa P. Mhadhiri. Chuo Kikuu Nairobi.

MAKUBALIANO YA KUSHIRIKI KUFANYIWA UTAFITI

Nimefahamishwa hatua zinazotakiwa, faida na hasara za kushiriki huu utafiti. Maswali yangu yote yamejibiwa vema.Nakubalikushiriki utafitiwakuchunguzwa jinsi mwili unavyofanya mabadiliko ninapokunywa dawa za ugonjwa wangu wa kuwa na huzuni pia uchangamfu uliokithiri.Ninaelewa kuwa nitahitajika kupimwa shinikizo la damu, uzito na uzio wa kiuno.
Nimekubali kushiriki utafiti huu kwa hiari yangu bila kulazimishwa na yeyote.
Jina la mshiriki utafiti_____
Sahihi ya mshiriki utafiti_____ Tarehe_____

Uapo wa mtafiti:

Nimetoa maelezo katika mkataba wa makubaliaono na mshiriki wa utafiti na kumpa nafasi ya kuuliza maswali. Nimejitahidi kujibu maswali yote. Nimeridhika kuwa mshiriki ameelewa vema maelezo kuhusu lengo, hatua, faida na hasara.
jina_____sahihi_____tarehe_____

KWA MAWASILIANO ZAIDI:

1. Mtafiti: Mumello Maria Benedicta OSB. Chuo Kikuu Nairobi. Shule ya Famasia. Idara ya dawa na tiba ya vitendo. SLP 19676-00202. Simu namba 0736924161.
2. Prof Okalebo F A. Kaimu Prof. Chuo Kikuu Nairobi. Idara ya Famakolojia na Famakognosia, Simu namba 0737 434 204.
3. Dr Amugune B, Mhadhiri. Chuo Kikuu Nairobi. Idara ya Madawa na Kemia. Simu namba 0722 802 074.
4. Dr Kigamwa P. Mhadhiri. Chuo Kikuu Nairobi. Shule ya Udaktari. Idara ya Akili. Simu namba 0722 521 261.
5. Prof. Chindia Hospitali ya Taifa Kenyatta / Chuo Kikuu Nairobi ERC. S.L.P 20723 00202 Nairobi. Simu 2726300 hadi 44102

C. CARE GIVER PROXY CONSENT FORM

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with the study investigator. I have had questions answered in a language I understand. The benefits and risks have been explained to me. I understand that my participation in this study is voluntary and that it is my rights as a participant to terminate the consent at any time with any dire awareness. I freely agree to participate in this research study. I understand that all efforts will be made to keep information regarding my personal identity confidential. By signing this consent form, I have not given up any of the legal rights that I have in a research study.

I agree to participate in this research study: Yes ☐ No ☐

Participant Printed Name: _____

Participant Signature/ Thumb stamp _____ Date

Researcher's statement:

I have explained information in the consent document to the participant and encourage them to ask questions which I took time to answer. I am satisfied that the participant has adequately understood explanation regarded study purpose, procedures, benefits and risks.

Researcher's Name: _____ Date: _____

Signature _____

C. CLINICIAN IN CHARGE PROBATE CONSENT FORM

Title: Prevalence and risk factors for metabolic and movement disorders in patients with bipolar disorders in Kenyatta National Hospitali na Mathare Hospitali ya Rufaa.

I, the signatories (Clinical in Charge) _____, do hereby give consent for the bipolar reprobate's participation in this study, whose nature and purpose have been fully explained by the researcher. I know that all the data gathered determination remain used in lieu of purposes of the study only.

Signature of participant _____Registration number _____

Date _____.**Contact information**:

1. Principal Investigator and Institutional affiliation: Mumello Maria Benedicta OSB. University of Nairobi. School of Pharmacy. Department of Pharmaceutics and Pharmacy Practice. P o Box 19676-00202.
2. Prof Okalebo F A. Associate Prof. University Of Nairobi. Department of Pharmacology and Pharmacognosy.
3. Dr Amugune B, Senior Lecturer. University of Nairobi. Department of Pharmaceutical Chemistry. Telephone number 0722 802 074.
4. Dr Kigamwa P. Senior Lecturer. University of Nairobi. School of Medicine. Department of Psychiatry. Telephone number 0722 521 261.
5. Prof Chindia Kenyatta National Hospital / University Of Nairobi. P o Box 20723 00202 Nairobi.

DEMOGRAPHIC DATA

Code: _____ Date: _____

Title: Prevalence and risk factors for metabolic and movement disorders in patients with bipolar disorders in Kenyatta National Hospital and Mathare Referral Hospital.

1. Study number_____ Gender: Female ☐ Male ☐

2. Date of birth _____month_____year_____

3. Marital status? (a) Married (b) single (c) Divorced/separated

4. Where have you been staying in the past 10 years? (a) Rural (b) urban (c) Rural then urban (d) Urban then rural

5. Level of education? (a) Primary (b) secondary (c) tertiary (d) none

6. Are you currently employed? (a) Yes (b) no

If yes, move to 7.

7. What is the nature of your employment? (a) Self-employed (b) salaried

8. Substance abuse YES ☐ NO ☐

9. Alcohol YES ☐ NO ☐

APPENDIX C: DATA ABSTRACTION FORM

BIPOLAR HISTORY

Year started: _____

Types of Bipolar: I_____

II_____

III_____

IV_____

Not indicated.

Other comorbidities:

1. Blood pres e ☐
2. Stroke ☐
3. Diabetes ☐
4. Renal disea ☐
5. Migraine ☐
6. Anxieties ☐
7. Thyroid ☐
8. Other_____

MEDICINES:

ANTIDEPRESSANTS

Name	Dose (mg)	Frequency	Duration	Date stated	Status

ANTIPSYCHOTICS

Name	Dose (mg)	Frequency	Duration	Date stated	Status

OTHERS DRUGS

Name	Dose (mg)	Frequency	Duration	Date started	Status

HISTORY OF METABOLIC AND MOVEMENT DISORDERS

Blood pressure	Diastolic (mmHg) ☐	Systolic (mmHg) ☐
Parkinsonism disorders	Acute parkinsonism ☐	Chronic parkinsonism ☐
Renal Diseases	Kidney failure ☐	Any kidney problem ☐
Diabetes	Type I ☐ Type II ☐	Prediabetes ☐
Lipid profile	Hyperlipidimia ☐	Triglycaemia ☐
Others	Systemic ☐	Dermatological ☐

A. PHYSICAL EXAMINATION

1. Measure with a scale weight in Kilograms _____

2. What is your current height (measure/confirm from clinic

Notes)._____ meters.

1. Body Mass Index_____

B. AUTONOMIC INVESTIGATION AND WAIST & ARM CIRCUMFERENCE

Supine blood pressure and heart rate are measured after 2 minutes of rest and again after 2 minutes of standing.

Systolic blood pressure

Supine

Standing (2 minutes)

Unable to record.

Diastolic blood pressure

Supine

Standing (2 minutes)

Unable to record.

Heart rate

Supine

Standing (2 minutes)

Unable to record.

Waist circumference_____

Upper Arm circumference _____

APPENDIX E: QUICK MOTOR ASSESSMENT

Part II: Motor Examination Scale

Always rate the worst affected limb

1. Facial expression

0 Normal.

1 Minimal hypomimia, could be normal (poker face)

2 Slight but definitely abnormal diminution of facial expression.

3 Moderate hypomimia; lips parted some of the time.

4 Masked or fixed facies with severe or complete loss of facial expression, lips parted 0.25 inch or more.

2. Speech

The patient is asked to repeat several times a standard sentence.

0 Normal.

1 Mildly slow, slurred, and/ or dysphonic. No need to repeat statements.

2 Moderately slow, slurred, and/ or dysphonic. Sometimes asked to repeat statements.

3 Severely slow, slurred, and/ or dysphonic. Frequently asked to repeat statements.

4 Unintelligible.

3. Ocular motor dysfunction

Eye movements are examined by asking the subject to follow slow horizontal finger movements of the examiner, to look laterally at the finger at different positions, and to perform saccades between fingers, each held at an eccentric position of approximately 30^0 .

The examiner assesses the following abnormal signs: (1) broken up smooth pursuit, (2) gaze evoked nystagmus at an eye position of more than 45^0 (3) gaze evoked nystagmus at an eye position of less than 45^0 (4) saccadic hypermetria. Sign 3 suggests that there are at least two abnormal ocular motor signs, because sign 2 is also present.

0 None.

1 One abnormal ocular motor sign.

2 Two abnormal ocular motor signs.

3 Three abnormal ocular motor signs.

4 Four abnormal ocular motor signs.

4. Tremor at rest (rate the most affected limb)

0 Absent.

1 Slight and infrequently present.

2 Mild in amplitude and persistent. Or moderate in amplitude, but only intermittently present.

3 Moderate in amplitude and present most of the time.

4 Marked in amplitude and present most of the time.

5. Action tremor

Assess postural tremor of outstretched arms (A) and action tremor on finger pointing (B). Rate maximal tremor severity in task A and/ or B (whichever is worse), and rate the most affected limb.

0 Absent.

1 Slight tremor of small amplitude (A). No interference with finger pointing (B).

2 Moderate amplitude (A). Some interference with finger pointing (B).

3 Marked amplitude (A). Marked interference with finger pointing (B).

4 Severe amplitude (A). Finger pointing impossible (B).

6. Increased tone (rate the most affected limb)

Judged on passive movement of major joints with patient relaxed in sitting position; ignore cogwheeling.

0 Absent.

1 Slight or detectable only when activated by mirror or other movements.

2 Mild to moderate.

3 Marked, but full range of motion easily achieved.

4 Severe, range of motion achieved with difficulty.

7. Rapid alternating movements of hands

Pro supination movements of hands, vertically or horizontally, with as large an amplitude as possible, each hand separately, rate the worst affected limb. Note that impaired performance on this task can be caused by bradykinesia and/or cerebellar incoordination. Rate functional performance regardless of underlying motor disorder.

0 Normal.

1 Mildly impaired.

2 Moderately impaired.

3 Severely impaired.

4 Can barely perform the task.

8. Finger taps

Patient taps thumb with index finger in rapid succession with widest amplitude possible, each hand at least 15 to 20 seconds. Rate the worst affected limb. Note that impaired performance on this task can be caused by bradykinesia and/or cerebellar incoordination. Rate functional performance regardless of underlying motor disorder.

0 Normal.

1 Mildly impaired.

2 Moderately impaired.

3 Severely impaired.

4 Can barely perform the task.

9. Leg agility

Patient is sitting and taps heel on ground in rapid succession, picking up entire leg. Amplitude should be approximately 10cm, rate the worst affected leg. Note that impaired performance on this task can be caused by bradykinesia and/or cerebellar incoordination. Rate functional performance, regardless of underlying motor disorder.

0 Normal.

1 Mildly impaired.

2 Moderately impaired.

3 Severely impaired.

4 Can barely perform the task.

10. Heel knee shin test

The patient is requested to raise one leg and place the heel on the knee, and then slide the heel down the anterior tibial surface of the resting leg toward the ankle. On reaching the ankle joint, the leg is again raised in the air to a height of approximately 40cm and the action is repeated. At least three movements of each limb must be performed for proper assessment. Rate the worst affected limb.

0 Normal.

1 Mildly dysmetric and ataxic.

2 Moderately dysmetric and ataxic.

3 Severely dysmetric and ataxic.

4 Can barely perform the task.

11. Arising from chair

Patient attempts to arise from a straight back wood or metal chair with arms folded across chest.

0 Normal.

1 Clumsy, or may need more than one attempt.

2 Pushes self-up from arms of seat.

3 Tends to fall back and may have to try more than once but can get up without help.

4 Unable to arise without help.

12. Posture

0 Normal.

1 Not quite erect slightly stooped posture; could be normal for older person.

2 Moderately stooped posture, definitely abnormal; can be slightly leaning to one side.

3 Severely stooped posture with kyphosis; can be moderately leaning to one side.

4 Marked flexion with extreme abnormality of posture.

13. Body sway

Rate spontaneous body sway and response to sudden, strong posterior displacement produced by pull on shoulder while patient erect with eyes open and feet slightly apart. Patient has to be warned.

0 Normal.

1 Slight body sway and/or retropulsion with unaided recovery.

2 Moderate body sway and/or deficient postural response; might fall if not caught by examiner.

3 Severe body sway. Very unstable. Tends to lose balance spontaneously.

4 Unable to stand without assistance.

14. Gait

0 Normal.

1 Mildly impaired.

2 Moderately impaired. Walks with difficulty, but requires little or no assistance.

3 Severely impaired. Requires assistance.

4 Cannot walk at all, even with assistance.

Total score Part II:

---

15. Dysarthria

0 Absent

1 Minimal (present but completely comprehensible, or speech easily understood)

2 Mild (less than 25% of the speech is incomprehensible, or some difficulty in understanding speech)

3 Moderate (25–50% of the speech is incomprehensible, or marked difficulty in understanding speech)

4 Severe (more than 50% of speech is incomprehensible)

17. Chorea (Test face and each limb)

0 Absent

1 Minimal (action chorea, or intermittent rest chorea)

2 Mild (continuous rest chorea, but without functional impairment)

3 Moderate (continuous rest chorea with partial functional impairment)

4 Severe (continuous rest chorea with complete functional impairment

18. Tongue protrusion

0 Can hold tongue protruded for more than 1 minute

1 Can hold tongue protruded for more than 30 seconds

2 Can hold tongue protruded for more than 10 seconds

3 Can hold tongue protruded for less than 10 seconds

4 Cannot protrude tongue

19. Finger taps (Patient taps thumb with index finger in rapid succession with widest amplitude possible. Test right and left)

0 Normal (_15/5 sec)

1 Minimally impaired (mild slowing and/or reduction in amplitude, 11–14/5 sec)

2 Mildly impaired (occasional arrests in movement, 5–10/5 sec)

3 Moderately impaired (frequent hesitation in initiating movements or arrests in ongoing movements, _5/5 sec)

4 Severely impaired (cannot perform the task)

20. Leg agility (Patients taps heel on ground in rapid succession with widest amplitude, picking up entire leg)

0 Normal

1 Minimally impaired (mild slowing and/or reduction in amplitude)

2 Mildly impaired (occasional arrests in movement)

3 Moderately impaired (frequent hesitation in initiating movements or arrests in ongoing movements)

4 Severely impaired (cannot perform the task)

21. Muscle tone (Test each limb. The value is the sum of the muscle tone for each limb divided by 4)

0 Normal

1 Minimal decrease (not apparent when the contralateral limb is simultaneously moved)

2 Mild decrease (apparent even when the contralateral limb is simultaneously moved, but without functional impairment)

3 Moderate decrease (apparent even when the contralateral limb is simultaneously moved and with functional impairment)

4 Severe decrease (loss of postural tone)

APPENDIX F: SELF-ADMINISTERINTERVIEW OF CONSENTING PARTICIPANT QUESTIONNAIRES

A. The Liverpool University Effect Rating Scale (LUNSERS)

Code: _____Date: _____

Title: Prevalence and risk factors for metabolic and movement disorders in patients with bipolar disorders in Kenyatta National Hospital and Mathari Referral Hospital.

This scale is for self-administered. Kindly indicate how much you have experienced each of the following symptoms in the last month by ticking a box for each of the 51 items.

Item	Not at all(0)	Very little(1)	A little(2)	Quite a lot(3)	Very much(4)
1.Rash					
2.Reduced sex drive					
3.Restlessness					
4.Runny nose					
5.Increased dreaming					
6.Increased sex drive					
7.Increased sweating					
8.Itchy skin					
9.Hair loss					
10. Headaches					
11.Depression					
12.Diarrhoea					
13.Difficulty in achieving climax					
14.Difficulty in concentrating					
15.Difficulty in getting to sleep					
16.Difficulty passing water					
17. Difficulty in remembering things					
18.Difficulty staying awake during the day					
19.Dizziness					
20.Dry mouth					
21.Sensitivity to sun					
22.Shakiness					
23.Sleeping too much					
24.Slowing of movement					
25.Swollen or tender chest					
26.Chilblains					
27.Constipation					

28.Urine darker than usual					
29.Painful joints					
30.Palpations					
31.Parts of body moving of their own accord e.g. foot moving up and down					
32.Passing a lot of water					
33.Periods less frequent					
34.Period problem					
35.Pins and needles					
36.Putting on weight					
37.Tension					
38.Tiredness					
39.Feeling sick					
40.Flushing of face					
41.Mouth ulcers					
42.Muscle spasms					
43.Muscle stiffness					
44.Lack of emotions					
45.Losing weight					
46.Weak fingernails					
47.Greasy skin					
48.Over wet or drooling mouth					
49.Blurred vision					
50.Neck muscles aching					
51.New or unusual skin marks					

KUJIBU MASWALI YA UTAFITI BINAFSI

The Liverpool University Effect Rating Scale (LUNSERS)

Code: _____tarehe _____

Jina la utafiti: uchunguzi wa ukuaji na visababishi vya kufanya mabadiliko mwilini ninapokunywa dawa za ugonjwa wa kuwa na huzuni pia uchangamfu unaokithiri katika Hospitali ya Taifa ya Kenyatta na Mathare Hospitali ya Rufaa**.**

Hii ni aina ya kujibu maswali binafsi ili kufanya utafiti ukamilike vema. Tafadhali onesha jinsi gani ulijisikia kwa kila dalili kwa mwezi uliopita kwa kuweka alama ya vema kwenye kisanduku kwa kila swali.

Hali	Sina kabisa	Kidogo sana	kiasi	Nasikia	Nasikia sana
1.upele					
2.kupungua nguvu za uzazi					
3.sipumziki					
4.kamasi kutoka mfululizo					
5.ndoto kuongezeka					
6.kuongezeka nguvu za uzazi					
7.kuongezeka kutoa jasho					
8.ngozi kuwasha					
9.nywele kunyonyoka					
10.kuuma kichwa					
11.msongo wa mawazo					
12.kuharisha					
13.ngumu kufikia lengo					
14.ngumu kufikiri kwa makini					
15.ngumu kupata usingizi					
16.ngumu kupitisha maji					
17.ngumu kukumbuka kitu					
18.ngumu kukaa macho mchana					
19.kizunguzungu					
20.mdomo kukauka					
21.kupata shida juani					
22.kutingisika					
23.kulala sana					
24.kutembea polepole					
25.kuvimba kifua					
26.kuvimba ngozi na kuuma					
27.kutopata choo					
28.mkojo mweusi kuliko kawaida					
29.viungo kuuma					
30.roho kuhangaika					

31.sehemu ya mwili kuondoka yenyewe mfano miguu juu/chini					
32.kupitisha maji mengi					
33.vipindi vifupi vifupi					
34. shida ya hedhi					
35.maumivu ya kuchoma sindano					
36.kuongezeka uzito					
37.wasiwasi					
38.kuchoka					
39.kujisikia mgonjwa					
40.kuvimba uso					
41.vidonda mdomoni					
42. misuli kuvutika					
43. misuli kukakamaa					
44. kukosa misisimko					
45. kupungua uzito					
46.kucha dhaifu					
47. ngozi ya mafuta					
48. kutoa mate au ulimi kuuchezesha					
49.kutoona vizuri					
50.misuli ya shingo kuuma					
51.alama za ngozi zisizokawaida					

APPENDIX F

B. Hillside Akathisia Scale [HAS]

Code: _____Date: _____

Title: Prevalence and risk factors for metabolic and movement disorders in patients with bipolar disorders in Kenyatta National Hospital and Mathari Referral Hospital.

Subjective Subscale (items 1 and 2):

0= Absent

1= Questionable

2= Present and easily controlled

3= Present and barely controlled

4= Present and not controlled

	sitting	standing	lying	total
Subjective items:				
1. Patient has sensation of inner restlessness:				
2. Patient has the urge to move:				
Objective items:				
3. Akathisia present in the head and trunk:				
4. Akathisia present in the hands and arms:				
5. Akathisia present in the feet and legs:				

Objective Subscale (items 3, 4 and 5):

0= No akathisia

1= Questionable

2=Small amplitude movements, all of the time

3= small amplitude movements, all of the time OR large amplitude movements, part of the time

4= Large amplitude movements, all of the time

Clinical Global Impression:	
Severity of Akathisia:	

Considering your total clinical experience with this particular population, how akathisic is the patient at this time?

0= Not assessed

1= Normal, not akathisic

2= Borderline akathisia

3= mildly akathisic

4= moderately akathisic

5= markedly akathisic

6= severely akathisic

7= among the most akathisic of patients

Global Improvement	Score

Rate total improvement whether or not, in your judgment, it is entirely due to drug treatment. Compared to his/her condition at admission to the study, how much has she/he changed?

0= Not assessed

1= Very much improved

2= Much improved

3= minimally improved

4= No change

5= minimally worse

6= Much worse

7= Very much worse

Subjective Awareness of Restlessness from Barnes rating……..☐

Absence of inner restlessness……..0

Nonspecific sense of inner restlessness……..1

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

Awareness of an intense compulsion to move most of the time and / or reports a strong desire to walk or pace most of the time…….3

Subjective Distress Related to Restlessness…… ☐

No distress…….0

Mild……1

Moderate…….2

Severe…….3

APPENDIX F

C. Abnormal Involuntary Movement Scale [AIMS]

Code: _____Date: _____

Title: Prevalence and risk factors for metabolic and movement disorders in patients with bipolar disorders in Kenyatta National Hospital and Mathari Referral Hospital.

Instructions: complete the examination procedure before making ratings. Circle score for each item.

Item	**none**	**Minimal, may be extreme normal**	**Mild**	**Moderate**	**Severe**
Facial and oral movements					
1. Muscles of facial expression e.g. movements of forehead, eyebrows, periorbital area, cheeks; include frowning, blinking, smiling, grimacing	0 0	1 1	2 2	3 3	4 4
2. Lips and perioral area e.g. puckering, pouting, smacking	0	1	2	3	4
3. Jaw e.g. biting, clenching, chewing, mouth opening, lateral movement	0	1	2	3	4
4. Tongue Rate only increases in movement both in and out of mouth, NOT inability to sustain movement					
Extremities Movements					
5.Upper (arms, wrists, hands, fingers) Include choreic movements (i.e., rapid, objectively purposeless, irregular, spontaneous); athetoid movements (i.e. slow, irregular, complex, serpentine). DO NOT Include tremor (i.e. repetitive, regular, rhythmic).	0 0	1 1	2 2	3 3	4 4
6.Lower (legs, knees, ankles, toes) e.g. lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot					
Trunk Movements					
7.Neck, shoulders, hips e.g. rocking, twisting, squirming, pelvic gyrations	0	1	2	3	4

Global Judgments					
8.Severity of abnormal movements	0	1	2	3	4
9.Incapacitation due to abnormal movements	0	1	2	3	4
10. Patient's awareness of abnormal movements (rate only patient's report) 0=not aware; 1= aware, no distress; 2=aware, mild distress; 3=aware, moderate distress; 4= aware, severe distress	0	1	2	3	4

Dental Status		
11. Current problems with teeth and/ or dentures?	No	Yes
Notes:		

AIMS Examination Procedure

Either before or after completing the examination procedure, observe the patient unobtrusively, at rest (e.g. in the waiting room)

The chair to be used in this examination should be a hard, firm one without arms.

1. Ask the patient whether there is anything in his/her mouth (i.e. gum, candy, etc.) and if there is, remove it.
2. Ask patient about the current condition of his/her teeth. Do teeth bother patient now?
3. Ask the patient whether he/she notices any movements in mouth, face, hands, or feet.
   Yes☐ No☐ If yes, ask to describe and to what extent they currently bother patient or interfere with his/her activities……
   ……..
   ……..
4. Have patient sit in chair with hands on knees, legs slightly apart, and feet flat on floor. (Look at entire body for movements while in this position).
5. Ask patient to sit with hands hanging unsupported. If male, between legs; if female and wearing a dress, hanging over knees. (Observe hands or other body areas).
6. Ask patient to open mouth. (Observe tongue at rest within mouth). Do this twice.

7. Ask patient to protrude tongue. (Observe abnormalities of tongue movement). Do this twice.
8. Ask patient to tap thumb, with each finger as rapidly as possible for 10 to 15 seconds; first with right hand, then with left hand. (Observe facial and leg movements).
9. Flex and extend patient's left and right arms (one at a time).
10. Ask patient to stand up. (Observe in profile. Observe all body areas again, hip included).
11. Ask patient to extend both arms outstretched in front with palms down. (Observe trunk, legs and mouth).
12. Have patient walk a few paces, turn, and walk back to chair. (Observe hands and gait). Do this twice.