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OCULAR SIDE EFFECTS AMONG ADULT PATIENTS TAKING ANTIPSYCHOTIC DRUGS IN MULAGO NATIONAL REFERRAL HOSPITAL PSYCHIATRY CLINIC.

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DECLARATION

I, OPYENE AMOS, hereby declare that the work submitted in this dissertation is original. It has never been submitted for any academic award in any university or to any public institution for publication.

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DEDICATION.

I dedicate this book to my parents, Mr Richard Ogwal TK (MHSRIP) and Mrs. Mary Ogwal who nurtured me into the person I am today.

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ACRONYMS

DM	Diabetes Mellitus.
EOM	Extra ocular muscle.
HIC	High Income Countries.
HIV	Human Immune deficiency Virus.
HTN	Hypertension.
IOP	Intraocular pressure.
LMIC	Low- and Middle-Income Countries
MNRH	Mulago National Referral Hospital.
NICE	National Institute for health and Care Excellence
PI	Principal Investigator.
SIGN	Scottish Intercollegiate Guidelines Network
SSRI	Selective Serotonin Receptor Inhibitor.
TCA	Tricyclic Antidepressants.
UKU	Task force for clinical investigations.
VA	Visual Acuity.
WHO	World Health Organisation.

OPERATIONAL DEFINITIONS.

Antipsychotic drug:

Any of the various medications used in the relief of symptoms of psychosis. They are used in management of common psychiatric conditions such as; bipolar affective disorder, schizophrenia, and other psychoses (National Collaborating Centre for Mental, 2014).

Ocular side effects.

These refer to abnormalities arising in the eye(s) documented to occur as a result of antipsychotic drug use as listed in the Food and Drug Administration drug side effects list. These include conjunctival injection, conjunctival pigmentation, corneal pigmentation, lens pigmentation, cataracts, ocular hypertension, glaucoma, retinopathy, maculopathy, ocular dystonia, refractive errors, and dry eye disease.

Psychotic disorder:

A condition in which a patient must have met at least two of the following; delusions, hallucinations, disorganized speech, or catatonic behavior, and a negative symptom. At least one of the symptoms must be the presence of delusions, hallucinations, or disorganized speech (Vahia, 2013).

Visual acuity: Is a measure of spatial resolution of the visual processing system. Visual acuity shall be measured for this study by using a Snellen's chart at 3m. Normal distance vision is denoted as a visual acuity of 6/6 to 6/12. Near visual Acuity measures the ability of a person to see objects at a working distance – usually about 40 cm or 16 inches (Naipal & Rampersad, 2018).

Visual impairment: Is visual Acuity worse than 6/12 up to the perception of light, with treatment and best possible refractive correction, or visual field less than 10 degrees from the point of fixation. It is classified into mild, severe and total blindness (Naipal & Rampersad, 2018).

E – charts: Is a visual acuity chart with tumbling E letters that is used for patients who are illiterate or unable to read letters on a Snellen chart**.**

Adult: A person 18 years and above (Canêo & Neirotti, 2017)

ABSTRACT.

Background: Ocular side effects resulting from the use of antipsychotic drugs represent a significant concern for the safety and long-term treatment adherence of patients with psychosis. These side effects can include blinding conditions such as abnormal pigmentation, cataracts, glaucoma, retinopathies and maculopathy. Despite the increasing prevalence of psychosis and widespread use of antipsychotic medications in Uganda, there is a notable lack of studies examining the ocular side effects among patients receiving these medications.

Objective: This study aimed to determine the prevalence and patterns of ocular side effects of antipsychotic drug use and associated factors among adult patients in the psychiatry outpatient clinic of Mulago national referral hospital.

Methods and materials: This was a hospital based cross sectional study, conducted in Mulago National referral Hospital Psychiatry Out-Patient clinic between 1st March and 1st May 2023. The principal investigator recruited 380 eligible adult patients consecutively and conducted, sociodemographic, medical, psychiatric, and a comprehensive ocular evaluation. Data was collected in a pre-tested questionnaire, entered in epi data, and analyzed using STATA version 14. Descriptive statistics were presented as means and standard deviation (SD), frequencies and proportions. Factors associated were assessed using a logistic regression to obtain odd ratios with their corresponding P-values and 95% confidence intervals.

Results: We assessed 380 patients with a median age of 35 years, age range 18 and 84 years, SD +/-14 years. Ocular side effect was found prevalent at 27.63%, the most frequent being; cataracts (35.65%) and dry eye disease (20%). Some of the factors associated with ocular side effects included; age 50 years and older ($p< 0.001$, AOR = 11.743, 95% CI: 3.667 – 37.599), having a history of eye disease ($p<0.001$), drug class type ($p<0.001$), a higher chlorpromazine dosage ($p<0.001$), and a higher number of antipsychiatry drugs taken ($p=0.073$).

Conclusion: The prevalence of ocular side effects among patients taking antipsychotics was high at 27.63%, with cataracts, dry eye as the commonest, whereas age above 50years, and history of eye disease were some of the factors associated with side effects of antipsychotic drug use.

Recommendation: Ophthalmic monitoring should be integrated into routine care for patients on antipsychotic medications with emphasis on risk factors such as hypertension and diabetes which may compound the ocular side effects seen with irreversible visual loss.

CHAPTER ONE

1.0 INTRODUCTION.

Psychosis refers to abnormalities in one or more of the following five domains; delusions, hallucinations, disorganized thought and speech, abnormal motor behavior (including catatonia) and negative symptoms(Vahia, 2013).

Antipsychotic drugs are commonly prescribed for the treatment of various psychiatric disorders including schizophrenia, bipolar disorders, mood disorders, and substance abuse(Arciniegas, 2015; Evins et al., 2017). First and second-generation antipsychotics are commonly used as primary treatment for these psychoses, effective in reducing symptoms and prevention of relapse, but do not cure the underlying psychotic disorder(Evins et al., 2017). The first-generation antipsychotics commonly used in Uganda are; (chlorpromazine, haloperidol, fluphenazine, thioridazine, clopixol, stelazine) and second generation are;(risperidone, olanzapine). Close to 90% of patients diagnosed with any psychotic disorder are treated with first-generation antipsychotic drugs in Uganda (Gardner et al., 2005).

While these medications have demonstrated efficacy in managing symptoms, they are associated with a range of adverse effects including ocular complications(Vahia, 2013). These ocular side effects include: eyelid and keratoconjunctival disorders; uveal tract disorders; accommodation interference; angle-closure glaucoma; cataract/ pigmentary deposits in the lens and cornea; retinopathy; and other disorders (Richa & Yazbek, 2010). Phenothiazines (chlorpromazine, thioridazine, haloperidol) cause abnormal pigmentation of eyelids, interpalpebral conjunctiva, cornea, and lens, with corneal edema occurring as well (Richa & Yazbek, 2010). The other side effect seen is mydriasis which may promote angle closure and glaucoma in susceptible patients (Richa & Yazbek, 2010). Pigmentary retinopathy is as well seen with thioridazine use at dose >800mg/day (Gardner & Teehan, 2010). The most prevalent side effect due to long term use of these antipsychotic drugs other than blurred vision due to impaired accommodation as a result of anticholinergic effects is anterior subcapsular cataracts which is less visually impairing compared to cataracts in the general population (Gardner & Teehan, 2010).

Factors that may be associated with occurrence of ocular side effects has been shown to include use of antipsychotics together with Selective Serotonin Receptor Inhibitors (SSRI) such as fluoxetine, which imposes an added risk of development of angle closure glaucoma in susceptible patients (those with narrow anterior chamber angles) (Richa & Yazbek, 2010). In addition, when systemic illnesses such as diabetes and hypertension are present, second-

generation antipsychotics such as olanzapine, quetiapine, and clozapine, may worsen the diabetes and its associated ocular complication. For example(e.g.) (dry eyes, corneal hypoesthesia, cataracts, glaucoma, and diabetic retinopathy). These are attributed to the weight gain which is an adverse effect of these medications (Bowers, 2020). Significant ocular side effects can also be seen when antipsychotic drugs are used in high doses, as seen when cataracts occur with chlorpromazine in doses >800mg/day (Richa & Yazbek, 2010).

Presence of these side effects impact on patients physical, social, occupational, and psychological functioning (Tandon et al., 2020). In a study by Tandon et al., several patients reported reduced physical activity, faced challenges interacting with friends and family, were unable to get and sustain a job, and reported unsatisfactory life (Tandon et al., 2020). The total quality of life satisfaction as shown by the Quality of Life Enjoyment and Satisfaction Questionnaire Short Form (Q-LES-Q-SF) however was moderate in these patients (Tandon et al., 2020).

In the psychiatry out-patient clinic Mulago National referral Hospital, Patients weight, blood pressure, blood sugar tests, liver function test were measured. These important parameters contribute to determining highly at-risk patients to developing ocular side effects of these antipsychotic drugs. Gaps lay in the fact that patients do not receive routine ophthalmology reviews during therapy for early identification, prevention, and treatment of ocular side effects. In conducting this study, the prevalence of ocular side effects, patterns and factors associated with occurrence of ocular side effects among patients on antipsychotic drugs was highlighted and results got will form a platform for discussions to implement improved eye care strategies among psychiatry patients.

1.1 PROBLEM STATEMENT.

Both first generation (typical) and second generation (atypical) antipsychotic drugs are widely used in the treatment of psychiatric disorders worldwide (Evins et al., 2017; National Collaborating Centre for Mental, 2014). While they are effective in managing symptoms, antipsychotic drugs are known to cause systemic side effects including ocular side effects (Evins et al., 2017). Ocular side effects significantly affect the patient's quality of life and may go unnoticed without proper monitoring. They are an important concern for the patient's safety and adherence. Additionally, some side effects such as ocular surface disorders, lenticular opacities and cataracts, and glaucoma, are potentially blinding if not treated early(Lieberman & First, 2018).

With the increasing number of patients seen in the eye clinic of MNRH presenting with ocular side effects of antipsychotic drugs, patients are at risk of visual impairment from preventable ocular side effects of these antipsychotics.

The lack of studies in this regards further compounds on the magnitude of these side effects as it is challenging to integrate ophthalmic care in existing psychiatry guidelines for improved patient care without scientific evidence in our setting.

1.2 JUSTIFICATION.

The significance and rationale of studying ocular side effects among patients taking antipsychotic drugs lies in several important factors at the patient, clinician and public health/policy level:

To achieve universal health coverage in these patients; ensuring patient safety and wellbeing through timely recognition of ocular side effects, prevention, and treatment of these side effects among the patients taking antipsychotic drugs by clinicians (Keel & Cieza, 2022)

To ensure integrated patient centred care as declared in the WHO vision 2020, by understanding patient factors such as age, presence of comorbidities, occupation, and education level that may compound on ocular side effects of antipsychotic drugs, and providing care based on these factors (Keel & Cieza, 2022).

Public Health and Policy: studying ocular side effects contributes to broader understanding of the medications safety profile. This would inform regulatory and policy makers aimed at improving medication guidelines, patient education, adverse event reporting systems and highlighting areas that require further research development (Burton et al., 2021; Keel & Cieza, 2022).

1.3 RESEARCH QUESTIONS:

1. What was the prevalence of ocular side effects among patients taking antipsychotic drugs?
2. What were the patterns of ocular side effects among these patients?
3. What were the factors associated with ocular side effects of antipsychotic drugs?

1.4 OBJECTIVES:

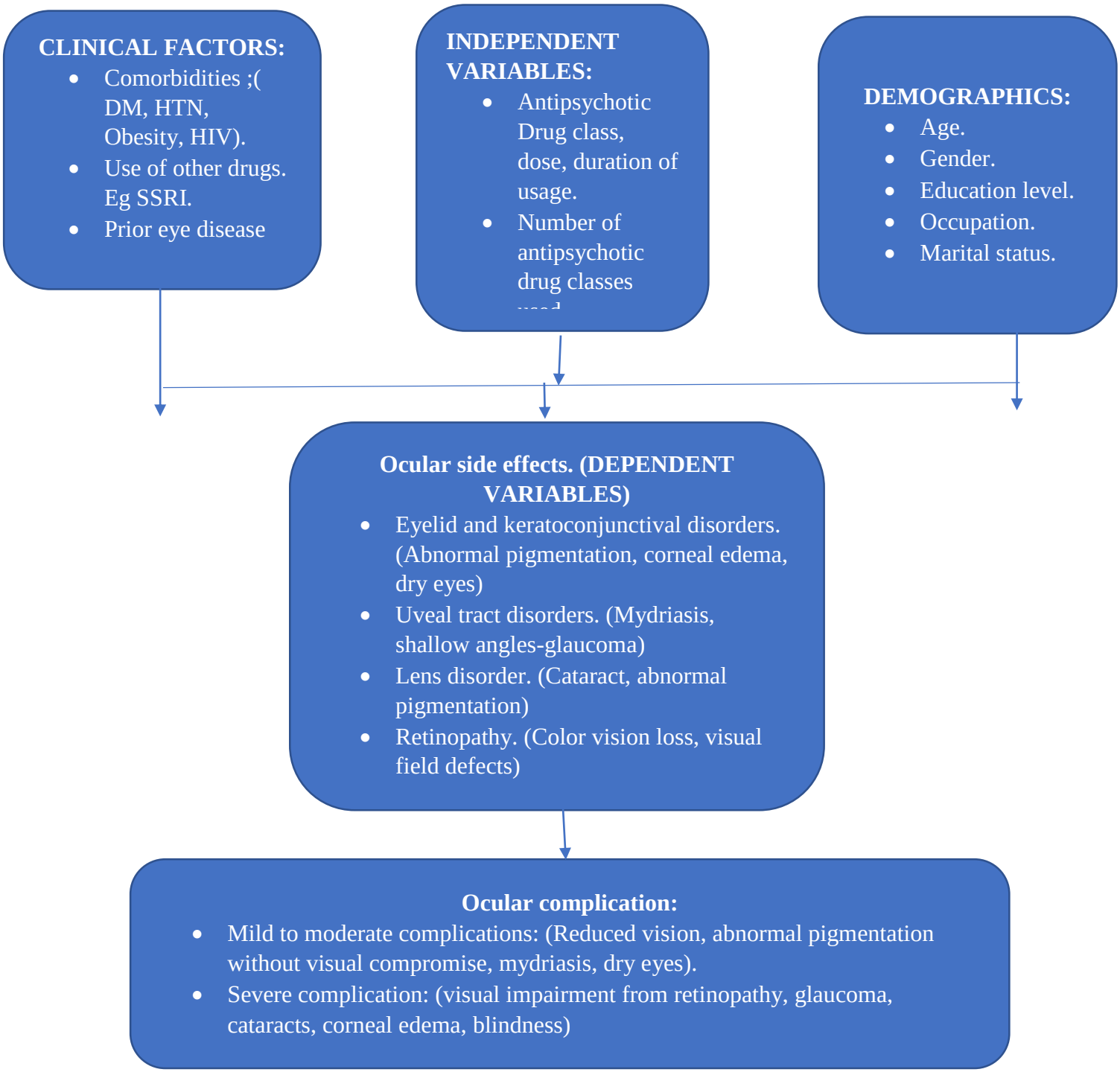
Broad objective:

To determine the prevalence, patterns of ocular side effects, and associated factors among patients taking antipsychotic drugs in Mulago National referral hospital psychiatry clinic.

Specific objectives:

1. To determine the prevalence of ocular side effects among patients taking antipsychotic drugs.
2. To determine the patterns of ocular side effects among patients taking antipsychotic drugs.
3. To determine the factors associated with ocular side effects among patients taking antipsychotic drugs.

1.5 CONCEPTUAL FRAMEWORK OF DEVELOPMENT OF OCULAR SIDE EFFECTS IN PATIENTS TAKING ANTIPSYCHOTIC DRUGS.



In this conceptual framework, we related three factors to the development of ocular side effects among patients taking antipsychotic drugs.

Independent variables in this study were those which are directly related to the development of ocular disease. The use of antipsychotic drug was an independent variable in this study, and factors such as the class, number, dose and duration of use of antipsychotic drugs determined

the occurrence and severity of ocular side effects in these patients. Phenothiazines like chlorpromazine cause pigmentary deposits in cornea and lens, and the severity can be increased when used with an additional antipsychotic drug class, and when used in high doses for prolonged periods.

Demographic factors such as age, gender, socioeconomic status, marital status also predispose, and exacerbate occurrence of ocular side effects. For patients already on antipsychotics, these factors directly relate to occurrence of ocular side effects and also relate to the clinical and pharmacological factors to exacerbate ocular side effects of antipsychotic drugs. For example, females react to smaller doses than males. Low socioeconomic status or unemployment force patients to stay longer on first generational antipsychotics which are more susceptible to causing ocular side effects. These factors were also determined in this study.

Also, concomitant use of other drugs such as Selective serotonin receptor inhibitors (SSRI), with antipsychotics may exacerbate occurrence of some side effects like angle closure which leads to glaucoma. Such patients also experience blurred vision and have accommodation challenges. In addition, comorbidities like DM, HTN also cause increased likelihood of ocular side effects through drug-drug interactions. These comorbidities are also visually disabling. Prior ocular disease may exacerbate the ocular side effect of the antipsychotic drug. In this study, these factors were measured.

CHAPTER TWO:

2.0 LITERATURE REVIEW.

2.0.1 Definition of psychosis.

Psychosis refers to abnormalities in one or more of the following five domains; delusions, hallucinations, disorganized thought and speech, abnormal motor behavior (including catatonia) and negative symptoms (Vahia, 2013). Its symptoms can occur in a range of disorders such as schizophrenia, mood disorders and substance misuse (Arciniegas, 2015).

2.0.2 The burden of psychoses.

Psychoses affect 21 million people globally (more common among men – 12 million than women – 9 million), with early onset in many (15–29 years old). People with psychoses are two and a half times more likely to die early than the general population, due to physical illnesses such as cardiovascular, metabolic, and infectious diseases (Bowers, 2020).

There is limited data on psychosis in sub-Saharan Africa, and existing data are disaggregated based on community populations in a few countries. A community survey in an urban setting in Tanzania reflected the prevalence of psychotic-like symptoms at 3.9 %, whereas a cross-sectional study in Kenya found a prevalence of 3.5% among Kenyan youth, and a Mozambique survey reflected a prevalence of 4.4% of these symptoms (Jenkins et al., 2010; Jenkins et al., 2012; Patel et al., 2007).

In Uganda, the burden of mental illness in Uganda could be higher than the estimated massive 35% incidence, and 15% requiring treatment (Molodynski et al., 2017). A community-based survey in a western district reflected a prevalence of 30.7% of severe mental illness (Kasoro et al., 2002). In comparison, another study done in eastern Uganda by Abbo et all found a 29.7% prevalence of psychosis among patients seeking services of traditional healers (Abbo et al., 2009).

2.0.3 Treatment and management of psychosis.

Antipsychotics are the primary treatment for psychosis and are effective in reducing the psychotic symptoms, however, they do not cure the underlying psychotic disorder. Evidence exists of their efficacy in treating acute psychotic episodes and preventing relapse over time (National Collaborating Centre for Mental, 2014) (Evins et al., 2017).

In High Income Countries, (HIC) second-generation antipsychotics which have less side effects are first-choice drugs, however, in Low- and Middle-Income Countries (LMIC), poor health financing dictates the use of first-generation antipsychotics which have more side effects as the first-choice drugs. Even though second-generation antipsychotics are now available, they are not easily available or affordable in these LMIC (Wang et al., 2021).

A cross-sectional quantitative study of psychotropic medication among 682 patients in 2 psychiatry hospitals in Uganda showed, that (close to 90% of patients with conditions diagnosed with any psychotic disorder were treated with first-generation antipsychotic drugs; chlorpromazine, haloperidol, trifluoperazine, and depot fluphenazine) (Annika Rukat et al., 2014).

About 63% of the patients were on a combination of first-generation antipsychotics and antidepressant (fluoxetine or amitriptyline) medication, and this was among patients presenting with depression as well (A. Rukat et al., 2014) whereas the use of second-generation antipsychotics was very low.

Both first and second-generation antipsychotics have similar effectiveness, however, the side effect profile of first-generation antipsychotics is a great limitation (Pakpoor & Agius, 2014). Ocular problems arising from the use of these drugs have an effect on patients' physical and psychical institutions, which already have a tendency to be crumpled, thus can worsen patients' condition. They can also affect adherence to medication (Pakpoor & Agius, 2014).

2.0.4 Overview of antipsychotic medication.

First-generation antipsychotics, also known as typical antipsychotics were earliest developed in the 1950s, however, due to their intolerable side effects, second-generation antipsychotics, also known as atypical antipsychotics were developed. In terms of efficacy, both generations of drugs are effective in the management of both acute and maintenance treatment of psychotic disorders (Enna & Coyle, 1998).

Table 1. Common antipsychotics used in Uganda (Hillary Irimaso, 2019).

Typical antipsychotics (low potency)	**Typical antipsychotics (high potency)**	**Atypical antipsychotics.**
Chlorpromazine HCL.	Fluphenazine.	Olanzapine.
Chlorprothixene.	Haloperidol.	Risperidone.
Thioridazine.	Pimozide.	Quetiapine.
Perphenazine.	Thiothixene.	Clozapine.
	Flupentixol.	Amisulpride.
	Zuclopentixol.	Aripiprazole.
	Prochloperazine.	
	Trifluoperazine.	

Typical antipsychotics reduce psychosis by blocking D2 receptors in the brain mesolimbic system. (Enna et al., 1998). The term potency denotes their ability to bind dopamine D2

receptors and linearly relates to the varying side effect profiles of these drugs (Muench & Hamer, 2010).

2.0.5 Antipsychotic medication and the eye.

Antipsychotic drugs are prescribed commonly to treat psychosis is patients presenting with psychotic disorders. Its use is not completely safe, with the eye being the second organ, after the liver to manifest toxicity due to these drugs. Clinicians need to monitor these patients for early detection and prevention of any complications that may result (Richa & Yazbek, 2010). Numerous mechanisms are implicated in the development of these ocular side effects some of which are; antipsychotics have weak anticholinergic effects which may contribute to impaired accommodation and tear film insufficiency (Dr. Dimple Shakeet*, 2019). Mydriasis and glaucoma can result from this anticholinergic effect as well (Gardner & Teehan, 2010). Some Photosensitizing drugs (chlorpromazine) denature proteins and render them vulnerable to sunshine in a way that they form opacities that are deposited in the lens, cornea, and skin. Another mechanism is that Endogenous melanin could also trap free radicals produced by antipsychotic drugs and resulting compounds manifest as lens discoloration (Richa & Yazbek, 2010).

2.0.6 Prevalence of ocular side effects.

Existing studies on prevalence of ocular side effects highlight individual side effect prevalence. The most prevalent ocular side effect due to antipsychotic drug use was found by Gardner and Teehan as blurred vision due to anticholinergic (impaired accommodation) side effects of these drugs (Gardner & Teehan, 2010). Cataract was the second most prevalent ocular side effect seen. A case control study showed a high prevalence of cataracts among patients of schizophrenia (26%) compared to the healthy counterparts (0.2%) (Gardner & Teehan, 2010). A cataract prevalence of 33% was also seen among young patients (mean age 35) living in the tropics on antipsychotic drugs.(Gardner & Teehan, 2010). Dr Dimple found the prevalence of dry eye at 32% among patients taking antipsychotic drugs (Dr. Dimple Shakeet*, 2019).

Few studies have been carried out to show the burden of these ocular side effects. Trude Seselie jahr iversen et al. in a study of side effect burden of antipsychotics in real life used the UKU side effect rating scale, clinical assessment, and pharmacologic data and found that a high occurrence of side effects was associated with use of antipsychotics, and that polypharmacy and female gender were risk factors to severe side effect burden (Iversen et al., 2018).

2.0.7 Patterns of Ocular side effects of antipsychotics.

Ocular side effects of antipsychotic drugs can be divided into seven major categories as listed below: eyelid and keratoconjunctival disorders; uveal tract disorders; accommodation

interference; angle-closure glaucoma; cataract/ pigmentary deposits in the lens and cornea; retinopathy; and other disorders (Richa & Yazbek, 2010).

2.0.7.1 Eyelid and keratoconjunctival disorders.

Eyelid and keratoconjunctival disorders refer to adverse effects seen in the eyelids, cornea, and conjunctiva. Phenothiazines such as chlorpromazine, and fluphenazine cause most of the side effects seen in these structures (Haylor, 2002)

a. Eyelid disorders.

Abnormal pigmentation of the eyelids occurs with phenothiazine use. It appears as hyperpigmented skin lesion over the eyelids. Commonly, chlorpromazine is the most causative antipsychotic to result in this and its related to high dose and longer duration of use (Richa & Yazbek, 2010). Another side effect reported in the eyelid is Meige syndrome occurring in patients taking risperidone. In a study by Miyamoto S et al, Japan, 3 cases of Meige syndrome were seen, 2 in adults and 1 in an adolescent male (An et al., 2008; Yoshimura et al., 2016). Other eyelid disorders seen with risperidone use include; eyelid edema, and eyelid margin crusting (Myers & Thase, 2001).

b. Conjunctival disorders.

Abnormal pigmentation of the conjunctiva is seen with antipsychotics, commonly phenothiazines. The palpebral conjunctiva is the most affected. This is not a visually impairing side effect. It is associated with use of high doses of chlorpromazine as reported by Richa. Et al (Richa & Yazbek, 2010) . Another side effect affecting the conjunctiva is hyperemia, and conjunctivitis. Risperidone has been shown in clinical trials to cause conjunctivitis, and hyperemia in < 1% of adult population (Myers & Thase, 2001).

c. Corneal complications.

Corneal side effects due to antipsychotic drugs include, abnormal pigmentary deposits, corneal opacity, keratopathy, and corneal edema.

Corneal toxicity was reported to occur within 6 months of therapy in 12% of patients receiving 2,000 mg of chlorpromazine daily but in only 1% of patients receiving 300 mg of chlorpromazine daily (Haylor, 2002; Hull et al., 1982). Epithelial keratopathy is a side effect seen and is described as swirling lines in the corneal epithelium, however rarely causes visual impairment, and diminishes after cessation of chlorpromazine (Richa & Yazbek, 2010). A worrisome side effect is corneal edema, caused by phototoxic lysis of corneal endothelial cells by chlorpromazine. It is a cause of irreversible vision impairment if not recognized early and offending drug removed (Richa & Yazbek, 2010).

Accumulation of chlorpromazine occurs in these tissues and being phototoxic, when exposed to sun light, it causes photosensitization of tissue proteins leading to the adverse effects seen(Richa & Yazbek, 2010).

Of all the above adverse effects, abnormal pigmentation is most commonly seen, whereas epithelial keratopathy is seen with large doses of chlorpromazine(>2g/day), and corneal edema, though visually disabling, is rare.

2.0.7.2 Refractive Errors:

Refractive errors are eye disorders that occur when the eye cannot clearly focus light rays from objects to retina resulting in blurry images (Besufikad et al., 2022). Myopia (short sightedness), hyperopia (long sightedness) and astigmatism (no single point of focus in the eye) are the three types of refractive errors (Besufikad et al., 2022). Aripiprazole, an atypical antipsychotic used in the treatment of psychotic disorders such as schizophrenia, bipolar disorder, depression, and obsessive-compulsive disorder in adults causes myopia. A case report by Bulgu et al, described a 34year female who presented with blurry vision after developing transient myopia following the first week of therapy. She was found to have a refractive error of -2DS, with best corrected visual acuity 10/10 in both eyes (Bulgu & Genc, 2020).

2.0.7.3 Dry Eye Syndrome.

Phenothiazines (chlorpromazine, thioridazine) exhibit anticholinergic side effects by blocking muscarinic and nicotinic receptors, and muscarinic 3 receptors in the conjunctiva and lacrimal gland (Dr. Dimple Shakeet*, 2019). This leads to decreased mucus and aqueous production. A persistent tear film instability results causing morphological and biochemical ocular surface changes that ultimately affect vision of the patient (Messmer, 2015).

2.0.7.4 Uveal tract problems.

Anticholinergic antipsychotic drugs with strong anticholinergic/ antiadrenergic actions such as chlorpromazine and fluphenazine can lead to mydriasis (Richa & Yazbek, 2010). Theoretically, this forms a risk factor for angle closure glaucoma. However no report of Angle closure glaucoma has been encountered in literature (Sönmez & Aykan, 2014). (Jain et al., 2021). Other effects include; disturbances in accommodation, and abnormal vision (Jain et al., 2021). Other psychotropic drugs used that may cause accommodation interference, and angle closure have been shown as TCAs such as amitriptyline, imipramine which act by anticholinergic mechanism (Richa & Yazbek, 2010). The same has been reported for SSRIs such as fluoxetine which may as well cause mydriasis and angle closure glaucoma (Richa & Yazbek, 2010)

2.0.7.5 Glaucoma (angle closure glaucoma).

Glaucoma can be defined as a heterogenous group of conditions which share common characteristic features of optic neuropathy and visual field loss. Increased IOP is an important risk factor (Bowers, 2020). Antipsychotics have weak anticholinergic effects and may result in acute angle closure glaucoma in predisposed patients. (Patients with narrow anterior chamber angles) (Richa & Yazbek, 2010). There have been reports of perphenazine, trifluoperazine and fluphenazine inducing Acute Angle Closure, as well as olanzapine in a predisposed patient with a brunescent cataract (Jain et al., 2021).

2.0.7.6 Cataractous and pigmentary deposits in the lens and cornea.

The lens is a biconvex, transparent structure located between the anterior and posterior segment of the eye. Clouding of the lens is termed cataracts and can be a result of insults from trauma, metabolic disease (diabetes, galactosemia), infections, radiation, advanced age, and drugs (Cochran et al., 2023). The cornea, as described earlier is a transparent glass like structure covering the anterior globe with majorly refractory and protective functions in the eye (Cochran et al., 2023).

Antipsychotics commonly phenothiazines cause pigmentary deposits in the lens and cornea (Richa & Yazbek, 2010). These deposits can cause opacities in both the lens and cornea. Two mechanisms have been shown to cause these pigmentary depositions as follows. First mechanism is that Photosensitizing drugs(chlorpromazine) denature proteins and render them vulnerable to sunshine in a way that they form opacities that are deposited in the lens, cornea, and skin. The second mechanism is that endogenous melanin could trap free radicals produced by antipsychotic drugs and resulting compounds show as lens discoloration (Richa & Yazbek, 2010).

Nearly all phenothiazines have shown these adverse effects, however the most implicated have been thioridazine, and chlorpromazine. These effects are drug, and dose dependent and chlorpromazine in doses >800mg/day for 2 year was found to manifest these adverse events in 31/61 patients examined in a study by Satanove A. (Richa & Yazbek, 2010). In addition atypical antipsychotics have a systemic side effect of metabolic syndrome, and hyperglycemic status in these people can lead to early diabetic cataracts formation (Richa & Yazbek, 2010).

A cross sectional study to determine cataract occurrence among two groups of antipsychotic drug users, one group on typical antipsychotic and another on atypical antipsychotics found

cataract prevalence of 33% with predominance of anterior sub capsular cataract, 40% prevalence among those on typical antipsychotics and 18% among those on atypical antipsychotics (Souza et al., 2008).

2.0.7.7 Retinal complications.

Retina is the part of the eye suffering most damage from drugs. It is made up of a thin nervous membrane that covers the eye-ball internally, within the thickness of which three types of cells are ordered. A disease to this membrane is termed retinopathy (M.S. Lee & A.I. Fern, 2004). Most documented retinal lesion is pigmentary retinopathy, and retinal degeneration resulting from phototoxicity of the drug in the eye (Richa & Yazbek, 2010). Pigments are deposited gradually from peripheral retina, with characteristic field loss. Patients complain initially of peripheral field loss, then central scotoma, and eventually blindness develops (Richa & Yazbek, 2010).

Thioridazine and chlorpromazine are the major drugs associated with retinopathy. Drug dose and duration are determinants of these side effects. For thioridazine doses >800mg/day are toxic to the retina, whereas chlorpromazine both dose and duration determine the retinopathy. (Richa & Yazbek, 2010). A case report showed Retinopathy in a patient on chronic flupentixol. A cumulative dose of 4380mg over 2 year period caused multiple, yellowish white refractile intraretinal deposits over the macula and peripapillary region shown on fundoscopy (Kumar et al., 2018).

Other retinal lesions reported have been retinal vein occlusion associated with olanzapine use. A case report of a 50year old male who was on olanzapine for 3 years, presented with central retinal vein occlusion (CRVO) with significant fundus feature (intraretinal hemorrhages in both superior and inferior poles). Other differentials diagnoses and risk factors that could lead to CRVO were ruled out in this patient. This calls for clinicians to questions patients who develop sudden CRVO on whether they are on antipsychotic drugs like olanzapine (Nowrouzi et al., 2021).

2.0.7.8 Maculopathy.

In a case report publication by Lee and Fern et al, fluphenazine was shown to singly cause maculopathy secondary to its accumulation in the retinal pigment epithelium and its toxic effects. Previous reports had shown maculopathy due to fluphenazine in association with exposure to other extreme forms of photochemical exposure for example welding arc lights (Mun Seng Lee & A. I. Fern, 2004)

In addition thioridazine in doses >800mg daily and chlorpromazine in doses > 1200mg daily cause course granular pigmentation, patchy RPE loss, in early disease, with late progression to geographical atrophy (Muchnick, 2008).

2.0.7.9 Ocular dystonias and oculogyric crisis.

Other visual problems of special concern are the ocular dystonias, and other eye movement disorders. Ocular dystonias can occur with antipsychotics especially high-potency ones. (Richa & Yazbek, 2010). Drugs causing extrapyramidal effects have been associated with ocular manifestations such as nystagmus, diplopia, extraocular muscle palsy, and oculogyric crisis (involuntary contraction of extra ocular muscles). Phenothiazines have been shown to cause diplopia. A study in 1995 by Tan et al. searched for oculogyric spasm among 2035 Asian psychiatric inpatients over a 2-month period. It was found that 1.7% of these patients developed oculogyric reactions; all of them had been receiving chlorpromazine (or another typical antipsychotic) maintenance treatment for >5 months, and those with recurrent oculogyric crises were taking a mean chlorpromazine equivalent dosage of 511 mg/day (Tan et al., 1994). Risperidone, in a study was shown to cause saccadic eye movements in patients 4 weeks after initiation of treatment, and was related to lack of acute tolerance to its powerful serotonergic antagonism which could disrupt brainstem neurophysiology responsible for saccadic eye movement control (Sweeney et al., 1997). Incidences of oculogyric crisis, nystagmus, and ophthalmoplegia have been reported with carbamazepine use as well (Richa & Yazbek, 2010).

2.0.8 Factors associated with ocular side effects among patients taking antipsychotic drugs.

Factors that may be associated with occurrence of ocular side effects has been shown to include use of antipsychotics together with Selective Serotonin Receptor Inhibitors (SSRI) such as fluoxetine, which imposes an added risk of development of angle closure glaucoma in susceptible patients (those with narrow anterior chamber angles) (Richa & Yazbek, 2010). In addition, when systemic illnesses such as diabetes and hypertension are present, second-generation antipsychotics such as olanzapine, quetiapine, and clozapine, may worsen the diabetes and its associated ocular complication. For example(e.g.) (dry eyes, corneal hypoesthesia, cataracts, glaucoma, and diabetic retinopathy). These are attributed to the weight gain which is an adverse effect of these medications (Bowers, 2020). Significant ocular side effects can also be seen when antipsychotic drugs are used in high doses, as seen when cataracts occur with chlorpromazine in doses >800mg/day (Richa & Yazbek, 2010). A study by Bahta et al., found smoking and having a secondary level education to be associated with occurrence

of side effects generally (Bahta et al., 2020). Few studies have highlighted factors associated with occurrence of ocular side effects among patients on antipsychotic drugs.

In conclusion, as prevalence of mental illness increase, chronic use of antipsychotic drugs also increases. Therefor understanding the adverse effects associated with antipsychotic drugs, the mechanisms underlying these complications becomes increasingly important. When psychiatrists, ophthalmologists and patients are aware of and attentive to medication induced adverse effects, early prevention and intervention can then easily circumvent the occurrence of the vast majority of cases of serious and potentially irreversible ocular damage.

CHAPTER 3

3.0 MATERIALS AND METHODS

3.1 Study design:

The study design was a cross sectional design.

3.2 Study site.

The study was carried out in the Psychiatry clinic (Bosa clinic) Out Patient Department of MNRH, located Northern side of Mulago Hill, near The AIDS Support Organisation (TASO) headquarter between March 2023 and May 2023. Specialised care to patients of schizophrenia, bipolar disorder, depression and other mental illnesses are offered in the clinic. These services were provided mostly on an outpatient basis, though an in-patient bed capacity of 4 patients existed to manage critical cases. The clinical team was composed of psychiatrists, psychiatric clinical officers, nurses and residents supervised by the clinical head.

The average daily patients seen in the clinic were about 30, seen during week days. On average 90% of patients seen were taking antipsychotic drugs on a daily basis. Patients seen in the clinic were generally stable on antipsychotic drugs which was desirable for conducting the study and meeting the required sample size.

3.3 Study participants.

3.3.1Target population.

The target population was adult patients taking antipsychotic medication and attending the psychiatry clinic at MNRH.

3.3.2 Accessible population.

Adult patients who were taking antipsychotics, attending clinic during the study period.

3.3.3 Study population.

Participants 18 years and above who had been on antipsychotics attending clinic during the study period who were eligible and had consented to participate in the study.

3.4 Selection criteria.

3.4.1 Inclusion criteria.

- All adults with a diagnosed psychotic disorder as seen in medical records.
- A patient who was stable on antipsychotic medication attending clinic at MNRH, determined using a Clinical Outcome in Routine Evaluation 10 (CORE-10) tool.
- A patient had been on antipsychotics for at least 2 weeks.
- A patient had consented to participate in the study.

3.4.2 Exclusion criteria.

- All patients triaged to be too ill to cooperate and undergo ocular exams.

3.5.1 Sample size estimation.

Sample size was determined using statistical formula adopted from Kish Leslie.

Given by $n = \frac{z^2\, pq}{d^2}$

N being the sample size required,

Z =1.96(constant for 95% confidence interval)

P being proportion of patients with ocular side effects,

q Being (1-**p**),

d the standard error of 5%.

Assume **p**=50%, since there is no documented prevalence of ocular side effects of antipsychotic in Uganda.

N=385

3.5.2 Sample size estimation for factors associated with ocular side effects of antipsychotic drugs.

n= $\frac{Z^2 p(1-P)}{E^2}$

Where:

n is the required sample size.

Z is the z-score corresponding to the desired confidence level. For a 95% confidence level, the z-score is approximately 1.96.

p is the estimated proportion of patients with ocular side effects (105/385 = 0.2763).

E is the desired margin of error, which is 5% or 0.05.

Using these values in the formula:

n=1.962*0.2763*(1−0.2763)0.052

n=0.052*1.962*0.2763*(1−0.2763)

n=225.

For statistical power and generation of more evidence we used the larger sample size (385) as calculated in the prevalence.

3.5.3 Sampling method.

Consecutive sampling technique was used. In this technique, an average of 10 patient was evaluated every day until the sample size was reached

3.6 Data collection, management, and analysis.

3.6.1 Data collection tools.

We used a pretested structured questionnaire to collect data from the participants.

3.6.2 Data collection procedure.

In conducting this study, the researchers included the supervisors who oversaw and provided guidance in design of the study. The principal investigator led in conducting the study. The research assistants who included an ophthalmic nurse and an ophthalmic clinical officer, were trained in filling the questionnaires.

Prior to consenting, a psychiatry evaluation was done aimed at ensuring that recruited patients were stable on antipsychotic drugs. This was done with the aid of a standardized Clinical outcome in Routine Evaluation-10 (CORE-10) assessment form, consisting of 10 questions with scores 0-4 and total score of 40, rating patient psychological distress while on therapy. Scores are interpreted as follows; <10 signify non clinical range, 11-14 signify mild psychological distress, 15-19 signify moderate psychological distress, 20-24 signify moderate to severe psychological distress, and scores 25 and above signify severe psychological distress. We recruited patients with non-clinical range of psychological distress on antipsychotic therapy.

All patients on antipsychotic medication were recruited consecutively, informed and consented to participate. Consent was sought from patient.

History.

A detailed history was obtained by the principal investigator from each patient and this included; relevant sociodemographic history, a medical history, psychiatry history, and an ocular history.

In the socio-demographic history, a unique identifier number was given to each patient for confidentiality. Thereafter, the patient age, sex, marital status, education level, and employment status were obtained. These were documented in the questionnaire used appropriately.

In the medical history, relevant history of any current medical illnesses such as hypertension, diabetes and HIV was obtained. This was done to look for comorbidities that could cause eye disease.

In the psychiatry history, the patient diagnosis was obtained from the file. The Patients history of antipsychotics and other drugs was obtained. This included the class, number, and total daily dose of each antipsychotic drugs used, and duration of use of these drugs.

In the ocular history; a history of previous eye check, previous eye disease, and previous eye surgery was obtained. Any history of present eye symptoms and duration, current and previous use of eye medication were also obtained. These were clearly documented in a questionnaire for each patient.

Examination.

The examination was done by the principal investigator and included a detailed general, medical, and ocular examination.

General examination.

The general examination involved assessment of patient general appearance, weight, body temperature, level of pallor, presence of edema, and lymphadenopathy. The patients Glasgow Coma Scale was also assessed.

Medical examination.

In the medical examination, the patients' blood pressures and pulse rates were measured using an automated Blood pressure machine. Other systemic examinations done included respiratory system, gastrointestinal system, central nervous system, for patients with significant complaints in the respective systems. Appropriate investigations, treatment, and referrals were made for such patients.

Ocular examination.

The ocular examination comprised a comprehensive ophthalmological evaluation, starting with the right eye and then moving on to the left eye. Visual acuity assessment was performed using a Snellen chart at a distance of 3 meters for literate participants and an E chart for illiterate participants. Distance visual acuity was classified as follows: normal vision for VA equal to or better than 6/12, mild visual impairment for VA worse than 6/12 to 6/18, moderate visual impairment for VA worse than 6/18 to 6/60, severe visual impairment for VA worse than 6/60 to 3/60, and blindness for VA worse than 3/60. A pinhole test was conducted for all participants with visual impairment, and refractive measurements were taken using a retinoscope. Near visual acuity was assessed using a Jaeger chart, and refractive measurements were performed for participants with near vision worse than N6. Patients with refractive errors were identified from the refraction measurement.

Visual fields were assessed by confrontation method compared with examiner (who had normal visual fields confirmed by automated perimeter). Patients with visual field abnormalities were suspected to have glaucoma and underwent further evaluation (fundoscopy and intraocular pressure assessment)

Extra ocular muscle movements were assessed, cover-uncover tests done to assess phorias and diplopia in all directions of gaze.

Amsler grid test to check for macular function for all participants.

A portables slit lamp microscope was used to fully evaluate the anterior segment signs or diseases and Schirmer strip test for dry eye. Dry eye was diagnosed as presence of Schirmer test result of < 10mm in 5 minutes(Li et al., 2012).

Intra-ocular Pressure measurement was done with a hand-held tonometer (I care tonometer).

Pupil dilatation was done using tropicamide 1% eye drops. Posterior segment assessment using indirect ophthalmoscope with a 20D VOLK lens was done. Glaucoma suspect: defined as cup disc ratio greater than 0.6 or IOP more than 21mmHg. Vitreous haemorrhage was presence of blood in the vitreous as seen with indirect ophthalmoscopy.

Retinopathies such as Pale retina and bony spicules were diagnosed as seen on indirect ophthalmoscopy. Diabetic retinopathy was diagnosed based on ETDRS protocol. Hypertensive retinopathy was diagnosed based on Schie classification.

Maculopathy was defined by any visible lesion (scar, thickening, hole, bleeding) seen with 1-disc diameter of the macular on indirect ophthalmoscopy.

Any ocular disease detected during the patient assessment was documented and managed where possible with consultation of the hospital ophthalmologist or referral to relevant specialty was done.

3.6.3 Data management.

Questionnaires were checked for accuracy, consistency and completeness. All complete data was entered using a data entry template developed using Epi data version 3.0 software package with its in-built quality checks. The final data shall be backed up and exported to STATA version 14.0 for cleaning and analysis. The data was stored in an encrypted folder in a password protected laptop to ensure safety.

3.6.4 Data analysis.

Descriptive analysis was conducted to describe continuous variables using median and standard deviations (±SD), and categorical variables expressed as frequencies and percentage (%). The clients' socio-demographic data and other characteristics of the study population was then stratified into two sub-populations: patients who had ocular side effects and those that did not have ocular side effects. The sub-groups were compared under non-parametric statistical methods using Pearson chi-square test for all patient demographics and other independent variables: Age group, gender, marital status, education level, employment status, drug class type, Chlorpromazine dosage, quantity of antipsychiatry drugs taken, duration on medication,

extra medication taken, presence of comorbidities and history of eye disease. Prevalence of ocular side effects among patients was determined as a proportion of patients who presented with any side effects in the anterior or posterior segment of the overall patients taking antipsychotic drugs.

To determine the factors associated with ocular side effects among patients taking antipsychotic drugs, an arbitrary P-Value of 0.2 was used and all variables at bi-variate analysis with P-Value greater than 0.2 were excluded from the multivariable analysis.

At multivariable analysis, we used a binary response variable of patients with ocular side effects as code (1) and those without any ocular side effects as code (0). Adjusted Odds Ratios from a multivariable binary logistic regression model was used to determine the variables associated with with ocular side effects of antipsychotic drugs at 5% significant level. The LR chi2 was used to determine 5% significance and the overall significance of the model was < 0.001. The results were populated in variation of un adjusted and adjusted logistic regression model results. The data was analyzed with the statistical package software Stata version MP 14.0

3.7 Quality control.

Ocular history and examination were done by the PI, pictures were taken and supervisors consulted for double checking. The research assistants were trained, and standardized filling of the questionnaire was done. The questionnaires were checked for completeness every after an interview/assessment by the PI. Supervisors were updated on the data collection process, for their input, weekly and daily as necessitated.

3.8 Ethical considerations.

Ethical clearance was sought from the different authorities as follows:

1. Permission was sought from the Department of Ophthalmology of Makerere University, and approval will be obtained from the School of Medicine Research and Ethics Committee (SOMREC) of Makerere University.
2. Administrative clearance was sought from Mulago Hospital.
3. Before joining the study, voluntary written informed consent was obtained from the participants.
4. To ensure anonymity and guarantee confidentiality, the consent forms were not combined with the questionnaire, and only had numerical identification.
5. The study tools were kept under lock and key, accessible only to the research team, to prevent any breach of confidentiality.

6. The principal investigator, with the guidance of their supervisors, periodically ran a plagiarism check to ensure that the work of this study was free from plagiarism.

3.9 Dissemination of results.

Results for the study were disseminated to:

1. Department of Ophthalmology.
2. Department of psychiatry.
3. Albert Cook Library, Makerere College of Health sciences.
4. Directorate of Graduate Studies, MUK
5. Peer reviewed journals.
6. National and International conferences

CHAPTER 4

4.0 RESULTS

In this chapter, we review a summary of results obtained during the study. Due to logistical, resource constraints and time limitations. We opted for a sample size of 380, which was more feasible to achieve within the available resources and time frame while still providing a substantial sample for analysis.

4.1 General characteristics of the study population.

A total of 380 patients were assessed, with a median age of 35 years, age range: (18-84 years) and a standard deviation of +/-14 years. The male to female ratio was 1:1.2. Among these, 12.37% (47/380) had comorbidities, of which 8.68% (33/380) had hypertension, and 3.68% (14/380) had diabetes.

Regarding the types of antipsychotic medications, it was found that the majority of patients, accounting for 55.79% (50.06-61.52 CI), were on typical antipsychotics such as chlorpromazine, clopixol, fluanxol, fluphenazine, stelazine, and haloperidol. On the other hand, 44.21% (38.34-50.08 CI) of the patients were on atypical antipsychotics including risperidone and olanzapine.

The median duration of psychotic drug use among the patients was 48 months, with the majority falling within an interquartile range of 12 to 120 months of medication usage.

The tables below address the sociodemographic and clinical characteristics of patients seen during the study.

Table 2: Sociodemographic characteristics of participants

Variable	N=380 (%)	95%CI
Gender		
Female	208, (54.74)	48.47- 61.01
Male	172, (45.26)	38.89-51.62
Age group.		
<30	111, (29.21)	23.18-35.24
30-39	106, (27.89)	21.75-34.03
40-49	74, (19.47)	12.85- 26.00
50+	89, (23.42)	17.03- 29.81
Marital status.		
Divorced	5, (1.32)	0-6.47
Married	122, (32.11)	26.75- 37.47
Separated	24, (6.32)	0-12.98
Single	212, (55.79)	50.06-61.52
Widowed	17, (4.47)	0-14.19
Education level.		
Informal	17, (4.47)	0-10.19
Primary	106, (27.89)	22.15-33.62
Secondary	171, (45.00)	38.94-51.06
Tertiary institution	86, (22.63)	18.69-26.57
Employment status.		
Full time employment	52, (13.68)	7.01- 20.35
Self-Employment	142, (37.37)	31.12-43.62
Student	41, (10.79)	4.32-17.26
Unemployment	145, (38.16)	32.09-44.23

Table 3: Clinical characteristics of study participants.

Variable	n (%)	95%CI
Comorbidities		
Had no comorbidity	333, (87.63)	84.75-90.51
Had a comorbidity of hypertension (33) or diabetes (14)	47, (12.37)	4.29- 20.45
History of eye Disease		
No history of eye disease	357, (93.95)	92.20-95.69
Had a history of eye disease	23, (6.05)	0-17.46
Drug class type		
Typical drug	212, (55.79)	50.06-61.52
Atypical drug	168, (44.21)	38.34-50.08
Chlorpromazine Dose		
Lower dose of chlorpromazine(<600mg/day)	25, (60.97)	94.01-97.57
High dose of Chlorpromazine(>600mg/day)	16, (39.02)	0-12.19
Number of antipsychiatry drugs taken		
1 Drug	275, (72.37)	68.53-76.21
More than 1 drug	105, (27.63)	19.56-35.70
Duration on antipsychiatry drugs		
≤ 12 Months	117, (30.79)	23.43-38.15
>12 Months	263, (69.21)	64.80-73.62
Combination of drugs taken		
Only Psychiatry drugs	2, (0.53)	0-1.05
Psychiatry drugs and others	378, (99.47)	98.23-100

4.1 Prevalence of ocular side effects.

Of the total 380 patients enrolled in the study taking antipsychotic drugs at Mulago NRH, 27.63% (105/380) were found with ocular side effects of these drugs.

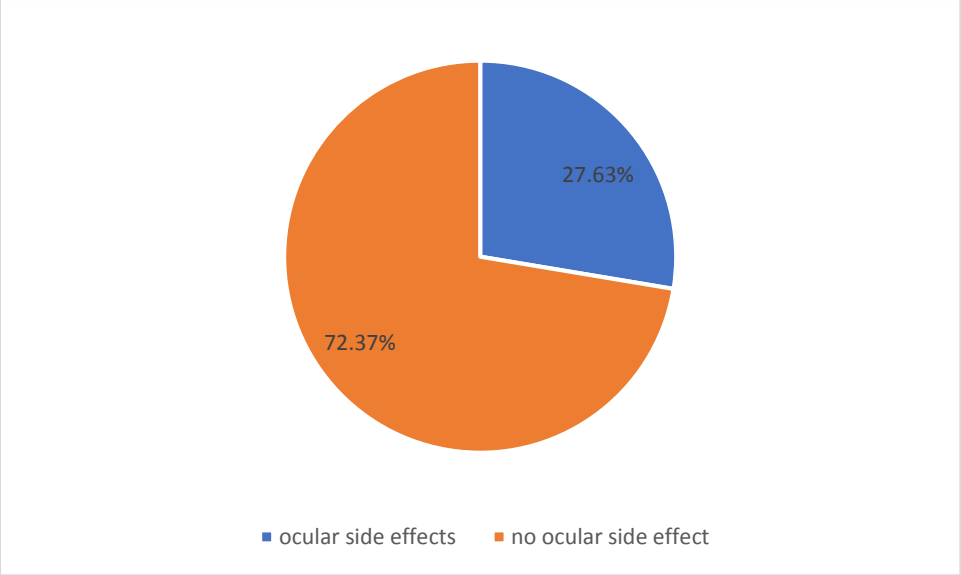


Figure 1: Ocular side effect prevalence in patients.

Prevalence of ocular side effects by sex.

There were more Females at 54.74% (208/380). The prevalence of ocular side effects was high among Females comprising of 50.48% (53/105), There was however no significant relationship of prevalence by gender (P-value; 0.303).

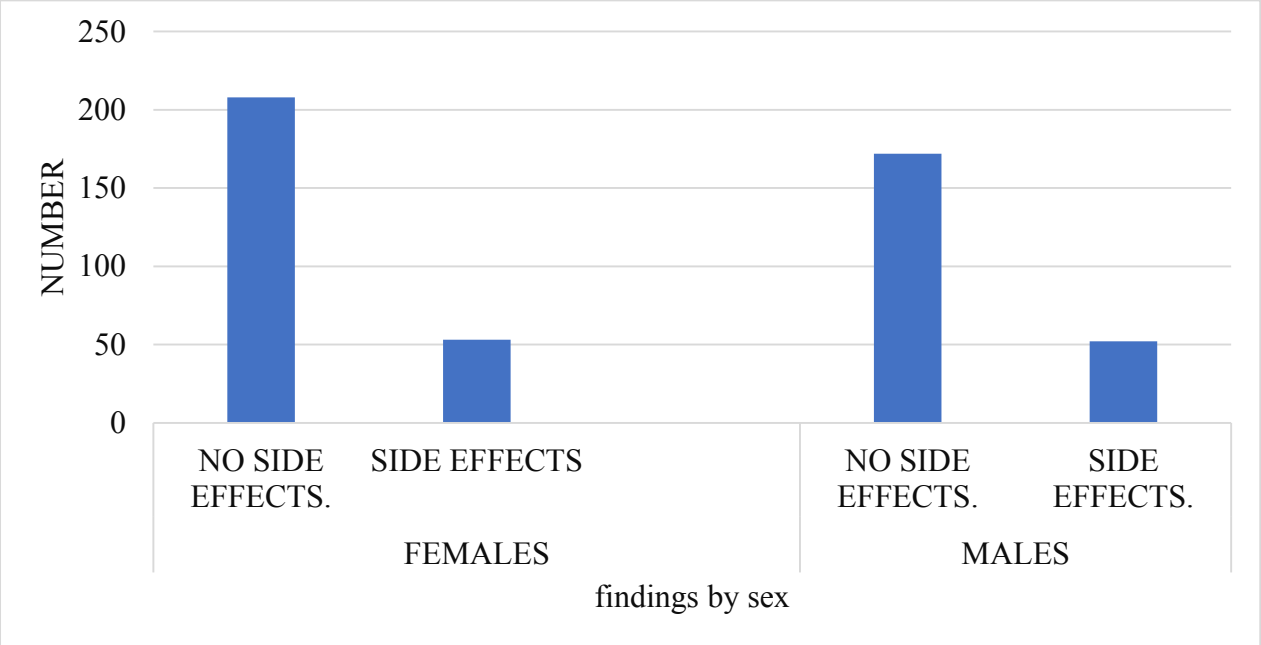


Figure 2: Histogram showing prevalence of ocular side effects of antipsychotic drugs among females and males.

4.2 Patterns of ocular side effects.

From the study, the most common ocular side effects seen were cataracts in 41 patients, followed by dry eye syndrome in 23 patients, and conjunctival pigmentation 12 patients from a total of the 110 ocular side effects seen in 105 patients.

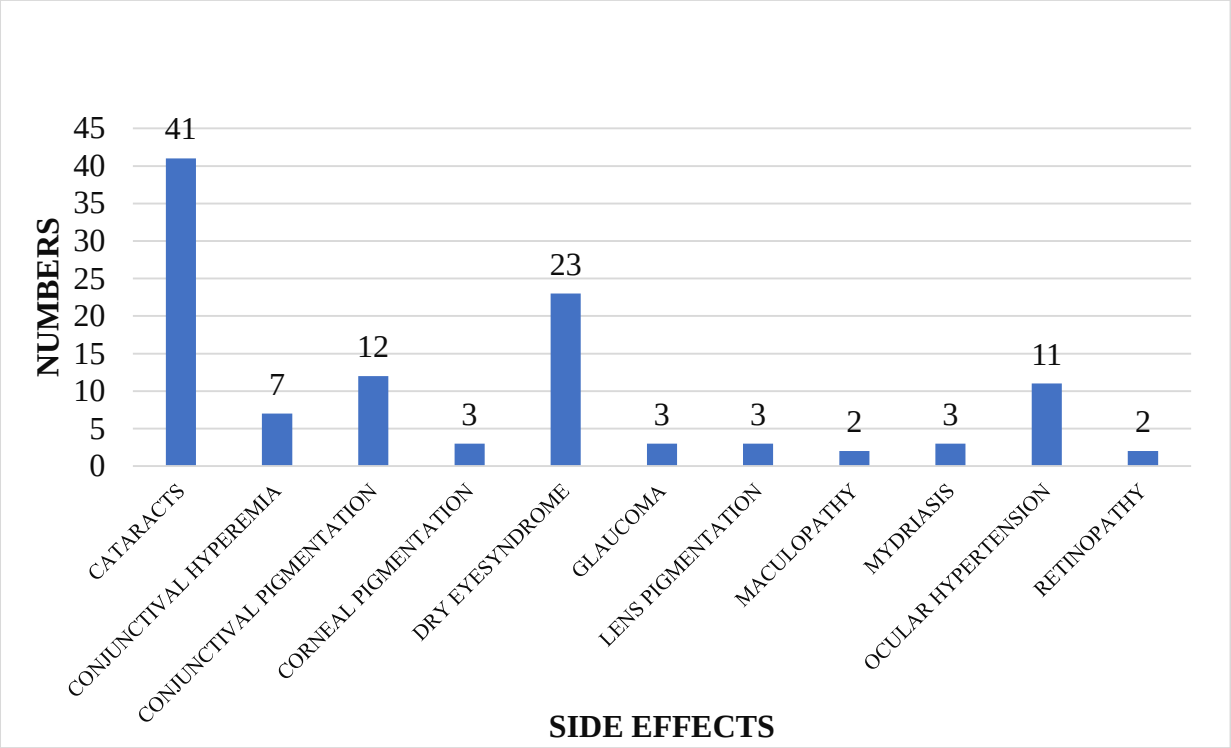


Figure 3: Histogram showing ocular side effects among adult patients taking antipsychotic drugs in MNRH Psychiatry Clinic.

Refractive errors.

A total of 99 (26.05%) had refractive errors.

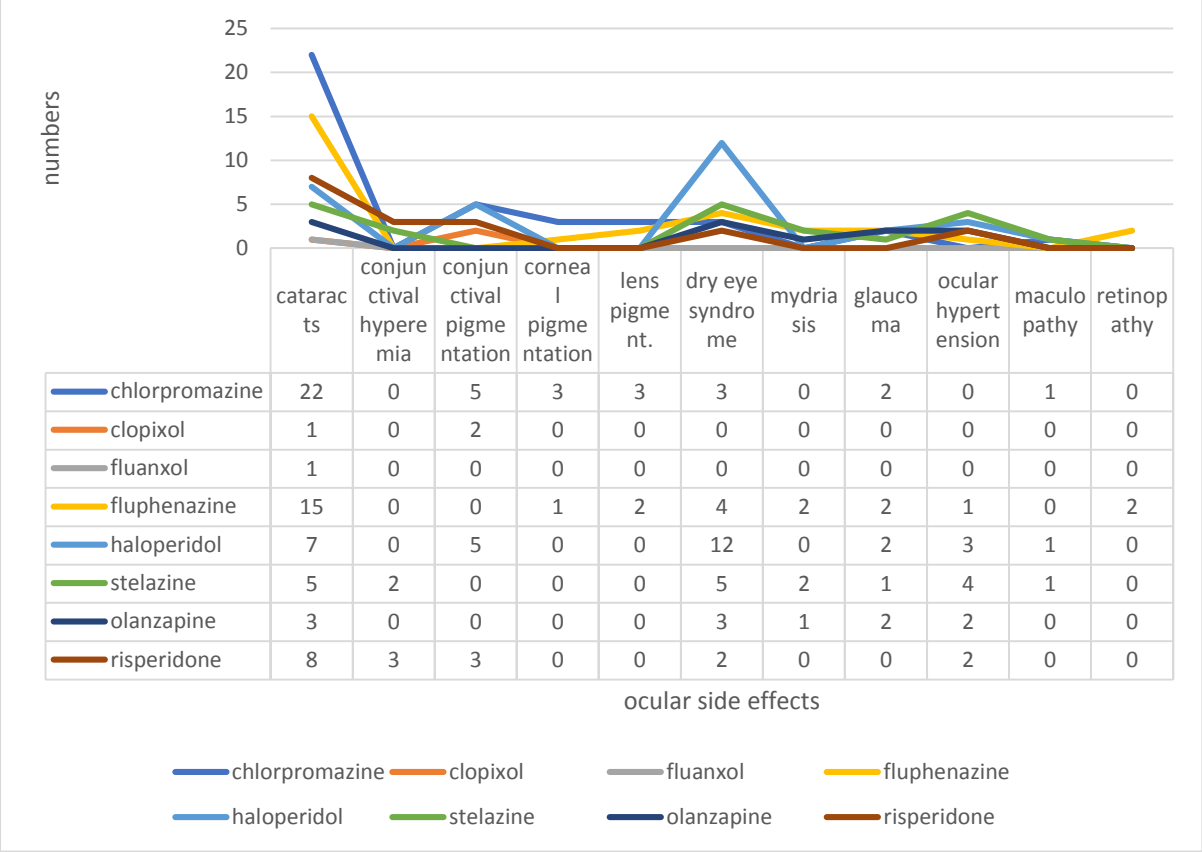
We found that most effects were myopia comprising 63 (63.64%) cases among patients. Hyperopia were also high comprising 29 (29.29%) cases.

Refractive Error	Frequency	Percent (%)
Myopia	63	63.44
Hyperopia	29	29.29
Astigmatism	6	6.06
Myopic astigmatism	1	1.01

Table 4: Showing proportions of refractive errors.

Distribution of ocular side effect by antipsychotic drug.

This study was able to show the different side effects associated with the different antipsychotic drugs used. More side effects were seen in patients taking typical antipsychotics, (chlorpromazine, clopixol, fluanxol, fluphenazine, haloperidol, and stelazine) p-value <0.001. It should however be noted that some patients could be taking more than one typical antipsychotic at a time during the study period.



	cataracts	conjunctival hyperemia	conjunctival pigmentation	corneal pigmentation	lens pigment.	dry eye syndrome	mydriasis	glaucoma	ocular hypertension	maculopathy	retinopathy
chlorpromazine	22	0	5	3	3	3	0	2	0	1	0
clopixol	1	0	2	0	0	0	0	0	0	0	0
fluanxol	1	0	0	0	0	0	0	0	0	0	0
fluphenazine	15	0	0	1	2	4	2	2	1	0	2
haloperidol	7	0	5	0	0	12	0	2	3	1	0
stelazine	5	2	0	0	0	5	2	1	4	1	0
olanzapine	3	0	0	0	0	3	1	2	2	0	0
risperidone	8	3	3	0	0	2	0	0	2	0	0

Figure 4: Distribution of ocular side effect by antipsychotic drug.

4.3 Factors associated with ocular side effects

At bivariate analysis, across several factors, the study found the following variations: by age group, occurrence of ocular side effects was highest among patients above 50 years contributing of 11.57% (44/380) and lowest among patients less than 30 years at 0.04% (16/380), the P-value was significant at **<0.001**. By marital status, being single was associated with higher prevalence at 14.47% (55/380) and lower among patients who divorced at a prevalence of 0.01% (2/380), P-value; **0.054**. By Employment status; prevalence was highest among patients unemployed at 15.00% (57/380) and least among students at 0.02% P-value; **0.001**. Participants who had comorbidities were 4.2 times more likely to have ocular side effects compared to their counterparts without comorbidities. This association was statistically significant at 95%CI 1.8-9.9, p-value; <**0.001**. Other 'significant predictors of ocular side

effects prevalence were: Drug class type, where more side effects were seen in patients taking typical antipsychotics, p-value; <**0.001**. Chlorpromazine dosage greater than 600mg was associated with more side effects, P-value; <**0.001**.

Table 5: Bivariate analysis of factors associated with ocular side effects of antipsychotic drugs among adult patients in MNRH Psychiatry Out-patient Clinic.

Patients' characteristics	No ocular side effects 275, (72.37) n, (%)	Had ocular side effects 105, (27.63) n, (%)	Chi square-values	P-Value
Age group				
<30	95, (34.55)	16, (15.24)	32.203	< **0.001**
30-39	82, (29.82)	24, (22.86)		
40-49	53, (19.27)	21, (20.00)		
50+	45, (16.36)	44, (41.90)		
Marital status				
Divorced	3, (1.09)	2, (1.90)	9.286	**0.054**
Married	91, (33.09)	31, (29.52)		
Separated	17, (6.18)	7, (6.67)		
Single	157, (57.09)	55, (52.38)		
Widowed	7, (2.55)	10, (9.52)		
Education level				
College	32, (11.64)	14, (13.33)	4.089	0.394
Informal	11, (4.00)	6, (5.71)		
Primary	72, (26.18)	34, (32.38)		
Secondary	127, (46.18)	44, (41.90)		
University	33, (12.00)	7, (6.67)		
Employment status				
Full time employment	43, (15.64)	9, (8.57)	16.403	**0.001**
Self-Employment	111, (40.36)	31, (29.52)		
Student	33, (12.00)	8, (7.62)		
Unemployment	88, (32.00)	57, (54.29)		
Comorbidities				
Had no comorbidity	256, (93.09)	77, (73.33)	27.367	< **0.001**
Had a comorbidity (Hypertension/DM)	19, (6.91)	28, (26.67)		

History of eye Disease				
No history of eye disease	269, (97.82)	88, (83.81)	26.224	< **0.001**
Had a history of eye disease	6, (2.18)	17, (16.19)		
Drug class type				
Typical drug	136, (49.45)	76, (72.38)	16.193	< **0.001**
Atypical drug	139, (50.55)	29, (27.62)		
Chlorpromazine Dose				
Less dose(<600mg/day)/ Not on Chlorpromazine	269, (97.82)	95, (90.48)	10.156	**0.001**
High dose of Chlorpromazine(>600mg/day)	6, (2.18)	10, (9.52)		
Number of antipsychiatry drugs taken				
1 Drug	206, (74.91)	69, (65.71)	3.213	**0.073**
More than 1 drug	69, (25.09)	36, (34.29)		
Duration on antipsychiatry drugs				
≤ 12 Months	91, (33.09)	26, (24.76)	2.474	**0.116**
>12 Months	184, (66.91)	79, (75.24)		
Combination of drugs taken				
Only Psychiatry drugs	1, (0.36)	1, (0.95)	0.503	0.478
Psychiatry drugs and others	274, (99.64)	104, (99.05)		

At multivariable analysis, variables which were fitted in the binary logistic regression model with P-value < 0.2 were as follows. The table shows factors statistically associated with ocular side effects among patients taking antipsychiatry drugs at Mulago National Referral Hospital.

Table 6: Multivariable analysis showing association between ocular side effects and patient characteristics at MNRH Psychiatry Out-patient Clinic.

Variable	Un adjusted OR [95% CI]	P-Value	Adjusted OR [95% CI]	P-Value
Age group				
<30	1		1	
30-39	1.738 [0.865-3.493]	0.121	2.739 [0.949-7.910]	0.063
40-49	2.353 [1.1314.892	0.022	6.048 [1.944-18.816]	**0.002**
50+	5.806 [2.961-11.382]	< 0.001	11.743 [3.667-37.599]	**< 0.001**
Marital status				
Divorced	1		1	
Married	1.903 [0.309-11.691]	0.487	0.502 [0.047-5.340]	0.568
Separated	0.972 [0.584-1.619]	0.914	0.521 [0.242-1.125]	0.097
Single	1.175 [0.463-2.986]	0.734	0.432 [0.129-1.441]	0.172
Widowed	4.078 [1.480-11.236]	0.007	0.939 [0.244-3.606]	0.927
Employment status				
Full time employment	1		1	
Self-Employment	0.323 [0.146-0.713]	0.005	0.403 [0.152-1.073]	0.069
Student	0.431 [0.257-0.725]	0.001	0.523 [0.265-1.033]	0.062
Unemployment	0.374 [0.161-0.868]	0.022	1.685 [0.488-5.813]	0.409
Comorbidities				
Had no comorbidity	1		1	
Had a comorbidity	4.899 [2.594-9.253]	< 0.001	4.228 [1.817-9.837]	**0.001**
History of eye Disease				
No history of eye disease	1		1	
Had a history of eye disease	8.661 [3.312-22.649]	< 0.001	19.408 [5.906-63.779]	**< 0.001**
Drug class type				
Typical drug	1		1	
Atypical drug	0.373 [0.229-0.609]	< 0.001	0.414 [0.204-0.843]	**0.015**
Chlorpromazine Dose				

Lower dose/ Not on Chlorpromazine	1		1		
High dose of Chlorpromazine	12.956 [5.918-28.363]	< 0.001	14.314	[5.589-36.657]	**< 0.001**
Number of antipsychiatry drugs taken					
1 Drug	1		1		
More than 1 drug	1.558 [0.958-2.534]	0.074	1.684 [0.848-3.343]		0.136
Duration on antipsychiatry drugs					
≤ 12 Months	1		1		
>12 Months	1.503 [0.903-2.501]	0.117	4.228 [1.817-9.837]		**0.001**

The adjusted binary logistic regression model identified the risk factors statistically associated with ocular side effects as:

Age group:

Patients with 50 years of age or more were more than eleven (11) times likely to have ocular side effects compared to patients with less than 30 years of age (P-value, < 0.001, AOR = 11.743, 95% CI: 3.667 – 37.599), Patients with age group 40-49 years of age were six (6) times likely to have ocular side effects compared to patients with less than 30 years of age (P-value, 0.002, AOR = 6.048, 95% CI: 1.944 – 18.816).

History of eye Disease:

Patients with a history of eye disease were about nineteen (19) times likely to have ocular side effects compared patients with no history to have any eye disease. (P-value, <0.001, AOR = 19.408, 95% CI: 5.906 – 63.779).

Comorbidities:

Patients with comorbidities of diabetes and hypertension were about four times likely to have ocular side effects compared to patients without these comorbidities. (P-value, <0.001, AOR=4.228, 95% CI: 1.817-9.837).

Chlorpromazine dose:

Patients on higher dose of chlorpromazine (>600mg /day) were about fourteen times more likely to have ocular side effects than their counterparts on lower daily doses. (P-value <0.001, AOR=14.314, 95% CI: 5.589-36.657)

Duration on antipsychiatry drugs.

Patients who had been on >12 months of antipsychotic drugs were about four times more likely to get ocular side effects compared to those who had been on it for less time. (P-value <0.001, AOR=4.228, 95% CI:1.817-9.837).

The model also identified protective factors statistically associated with ocular side effects as:

Drug class type:

Patients on Atypical drug medication were 58.6% less likely to have ocular side effects compared to those on Typical drugs (P-value, 0.015, AOR = 0.414, 95% CI: 0.204 – 0.843).

CHAPTER 5

5.0 Discussion.

This was a hospital based cross sectional study, conducted between March 2023, and May 2023, with an aim of determining the prevalence, patterns of ocular side effects, and associated factors among adult patients taking antipsychotic drugs in MNRH psychiatry out-patient clinic. A total of 380 research participants were evaluated during the study period. The following discussion elaborates on the different findings during the study.

5.1 Prevalence of ocular side effects among adult patients taking antipsychotic drugs.

The prevalence of ocular side effects was found to be 27.63% in the study conducted on a sample size of 380. There have been no comparative studies documenting general prevalence of ocular side effects among patients taking antipsychotic drugs. In this study though, females were found to have higher prevalence of ocular side effects than males contributing 54% of prevalence of these side effects by gender. In the BeSt InTro study, females were found to experience more side effects from antipsychotic drug use than males. This was attributed the difference in pharmacokinetic properties of the drugs in both genders, with females having higher serum levels, and delayed renal clearance of antipsychotics drugs than their male counterparts. These could explain the higher prevalence of side effects in the females (Hoekstra et al., 2021). This study showed a similar prevalence of ocular side effects in the two genders as in the best InTro study.

5.2 Patterns of ocular side effects of antipsychotic drugs.

Conjunctival hyperemia.

Conjunctival hyperemia was prevalent at 1.8% (7/380) in this study. Phenothiazines (chlorpromazine, thioridazine) exhibit anticholinergic side effects by blocking muscarinic and nicotinic receptors, and muscarinic 3 receptors in the conjunctiva and lacrimal gland. A persistent tear film instability results causing morphological and biochemical ocular surface changes (conjunctival hyperemia inclusive) that ultimately affect vision of the patient (Wong et al., 2011). Risperidone has been shown to cause conjunctival hyperemia in <1% adult population (Myers & Thase, 2001). This relates to this study, where ocular hyperemia was found in 1.8% (7/380) of the study participants, with risperidone being one of the causative antipsychotic drugs.

Dry eye disease

Dry eye was found in 18.10% of the participants with side effects during this study. This was seen mostly in patients taking haloperidol, stelazine, and fluphenazine. A similar study by Dr Dimple Shakeet. Found a prevalence of 32% among patients taking antipsychotic drugs. This

can be related to the anticholinergic side effects of blocking muscarinic and nicotinic receptors, and muscarinic-3 receptors in the conjunctiva and lacrimal gland as well by these drugs. This leads to decreased mucous and aqueous secretion (Dr. Dimple Shakeet*, 2019). The findings in this study were however lower than the findings reported in the study by Dr Dimple Shakeet. This could be because Dr Dimples' study had a smaller sample size of only 50 patients.

Cataracts.

In this study, cataracts had a proportion of 35.65%. this was mostly seen with use of phenothiazines (chlorpromazine and fluphenazine). The type of cataract seen was anterior subcapsular cataracts causing only minimal visual impairment. A cross sectional study to determine cataract occurrence among antipsychotic drug users, found cataract prevalence of 33% with predominance of anterior sub capsular cataract among patients taking typical antipsychotic drugs (Souza et al., 2008). This finding relates similarly to our study.

Cataracts can occur due to several risk factors such increasing age, diabetes mellitus, trauma, galactosemia, and radiation (Richa & Yazbek, 2010). Some of these risk factors (diabetes, increasing age) were present in these patients. However, most of the cataracts due to these risk factor can be cortical, nuclear, or posterior subcapsular with more visual impairment (Gardner & Teehan, 2010). The findings in our study were mostly anterior subcapsular cataracts, with minimal visual impairment, which differentiated it from cataracts due to these risk factors.

Ocular hypertension, mydriasis and glaucoma.

During the study, 2.61% of patients with ocular side effects had mydriasis, 9.57% had ocular hypertension, and 5.22% had glaucoma. Antipsychotics have weak anticholinergic effects and may result in acute angle closure glaucoma in predisposed patients. (Patients with narrow anterior chamber angles). In this study, of the 6-patients found with glaucoma, only one was on atypical antipsychotics and the rest were on typical antipsychotics. 2 patients were on TCAs, and 1 on SSRI. There have been reports of perphenazine, trifluoperazine and fluphenazine inducing Acute Angle Closure, as well as olanzapine. Concurrent use of TCAs, SSRIs drugs exacerbates anticholinergic side effects. This results from side effect of mydriasis (Jain et al., 2021). These reports show similar findings as seen in this study.

Retinopathy.

In this study, retinopathy was seen to constitute 1.74% of the ocular side effects. This was seen in patients who were on fluphenazine. In these patients, there were retinal pigmentary changes. Retina is the part of the eye suffering most damage from drugs. Retinopathy has been shown to be related to high dosages of typical antipsychotics, mainly chlorpromazine and thioridazine.

Thioridazine causes retinal pigmentary changes, disturbance of dark adaptation, color vision loss, and visual field defects. The frequency of occurrence of retinal effects seems to be proportional to the total amount of drug used over a long period of time (Richa & Yazbek, 2010). In our study, pigmentary retinopathy was seen with the typical antipsychotic fluphenazine.

Maculopathy.

In this study, maculopathy was seen in 1.74% of the ocular side effects. This were noted in a patient taking fluphenazine and another on both fluphenazine and haloperidol. In a case report publication by Lee and Fern et al, fluphenazine was shown to singly cause maculopathy secondary to its accumulation in the retinal pigment epithelium and its toxic effects. (Mun Seng Lee & A. I. Fern, 2004), Which related to this study in terms of causative drug.

5.3 Factors associated with ocular side effects among adult patients taking antipsychotic drugs.

Older age.

Older age above 50 years was associated with more ocular side effects. Ocular side effects in this age group contributed 44% (p-value 0.001) of the ocular side effects. Age 40-49 was also significantly associated with occurrence of ocular side effects. This could be because older age was associated with other co morbidities such as hypertension, diabetes, that also affect the eye. In addition, older age may confer poor drug pharmacokinetics within the body and lead to toxicity that can manifest as side effects.

A study by Gardner found prevalence of ocular side effects to be higher among age group 60 years and older at 33% (Gardner & Teehan, 2010). The higher prevalence could be because of the larger sample size used in our study against the 100 patients in the study by Gardner.

History of eye disease.

The study found that patients with a history of eye disease were about nineteen (19) times likely to have ocular side effects compared patients with no history to have any eye disease. (P-value, <0.001). This was a novel finding in this study, with no similar related studies. A history of eye disease possibly poses a detrimental effect to the eye in regards to its protection. With introduction of antipsychotic drugs, patients' eyes are already predisposed to injury and further insult is mediated by these drugs. The implication is that patients with history of eye disease on antipsychotic have an increased risk of toxic injury due to these drugs and hence a higher chance of visual impairment. It would be imperative to perform baseline ophthalmic evaluation

to patients started on antipsychotic drugs to identify these categories of patients for closer monitoring.

Class of antipsychotic drug.

Patients on Atypical drug medication were 58.6% less likely to have ocular side effects compared to those on Typical drugs (P-value, 0.015, AOR = 0.414, 95% CI: 0.204 – 0.843). Chlorpromazine, a typical antipsychotic was found to have greatest side effects than all other antipsychotics (P-value, <0.001), and this was associated with longer duration of use. Typical antipsychotics have been shown to have more side effects compared to the atypical antipsychotics (Enna & Coyle, 1998). This study supports the findings obtained during this research. However, it is imperative to note that majority (55.79%) of patients were on typical antipsychotics. In addition, the only atypical antipsychotics in use during the study were olanzapine and risperidone, against the many typical antipsychotics which were in use. It is possible that this could have contributed to the higher occurrence of side effects among those on the typical antipsychotics.

Antipsychotic drug dose.

A higher total daily dosage of chlorpromazine >600mg was significantly related to side effect occurrence.(P-value <0.001). A study by Satanove A reports occurrence of pigmentary changes in conjunctiva, cornea, and lens with total daily doses of chlorpromazine > 800mg/day (Richa & Yazbek, 2010). Higher doses are related to higher plasma drug concentrations to toxic levels resulting to side effects developing (Haylor, 2002). The ocular side effects in the study by Satanove A occurred at a slight higher total daily dose of chlorpromazine compared to our study. It is unclear what could cause this difference but an existence of several associating factors that could aggravate occurrence of ocular side effects in this study such as old age, longer duration of drug use, presence of comorbidities could explain this.

Duration on antipsychotic drugs.

Patients who had taken antipsychotics for longer durations of greater than 12 months were four times more likely to develop ocular side effects compared to their counterparts who had taken drug for less than twelve months. In a study by Richa et al., side effects were seen to occur more frequently in patients who had taken antipsychotics for longer durations (Richa & Yazbek, 2010). This could be explained by the increased cumulative dose which occurs with longer duration of use leading to toxicity (Haylor, 2002). The findings were similar in both studies.

Presence of comorbidities.

Presence of comorbidities like hypertension, diabetes was related to higher occurrence of ocular side effects. (P-value 0.001). A similar study showed that higher complications of comorbidities occurred with antipsychotic drug use, for example microvascular complications of Diabetes increased with antipsychotic drug use and the same was found in patients with hypertension (Holt, 2019). These side effects were commonly seen in patients taking atypical antipsychotics olanzapine and clozapine (Holt, 2019). In this study, one patient with retinopathy had diabetes and was using olanzapine. This exacerbation could be because of antipsychotic drug use as seen in the study by Holt.

6.2 Study Limitations.

- This was cross sectional study; therefore, causal relationship could not be established.
- There were no control group of normal patients included in this study due to time/cost constraints, therefore we could not compare or relate prevalence of some ocular side effects with normal population in our setting.

CHAPTER 6

6.0 Conclusion.

1. The prevalence of ocular side effects was found to be significant at 27.63% among adult patients taking antipsychotics in psychiatry clinic MNRH.
2. The commonest ocular side effects encountered included; cataracts, dry eye disease, and conjunctival pigmentation.
3. Significant factors associated with occurrence of ocular side effects included; older age, class of antipsychotic drug, dose of chlorpromazine, presence of comorbidities, and duration on antipsychotic drugs.

6.1 Recommendations.

For Clinical care.

1. Patients taking typical antipsychotics should be regularly monitored for ocular side effects.
2. Patients with comorbidities such as diabetes and hypertension should be regularly monitored for ocular side effects while on antipsychotic drugs.
3. Patients taking higher doses of antipsychotic drugs and who have been on antipsychotic drugs for longer duration >12 months should be evaluated for ocular side effects.

For Policy formulation.

4. We recommend that psychiatry management guidelines stipulate definite periodic eye care evaluation for patients taking antipsychotic drugs.

For future study.

5. We recommend a cohort follow up to establish causality among antipsychotic drug users and normal cohorts.

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APPENDIX I: CONSENT FORM (ENGLISH VERSION)

TITLE OF THE STUDY.

OCULAR SIDE EFFECTS AMONG ADULT PATIENTS TAKING ANTIPSYCHOTIC DRUGS IN MULAGO NATIONAL REFERRAL HOSPITAL PSYCHIATRY CLINIC.

PRINCIPAL INVESTIGATOR

Dr. OPYENE AMOS, Eye department, Makerere University College of Health Sciences.

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Background and rationale for the study:

Antipsychotic medications are drugs for the primary treatment for psychoses. They are effective in reducing symptoms of psychosis, both acute and relapse prevention, but do not cure the underlying psychotic disorder.

All antipsychotics have the potential to cause numerous unwanted ocular effects. These can include; eyelid and corneal disorder (abnormal pigmentation, corneal edema, dry eyes), anterior eye abnormality like shallowing of angles and glaucoma, cataracts, color vision abnormality, visual field defects, abnormal eye movements (nystagmus, extraocular muscle palsies). These can lead to mild, moderate, or severe visual impairment. The major objective of this study is to find out the eye problems and associated factors and the study will enroll 365 study participants. You are kindly being asked to participate in this study which will run for a period of 3 months.

Sponsors of the research project: this will be self-sponsored research.

PURPOSE OF THE STUDY.

The purpose of the study is to determine the ocular side effects among those taking antipsychotic drugs (manifestations, prevalence and associated factors) in Psychiatry Clinic MNRH. This will help raise awareness and improve patient quality of care thereafter.

STUDY PROCEDURE.

If you decide to participate in this study, you shall be asked about your general health, eyes and drugs, thereafter, a full general and eye examination will be done to look for any ocular findings. You are informed that during the examination, some eye drops (tropicamide) will be instilled into eyes to allow clear viewing of inner part of the eye in assessing for causes of your eye problems.

A comprehensive eye exam including checking whether you can see (a 3m Snellen chart will be used), measuring the pressure of your eyes, eye movements to determine muscle paralysis,

checking whether you can see in all visual field, eye surface and anterior segment examination, and posterior segment examinations will be conducted. All these will be done to determine whether any complications exist from taking antipsychotic drugs.

In case you are found with any ocular complication, you will be advised accordingly;

Those with mild complications not visually impairing will be reassured and provided health education accordingly.

Those found with visually impairing complications will be provided the necessary treatment and referral.

All these shall be decided with consultation from supervisors (consultants) on best management practice.

You will spend a short time of 40 minutes to participate in the study.

Who will participate in the study:

All who are from 18 years and above who are on antipsychotic medications who meet the inclusion criteria and have accepted to participate in the study.

RISKS.

Participation in the study has no foreseeable risks to you. However, the examination is a bit discomforting due to the bright light and eye drops used in the process. The eyedrops may cause stingy sensation that lasts a few seconds and may reduce vision for only a few hours (1-2hours of reduced near vision); however, this does not leave a permanent damage.

POTENTIAL BENEFITS.

Results from this study are expected to be used in screening, early identification and treatment of ocular disease in patients taking antipsychotics. Also, in case any eye diseases are found in yours, necessary treatment or referral shall be done.

CONFIDENTIALITY.

A study number known to the authorized study personnel and yourself will be used instead of your name. The records of the study will be kept strictly confidential, under lock and key, and electronically with password protection.

The principal investigator, research assistant, supervisors, and the local research ethics committee and Uganda national council for science and technology are entities that may have access to private information that identifies the research participants by name. You will not be identified in any of the publications or presentations about this study.

COSTS

During the study, there are no predetermined costs to be met, however if found to have any ocular disease that warrants treatment, the costs of medication shall be met by the study

participant unless, the medications are available in the government pharmacy in the hospital for which you will be provided a prescription to pick the medications.

COMPENSATIONS.

This is a relatively safe study, and there are no foreseeable risks to injury or permanent damage during the study. However, should any injury occur during the study, you will be given priority in management, that will be instituted immediately and supervisors will be consulted and reference made if required.

In addition, a modest amount of 10,000 Ug shs, will be given to patients as compensation for their time in participation in the study.

REIMBURSEMENT.

There will be no re imbursement during the study, as patients will be recruited when they come to the clinic.

ALTERNATIVES

Participation in this study is not mandatory and other options to have your eyes assessed can be from the eye clinic in Mulago or from private centers.

QUESTIONS REGARDING THE STUDY.

If you have questions about this study, you may contact the principal investigator, Dr. Opyene Amos. Department of Ophthalmology, Makerere University, Tel no. 0777101724.

QUESTIONS REGARDING PARTICIPANT'S RIGHTS.

If you have any questions at any time about your rights as a study participant, you may contact the chairman of school of medicine research ethics committee, Prof. Ocama Ponsiano, 0772421190.

VOLUNTARY PARTICIPATION.

Participation in this study is entirely voluntary, you are free to accept to participate in this study; completely refuse to participate or withdraw from the study any time. There is no penalty if you decide to withdraw or refuse to participate in this study. You will still get the medical care she/he has been entitled to in this clinic.

DISSEMINATION OF RESULTS:

The findings from this study will also be disseminated to psychiatry department, department of ophthalmology, scientific journals, and scientific conferences.

ETHICAL APPROVAL:

This study has been approved by the school of medicine research and ethics committee, which is an accredited Ugandan based research and ethics committee.

PARTICIPANT'S CONSENT.

I have been made to understand what is going to be done, the risks, hazards, my rights as a study participant and the benefits of the study. I understand that my decision to allow me participate in this study is not my usual medical care, and that my identity and information from this study will be confidential. I do not waive any of my legal rights but merely indicate that I have been informed about the study in which I am voluntarily agreeing to participate. A copy of this form will be provided to me.

Participant's name	Signature /thumb	Date
……	……..	……
Witness	Signature	Date
……	……..	……
Person obtaining consent.	Signature	Date
……	……..	……

APPENDIX II: CONSENT FORM (LUGANDA VERSION)

OMUTWE GW' OKUNONNYEREZA:

EBIKOZSEBWA MU BALWADDE ABAMIMIRA EDDAGALA ERYA OBUBAKA MU MULAGO NATIONAL REFERAL HOSPITAL PSYCHIATRY CLINIC.

OMUNONYEREZA OMUKULU:

Musawo Opyene Amos, ku kitongole ky'ebyamaaso e Makerere.

Esiimu: 0777101724.

EKIGENDERERWA KYO KUNONYEREZA

Ekigendererwa ky'okunoonyereza kuno kwe kuzuula ebizibu ebiva mu maaso mu abo abamira eddagala eriweweeza ku bwongo (okwolesebwa n'ensonga ezikwatagana nabyo) mu Psychiatry Clinic MNRH. Kino kijja kuyamba okumanyisa abantu n'okutumbula omutindo gw'okulabirira omulwadde oluvannyuma lw'ekyo.

Emitendera gyo kunonyereza

Bw'osalawo okwetaba mu kunoonyereza kuno, ojja kubuuzibwa ku bulamu bwo obw'awamu, amaaso n'eddagala, oluvannyuma, okukeberebwa okujjuvu okwa bulijjo n'amaaso kujja kukolebwa okunoonya byonna ebizuuliddwa mu maaso. Otegeezebwa nti mu kiseera ky'okukeberebwa, amatondo g'amaaso agamu (tropicamide) gajja kuteekebwa mu maaso okusobozesa okulaba obulungi ekitundu ky'eriiso eky'omunda mu kwekenneenya ebivaako obuzibu bw'amaaso go.

Okukebera amaaso okujjuvu omuli okukebera oba osobola okulaba (ekipande kya snellen ekya mmita 3 kijja kukozesebwa), okupima puleesa y'amaaso go, entambula y'amaaso okuzuula okusannyalala kw'ebinywa, okukebera oba osobola okulaba mu bifo byonna eby'okulaba, okukebera amaaso kungulu n'ekitundu eky'omu maaso , n'okukeberebwa kw'ekitundu eky'emabega kujja kukolebwa. Bino byonna bijja kukolebwa okuzuula oba waliwo ebizibu byonna ebibaawo okuva mu kumira eddagala eriweweeza ku bwongo.

Singa osangibwa ng'olina ekizibu kyonna mu maaso, ojja kuwabulwa okusinziira ku bino wamanga;

1. Abo abalina ebizibu ebitonotono ebyo butalaba bulungi bajja kugumizibwa era baweebwe okusomesebwa ku by‟obulamu okusinziira ku ekyo okunonyerezebwa kwe kinaba kizudde.
2. Abo abazuuliddwa nga balina ebizibu byo butalaba bulungi bajja kuweebwa obujjanjabi obwetaagisa n’okwongelwayo.
3. Bino byonna ebinaasalibwawo kunabako okweebuuzibwako okuva mu batukulila(abakugu) ku nkola ennungi ey’okuddukanya emirimu.
4. Ojja kumala akaseera katono ak’eddakiika 40 okwetaba mu kunonyereza kunno.

Bani abagenda okwetaba mu kunoonyereza kuno:

Abo bonna ab’emyaka 18 n’okudda waggulu ngabali ku ddagala eriweweeza ku bwongo era nga batuukana n’ebisaanyizo by’okuyingizibwa mu kunoonyereza kuno era nga bakkirizza okwetaba mu kunoonyereza kuno.

Ebiggwa bitalaze

Okwetaba mu kunoonyereza kuno tekirina bulabe bwonna busubirwa mu maaso gy’oli. Wabula okukebera kuno kuzibuwalira katono olw’ekitangaala ekimasamasa n’amatondo g’amaaso agakozesebwa mu nkola eno. Amatondo g’amaaso gayinza okuleeta okuwulira okw’obusungu okumala sekondi ntono era gayinza okukendeeza ku kulaba kwo okumala essaawa ntono zokka (12hours of reduced near vision); wabula kino tekireka kwonooneka kwa lubeerera.

EMIGASO EGIYINZA OKUGANYIBWAMU

Ebivudde mu kunoonyereza kuno bisuubirwa okukozesebwa mu kukebera, okuzuula amangu n’okujjanjaba obulwadde bw’amaaso mu balwadde abamira eddagala eriweweeza ku bulwadde ku bwongo. Era, singa wabaawo endwadde z’amaaso ezisangibwa mu gwe, obujjanjabi obwetaagisa oba okusindikibwa mu bakugu kujja kukolebwa.

Okukuuma ebyama

Ennamba emannyidwa gwe n’omunonyereza omukulu y’ejja okukozesebwa. Elinnya lyo terijja kulabikira ku kukiwandiko kyona ekikwatagana n’okunonyereza kuno.
Omunonnyereza omukulu, amumyuka, bakalabalaba b’okunonnyereza kuno n’akakiiko ke’byassayansi balina obusobozi okufuna ebiwandiko ebiriko amannyago singa kinaaba kyetagisiza.

Esasaanya

Mu ku nonyerezebwa kuno, teli miwendo gilowozebwako, wabula mu kutekera ekirwadde kyona ekyetagisa obujanjabi, enzijanjaba enaba eli oyo yena anaaba eyetabye mukunonyereza kuno okujjako nga obujanjabi ne'dagala nga gyelili mu Dwaliro lya Gavumenti.

Okulilirwa: buli anetaba munkunonnyereza aja kuwebwayo ekyokunywa no mutwalo gumu nekulwobude bwanaba atuwadde.

Engeri endala

Okwetaba mu ku nonyereza kuno sikya teeka era emitendera emilala egyokukebera amaso giyinza okukolebwa ku dwaliro elya'amaso emulago.

Ebibbuzo:

Bwobera olina ebibuuzo ebikwatta ku kunonnyereza kuno, osobola okubuza Musawo Amos Opyene ku nnamba y'essimu 0777 101 724.

Bwobera olina ebibbuzo ebikwata ku ddembe lyo, osobola okutukirira akulira akakiiko akakwasisa empisa Pulofesa Ocama Ponsiano ku nnamba 0772 421 190.

Eddembe lyo:

Foomu eno ekutegeza ebikwatta ku kunonyereza. Bwobera obitegedde nokirizza okwetaba mu kunonnyereza, ojja kwetagibwa okuteka omukono ku kiwandiko kino era ojja kuweebwako kkopi yakyo.

Okukirizibwa okunonyereza:

Okunonyereza kuno kwakirizibwa okukolebwa ekitongole ekikwasa empisa mukunonnyereza ekya Research Ethics Committee ku somero ly'abasawo ku ssetendekero lya Makerere University.

Enkozesa yebinaava mukunonnyereza:

Ebinaava mukunonnyereza nga byamugaso eri abaneetaba mukunonnyereza oba buli nkyukakyuka mukunonnyereza eja kuba ebulirwa abaneetaba mukunonnyereza kuno.

OKUKIRIZA OKWETABA MU KUNONNYEREZA KUNO

Annyinnyonnyole ebigenda okukolebwa, obuzibu nebyokuganyulwa ebiri mu kunonnyereza kuno. Ntegedde nenzikiriza okwetaba mu kunonnyereza kuno era ebinkwatako tebijja kwasanguzibwa eri abantu abalala. Nkitegedde inti nsobola okuva mu kunonnyereza kuno essawa yonna. Okutekako omukono ku kiwandiiko kino kiraga nti nzikiriza okukwetabamu.nja kuweebwako kkopi yo foomu eno.

Erinnya …….

Omukono ……..……. Olunaku…….

Omujulizi …….

Omukono…….Olunaku …….

Omuntu abuziiza …….

Omukono……. Olunaku …….

APPENDIX III: QUESTIONNAIRE

OCULAR SIDE EFFECTS AMONG ADULT PATIENTS TAKING ANTIPSYCHOTIC DRUGS IN MULAGO NATIONAL REFERRAL HOSPITAL PSYCHIATRY CLINIC.

SOCIODEMOGRAPHIC DATA AND PATIENT CLINICAL DATA.

Participants' number: ……

Date: …….

Age: ……

Gender: male ( ), female ( )

Marital status: Single ( ), married ( ), divorced ( ), separated ( ), widowed ( ).

Education level: Informal ( ), Primary ( ), Secondary ( ), College ( ), or University ( ).

Employment status: Full time employment ( ), Self-employment ( ), Unemployed ( ), Student ( ).

PATIENTS CLINICAL DATA:

Psychiatry diagnosis:……

Antipsychotic medication (s) and total daily dose.

1. ……..
2. ……..
3. ……..
4. ……..

Other medications:

1. ……..
2. ……..
3. ……..
4. ……..

Duration on antipsychotics: ……

Comorbidities:

Hypertension: Yes ( ), No ( )

Diabetes mellitus: Yes ( ), No ( )

Others:

1. …….
2. …….

OCULAR ASSESSMENT:

OCULAR HISTORY

1. Have you ever had an eye check-up? 1. Yes ( ) 2. No ( )

2. If yes, when? ……..

3. Do you have any eye complaints?

SYMPTOMS	DURATION
Blurry vision.	
Itching.	
Tearing.	
Foreign body sensation.	
Dryness of eye.	
Pain.	
Tearing.	
Photophobia.	
Discharge.	
Other.	

4. Do you have any past eye disease?

.....

5. Have you had any ocular treatment before?

i. History of using eye drops; yes ( ), no ( )

ii. If yes specify…….

iii. History of using spectacles; yes ( ), no ( )

iv. History of using contact lens; yes ( ), no ( )

v. History of ocular surgery; yes ( ), no ( )

EXAMINATION

1. General examination

i. General condition: Fair ( ), sick looking ( ), very sick looking ( )

ii. Conjunctival Pallor: Present ( ), Absent ( )

iii. Oedema: Present ( ), Absent ( )

iv. Jaundice: Present ( ), Absent ( )

v. Blood pressure: Low ( ), Normal ( ), High ( )

vi. Specify …….

vii. Pulse rate ……

viii. GCS ……..

2. Ocular examination

Eye exam

A

	Right eye	Left eye.
Visual acuity		
Pinhole acuity.		
Best corrected visual acuity.		
Refraction status		

B. Intraocular pressure …… …….

C. Periorbita 1. Normal ( ), 2. Abnormal ( )

3. If 2, Specify …… …….

D. Eyelids 1. Normal ( ), 2. Abnormal ( ),

3. If 2, specify……

E. Conjunctiva 1. Normal ( ), 2. Injection ( ), 3. Pingueculum ( ), 4. Pterygium ( ), 5. Calcification ( ) 6. Hyperpigmentation ( )

6. Others, specify …… …….

F. Tear meniscus 1. Normal ( ), 2. Reduced ( )

G. Schirmer's test without anesthesia 1. Normal (>10mm/5minutes) ( ),

2. Abnormal,≤10mm/5minutes ( )

H. Cornea 1. Normal ( ), 2. Pigmentation ( ), 3. Ulceration 4. Foreign body

5. Others, specify…….

I. Anterior chamber 1. Normal ( ), 2. Shallow ( ), 3. Flare/Cells ( )

4. Others, specify……..

J. Iris 1. Normal ( ), 2. Abnormal ( )

3. Specify…… ……..

K. Lens 1. Clear ( ), 2. Opacity ( ) 3. Aphakia ( ), 4. Pseudophakia ( )

5. Others, specify ……

L. Vitreous 1. Normal ( ), 2. Vitreous opacity ( ), 3. Vitreous hemorrhage ( )

4. Others, specify ……

M. Optic disc 1. Normal ( ), 2. Cupped ( ), 3. Atrophy ( )

4. Others, specify……..

N. Macular 1. Normal ( ), 2. Maculopathy ( )

3. Specify……

O. Peripheral retina 1. Normal ( ), 2. Abnormal ( )

3. Specify ……

P. Confrontational visual field 1. Normal ( ), 2. Abnormal ( ).

DIAGNOSIS

Anterior segment diagnosis …….

Posterior segment diagnosis …….. ……

V.A (WHO) Grade …….. …….

APPENDIX IV. BUDGET.

ITEM	ITEM QUANTITY	UNIT COST UGX	TOTAL COST UGX
PROPOSAL AND IRB			
Printing proposal to department of ophthalmology and psychiatry.	11 copies * 50 pages	100 Ugx	55000Ugx
Printing proposal to IRB	11 copies *50 pages.	100 Ugx	55000Ugx
IRB Fee			100000Ugx
DATA COLLECTION TOOLS AND EQUIPMENT.			
Consent forms.	390 * 4 pages	100Ugx	156000ugx.
Questionnaire forms.	390 * 5 pages.	100Ugx	195000Ugx.
Dilating eye drops	10	5000Ugx	50000Ugx
STATIONARY			
Box file	5	5000Ugx	25000Ugx
Pens.	1 box	20000Ugx	20000ugx
Punching machine	1	20000ugx	20000Ugx
HUMAN RESOURCE			
Research assistant.	1	500000Ugx	500000ugx
Statistician.	1	1500000Ugx	1500000Ugx
Reimbursement of study participants	384	10000ugx	3840000ugx
RESULTS PRESENTATION			
Printing final book	5	20000ugx	100000Ugx
Miscellaneous.			200000ugx
TOTAL			**6816000Ugx.**

APPENDIX V. WORK PLAN.

Activities.	December 2021	January 2022	November 2022.	March-May 2023	May 2023.	June 2023.
Proposal development.						
Proposal presentation and clearance by department.						
Proposal submission to IRB for approval.						
Data collection						
Data entry and analysis.						
Report writing, results presentation, and submission of dissertation and manuscript.						

Clinical Outcomes in Routine Evaluation 10 (CORE-10)

Instructions:

This form has 10 statements about how you have been OVER THE LAST WEEK.
Please read each statement and think how often you felt that way last week.

		Not at all	Only occasionally	Sometimes	Often	Most or all of the time
1	I have felt tense, anxious or nervous	0	1	2	3	4
2	I have felt I have someone to turn to for support when needed	4	3	2	1	0
3	I have felt able to cope when things go wrong	4	3	2	1	0
4	Talking to people has felt too much for me	0	1	2	3	4
5	I have felt panic or terror	0	1	2	3	4
6	I made plans to end my life	0	1	2	3	4
7	I have had difficulty getting to sleep or staying asleep	0	1	2	3	4
8	I have felt despairing or hopeless	0	1	2	3	4
9	I have felt unhappy	0	1	2	3	4
10	Unwanted images or memories have been distressing me	0	1	2	3	4

Interpretation; < 10-non clinical range; 11-14, mild psychological distress; 15-19, moderate psychological distress; 20-24, moderate to severe psychological distress; >25, severe psychological distress.