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PREVALENCE OF EXTRAPYRAMIDAL SYMPTOMS AMONG PATIENTS ON ANTIPSYCHOTIC MEDICATIONS AT MATHARI NATIONAL TEACHING AND REFERRAL HOSPITAL NAIROBI CITY COUNTY, KENYA

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Abstract*: Extrapyramidal symptoms (EPS) are a group of movement disorders that are common with conventional antipsychotics. They include dystonia, akathisia, parkinsonism and tardive dyskinesia. First generation antipsychotics drugs are associated with extrapyramidal symptoms in 61.6% of institutionalized patients with Schizophrenia. Extrapyramidal symptoms lead to poor medication adherence, relapse and hospitalization, stigma, distress and impaired quality of life. The study aimed to determine the prevalence of EPS among patients taking antipsychotics at Mathari National Teaching and Referral Hospital in Nairobi county, Kenya. In this hospital 80% of antipsychotic drugs used are first generation while only 20% are second generation. A cross-sectional review of medical files for patients on antipsychotics was done at Mathari National Teaching and Referral hospital. Patients diagnosed with Extrapyramidal symptoms and were on treatment with antipsychotics were selected from the Psychiatric outpatient department clinic. Systemic random sampling was also used to select 80 medical records for review. Data was collected using data abstraction forms. The data collected was coded and analyzed using SPSS version 28. Categorical variables were summarized and presented using frequency tables, pie charts and bar charts while continuous variables mean, standard deviation and histograms were used. Majority of the patients were male 61.3% with females accounting for 38.8%. The study findings also indicated that 20% were married and 57% single while the rest 23% are divorced, separated or widowed. The most common extrapyramidal symptom was akathisia 30% while the least prevalent was tardive dyskinesia. Most of the patients smoked tobacco (67.5%), and non-smokers accounted for 32.5%. The highest level of education among the respondents was secondary education at 52.5% while 23.8% had attained college education and 8.8% university education. The most prescribed antipsychotic were first generation antipsychotics 80% and second generation 20%. The most prevalent extrapyramidal symptom was akathisia at 30%, parkinsonism was the second most prevalent at 27.5% while acute dystonia was at 25% and tardive dyskinesia at 17.5%. The first-generation antipsychotics were the mostly prescribed antipsychotic drugs

***Keywords:* extrapyramidal symptoms, antipsychotic drugs, psychiatric.**

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1. INTRODUCTION

1.1 Background of the study

Psychotic disorders are constellation of symptoms resulting in a loss of touch with reality. They comprise one or more of the following five categories namely delusions, hallucinations, disorganized thought, disorganized behaviour, and negative symptoms. The peak onset of a psychotic disorder is earlier in males than females. It is estimated that 1.5%–3.5% of the population suffers from some form of affective or nonaffective psychotic disorder (Calabrese and Al Khalili, 2023). Black individuals have a 2.13-fold greater risk in the incidence of nonaffective psychoses, and a 1.76-times of affective psychoses increased risk compared with White individuals (Kalin, 2023). In sub-Saharan Africa, mental disorders account for approximately 10% of the disease burden, and studies on the prevalence of Psychotic-like experiences among Kenyan youth found a prevalence of 3.5% (Ndetei *et al*., 2012). Those with psychotic disorders have increased odds of suicide, premature death and metabolic-related and cardiovascular illnesses (Kalin, 2023).

Treatment of psychotic disorders involves a combination of psychotherapy, pharmacotherapy, and social support. In most middle-income and low-income economies, pharmacotherapy especially with first generation antipsychotics is the mainstay treatment (Matheri *et al*., 2021). Many antipsychotic medications are available with improved efficacy in reducing acute and chronic symptoms of various psychotic disorders. However, antipsychotic drugs are associated with severe side-effect profiles, sometimes hampering a person's or patient's quality of life (Sadock *et al*.,2017). This often leads to poor medication adherence. People with psychotic disorders face stigma and reduced quality of life.

Among the various side effects of antipsychotics, extrapyramidal symptoms (EPS) constitute one of the most important side effects interfering with patients' compliance towards medication. Kenya's mental health care system faces particular challenges, including insufficient drug supply and low affordability, which influence the choice of antipsychotics. Many of the patients opt to buy drugs they can afford, which are mostly first-generation antipsychotics and usually associated with the highest frequency of side effects. Additionally, inadequate human resources, lack of prioritization of mental health, stigma, traditional and religious beliefs and insufficient training, especially in rural and informal settings, affect the management process (Ambikile and Iseselo 2017; Musyimi *et al*., 2017)

Extrapyramidal symptoms were first identified in 1952 among patients on chlorpromazine and who demonstrated symptoms similar to Parkinson's disease (Rifkin, 1987) hence EPS was characterized as a Chlorpromazine-induced side-effect. The appearance of these movement disorders is generally time and dose-dependent. Some common antipsychotics that cause EPS include phenothiazine neuroleptics such as chlorpromazine and butyrophenones, such as haloperidol. Other agents that cause EPS besides antipsychotic drugs are antiemetics such as droperidol, metoclopramide and prochlorperazine, lithium, serotonin reuptake inhibitors (SSRIs), stimulants, and tricyclic antidepressants (TCAs) (Farahmadilah and Amris, 2023). Also, some antivirals, antiarrhythmics, and valproic acid can cause EPS (Chokhawala and Stevens, 2023)

Extrapyramidal symptoms represent a collection of side effects that primarily present as movement disorders. These symptoms are commonly associated with antipsychotic medications, particularly first-generation or "typical" antipsychotics. They cause postsynaptic blockade of dopamine D2 receptors in the mesolimbic system of the CNS leading to movement disorders. The blockade leads to increased cholinergic activity, resulting in acute dystonia, akathisia, antipsychotic-induced parkinsonism and the various forms of tardive syndromes, such as dyskinesia, and akathisia (Ameer and Saadabadi, 2023). The antidopaminergic action in the caudate nucleus and basal ganglia thus also contributes tremendously to EPS as these areas are predominantly involved in the coordination of voluntary movements and fine-tuning motor coordination between the thalamus and the cortex. Nonetheless, the blockade of receptors in these pathways is useful in the treatment of positive symptoms such hallucinations, delusions and disorganized speech (Horga *et al*., 2016) but also increased worsening of negative symptoms such as alogia, evolution and anhedonia (Howes *et al*., 2009).

Many second-generation or atypical antipsychotics, have reduced prevalence EPS. This is attributed to their mechanism of action which is by blocking D2 dopamine receptors as well as serotonin receptor antagonist action especially 5- HT2A subtype. They differ from first-generation by transiently occupying D2 receptors, followed by rapidly dissociating, allowing normal dopamine neurotransmission thus have fast D2 dissociation. They also have antagonistic properties on the 5HT2A receptor, and 5HT1A agonism although at a lower rate (Ameer and Saadabadi, 2023).

In most patients with antipsychotic-medication-induced EPS, akathisia and dystonia are acutely observed. Some chronic side effects include tardive dyskinesia or tardive akathisia. Parkinsonism is particularly challenging among EPS because it may unmask a neurodegenerative disease. (Roiter *et al*., 2020). Despite advancements in medication and treatment, extrapyramidal symptoms continue to plaque patients undergoing antipsychotic treatments. The prevalence, incidence and course of extrapyramidal symptoms associated with antipsychotic medications vary due to different criteria to identify and define EPS among clinicians. However, Ali *et al*., (2021) estimated the prevalence of antipsychotic-induced parkinsonism, akathisia, and tardive dyskinesia at 20%. The extrapyramidal symptoms rating scale (ESRS) is the most comprehensive since it accesses all types of EPS while other scales access only one symptom (Chouinard and Margolese, 2005). Many treatment guidelines recommend long-term antipsychotic treatment for Schizophrenia and related disorders because intermittent treatment may be associated with potentially avoidable risk of relapse (Taipale *et al*., 2020). Even with well-documented nature of EPS, gaps remain in the understanding of its prevalence and risk factors across diverse populations, highlighting the need for a more comprehensive study.

There is limited data on the prevalence and detection rates of psychotic disorders in Kenyan hospitals as well as documentation of the side effects of the antipsychotic medications and how they may affect the patients' compliance to treatment. The aim of this study was to determine the prevalence and clinical correlates associated with extrapyramidal symptoms as well as to bring awareness to the gap in antipsychotics and sensitize prescribers on the importance of recognizing the different types of extrapyramidal symptoms. Comprehensive data is needed to quantify the prevalence of EPS across different demographics and medication regimens, bridging the gap between the current and ideal state of patient care.

2. MATERIALS AND METHODS

Study site

The study was carried out in the Outpatient Psychiatric clinic at Mathari National Teaching and Referral Hospital. It is the largest public teaching and referral psychiatric hospital in Kenya with a bed capacity of 700 beds. There is a total of ten wards, with two of them being the maximum-security wards and the remaining eight civil unit wards, consisting of 4 female wards and four male wards. The hospital staff numbers 386 staff. This is against the international recommended staff of 1077 (GoK, 2019). There are 104 psychiatric nurses, 11 consultant Psychiatrists, two clinical pharmacists, eight pharmacists, one pharmacy technologist, five clinical officers and zero psychologists (GoK, 2017&2019). The hospital Outpatient unit serves patients discharged from the wards and at least 1500 clients monthly (GoK, 2017; Muhia *et al*., 2021).

Study design

A hospital-based retrospective cross-sectional study design was used. This study allows for review assessment, which is beneficial for understanding the current prevalence of EPS in selected settings. The study design also requires fewer resources compared to other study designs like longitudinal designs. Due to ethical considerations and given that EPS is a sensitive issue with potential ethical constraints, a cross-sectional study provided the necessary data without interfering with patient care.

Target population

Adult patients undergoing antipsychotic treatment at the Outpatient department clinic were targeted for the study. Patients undergoing antipsychotic treatments were chosen due to the prevalence and potential of EPS associated with these medications. The inclusion criteria were patients and their file records who were on antipsychotic medications for at least two weeks, those aged above 18 years and were clinically stable. Those who had with incomplete or missing information in the medical files, a history of neurological disorders that could mimic EPS or those severe mental illness were exclude from the study.

Sampling procedure

Sample size was obtained based on the prevalence of tardive dyskinesia, the main long-term extrapyramidal effect associated with patients on treatment with antipsychotic medications. (A study conducted at the Mathari Hospital found the prevalence of Tardive dyskinesia to be 11.9% among patients on typical antipsychotic treatments. (Gatere *et al*.,2002). The sample size was determined using the statistical formula by Fisher *et al*, (1998) for estimating sample size.

There are about 1,500 patients who attend the Outpatient clinic every month and a sample size of 165 patients will be required.

$N=Z^2\times P(1-P)/d^2$

Z=1.96(Z-value from the standard normal distribution for 95% confidence)

P=0.5(The proportion in the target population estimated to have characteristics being measured)

d=0.05(Level of statistical significance that is set for example 0.05% represents a 5% error)

$n=1.96^2\times 0.119(1-0.119)/0.05^2 =161$

A sample size 165 was recruited with a 3% overage to cater for incomplete data and misinformation.

Data collection tools

Data collection for the study was done using data abstraction forms from the paper filing forms, e.g. patients' medical forms and prescriptions and computerized medical records. The form collected the patient's socio-demographic data and helped analyze the different types of EPS from the patients eligible for the study. The two main data collection tools included the extrapyramidal symptoms rating scale and demographic data forms.

Extrapyramidal symptoms rating scale

The extrapyramidal symptom rating scale (ESRS)is the most comprehensive as it accesses all types of EPS. It is a clinician-administered rating scale that includes four subspaces and four clinical global impression severity(CGI-S). The four subscales include drug-induced movement disorders, which is a (12-item questionnaire rated on a 4-point scale), parkinsonism and akathisia (7-item examination rated on a 7-point scale), dystonia which is a (10-item examination rated on a 7-point scale) and dyskinesia (7-item examination rated on a 7-point scale). The four Clinical global impression severity scales capture tardive dyskinesia, parkinsonism, acute dystonia and akathisia and are rated according to the physician's experience using an 8-point rating scale.

Ethical considerations

Approval to conduct the study was granted by the Kenyatta University ethical review committee number PKU 3845/11968. Authorization was also sought from the Mathari Teaching and Referral Hospital Ethics Committee. Once the written permission was granted, the patients eligible for the study after fulfilment of the inclusion/exclusion criteria were selected from both the inpatient and outpatient units after giving a full informed consent. systematic random sampling technique was employed to single out the required sample population for the research study. The data abstraction form acted as a guide to collect the necessary data variables for the research study. Additional information was extracted from the patient's file after confirming that their identification details correspond to those on the file, e.g. sex of patient. Only the patient files that were with complete medical information. The data on the medications that they were currently on was extracted from the in-patient treatment sheets and patients' prescriptions at the pharmacy department. Data abstraction forms were filled according to the information obtained from each study participant. The survey was anonymous; only the unique code number allocated was recorded. The patients' data was identified with a unique code number to maintain their privacy. In order to gain important additional data, their psychiatrists were consulted. All the patients during the study were on neuroleptic medication. Data was entered into Microsoft Excel® and then analyzed using SPSS Version 28.

3. RESULTS

A total of 165 participants were selected for the study but 85 were excluded for various reasons. Five of those excluded were below 18 years of age after confirming in their medical records, 58 of them had incomplete or inconsistent medical records, and 22 remaining had incorrect identification numbers, therefore their medical files were not easily retrievable, leaving 80 participants. Of the participants, about sixty one percent (61.3%) were males and 38.8%) were females. The mean age of the sample was 36yrs (SD+ 11.642) and the median age was 35 years, with a range of 18-75 years. More than half of the patients had no previous history of psychiatric admission while (31.3%) had been previously admitted.

About seventy five percent (75%) indicated that they were Christians, 12.5% being Muslim and 12.5% ascribed to other religious affiliations. About 46% were self-employed doing various businesses while 36.3%were unemployed, 5% were

students and 12.5% were full-time employees. Most of the patients took alcohol (65%) while 67.5% admitted to smoking cigarettes or taking tobacco and some other illicit drugs. Majority had some form of education with the highest academic achievement being secondary (52.5%), primary education at 11.3%, college at 23.8% and university education at 8.8%.

About fifty eight percent (57.5%) were single, 20% were married, 8.8% were divorced, 10% were separated and 3.8% were widowed. Of the antipsychotic drugs, 80% used were first generation while only 20% are second generation. The most prevalent side effect of the drugs was Akathisia 24 (30%) Parkinsonism 22 (27.5%), Acute dystonia 20 (25%) and at 14 (17.5%) being tardive dyskinesia.

TABLE 1: Prevalence of EPS

Symptom		Frequency	Percent
	Akathisia	24	30.0
	Acute dystonia	20	25.0
	Parkinsonism	22	27.5
	Tardive dyskinesia	14	17.5
	Total	80	100.0

There was a correlation between the type of antipsychotic drug and the appearance of extrapyramidal side effects. Thus, the null hypothesis that he prevalence of EPS varies significantly among patients taking different types of antipsychotic treatments could not be rejected.

Table 2: correlation between type of antipsychotic and diagnosis of extrapyramidal symptoms

Correlations			
		Type of antipsychotic	Diagnosis of EPS
Type of antipsychotic	Pearson Correlation	1	.100
	Sig. (2-tailed)		.376
	N	80	80
Diagnosis of EPS	Pearson Correlation	.100	1
	Sig. (2-tailed)	.376	
	N	80	80
	Sig. (2-tailed)		0.376
	N	80	80

4. DISCUSSION

The population was predominantly male at 61.3% indicating that mental illness was more common in males than females. This was similar to a study in nearby Uganda with predominance male gender (66.5%) at sex ratio of 2:1 male to female (Kalume *et al*., 2024) and another in Thailand, where the majority were the males (Suanrueang *et al*., 2022). Other studies have had more females with mental disorders than males (Engidaw et al., 2020, Otten *et al*., 2021, Muze *et al*., 2021, Mohammed et al., 2022). In this study, mental illness requiring antipsychotics was more prevalent among those aged below 45 years. The median age was 35 years. This indicates that the condition affects mostly the middle-aged Kenyan population. This was similar to a study done in Kenya where the median age was 34 years (Kwobah *et al*., 2017). and in Uganda at whereby the participant had an average age of 35.9 years (Kalume *et al*., 2024)

Majority of patients were single and have never been married (57.5%) and only 20% were married. This observation was similar to studies done in Finland (Van der Sanden *et al*., 2014) and Ethiopia (Mohammed *et al*., 2022) which indicated that marital status and an intimate relationship are of vital importance for mental wellbeing. Generally, the mentally ill may have limited ability to form consistent and long-term social engagements due to the occupational and social disability that arises from the illness. According to a study, partners with mental illness feel isolated and misunderstood by their partners. Similarly, partners with mental illness are reported to be unable to meet their established obligations and they experience social exclusion which are a trigger to poor interpersonal relationships as evidenced by the high rates of separation (Mohammed *et al*., 2022, Van der Sanden *et al*., 2014).

Mental illness significantly affects the concentration, dependability, mental ability and optimism hindering performance. There is an association with school termination before completing primary education. this corresponds to studies in Ethiopia that showed majority of the people with mental health disorders had no formal education or only attained primary education (Mohammed *et al*., 2022; Muze *et al*., 2021). In another study done in the USA, the chances of school termination among the mentally ill to be 1.3% to 7.0% as compared to the rest of the population (Breslau *et al*., 2008). The early onset of illness hinders educational attainment. This is indicative of this study whereby more than half of the patients had attained secondary education with only 23% having college education and 8.8% with university education.

Most of the participants were Christians (75%) while 12.5% were Muslims. This reflects the Kenyan population with 80% being Christians while 11% being Muslim and 25% representing other religious affiliations. The use of alcohol especially heavy drinking has been linked to depressive symptoms. It is estimated that 32% of the global population consume alcohol. There is evidence that links worsening mental health and increased alcohol use. People with common mental disorders such as depression, anxiety and phobia are twice as likely to report an alcohol use disorder than people without it (Jane-Llopis *et al*.,2016).

In Africa, the prevalence of tobacco use is about 20% compared to the global usage rate of 15%. The study found that 67.5% of the participants were smokers which is twice that of the general population. Some studies have linked smoking to severity of drug induced extrapyramidal symptoms (Chong *et al*., 2003; Abu-Naser *et al*., 2021, Kalume *et al*., 2024). Smoking reduces the negative affect among the mentally ill and individuals with anxiety disorders and depressive states have demonstrated higher smoking rates than the general population. According to Kalume *et al*, (2024), smoking increases dopaminergic activity from nicotine, leading to nigrostriatal hypersensitivity to dopamine, and neurotoxicity from the free radicals in cigarette smoke, causing damage to catecholaminergic neurons in the basal ganglia. On the other hand, Smoking also increases the risk of cerebrovascular pathology, which may lead to increased risk of developing extrapyramidal side effect. Smoking, substance abuse and positive family history of substance abuse are among factors associated with mental illness (Mohammed *et al*., 2022)

Employment is important for mental healthcare. Joblessness worsens mental health and gaining employment has been shown to improve mental healthcare. The study found that majority of the participants were self-employed (46.3%) while 36% unemployed, 5% were students and 12.5% were full-time employees. This study agrees with Mohammed *et al*, (2022) which identified joblessness as a risk factor for mental illness, In the UK and USA and other high-income countries, 10-15% of the mentally ill individuals are full-time employees (Drake and Wallach,2020). This could be attributed to the chronic nature of the illness which is characterized sometimes with positive and negative symptoms, especially in a working environment. Many people with mental disorders desire employment as a primary treatment goal and legal standards in several high-income countries have issued directives for creating opportunities for employment. Employment ensures self-reliance and leads to other valued outcomes including self-confidence, respect of others, personal income and community integration. It is not only a short-term treatment but also one of the only interventions that lessen dependence on mental health system over time.

In this study, majority of the patients resided in urban centers which comprised 58.8% while those residing in rural areas were 41. 3%. Mental illness and associated social problems such as substance abuse, homelessness, and crime which are often concentrated in urban neighborhoods. Urban environments also tend to be noisy and busy which stimulates fear and stress among new comers. Higher mental illness and unhappiness rates in cities may result largely from the concentration of people with elevated risk factors such as poverty, disability and minority status because urban areas offer more economic opportunities, services and tolerance (Todd, 2017). The majority of this study participants had no positive history of previous admission while 31.3% had been admitted prior, indicating a relapse or chronic nature of the mental illness.

This study reports that EPS is prevalent with first generation antipsychotics. Kalume *et al*, (2024) reported similar observations in psychiatric units in Uganda. The most reported EPS was akathisia which was most notably interpreted as a sense of restlessness and compulsion to move and was identified as one of the most troublesome with a prevalence of 30%. It is mostly associated with most discontinuation of medication the acute treatment phase. The most notable symptoms also include stamping feet while sitting, inability to sit down for short periods of time and walking or moving constantly.

The second most prevalent EPS was parkinsonism which was at 27.5%. This was reported as tremors in various body parts, slowness in movement (bradykinesia) and difficulty in initiating movements and rigidity. Most of the participants had tremors as the most notable type of drug induced parkinsonism symptom. Acute dystonia was prevalent in 25% of the

patients and this was mainly identified as oculogyric crisis among majority of the participants and some degree of torticolic crisis and buccolingual crisis in the rest of the patients. Younger patients seem to be more susceptible to develop acute dystonic reactions while older patients are more likely to develop drug-induced parkinsonism. The incidence of acute dystonia can sometimes be twice as high in males than females. The clinical features of acute dystonia appear to differ in different age groups with younger patients showing more generalized involvement of the trunk and the extremities while older individuals tend to show restricted movement of neck, face tongue and upper extremities (Lewis and O'Day 2023).

Tardive dyskinesia was the least prevalent among the Extrapyramidal symptoms with 17.5% being diagnosed with it. This was mainly identified by drooling and lip smacking as the most notable symptoms. It was within the same range as a previous study that was carried out in MNTRH that found the prevalence of tardive dyskinesia to be at 11.9 % (Katayi, 2014). The prevalence of tardive dyskinesia is most commonly experienced in patients who are on antipsychotic and increases steadily with age. It is also associated with older age, female sex, previous brain injury or dementia, early extrapyramidal symptoms, use of stimulants like amphetamines and African and African American race. Patients with other conditions like schizophrenia and depression are also most prone to severe forms of tardive dyskinesia (Cornett *et al*., 2017). In a study on 903 patients with schizophrenia, the prevalence of drug induced parkinsonism was 17.7%, 13.2% had only tardive dyskinesia, and 13.6% had both drug induced parkinsonism and tardive dyskinesia (Rekhi *et al*., 2022)

The most prescribed antipsychotics were the first-generation antipsychotics with a prevalence of 80% while the second-generation antipsychotics were 20%. This was substantially lower than the rate of SGAs used in developed countries in the world such as China at about 84% (Guo *et a*l., 2021) while in India is at about 94% (Mathew *et al*.., 2019). This can be explained by the cost of SGAs in Kenya and low affordability of patients to these medications. Second generation antipsychotics are more associated with metabolic disorders but they can cause movement disorders such as EPS although atypical antipsychotics are more implicated in EPS due to their high potency dopaminergic binding (Chokhawala and Stevens, 2023)

5. CONCLUSION

Mental illness, substance abuse, smoking, frequent alcohol use, male gender, joblessness, being single and use of first-generation antipsychotic drugs were some of the factors identified by this study as triggers and causes of extrapyramidal symptoms. Extrapyramidal symptoms affected many patients in this hospital as majority of the patients were on first generation antipsychotics at 80% while the rest were on second generation at 20%. The most prevalent EPS symptom was akathisia (30%), parkinsonism was the second most prevalent at 27.5% while acute dystonia was at 25% and tardive dyskinesia was the least prevalent with 17. 5%.

6. RECOMMENDATION

Further studies should focus on getting the specific prevalence of each Extrapyramidal symptom and the specific agents that are responsible for each symptom. This will be beneficial in developing the personalized treatment plans for each patient depending on the antipsychotic medication they are taking.

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