

FACTORS CONTRIBUTING TO INCREASED ADVERSE DRUG EFFECTS OF ANTI-CANCER DRUGS AMONG CANCER PATIENTS AT MULAGO NATIONAL REFERRAL HOSPITAL, KAMPALA CITY; A CROSS-SECTIONAL STUDY.

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ABSTRACT.

Background:

The purpose of the study was to assess factors contributing to increase Advance Drug Effects among patients taking anti-cancer drugs attending Mulago National Referral Hospital, Kampala City.

Methodology:

A cross-sectional study design was employed using a simple random-sampling technique on a sample size of 50 respondents. Semi-structured questionnaires with closed-ended questions were used. Data was analyzed manually using tally sheets and entered into a computer using the Microsoft Excel computer program to generate tables and figures.

Results:

All respondents 50(100%) who were interviewed reported having experienced at least a side effect from the anti-cancer drugs they were taking despite being varying in severity of symptoms. The majority of the respondents were females 28 (56%), Most of the severe Advance Drug Effects of alopecia and severe vomiting were seen in patients. Patients having other co-morbidities like Hypertension, Diabetes, and sickle cell anemia indicate that most of these respondents were taking more than one or two types of drugs as a result of the multiple diagnoses.

Conclusion:

Advance Drug Effects impact on overall treatment outcomes may result in treatment failure or abrupt adherence to medications however with early detection and reporting, minimization of damage can be achieved. Individual factors like having related medical co-morbidities like hypertension, and diabetes. Healthcare-related factors like a high pill burden and frequent dosages of the prescribed drugs contributed to the occurrence of Advance Drug Effects among the patients.

Recommendations:

Since most of the Advance Drug Effects in hospitalized oncology patients are predictable and at least probably preventable, the researcher, therefore, recommends that the hospital sets up an effective ADE monitoring and reporting system and create awareness among healthcare workers regarding the importance of this system, the government should encourage rational use of drugs.

Keywords: Cancer patients, Anti-Cancer Drugs, Mulago National Referral Hospital, Advance Drug Effects
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BACKGROUND OF THE STUDY.

Globally cancer remains the leading cause of death accounting for nearly 18 million cases with approximately one in every six deaths i.e. 6 million cases annually globally and a projection of increase to 29 million cases by the year 2040 which poses both an economic and public health burden as it contributes to reduction in the Disability Adjusted Life Years (DALYs) globally by 16.8% (WHO, 2019).

In Uganda, the Global Cancer Observatory Assessment indicated that Uganda cancer institute through its main two registries at Gulu and Kampala cancer registry

reported that as of 2020, 34008 new cancer cases and 22,992 associated deaths of cancer were recorded with more than 4000 new cancer patients of which only about 7400 cases make it for care while over 60% of all the registered cases (21,000) are deaths as a result of presentation as a late-stage disease at the cancer institute, Mulago annually with cancer of the cervix, prostate, breast, and Kaposi sarcoma being the most prevalent types in the country (WHO M., 2021) Almost all patients who had been enrolled on anticancer treatment (80%) had ever reported having an episode of side effects following anticancer drug use like weakness, loss of appetite, loss of hair among others 52% of which reported having ever

sought medical help 14% others opted for possible other remedies like herbal medicine following side effects (Nakaganda, 2021).

There is limited literature assessing factors contributing to the increasing ADE's among cancer patients attending Mulago national referral hospital, this therefore prompted the researcher to probe into the factors that may be a foundation for modulation of interventions to curb the variation. This study aims to determine the factors contributing to the increased adverse drug effects of anticancer drugs among cancer patients at Mulago National Referral Hospital, Kampala City.

METHODOLOGY.

Research Design.

An institution cross-sectional study was carried out to determine the factors predisposing to the increased cases of adverse drug effects of anticancer drugs among patients on anticancer drugs attending Mulago Hospital National Referral Hospital.

Study Site.

The study was carried out at Mulago National Referral Hospital in Kampala City, Uganda. The study period was from April to November 2023 in which the proposal was developed.

Study Population.

The source populations for the study were the cancer patients admitted at Mulago National Referral Hospital.

Sample Size Determination.

The sample size was calculated using Burton's formula. $S=2(QR) O$: where
S=required sample size.

Q=number of days that were spent while collecting data

R=maximum number of people per day

O= maximum time the interviewer spent on each participant

$2 \times 5 \times 10 \times 0.5hr = 50$

Therefore, the sample size was 50 respondents

Sampling Technique.

A simple random sampling technique was used to select the patients at the cancer unit.

Sampling Procedure.

The researcher explained the procedure to the respondents about the study, and those who turned positive (willing) were given tools (questionnaires) for capturing data and they filled them out at their convenience/ free time. Those who were not able to read and write were interviewed while using an interview guide.

Data Collection Method.

Data was collected using both interview guides and questionnaire methods. This is because the study involved gathering information from men and women, where some could write yet others couldn't.

Data Collection Tool.

Both interview guides and closed-ended questionnaires were used to collect data from the respondents. Questionnaires were written in English language and later translated into local languages that is to say; Luganda Interview guides were used to guide the researcher during the process of data collection.

Data Collection Procedure.

An introduction letter was obtained from the Principal of Kampala School of Health Sciences and then taken to the director of Mulago National Referral Hospital. After getting permission, the researcher explained the purpose of the study to the respondents, then the researcher administered the questionnaires to the respondents and translated interview guides were used. Verbal or written consenting was allowed, and then data collection. Participants were thanked for taking part in the study.

Study Variables.

The study's independent variables were factors that contributed to increased adverse drug effects of anti-cancer drugs among cancer patients. While the dependent variables were the anti-cancer drugs.

Quality Control.

To ensure quality control questionnaires were pre-tested by administering the tool to volunteers and adjustments were made accordingly before being given out to the patients.

Inclusion Criteria.

All patients were diagnosed with cancer and were currently on anti-cancer drugs and admitted to the cancer ward of Mulago National Referral Hospital.

Exclusion Criteria.

Cancer Patients who were not on anti-cancer therapy. Patients who didn't have confirmatory cancer results.

Data Analysis and Presentation.

Data was tallied and analyzed manually using a pen and A4 sheets of paper. It was then entered into Microsoft Excel to generate tables, graphs, and pie charts for easy analysis.

Ethical Consideration.

A letter of approval from the research committee of Kampala School of Health Sciences was obtained together with approval from the hospital Executive Director of Mulago National Referral Hospital before data was collected. Initials were used to provide privacy and confidentiality of the patient’s data. Before data

collection, the objectives of the study were fully explained to the records manager and the research section of Mulago National Referral Hospital to obtain their permission to do research at the hospital.

RESULTS.

Socio-demographic data of the respondents.

Table 1: Showing the socio-demographic data of the respondents.

Variable	Category	Frequency, N=50	Percentage (%)
Marital status	Single	14	28
	Married	19	38
	Widow	6	12
	Divorced	11	22
Sex	Female	28	56
	Male	22	44
Age	<18years	08	16
	18-30 years	10	20
	30-45years	09	18
	>45 Years	23	46
Tribe	Bantu	23	46
	Luo	09	18
	Nilo-hamites	08	16
	Others	10	20
Education level	None	10	20
	Primary	16	32
	Secondary	14	28
	Tertiary	10	20
Residence	Urban	18	36
	Rural	32	64
Religion	Muslim	11	22
	Catholic	18	36
	Anglican	13	26
	Others	08	16
Occupation	Peasant	21	42
	Civil servant	12	24
	Casual labourer	10	20
	Others	07	14
Income level	100,000-200,000	20	40
	200,000-300,000	14	28
	300,000-400,000	06	12
	400,000-above	10	20

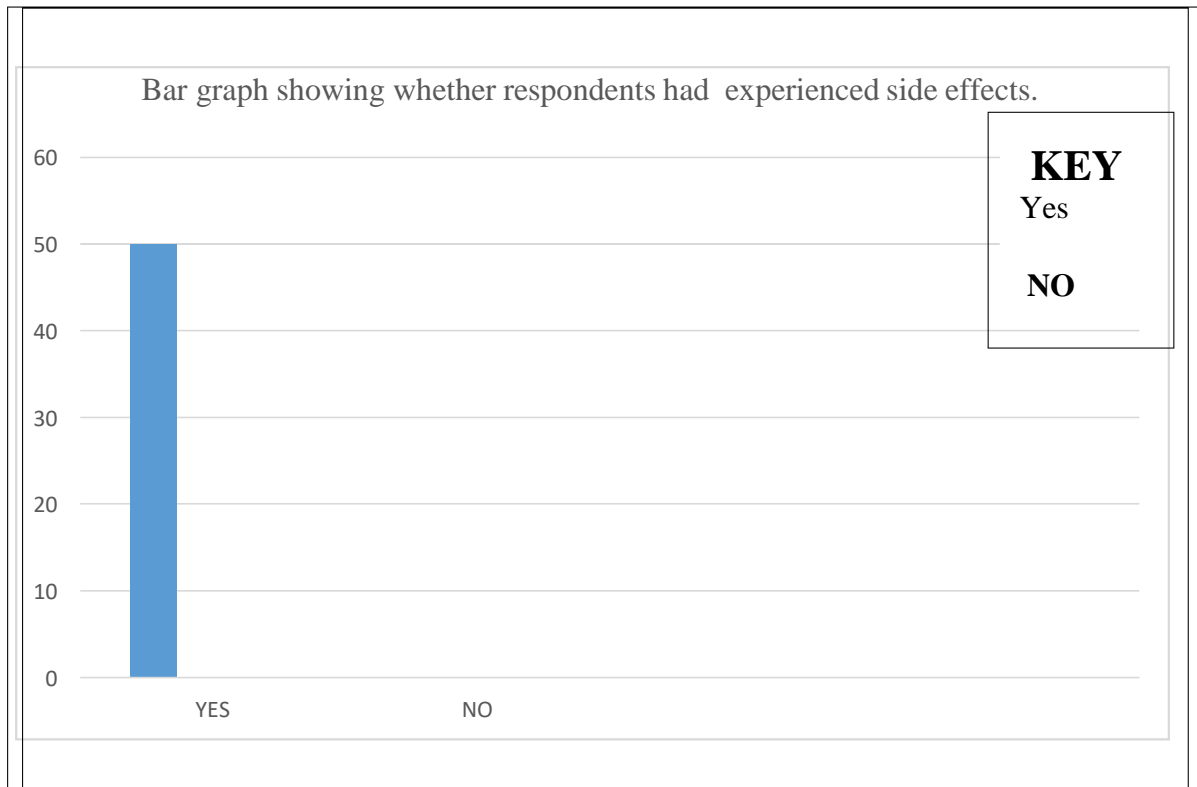
From the research findings, results for the socio-demographic data showed that the majority of the respondents 109(56%) were females whereas the least 84(44%) were males. The majority of the respondents 23(46%) were above 45 years of age, whereas at least 18

years were 08(16%). Most of the respondents were married 19(38%) whereas the least 6(12%) were widows. Based on the study findings, most 18(36%) were Catholics whereas the least 8(16%) belonged to other religions. The study findings further revealed that most 23(46%) were Bantu whereas the least8(16%) were nilo-hamites. The majority 32(64%) of the respondents were rural

residents whereas the minority 18(36%) were from urban areas. Most of the respondents had a primary education 16(32%), whereas only 10(20%) had tertiary education. From the study findings, almost half 21(42%) were earning less than 200,000 Ugx monthly whereas 12(24%) were civil servants. (Table 1)

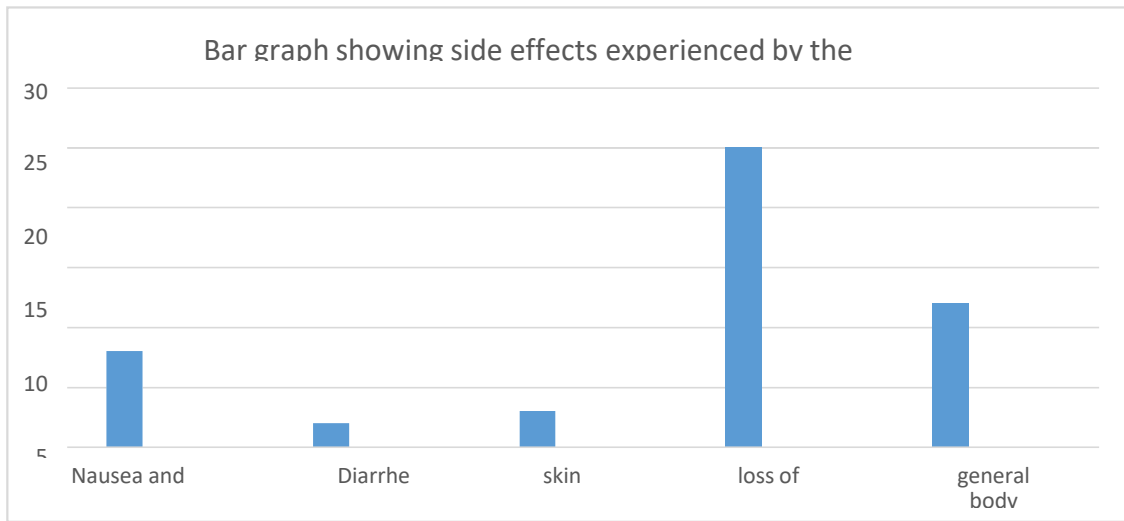
Individual Factors contributing to increased adverse drug effects of anticancer drugs among cancer patients.

Figure 1: Patients' responses if they had ever gotten side effects.



From the results of the study, all the respondents 50(100%) reported having experienced atleast a side effect from the drugs being taken.

Figure 2: Showing the distribution of side effects experienced by the patients.



From figure 2, half of the respondents 25(50%) reported that among the side effects they experienced was loss of hair whereas the least 2(04%) experienced diarrhea.

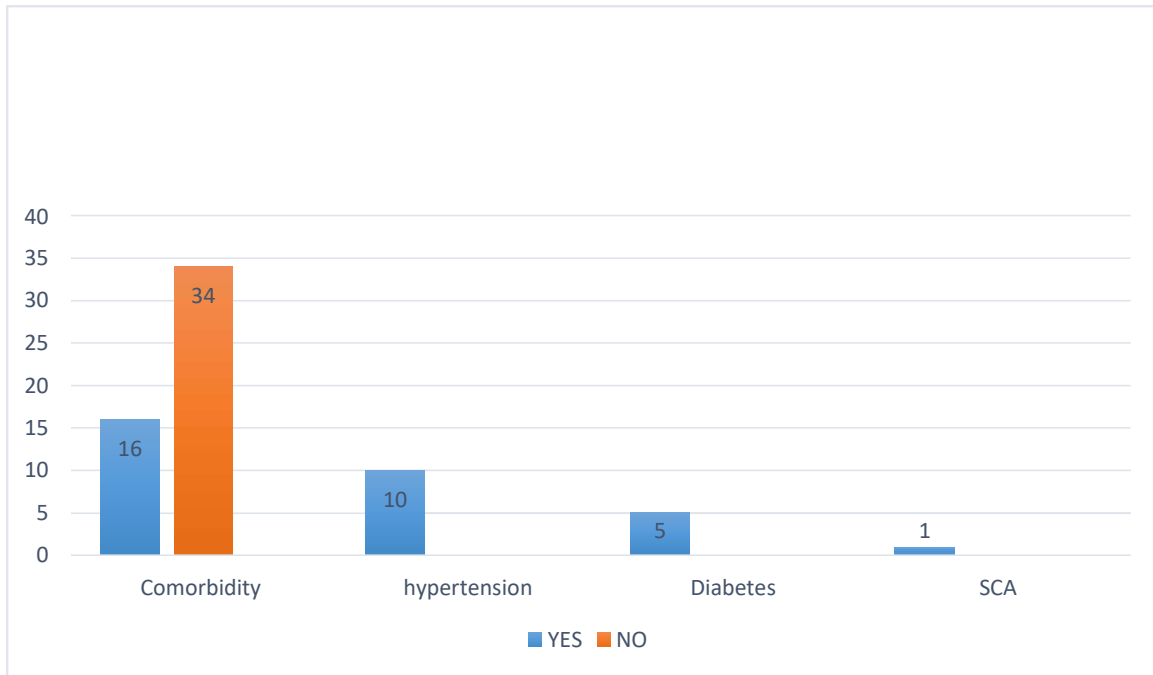
Table 2: Showing the Cancer family history and where they were treated.

Variable	Category	Frequency, N=50	Percentage (%)
Family history of cancer	Yes	11	22
	No	39	78
Where did family members get the cancer from	Hospital	49	98
	Herbalist	01	02
	Never treated.	00	00
	Others	00	00

The majority of 39(78%) of the total respondents reported having had a family history of cancers whereas the minority 11(22%) of the respondents reported not having had any family history of cancer.

The majority 49(98%) of the respondents were treated for cancers in the hospital and the minority 01(2%) were treated by herbalists. (Table 2)

Figure 3: Showing the distribution of the respondents according to the associated co-morbidities.



The majority of respondents 34(68%) did not report any associated co- morbidities however of those who reported having a co-morbidity, 10(63%) had hypertension while

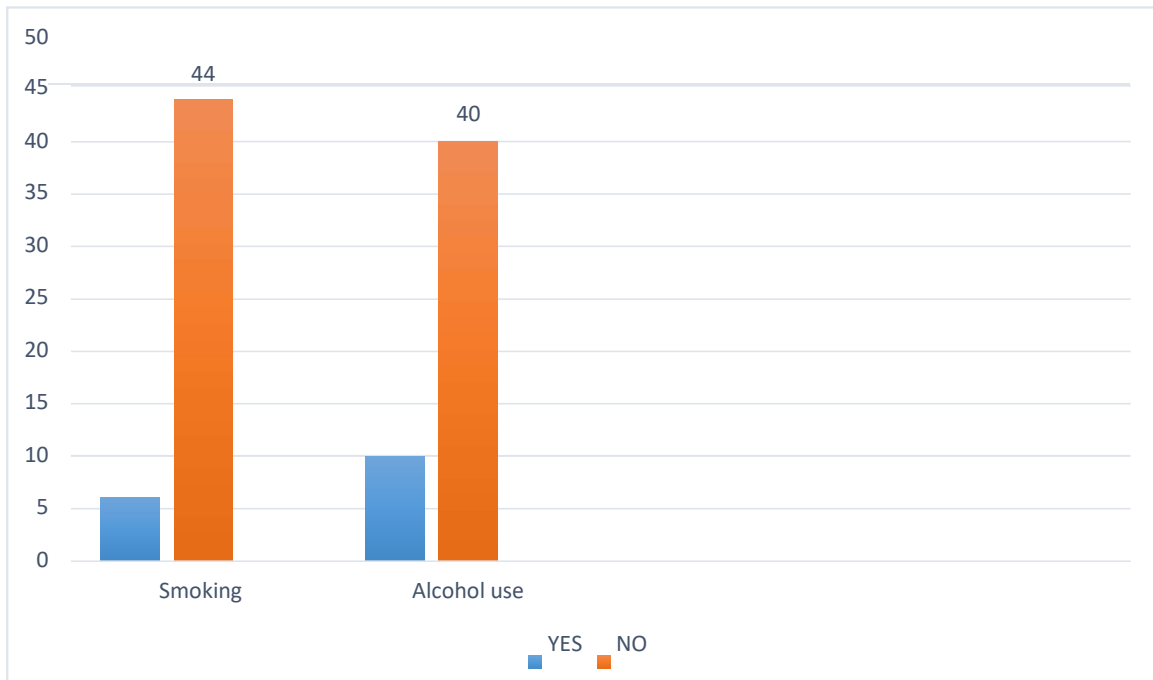
only 5(31%) and 1(06%) had Diabetes and SCA respectively.

Table 3: Showing the history of Allergies among respondents.

Variable	Category	Number N=50	Percentage (%)
History of allergies	Yes	09	18
	No	41	82

The majority of the respondents 41(82%) reported never having had any history of any related allergies while only 09(18%) reported having had some history of a drug allergy before the start of the anticancer drugs.

Figure 4: Showing distribution of the respondents depending on alcohol or smoking habits.



The bar graph shows that from the research findings, the majority of the respondents were neither smokers nor alcoholics with 44(88%), and 40(80%) respectively not involved.

Health facility-related factors contributing to increased Adverse Drug Effects of anticancer drugs among cancer patients.

Figure 5: Showing Distance traveled to reach the hospital.

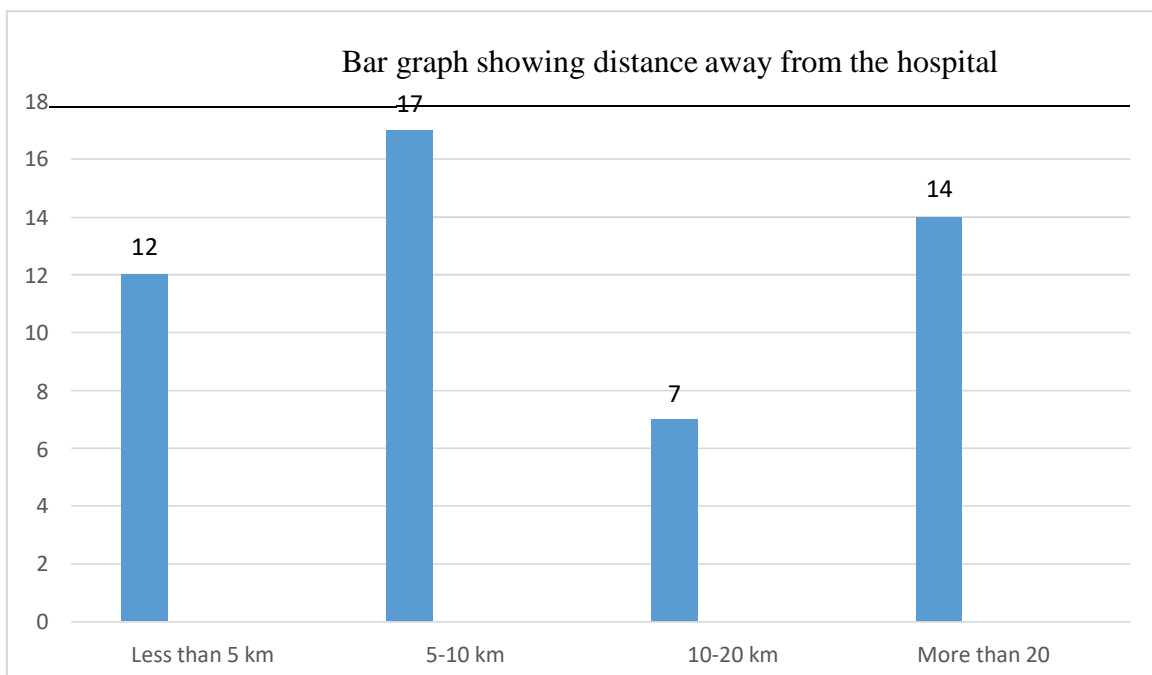


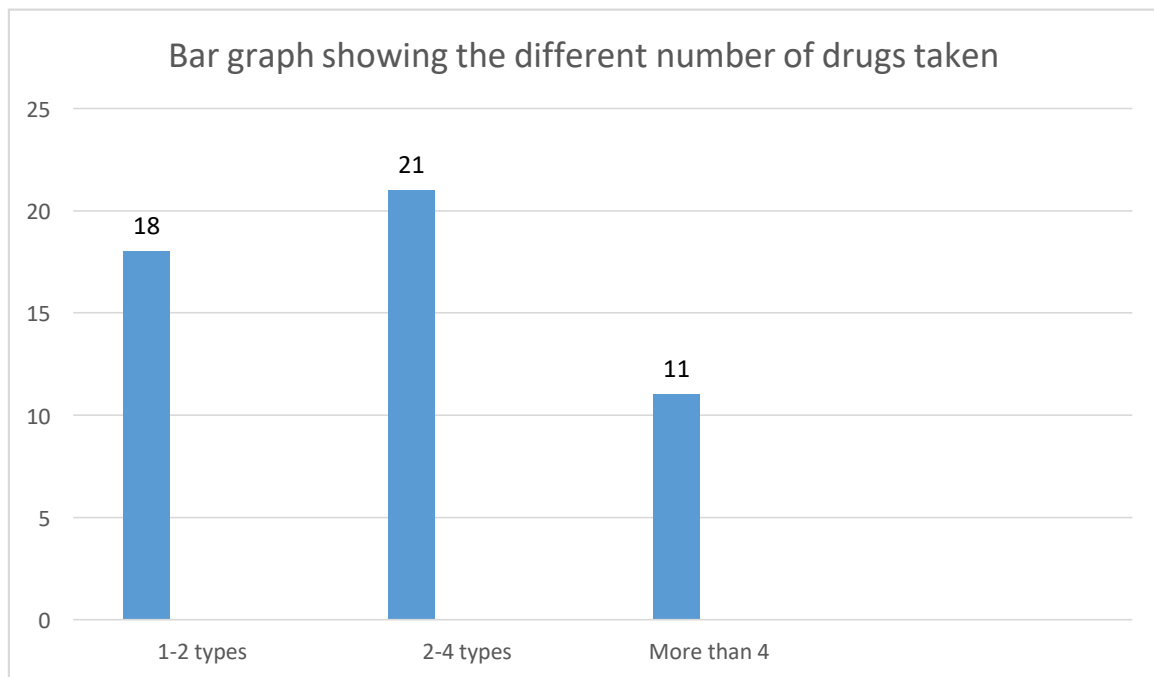
Figure 5 shows that the majority of the respondents traveled longer distances of 5-10 km and more than 20km distances 17(34%) and 14(28%) respectively to reach the hospital for treatment as compared to the 12(24%) who traveled few distances of less than 5km to reach the hospital.

Table 4: Shows why the respondents had not reported the side effects to the health workers.

Variable	Category	Number N=08	Percentage (%)
Reasons for not reporting to health workers.	Overcrowding at hospitals	06	75
	Unsupportive	02	25
	Not available	00	00
	Others	00	00
			100

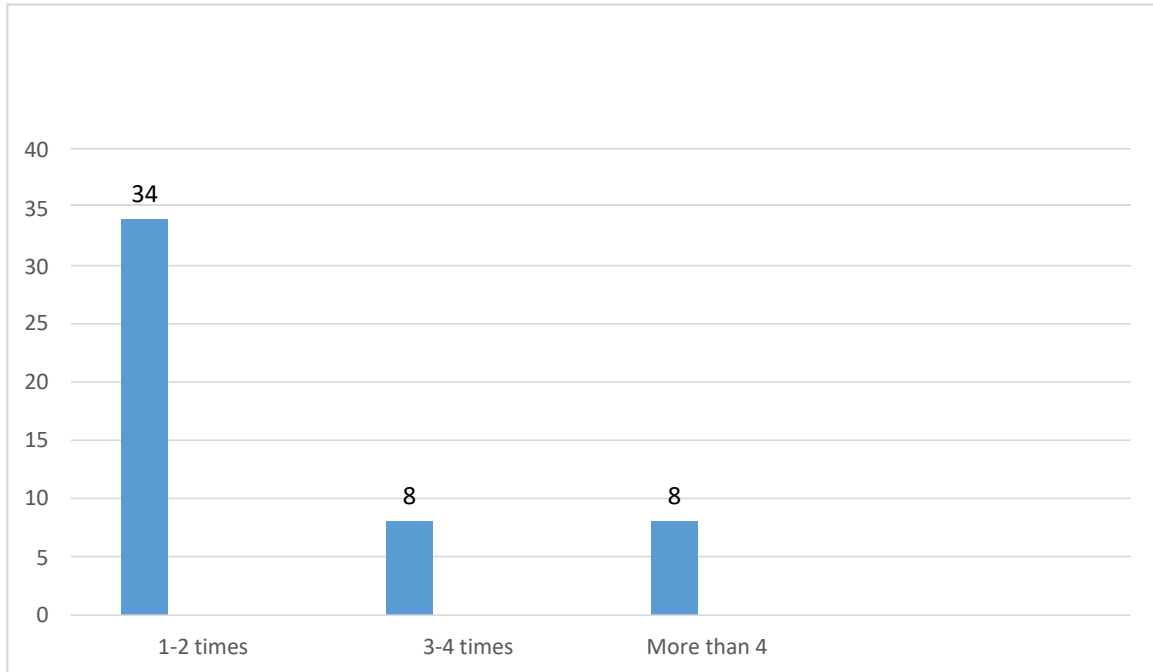
From the figure, the majority 06(94%) of the respondents had not reported the side effects they got to the health workers due to overcrowding whereas the minority 2(25%) reported that the health workers were not supportive of them hence not reporting the presence of the side effects.

Figure 6: Showing the distribution of the several drugs that are taken by therespondents.



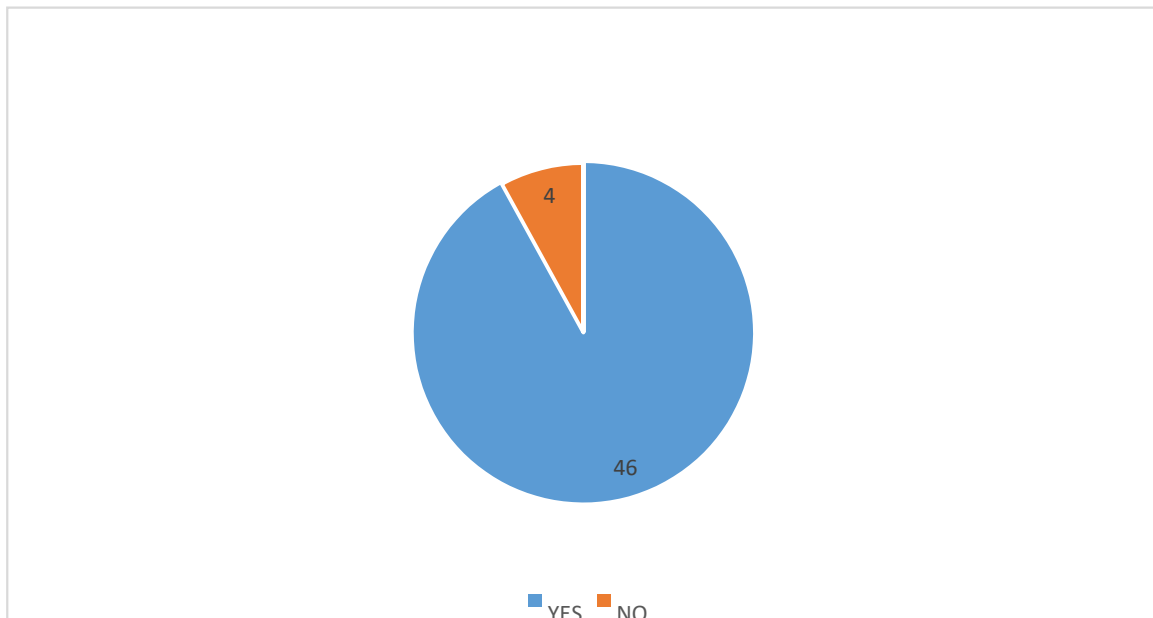
From figure 6, the majority 21(42%) of the respondents were taking between 2-4 types of drugs, whereas the least 11 (22%) were taking more than 4 types of drugs.

Figure 7: Showing the frequency of taking the given drugs.



Findings from figure 7, the majority of the respondents 34(74%) took the drugs once or twice whereas the least 08(16%) took more than four times a day.

Figure 8: Showing if the respondents had ever reported the side effects.



From the research findings in figure 8, the majority of the respondents 46(92%) had ever reported the side effects they got yet the least 4(8%) had never reported the side effects anywhere.

Table 5: Showing where the respondents reported the side effects that they got.

Variable	Category	Number N=50	Percentage (%)
Where they reported	Health worker	47	94
	Herbalist	01	02
	Church elders	02	04
	Others	00	00
			100

From table 5, the majority of the respondents 47(94%) reported the side effects that they felt to the immediate health workers whereas the least 01(2%) reported the side effects to the herbalists.

DISCUSSION.

Individual factors contribute to the increased adverse drug effects among cancer patients.

In this study, the majority of the patients were females 28 (56%) which is consistent with findings in other studies. (Baniyadi S 2014) which also showed that the greatest number of respondents were female as compared to their male counterparts. However, some other studies like one done by Prasad A 2013, showed a male preponderance. Interestingly all the respondents 50(100%) who were interviewed reported having experienced at least an adverse effect from the anti-cancer drugs they were taking despite being varying in severity of symptoms. These findings are coherent with the fact that the majority of the prescribed anticancer agents are not devoid of adverse effects however presentations of effects vary from one patient to another patient and according to the administered drugs because cancer chemotherapeutic agents have a high propensity to cause ADE's as they are toxic to rapidly dividing cells in the body. (Pardmanee Sharma, 2015) The findings are therefore in line with one of the studies conducted in Uganda at the Uganda Cancer Institute (Nakaganda, 2021) which also showed almost all the respondents had reported a complaint of adverse effects in the course of management.

Most of the severe ADE's of alopecia, severe vomiting, and General body malaise were seen in patients in the age group above 45 years of age which is again similar to reports of studies done by Prasad 2013. This could be because, in elderly patients, the metabolizing capacity and the excretory functions are reduced, leading to the accumulation of drugs in the body and thus increasing the risk of ADE's. Similarly, at an advancing age, such patients tend to have many co-morbidities which increase the number of drugs taken hence the pill burden that precipitates drug reactions leading to ADE's.

In this study, the majority of the respondents were non-smokers (88%) and also non-alcoholics (80%). These findings were coherent with similar findings on research conducted in India where the majority of the cancer patients interviewed (82.6%) were nonsmokers. (Pardmanee Sharma, 2015)

In the research findings, 16(32%) respondents reported having other co-morbidities like Hypertension, Diabetes,

and sickle cell anemia indicating that most of these respondents were taking more than one or two types of drugs as a result of the multiple diagnoses hence as a result, these patients on various medications are more likely to experience more ADE's. This is because these patients with co-morbidities and complications were also more likely to receive multiple medications with different safety profiles, which can cause ADE's. These findings were in line with other studies in which the presence of co-morbidities and complications, and a higher number of medications were found to have a significant association with the incidence of ADE's in which patients with a higher number of medications were found to be more likely to have ADE's compared with those who received a lower number of medications (Kumar A, 2017) and (P, 2021)

Factors like Familial history, and familial previous cancer treatment were noted to not correlate with one's tendency to have an adverse effect as each patient experienced symptoms depending on the factors and their genetic makeup.

Health facility-related factors contributing to the increased adverse drug effects among cancer patients.

In the findings from this study, despite the majority (68%) of the patients reporting having gotten the prescribed drugs, a section of them (32%) did not receive the prescribed drugs prompting them to secure them from an outside source at an expensive cost from the neighboring onto- pharmacies. Similarly, of those who received the prescribed drugs from the unit, almost all (94%) confirmed having been given advice and instruction for the drugs as compared to the 6% who reported not having been given the drug instructions from the health workers citing the reason they could have received the adverse effects. These findings were similar to those done by (P, 2021) which showed that up to 60% of cancer patients do not receive the prescribed drugs as a result of the cost of procurement and the diversity in the drugs taken that are not met by the different public health care systems.

In line with this study, a higher number of medications 2-4 types 21(42%) as well as more than 4 types of medicines 11(22%) was found to have a significant association with the incidence of worse ADE's. This is because patients are exposed to different classes of medication with different safety profiles associated with the presence of multi-morbidity hence these patients on various medications are more likely to experience ADE's due to an increase in the number of new drug classes that easily react. The many

drugs that are given to patients due to the co-morbidities and complications were also more likely to receive multiple medications compared with those who received a lower number of medications. These findings were in line with other studies in which the presence of co-morbidities and complications, and a higher number of medications were found to have a significant association with the incidence of ADEs in which patients with a higher number of medications were found to be more likely to have ADE's compared with those who received a lower number of medications (Kumar A, 2017) and (P, 2021)

Patient health worker relation in terms of conduct and attitude has a greater influence on the treatment outcomes of patients taking long courses and seemingly chronic illnesses like cancer. In this study, a section of patients 4(8%) reported that the negative attitude of the health workers deterred them from accessing consultation as a result of the adverse effects that they had experienced and therefore they opted to get help and advice from others like the church (4%) and the traditional leaders and the herbalists (2%) other than the health workers. These findings were similar to those found by Mwamba 2023 where he discovered that many health workers handling patients did not care about their complaints because they acted rude, judgmental, and not empathetic.

In the research findings, among other reasons the respondents were reluctant to report the adverse effects of the drugs was that there were long waiting hours coupled with overcrowding at the hospital, (94%) given the low numbers of health workers at the unit hence they expected no replies and immediate care offered to them. This finding was similar to those findings by Kumar A 2017 who stressed that overcrowding and long waiting hours were some of the major challenges that affected cancer patients in their course of management.

More than half of the respondents 76% travelled more than 5km to reach hospital for the cancer care. This coupled with the living expenses in terms of accommodations as a result of long journeys traveled from various areas upcountry to reach the hospital was a great impingement to the care and follow-up in terms of effectively taking drugs thus contributing to the respondent's failure to effectively take drugs as many reported missing their appointment dates. These findings were coherent with those conducted at the Uganda Cancer Institute by Nakaganda A 2021 which showed that the majority of the patients traveled longer distances to reach the cancer unit.

STUDY LIMITATIONS.

Because most patients were from all over the country with different languages, others educated, the researcher anticipates the challenge of interpretation, financial constraints, and Limited time for collecting data.

CONCLUSION.

ADE's impact on patient treatment outcomes may result

in multiple patients' treatment failure and medication discontinuation or abrupt adherence to medications. Nevertheless, early detection and reporting of these ADE's may help in minimizing the damage by either modifying the dose or changing the offending agent thereby providing an appropriate advice management plan.

In these research findings, All the respondents (100%) interviewed in the study reported at least an episode of an ADE during the management with personal factors like having an advanced age above 45 years, having related medical co-morbidities like hypertension, diabetes, or SCA together with the use of social abuse agents like Alcohol, smoking increase likelihood to developing the ADE's among patients while health care related factors like longer distances traveled by the patients to access the hospital, a high pill burden and frequent dosaging of the prescribed drugs as well as drug stock outs contributed to occurrence of the ADE's among the patients.

RECOMMENDATIONS.

From the evident fact that any prescribed anticancer agent will cause a side effect and most of the ADE's in hospitalized oncology patients are predictable and at least probably preventable., it is therefore pertinent to the knowledge gaps of patients to prevent the occurrence of similar such reactions in the future.

There is also a great need to set up an effective ADE monitoring and reporting system in all hospitals and also create awareness among healthcare professionals regarding the importance of this system.

The Ministry of Health should encourage rational and judicious use of drugs in terms of proper prescription of appropriate drugs and reducing pill burden as well frequency of intake will lead to a reduction in the incidence and severity of ADE's.

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2. Kalungi Vincent Charles, lecturer at the Kampala School of Health Sciences.

LIST OF ABBREVIATIONS AND ACRONYMS.

5FU: 5- Flouro- Uracil.
ADE's: Adverse Drug Effects.
AE: Adverse Event.
HCP: Health care professional.
HW: Health worker.
KSHS: Kampala School of Health Sciences.
MDG: Millennium Development Goal.
MOH: Ministry of Health.
NDA: National Drug Authority.
NPC: National Pharmacovigilance Center.
PV: Pharnacovigilance.
SPSS: Statistical Package for Social Scientists.
UBOS: Uganda Bureau of Statistics.
UDHS: Uganda Demographic and Health Survey.
UNICEF: United Nations International Children funds.
WHO: World Health Organization.

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CONFLICT OF INTEREST.

The author declares no conflict of interest.

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