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Research Article

Antiretroviral-Related Adverse Reactions: A Cause for Concern

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ABSTRACT

Background: Safety monitoring of medicines is key to the overall quality of care for Persons Living with HIV on Antiretroviral Therapy. As Ghana scales up access to Antiretroviral treatment towards ending the global AIDS pandemic by the year 2030, there is a need to monitor and evaluate treatment-related Adverse Drug Reactions amongst Persons Living with HIV at all levels, including district hospitals.

Objective: To determine the prevalence, types, causes, and outcomes of Adverse Drug Reactions in patients being managed with Antiretrovirals at a secondary health facility in Ghana.

Method: A quantitative retrospective study was conducted to collect data on Adverse Drug Reactions that had occurred amongst HIV-positive patients on Antiretroviral Therapy (ART). A total of 350 active HIV-positive adults on ART were interviewed at the Antiretroviral Center from June 2020 to August 2020. The results of 109 out of 350 patients who reported ADRs were analyzed using Statistical Package for Social Sciences (SPSS) version 20. Naranjo's and Hartwig's assessment scales were used for causality and severity assessments of ADRs, respectively. Prevalence was determined as a proportion of the study population with ADRs.

Results: The prevalence of Adverse Drug Reactions (ADRs) was 31%. More females (84%) than males (16%) reported ADRs with the highest number of ADRs reported amongst the middle age group (41-50 years). Dizziness (32.5%) was the most common type of ADR reported, followed by abnormal dreams (7.7%), palpitations (7.1%), and vomiting (5.9%). The fixed-dose combination, Tenofovir/Lamivudine/Efavirenz, was the Antiretroviral most frequently associated with ADRs (49.1%); followed by Zidovudine/Lamivudine/Nevirapine (14.7%) and the single-dose Efavirenz (8.6%). Most of the ADRs were mild (55%) to moderate (32%). Almost 12% of ADRs were severe and 8% were life-threatening. ADRs were categorized as "possible" (84%) and "probable" (16%) according to Naranjo's probability scale. Actions taken in response to ADRs included no change of active medications (73%); changing of medications to a new regimen (22%) and withdrawal of the suspected drug(s) (5%).

Conclusion: The prevalence of ADRs is high amongst HIV-positive patients being managed on Antiretroviral Therapy at the study facility. This calls for pragmatic steps to enforce pharmacovigilance at all levels of HIV treatment centers to forestall non-adherence and reduce mortality.

Keywords: Acquired Immune Deficiency Syndrome, Adverse Drug Reaction(s), Highly Active Antiretroviral Therapy, Human Immunodeficiency Virus, Pharmacovigilance

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INTRODUCTION

According to Global AIDS Update 2017, more than half (53%) of all Persons Living with HIV worldwide have access to life-prolonging Antiretroviral (ARV) drugs with an appreciable decrease in HIV-related morbidity and mortality.

In Ghana, the National HIV prevalence and AIDS estimates reports show much improvement in the HIV therapy response. The national HIV prevalence decreased from 2.4% in the year 2016 to 2.1% in 2017 with HIV prevalence of below 2.0% recorded between the years 2013 and 2015. These remarkable achievements are largely due to life-prolonging Antiretroviral medicines which reduce the degree of infectivity of HIV-positive patients (Eluwa GI, *et al.*, 2012). However, Antiretroviral Therapy, like most treatments for chronic diseases, is not without toxicities and adverse effects. Adverse Drug Reactions (ADRs) to Antiretroviral Therapy range from mild to life-threatening, with short and long-term effects.

Studies on the incidence of ADRs reported in both developed and developing countries revealed that ADRs amongst patients on Antiretroviral Therapy range between 11% to 35% with an incidence as high as 54% in the presence of opportunistic infections (Severe P, *et al.*, 2010). The use of complex Antiretroviral regimens, coupled with compromised immune systems puts HIV patients at increased risk of developing ADRs (van Graan R, *et al.*, 2018). Other studies on ADRs due to Antiretroviral Therapy also indicate that ADRs is a major cause of non-adherence and play a key role in therapy change/modification which affects treatment outcomes negatively. This, unfortunately, poses a challenge in the fight against HIV/AIDS.

A recent study at Korle Bu Teaching Hospital (KBTH) in Ghana revealed that one (1) out of every five (5) HIV-positive patients on a Tenofovir-based Antiretroviral regimen develops renal impairment over 5 years and 2.3% of these patients develop severe renal impairment (Tetteh RA, *et al.*, 2018). Another study on "association between the occurrence of adverse drug events and modi-

fication of first-line Antiretroviral Therapy in Ghanaian HIV patients" revealed that more than half (52.7%) of patients on Highly Active Antiretroviral Therapy (HAART) in KBTH had at least one documented adverse drug events. The commonest ADR was anaemia which was recorded in 18.5% of modified therapy patients treated with the Zidovudine-based regimen (Tetteh RA, *et al.*, 2016).

In developing countries such as Ghana, there is limited information on the prevalence and cost of ADRs although the impact of these ADRs seems to be devastating. Available data from the Food and Drugs Authority indicates that 5%, 1%, and 2.5% of ADR reports submitted to the National Pharmacovigilance Center of Ghana in the years 2012, 2013, and 2014 respectively, resulted in death. Although there is some data on ADRs amongst Persons Living with HIV (PLHIV) in some tertiary hospitals in Ghana, this information at the secondary hospital level is lacking. Whilst research for new and less toxic ARVs continues, it is important to monitor and evaluate treatment-related ADRs at all levels to understand and manage them appropriately. The overall aim of the study was to evaluate treatment-related Adverse Drug Reactions (ADRs) amongst PLHIV on Highly Active Antiretroviral Therapy (HAART) at a secondary health facility.

METHODS

Study area

The study was conducted at the Antiretroviral Therapy (ART) Center in the Kwahu Government Hospital (KGH), Atibie, in the Eastern Region of Ghana. The hospital's ART Center offers ART services to patients within the Kwahu-South District. Also, communities within neighboring districts (Kwahu East, Kwahu West, Kwahu Afram Plains South, and Brim North Districts) receive care from the KGH. Once a patient is diagnosed with HIV and eligible to start ART, a unique identification number is issued and the patient is provided with ART services free of charge. Records available at the ART Center indicate that Antiretroviral drugs are usually supplied to patients for a minimum duration of (2) weeks and a maximum duration of two (2) months, depending on whether the individual is a new or a known ART patient.

Study design

A descriptive quantitative retrospective study was conducted. HIV-positive adult patients on ART who visited the KGH ART Center for their refills, from June 2020 to August 2020, were interviewed after a signed informed consent was given.

Study population

The study population consisted of all HIV-positive adult patients on ART who received care from the Kwahu Government Hospital, Atibie, at the time of the study.

Inclusion criteria

All HIV-positive patients, aged 15 years and above, on ART who consented to the study.

Exclusion criteria

All HIV-positive patients who were less than fifteen (15) years of age at the time of the study or potential study subjects who did not give consent to participate in the study.

Sampling technique

Convenient sampling was used to select 350 HIV-positive patients out of a total of 688 active HIV-positive patients receiving ART at KGH. The patients were sampled, assessed for inclusion, and interviewed after signed informed consent was granted.

Development of questionnaire

A structured data extraction tool was designed to interview patients and obtain information from patients' medical records on the types, causes, and outcomes of ADRs. The tool was subjected to a validity and reliability assessment in an attempt to improve quality. The questionnaire consisted of open- and close-ended questions divided into four (4) sections: demographic information, type of adverse drug reaction(s), cause(s) of adverse drug reaction(s), and the actions that were taken to address these Adverse Drug Reactions.

Data collection methods and tools

The data collection involved a face-to-face interview between the researchers and the participants at the ART Center. The data was collected by the principal investigator together with the help of three (3) trained research assistants. The structured questionnaires were administered to participants and filled by the researchers. A 2-month duration, 15th June 2020 to 14th August 2020, was selected for the data collection. This was to present a near equal chance to every patient attending the Center of getting enrolled in the study, based on the evidence from patients turnover at the Center. To avoid the possibility of a patient being selected twice for the study, patients interviewed were designated unique identification codes.

Naranjo's probability scale was used to assess the cause and effect relationship of ADRs. Patients were asked ten (10) objective questions from Naranjo's algorithm scale to obtain three possible responses: yes, no, or do not know. The scores obtained for each question were totaled and drug reactions classified as follows: >9=definite ADR, 5-8=probable ADR, 1-4=possible ADR, 0=doubtful ADR. Hartwig's severity assessment scale was used to assess ADR severity by respondents. Patients were asked questions on the outcome of ADR and the severity classified as mild (level 1-2), moderate (level 3-4), or severe (level 5-7) based on the application of the Hartwig's scale.

Data analysis

The data captured was entered into Statistical Package for Social Sciences (SPSS) version 20 software and analyzed. Relevant tables were created from the data to allow for easy analysis and interpretation. Categorical variables were presented as frequencies and percentages in tables and figures.

Ethical consideration

Approval for the study was sought from the management of the Kwahu Government Hospital. Ethical clearance was obtained from the Committee on Human Research, Publication, and Ethics (CHRPE), Kwame Nkrumah University of Science and Technology (KNUST), Kumasi. To ensure confidentiality and anonymity, codes were used instead of patient names. Participants responded to questionnaires after a signed consent was obtained. All reports and findings were treated with confidentiality.

RESULTS

Socio-demographics of respondents

The prevalence of ADR amongst retroviral patients being managed at the KGH for the period was 31%. A total of 109 patients reported ADRs out of a total of 350 patients interviewed. Amongst the 109 participants who reported ADRs, 84% (n=92) were females and 16% (n=17) were males. The 241 respondents who reported no ADRs consisted of 83% (n=200) females and 17% (n=41) males. Most of the respondents presenting with ADRs fell in the age range between 41-50 years (n=35), followed by 31-40 years (n=30). Patients in the age range of 15-20 years (n=2) constituted the least number of respondents with ADRs. A similar trend was observed in patients with no ADRs where patients aged 41-50 years (n=77) constituted the highest number, and patients aged 15-20 years (n=5) constituted the least. These findings are detailed in *Table 1*.

Table 1: Respondents with and without ADRs and their age ranges

Respondents		ADR respondents		No-ADR respondents	
Age ranges (years)	Number (n)	Number (n)	Percentage (%)	Number (n)	Percentage (%)
15-20	7	2	1.8	5	2.1
21-30	32	5	4.6	27	11.2
31-40	100	30	27.6	70	29
41-50	112	35	32.1	77	32
51-60	63	20	18.3	43	17.8
> 60	36	17	15.6	19	7.9
Total	350	109	100	241	100

In terms of educational background, most of the respondents with ADRs had junior high education (n=53); followed by primary (n=35), senior high (n=10), and tertiary education (n=1). A similar trend was observed in respondents with no ADRs, with junior high education (n=115) being the highest number of respondents reporting no ADRs and tertiary education respondents (n=13) reporting the least. 17.8% of respondents with no ADRs were uneducated compared to 9.2% of respondents with ADRs.

G6PD status of respondents

A significant number of respondents did not have their G6PD status laboratory investigations available at the time of the study. Out of the 109 respondents with ADRs, 72 had their G6PD status available. 87.5% (n=63) of this number with G6PD laboratory investigations available had no defect, 9.7% (n=7) had partial defect and 2.8% (n=2) had full defect. 34.2% (n=37) of respondents with ADRs had no G6PD laboratory results available.

Viral load status of respondents

Viral load test results were not available for the majority of patients interviewed. Out of the number of respondents with ADRs who had viral load test results available, most of them either had a viral load count of 1000 copies/ml (n=14) or a target not detected (n=14). A total of 12 respondents had a viral load count of fewer than 20 copies/ml (cp/ml) *(Figure 1)*.

Treatment duration of respondents

Most patients interviewed had been on ART for between 1 year and 5 years; followed by those on ART for more than 5 years. A total of 12 respondents with ADRs had been on ART between 6 months and 1 year, whilst the least number of respondents had been on ART for 2- 4 weeks. A similar trend was observed in respondents with no ADRs *(Figure 2)*.

Co-morbidities of respondents

The majority of respondents, either with a report of ADRs (89%) or not (98%), had no co-morbidities. Hypertension (9.2%), diabetes mellitus (0.9%), and hepatitis B (9.2%) were the co-morbidities that were identified amongst respondents with ADRs.

Other medications of respondents with ADRs aside ARVs

Iron III Polymaltose complex (n=108) and Co-trimoxazole (n=99) were the two major medications taken by respondents aside from their usual ARV medications. Less frequent medications taken by respondents were antihypertensive, antidiabetic, and herbal medicines. The details are shown in *Table 2*.

Types and severity of ADRs experienced by respondents

Dizziness was the most frequently experienced ADR with a percentage of 32% (n=55) patients reporting this. This was followed by abnormal dreams in 7.7% of respondents (n=13), palpitations in 7.1% (n=12) of respondents and vomiting in 5.9% (n=10) of study subjects. Other reactions such as anorexia, constipation, urticaria, amenorrhea, facial puffiness, etc. altogether constituted 13.6% (n=23). The majority of ADRs experienced by respondents were mild (55%) followed by moderate (33%) and severe (12%). Further details are available as supplemental online materials.

Duration of ADRs

Most ADRs experienced by respondents lasted for more than 1 month (45.9%) with a few lasting for 1-3 days only (4.6%). Some respondents (8.3%) indicated their reactions were ongoing at the time of the data collection for this study. The details are shown in *Figure 3*.

Table 2: Other medications of respondents with ADRs

Medication	Frequency (n)	Percentage (%)
Co-trimoxazole	99	90.8
Iron (III) Polymaltose	108	99.1
Amlodipine	6	5.5
Bendrofluazide	4	3.7
Nifedipine	3	2.8
Lisinopril	4	3.7
Metformin	1	0.9
Glimepiride	1	0.9
Atenolol	1	0.9
Losartan	1	0.9
Herbal	2	1.9

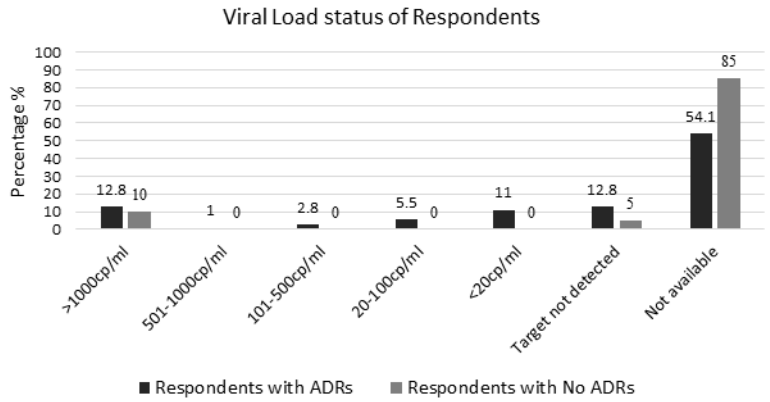

Figure 1: Viral load status of respondents

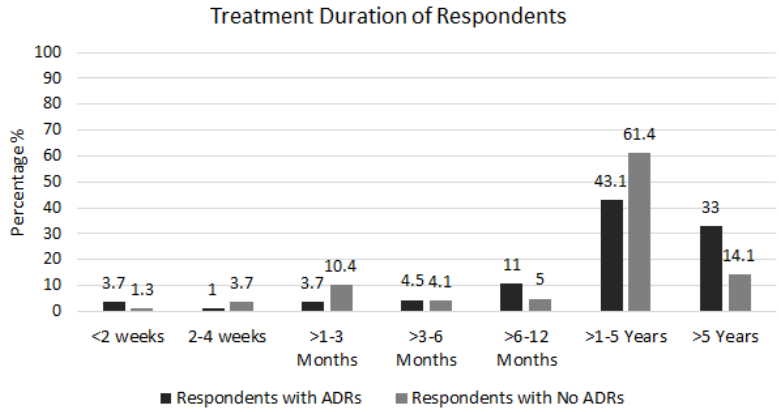

Figure 2: Treatment duration of respondents

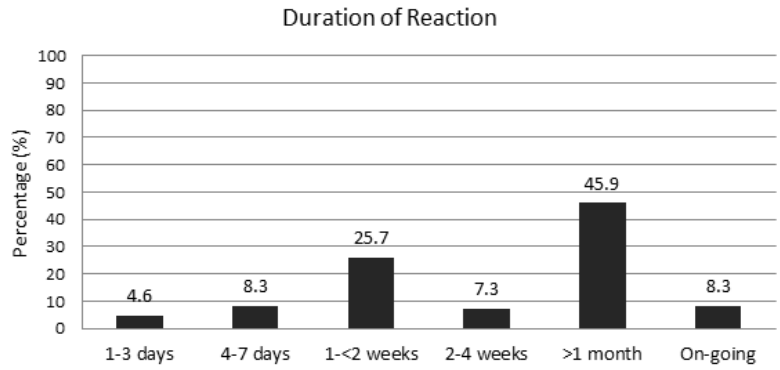

Figure 3: Duration of ADRs

Possible causes of ADR

As expected, Antiretrovirals (ARVs) accounted for 91% of all ADRs reported in the study population. Only 9% of patients on ARVs experienced ADRs, not due to ART. Co-trimoxazole and Iron III Polymaltose complex were responsible for ADRs not due to ART, accounting for 8% and 1% of ADRs respectively. Further details are available as supplemental online materials.

Types of ADRs caused by ARVs

Fixed-dose combination of Tenofovir/Lamivudine/Efavirenz (TDF/3TC/EFV) accounted for the highest number of ADRs (49.1%), which was mostly dizziness (n=30), palpitations (n=9), and abnormal dreams (n=5). Zidovudine/Lamivudine/Nevirapine (AZT/3TC/NVP), a fixed-dose combination ARV accounted for 14.7%, and Efavirenz (EFV), a single-dose ARV accounted for 8.6% *(Table 3)*.

Actions that were taken to address ADRs

The majority of patients (73%) continued with their treatment regimen despite experiencing various forms of ADRs. Some 22% of respondents had their medications changed whilst another 5% had their medications withdrawn or discontinued. Medications withdrawn were all cases of ADRs associated with Co-trimoxazole. Twenty-two percent of (n=24) respondents with ADRs had their medications changed. The details of respondents whose medications were changed as a result of ADRs are available as supplemental online materials.

Table 3: Types of ADRs caused by ARVs

Type of ADR	If ADR is due to ARVs, which regimen or drug molecule?										
	TDF/3TC/EFV	TDF/FTC/EFV	AZT/3TC/NVP	TDF/3TC	AZT/3TC	ABC/3TC	NVP	EFV	LPV/r	TDF/3TC/DTG	Total
Rash	2	0	3	1	1	1	0	0	0	1	9
Diarrhoea	2	1	0	1	0	1	0	0	0	0	5
Neuropathy	2	0	1	0	0	0	0	0	1	0	4
Anaemia	1	1	2	0	2	0	0	1	0	0	7
Palpitation	9	1	1	0	0	0	0	0	0	0	11
Dizziness	30	1	4	2	4	0	1	2	0	2	46
Nausea	1	0	0	0	0	0	0	0	0	0	1
Vomiting	1	0	1	2	0	0	1	0	1	0	6
Headache	0	0	1	0	0	0	0	1	0	0	2
Insomnia	1	0	1	0	1	0	0	1	0	0	4
Abnormal dreams	5	0	0	0	0	0	0	3	0	0	8
General weakness	1	1	0	0	0	0	0	1	0	0	3
Others	2	1	3	2	1	0	0	1	0	0	10
Total (frequency)	57	6	17	8	9	2	2	10	2	3	116
Total (%)	49.1	5.2	14.7	6.9	7.8	1.7	1.7	8.6	1.7	2.6	100

DISCUSSION

Patient safety is a key element in the overall quality of care for persons accessing Antiretroviral treatment. The absence of comprehensive drug safety monitoring systems to recognize ADRs and events in patients is a shortfall to this therapy (Olsson S, *et al.*, 2015). The World Health Organization's report indicates that there is limited data on local documentation of Adverse Drug Reactions (ADRs) related to Antiretroviral use in public health practice (WHO, 2010). With the increasing access to Antiretroviral Therapy in Ghana, adequate reporting of suspected and unexplained serious ADRs is of great importance. Also, continued insight into ADRs is needed for adequate information on the safety of ARVs in clinical practice. It is in response to these challenges that this study was conceptualized and conducted to evaluate the treatment-related ADRs amongst PLHIV on HAART at the Kwahu Government hospital.

The overall ADR prevalence for the population was 31%. This was similar to the ADR prevalence of 37% previously recorded in South Africa (Masenyetse LJ, *et al.*, 2015). The result of the study is however lower compared to ADR prevalence data reported by several studies in sub-Saharan Africa: i.e. 70.8% in Ethiopia (Tatiparthi R and Mamo Y, 2014), 61.2% in Mali (Oumar AA, *et al.*, 2017), and 53.4% in Nigeria (Bassi P, *et al.*, 2017). Comparable to studies in Ghana, the prevalence of ADR recorded was higher than 9.4% (Lartey M, *et al.*, 2014) and lower than 52.7% (Tetteh RA, *et al.*, 2016). The difference in prevalence observed with other studies may have resulted from variations in sampling techniques and study designs used. In addition, changes in ART treatment guidelines over the years may have contributed to these findings. These, probably, are the reasons for the different values reported in this study compared to similar pharmacovigilance studies.

The demographic characteristics of the participants indicated that more females reported ADRs (84% females). This observation is similar to findings from other studies (Chioma AD, *et al.*, 2019; Ejigu A, *et al.*, 2018; Van Graan R, *et al.*, 2018). A possible reason for this observation is the higher number of females compared to males on ART at the time of the study. The ART center had a female-to-male ratio of 3:1. This could be because females are known to more readily seek medical attention compared to males (Alomar MJ, 2014).

It was observed that the majority of the patient (91%) who reported with ADRs had formal education, thus, were able to provide accurate descriptions and gave a better assessment of the ADRs they had experienced.

Adverse drug reactions were mainly observed amongst patients of the middle age group (41-50 years) (n=35), the majority of whom had been on ART between 1-5 years (n=47). This finding is similar to a study in Malaysia in which ADRs were highly prevalent amongst ART patients in the middle age group (31-50 years) (Khan UK, *et al.*, 2017). The duration of treatment for most patients with ADRs on ART (1-5 years) served as means to evaluate both short-term and long-term adverse effects of Antiretroviral Therapy. ADRs were prevalent in the elderly population, therefore routine monitoring for signs of drug toxicity is essential in this population. Also, laboratory investigations such as liver and renal function tests should be carried out routinely to monitor for possible drug-induced organ damage.

Results from the study indicate that viral load count was not available for most of the patients who were interviewed. A significant number of respondents with ADRs (34.3%) did not have Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency laboratory test results at the time of the study. This outcome made it difficult to evaluate the impact of viral sup-

pression and G6PD status of patients in the development of ADRs due to ART. One of the reasons that may have accounted for this observation was the lack of logistics and laboratory reagents for viral load assessment which led to the delay in obtaining results. Samples for viral load assessment were sent to the Eastern Regional Hospital and this further contributed to the unavailability of viral load results. Also, according to the Ghanaian policy on ART, viral load testing is done after six months and yearly thereafter for patients who are stable on ART. Therefore, all patients who had been on ART for less than six months were not offered a viral load test according to the eligibility criteria outlined in the ART policy document. Forgetfulness on the part of clinicians to request for G6PD test for patients before initiation of Co-trimoxazole prophylaxis was the main reason why the G6PD status of patients was lacking. The majority of the patients who were interviewed did not know their G6PD status, making it difficult to evaluate this variable on the development of ADRs. It is known that individuals who are G6PD deficient (partial or full defect) have difficulty in metabolizing drugs such as Co-trimoxazole, hence are prone to developing ADRs.

Hypertension, diabetes mellitus, and hepatitis B infections were the main co-morbidities that were identified amongst 11% of patients with ADRs on ART. The majority of patients interviewed did not have any co-morbidity with HIV infection that required the use of other medications. However, Co-trimoxazole prophylaxis (n=99) and Iron III Polymaltose complex (n=108) were prescribed routinely as prophylaxis against opportunistic infections and anaemia respectively, for the majority of patients with ADRs on ART. Amlodipine (n=6), Bendrofluazide (n=4), Nifedipine (n=3), and Lisinopril (n=4) were some of the antihypertensive medications prescribed for patients with hypertension whilst Metformin (n=1) and Glimepiride (n=1) were prescribed for the management of diabetes mellitus in patients with ADR. There were no drug-drug interactions between ARVs and these medications. A few patients who developed ADRs (n=2) were taking herbal medicines aside ARVs. This has the potential for drug-drug interactions requiring appropriate monitoring.

Dizziness (32.5%), abnormal dreams (7.7%), and vomiting (5.9%) were the most common ADRs that were observed amongst the participants. Most ADRs lasted for more than one month (45.9%) with some 25.7% lasting up to 2 weeks' duration. A few ADRs (8.3%) were ongoing at the time of data collection. The types of ADRs that were observed, associated with the Central Nervous System and gastrointestinal tract, were similar to findings from other studies reporting on ADRs in ART (Bhatnagar S, *et al.*, 2013; Chowta MN, *et al.*, 2018; Kumar A, *et al.*, 2017). Notably, palpitations (7.1%) were observed as one of the most reported ADRs, similar to findings by a study in Nigeria (Agada PO, *et al.*, 2016). Other types of ADRs that were reported included anaemia (5.3%), rash (5.3%), general weakness (5.3%), headache (3.9%), insomnia (3.6%), nausea (3.6%), and neuropathy (2.4%). In general, a total of 169 types of ADRs were recorded amongst 109 patients on ART. Most of the ADRs observed were Central Nervous System (CNS) manifestations, therefore, retroviral patients on ART should always be counselled to be cautious when driving or working with machines with revolving parts.

ADRs were mostly attributed to Antiretroviral drugs (91%). Similar to findings by Kumar A, *et al.*, 2017 regimens containing Tenofovir/Lamivudine/Efavirenz (TDF/3TC/EFV) accounted for the highest number of ADRs (49.1%) recorded amongst patients on ARVs alone. Also, TDF/3TC/EFV was responsible for the majority of frequently reported ADRs, i.e. dizziness, palpitations, and abnormal dreams. Zidovudine/Lamivudine/Nevirapine (AZT/3TC/NVP) and Efavirenz were identified as second and third highest causes of ADRs respectively. The driving force behind this observation was the use of TDF/3TC/EFV as one of the first-line recommended Antiretroviral treatment regimens given to ART-naive patients in Ghana (UNAIDS J, 2013). Hence a comparably higher number of patients were put on this regimen as compared to the other regimens. More so, TDF/3TC/EFV fixed-dose combination therapy is preferred to separate doses of the same drug because it addresses the issue of pill burden which translates to poor compliance. Other causes of ADRs identified were Co-trimoxazole (8%) and Iron III Polymaltose complex (1%). The majority of ADRs were caused by ARVs, therefore, retroviral patients on ART should be routinely offered adherence and follow-up counselling to ensure compliance to therapy.

Assessment of ADR severity was done with Hartwig's ADR severity scale; i.e. level (1-2) mild, level (3-4) moderate, and level (5-7) severe. The outcome of the study indicates that the majority of ADRs were mild (55%) with the remaining being moderate (33%) and severe (12%). This outcome conforms to several studies that have reported ADRs due to ART to be mostly of mild and moderate severity (Gudina EK, *et al.*, 2017; Kumar A, *et al.*, 2017; Malalur C, *et al.*, 2016; Sadiq S, *et al.*, 2016). However, severe grade of ADRs recorded in the study i.e. 12% was relatively higher than 9.5% (Gudina EK, *et al.*, 2017), 3.04% (Kumar A, *et al.*, 2017), 3.57% (Malalur C, *et al.*, 2016), and 1.78% (Sadiq S, *et al.*, 2016). The higher number of severe grade forms of ADR observed in the study may have resulted from variations in the mode of assessment and the type of scale used in measuring ADR severity. According to the WHO definition of serious ADR, 12% of ADRs reported were classified as 'serious' ADR. Out of this number, 8% were life-threatening while 4% resulted in hospitalization.

Naranjo's probability scale was used for the causality assessment of ADR. This assessment established the extent of the relationship between ADRs and the suspected drugs. The outcome of the study revealed that the majority (84%) of ADRs were 'possible' and the remaining (16%) were 'probable' ADRs. This outcome of the study is similar to findings by Kumar A, *et al.*, 2017 in which the majority (88.6%) of ADRs were classified as 'possible', according to Naranjo's probability scale.

The majority of suspected drugs were continued for patients (75%) despite the presentation of ADRs. This was partly because most ADRs were mild and moderate in severity. In addition, most ADRs were common and known side effects associated with the use of these suspected drugs. Patients were asked to continue their medications after they were offered the needed adherence counselling. A significant number of patients (22%) had their medications changed or switched to the new regimen(s) because of the presence of ADRs whereas few patients (5%) had their medications withdrawn or discontinued due to severe ADRs. The drugs withdrawn or discontinued for patients were Co-trimoxazole.

LIMITATIONS

The sampling method used, i.e. convenient sampling, was not a true representation of the target population, making the study difficult to generalize. Study participants who failed to visit the ART Center during the data collection period did not have the opportunity to be included in the study. However, to reduce these biases, data were collected over a two (2)-month period where it was assumed that all patients receiving treatment at the hospital would have visited the ART Center. The study would be strengthened if all required blood results were available for all participants, including all viral load and G6PD results.

CONCLUSION

The findings from the study indicate that ADRs are highly prevalent amongst retroviral patients being managed at the Kwahu Government Hospital. Dizziness was the commonest type of ADR and was mainly caused by Tenofovir/Lamivudine/Efavirenz Antiretroviral drug regimen. The majority of ADRs were mild and moderate, resulting in the continuation of suspected drugs for most patients who experienced ADRs. A significant number (12%) of ADRs were however severe, leading to discontinuation or changing of drug regimen. 8% of ADRs were life-threatening while 4% resulted in hospitalization. It is therefore recommended that active surveillance measures be implemented to identify and monitor ADRs at all times at various ART centers across the country.

DECLARATIONS

Acknowledgment

The authors acknowledge participants of the study and the management of the Kwahu Government Hospital.

Author's contribution

All the listed authors contributed significantly to the design, implementation, and development of the manuscript for publication, with approval.

Ethics approval and consent to participate

A study site approval was obtained from the management of the Kwahu Government Hospital. Ethical clearance was granted by the Committee on Human Research, Publication and Ethics (CHRPE), Kwame Nkrumah University of Science and Technology (KNUST), Kumasi. Ethics approval number CHRPE/AP/181/20. The participants gave a signed informed consent to participate.

Paper context

This study investigated the Adverse Drug Reactions presented by patients who are put on life-long Antiretroviral Therapy. The study findings call on caregivers to adopt strategies to encourage these patients to take their medications as required and to immediately report adverse reactions.

Data availability statement

Data is available. However, it will not be shared in response to ethical requirements.

Supplemental online material

Supplemental materials on the study are available at; https://figshare.com/s/b582077de1a28fdb74fb

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