


Prevalence of Adverse Drug Reactions among Pediatric Patients on Antiretroviral Therapy in Selected Hospitals in Eastern Ethiopia: 8-Year Retrospective Cross-Sectional Study

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Abstract

Background: Antiretroviral-related adverse drug reactions (ADRs) are one of the leading causes of drug changes, poor adherence, and treatment failure. Therefore, this study was designed to assess the magnitude of ADR and associated factors among pediatric patients on antiretroviral therapy (ART). **Methods:** A retrospective cross-sectional study was conducted by reviewing the medical records of pediatric patients on ART at Hiwot Fana Specialized University Hospital and Jugal Hospital ART clinics. The collected data were coded, entered, and analyzed using SPSS, IBM version 16. The associations of selected categorical variables were done using binary logistic and multivariate logistic regression. **Results:** Of 186 medical records of pediatric patients on ART, 153 (82.25%) were reviewed. From the total medical records assessed, ADRs were observed in 23 (15.03%) of pediatric patients on ART, of which the most commonly encountered ADRs were anemia (34.8%) and followed by rash (17.4%). Most of ADRs were ranked as grade 3 (39.13%) and followed by grade 2 (30.4%) based on the degree of their severity. The likelihood of developing ADR was significantly associated with the regimen AZT/3TC/NVP (adjusted odds ratio: 6.420; 95% confidence interval: 1.056-39.018) relative to pediatric patients on D4T/3TC/NVP regimen. **Conclusion:** This study indicated that few pediatric patients on ART experienced ADRs. Most of the observed ADRs were ranked as grade 2 and 3 in terms of their severity. Drug out of stock and ADRs were the 2 most common reasons for antiretroviral (ARV) drug regimen change that could affect patient's treatment outcome and limited future option.

Keywords

HIV/AIDS, ADRs, ART, HAART, pediatrics

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Introduction

According to the report from United Nations Program on HIV and AIDS (UNAIDS) by the end of 2015, about 36.7 million people were living with HIV of which only 18.2 million were getting antiretroviral therapy (ART) across the world. On the other hand, a previous report of UNAIDS in 2012 showed that about 330 000 children were newly infected with HIV of which 90% of them were living in Sub-Saharan Africa. By the end of the same year, approximately 3.3 million children less than 15 years of age were infected.¹ In addition, recent global report in 2016 demonstrated that there were 2.1 million children living with HIV, whereas the number of newly infected children were estimated to be 160 000. This report also showed that annual death of children from AIDS is accounted for 120 000.² This number implies that still HIV is significantly affecting the

quality of life of children which in turn increasing childhood mortality rates in a number of sub-Saharan Africa.^{1,2}

The aim of using highly active ART (HAART) is to limit HIV viral replication and bring back immune function of the

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What Do We Already Know about This Topic?

Little is known about the prevalence of ADRs of commonly used ARV drugs among pediatric patients on antiretroviral therapy (ART) particularly in our country Ethiopia.

How Does Your Research Contribute to the Field?

Therefore, the finding of this study may provide input for the health care providers as they closely monitor pediatric patients on ART in order to maintain future option for them.

What Are Your Research's Implications toward Theory, Practice, or Policy?

It may provide insight for the health care providers as they look for relatively safe and tolerable drugs for pediatrics to wisely use the limited available formulation for pediatrics.

patients. Effective treatment results in decrease in viral load, boosting in the number of CD4 counts, and clinical improvement of the patient.³ Therefore, antiretroviral drugs (ARVs) have brought an ample of hope to people living with HIV.⁴ In developing countries, HAART has changed the face of HIV/AIDS disease among pediatric patients. Moreover, presently children who are contracted with HIV infection are able to survive to adolescence and adult hood. According to the report from resource rich countries and some areas of developing countries which have started implementing pediatrics ART, the rate of HIV linked morbidity and mortality in children as well as the risk of opportunistic infections are significantly reduced.⁵⁻⁷

Despite this, ARV drugs have appeared with its own risk that is observed in patients with various age groups from the very beginning of its initiation. Chronic use of the drugs, multiple pills taken at a time, exclusion from the society and being lonely due to stigma and discrimination, adverse drug reaction (ADR), and treatment failure are the major problems associated with HAART.⁸ Adverse drug reactions are significantly contributed for treatment interruption, regimen changes, nonadherence, and treatment failure among patients on ART.^{4,8} Adverse drug reactions of ARV drugs and other drugs have been considered to be the most important causes of mortality among people living with HIV/AIDS despite the fact that many of them are preventable as well as manageable.⁹ Variations are there among general population in terms of degree of severity of ADRs to occur among different people because of differences in their genetic makeup. Therefore, it is imperative to continuously monitor patients on ARV drugs in order to maximize the potential benefits and minimize the risks associated

with ARV drugs that will help achieve the ultimate goal of HIV/AIDS treatment.¹⁰⁻¹²

To date, there are a few reports on the prevalence of ADRs among pediatric patients on ART in Ethiopia. Since most of available data are from adult HIV-positive patients, extrapolating to children is not possible as long as the 2 populations have no similar drug dynamics.¹³ Therefore, this study was aimed to assess the prevalence of ADRs and associated factors among pediatric patients on ART at ART clinics of Hiwot Fana Specialized University Hospital (HFSUH) and Jugal Hospital (JH).

Methodology

Study Design and Study Period

The study was conducted in HFSUH and JH ART clinics which are located in Harar-town, 526 km from Addis Ababa, the capital of Ethiopia. Both hospitals provide services for the surrounding community at different wards such as internal medicine, gynecology/obstetrics, surgery, antenatal care, ophthalmology, hospital pharmacy, and ART clinic, among many others. A retrospective cross-sectional study was used to review 8-year medical records of pediatric patients on ART from March 2007 to April 2015. The data were collected from May 01 to 30, 2016.

Source Population

The source populations are all medical records of pediatric patients on ART registered at ART clinics of HFSUH and JH.

Study Population

Medical records of pediatric patients on ART from March 2007 to April 2015 that fulfilled the inclusion criteria of the study in both hospitals.

Sample Size Determination

All medical records of pediatric patients on ART registered within the study period in both hospitals who met the inclusion criteria were considered for data collection. This is because of the fact that the number of pediatric patients on ART at both hospitals is very small which is not feasible for sample size calculation.

Inclusion and Exclusion Criteria

Inclusion Criteria. All patients living with HIV whose ages are less 15 years and registered for ARV treatment at HFSUH and JH ART clinics from March 2007 to April 2015 were included in the study.

Exclusion Criteria. Age ≥ 15 years old, missing clinical records, and incomplete medical records as well as medical records of pediatric patients on ART that did not fall in the study period were excluded from the study.

Data Collection Instruments

Data collection tools adapted from previous studies were used to collect the desired information from the patients' medical records. The questionnaire used for data abstraction had 5 major parts which includes sociodemographic characteristics, WHO stage of the diseases, clinical and laboratory state at the beginning of ART, ART regimens, drugs used other than ARV drugs, and ADRs.

Data Quality Control and Analysis

The collected data were checked by the principal investigator for its accuracy, consistency, completeness, and those found to be incomplete or missing were excluded. The collected data were coded sequentially and entered into SPSS software version 16, IBM for analysis. A descriptive analysis was conducted as well as some tests of associations among selected categorical variables were done using binary logistic and multivariate logistic regression.

Operational Definitions

1. Adverse drug reaction is a response to a medicine which is noxious and unintended, and which occurs at doses normally used in human for diagnosis, prevention and treatment.
2. Side effect is any unintended effect of a pharmaceutical product occurring at doses normally used by a patient which is related to the pharmacological properties of the drug.
3. ART-clinic is a unit in a hospital that is responsible for counseling, investigating, and treating HIV-infected persons with ARV drugs.
4. Pediatric refers to those who are less than 15 years old.

Ethical Considerations

Ethical clearance and study approval was obtained from School of Pharmacy, College of Health and Medical Sciences, Haramaya University, and official letter was written to HFSUH and JH to secure permission with reference number of SOP/879/03/2016. After permission was obtained from the hospital administrators, the investigators communicate verbally with the head of ART clinics to explain the purpose of the study and ensuring that confidentiality of patients is maintained in such a way that no disclosure of any name of the patients was made during and after data collection. Since the data were collected from medical records and not directly from the patients, informed consent was not sought from the guardian of the children.

Results

Of 186 medical records of pediatric patients on ART at the 2 hospitals, 153 (82.25%) were reviewed while the remaining 33 medical records were excluded because of the absence of pertinent sociodemographic and medical information. The study indicated that of 153 pediatric patients on ART, 87 (56.86) of

Table 1. Sociodemographic Characters, Clinical Conditions, and Laboratory Conditions of Pediatric Patients on ART at the Time of Initiation of ARV Drugs at HFSUH and JH ART Clinics, Harar, Eastern Ethiopia, from March 2007 to April 2015.

Variables	Category	N = 153 (%)
Sociodemographic characteristics		
Age (years)	<3	11 (7.2%)
	3-10	55 (35.95%)
	11-15 ^a	87 (56.86%)
Sex	Male	71 (46.4%)
	Female	82 (53.6%)
Clinical conditions of pediatric patients on ART		
Reason for starting ARV	Treatment	148 (96.7%)
	PEP	0
	PMTCT	0
	Unknown	5 (3.3%)
Stage of the disease	Stage I	76 (49.7%)
	Stage II	49 (32%)
	Stage III	26 (17%)
	Stage IV	2 (1.3%)
	Functional stage	Working
	Ambulatory	75 (49%)
	Bedridden	2 (1.3%)
Weight (kg)	3-10	21 (13.7%)
	11-20	106 (69.3%)
	>20	26 (17%)
	Laboratory conditions of pediatric patients on ART	
CD4 (cell/mm ³)	50-100	3 (1.96%)
	101-200	7 (4.6%)
	201-500	36 (23.5%)
	>500	107 (69.9%)
	Hemoglobin (g/dL)	<7
7.1-10		39 (25.5%)
10.1-13		95 (62.1%)
>13		10 (6.5%)
Unknown		8 (5.2%)
ALT		<50
	50-100	12 (7.8%)
	101-200	3 (2%)
	Unknown	45 (29.4%)

Abbreviations: ALT, alanine aminotransferase; ART, antiretroviral therapy; ARV, antiretroviral; HFSUH, Hiwot Fana Specialized University Hospital; JH, Jugal Hospital; PEP, postexposure prophylaxis; PMTCT, prevention of mother-to-child transmission.

^aChildren of the age 15 years old were not included in the study.

them were in the age range of 11 to 15 years. Regarding gender, females accounted for 53.6% of the study participants. Most of the patients, 148 (96.7%), were using ARV drugs for the treatment purpose. In terms of disease clinical conditions, 76 (49.7%) of the patients were categorized under World Health Organization (WHO) clinical stage I. On the other hand, about half of the patients were found to be in a good functional state (49.7%). Based on the laboratory results, the study indicated about 107 (69.9%) patients were found to have CD4 count greater than 500 cell/mm³, whereas 135 (88.3%) of them had initial hemoglobin (Hgb) count less than 13 g/dL at the time of initiation of ARV drugs. At the time of initiation of ARV drugs most of the patients, 93 (60.8%), had ALT count <50 (Table 1).

Table 2. Antiretroviral Regimens, Treatment Status, and Drugs Used for Prophylaxis for Pediatric Patients on ART at HFSUH and JH ART Clinics, Harar, Eastern Ethiopia, from March 2007 to April 2015.

Variables	Category	Percent (%)
Treatment and follow-up status of pediatric patients on ART		
Treatment experience	Yes	0
	No	153 (100%)
Initial regimen	D4T/3TC/NVP	66 (43.1%)
	AZT/3TC/NVP	56 (36.6%)
	AZT/3TC/EFV	18 (11.8%)
	ABC/3TC/EFV	2 (1.3%)
	TDF/3TC/EFV	11 (7.2%)
	Current treatment status	On initial regimen
	Only 1 drug changed	65 (42.5%)
	Changed to other regimen	3 (2%)
Current regimen	AZT/3TC/NVP	95 (62%)
	AZT/3TC/EFV	31 (20.3%)
	AZT/3TC/LPV/r	4 (2.6%)
	ABC/3TC/EFV	8 (5.2%)
	TDF/3TC/EFV	15 (9.9%)
Drugs used for prophylaxis and TB treatment status by pediatric patients on ART		
Co-trimoxazole prophylaxis	Yes	146 (95.43)
	No	7 (4.57)
Isoniazid prophylaxis	Yes	124 (81)
	No	29 (19)
Patient on TB treatment	Yes	10 (6.5)
	No	143 (93.5)

Abbreviations: ART, antiretroviral therapy; HFSUH, Hiwot Fana Specialized University Hospital; JH, Jugal Hospital; TB, Tuberculosis.

Antiretroviral Regimens and Other Drugs Used for Prophylactic Purpose

The most commonly prescribed initial regimen was D4T/3TC/NVP in 66 (43.1%) of cases and followed by AZT/3TC/NVP in 56 (36.6%) patients. About 85 (55.6%) of the patients were still on initial regimen, whereas 65 (42.5%) of the patients did change at least 1 drug. On the other hand, 95 (62%) of pediatric patients were currently on AZT/3TC/NVP-based regimen. The most commonly used drugs other than ARV drugs were co-trimoxazole in about 146 (95.43%) patients and followed by isoniazid prophylaxis that accounted for 124 (81%) (Table 2).

Reasons for Changing ARV Drugs

The main reasons for changing ARV drugs before 1 year of treatment were due to toxicity in 23 (33.8%) of cases, whereas drug out of stock is attributed for 22 (32.4%) cases (Figure 1).

Frequency of ADRs, Severity, and Duration of Treatment

Among pediatric patients on ART at both hospitals, about 23 (15.03%) of them experienced ADRs. The most frequently diagnosed ADRs were anemia ($n = 8$; 34.8%) and rash ($n = 4$; 17.4%). Of the 23 patients encountered ADRs, 9 (39.13%) of

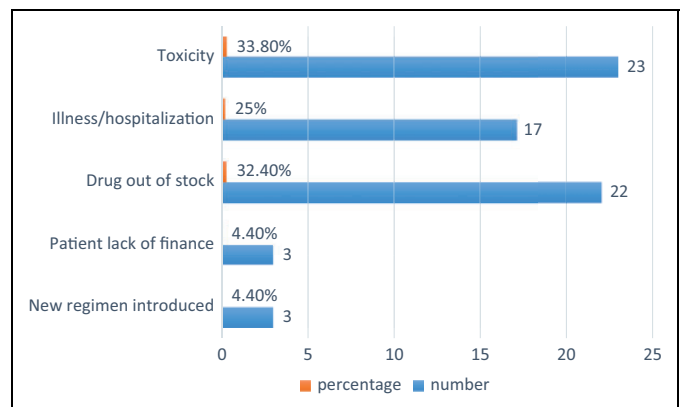


Figure 1. Reasons for changing antiretroviral (ARV) drugs at Hiwot Fana Specialized University Hospital (HFSUH) and Jugal Hospital (JH) antiretroviral therapy (ART) Clinics, Harar, Eastern Ethiopia, from March 2007 to April 2015.

Table 3. Distribution and Severity of ADRs associated with Antiretroviral Drugs at HFSUH and JH ART Clinics, Harar, Eastern Ethiopia, from March 2007 to April 2015.

Variables	n (%)
Adverse drug reaction	
Yes	23 (15.03)
No	130 (84.97)
Types of adverse drug reaction	
Diarrhea	3 (13.04)
Vomiting	2 (8.7)
Hepatitis	2 (8.7)
Rash	4 (17.4)
Anemia	8 (34.8)
Alteration in personality behavior or mood	2 (8.7)
Headache	2 (8.7)
Severity	
Grade 1	4 (17.4)
Grade 2	7 (30.4)
Grade 3	9 (39.13)
Grade 4	3 (13.04)
Total duration on follow-up (years)	
<2	27 (17.6)
2-5	66 (43.1)
6-10	60 (39.2)

Abbreviations: ADR, adverse drug reaction; ART, antiretroviral therapy; HFSUH, Hiwot Fana Specialized University Hospital; JH, Jugal Hospital.

them developed grade 3 ADRs, whereas 7 (30.4%) of them developed grade 2 ADRs (Table 3).

Variables Associated with the Development of ADR in Pediatric Patients on ART

To assess factors associated with the development of ADRs among pediatric patients on ART, regression analysis was conducted. Based on this, bivariate analysis showed that the duration of follow-up from 2 to 5 years (crude odds ratio [COR]: 0.19; 95% CI: 0.051-0.705) was significantly associated with

Table 4. Bivariate and Multivariate Logistics Analyses showing the association of Variables with the Development of ADRs Among Pediatric Patients on ART at HFSUH and JH ART Clinics, Harar, Eastern Ethiopia, from March 2007 to April 2015.

Variables	COR (95% CI)	P Value	AOR (95% CI)	P Value
Age (years)				
<3	1		1	
3-10	0.312 (0.070-1.391)	.127	.399 (0.064-2.470)	.323
11-15	0.538 (0.203-1.421)	.211	.741 (.234-2.352)	.611
Sex				
Male	1		1	
Female	0.55 (0.220-1.376)	.201	.388 (.132-1.140)	.085
Initial regimen				
D4T/3TC/NVP	1		1	
AZT/3TC/NVP	6.971 (1.510-32.19)	.013 ^b	6.420 (1.056-39.018)	.043 ^b
AZT/3TC/EFV	3.429 (0.814-14.45)	.093	3.931 (.790-19.549)	.094
ABC/3TC/EFV	2.0 (0.382-10.482)	.412	1.114 (.171-7.268)	.910
TDF/3TC/EFV	0.571 (0.028-11.849)	.718	–	–
INH prophylaxis				
No	1		1	
Yes	0.173 (0.022-1.346)	.094	–	–
Total duration of follow-up (years)				
<2	1		1	
2-5	0.190 (0.051-0.705)	.013 ^b	.455 (.091-2.261)	.336
6-10	0.496 (0.147-1.677)	.259	.810 (.199-3.307)	.770

Abbreviations: ADR, adverse drug reaction; AOR, adjusted odds ratio; ART, antiretroviral therapy; COR, crude odds ratio; HFSUH, Hiwot Fana Specialized University Hospital; INH, Isonicotinic Acid Hydrazide; JH, Jugal Hospital.

^bP < .05 is considered to be statistically significant.

the decrease in ADR compared to pediatric patients on ART for less than 2 years. However, with multivariate logistic analysis, the duration of follow-up did not show statistically significant association with the occurrence of ADRs. From the initial regimen of ARV drugs used, AZT/3TC/NVP regimen was found to be significantly associated with the development of ADRs both using bivariate (COR: 6.971; 95% CI: 1.510-32.19) and multivariate logistic analysis (adjusted odds ratio: 6.420; 95% CI: 1.056-39.018) relative to pediatric patients on D4T/3TC/NVP regimen (Table 4).

Discussion

This retrospective cross-sectional study was concerned with assessing the prevalence of ADRs, characterizing its effects and associated factors among pediatric patients on ART at HFSUH and JH. Accordingly our finding showed that more than 95% of pediatric patients using ARV drugs for the treatment purpose and about 50% of them were in WHO clinical stage I. This could be attributed to that earlier children born to a mother with HIV are more likely to be caught with HIV during pregnancy, delivery, and breastfeeding since option B+ was recently introduced in 2013 which is significantly reducing viral load in pregnant woman with HIV and in turn reducing the risk of HIV/AIDS transmission to new born and in turn reduce high risk of HIV/AIDS transmission to new born.¹⁴ This could suggest that after establishment of infection among exposed children, ARV drugs are used for the management of infection to improve the quality of life as well as prolong their survival time.

Our study showed that most of pediatric patients on ART had CD4 counts greater than 500 cell/mm³. This is not consistent with another study conducted in a selected hospitals in Addis Ababa which illustrated about 49.5% of children were in stage III based on WHO disease classification whereas similar proportion of children had CD4 count \geq 500 cell/mm³.¹⁵ This difference might probably arise from the fact that in our study ART was initiated as early as possible before significant reduction of CD4 count in most pediatric patients that maintained their CD4 count above 500 cell/mm³ or most children might be well respond to ART that increased their CD4 count to more than 500 cell/mm³ and kept them in stage I disease state. On the other hand, about 88.3% of them were found to have initial hemoglobin(Hgb) count <13 g/dL at the time of starting ART. Probably, this condition might be attributed by nutritional deficiency that prevails across such patients who are in a low-income country setting. This finding is concordant with other study that assessed the role of multiple factors such as nutritional deficiencies, chronic infections, immunosuppression of erythropoiesis, and genetic condition's contribution for the reduction in Hgb level and induction of anemia among pediatric patients.¹⁶⁻¹⁸

The regimen D4T/3TC/NVP was used in more than 40% of pediatric patients on ART and followed by AZT/3TC/NVP which accounted for 36.6%. This could have resulted from the fact that initially at the time of its introduction D4T was better tolerated than AZT and did not require Hgb or laboratory monitoring.¹⁹ This finding is in line with the study conducted at St. Paulo's and Ethio-Tebib hospitals and Addis Ketema Health Center in Addis Ababa city, which indicated that about 63% of

initial regimen was D4T/3TC/NVP followed by D4T/3TC/EFV and AZT/3TC/NVP regimens.²⁰ On the other hand, about 62% of the current regimen was AZT/3TC/NVP-based regimen which could imply that after D4T-associated long-term toxicity such as lipodystrophy, lactic acidosis, and other ADRs necessitate removal of D4T from the market,¹¹ the number of patients on AZT-based regimen tends to be escalated. The result of our study is consistent with the study conducted at Jos University teaching hospital in Nigeria in which AZT/3TC/NVP regimen constituted about 70.1% of all regimens used for pediatric patients.²¹

Regarding ARV drug regimen changes, the study showed that about 55.6% of the pediatric patients on ART were on initial regimen, whereas 42.5% of them did change at least one drug. According to our finding, the most common reasons of ARV drug regimen change among pediatric patients on ART is drug-related side effects which was accounted for 33.8% whereas drug out of stock was attributed to 32.4%. This change might be due to the fear of that ADRs were lead to patient's nonadherence and treatment failure. In similar fashion, stock out of drugs interrupt with the treatment and may contribute for ARV drug resistance that could urge for regimen change to deter ARV drug resistance. This study is consistent with another study in which the main reason for ARV drug regimen change was the occurrence of ADRs.²⁰ It is also in line with another study that observed ADRs were reasonably linked with nonadherence to treatment, discontinuation of ART, treatment failure, and changes in ART regimens.²²⁻²⁷

In this study, about 15% of pediatric patients on ART experienced ADRs in which anemia and rash were the 2 most commonly diagnosed cases. On the other hand, in terms of severity 39.13% of the patients were developed grade 3 ADRs whereas 30.4% of them developed grade 2 ADRs. This might probably associated with AZT/3TC/NVP-based regimen which was the most commonly used regimen in this study next to D4T/3TC/NVP. This result is in agreement with the study conducted in Nigeria in which about 41% of the patients on AZT-based regimen were developed pallor²² and another study in which AZT-based regimen associated with severe anemia and neutropenia.²⁸ However, our finding is higher in terms of severity of ADRs observed among pediatric patients on ART than the result reported from children in Sikasso Mali in which most of the cases were grade 1 in terms of its severity.²⁹ This difference could be ascertained by the low level of baseline Hgb in our study that could augment ADR associated with ART drugs.

Moreover, this study also revealed that pediatric patients on AZT/3TC/NVP regimen were 6.42 (95% CI: 1.056-39.018; $P < .05$) times more likely to experience ADR than those who were on another regimens. However, age, sex, and the use of Isoniazid (INH) prophylaxis failed to show statistically significant association in both bivariate and multivariate analyses with the occurrence of ADR among pediatric patients on ART. This result is in agreement with another study conducted in Mumbai, India in which sex, age, immune category, viral load at onset, and CD4 count were not significantly associated with the development of ADRs ($P > .05$), while AZT and NVP were

reported to induce anemia and rash among pediatric patients on ART, respectively.⁷

Limitations of the Study

The results of this study may not represent the national picture as it was done only in 2 hospitals. The diagnosis and severity were taken as documented on the medical records of patients. It was also difficult to find follow-up report from the clinical records of patients who developed ADRs. The clinical records were very often incomplete, lacking important sociodemographic, and clinical variables. Therefore, the findings of this study were interpreted in context of these limitations.

Conclusion

This study demonstrated that few pediatric patients on ART were encountered ARV drug-associated ADRs. However, most of them were experienced grade 2 and 3 ADRs in terms of severity. On the other hand, of all ARV drug regimens used by pediatric patients, AZT/3TC/NVP was observed to be strongly associated with the occurrences of ADRs. Therefore, taking baseline laboratory results of pediatric patients with HIV into account and considering ARV drugs that do not exacerbate preexisting conditions must be strategically planned so as to limit these ADRs while upholding adherence and better treatment outcome among pediatric patients on ART.

Authors' Note

All authors have made a substantial contribution to the development of concept and design, analysis and interpretation of data, prepared the manuscript and revised it critically for important intellectual content, and approved for publication.

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Declaration of Conflicting Interests

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References

1. Joint United Nations Programme on HIV/AIDS. *Global Report: UNAIDS Report on the Global AIDS Epidemic 2013*. Geneva, Switzerland: UNAIDS; 2013.
2. United Nations Programme on HIV/AIDS. *AIDSinfo website*; accessed July 2018; UNAIDS. *Core Epidemiology Slides*; http://www.unaids.org/en/resources/documents/2017/20170720_Core_epidemiology_slides. Accessed June 2017.
3. World Health Organization. *Antiretroviral Therapy of HIV Infection in Infants and Children: Towards Universal Access: Recommendations for a Public Health Approach-2010 Revision*. Geneva Switzerland: World Health Organization; 2010.
4. Cooper CL, Breau C, Laroche A, et al. Clinical outcomes of first antiretroviral regimen in HIV/hepatitis C virus co-infection. *HIV Med*. 2006;7(1):32–37.
5. Dollfus C, Le Chenadec J, Faye A, et al. Long-term outcomes in adolescents perinatally infected with HIV-1 and followed up since birth in the French perinatal cohort (EPF/ANRS CO10). *Clin Infect Dis*. 2010;51(2):214–224.
6. Verweel G, van Rossum AM, Hartwig NG, et al. Treatment with highly active antiretroviral therapy in human immunodeficiency virus type 1-infected children is associated with a sustained effect on growth. *Pediatrics*. 2002;109(2):e25.
7. Shah I. Adverse effects of antiretroviral therapy in HIV-1 infected children. *J Trop Pediatr*. 2006;52(4):244–248.
8. Parchure RS, Kulkarni VV, Darak TS, et al. Growth patterns of HIV infected Indian children in response to ART: a clinic based cohort study. *Indian J Pediatr*. 2015;82(6):519–524.
9. Mulcahy F, Hoffman C. ART 2006. *Perspective HIV Med*, 2006: 89e93.
10. Highleyman L. Adverse effects associated with antiretroviral therapy. *Bull Exp Treatm AIDS*. 2000;13:23–31.
11. Ethiopia Drug Administration and Control Authority. *Adverse Drug Reaction Reporting Guideline*. Addis Ababa, Ethiopia: Publisher-Food, Medicine and Health Care Administration and Control Authority (FMHACA), 2003.
12. Ethiopia Drug Administration and Control Authority. *Adverse Drug Reaction Monitoring and Promotion Control Division Report*. Addis Ababa, Ethiopia: Publisher-Food, Medicine and Health Care Administration and Control Authority (FMHACA), 2006.
13. Vidal F, Gutierrez F, Gutierrez M, et al. Pharmacogenetics of adverse drug reactions due to antiretroviral drugs. *AIDS Rev*. 2010;12(1):15–30.
14. Country/Regional Operational Plan (COP/ROP) 2017: Strategic Direction Summary; Ethiopia, April 2017. <https://www.pepfar.gov/documents/organization/272012>. Accessed March 4, 2018.
15. Biadgilign S, Deribew A, Amberbir A, et al. Adherence to highly active antiretroviral therapy and its correlates among HIV infected pediatric patients in Ethiopia. *BMC Pediatr*. 2008;8(1): 53. doi:10.1186/1471-2431-8-53.
16. Ethiopia Demographic and Health Survey 2016. <https://dhsprogram.com/pubs/pdf/FR328/FR328>. Accessed March 7, 2018.
17. Calis JC, van Hensbroek MB, de Haan RJ, et al. HIV-associated anemia in children: a systematic review from a global perspective. *AIDS*. 2008;22(10):1099–1112.
18. Shet A, Arumugam K, Rajagopalan N, et al. The prevalence and etiology of anemia among HIV-infected children in India. *Eur J Pediatr*. 2012;171(3):531–540.
19. Viganò A, Thorne C, Brambilla P, et al. Antiretroviral therapy, fat redistribution and hyperlipidaemia in HIV-infected children in Europe. European Paediatric Lipodystrophy Group. *AIDS*. 2004; 18:1443–1451.
20. Jima YT, Angamo MT, Wabe NT. Causes for antiretroviral regimen change among HIV/AIDS patients in Addis Ababa, Ethiopia. *Tanzan J Health Res*, 2013: 15(1)
21. Ejeliogu EU, Ebonyi AO, Okpe SE, et al. Pattern of adverse drug reaction in HIV-infected children on anti-retroviral therapy in Jos, Nigeria. *Open Sci J Clin Med*. 2014;2(4):89–93.
22. Monforte AD, Lepri AC, Rezza G, et al. Insights into the reasons for discontinuation of the first highly active antiretroviral therapy (HAART) regimen in a cohort of antiretroviral naive patients. *AIDS*. 2000;14(5):499–507.
23. Mocroft A, Phillips AN, Soriano V, et al. Reasons for stopping antiretrovirals used in an initial highly active antiretroviral regimen: increased incidence of stopping due to toxicity or patient/physician choice in patients with hepatitis C coinfection. *AIDS Res Hum Retroviruses*. 2005;21(9):743–752.
24. Sabundayo BP, McArthur JH, Langan SJ, Gallant JE, Margolick JB. High frequency of highly active antiretroviral therapy modifications in patients with acute or early human immunodeficiency virus infection. *Pharmacotherapy*. 2006;26(5):674–681.
25. Yuan Y, L'italien G, Mukherjee J, et al. Determinants of discontinuation of initial highly active antiretroviral therapy regimens in a US HIV-infected patient cohort. *HIV Med*. 2006;7(3):156–162.
26. De F, Bonolo P, César CC, et al. Non-adherence among patients initiating antiretroviral therapy: a challenge for health professionals in Brazil. *AIDS*. 2005;19(suppl 4):S5–S13.
27. Pádua CA, César CC, Bonolo PF, et al. Self-reported adverse reactions among patients initiating antiretroviral therapy in Brazil. *Braz J Infect Dis*. 2007;11(1):20–26.
28. Van Dyke RB, Wang L, Williams PL, Pediatric AIDS Clinical Trials Group 219C Team. Toxicities associated with dual nucleoside reverse-transcriptase inhibitor regimens in HIV-infected children. *J Infect Dis*. 2008;198(11):1599–1608.
29. Oumar AA, Diallo K, Dembélé JP, et al. Adverse drug reactions to antiretroviral therapy: prospective study in children in sikasso (mali). *J Pediatr Pharmacol Ther*. 2012;17(4):382–388.