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PREVALENCE OF CO-MEDICATION AND POTENTIAL DRUG-DRUG INTERACTIONS IN HUMAN IMMUNODEFICIENCY VIRUS INFECTED PATIENTS ON HIGHLY ACTIVE ANTI-RETROVIRAL THERAPY

Behailu Terefe Tesfaye*, Teshale Ayele Mega, Tsegaye Melaku Kebede

Institute of health science, School of Pharmacy, Clinical pharmacy unit, Jimma University, Ethiopia.

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ABSTRACT

Background:-Drug interaction is an important therapeutic challenge among Human Immunodeficiency Virus infected patients. They are often observed in these patients because they frequently receive multiple medications. Though this may have clinical and economic impact, its prevalence is unknown in Ethiopia. So this study was aimed at addressing this issue by determining the prevalence of Co-medication and potential drug-drug interaction (PDDIs) in HIV infected patients. Method:- initially, checklist containing the relevant variables for the study was developed; ethical approval for patient medical history card (PMHC) access was requested and obtained from the hospital. Then, before the actual data collection process takes place, pre-test was done on 18 PMHCs. After assessing the check list, data of 350 HIV infected patients was reviewed retrospectively and recorded from cards using simple random sampling method. Subsequently, PDDI was assessed using Meds cape online drug interaction checker database and Drug.com (as supportive DDI checker). Then, the data was checked for completeness, entered and analyzed using Statistical Package for Social Science (SPSS) version 20 and Microsoft excel and presented using tables and figures. Result:-out of 350 HIV infected patients on HAART; only 53(15.1%) patients were not co-medicated along with Anti-Retroviral drugs. Then, a total of 2431 PDDIs were identified, and pharmacokinetic and pharmacodynamic interactions were found to occur almost in comparable frequency and almost all of the interactions were found to be moderate or minor in their severity. Conclusion:-in this study more than half of the HIV infected patients were found co-medicated and high numbers of PDDIs were identified. Accordingly, the authors of this study concluded that co-medication and PDDIs are common and, though unavoidable, since almost all of the identified PDDIs were moderate or minor in their severity, the authors' recommend close monitoring of patients for therapeutic or toxic response.

Corresponding author
Behailu Terefe Tesfaye
Jimma town, Ethiopia-378.
terefebh@gmail.com or behailu.terefe@ju.edu.et
+251 920194883 / +251 943302087

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INTRODUCTION

Human Immunodeficiency Virus/ Acquired Immunodeficiency syndrome (HIV/AIDS) is a disease caused by a virus called Human immunodeficiency virus (HIV), a member of the lentivirinae subfamily of retroviruses [1]. Treatment of HIV infection commonly requires a combination of 3 to 4 Anti-retroviral, termed as Highly Active Antiretroviral Therapy (HAART) [2]. HAART consists of a backbone of two NRTIs and one NNRTI or one or two PIs, with a high potential for drug-drug interactions (DDIs) [3]. The consumption of multiple therapeutic agents often results in clinically significant DDIs, the consequence of which might be serious. Among the enormous consequences of DDIs: toxicity, treatment failure, organ damage, increased mortality and/or development of viral resistance to ART can be mentioned [4]. ART drugs categorized under the PIs and NNRTIs are extensively metabolized by cytochromeP450 (CYP450) enzymes, and can inhibit and/or induce different CYP450 isozymes [5]. Therefore, identification, prevention, and management of drug interactions crucial for better patient care [6]. Taking multiple medications, which account for 3% to 5% of all in-hospital medication errors, may result in drug-drug interactions, which could be clinically significant (CSDIs) [7]. In large cohort study conducted to assess the prevalence of the potential for DDI involving ARV in Kenya, 1 in 3 patients on ARV drugs was found to be at the risk of clinically significant DDI [8].

In a study done in French, to analyze potential DDI between ART drugs and co-medication in elderly patients (median age 65.3 ± 5.2 years), 45% of the prescriptions were found to have clinically relevant DDI. In this study, in 85% of the Patients a combination of three ARV drugs and in 94% of them a concomitant treatment with non-ARV drugs was found. Beside, 4.6 ± 3.3 drugs were prescribed per patient [9]. A cohort study done in Chile (n=150) revealed 10.7% of patients were not receiving any co-medications. The most frequently used drugs were analgesics (31%), antibiotics (11.2%), and GI medications (7.7%) [10]. In a review of HIV infected children's case file done in Lagos University teaching Hospital, wide range of medications were co-prescribed for the patients while on HAART regimen. The drugs were used to treat co morbid conditions, opportunistic infections, or concurrent infections. Other co-medicated drugs include drugs for the treatment of malaria 208(67.1%), pneumonia 70(22.6%), and sepsis 4(1.3%) were the concurrent infections frequently treated in the patients [11]. Report from Uganda assessed the prevalence and type of drug-drug interactions involving anti-retroviral in patients, showed that, almost all patients were taking one or more co-medication along with ARV regimen, with a mean of 1.9 co-medications per patient [12]. Swedish report (n= 600,000) from a Swedish drug register, indicates 26% type C and 5% type D potential DDI prevalence were seen [4]. Prospective study was conducted at Gulbarga (n=72) analyzed potential DDIs by using multiple DDI checker databases. Out of 72 enrolled patients 52.77% and 47.23% were males and females respectively and 58.33% of them were in the age group between 31-45 years. In this study, out of the 72 patients, DDIs were seen in 63 of them. The total DDIs identified were 337, of these, 50.74% DDIs were between others with others, 49.25% DDIs were between ARTs with others. No DDIs were found between ARTs themselves. On Classification wise, 75.3% pharmacokinetic, 21.66% major, 51.33% moderate, 27.01% minor and 72.4% delayed DDIs were revealed. Major DDIs were between ARTs with other [6]. Study done in India (n=118) on hospitalized HIV infected patients, 90 were males and 49.1% of them were in age group between 41 to 59 years. DDIs were seen in 77 patient prescriptions. The total DDIs detected was 175 and the overall incidence of DDIs was 65.2%. This incidence was found to be higher in female population 67.8%, as compared to males which are 64.4%. Of the 175 detected DDIs, 89% were pharmacokinetic in type and in severity wise; 50.8% were minor, 26.9% were moderate and 22.3% were major DDIs [13]. Swiss study (n=1497) showed antibiotics, self-prescribed drugs and herbal supplements are co-medicated with HAART. The study revealed 51% frequency of DDI in the upper age group compared to the 35% in the lower. In this older population group, 27% and 22% DDIs occurred with cardiovascular and CNS drugs, respectively. The study attributed the higher incidence of DDI in the older group due to the consumption of higher number of drugs (82% against 61%) with median number of 2 compared to 1 in the younger individuals [14].

In a retrospective review of 47085 ARV prescriptions in South Africa shows, 960 DDIs were detected, of these 60.21% were seen in patients of age group between 40 and 60, 1.88% in patients of age ≤ 6 years, 4.27% in patients of age between 6-12 years, 0.63% in patients of age between 12-19 years, 32.4% in patients of age between 19-40 and lowest DDI prevalence were Seen in patients of ≥ 60 [2]. DDIs observed after multiple drug administration could be either positive or negative i.e. the interaction may result in improved therapeutic effect or result in deleterious effect. The negative impacts of DDIs may include, toxicity-if one of them increases the effect of the other resulting in overdose, increased risk of side effects, therapeutic failure-if the action of the drug is reduced due to the interaction, increased cost of treatment, emergency of drug resistance and so on. These negative consequences of DDI are pathologically significant and may even go unnoticed [10]. As a result, managing drug-drug interactions remains as one of the major challenges in the optimization of HIV therapy [15]. The magnitude of this problem is unknown in Ethiopia, a country were a great share of Human Immunodeficiency Virus (HIV) infection burden reside. In this country the use of DDI checker data base is less likely both during prescription and dispensing. So studying the prevalence will enable the concerned bodies to appreciate the degree of this problem and to give attention to it. To address this issue, the study was conducted with the aim of determining and assessing the prevalence of co-medication and potential drug-drug interactions (PDDIs) in HIV infected patients on HAART in a single set up, BGH, East Ethiopia.

METHODS AND MATERIALS

Study Area and Period:

The study was conducted in BGH found in Bishoftu town, which is 47 km far away from the capital city of Ethiopia / Addis Ababa/. The study was conducted from March 21, 2014-May 22, 2014.

Study Design:

A descriptive cross sectional study on PMHCs was used.

Exclusion Criteria:
Patients whose medical card shows inadequate information and medical card with high degree of illegibility problem were excluded from the study.

Study Population:
All medical cards of HIV infected patients on HAART attending treatment in ART Clinic of BGH during the study period.
Sample Size Determination & Sampling Technique: The sample size was determined as follows,

$$\mathbf{n}= \frac{Z\,2\,p\,(1-p)}{w2} \quad \text{for very large population (N>10,000)}$$

=384

Where, n=the required sample size, p=Assumed proportion, P=50%, w=margin of error (precision) =5%
Z= the value of Z in the standard normal distribution that corresponds to a-level 0.05.
Since, N <10,000 which was 2889, the required minimum sample size is,

$$= n/ (1+n/N) = 350$$

Sampling Procedure:
Simple random method of sampling was used to select sample populations medical history card for incorporation into the study by passing over any medical history card with high degree of illegibility problem.

Data Collection Instrument:
Data collection format containing the variables to be measured was developed and pre-test was done by collecting data from 18 patient`s medical history card to make sure that the format provides the required information.

Data analysis and quality:
Data was cleared, categorized, compiled and coded before analyzed by using the SPSS version 20.0 software for windows. Completeness, accuracy and clarity of the collected data were checked carefully before data analysis was made. Any erroneous, ambiguous and incomplete data was excluded. Percentages and proportions were used to describe the completeness of different components of the prescription.

Ethical Consideration:
A formal letter written from Department of pharmacy, Ambo University to BGH and permission was obtained from Ethical Approval Committee. Strict confidentiality was assured through anonymous recording and avoiding patient identifying information. The raw data were kept secured in a locked cabinet in the researchers' office.

Funding source:
Financial support was obtained from students' research project of Ambo University.

Definition of terms
- Clinically significant drug interaction-drug interaction requiring close monitoring or contraindicated drug combination .i.e., major and/or moderate drug interactions.
- Co-medication:- drugs used to treat opportunistic infections and other co-morbidities in HIV infected Patients other than antiretroviral drugs.
- Major DDI: - is a type of highly clinically significant interaction which requires avoiding of combinations, because, the risk of the interaction outweighs the benefit. i.e. serious DDIs.
- Minor DDI: - clinically non-significant type of interactions
- Moderate DDI:-Moderately clinically significant. Usually avoid combinations; use it only under special circumstances.
- Supplements:-vitamins and minerals taken either because of deficiency, treatment or as prophylaxis excluding supplemental medicated foods such as plumpy nut.

Limitation of the Study:
Medscape online drug interaction checker database cannot point out DDIs that occur between drugs and multivitamin. Although Drug.com interaction checker database can point out these DDIs, it overstates the extent of interaction. Also, majority of the interactions are clinically non-significant or at most requires monitoring. This made multivitamin exclusion in DDI study compulsory. DDIs were evaluated for clinical significance according to the criteria Stated in Medscape online drug interaction checker database and Drug.com.

RESULTS

Demographic Results

Three hundred fifty (n=350) patients medical card were reviewed during the study, of these, 114 (32.6%) were male and 236 (67.4%) were female patients. Among them, 15(4.3%) patients were ≤ 6 years of age, 24(6.9%) patients were in the age group of 6-12 years, 13(3.7%) patients were in the age group of 12-19 years, 241(68.9%) patients were in the age group of 19-40 years and 57(16.3%) patients were in the age group of 40-60 years. The regional status of patients whose medical cards were reviewed during the study showed that, 252(72%) patients were from the urban area, whereas 98(28%) patients were from the rural area. Of these, 61(17.4%) patients have had body mass index (BMI) of less than 18 kg/, 197(56.3%) patients have had a BMI of 18.5-24.9 kg/ and 50(14.3%) patients have had a BMI above 24.9 kg/.CD4 count of patients included in the study showed that there were 250(71.4%) patients having CD4 counts 200 and 43(12.3%) patients having a CD4 count of. The CD4 count of 57(16.3%) patients was not available during the study period (See Table4).

Prevalence of Co-Medication

In this study, out of 350 patients, only 53(15.1%) patients were not taking co-medications together with ARV drugs. The rest, 297(84.9%) patients were concomitantly receiving at least one non-ARV drug with ARVs. Of the 350 patients, 322(92.0%) patients were receiving three ARV drugs, while 28(8.0%) patients were receiving four ARV drugs (second line regimen). The most frequently co-prescribed class of drugs were: antibiotics (65.8%), supplements (16.2%), analgesics (7.1%), acid-suppressants (3.3%), and anti-helminthes (1.8%) (Figure1). The most commonly co-prescribed antibiotic is Cotrimoxazole (See Table 1). In addition to these, the study showed that the amount of drugs prescribed per patient was 4.8±1.4 and highest number of drugs prescribed per patient was 10 and the lowest was 3 (See Table 5).

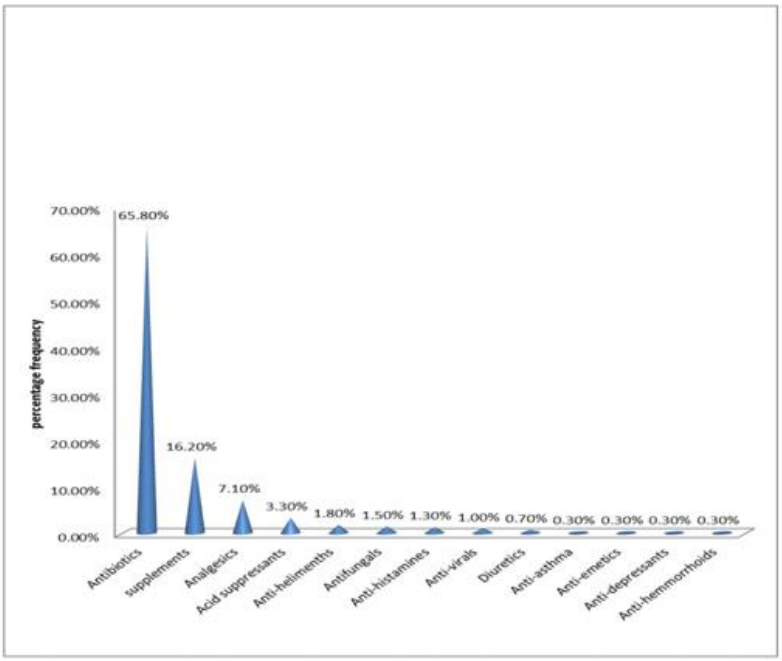

Figure1: Percentage of patients using one or more drugs of the Corresponding class as identified at Bishoftu General Hospital from March 21, 2014-May 22, 2014

Table 1: Shows some of co-prescribed non-ARV drugs with their frequency revealed by this study.

ARV Regimens	Co-medicated drugs	Frequency of co-medicated Drugs with each specific regimen
TDF/3TC/EFV	Cotrimoxazole	109
	Isoniazide	28
	Amoxicillin	12
	Rifampin	9
	Multivitamin	22
	Albendazole	8
AZT/3TC/EFV	Cotrimoxazole	62
	Isoniazide	11
	Amoxicillin	9
	Pyridoxine	11
	Diclofenac	6
AZT/3TC/NVP	Cotrimoxazole	40
	Isoniazide	8
	Acyclovir	3
TDF/3TC/NVP	Cotrimoxazole	13
	Isoniazide	6
D4T/3TC/NVP	Cotrimoxazole	9
	Amoxicillin	7
	Paracetamol	5
ABC/3TC/NVP	Cotrimoxazole	2
AZT/3TC/LP/r	Cotrimoxazole	4
	Clotrimazole	2
	Spironolactone	2
	Salbutamol	2
TDF/3TC/LP/r	Cotrimoxazole	4
	Omeprazole	2
	Amitriptyline	2
TDF/3TC/ATV/r	Cotrimoxazole	4
D4T/3TC/LP/r	Cotrimoxazole	2

† AZT-Zidovudine, TDF-Tenofovir, D4T-Stavudine, 3TC-lamivudin, EFV-Efavirenz, NVP-Nevirapine, ABC-Abacavir, LP/r-Lopinavir/ritonavir, ATV/r-Atazanavir/ritonavir

Prevalence of DDIs

In this study, out of 350 patients' medical card, using Meds cape online drug interaction checker database and using drug.com as a supportive DDI checker database, DDIs were seen in all (100%) during the study period. A total of 2431 DDIs were identified, out of which, 1221(50.2%) DDIs were between ART themselves (See Table 2), 1039(42.7%) DDIs were between ART and co-medicated drugs, and 171(7.1%) DDIs were between co-medicated drugs themselves (See Table 3). Of the 2431 DDIs, pharmacologically, 1059(43.6%) DDIs were pharmacokinetic, 1335(54.9%) DDIs were pharmacodynamic and 37(1.5%) DDIs were, DDIs of unknown pharmacologic mechanism of interaction. On severity wise, 2(0.1%) major, 1767(72.7%) moderate, and 661(27.2%) minor DDIs were identified (See Figure 2). The highest DDIs (69.3%) were observed in the age group of 19-40 years and the lowest DDIs (2.9%) were observed in the age group of 12-19 years (See Table 6).

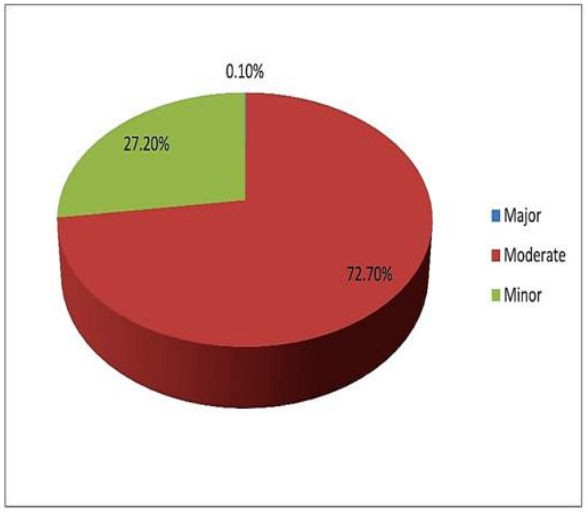

Figure-2: Level of severity of potential Drug-drug interactions identified at Bishoftu General Hospital from March 21, 2014-May 22, 2014

Table 3: Shows inter-ARV drug Interactions with their frequency, degree of severity and Pharmacologic classification.

Index drug	2nd Drug	Frequency	Pharmacologic Classification		Severity classification		
			PK	PD	M	MO	m
Tenofovir	Atazanavir	6(0.2%)					
Lamivudine	Zidovudine	278(11.4%)					
	Stavudine	18(0.7%)					
	Tenofovir	185(7.6%)					
	Nevirapine	91(3.8%)					
Efavirenz	Zidovudine	70(2.9%)					
	Tenofovir	149(6.1%)					
	Lamivudine	216(8.9%)					
Nevirapine	Zidovudine	71(2.9%)					
	Tenofovir	23(1.0%)					
	Stavudine	15(0.6%)					
Atazanavir	Tenofovir	6(0.2%)					
	Lamivudine	6(0.2%)					
	Ritonavir	12(0.5%)					
Ritonavir	Zidovudine	11(0.5%)					
	Stavudine	2(0.1%)					
	Tenofovir	26(1.1%)					
	Abacavir	2(0.1%)					
	Lamivudine	28(1.2%)					
	Atazanavir	6(0.2%)					

† PK-Pharmacokinetic, PD-Pharmacodynamic, U-Unspecified, M-Major, MO-Moderate, m-Minor, ✓ Pharmacologic classification of the respective DDI.

Table 4: Shows some of ART with other and other with other DDIs with their frequency, severity and Pharmacologic classifications from data of Aug.10, 2013-Jan.8, 2014 in BGH.

Drug-drug interactions	Frequency of the DDIs with percent	Pharmacologic classification of the DDI		
		PK	PD	U
1.ART-Other				
Moderate				
3TC with Sulfamethoxazole	9.8%			
EFV with INH	1.6%			
AZT with Rifampin	0.8%			
EFV with Diclofenac	0.4%			
Minor				
AZT with Cotrimoxazole	8.7%			
EFV with Miconazole	0.2%			
EFV with Metronidazole	0.3%			
2.Other-Other				
Major				
INH with Omeprazole	0.1%			
Moderate				
Diclofenac with Ibuprofen	0.2%			
Metronidazole with Sulfamethoxazole	0.2%			
Amoxicillin with Acyclovir	0.1%			
Minor				
Ibuprofen with Acyclovir	0.2%			
Sulfamethoxazole with Diclofenac	0.4%			
Trimethoprime with Pyridoxine	0.7%			
INH with Pyridoxine	1.0%			

† INH-Isoniazid, ✓ Pharmacologic classification of the respective DDI, PK-Pharmacokinetic, PD-Pharmacodynamic U-Unspecified, M-Major, MO-Moderate, m-Minor.

Tabular summary of demographic and main study results

Table 4: Demographic results of the sample populations in BGH from Aug.10, 2013-Jan.8, 2014.

Demographic data	Male	percentage	Female	Percentage	Total no of patients	% of total no of patients
Gender	114	32.6%	236	67.4%	350	100%
Regional status	76	21.7%	176	50.3%	252	72%
-Urban	38	10.9%	60	17.1%	98	28%
-Rural						
Age distribution	8	2.3%	7	2.0%	15	4.3%
≤6	11	3.1%	13	3.7%	24	6.9%
(years)	6	1.7%	7	2.0%	13	3.7%
6-12	61	17.4%	180	51.4%	241	68.8%
12-19		8.0%				16.3%
19-40						
40-60						
CD4 counts in cells/µI	76	21.7%	174	49.7%	250	71.4%
≥200	26	7.4%	17	4.9%	43	12.3%
<200		-	-	-	57	16.3%
Not available						
BMI in kg/m^2						
<18.5	33	9.4%	28	8.0%	61	17.4%
18.5-24.9	56	16.0%	141	40.3%	197	56.3%
>24.9	9	2.6%	41	11.7%	50	14.3%

Table 5: Study results of co-medication Prevalence in BGH from Aug.10, 2013-Jan.8, 2014.

Co-medication data	Total number	% of total
No. of ARV drugs per patient		
Three(3)	322	92.0%
Four(4)	28	8.0%
Prevalence of co-medication		
Non-co-medicated patients	53	15.1%
Co-medicated patients	297	84.9%
Most commonly co-prescribed Drugs		
Antibiotics	399	65.8%
Supplements	98	16.2%
Analgesics	43	7.1%
Acid-suppressants	20	3.3%

Table 6: Results Of Prevalence of PDDIs identified from HIV Infected Patients on HAART in BGH from data of Aug.10, 2013-Jan.8, 2014.

DDI prevalence data	ART-ART	ART-Other	Other-Other	Total number of DDIs	Percent of total no
Patients without DDI				No	No
Patients with DDI	1221(50.2%)	1039(42.7%)	171(7.1%)	2431	100.0%
Classification of DDI					
Pharmacologically					
Pharmacokinetic	25(1.0%)	904(37.2%)	130(5.3%)	1059	43.6%
Pharmacodynamic	1190(48.9%)	133(5.5%)	12(0.5%)	1335	54.9%
Unknown	6(0.2%)	2(0.1%)	29(1.2%)	37	5%
Based on Severity					
Major	0	0		2	0.1%
Moderate	1076(44.3%)	667(27.4%)		1767	72.7%
Minor	145(6.0%)	372(15.3%)		662	27.2%

DISCUSSION

Demographic result of this study shows that there are more HIV infected females (236) than males (114). But, in the study done in India, HIV infected male individuals were much greater than females (90 and 28 respectively) during the study period [13]. Regional status of patients from reviewed medical cards shows higher number of patients were from the urban area (72%) which is inconsistent with results of study done at Gulbarga showing patients from rural back grounds being higher (68.06%) [6]. This difference might have resulted from factors such as time to time increase in the number of prostitution houses in the town which might have paved a away to unprotected sexual intercourse for urban dwelling peoples or migration of infected peoples from rural to urban areas for different reasons or the emerging local access of treatments for the rural dwelling peoples. Body mass index (BMI) of the sample population in this study shows the majority of patients (56.3%) were in the BMI range of 18.5-24.9kg/m^2. This result agrees with study conducted in India which revealed that the highest number of patients (55.9%) were in the BMI range of 18.5-24.9 kg/m^2 [13]. In this study, 71.4% of patients have a CD4 count ≥200 which is inconsistent with the results obtained from study conducted in India showing higher number of patients involved in the study have had CD4 count<200 [6,13]. This difference might have resulted because of unfortunate discrepancy creating factors, such as, difference in adherence of patients to their Medications during the study period, difference in time of initiation or duration after initiation of ART. In this research finding, 92.0% of patients were taking three ARV drugs which closely agree with the results of study done in French, which is 85% [9]. These ART regimens are: TDF/3TC/EFV (41.7%), AZT/3TC/EFV (20.0%), AZT/3TC/NVP (19.7%), D4T/3TC/NVP (4.3%), TDF/3TC/NVP(6.3%). The rest are second line regimens including: AZT/3TC/LP/r (3.1%), TDF/3TC/LP/r (2.0%), TDF/3TC/ATV/r (1.7%), D4T/3TC/LP/r (0.6%), and ABC/3TC/LP/r (0.6%) (See figure 3). Besides, in this current study only 53(15.1%) patients were not co-medicated. This result of the study is consistent with results of studies conducted in French and Chiles showing the co-medicated patients being higher in number than non-co-medicated patients. In these two studies the non-co-medicated patients were 6% and 10.7% respectively [9, 10].

In this study the most frequently co-prescribed class of drugs was: antibiotics (65.8%), supplements (16.2%), analgesics (7.1%), acid-suppressants (3.3%), and anti-helminthes (1.8%). This result disagrees with finding of study conducted in Chile, which claimed the most frequently co-prescribed drugs as analgesics (31%), antibiotics (11.2%), and GI medications (7.7%) [10]. This difference might have occurred because of the difference in the living standards of patients included in the two studies, which in turn determines to some extent, the immunity status of the patient. In the area where this study was conducted, in majority of cases, patients receive at least one prophylactic antibiotic, in addition to antibiotics they receive for treatment of opportunistic infections and other diseases. In addition to this, supplements might not have been considered in the above study. In this study, the average number of drugs prescribed per patient was found to be 4.8 with a standard deviation of 1.4, which is almost closer to the result claimed by study conducted in French, which is 4.6±3.3 [9]. In this study finding, PDDIs were observed in all patient`s (100%) medical card reviewed during the study period. This result is inconsistent with results of study conducted in South Africa, Swedish and India [2, 4, and 13]. This difference might have occurred because of the difference in DDI checker databases used or due to difference in study design. A total of 2431 PDDIs were identified, out of which, 1221(50.2%) DDIs were between ART themselves, 1039 (42.7%) DDIs were between ART and co-medicated drugs, and 171(7.1%) DDIs were between co-medicated drugs themselves. But, the results of study done at Gulbarga claimed most DDIs to exist between others with others (50.74%) and no DDIs between ARTs themselves [6]. This might have occurred because of the difference in DDI checker databases used and the availability of a number non-ARV drugs which may not be available in our country. Pharmacologically, of the 2431 PDDIs identified in this study, higher numbers of DDIs were pharmacodynamic (43.6%).On severity wise, 2(0.1%) major, 1767(72.7%) moderate, and 662(27.2%) minor DDIs were identified, showing 1769 DDIs being CSDIs. With regard to severity, this result is consistent with results of study done at Gulbarga, which claimed highest number of moderate (51.33%) DDIs followed by minor (27.01%) DDIs.[6] But, in the study done at Gulbarga, 75.3% of DDIs were pharmacokinetic, which is inconsistent with result of this current study which shows dominance of Pharmacodynamic DDIs (43.2%) [6]. This is because, in this study the majority of ARV drugs were found to interact with each other pharmacodynamically by causing immune reconstitution syndrome, which have highly contributed to the predominance of pharmacodynamic DDIs over pharmacokinetic DDIs. This effect might have resulted from difference in DDI checker databases used in classifying the specific DDIs pharmacologically. With regard to the clinical significance of the identified PDDIs, this current study supports results of study done in Kenya [8]. In this study the highest numbers of DDIs (69.3%) were observed in the age group of 19-40 and the lowest DDIs (2.9%) were observed in the age group of 12-19. But, in the study done in South Africa 60.21% of DDIs were seen in patients of age group between 40 and 60 and lowest DDI prevalence were Seen in patients of ≥ 60 [2]. This inconsistence might have arisen due to inconsistent types and patterns of drugs prescribed in the two countries based on their respective standard treatment guide line. Beside, in this study no patients were above 60 years of age.

CONCLUSION

In this study more than half of the HIV infected patients were found co-medicated and high numbers of PDDIs were identified. Accordingly, the authors of this current study concluded that co-medication and PDDIs are common. This is of more concern as they may lead to therapeutic failure; increase hospital admissions, cost of therapy and morbidity and mortality rates, if not appropriately managed. Since almost all of the identified PDDIs were moderate or minor in severity, the authors' of this study recommended close monitoring of patients for therapeutic or toxic responses. Appropriate advice on good adherence to ART is also indispensable in these patient populations to minimize the occurrence of diseases associated with immunodeficiency, as these leads to co-medication and further DDIs. In addition, clinicians should have to understand how to monitor drug interactions in order to prevent drug toxicities or treatment failure in these patient populations. Finally, the authors of this study recommend further prospective studies on these patient populations to reveal the actual effect of DDIs.

Conflict of Interest:
no conflict of interest

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List of abbreviations and acronyms

ART	Anti-Retroviral Therapy
ARV	Anti-Retroviral
BGH	Bishoftu General Hospital
BMI	Body mass index
CSDI	Clinically Significant Drug Interaction
CYP450	CytochromeP450
DDIs	Drug-Drug Interaction
FMOH	Federal Ministry Of Health
HAART	Highly Active Anti-Retroviral Therapy
HIV/AIDS	Human Immunodeficiency Virus
MUAC	Mid upper arm circumference
NNRTIs	Non-Nucleoside Reverse Transcriptase Inhibitors
NRTIs	Nucleoside Reverse Transcriptase Inhibitor
OI	Opportunistic Infection
PIs	Protease Inhibitors
PMHC	Patient Medical History Card
RVI	Retroviral Infection
SPSS	Statistical Package for Social Science

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