

Drug Interactions in Cardiovascular Patients in Yekatit 12 Hospital, Addis Ababa Ethiopia

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Abstract

Background: Cardiovascular patients are more often reported with drug-drug interactions as compared to patients with other diseases. The high rate of prescribed drugs in elderly patients increases the likelihood of drug interactions and thus the risk that drugs themselves can be the cause of hospitalization.

Purpose: The objective of the research is to assess drug interaction in cardiovascular patients at Yekatit 12 Hospital, Addis Ababa, Ethiopia.

Patients and Methods: Retrospective cross-sectional study design was involved to assess drug-drug interaction and associated factors in cardiovascular patients admitted in Yekatit 12 Hospital Medical College. A total of 209 medical charts of cardiovascular patients were included to this study. Drug-drug interaction was checked using standard drug interaction checker software (Micromedex). A test of association was done using Chi-square test. In addition, the significance for the association of variable with the dependent variable was tested at p value less than 0.05.

Result: The medical records of 209 cardiovascular patients were included to this study. From these, 55.5% were female whereas, 45% were in the age group of less than 65 years. The mean hospital stay of patients was 11.2 days. Nearly half (44.5%) of the patients had a diagnosis of CHF. A total of 1485 drugs were prescribed during the mean hospital stay of 11.2 days, with a mean of 7.1 medications per patient. Sixty-eight patients (32.5%) had at least one major drug-drug interaction. DDI was found significantly associated with increase in number of drugs (polypharmacy) ($p=0.001$; $\chi^2=31.04$). In addition patients with prolonged hospital stay were associated with potential drug interactions ($p=0.012$; $\chi^2=5.75$).

Conclusion: The finding of present study reveals that nearly one third of the elderly patients are exposed to at least one major DDI. The most common drug interaction in these cardiovascular patients is between omeprazole and digoxin. Clinical pharmacists must remain vigilant in monitoring potential DDIs and making appropriate dosage or therapy adjustments.

Keywords: Drug-drug interaction; Yekatit 12 hospital; cardiovascular patients

List of Abbreviations ADR: Adverse Drug Reaction; CAD: Coronary Artery Disease; CVD: Cardiovascular Disease; DDIs: Drug-Drug Interactions; MI: Myocardial Infraction; WHO: World Health Organization

Introduction

Drug therapy is growing more complex thus making appropriate decision on drug therapy is increasingly challenging. Drug interactions are most important in this situation and proper management of drug-drug interactions (DDI) may prevent harmful events. DDIs are a major cause for concern in patients with cardiovascular disorders due to multiple co-existing conditions and the wide class of drugs they receive [1]. DDI in patients receiving multi drug therapy is a major concern as it may lead to an increase risk of hospitalization and higher health care

cost [2]. Many adverse events can be prevented by identifying DDIs [3].

Various studies suggest that cardiovascular patients are more often reported with DDI as compared to patients with other diseases. The possible reason behind higher DDI rate in cardiovascular disease may include elder age, polypharmacy and pharmacokinetic or pharmacodynamics nature of drugs used in cardiology [4].

The probability of interactions increases with the number of drugs taken. The high rate of prescribed drugs in elderly patients increases the likelihood of drug interactions. Furthermore, DDIs are common and growing in frequency due to increasing numbers of medications available and the number of patients on multiple medications [5].

Drug interactions can have desired, reduced or unwanted effects. It may transform the diagnostic, prevents or therapeutic activity of any drug [6]. Drug interactions can be an extremely main contributory factor for the incidence and occurrence of adverse drug events. It may result in the alteration of therapeutic response. Hospitalized cardiac

patients need more attention regarding drug-drug interactions due to complexity of their disease and therapeutic regimen. Cardiovascular drugs are the most frequently prescribed medicines for older people. The high rate of prescribed drugs in elderly patients increases the likelihood of drug interactions and thus, the risk that drugs themselves can be the cause of hospitalization [7].

Cardiovascular patients who were admitted in a medical ward in India, 61.36% of them were having moderate DDI in severity. This DDIs are responsible for up to 2.8% of hospital admissions [2]. In addition, a study performed in hospitalized cardiac patients at Ayub Teaching Hospital, Abbotabad, Pakistan has shown that 91.6% of patients have at least one DDI from study subjects[4].

Few studies conducted in Ethiopia showed that DDIs are common in chronic patients. A study performed among cardiovascular patients admitted to medical ward of Ayder Referral Hospital, Northern Ethiopia, showed that 62.2% DDIs from all patients participated in the study [8]. Another study that assessed DDIs and risk factors in patients taking cardiovascular drugs at Jimma University Specialized Hospital explored that 72.2% of patients were at risk for DDIs [9].

Despite the above few studies, extensive researches related to DDIs in cardiovascular patients are limited in Ethiopian settings. Therefore, we conducted this study to find out the extent of drug interactions and associated factors in cardiovascular patients at Medical Ward of Yekatit 12 Hospital, Addis Ababa, Ethiopia.

Material and Methods

Study design and study setting

Retrospective cross-sectional study design was employed to assess DDIs and associated factors in cardiovascular patients at Yekatit 12 Hospital. The hospital has more than 339 beds that provide diagnostic and treatment services for about 1.5 million patients per year. The study was conducted in the Medical Ward. Data was collected from December 20, 2017 to January 5, 2018. We included six months data in cardiovascular patients who were admitted in the Medical Ward from May 2017 to October 2017.

Sample size determination and sampling technique

Cardiovascular patients above the age of 50 who were admitted for at least 24 hours in the hospital's medical ward were included in the

study. Cardiovascular patients with incomplete medical chart information were excluded from the study. Sample size of 209 was computed based on single population proportion formula by using the proportion (P) of drug-drug interaction of 0.726 from a previous study in Jimma, Ethiopia [9].

Data collection process

Data collection tool was developed based on the context of the study. Approval and permission was sought from Ethical Review committee of Addis Ababa Health Bureau. Four clinical pharmacists collected data on current medications, co-morbidities, length of hospitalization, and relevant previous medical and medication histories. The research team supervised consistency of data collection process, observation and data cleaning was done daily by research team. Research team were gave code for each medical record card to reduce redundancies and possible error.

Data analysis

Once the raw data was collected, data analysis was done using SPSS version 23. A test of association was done using Chi-square test. In addition, the significance for the association of variable with the outcome variable was tested at p-value less than 0.05. Drug-drug interaction was checked using standard drug interaction checker software (Micromedex). The result is presented using tables, figure and descriptive statistical interpretation was made in the context of study objectives and based on the study result, and conclusion and recommendation were forwarded.

Results

The medical records of 209 cardiovascular patients were included to this study. Of these, 116 (55.5%) were female whereas, the rest 93 (44.5%) were males. From the study participants -45% were in the age group of less than 65 years and the other 55% were 65 and above. The mean age (\pm SD) of participants was 65.6 (\pm 9.9) years (Table 1).

Variable	Frequency	Percentage (%)	
Sex	Male	93	44.5
	Female	116	55.5
Age	Mean (\pm SD)	65.6 (\pm 9.9)	
	<65 Years	94	45
	\geq 65 Years	114	55

Table 1: Characteristics of elderly cardiovascular patients admitted in Yekatit 12 Hospital Medical College, 2018.

The mean hospital stay of patients was 11.2(\pm 6.9) days. 88.5 % of the participants had co-morbid conditions while 24 (11.5%) of them

had a single diagnosis. Nearly half (44.5%) of the patients had a diagnosis of CHF followed by corpulmonale (20.1%) (Table 2).

Characteristics	Frequency	Percentage (%)	
Current Diagnosis	CHF	93	44.5
	Corpulmonale	42	20.1
	DVT	28	13.4
	Hypertension	17	8.1
	Ischemic stroke	10	4.8
	IHD	8	3.8
	Rheumatic Valvular Heart Disease	5	2.4
	Others ^a	6	2.9
Hospital Stay (days)	Mean (± SD)	11.2 (± 6.9)	
	<11	114	54.5
	≥ 11	95	45.5
Comorbidity	Yes	185	88.5
	No	24	11.5
Physicians involved with the patient care	Intern	209	100
	General Practitioner	198	94.7
	Resident	188	90
	Senior Physician	163	78

Note: ^aHemorrhagic stroke, dilated cardiomyopathy; Abbreviations: CHF: Congestive Heart Failure; DVT: Deep Vein Thrombosis; IHD: Ischemic Heart Disease; SD: Standard Deviation

Table 2: Clinical characteristics of elderly cardiovascular patients admitted in Yekatit 12 Hospital Medical College, 2018.

A total of 1485 drugs were prescribed during the mean hospital stay of 11.2 (± 6.9) days, with a mean of 7.1(± 2.6) medications per patient. 35 (16.7%) patients had <5 prescribed drugs while 95 (45.5%) and 79 (37.8%) of them had 5-7 and 8 and above prescribed drugs, respectively (Figure 1).

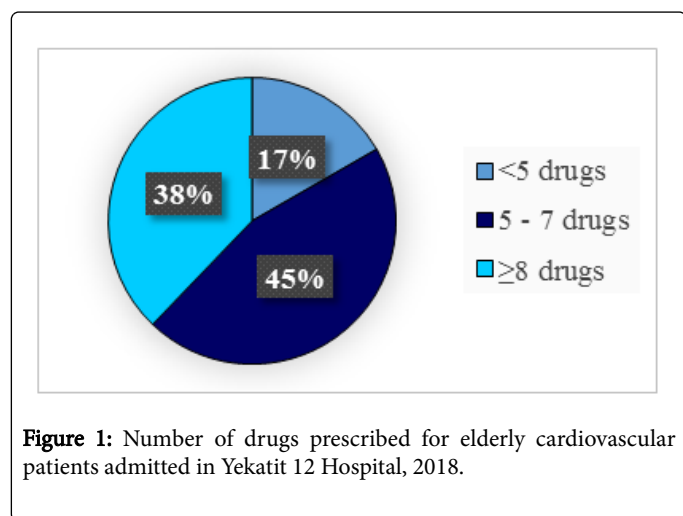


Figure 1: Number of drugs prescribed for elderly cardiovascular patients admitted in Yekatit 12 Hospital, 2018.

According to Micromedex[®] 2.0 online drug reference, majority (88%) of the participants were exposed to potential moderate DDIs.

Sixty-eight patients (32.5%) had at least one major drug-drug interaction. One patient has got a contra-indicated medication with ceftriaxone and calcium gluconate (Figure 2).

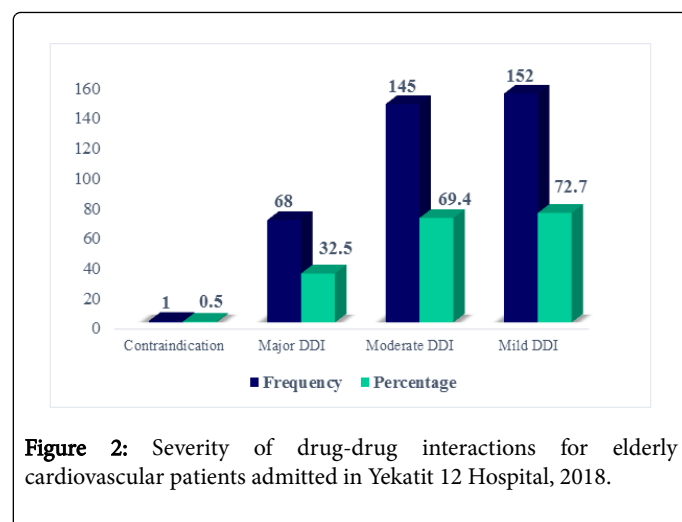


Figure 2: Severity of drug-drug interactions for elderly cardiovascular patients admitted in Yekatit 12 Hospital, 2018.

The most frequently prescribed major DDI was the combination of omeprazole and digoxin that occurred on 17 cardiovascular patients. Spirinolactone and KCl combination was the second most common

major drug-drug interaction (15 patients) administered for these patients. The third most important drug interaction was with azithromycin and digoxin in 12 individuals (Table 3).

Interacting drugs	Number of patients	Potential risk
Omeprazole+Digoxin	17	Risk of digoxin toxicity (nausea, vomiting, cardiac arrhythmias)
Spirolactone+KCl	15	Increase potassium levels in the blood
Azithromycin+Digoxin	12	Risk of digoxin toxicity (nausea, vomiting, cardiac arrhythmias)
Omeprazole+Clopidogril	9	Reduced plasma concentrations of clopidogrel active metabolite and reduced antiplatelet activity
Azithromycin+Warfarin	7	Increased risk of bleeding
Cimetidine+Atorvastatin	3	Increased atorvastatin toxicity
Fluoxetine+Warfarin	3	Increased risk of bleeding
Rifampicin+Atorvastatin	1	Decreased effect/level of atorvastatin
Efavirenz+Warfarin	1	Risk of bleeding
KCl: Potassium Chloride		

Table 3: List of major drug–drug interactions with their potential risks for elderly cardiovascular patients admitted in Yekatit 12 Hospital Medical College, 2018.

There was no significant difference in the occurrence of DDI with respect to age, sex and presence of co-morbidities. DDI was found significantly associated with increase in number of drugs (polypharmacy) ($p=0.001$; $\chi^2=31.04$). In addition patients with prolonged hospital stay were associated with potential drug interactions ($p=0.012$; $\chi^2=5.75$). (Table 4).

Variable	Category	DDIa (%)		χ^2	p-value
		Yes	No		
Sex	Male	30 (32.3)	63 (67.7)	0.006	0.529
	Female	38 (32.8)	78 (67.2)		
Age	<65 years	29 (30.6)	65 (69.1)	0.22	0.375
	>65 years	39 (33.9)	76 (66.1)		
Co-morbidity	Yes	61 (33)	124 (67)	0.14	0.452
	No	7 (29.2)	17 (70.8)		
Hospital stay	<11 days	29 (25.4)	65 (74.6)	5.75	0.012
	≥ 11 days	39 (41.1)	56 (58.9)		
Number of drugs prescribed	<5 drugs	1 (2.9)	34 (97.1)	31.04	0.001
	5-7 drugs	25 (26.3)	70 (73.7)		
	≥8 drugs	42 (53.2)	37 (46.8)		
DDI: Drug-drug interactions					

Table 4: Statistical association of variables with drug–drug interaction for elderly cardiovascular patients admitted in Yekatit 12 Hospital Medical College, 2018.

Discussion

The mean (\pm SD) number of drugs prescribed per patient in this study was $7.1(\pm 2.6)$ which is higher than study reports from Mekelle, [8] Jimma; [9] which was 6 ± 4 and 3.8 , respectively. These differences could be due to the discrepancy in study set-up and difference in burden of co-morbidity and medication use pattern in these settings. From the total patients, 38% of patients had received more than seven drugs. This is greater than the study in Mekelle, which is 11.8% [10]. This difference could be the inclusion of elderly patients only in the current study

In this study, 68 (32.5%) of the study participants were exposed to at least one major DDI. This is in line with the findings in Jimma [9] and Mekelle, [8] which reported a prevalence of 29.6 and 32.9% major DDIs, respectively. In contrast to this, lower prevalence of DDIs was reported from a study in Tikur Anbesa Specialized Hospital, which is 13.1% [11]. This variation could be due to difference in availability of alternative drugs and absence of clinical pharmacists and drug information software to provide drug information in the inpatient settings of hospitals during the study period

Omeprazole and digoxin were the most common drugs responsible for DDIs in this study. The interaction between KCl and Spironolactone was the second most important interaction. This finding is different from studies in Mekelle [10] and Tikur Anbesa Specialized Hospital [11] in which clarithromycin–clopidogril and ceftriaxone–heparin were the most common drug-drug interactions. This variation could be explained by the disparity of the scope of the hospital settings and prescribers level of education.

In this study polypharmacy (taking five drugs or more) was identified to be associated with the occurrence of DDI ($p=0.001$; chi-square=31.04). A number of other studies have also identified an increase number of medications to be associated with DDI in the cardiovascular patients [4,8-10]. A study from Tikur Anbesa Specialized Hospital reported that the potential drug interaction risk when patients are taking more than 5 medications [11]. The other factor found to be associated with major DDIs is prolonged hospital stay ($p=0.012$; chi-square=5.75) similar to the study in Abbottabad [4]. But, this was not accordance with studies in Jimma, [9] Mekelle [8,10] and Tikur Anbesa Specialized Hospital [11]. The reason for this discordance could be the prolonged time patients spent in the current study. Despite that age is not an associated factor with DDI in the current study, the incidence of DDIs was associated with old age in another study in Pakistan [4]. These could be because of the homogeneity of participants' age in the current study. Other variables such as age, sex and comorbidity were not found to be associated with the occurrence of drug-drug interaction. This is in line with other findings in Jimma, [9] Mekelle [8,10] and Tikur Anbesa Specialized Hospital [11].

A contraindicated drug combination was administered in one patient. The interaction was involving ceftriaxone with calcium gluconate. Co-administration of ceftriaxone with calcium-containing solutions, even *via* different infusion lines, may cause precipitation of ceftriaxone-calcium salt [12].

Conclusion

The finding of present study revealed that nearly one third of the patients are exposed to at least one major DDI. As cardiovascular patients with polypharmacy and prolonged hospital stay are associated

with the occurrence of DDIs, they need close monitoring to identify and manage drug-drug interactions. Identifying and preventing potentially harmful DDIs is a critical component of a pharmacist's mission. Clinical pharmacists must remain vigilant in monitoring potential DDIs and making appropriate interventions. Further longitudinal studies using larger number of participants are necessary to observe the actual clinical outcomes drug-drug interactions.

Ethical Consideration

Approval and permission was obtained from Ethical Review committee of Addis Ababa Health Bureau. Verbal consent obtained from chief of medical record room and each staff in the room to extract data from patient medical record cards. Privacy and confidentiality was ensured during review of patients' medical record card. Data obtained from patients chart was used only for the study purpose.

Author Contributions

All authors contributed toward data analysis, drafting and critically revising the paper. All the authors agree to be accountable for all aspects of the work

Disclosure

The authors report no conflicts of interest in this work

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References

1. Shukla AK, Mehani R (2016) Cost analysis of antiepileptic drugs available in India. *Int J Basic Clin Pharmacol* 5: 1636-1640.
2. Mateti UV, Rajakannan T, Nekkanti H, Rajesh V, Mallaysamy SR, et al. (2011) Drug-drug interactions in hospitalized cardiac patients. *J Young Pharm* 3: 329-333.
3. Sunanda NP, Master SA, Raj KN, Sushen G, Laxshmi MS (2015) Assessment of quality of life in hypertensive patients at a tertiary care hospital. *Int Res J Pharm* 6:720-3.
4. Murtaza G, Khan MYG, Azhar S, Khan SA, Khan TM (2016) Assessment of potential drug-drug interactions and its associated factors in the hospitalized cardiac patients. *Saudi Pharm J* 24(2):220-5.
5. <https://www.ahajournals.org/doi/10.1161/CIR.0000000000000456>
6. Cascorbi I (2012) Arzneimittelinteraktionen: Prinzipien, Beispiele und klinische Folgen. *Dtsch Arztebl Int* 109:546-556.
7. https://www.ccs.ca/images/Guidelines/Guidelines_POS_Library/HD_CC_2002_Eld.pdf
8. Teka F, Teklay G, Ayalew E, Teshome T (2016) Potential drug-drug interactions among elderly patients admitted to medical ward of ayder referral hospital, Northern Ethiopia: A cross sectional study. *BMC Res Notes* 9: 1-8.
9. Chelkeba L, Alemseged F, Bedada W (2013) Assessment of potential drug-drug interactions among outpatients receiving cardiovascular medications at Jimma University specialized hospital, South West Ethiopia. *Int J Basic Clin Pharmacol* 2: 144.
10. Aklilu Yesuf T, Zeleke Belay A, Ayalew Sisay E, Gebreamlak ZB (2017) Prevalence and clinical significance of potential drug-drug interactions at Ayder Referral Hospital, Northern Ethiopia *J Dev Drugs* 6.

11. Tesfaye ZT, Nedi T (2017) Potential drug-drug interactions in inpatients treated at the Internal Medicine ward of Tikur Anbessa Specialized Hospital. *Drug Healthc Patient Saf* 9:71–6.
12. Steadman E, Raisch DW, Bennett CL, Esterly JS, Becker T, et al. (2010) Evaluation of a potential clinical interaction between ceftriaxone and calcium. *Antimicrob Agents Chemother* 54:1534–40.