

A prospective study on impact of clinical pharmacist interventions in management of patients with cardiovascular diseases in a tertiary care hospital, India

Un estudio prospectivo sobre el impacto de las intervenciones de los farmacéuticos clínicos en la gestión de pacientes con enfermedades cardiovasculares en un hospital de atención terciaria, India

Shahin Mojra , **Mekkanti Manasa Rekha** 

Doctors of Pharmacy, Department of pharmacy practice, Gautham College of Pharmacy, Bengaluru, India.

Corresponding author

Shahin Mojra
Department of pharmacy practice,
Gautham College of Pharmacy, Bengaluru, India
E-mail: mojra4133@gmail.com

Received: 17 - X - 2021

Accepted: 15 - XII - 2021

doi: 10.3306/AJHS.2022.37.01.110

Abstract

Objective: To evaluate the impact of clinical pharmacist interventions in the management of patients with cardiovascular diseases in a tertiary care hospital.

Methodology: The Present Study was a Prospective Interventional study conducted over a minimum period of 6 months from October 2019 to March 2020 in Cardiology and General Medicine Departments In a Tertiary Care Hospital, India. 220 prescription was evaluated out of which 140 prescription had pDDIs. The patient demographics and all medically relevant information were noted in a predefined data collection form. Alternatively, these case charts were reviewed for potential drug interactions, drugs involved in interactions, laboratory investigations, followed up for assessing observed adverse drug interaction, and pharmacist's intervention.

Result: Out of 220 prescriptions analyzed, 140 prescriptions comprised of potential drug interactions and it was found that 234 drug interactions were present. The incidence of potential drug interaction was 63.64%, A total of 28 adverse drug reactions were recorded among 234 pDDI.

Conclusion: This study attempted to assess the potential drug-drug interaction in the prescription of cardiac patients in the inpatient hospital setting. This study also examined patient, drug characteristics, causality, and severity of pDDIs. This study shows that DDIs are frequent among hospitalized cardiac patients. About 234 drug interactions were reported during the study period with a median number of 1.67 pDDIs in the cardiac patients. This study emphasizes the need to consider pDDIs during therapeutic planning, protect patients from the consequence of drug interactions. In addition, providing DDI-related information to the prescribers and drug interaction alert software to the dispensing pharmacist can play a vital role in minimizing the incidence rate of DDI.

Keywords: Cardiovascular, Potential drug-drug interaction, Drug interaction.

Resumen

Objetivo: Evaluar el impacto de las intervenciones del farmacéutico clínico en el manejo de pacientes con enfermedades cardiovasculares en un hospital de tercer nivel.

Metodología: El presente estudio fue un estudio prospectivo de intervención realizado durante un período mínimo de 6 meses desde octubre de 2019 hasta marzo de 2020 en los departamentos de cardiología y medicina general en un hospital de atención terciaria, India. Se evaluaron 220 prescripciones de las cuales 140 tenían pDDIs. Los datos demográficos del paciente y toda la información médicamente relevante se anotaron en un formulario de recogida de datos predefinido. Además, se revisaron las historias clínicas para determinar las posibles interacciones farmacológicas, los fármacos implicados en las interacciones, las investigaciones de laboratorio, el seguimiento para evaluar la interacción farmacológica adversa observada y la intervención del farmacéutico.

Resultado: De las 220 prescripciones analizadas, 140 incluían posibles interacciones farmacológicas y se descubrió que había 234 interacciones farmacológicas. La incidencia de interacciones farmacológicas potenciales fue del 63,64%, y se registraron un total de 28 reacciones farmacológicas adversas entre las 234 pDDI.

Conclusión: Este estudio trató de evaluar la potencial interacción farmacológica en la prescripción de pacientes cardíacos en el ámbito hospitalario. Este estudio también examinó las características del paciente, del fármaco, la causalidad y la gravedad de las pDDI. Este estudio muestra que las IDP son frecuentes entre los pacientes cardíacos hospitalizados. Se notificaron unas 234 interacciones farmacológicas durante el periodo de estudio, con una mediana de 1,67 IDP en los pacientes cardíacos. Este estudio enfatiza la necesidad de considerar las pDDIs durante la planificación terapéutica, para proteger a los pacientes de las consecuencias de las interacciones farmacológicas. Además, el suministro de información relacionada con las IDP a los prescriptores y el software de alerta de interacciones farmacológicas al farmacéutico dispensador pueden desempeñar un papel vital para minimizar la tasa de incidencia de las IDP.

Palabras clave: Cardiovascular, posible interacción medicamentosa, interacción medicamentosa.

Introduction

By causing an estimated 17.9 million passing's every year, cardiovascular diseases (CVDs) are the main deadly diseases all around the world, making 31% of all-cause mortality¹. As a result of various etiologies and simultaneous comorbidities, CVD patients are treated with a mind-boggling therapeutic routine containing numerous various drugs. For instance, in the United States of America, the elderly CVD patients (age > 65 years) had eight simultaneous comorbidities and took 13 drugs on normal². In like manner, prescription of countless various drugs (range 2-24 drugs) to CVD patients have been accounted for by studies directed somewhere else.^{3,4,5,6}

Cardiovascular diseases (CVDs) remain the biggest cause of death worldwide. A WHO report (2012) estimated that 17.5 million people die of CVDs each year representing 31% of all deaths. Of these, about 7.4 million are due to coronary heart disease and 6.7 million dues to stroke. By 2030, an estimated 23.6 million people will kick the bucket from CVDs basically from coronary illness and stroke. These are projected to stay the single driving reason for death⁷.

Even though pharmacotherapy in cardiovascular diseases can further develop prosperity, its benefit can be undermined by drug-related problems (DRPs). A drug-related problem is any occasion or situation including drug therapy that meddles with the patient accomplishing an ideal result of clinical consideration⁸⁻¹¹. They act as a huge danger, prompting huge morbidity and mortality. In a survey of worldwide examinations, it was tracked down that about 28% of all crisis division visits were related to DRPs and 24% of them brought about medical clinic confirmation. In a review directed by Zaredar, N⁹ et al in 2017, it was seen that about 87% of hospitalized patients have drug-related problems. In one more review directed by Nascimento¹⁰ et al in 2009, the incidence of DRPs was accounted for as 91.7. An Indian review announced that the incidence of DRPs was observed to be more noteworthy than cited in created nations. The high incidence of unseemly measurement and ill-advised drug choice saw in the review was ascribed to the absence of standard therapy conventions and the varying therapy designs between the clinical wards in every Indian medical clinic.¹¹ Cardiovascular drugs are one of the drug classifications frequently engaged with drug-related problems. A concentrate by Andreazza⁸ et al in 2011 reported cardiovascular drugs to account for the majority of all DRPs. Detection and prevention of DRPs can save lives along with enhancing patients' quality of life and optimizing healthcare costs. Among DRPs potential drug-drug interaction is the most important part of cardiovascular pharmacotherapy.

The role of drug-drug interaction during medicinal therapy can be considered a bivalent outcome that can be either

beneficial or profoundly unintended and distressful. The identification of such unintended interaction is the primary goal of this research. As it has been already identified by the Committee for Human Medicinal Product (CHMP) of the European Medicines Agency that drug-drug interaction is a common problem during drug treatment and is the major reason behind numerous hospitalizations as a result of adverse drug reactions, sometimes serious or even fatal adverse events¹²⁻¹⁶. Drug-drug interaction may also result in a decrease or completely inhibit treatment efficacy. Many studies have proven the significance of pharmacists in identifying and resolving potential drug-drug interactions through timely interventions. Gattis et al¹⁴ observed that including a drug specialist as an individual from a multidisciplinary heart failure (HF) group altogether diminished mortality and HF occasions. Studies evaluating the pervasiveness of potential drug-drug cooperation's in hospitalized cardiovascular patients and the meaning of drug specialist mediation in such cases are lacking in India. The potential for drug collaboration is higher with cardiovascular drugs^{15,16,17} and there is gives an account of expected DDIs in the cardiology division from India.^{18,19} No examinations are detailing the real incidence of DDIs in the Indian setting. Henceforth, the current review was intended to evaluate the incidence and example of DDIs in hospitalized heart patients in a tertiary consideration emergency clinic, with the appraisal of a planned report on the effect of clinical drug specialist intercessions in the management of patients with cardiovascular diseases.

Materials and methods

Prospective Interventional Study was conducted in Cardiology and General Medicine Departments. 220 prescription was evaluated out of which 140 prescription had pDDIs. The patient demographics and all medically relevant information were noted in a predefined data collection form. On the other hand, these case outlines were reviewed for potential drug interactions, drugs associated with interactions (route, indication frequency, dose, therapy duration), lab examinations, followed readily for evaluating drug connection and drug specialist's intercession. The progressions and the everyday notes in the case sheets were followed until the patient was released or moved to different wards. The Micromedex, Medscape, and references books were utilized as instruments to audit the prescription and case diagrams. drug interactions were sorted as minor, moderate, or significant which shows the potential dangers of the event of the potential drug interactions which can happen in patients, however not the real seriousness of drug interactions. The information acquired was utilized to classify interactions dependent on the instrument as pharmacokinetic or pharmacodynamics. The pharmacokinetic drug interactions were additionally sorted into interactions dependent on ingestion, conveyance, digestion, and end. The severities of the

interactions were evaluated and classified as major (can cause permanent harm or life hazard), moderate (can cause mischief and treatment are required) or minor (can cause little or no clinical impact, with no treatment required). The information was put away privately and exposed to additional examination utilizing appropriate programming.

Result and discussion

The present study identified the pattern of pDDIs among patients admitted to the cardiac unit of the general medicine ward. The data of 220 patients admitted to the inpatient ward during the period October 2019 and March 2020 were analyzed for assessment of potential drug interaction. Among them, 140 patients had at least one potential drug interaction. The mean age of the study population was 64.43 (± 14.58) years which is in agreement with the study conducted in Nepal²⁰. However, another study conducted in the cardiology ward of South Indian hospital reported lower mean age of 57.27 \pm 14.0 years. In the group of 140 cardiac patients, 67.85% were males that are in line with the fact that men are more prone to heart disease compared to women of similar age¹⁷. A study conducted in Bangladesh showed higher (72%) men's dominance in cardiac patients¹⁶. The majority of the study subjects were in a group of geriatric (75.71%), which is related to more incidence of

heart disease in the older population. In general, elderly patients are at higher risk for DDIs because they are likely to have multiple diseases and polypharmacy that usually occur with an increased duration of disease conditions and altered physiology. In many of the reported studies, age more than 60 was reported as an independent risk factor for DDIs.²¹

It was observed that 83 (59.28%) had diabetes mellitus type 2 as a major co-morbidity which is similar to a study conducted in Tamil Nadu⁵³. Comorbidity increases the total burden of the illness in a patient and also contributes to clinical outcomes as well as to economic outcomes. Hypertension (65%) was the most common diagnosis followed by CHF (28.67%) and MI (19.28%). A similar result was reported by other studies conducted on cardiac patients. [20] Most of the patients had a hospital stay of five to ten days. The median hospital stay was 7 days. A study conducted in Pakistan showed a median hospital stay of 6 days²² (**Table I**).

Among 140 study population, most of the patients had hypertension (65%) as a major diagnosis. Another main diagnosis was CHF (28.67%) and MI (19.28%). The pattern of primary cardiovascular disorder is shown in **table II**.

Out of 220 prescriptions analyzed, 140 prescriptions comprised of potential drug interactions and it was found

Table I: Study patient's demographic details.

Parameter	Gender				Total	
	Male		Female		n	%
	n	%	N	%		
Patient age (Years)						
20-30	2	1.42	1	0.71	3	2.14
31-40	5	3.57	1	0.71	6	4.28
41-50	14	10	6	4.28	20	14.28
51-60	11	7.85	4	2.85	15	10.71
61-70	28	20	15	10.71	43	30.71
71-80	27	19.28	13	9.28	40	28.57
81-90	8	5.71	5	3.57	13	9.28
Sub total	95	67.85	45	32.14	140	100
Special population						
Geriatric	70	50	36	25.71	106	75.71
Renal impairment	5	3.57	2	1.42	7	5
Hepatic impairment	3	2.14	0	0	3	2.14
Co-morbidities						
Diabetes Mellitus	50	35.71	33	23.57	83	59.28
CKD	2	1.42	2	1.42	4	2.857
Pulmonary Disorder	9	6.42	3	2.14	12	8.57
Seizure Disorder	3	2.14	2	1.42	5	3.57
Other	67	47.85	41	29.28	108	77.14

Table II: Primary cardiovascular diagnosis in study patients.

Main Diagnosis	Male		Female		Total	
	N	%	n	%	n	%
Hypertension	58	41.42	33	23.57	91	65
MI	22	15.71	5	3.57	27	19.28
CHF	26	18.57	14	10	40	28.57
Atrial fibrillation	2	1.42	1	0.71	3	2.14
ACS	4	2.85	4	2.85	8	5.71
CVA	6	4.28	2	1.42	8	5.71

that 234 drug interactions were present. The incidence of potential drug interaction was 63.64%. Among 234 drug interactions, 90 types of interaction combinations were identified. The studied prescription comprised 58.11% moderate interaction, 40.59% major drug interactions, and 1.28 minor drug interactions. Among them, 57.26% were pharmacodynamic drug interactions followed by 36.75% of pharmacokinetic interaction and 5.98% of unknown mechanism interactions. The summary of potential drug-drug interactions is listed in **table III**.

Table III: Summary of potential drug-drug interaction.

Parameters		Total	
		N	%
Severity	Major	95	40.59
	Moderate	136	58.11
	Minor	3	1.28
Pharmacodynamic Interaction		134	57.26
Pharmacokinetic Interaction		86	36.75
Unknown Mechanism		14	5.98
Management	Monitoring	173	73.93
	Dose adjustment	32	13.67

Among 234 drug interactions, 90 types of interaction combinations were identified. However, another study

of South Indian teaching hospital identified 388 pDDIs in 249 patients involving 51 different drugs with a total of 74 different drug combinations. Cardiac patients have previously been found to have a higher chance of having drug interactions compared to other groups of patients.²³

In most patients, the cases of one potential drug interaction were identified with a median of 1.67 potential drug-drug interactions. Among them, 30% of prescriptions had two potential drug-drug interactions. The frequency of pDDIs is shown in **table IV**.

Out of 234 drug interactions, aspirin/clopidogrel and clopidogrel/atorvastatin were the most common drug interaction pairs observed among prescribed medications. The clinical important and most common potential drug interaction pair is summarized in **table V**.

Most interactions were documented as good (44.44%) followed by fair (41.45%) and excellent (14.10%). The documentation of pDDIs is shown in **table VI**.

Most interactions were classified as not specified, accounting for 60.25%. Whereas 31.19% were of delayed-type. The onset of pDDI is listed in **table VII**.

Table IV: Frequency of drug interaction in the study population.

Frequency of pDDI	Male		Female		Total	
	N	%	n	%	n	%
1	52	37.14	23	16.42	75	53.57
2	25	17.85	17	12.14	42	30
3	14	10	5	3.57	19	13.57
4	2	1.42	0	0	2	1.42
5	2	1.42	0	0	2	1.42

N=140

Table V: Top 10 common pDDI.

pDDI pair	Effect	Male		Female		Total	
		N	%	N	%	n	%
Aspirin/Clopidogrel	bleeding	13	5.55	3	1.28	16	6.83
Clopidogrel/atorvastatin	Decreased efficacy	11	4.70	5	2.13	16	6.83
Atorvastatin/amiodarone	rhabdomyolysis	7	2.99	0	0	7	2.99
Aspirin/Acenocoumarol	bleeding	3	1.28	3	1.28	6	2.56
Atorvastatin/Azithromycin	rhabdomyolysis	5	2.13	1	0.42	6	2.56
Atorvastatin/Clarithromycin	rhabdomyolysis	3	1.28	3	1.28	6	2.56
Acenocoumarol/Clopidogrel	bleeding	3	1.28	2	0.85	5	2.13
Carvedilol/aspirin	Decreased efficacy	3	1.28	2	0.85	5	2.13
Insulin/aspirin	hypoglycaemia	3	1.28	2	0.85	5	2.13
Ramipril/Spirolactone	hyperkalaemia	3	1.28	2	0.85	5	2.13

Table VI: Documentation of Pddi.

Documentation of pDDI	Male		Female		Total	
	N	%	n	%	n	%
Excellent	22	9.401	11	4.700	33	14.10
Good	64	27.35	40	17.09	104	44.44
Fair	64	27.35	33	14.10	97	41.45

Table VII: Onset of pDDI.

Onset of pDDI	Male		Female		Total	
	N	%	n	%	n	%
Rapid	12	5.12	8	3.41	20	8.54
Delayed	47	20.08	26	11.11	73	31.19
Not Specified	91	38.88	50	21.36	141	60.25

Of the pDDIs identified, 60.25% were not specified and 31.19% were of delayed onset in nature. This implies that even if there was an interaction occurring during the concomitant administration, it may not manifest itself immediately. On the off chance that these combinations of drugs were to be forged ahead an outpatient premise, this might actually prompt decreased efficacy prompting therapeutic failures or potential for delayed adverse events. Subsequently the duration of concomitant medication use ought to likewise be considered while prescribing pertinent associating drugs. Most of the interactions were documented as good (44.44%). This suggested that most of the interaction ratings were reliable.

Among 234 drug interactions aspirin (19.65%) and atorvastatin (17.09%) were the most common object drug involved in potential drug interactions. Common object drug involved in drug interaction is given in **table VIII**.

Among 234 drug interactions, aspirin (10.68%) and clopidogrel (9.48%) were the most common precipitant drug involved in drug interaction, which is shown in **table IX**.

Many of the commonly used cardiovascular drugs interact with one another. These drugs can be utilized together to treat heart conditions following a danger advantage appraisal. Numerous clinicians probably balance the dangers of pDDIs against the advantages while prescribing patients with multidrug regimens. A model would be joined anticoagulant antiplatelet treatment where an expansion in the danger of drain with the consolidated treatment should be considered against the dangers of thromboembolism without it. Benefits with multidrug regimens are unlikely to always outweigh their risks; therefore, decisions regarding prescriptions must

always be tailored to suit each patient.

This study showed the median number of 1.67 pDDIs in cardiac patients. A study held earlier at ATH reported a similar median number of pDDIs in cardiac patients²³. On analyzing the mechanism of drug interaction identified here, pharmacodynamic type interaction (57.26%) was found in a higher number compared to pharmacokinetic type (36.75%) (). The findings obtained here are in contrast to those reported by Vonbach *et al.*²⁴ and Aparasu *et al.*²⁵ who reported 76% of pharmacokinetic and 22% of pharmacodynamic interactions respectively.

The significance of pDDIs was classified according to three levels of scale. Of 234 drug interactions, the majority were moderate and major drug interactions. Moderate interaction comprised 54.11% followed by major 40.59%. The severity of pDDIs is shown in **table X**.

Of the total pDDIs identified, the interacting combination of moderate severity (58.11%) constituted the majority of pDDI. The major severity interacting combination identified was 40.59%. This finding is similar to most of the DDI studies conducted worldwide.

Among major drug interactions, aspirin/clopidogrel¹⁶ was the most common pDDI. The important and common major drug interaction is summarized in **table XI**.

Among moderate drug interactions, clopidogrel/atorvastatin¹⁶ was most commonly observed. The common moderated drug interaction is listed in **table XII**.

The most common interacting pair identified were aspirin/clopidogrel, clopidogrel/atorvastatin, atorvastatin/amiodarone, and atorvastatin/azithromycin. The pDDIs

Table VIII: Common object drug involved in drug interaction.

Object Drug	Male		Female		Total	
	N	%	n	%	n	%
Aspirin	28	11.96	18	7.69	46	19.65
Atorvastatin	28	11.96	12	5.12	40	17.09
Clopidogrel	18	7.69	9	3.84	27	11.53
Insulin	11	4.700	6	2.56	17	7.26
Metformin	12	5.12	5	2.13	17	7.26

Table IX: Common precipitant drug involved in drug interactions.

Precipitant Drug	Male		Female		Total	
	N	%	n	%	n	%
Aspirin	15	6.41	10	4.27	25	10.68
Clopidogrel	16	6.83	6	2.56	22	9.40
Atorvastatin	11	4.70	5	2.13	16	6.83
Amlodipine	7	2.99	5	2.13	12	5.12
Nebivolol	6	2.56	4	1.709	10	4.27

Table X: Severity of pDDIs.

Severity of pDDI	Male		Female		Total	
	N	%	n	%	n	%
Major	59	25.21	36	15.38	95	40.59
Moderate	88	37.60	48	20.51	136	54.11
Minor	3	1.28	0	0	3	1.28

Involving aspirin (19.65%) and atorvastatin (17.09%) were most common. The values obtained here are similar to a study in India where Patel et al reported aspirin (44.85%) followed by atorvastatin (7.22%). Similarly, Smithburger *et al.* (2010)²⁶ reported the involvement of blood coagulation modifier in a maximum number of pDDIs. This might be due to the frequent use of this drug class among the cardiac patients in the present study. Decreased efficacy was the commonest clinical consequence in 56(23.93%) cases followed by bleeding (21.36%). A study conducted in the cardiology department of Kasturba Medical College reported bleeding (86.63%) as the commonest clinical consequence. The most common management plan found in the present study for most of the drug interaction was monitoring and dose adjustment; this is similar to the

results reported by Bergk and colleagues²⁷.

The classification of potential drug-drug interactions was made based on their mechanism like pharmacodynamic, pharmacokinetic or unknown. Among 234 drug interactions, 57.26% were pharmacodynamic, 36.75% were pharmacokinetic and 5.98% were unknown. Among pharmacokinetics, 23.98% were metabolism interaction. The mechanism of pDDIs is shown in **table XIII**.

Decreased efficacy was the commonest clinical consequence in 56(23.93%) cases. Bleeding (21.36%) and hypo or hyperglycemia (19.23%) were other common clinical effects of interaction. The clinical effect of pDDIs are summarized in **table XIV**.

Table XI: Top 10 Major pDDI.

Object Drug	Precipitant Drug	Effect	Documentation	Frequency	Management
Acenocoumarol	Clopidogrel	bleeding	fair	5	Monitor INR
Aspirin	Acenocoumarol	Bleeding	Fair	6	Monitor INR
Aspirin	Clopidogrel	Bleeding	Fair	16	Monitor INR
Aspirin	Heparin	Bleeding	Fair	4	Monitor INR
Atorvastatin	Clarithromycin	Rhabdomyolysis	Good	6	Dose adjustment
Atorvastatin	Diltiazem	Rhabdomyolysis	good	4	Dose adjustment
Atorvastatin	Fluconazole	Rhabdomyolysis	fair	3	Monitor for toxicity
Domperidone	Amlodipine	QT prolong	Fair	4	Monitor ECG
	Cilnidipine	QT prolong	fair	4	Monitor ECG
Ramipril	Spironolactone	Hyperkalaemia	good	5	Monitor Serum K

Table XII: Top 10 moderate pDDI.

Object Drug	Precipitant Drug	Effect	Documentation	Frequency	Management
Aspirin	Furosemide	Decreased efficacy	good	4	Monitor BP
Aspirin	Spironolactone	toxicity	excellent	4	Monitor for toxicity
Atorvastatin	amiodarone	Rhabdomyolysis	good	7	Monitor for toxicity
Atorvastatin	azithromycin	Rhabdomyolysis	good	6	Monitor for toxicity
Atorvastatin	phenytoin	Decreased efficacy	good	4	Dose adjustment
Atorvastatin	Domperidone	QT prolong	fair	4	Monitor ECG
Carvedilol	Aspirin	Decreased efficacy	good	5	Monitor BP
Clopidogrel	atorvastatin	Decreased efficacy	excellent	16	Alternative therapy
Insulin	Aspirin	Hypoglycemia	fair	5	Monitor blood glucose
Ramipril	Aspirin	Decreased efficacy	fair	4	Monitor BP

Table XIII: Mechanism of potential drug interaction.

Mechanism		Male		Female		Total	
		N	%	N	%	n	%
Pharmacokinetic	Absorption	2	0.85	0	0	2	0.854
	Distribution	16	6.83	7	2.99	23	9.82
	Metabolism	39	16.66	17	7.26	56	23.93
	Excretion	1	0.42	4	1.70	5	2.13
Subtotal		58	24.78	28	11.96	86	36.75
Pharmacodynamic	Synergism	67	28.63	35	14.95	102	43.58
	Antagonism	18	7.69	14	5.98	32	13.67
Subtotal		85	36.32	49	20.94	134	57.26
Unknown		7	2.99	7	2.99	14	5.98

Table XIV: Clinical effect of pDDI.

Clinical effect	Male		Female		Total	
	N	%	n	%	n	%
Bleeding	33	14.10	17	7.26	50	21.36
Decreased efficacy	31	13.24	25	10.68	56	23.93
Hypotension	4	1.70	5	2.13	9	3.84
Rhabdomyolysis	20	8.54	7	2.99	27	11.53
Increased Toxicity	21	8.97	13	5.55	34	14.52
Hypo or hyperglycaemia	32	13.67	13	5.55	45	19.23
QT prolongation	9	3.84	4	1.709	13	5.55

The drug interaction software by Micromedex-2 showed that monitoring for the adverse drug effects 173 (73.93%) was the most popular intervention followed by dose adjustment 32 (13.67%) and use of alternative 24 (10.25%) following potential drug-drug interactions. The detailed management of potential drug interaction is listed in **table XV**.

Conclusion

This study attempted to assess the potential drug-drug interaction in the prescription of cardiac patients in an inpatient hospital setting. This study also examined patient, drug characteristics, causality, and severity of pDDIs. This study shows that DDIs are frequent among hospitalized cardiac patients. About 234 drug interactions were reported during the study period with a median number of 1.67 pDDIs in the cardiac patients. This study emphasizes the need to consider pDDIs during therapeutic planning, protect patients from the consequence of drug interactions. In addition, providing DDI-related information to the prescribers and drug interaction alert software to the dispensing pharmacist can play a vital role in minimizing the incidence rate of DDI.

The majority of interactions were pharmacodynamic, having moderate severity. Anti-platelets and anti-coagulants were commonly implicated in many PDDIs in this study and therefore require intensive monitoring during therapy. The most common management plan found in the present study for most of the drug interaction was monitoring and dose adjustment. The study reported that about 26% of interventions proposed were accepted by physicians. The current study demonstrated the importance of routine medication review and the need for a pharmacist in a multidisciplinary team.

The incidence rate of adverse drug interactions was found to be 20%. The results provided an insight to the healthcare providers on the importance of monitoring and reporting adverse drug interactions. The active involvement of a well-trained clinical pharmacist for detecting the adverse drug interactions and delivering the awareness classes for the healthcare professionals regarding the need of reporting the incident could improve the scenario in under-reported hospitals.

Interests conflict

The authors declare no conflict of interest.

Table XV: Management of pDDI.

Management of pDDI	Male		Female		Total	
	N	%	n	%	n	%
Avoid concurrent use	0	0	1	0.42	1	0.42
Use of alternative drug	15	6.41	9	3.84	24	10.25
Discontinuation of drug	3	1.28	1	0.42	4	1.70
Dose adjustment	17	7.26	15	6.41	32	13.67
Continue with monitoring	115	49.14	58	24.78	173	73.93

References

- Forouzanfar MH, Liu P, Roth GA, Ng M, Biryukov S, Marczak L, Alexander L, Estep K, Abate KH, Akinyemiju TF, Ali R. Global burden of hypertension and systolic blood pressure of at least 110 to 115 mm Hg, 1990-2015. *Jama*. 2017 Jan 10;317(2):165-82.
- Isetts BJ, Schondelmeyer SW, Artz MB, Lenarz LA, Heaton AH, Wadd WB, Brown LM, Cipolle RJ. Clinical and economic outcomes of medication therapy management services: the Minnesota experience. *Journal of the American Pharmacists Association*. 2008 Mar 1;48(2):203-14.
- Murtaza G, Khan MY, Azhar S, Khan SA, Khan TM. Assessment of potential drug-drug interactions and its associated factors in the hospitalized cardiac patients. *Saudi Pharmaceutical Journal*. 2016 Mar 1;24(2):220-5.
- Kovačević M, Vezmar Kovačević S, Radovanović S, Stevanović P, Miljković B. Adverse drug reactions caused by drug-drug interactions in cardiovascular disease patients: introduction of a simple prediction tool using electronic screening database items. *Current medical research and opinion*. 2019 Nov 2;35(11):1873-83.
- Shakeel F, Khan JA, Aamir M, Hannan PA, Zehra S, Ullah I. Risk of potential drug-drug interactions in the cardiac intensive care units: a comparative analysis between 2 tertiary care hospitals. *Saudi medical journal*. 2018;39(12):1207.
- Diksis N, Melaku T, Assefa D, Tesfaye A. Potential drug-drug interactions and associated factors among hospitalized cardiac patients at Jimma University Medical Center, Southwest Ethiopia. *SAGE open medicine*. 2019 Jun;7:2050312119857353.
- Abraham RR. Drug related problems and reactive pharmacist interventions for inpatients receiving cardiovascular drugs. *International Journal of Basic Medical Sciences and Pharmacy (IJBMS)*. 2014 Jan 26;3(2).
- Andreazza RS, De Castro MS, Köche PS, Heineck I. Causes of drug-related problems in the emergency room of a hospital in southern Brazil. *Gaceta Sanitaria*. 2011 Nov 1;25(6):501-6.
- Zaredar N, Koneri R, Swamy T. Assessment of Drug Interactions in Hospitalized Cardiac Patients at a Tertiary Care Hospital, Baptist Hospital, Bangalore. *World J Pharm Med Res*. 2017;3(1):210-5.

10. Nascimento YD, Carvalho WD, Acurcio FD. Drug-related problems observed in a pharmaceutical care service, Belo Horizonte, Brazil. *Brazilian Journal of Pharmaceutical Sciences*. 2009;45:321-30.
11. Rashid K, Khan Y, Ansar F, Waheed A, Aizaz M. Potential Drug-Drug Interactions in Hospitalized Medical Patients: Data From Low Resource Settings. *Cureus*. 2021 Aug;13(8).
12. Garin N, Sole N, Lucas B, Matas L, Moras D, Rodrigo-Troyano A, Gras-Martin L, Fonts N. Drug related problems in clinical practice: a cross-sectional study on their prevalence, risk factors and associated pharmaceutical interventions. *Scientific reports*. 2021 Jan 13;11(1):1-1.
13. Origi FC, Jacobson ER. Diseases of the respiratory tract of chelonians. *Veterinary Clinics of North America: Exotic Animal Practice*. 2000 May 1;3(2):537-49.
14. Gattis WA, Hasselblad V, Whellan DJ, O'Connor CM. Reduction in heart failure events by the addition of a clinical pharmacist to the heart failure management team: results of the Pharmacist in Heart Failure Assessment Recommendation and Monitoring (PHARM) Study. *Archives of internal medicine*. 1999 Sep 13;159(16):1939-45.
15. Hartshorn EA. Drug Interaction 1. General Considerations. *Drug Intelligence*. 1968 Jan;2(1):4-7.
16. Murtaza G, Khan MY, Azhar S, Khan SA, Khan TM. Assessment of potential drug–drug interactions and its associated factors in the hospitalized cardiac patients. *Saudi Pharmaceutical Journal*. 2016 Mar 1;24(2):220-5.
17. Nolan Jr PE, Marcus F. Cardiovascular drug use in the elderly. *The American journal of geriatric cardiology*. 2000 May;9(3):127-9.
18. Parthasarathi G, Ramesh M, Kumar JK, Madaki S. Assessment of drug-related problems and clinical pharmacists' interventions in an Indian teaching hospital. *Journal of Pharmacy practice and Research*. 2003 Dec;33(4):272-4.
19. Patel VK, Acharya LD, Rajakannan T, Surulivelrajan M, Guddattu V, Padmakumar R. Potential drug interactions in patients admitted to cardiology wards of a south Indian teaching hospital. *The Australasian medical journal*. 2011;4(1):9.
20. Sharma S, Chhetri HP, Alam K. A study of potential drug-drug interactions among hospitalized cardiac patients in a teaching hospital in Western Nepal. *Indian journal of pharmacology*. 2014 Mar;46(2):152.
21. Nag KA, Umesh M, Churi SH. Assessment of drug-drug interactions in hospitalised patients in India. *Asian J Pharm Clin Res*. 2011;4(1):62a.
22. Murtaza G, Khan MY, Azhar S, Khan SA, Khan TM. Assessment of potential drug–drug interactions and its associated factors in the hospitalized cardiac patients. *Saudi Pharmaceutical Journal*. 2016 Mar 1;24(2):220-5.
23. Ismail M, Iqbal Z, Khattak MB, Khan MI, Javaid A, Khan TM. Potential drug-drug interactions in cardiology ward of a teaching hospital. *Health Med*. 2012 Jan 1;6:1618-24.
24. Vonbach P, Dubied A, Krähenbühl S, Beer JH. Prevalence of drug–drug interactions at hospital entry and during hospital stay of patients in internal medicine. *European journal of internal medicine*. 2008 Oct 1;19(6):413-20.
25. Aparasu R, Baer R, Aparasu A. Clinically important potential drug-drug interactions in outpatient settings. *Research in Social and Administrative Pharmacy*. 2007 Dec 1;3(4):426-37.
26. Smithburger, P. L., Kane-Gill, S. L., & Seybert, A. L. (2010). Drug-drug interactions in cardiac and cardiothoracic intensive care units. *Drug safety*, 33(10), 879-88.
27. Bergk V, Gasse C, Rothenbacher D, Loew M, Brenner H, Haefeli WE. Drug interactions in primary care: impact of a new algorithm on risk determination. *Clinical Pharmacology & Therapeutics*. 2004 Jul;76(1):85-96.