ASSESSMENT OF POTENTIAL DRUG INTERACTIONS AMONG HOSPITALIZED PATIENTS AT THE CARDIAC AND PULMONARY DEPARTMENTS IN TERTIARY CARE HOSPITALS

KAMESWARAN RAMALINGAM[1]*, SHANMUGA SUNDARAM RAJAGOPAL[2], KRISHNAVENI KANDASAMY[1], KARTHIKEYAN KRISHNAN[1]

[1]Department of Pharmacy Practice, Faculty of Pharmacy, Pacific Academy of Higher Education and Research University, Udaipur, Rajasthan, India. [2]Department of Pharmacology, J.K.K. Nattraja College of Pharmacy, Kumarapalayam, Tamil Nadu, India.
Email: kamesjohashwanth@gmail.com

ABSTRACT

Objective: The aim of this study was to assess the potential drug interactions among hospitalized patients in cardiac and pulmonary wards in three tertiary care hospitals.

Methods: A prospective, observational study was carried out for 12 months. A sample of 1150 patients were assessed for potential drug-drug interactions (pDDIs) using Micromedex®- 2.7 and Drugs.com.

Results: A total of 1150 patients were analyzed, and it was found that 685 were cardiac and 465 were pulmonary patients. The study identified 524 (76.49%) cardiac patients and 345 (74.19%) pulmonary patients, with pDDIs higher in male cardiac (298 [56.87%]) and male pulmonary (199 [57.68%]) patients, compared to females. Incidences of pDDIs were found to be higher in the age group of 60–70 years in cardiac (193 [36.83%]) and pulmonary (146 [42.31%]) patients and incidences of interactions based on duration of 4–6 days' hospital stays in cardiac were 380 (72.53%) and 215 (62.31%) in pulmonary patients, respectively. Moreover, 51.90% of cardiac patients and 56.52% of pulmonary patients were found to be prescribed with more number of drugs (cardiac 7 drugs and pulmonary 5–6 drugs) causing higher incidences of pDDIs. Some of the most common drug interacting pair was aspirin and clopidogrel combination observed in 245 cardiac patients, whereas in the pulmonary department, it was ranitidine-theophylline combination with a frequency of 195 pDDIs. Drug-food interactions were found with atorvastatin–citrus fruits in cardiac and theophylline–caffeine in pulmonary patients. The most common drug-disease interaction was found to be isosorbide dinitrate–myocardial infarction in cardiac and diazepam–COPD in pulmonary, respectively.

Conclusion: Pharmacists must take responsibility in the monitoring of drug interactions and notifying the physician and patient about potential problems. With their detailed knowledge of drugs, pharmacists have the ability to relate unexpected symptoms experienced by patients to possible adverse effects of their drug therapy.

Keywords: Cardiac, Drug-drug interactions, Pulmonary, Aspirin, Clopidogrel, ISDN–MI.

INTRODUCTION

A drug interaction occurs when a patient's response to a drug is modified by food, nutritional supplements, formulation excipients, environmental factors, other drugs, or disease. Drug interactions are a major area of concern these days. The study of drug-drug, food-drug, and disease-drug interactions and of genetic factors affecting pharmacokinetics and pharmacodynamics is expected to improve drug safety and will enable individualized drug therapy. Drug-drug interactions are said to account for a number of severe adverse drug reaction, resulting in hospitalizations and emergency department visits. It is estimated that, in 2011, DDI contributed to about 56.4% of all ADR [1]. Furthermore, ADR due to DDI accounts for about 2.8% hospital admission every year [2]. Many adverse events can be prevented by identifying potential drug interactions (pDIs). However, certain conditions such as multiple disorders, chronic diseases, and polypharmacy may increase the risk of potential drug-drug interaction. In the elderly, concomitant use of several drugs (polypharmacy) is very common and carries a high risk of both drug-drug interaction and drug-disease. A study in 2010 reported that 558 (26.5%) of elder people taking medicines were exposed to at least one DDI [3]. It was reported in 2011 that 164 (75.9%) patients taking 7 or more drugs were having at least one potential drug-drug interactions (pDDIs) while 76 (73.8%) patients with a hospital stay of seven or more were at risk of DDIs [4]. Patients with cardiovascular disorders are even at higher risk of DDI due to the number and types of drug they receive and the influence of heart disease on drug metabolism. A prospective study conducted in one of the teaching hospitals in India in 2011 indicated that the incidence of pDI among cardiac drugs in hospitalized patients is 30.67% [5]. A cross-sectional study conducted in the Pulmonology Department, Ayub Teaching Hospital, Pakistan, in 2011 showed that among 558 pDDIs, most were of moderate (53.6%) or major (34%), good (74.2%) or fair (16.3%), and delayed onset (70%) [4].

Diet and lifestyle can sometimes have a significant impact on drugs. These may occur of accidental misuse or due to lack of knowledge about the active ingredients involved in the relevant substances. Interactions between food and drugs may inadvertently reduce or increase the drug effect. Major side effects of some diet (food) on drugs include alteration in absorption of fatty, high protein, and fiber diets. Sixteen cohort and case–control studies reported an elevated risk of hospitalization in patients who were exposed to pDDIs [6]. Studying the drug-drug interactions, food-drug interactions, and disease-drug interactions is essential for the management of drug therapy. The exhaustive literature review revealed that studies have been conducted on the pDDIs in the departments. Hence, we carry out a study to assess the prevalence of drug-drug interactions, food-drug interactions, and disease-drug interactions.

METHODS

The research was conducted in three tertiary care hospitals, in Erode, for 12 months at the hospitalized cardiac and pulmonary patients. 1150 patients were taken in for the study, of which 685 were cardiac, and 465 were pulmonary patients. Exclusion criteria included out patients, patients <18 years of age, medical disability, and patients who are on Ayurveda, Siddha, or other alternative system of medicine. Consent was obtained from hospital authority and hospitalized patients. The data were collected from case sheets of hospitalized patients and direct patient interview from cardiac and pulmonary departments. Demographic information (age and sex), length of hospital stay, main diagnosis, number of drugs, and details of comorbidities were obtained from the clinical records. All medications that were prescribed, including routine and *pro re nata* (means as required) medications, were screened for pDDIs. pDDIs were detected using the Drug Interactions Checker within Micromedex®-2.7 and www.drugs.com. The detected DDIs were classified as major, moderate, and minor, relying on their severity of clinical significance and cross-over checked manually for the presence of enough published medical evidence for the recognized interacting marketers. Primarily, based on the profile of medicines prescribed, the DDIs had been recognized and classified in step with the Micromedex®- 2.7 and www.drugs.com. In line with the types, pDDIs have been categorized as: Pharmacokinetics - absorption, distribution, metabolism, and excretion and pharmacodynamics - antagonism, synergism, and additive. In line with severity, pDDIs were labeled as: Major - the consequences are probably life threatening or capable of inflicting permanent harm; moderate - the outcomes may also cause deterioration in patients' scientific fame and additional treatment or extension of hospital stay; and minor- the consequences are typically moderate. The effects can be bothersome or unnoticeable, but need to now, not considerably affect the healing outcome. Frequencies expressed as possibilities were used to summarize sex, diagnosis, number of medication disbursed frequency of pDDIs, the drugs concerned with the pDDIs, period of hospital stay and types, and severity of pDDIs.

RESULTS

A total of 1150 patients were admitted at the department of cardiac and pulmonary during the study period. Among these, 685 were cardiac and 465 were pulmonary patients. Of 685 cardiac patients, 524 (76.49%) had found to be pDDIs, 856 pDDIs were found at 524 cardiac patients, and 675 pDDIs were found at 465 pulmonary patients. It was found that patients were confirmed with minimum one or two pDDIs in both cardiac and pulmonary patients. Of which, 298 (56.87%) cardiac males and 199 (57.68%) pulmonary males were found to be higher pDDIs, compared to females. Incidences of pDDIs were found to be higher in the age group of 60–70 years in cardiac (193 [36.83%]) and pulmonary (146 [42.31%]) patients and incidences of interactions based on duration of (4–6 days) hospital stay were 380 (72.53%) and 215 (62.31%) in cardiac and pulmonary patients, respectively. 51.90% of patients prescribed with more than seven drugs in cardiac and 56.52% of patients prescribed with between five and six drugs in pulmonary patients were found to have developed a higher number of pDDIs (Table 1).

On average, each patient had one or two coded diagnosis in which hypertension was the most common condition 165 (31.48%), followed by angina with diabetes mellitus 111 (21.18%) in cardiac patients and asthma 92 (26.66%), followed by the asthma with LRTI 75 (21.73%) in pulmonary patients (Tables 2-11).

DISCUSSION

DIs are a major area of concern these days for the effective management of patient illness. It may create a considerable health hazard to the patients when the risk-benefit ratio of combining interacting drugs is not accurately estimated. It has already been approximated that the effect of drug interactions can range from any minor morbidity to fatal consequences. The study of drug-drug, drug-food, and drug-disease interactions and genetic factors affecting pharmacokinetics and pharmacodynamics is expected to improve drug safety and will enable individualized drug therapy.

The present study identified a total of 1150 patients admitted at the department of cardiac and pulmonary, during the study period. Among these, 685 were cardiac and 465 were pulmonary patients. Of 685 cardiac patients, 524 (76.49%) had found to be pDDIs, 856 pDDIs were found in 524 cardiac patients (Fig. 1). 675 pDDIs were found in 465 pulmonary patients. Out of which 298 (56.87%) cardiac male, and 199(57.68%) pulmonary male were found to be higher pDDIs, compared to females (Table 1), similar to the study conducted by Mukesh *et al*, where male patients (67%) had a high frequency of cardiovascular incidence as compared to female patients (33%) [7]. Another study conducted by Murtaza *et al*. also reported that male patients had a higher cardiology (50.94%), pulmonary (56.41%), and pDDIs possible when compared to females in the present study may be the primary reason [8]. Another reason possibly will be the greater risk of cardiovascular and pulmonary disorders among male gender in comparison to female, and hence, there is a need for multiple drugs which ultimately result in drug interactions.

The study showed that the majority of the incidences of pDDIs were found to be higher in the age group of 60–70 years in 193 (36.85%) cardiac and 146 (42.33%) pulmonary patients (Table 1). A study conducted by Chelkeba *et al*. reported an age group of 59–69 years [9], whereas a study conducted by Fita *et al*. reported that the majority of patients ages were between 70 and 74 years [10]. Older people were at high risk of developing an ADR due to pDDIs for several reasons. They are likely to have higher commodities and thus take several prescriptions and over the counter drugs. As people get older, the liver loses the ability to metabolize drugs. Furthermore, older people are more than twice as susceptible to ADRs as younger people. As people age, the amount of water in the body decreases and the amount of fat tissue relative to water increases. Furthermore, as people age, the kidneys are less able to excrete drugs into the urine, and the liver is less able to metabolize many drugs.

The study revealed 72.53% of cardiac and 62.31% of pulmonary cases, that the number of hospital stay was between 4-6 days (Table 1). Lubinga *et al*, conducted a study which showed that the majority of the cases the number of hospital stay were less than 6 days [11]. The likelihood of getting the multiple drugs increases with the increased length of hospital stay which in turn will increase the likelihood of pDDIs.

In our study, 51.90% of patients were prescribed with more than seven drugs in the cardiology department (Table 1). The study conducted by de Andrade *et al*. revealed that 40.6% of cases were prescribed between 13 and 16 drugs [12]. 56.52% of patients prescribed with between 5 and 6 drugs in the pulmonology department. A study conducted by Ismail *et al*. showed that 54% of cases had more than seven drugs prescribed [4]. Mannesse *et al*. reported the concurrent use of three or more drugs increased the risk of ADE's by 9.8 times [13]. More the medications that are prescribed, the more the possibility of irrational polypharmacy. A study conducted by Doan *et al*. determined the probability of potent cytochrome P450 (CYP 450) interactions in older hospitalized people taking more than five concurrent medicines [14]. Potential drug-drug interactions were present in 80% of people taking more than five concurrent medicines. People taking five concurrent medicines had a 50% probability of at least one drug interaction, each additional medicine adds a 12% increase in the risk of drug interactions.

The most common interacting pair at the cardiac department was found to be aspirin and clopidogrel, causing major pharmacodynamic interaction, with a frequency of 245 (Table 3). The finding of the study is similar to the study conducted by Murtaza *et al*., in which the most common interacting pair was identified as aspirin–clopidogrel followed by clopidogrel–fondaparinux [8]. Another study conducted by Yanti *et al*.

Table 1: Demographic profile of cardiac and pulmonary patients

Parameter	Cardiac total number of patients n=524 (%)	Pulmonary total number of patients n=345 (%)
Gender-wise distribution		
Male	298 (56.87)	199 (57.68)
Female	226 (43.13)	146 (42.32)
Age-wise distribution		
18–30	21 (4.00)	33 (9.56)
31–45	69 (13.17)	35 (10.14)
46–59	164 (31.29)	86 (24.93)
60–70	193 (36.85)	146 (42.33)
Above 70	77 (14.69)	45 (13.04)
Number of hospital stay (in days)		
<3	83 (15.83)	85 (24.63)
4–6	380 (72.53)	215 (62.31)
>7	61 (11.64)	45 (13.06)
Number of prescribed drugs per day		
<4	94 (17.93%)	54 (15.65)
5–6	158 (30.15)	195 (56.52)
>7	272 (51.90)	96 (27.82)

Table 2: Types of diseases in each department

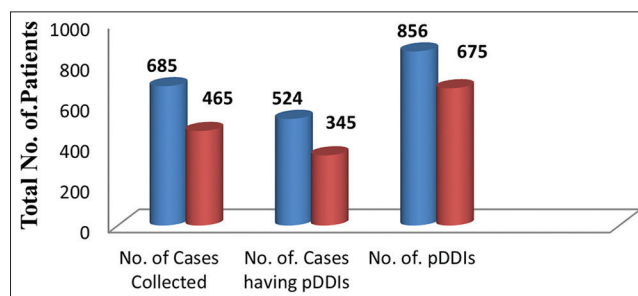| Cardiology (n=524)		Pulmonary (n=345)	
Type of diseases	Number of patients	Type of diseases	Number of patients
Myocardial infarction	87 (16.60)	Asthma	92 (26.66)
Angina+diabetes mellitus	111 (21.18)	Asthma+LRTI	75 (21.73)
Hypertension	165 (31.48)	Pneumonia	48 (13.91)
Ischemic heart disease	46 (08.77)	Pneumonia+bronchitis	34 (09.85)
Coronary artery disease	34 (06.48)	Bronchitis	47 (13.62)
Chronic heart failure	81 (15.45)	COPD	49 (14.20)

LRTI: Lower respiratory tract infection, COPD: Chronic obstructive pulmonary disease

Table 3: Highest potential drug-drug interaction combinations in cardiology
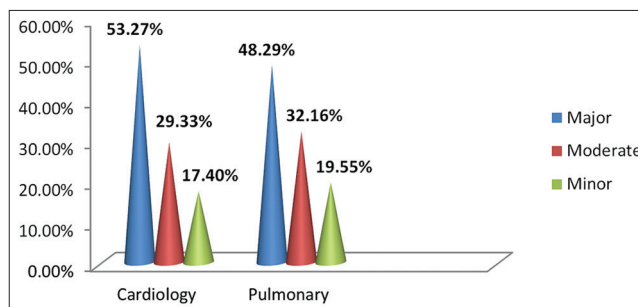
pDDI combination	Type	Severity	Frequency n=856 (%)
T. aspirin+ T. clopidogrel	PD	Major	245 (28.62)
T. aspirin+ T. enalapril	PD	Moderate	69 (8.06)
T. atorvastatin+ T. clopidogrel	PK	Moderate	78 (9.11)
T. aspirin+ T. atenolol	PD	Moderate	25 (2.92)
T. clopidogrel+ T. amlodipine	PK	Moderate	80 (9.34)
T. atenolol+ T. metformin	PK	Major	25 (2.92)
T. spironolactone+ T. enalapril	PD	Moderate	18 (2.10)
T. enalapril+ T. metformin	Unknown	Major	15 (1.75)
T. enalapril+ T. furosemide	PD	Moderate	12 (1.40)
T. aspirin+ T. spironolactone	PD	Major	41 (4.78)

PD: Pharmacodynamics, PK: Pharmacokinetics, pDDIs: Potential drug-drug interactions

Fig 1: Distribution of drug interactions in various departments

Fig 2: Prevalence of potential drug-drug interactions

observed a combination of diltiazem–amlodipine and spironolactone–potassium chloride [5]. Diltiazem may increase the serum amlodipine level by affecting CYP3A4, while the combination of spironolactone and potassium chloride will potentially increase potassium levels. The most common interacting pair at a pulmonology department in the present study was ranitidine–theophylline, which is a minor pharmacokinetic interaction, with a frequency of 195 (Table 4). Another study conducted

by Ismail *et al.* showed dexamethasone–rifampicin as the most common interacting pair [4]. Rifampin can reduce the pharmacological effects of corticosteroids (dexamethasone and prednisolone). It is suggested to monitor corticosteroid effects and increase the dose if necessary. A dose reduction may be necessary if rifampin is discontinued.

Table 4: Interactive effect, M.O.A, clinical management of common potential drug-drug interactions in cardiology

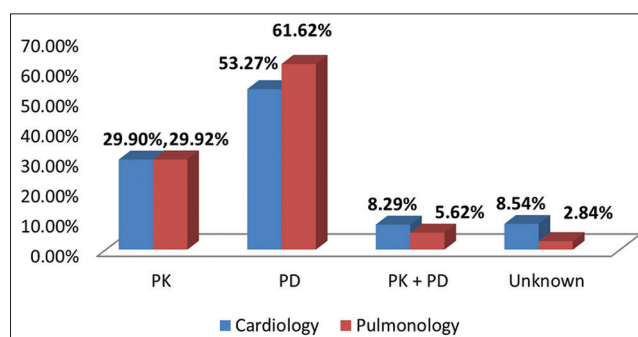| pDDI combination	Mechanism of action	Interactive effect	Clinical management
T. aspirin+T. clopidogrel	Increased risk of bleeding	Additive effect	Monitor for blood counts if coadministration is needed
T. aspirin+T. enalapril	Decreased effectiveness of enalapril	Antagonistic effect	Weigh benefit and risk
T. atorvastatin+T. clopidogrel	Decreased formation of the clopidogrel active metabolite resulting in higher on-treatment platelet reactivity	Metabolism	Discontinue the statin and substitute a statin that is not metabolized by CYP3A4 (i.e, pravastatin or rosuvastatin)
T. aspirin+T. atenolol	Decreased antihypertensive effect	Antagonistic effect	Monitor for the patient's blood counts and dose adjustment for beta blockers if necessary
T. clopidogrel+T. amlodipine	Decreased antiplatelet effect and increased risk of thrombotic events	Inhibit CYP3A (metabolism)	The addition of cilostazol may reduce the potential harmful interactions
T. atenolol+T. metformin	Result in hypoglycemia or hyperglycemia	Altered glucose metabolism	Monitor for patient's glucose level
T. spironolactone+T. enalapril	Result in hyperkalemia	Additive effect	Monitor for serum potassium level
T. enalapril+T. metformin	Increased risk of hypoglycemia	Unknown mechanism	Avoid concurrent use
T. enalapril+T. furosemide	Result in postural hypotension	Synergistic effect	Discontinue the diuretic 2 or 3 days before ACEI
T. aspirin+T. spironolactone	Result in hyperkalemia, or possible nephrotoxicity	Additive effect	Avoid aspirin doses of>650 mg daily in adults receiving spironolactone

pDDIs: Potential drug-drug interactions

Table 5: Highest potential drug-drug interaction combinations in pulmonary

pDDI combination	Type	Severity	Frequency n=675 (%)
Injection ranitidine+Injection theophylline	PK	Minor	195 (28.88)
Injection furosemide+Injection hydrocortisone	PD	Moderate	68 (10.07)
Injection ciprofloxacin+Injection theophylline	PK	Major	82 (12.14)
C. omeprazole+ T. clopidogrel	PK	Major	55 (8.14)
Injection furosemide+Injection theophylline	Unknown	Minor	86 (12.74)

pDDIs: Potential drug-drug interactions

Fig 3: Classification of types of potential drug-drug interactions

The prevalence of pDDIs in the cardiac department in our study was 53.27% (Table 7 and Fig. 2). A similar study performed by Ismail *et al.* showed an overall 77.5% PDDI prevalence rate among randomly selected cardiac patients [4]. A study conducted by Murtaza *et al.* in the department of cardiology showed that the prevalence rate of PDDIs was 91.6% among the studied cardiac patients [8]. The prevalence of pDDIs in the pulmonary department in our study was 48.29% (Table 7). A similar study that was conducted by Ismail *et al.* reported an overall prevalence of 45% [4].

In our study, the prevalence of pDDIs was higher in major severity accounted at 456 (53.27%) cardiology and 326 (48.29%) pulmonary patients. Fokter *et al.* reported pDDIs of major severity in 13% of patients [15] and Ismail *et al.* in 24.25% of patients [3]. Prevalence of pDDIs of moderate severity was 30.94%. Patel *et al.* reported moderate severity in 60.3% of patients [5]. This study contrasts the other studies which report moderate severity. These potential DDIs suggest that there is a need for modification or alteration of therapy such as dosage adjustment. To prevent these DDIs, health-care providers should have adequate information about DDIs not

only through drug information center, which can provide evidence-based information to health-care professionals, but also through encouraging the empowerment of clinical pharmacists that can provide an evidence-based approach to drugs and thereby prevent drug therapy problems of which DDIs is one.

Of 524 cardiac cases, there were 82 interacting pairs identified during the study. Among 856 pDDIs, 256 (29.90%) were due to pharmacokinetic interactions, and 456 (53.27%) were pharmacodynamic interactions. 71 (8.29%) show both mechanisms and 73 (8.54%) were due to unknown mechanisms. Among 256 pharmacokinetic drug interactions, 39 (15.23%) were due to absorption, 41 (16.01%) were due to distribution, 141 (55.07%) were due to metabolism, and 35 (13.67%) were due to excretion. Among 456 pharmacodynamic interactions, 28 (6.14%) were synergistic, 115 (25.21%) were antagonistic, 294 (64.47%) were added, and 19 (4.18%) with both additive and antagonistic effects. According to Chavda *et al.*, among 423 pDDIs, 50.83% were pharmacodynamic drug interactions, 38.53% were pharmacokinetics, and 10.64% were both kinds of mechanisms (Fig. 3) [16]. From 163 pharmacokinetics pDDIs, 45.41% were altered the absorption, 28.99% were altered the metabolism, and 25.60% were altered the excretion. Of the 215 pharmacodynamic pDDIs, 67.44% were synergistic, 30.70% antagonistic, and 1.86% unknown in nature. The reason for the majority being pharmacodynamic interaction is that these types of interactions derive from modification of the action of one drug at the target site by another drug, independent of a change in its

Table 6: Interactive effect, M.O.A, clinical management of common potential drug-drug interactions in pulmonology

pDDI combination	Mechanism of action	Interactive effect	Clinical management
Injection ranitidine+Injection theophylline	Theophylline toxicity (nausea, vomiting, palpitations, seizures)	Decrease metabolism	Dosing adjustments of theophylline may be necessary
Injection furosemide+Injection hydrocortisone	Result in hypokalemia	Antagonistic effect; additive effect	Potassium balance should be carefully monitored during concomitant therapy
Injection ciprofloxacin+Injection theophylline	Theophylline toxicity (nausea, vomiting, palpitations, seizures)	Decreased metabolism	Serum levels of theophylline should be monitored and dosage adjustments made as appropriate
C. omeprazole+T. clopidogrel	Reduction in clinical efficacy of clopidogrel and increased risk for thrombosis	Inhibit metabolism	Avoid concomitant use of clopidogrel and omeprazole. Rabeprazole (given 4 hours after clopidogrel), pantoprazole, and dexlansoprazole have less effect on the antiplatelet activity of clopidogrel
Injection furosemide+Injection theophylline	Altered theophylline concentrations	Unknown	Dosing adjustments of theophylline may be necessary

pDDIs: Potential drug-drug interactions

Table 7: Prevalence of pDDIs

Type of prevalence	Cardiology	Pulmonary
Severity of pDDIs	Frequency n=856 (%)	Frequency n=675 (%)
Major	456 (53.27)	326 (48.29)
Moderate	251 (29.33)	217 (32.16)
Minor	149 (17.40)	132 (19.55)

pDDIs: Potential drug-drug interactions

concentration. This may result in enhanced response (synergism), an attenuated response (antagonism), or an abnormal response.

Of 345 pulmonary cases, 68 interacting pairs were identified during the study. Among 675 pDDIs, 202 (29.92%) were pharmacokinetic interactions, 416 (61.62%) were pharmacodynamic interactions. 38 (5.62%) show both mechanisms, and 19 (2.84%) were unknown mechanism. Among 202 pharmacokinetic drug interactions in pulmonary department, 114 (56.43%) were due to metabolism. Among 416 pharmacodynamic interactions, 276 (66.34%) were synergistic, identified to a study reported by Chavda *et al*, where 67.44% were synergistic followed by 30.7% antagonistic [16]. From pDDIs detected in the study by Chavda *et al.*, the majority were of pharmacodynamic (58.83%) in nature, followed by pharmacokinetics (38.53%) interactions [16]. These findings are in contrast to the study reported by Vonbach *et al.* [17] and Aparasu *et al.*, wherein it was reported that 76% of pharmacokinetics and 22% of pharmacodynamic interactions (Fig. 3) [18].

Diet and lifestyle can sometimes have a significant impact on drugs. These may occur out of accidental misuse or due to lack of knowledge about the active ingredients involved in the relevant substances. Interactions between food and drugs may inadvertently reduce or increase the drug effect. Major side effects of some diet (food) on drugs include alteration in the absorption of fatty, high protein, and fiber diets.

According to this study, a total of 1150 patients were studied at cardiology and pulmonary departments. Among this, 685 were cardiac and 465 were pulmonary patients. Of 685 cardiac patients, 290 (42.33%) were found to be drug-food interactions (DFIs). 457

pDFIs were found in 290 cardiac patients. 278 pDFIs were found in 165 pulmonary patients. The most common pDFIs were between atorvastatin and citrus fruits, in cardiac patients, with a frequency of 144 (Table 8), which may cause decreased first-pass metabolism and increased bioavailability of atorvastatin that further results in muscle breakdown, liver damage, digestive problems, increased blood sugar, and neurological side effects. The reason for these interactions is due to furanocoumarins. The interaction between citrus fruits and medications poses dangers only if a drug is taken orally because the interaction occurs in the digestive tract. The second most common interaction was banana interacting with the ACE inhibitors, with a frequency of 83, to cause hyperkalemia [19]. Bananas are high in potassium. Too much potassium can cause an irregular heartbeat and heart palpitations.

Of 278 pDFIs, 165 were found in pulmonary patients. The most common pDFIs were found between theophylline and caffeine (coffee/tea) with a frequency of 120 (43.16%) (Table 9), followed by theophylline–protein-rich foods (fish, milk, and egg) with a frequency of 55 (19.78%). Tse *et al.* conducted a study that suggested that interactions between theophylline and caffeine may be attributed to changes in drug distribution and drug elimination characteristics [20].

A total of 1150 patients were studied at cardiology and pulmonary departments. Among these, 685 were cardiac and 465 were pulmonary patients. Of 685 cardiac patients, 175 (42.06%) had found to be pDDIs. 289 pDDIs were found in 175 cardiac patients. 138 pDDIs were in 93 (22.35%) pulmonary patients. The most common drug-disease interaction was found between ISDN and MI (Table 10). The interaction may result in systemic hypotension and tachycardia. It may also exacerbate myocardial ischemia. The second common drug-disease interaction was found to be furosemide with DM. This interaction may result in latent diabetes which may become overt: Insulin requirements in established diabetes may increase. Therefore, it is advisable to stop furosemide before a glucose tolerance test. The most common pDDIs found between diazepam and COPD in pulmonary patients (Table 11). This interaction may result in risk of respiratory depression. Dimitriadis *et al.* conducted a study which reported that the effects of furosemide may contribute to the decrease in glucose utilization [21].

Table 8: Distribution of potential DFIs in cardiology

Drug-food	Interactive effect	Type of DFI	Severity	Frequency n=457 (%)
T. atorvastatin with citrus fruits	Decreased first-pass metabolism and increased bioavailability	PK	Moderate	144 (31.50)
T. enalapril with banana	Hyperkalemia	Unknown	Moderate	47 (10.28)
T. atenolol with orange juice	Decrease the mean peak plasma concentration of atenolol; excretion of drugs in urine decreased	PK	Moderate	79 (17.28)
T. diazepam with tea/coffee	Antagonistic effect. Caffeine generally antagonized the diazepam-induced ratings of sedation and impairment of psychomotor performance	PD	Minor	83 (18.16)
T. Bisacodyl with milk	Increase the risk of stomach upset and nausea	Unknown	Minor	91 (19.91)
T. paracetamol with cabbage	Decrease effectiveness of the drug	PK	Moderate	38 (8.31)

Table 9: Distribution of potential DFIs in pulmonology

Drug-food	Interactive effect	Type of DDI	Severity	Frequency n=278 (%)
T. theophylline with coffee/tea (caffeine)	Increased plasma concentration by inhibiting metabolism	PK	Moderate	120 (43.16)
T. theophylline with protein-rich foods (fish, milk, egg, meat)	Increased clearance of the drug	Unknown	Moderate	55 (19.78)
T. paracetamol with cabbage	Decrease effectiveness of the drug.	PK	Moderate	22 (7.91)
T. ciprofloxacin with tea/coffee (caffeine)	Increased caffeine concentrations and enhanced CNS stimulation	PK	Moderate	68 (24.46)
T. ciprofloxacin with milk/curd	Decreased drug concentration	PK	Moderate	65 (23.38)

DFIs: Drug-food interaction

Table 10: Distribution of potential drug-disease interactions in cardiology

Drug-disease	Interactive effect	Severity	Frequency n=289 (%)
T. ISDN with MI	Systemic hypotension and tachycardia	Major	42 (14.53%)
Injection furosemide with diabetes mellitus	Latent diabetes may become overt: Insulin requirements in established diabetes may increase: Stop furosemide before a glucose tolerance test	Moderate	56 (19.37)
T. atenolol with DM	Inhibit catecholamine-mediated glycogenolysis, thereby potentiating insulin-induced hypoglycemia and delaying the recovery of normal blood glucose levels	Major	24 (8.30)
T. enalapril with CHF	Oliguria and/or progressive azotemia, and rarely, renal failure, myocardial ischemia, and death	Major	28 (9.68)
T. amlodipine with CAD	Unknown mechanism	Major	18 (6.22)

ISDN: Isosorbide dinitrate, MI: Myocardial infarction, DM: Diabetes mellitus, CHF: Congested heart failure, CAD: Coronary artery diseases

Table 11: Distribution of potential drug-disease interactions in pulmonology

Drug-disease	Interactive effect	Severity	Frequency n=138 (%)
T. diazepam with COPD	Risk of respiratory depression	Moderate	76 (55.07)
T. chlorpheniramine with COPD	Reduce the volume and cause thickening of bronchial secretions, resulting in obstruction of the respiratory tract	Moderate	62 (44.93)

COPD: Chronic obstructive pulmonary diseases

CONCLUSION

This study concluded that the overall incidence of the pDDIs was very high in cardiology when compared to pulmonology department. It was found that the incidence of pDDIs was associated with older age, male gender, number of medication given, and increased length of hospital stays. To reduce pDDIs, the number of medications for the patients need to properly controlled and it is recommended to eliminate all medications without therapeutic benefit, the goal, and indication. All potential DDIs are not equally harmful; therefore, identification of the level of each potential DDIs is integral to assess the clinical importance and appropriate management. Food-drug interactions can produce negative effects on the safety and efficacy of drug therapy as well as nutritional status of patients. Often, such interactions can be avoided by taking 1 h before or 2 h after eating. Therefore, providing information regarding the different food and drug interactions will help

the physicians to prescribe drugs cautiously with only suitable food supplement to get maximum benefit for the patient. Our study reports several examples of interactions between drugs and diseases. Guideline developers could consider a more systematic approach regarding the potential for drug-disease interactions, based on epidemiological knowledge of the commodities of people with the disease, the guideline is focused on and should particularly consider whether cardiovascular diseases are common in the target population. Knowledge of such predictable or possible interactions is necessary for their timely detection and prevention of associated morbidity.

Pharmacists must take responsibility for observing for drug interactions and informing the doctor and the patient about potential issues. With their point-by-point information about drugs, pharmacists have the capacity to relate unforeseen side effects experienced by patients inconceivable adverse effects of their drug therapy.

AUTHORS' CONTRIBUTION

All the authors have contributed equally.

CONFLICTS OF INTEREST

All authors have no conflicts of interest to declare.

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