European Review for Medical and Pharmacological Sciences 2023; 27: 737-743

Detection and analysis of potential drug-drug interactions among patients admitted to the cardiac care unit in a tertiary care hospital

A. KHALED[1,2], D. ALMAGHASLAH[2], R. NAGIB[3], S. MAKKI[2], A. SIDDIQUA[2]

[1]Department of Clinical Pharmacy, Beni-Suef University Hospital, Beni-Suef University, Egypt
[2]Department of Clinical Pharmacy, College of Pharmacy, King Khalid University, Abha, Saudi Arabia
[3]Clinical Pharmacy Department, Ministry of Health, Alexandria, Egypt

Abstract. – OBJECTIVE: This study aimed to estimate how prevalent potential drug-drug interactions (pDDIs) were in patients with cardiovascular diseases who were hospitalized for more than 24 hours, and to determine the risk factors associated with these pDDIs.

PATIENTS AND METHODS: A prospective observational study was conducted on patients admitted to the cardiac care unit in a tertiary care hospital. We included two hundred medical records of cardiovascular disease patients who were prescribed more than one drug. These medical records were analyzed for pDDIs using the Micromedex drug interaction checker database. Data were analyzed using Descriptive statistics. Chi-square test and the Pearson correlation coefficient were applied.

RESULTS: PDDIs were prevalent in 95% of the analyzed medical records, with at least one detected pDDI per record. Within the 200 medical records, 430 potentially interacting drug pairs were identified, with the majority resulting in moderate and major interactions. Aspirin/clopidogrel (111), furosemide/aspirin (89), enoxaparin/clopidogrel (89) and Lisinopril/aspirin (60) were the most common interacting pairs. Whereas, aspirin, heparin, clopidogrel, furosemide, ranitidine and Lisinopril were the most frequently implicated drugs in DDIs.

CONCLUSIONS: PDDIs were common among hospitalized cardiovascular patients. PDDIs were associated with age and number of drugs prescribed. The routine integration of an online drug interactions screening tool may improve the ability of pharmacists to identify cardiac patients at higher risk of potential drug interactions and conduct appropriate interventions thereafter.

Key Words:
Hospitalized cardiac patients, Micromedex, Drug-related problems, Tertiary care hospital, pharmacist, Saudi Arabia.

Introduction

Drug-related problems (DRPs) remain a major challenge in clinical practice[1]. Because of the adverse health outcomes and excess healthcare costs associated with these problems, identifying and addressing DRPs have become integral patient safety measures in healthcare systems[2,3].

There are different DRPs classification schemes. These schemes categorize DRPs into drug selection problems, inappropriate doses, therapeutic duplication, adverse drug reactions or allergies, drug interactions, adherence issues and other problems[4]. Potential drug-drug interactions refer to the possibility of a drug to interact with another when concurrently prescribed, regardless of whether adverse events occurred, i.e., pDDIs can be considered as precursors of DDIs. Hence, preventing, identifying, and addressing potential drug-drug interactions may improve patient safety[5].

The reported prevalence of drug interactions varies significantly among studies. Moreover, some studies[6-8] report incident DDIs, sometimes clinically significant DDIs, and others report pDDIs. This variability complicates the comparison of rates of DDIs among different settings or different populations. However, many studies[6,9-14] suggest that cardiac patients are among the populations at highest risk of DDIs and that many cardiovascular medications are associated with high risk of potential and actual DDIs in various settings.

PDDIs are mostly predictable and preventable if proper monitoring is performed. Studies[15-17] exploring the occurrence and characteristics of pDDIs may aid healthcare professionals in predicting and preventing these interactions. Clinical pharmacists are healthcare professionals

Corresponding Author: Dalia Almaghaslah, MD; e-mail: damoazle@kku.edu.sa

primarily concerned with optimizing medication management and minimizing potential or actual drug-related problems, including DDIs in different healthcare settings[18-20]. Studies[19,21-23] have shown that cardiology clinical pharmacists were able to reduce the occurrence of pDDIs and other DRPs in patients with cardiovascular diseases.

This study aimed to identify the prevalence and assess the severity of pDDIs in hospitalized cardiac patients in a tertiary care hospital at the Asir region of Saudi Arabia and assess the correlation between the number of prescribed drugs and association of certain comorbidities with the incidence of DDIs.

Patients and Methods

A cross sectional study was conducted over a period of three months, in a tertiary care hospital in the Asir region. Ethical approval was obtained from the Research Ethics Committee at King Khalid University (HA-06-B-001) The study included hospitalized cardiac patients aged 18 years or older who were taking more than one drugs during their hospital stay, including the PRN drugs (as needed). We excluded patients who were referred to the cardiology unit for assessment, were visiting on an outpatient basis or died during their hospital stay. A predefined form was used to collect data including patient demographics and medical information. The Patients' medication orders and electronic medication lists were evaluated. Micromedex interaction databases were used to objectively assess the presence and severity rating of pDDIs. PDDIs were classified as either major, moderate, or minor. After the Micromedex database detected a pDDI and identified its severity level, the clinical pharmacist recorded other drugs involved in the interaction, their doses, and routes of administration.

Statistical Analysis

Demographic data like mean age and male to female ratio were described. Descriptive statistics were performed to develop a list of the most frequent and clinically significant pDDIs. Results were expressed as percentages for age, gender, diagnosis, number of drugs prescribed, severity and risk involved. A Chi-square test was done to study the potential association between the number of drugs prescribed, comorbidities, age and sex with the pDDI. Analysis was carried out using SPSS version 25 (IBM Corp., Armonk, NY, USA). The association between age and number of drugs prescribed and the number of pDDIs were analyzed using Pearson correlation. Continuous variables were expressed as means ±standard deviations (SD), while categorical variables were expressed as a count (percentage). *p*-value of <0.05 was considered significant.

Results

A total of 200 medical records of hospitalized cardiac patients were evaluated during the study period. Ninety three percent of the medical records contained drug combinations that exhibited moderate interactions; while 91.5% exhibited major interactions and 30.5% exhibited minor interactions (Table I).

Demographics and Clinical Characteristics

Of the 200 patients participating, a higher number of males [120 (60%)] were studied, compared to females (80 [40%]). The majority of patients were in the age group older than 70 years old [63 (31.5%)], followed by the age group 54-60 years [48 (24%)]. The most common diagnosis was hypertension [145 (72.5%)], followed by coronary artery diseases [97 (48.5%)] and congestive heart failure [58 (29%)]. Diabetes mellitus [121 (60.5%)], dyslipidemia [90 (45%)] and chronic

Table I. Prevalence of potential DDIs according to severity.

		Frequency	Percent	X^2	*p*-value
Major interaction	Yes	183	91.5	137.780	$p < 0.001$
	No	17	8.5		
Moderate interaction	Yes	186	93.0	147.920	$p < 0.001$
	No	14	7.0		
Minor interaction	Yes	61	30.5	30.420	$p < 0.001$
	No	139	69.5		

Table II. Patient's demographic and clinical characteristics.

Characteristics	N (%) or mean ± SD (range)
Gender	
Male	120 (60)
Female	80 (40)
Age (y)	62.8 ± 14.61
30-40	10 (5)
41-50	37 (18.5)
51-60	48 (24)
61-70	42 (21)
> 70	63 (31.5)
Number of drugs	10.9 ± 3.55
1-3	1 (0.5)
4-6	15 (7.5)
7-10	67 (33.5)
>10	117 (58.5)
Reason for hospitalization	
Hypertension	145 (72.5)
Coronary artery disease	97 (48.5)
Congestive heart failure	58 (29)
Atrial fibrillation	18 (9)
Cardiomyopathy	11 (5.5)
Valvular heart disease	2 (1)
Length of the hospital stay (days)	4.5 ± 1.3
< 3	10 (5)
3-5	129 (64.5)
> 5	61 (30.5)
Comorbidities	
Diabetes	121 (60.5)
Dyslipidemia	90 (45)
CKD	15 (7.5)
Respiratory disease	9 (4.5)
Gastrointestinal disease	3 (1.5)
Endocrine disease hypothyroidism	2 (1)

kidney disease (CKD) [15 (7.5%)] were the most common co-morbidities. The mean length of hospital stay was 4.5±1.3 days, during which a majority of the patients received more than 10-drugs concurrently [117 (59%)], 7-10 drugs [67 (33.5%)] and 4-6 drugs [15 (7.5%)]. The anticoagulants and antiplatelet drugs [195 (97.5%)], antihypertensive [123 (77%)], angiotensin converting enzyme inhibitors (ACE inhibitors) [113 (56.5%)] and diuretic drugs [112 (56%)] were also used frequently (Tables II and III).

Prevalence and Severity of DDIs

Among the 200 checked prescriptions**,** 430 drug interactions were identified. The majority of the identified drug interactions were of moderate severity [186 (93%)], although nearly as many severe interactions [183 (91.5%)] were noted. Relatively few interactions of minor severity [61 (30.5%)] were found. The most common interacting drug pairs with severe consequences were aspirin/clopidogrel [111 (18.5%)], furosemide/aspirin [89 (10.5%)] and Heparin/aspirin [52 (7%)]. Among the moderate interacting drug pairs, Lisinopril, and aspirin [60 (12.3%)] was followed by Metoprolol and aspirin [58 (10.8%)], then insulin and aspirin [49 (10.3%)]. The interacting drug pairs of minor severity included ranitidine/aspirin [41 (58.5%)] and furosemide/hydralazine [24 (34.3%)] (Table IV).

Risk Factors

The prevalence of major and moderate DDIs increased in patients more than 70 years old

Table III. The most commonly prescribed drugs.

		Frequency	Percent	Chi-Square	*p*-value
Anticoagulants and antiplatelet	Yes	195	97.5	183.322	< 0.001
	No	4	2.0		
Diuretics	Yes	112	56.0	2.880	0.090
	No	88	44.0		
Antihypertensive	Yes	123	61.5	10.580	0.001
	No	77	38.5		
Calcium channel blocker	Yes	30	15.0	97.090	< 0.001
	No	169	84.5		
ACE inhibitors	Yes	113	56.5	3.663	0.056
	No	86	43.0		
Adrenergic inhibitors	Yes	116	58.0	5.472	0.019
	No	83	41.5		
Vasodilators	Yes	57	28.5	36.307	< 0.001
	No	142	71.0		
ARB	Yes	17	8.5	135.838	< 0.001
	No	181	90.5		
Inotropic agents	Yes	16	8.0	140.146	< 0.001
	No	183	91.5		

p-value is significant at $p < 0.05$.

Table IV. The most common drug pairs involved in pDDIs.

Risk rating	Interacting drug pairs	Frequency	Percent	Effect	Type
Severe	Aspirin and Clopidogrel	111	18.5	Aspirin, clopidogrel. Either increases toxicity of the other by pharmacodynamics synergism	PD
	*Aspirin and Furosamide	89	10.5	aspirin increases and furosemide decreases serum potassium	PD
	Clopidogrel and Enoxaparin	89	10.5	Either increases effects of the other	PD
	Clopidogrel and Omeprazole	69	8.1	Decreased Clopidogrel effect	PK
	Aspirin and Heparin	52	7	Aspirin, heparin. Either increases toxicity of the other by anticoagulation	PD
	Spironolactone and Aspirin	29	11.5	Aspirin decreases effects of spironolactone and both increase the potassium level	PD
	Ticagrelor and Aspirin	18	2.1	Increased risk of bleeding	PD
	Heparin and Clopidogrel	16	3.6	Bleeding	PD
Moderate	Lisinopril and Aspirin	60	9.3	Co administration may result in a significant decrease in renal function	PD
	Metoprolol and Aspirin	58	10.8	Aspirin decreases effects of metoprolol	PD
	Insulin and Aspirin	49	10.3	Hypoglycemia aspirin increases effects of insulin	PD
	Carvedilol and Aspirin	40	5.3	Aspirin decreases effects of carvedilol	PD
	Lisinopril and furosemide	32	5.0	pharmacodynamic synergism	PD
	Insulin and Lisinopril	27	4.2	lisinopril increases effects of insulin	PD
	Enalapril and Aspirin	26	6.7	Coadministration may result in a significant decrease in renal function. Decreased efficacy	PD
	Levofloxacin and Aspirin	16	7	Coadministration may result in a significant stimulation of the central nervous system	PD
	Clopidogrel and Atorvastatin	12	1.9	Decreased efficacy	PK
Minor	Ranitidine and Aspirin	41	58.5	Reduce the absorption of aspirin	PK
	Furosemide and Hydralazine	24	34.3	Increase the Furosemide renal clearance	PK
	Dobutamine and Metoprolol	2	2.8	Metoprolol decreases effects of Dobutamin by pharmacodynamic antagonism	PD

*The interaction depends on the dose.

(58% and 59%, respectively), patients taking a higher number of drugs (more than 10 drugs) and patients having diabetes mellitus. No association was found between gender and the prevalence of pDDIs (Tables V and VI).

Discussion

We found that pDDIs were highly prevalent among hospitalized cardiac patients in a tertiary care hospital (95%), and that pharmacodynamic interactions were more common than pharmacokinetic ones.

The Micromedex database was used to detect pDDIs. Among the 200 prescriptions analyzed, 430 potential drug interactions were identified, with a prevalence rate of 95%. Our results are in accordance with many previous studies[1,16,24,25], which also indicated a high prevalence rate of pDDIs among hospitalized cardiac patients. The study done by Kovačević et al[24] reported a prevalence of 94.7%, while Murtaza et al[1] reported 91.6% and Shakeel et al[25] reported 96.9% prevalence of pDDIs in their studies. By contrast, a study[16] in a South Indian hospital showed a low prevalence rate for pDDIs (30.67%) among the cardiac patients studied. The high variability of reported prevalence rates among different studies may be attributed to the use of different methods to detect pDDIs[16,25].

The majority of the identified pDDIs in our study were moderate in severity, followed by those major in severity. These results are in accordance with previous studies[1,26] which also reported a high prevalence of pDDIs of moderate severity among cardiac patients.

Table V. Prevalence of potential DDIs, according to patient demographics and clinical characteristics.

Risk rating	Major			Moderate			Minor		
	N	*p*-value	X^2	N	*p*-value	X^2	N	*p*-value	X^2
Gender									
Male	113	0.098	$X^2 = 2.743$	114	0. 175	$X^2 = 1.483$	38	0.661	$X^2 = 0.193$
Female	70			72			23		
Age									
30-40	6	0.04	$X^2 = 14.484$	6	0.001	$X^2 = 18.697$	1	0.556	$X^2 = 3.011$
41-50	36			35			10		
51-60	44			47			14		
61-70	39			39			15		
> 70	58			59			21		
Number of drugs prescribed									
4-6	11	0.001	$X^2 = 13.66$	12	0.013	$X^2 = 8.702$	2	0.135	$X^2 = 4.002$
7-10	60			63			18		
> 10	112			111			41		
Comorbidities									
Diabetes	112	0.505	$X^2 = 13.66$	112	0.764	$X^2 = 16.45$	41	0.198	$X^2 = 1.76$

A significant association was found between polypharmacy and the prevalence of pDDIs. We found a high prevalence of pDDIs in patients who received more than 10 drugs, as well as by those who received 7-10 drugs. Moreover, the results of this study indicated a high prevalence of moderate and severe interactions in the elderly patients. Many other studies[1,24,27,28] have proposed ploypharmacypDDIs, especially among cardiac and elderly patients. For example, Schuler et al[11] found a high prevalence of pDDIs among their elderly patients, with a mean number of 7.5+/-3.8 drugs taken.

Patients diagnosed with diseases like hypertension, diabetes mellitus, heart failure and atrial fibrillation – which are more common in the elderly population – end up receiving at least 6 different drugs which promotes the practice of polypharmacy[11]. Nevertheless, other studies[25] reported that the association between age and prevalence of pDDIs is not consistent after the adjustment of polypharmacy and the management of co-morbidities. Sometimes, the use of polypharmacy is essential in the management of patients with multiple co-morbidities, and it is a major challenge for the healthcare system and professionals to optimize medication management and avoid adverse drug reactions (ADRs) and DDIs[10].

Table VI. Risk factor correlation with pDDIs.

Risk factor	r	*p*-value
Age	0.247**	0.001
Number of drugs prescribed	0.658**	0.001

p-value calculated using Pearson correlation; significant at $p < 0.05$.

In our study, no association was noted between gender and pDDIs. This result is similar to some previous studies[1,2,4,12,14] performed in different countries. However, other studies[17,29,30] have previously shown contradictory results. For instance, the study by Ismail et al[17] demonstrated a significant association between the male gender and the prevalence of pDDIs. Another study carried out by Mateti et al[29] noted a significant association between females and the prevalence of pDDIs, as did Shanbhag et al[30] study.

Drugs used for the management of cardiovascular disease (CVD) are usually prescribed in combinations, which increases the likelihood of pDDIs[24]. In our study**,** the most commonly prescribed drug pairs that were found to be associated with pDDIs were anticoagulants and antiplatelets, followed by antihypertensives and diuretics. Our study is in accordance with previous studies[31] which stated that the drugs used for CVD, inflammation, diabetes, and infection were the major factors for hospitalization due to adverse drug reactions and drug-related problems. The consequences of the pDDIs reported in our study included bleeding, effects on heart rate and blood pressure, decreased renal function, disturbance in the potassium level and impaired glucose level.

Finally, the decision to use the drug pairs which cause pDDIs depends on several factors, such as the patient›s condition and the risk/ben-

efit ratio. If the potential benefits outweigh the risks, the physician may prescribe them together and monitor the patient closely. For example, in our study, the combination of aspirin and clopidogrel was the highest reported drug pair identified as a pDDI that may result in bleeding. However, physicians frequently prescribe them to prevent thromboembolisms as they are class I recommendation in multiple guidelines to prevent major adverse cardiac events (MACE).

Limitations

This study has several limitations. A single hospital was used as the study site, so the patient pool was limited. The monitoring of pDDIs was based on drug interaction screening software, which checks only the interactions; therefore, the consequences of these interactions are not considered. Future studies to monitor the actual adverse consequences of the identified pDDIs are recommended.

Recommendations

Healthcare professionals are encouraged to use screening software programs for the detection of pDDIs. The clinical pharmacist should be consulted in order to minimize medication errors, including the detection and prevention of pDDIs.

Conclusions

Patients having CVD are at high risk for pDDIs. Most of the detected pDDIs in this study were of moderate and high severity. The presence of diabetes mellitus, advanced age, and polypharmacy are the major risk factors for pDDIs. These factors can be used as triggers for more careful prescription and monitoring of DDIs.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Acknowledgements

The authors extend their appreciation to the Deanship of Scientific Research at King Khalid University, Saudi Arabia, for funding this work through General Research Program under grant number (GRP-75/43). The authors are grateful to King Khalid University for providing assistance in the implementation of this study. Also, the authors would like to thank Abeer Abdullah, Afnan Ali, Soad Ahmed, Tahani Zaid, Tahani Mohammed and Wajd Yahya for helping in data collection.

Funding

The authors extend their appreciation to the Deanship of Scientific Research at King Khalid University, Saudi Arabia, for funding this work through General Research Program under grant number (GRP-75/43).

Ethics Approval

Ethical approval was obtained from the Research Ethics Committee at King Khalid University.

Informed Consent

Written informed consent was obtained for all participants.

ORCID ID

Dalia Almaghaslah :0000-0002-3094-0808; Arwa Khaled: 0000-0002-0064-7870.

References

1) Murtaza G, Khan MYG, Azhar S, Khan SA, Khan TM. Assessment of potential drug-drug interactions and its associated factors in the hospitalized cardiac patients. Saudi Pharm J 2016; 24: 220-225.
2) Kjeldsen LJ, Nielsen TRH, Olesen C. Investigating the Relative Significance of Drug-Related Problem Categories. Pharmcy 2017; 5: 31-49.
3) Zheng WY, Richardson LC, Li L, Day RO, Westbrook JI, Baysari MT. Drug-drug interactions and their harmful effects in hospitalised patients: a systematic review and meta-analysis. Eur J Clin Pharmacol 2018; 74 :15-27.
4) Van Mil JWF, Westerlund LOT, Hersberger KE, Schaefer MA. Drug-related problem classification systems. Ann Pharmacother 2004; 38: 859-867.
5) Zhang T, Leng J, Liu Y. Deep learning for drug-drug interaction extraction from the literature: a review. Brief Bioinform 2020; 25; 21:1609-1627.
6) Espinosa-Bosch M, Santos-Ramos B, Gil-Navarro MV, Santos-Rubio MD, Marín-Gil R, Villacorta-Linaza P. Prevalence of drug interactions in hospital healthcare. Int J Clin Pharm 2012; 34: 807-817.
7) Thompson MD, Thompson HJ. A systems pharmacokinetic and pharmacodynamics approach to identify opportunities and pitfalls in energy stress-mediated chemoprevention: the use of metformin and other biguanides. Curr Drug Targets 2012; 13: 1876-1884.
8) Janković SM, Pejčić AV, Milosavljević MN, Opančina VD, Pešić NV, Nedeljković TT, Babić GM. Risk factors for potential drug-drug interactions in intensive care unit patients. J Crit Care. 2018; 43: 1-6.
9) Bjerrum L, Gonzalez Lopez-Valcarcel B, Petersen G. Risk factors for potential drug interactions

in general practice. Eur J Gen Pract 2008; 14: 23-29.

10) Guthrie B, Makubate B, Hernandez-Santiago V, Dreischulte T. The rising tide of polypharmacy and drug-drug interactions: population database analysis 1995-2010. BMC Med 2015; 13: 1-10.
11) Schuler J, Dückelmann C, Beindl W, Prinz E, Michalski T, Pichler M. Polypharmacy and inappropriate prescribing in elderly internal-medicine patients in Austria. Wien Klin Wochenschr 2008; 120: 733-741.
12) Hamilton RA, Briceland LL, Andritz MH. Frequency of hospitalization after exposure to known drug-drug interactions in a Medicaid population. Pharmacotherapy 1998; 18: 1112-1120.
13) Baniasadi S, Farzanegan B, Alehashem M. Important drug classes associated with potential drug-drug interactions in critically ill patients: highlights for cardiothoracic intensivists. Ann Intensive Care 2015; 5: 1-8.
14) Magro L, Moretti U, Leone R. Epidemiology and characteristics of adverse drug reactions caused by drug-drug interactions. Expert Opin Drug Saf 2012; 11: 83-94.
15) Alhomaidan HT. Primary Prevention of Coronary Heart Disease (Chd) in Saudi Arabia: Meeting the Challenge. International Journal of Medical Science and Education 2018; 5: 23-29.
16) 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. Australas Med J 2011; 4: 9-14.
17) Ismail M, Iqbal Z, Khattak MB, Khan MI, Javaid A, Khan TM. Potential drug-drug interactions in cardiology ward of a teaching hospital. HealthMED 2012; 6: 1618-1624.
18) Guignard B, Bonnabry P, Perrier A, Dayer P, Desmeules J, Samer CF. Drug-related problems identification in general internal medicine: The impact and role of the clinical pharmacist and pharmacologist. Eur J Intern Med 2015; 26: 399-406.
19) Al-Hajje AH, Atoui F, Awada S, Rachidi S, Zein S, Salameh P. Drug-related problems identified by clinical pharmacist's students and pharmacist's interventions. Ann Pharm Fr 2012; 70: 169-176.
20) Sell R, Schaefer M. Prevalence and risk factors of drug-related problems identified in pharmacy-based medication reviews. Int J Clin Pharm 2020; 42: 588-597.
21) Roblek T, Deticek A, Leskovar B, Suskovic S, Horvat M, Belic A, Mrhar A, Lainscak M. Clinical-pharmacist intervention reduces clinically relevant drug-drug interactions in patients with heart failure: A randomized, double-blind, controlled trial. Int J Cardiol 2016; 203: 647-652.
22) Georgiev KD, Hvarchanova N, Georgieva M, Kanazirev B. The role of the clinical pharmacist in the prevention of potential drug interactions in geriatric heart failure patients. Int J Clin Pharm 2019; 41: 1555-1561.
23) Rekha MM. A Study on Role of Doctor of Pharmacy in Identifying and Reporting of Drug Related Problems and its Comorbidities in Inpatient Units of a Teritary Care Teaching Hospital. Pharmatutor 2017; 5: 68-73.
24) Kovačević M, Vezmar Kovačević S, Miljković B, Radovanović S, Stevanović P. The prevalence and preventability of potentially relevant drug-drug interactions in patients admitted for cardiovascular diseases: A cross-sectional study. Int J Clin Pract 2017; 71: 1-9.
25) Shakeel F, Khan JA, Aamir M, Shareef R, Shah N. Identification of clinically significant drug-drug interactions in cardiac intensive care units of two tertiary care hospitals in Peshawar, Pakistan. Trop J Pharm Res 2016; 15: 2289-2295.
26) Bacic-Vrca V, Marusic S, Erdeljic V, Falamic S, Gojo-Tomic N, Rahelic D. The incidence of potential drug-drug interactions in elderly patients with arterial hypertension. Pharm World Sci 2010; 32: 815-821.
27) Moura CS, Acurcio FA, Belo NO. Drug-drug interactions associated with length of stay and cost of hospitalization. J Pharm Pharm Sci 2009; 12: 266-272.
28) Saedder EA, Lisby M, Nielsen LP, Bonnerup DK, Brock B. Number of drugs most frequently found to be independent risk factors for serious adverse reactions: a systematic literature review. Br J Clin Pharmacol 2015; 80: 808-817.
29) Mateti U, Rajakannan T, Nekkanti H, Rajesh V, Mallaysamy S, Ramachandran P. Drug-drug interactions in hospitalized cardiac patients. J Young Pharm 2011; 3: 329-333.
30) Shanbhag A, G. H, Sadananda K. Potential drug-drug interactions among hospitalized cardiac patients. Int J Basic Clin Pharmacol 2016; 5: 2251-2256.
31) Al Hamid A, Ghaleb M, Aljadhey H, Aslanpour Z. A systematic review of hospitalization resulting from medicine-related problems in adult patients. Br J Clin Pharmacol 2014; 78: 202-217.