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Original Research Article

Evaluation of Polypharmacy Induced Drug Interactions of General Medicine in a Tertiary Care Hospital

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Abstract

The study outcome measure was, to find out the relationship between the Drug interactions and polypharmacy and other factors such as age, gender, hospital stay. A prospective cross-sectional study was performed in general medicine department of tertiary care teaching hospital, Ongole, over a period 6 months. All the patients admitted to the general medicine department were included using appropriate criteria and analyzed for Drug–Drug Interactions (DDIs). These drug interactions in the study were analyzed using the Micromedex Drug Interactions. 905 cases were screened for DDIs, among them 45% of cases with more than 1DDIs. With a total of 848 interactions, aspirin + clopidogrel is the most common interaction pair and is reported by 10.81%, while atorvastatin + clopidogrel is the second most common interaction pair with 9.03% prevalence. 5% of the incidence of interaction was observed in the cases of 408 cases. The regression analysis results the significance level at 95% Confidence Interval ($p \leq 0.05$) of DDIs and polypharmacy. This study concludes that there is a significant association between prescription drugs and DDIs. This type of study helps improve the quality of life. Estimating the most common DDIs can assistance the medical practitioner to recommend the minimal risk prescriptions and the combination of drugs.

Keywords: Drug-Interactions, Polypharmacy, Pharmacokinetic, Pharmacodynamics, Hospital stay.

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INTRODUCTION

Today, disease prevalence is greater, some people have a single disease and few have comorbidities. To treat these, monotherapy or combination therapy can be used for better result. Of these therapies, most of the drugs have side effects and adverse effects, some of the drugs can interact with food, drugs, and disease. Rational drug therapy without drug-drug interactions (DDIs) becomes very difficult with polypharmacy and complex drug therapies. Drug interactions are the most important concept in prescribing a prescription [1]. Drug interactions are a major problem in daily practice. Polypharmacy was observed in 85% of prescriptions and drug interactions in 58.5% of prescriptions [2].

A drug–drug interaction (DDI) is defined as a modification of pharmacokinetic or pharmacodynamic effect of drugs on each other, which may result in wanted effects, in reduced efficacy and effectiveness or augmented toxicity [1,3]. Recurrently ill, critically disease and elderly patients are predominantly at risk of drug interactions due to polypharmacy as well as reduced homeostatic mechanisms [4]. DDIs are predictable to account for 6%-30% of all the ADRs, and they remain to stance a significant risk to the patient's health quality and a considerable economic burden on the health care system [5]. The important ones are Harmful drug–drug interactions, as they cause 10–20% of the adverse drug reactions requiring hospitalization and they can be avoided [6].

Interactions between the two drugs, when they are given simultaneously or within a short timeframe, are known as drug interactions. When multiple medications are provided to a patient, drug interactions are more likely. In most cases, however, the severity of these interactions is impossible to predict [7].

Patient safety is more important for physicians to improve health care. But, now a day's prevalence of polypharmacy is greater for treat multiple health conditions, these results increased chance of potential drug-drug interactions. Because of vast use of medicines for co-morbidities, day by day risk of drug-drug interactions are increasing. These interactions may

be beneficial as well harmful. Harmful drug interactions result in consequences like developing ADR, toxicity, loss of treatment efficacy and drug resistance. However, knowledge about the significant DDIs and risk factors for DDIs are the basis for taking measures to their management [8]. Thus, this study aimed to determine the evaluation of polypharmacy induced Drug- Drug Interactions (DDI's) in general medicine department. And the primary objective of the study was to determine the drug-drug interaction in prescription; secondary objective was to estimate the prevalence of drug interaction in different disease conditions. The other objective of the study was to estimate the severity of drug-drug interactions. This type of study helps in providing individualized treatment to each patient that increases the quality of life and further expect outcomes prior to and increasing the safety of drug use [9].

METHODS

A prospective cross-sectional investigation was conducted among the Subjects who are admitted in general medicine department of a tertiary care teaching hospital Ongole for a period 6 month. Patients were well diagnosed by the physician based on the laboratory parameters, diagnostic tests and treated with respective medications, are recruited in the study.

The study criteria include, the subjects those are willing to participate in to the study, all disease conditions along with co-morbidities, subjects with the age of 12yrs – 70yrs, Polypharmacy prescriptions, and hospital stays for more than 4 to 6 days. The exclusion criteria as described in the figure 1 Subjects with HIV, TB, Cancer, Poisoning cases, Pediatrics and children, Pregnant women and lactating women, Subjects with psychiatric illness, comatose, Subjects undergoing for surgery, Prescriptions with <2 drugs, topical medications containing prescription were excluded.

Prior to collection of data, an approval was acquired from the respected hospital committee. Adapted drug interactions proforma which consist demographic patient data such as their age, gender, date of admission and discharge and treatment plan which contains drugs, dose and frequency, time of drug direction, complaint on day-to-day follow-up and drug interaction information regarding onset, severity, mechanism and documentation, those are checked in Micromedex drug interactions checker software [10]. Microsoft Excel 2010 was used to recoding the collected data and also draws graphs and bar charts.

Drug Interaction Probability scale (DIPS) was applied to estimate the likelihood of the interaction. This scale contains 10 questions related to the interaction, each question caries score from -1 to +1. Depends on the selection the interaction gets a score, based on the score it can be classified (Table 1) [11].

Table-1: DIPS scoring scale

Points	Drug Interaction
<2	Doubtful
2 to 4	Possible
5 to 8	Probable
≥ 9	Highly probable

CDSCO guidelines were followed for good clinical practice. Informed consent was collected from the patients and data was extracted from by treatment charts review of the patients, for which the hospital committee approved [12].

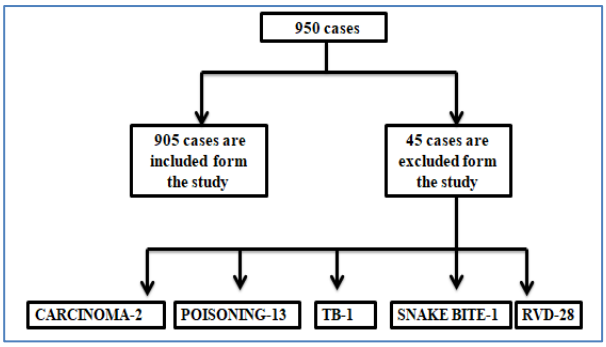

Fig-1: Schematic description of study criteria flowchart

RESULTS

A total of 950 case sheets were reviewed during study period, among which 45 cases were excluded from the study as they were RVD, TB, Carcinoma, and Poisoning cases as described in (Figure 1). From them, using Micromedex Drug Interactions checker, 905 prescriptions were recruited and screened for potential Drug-Drug Interactions (PDDIs), among them 55% (n=497) of prescriptions presented with 0 DDIs and 45% (n=408) with more than 1DDIs.

Age group analysis in study subjects

Age group analysis shown that 27.2% of the DDIs were observed in the age group of 45-53, followed by 23.3% of age 63-71, 19.8% of age group 54-62, 13.4%, 9.3% & 6.8% of age groups 36-44, 27-35 and 18-26 respectively.

Relation between Length of the hospital stay and no. of DDIs

The more DDIs were reported in 5days cases i.e., 32.1%, and the remaining were as followed 31.6%, 16.2%, 14%, & 4% in 6, 4, 7and 8 days respectively. The average length of the hospital stay is found to be 6.5 days.

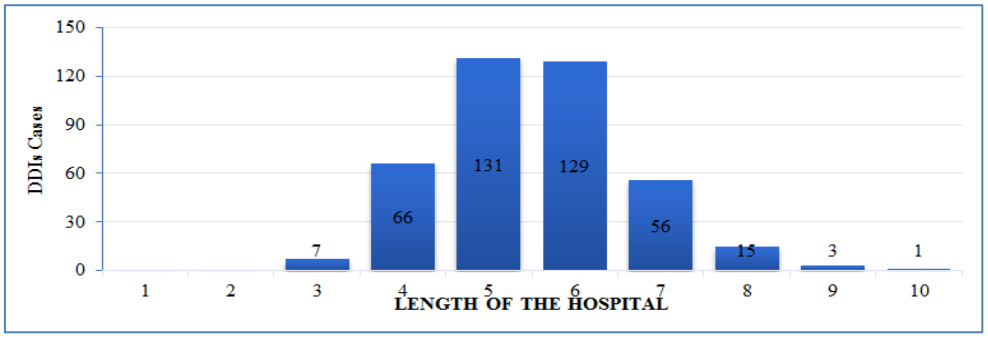

Fig-2: Length of the hospital stay and no. of DDI cases

Distribution of potential DDIs

The potential DDIs showed up between 1 to 10; in which 44% cases showed one PDDI, 26% cases showed two PDDIs, 18% cases showed three PDDIs and 12% cases showed more than 3 potential drug-drug interactions (Table 2).

The potential DDIs had a range of 1 to 10; for which 44% of the patients had one PDDI, 26% of the cases had two PDDI, 18% of the cases had three PDDI, and 12% of the cases had three or more PDDI.

Table-2: Distribution of cases with number of drug-drug interactions

No. DDIs per Rx	Frequency (n=408)	Percentage (%)
1 DDI	179	44%
2 DDIs	106	26%
3 DDIs	74	18%
4 DDIs	24	6%
5 DDIs	15	3.6%
6 DDIs	9	2.2%
10 DDIs	1	0.2%

Distribution of potential DDI's in study subjects

The risk of potential DDIs observed based on the diagnosis, out of 905 cases 80.66% (n=730) cases were single diagnosis cases among them 41% (n=299) DDIs case were observed. Of 19.33% (n=175) co-morbid condition cases 62.28% (n=109) DDIs cases were observed (Figure 2).

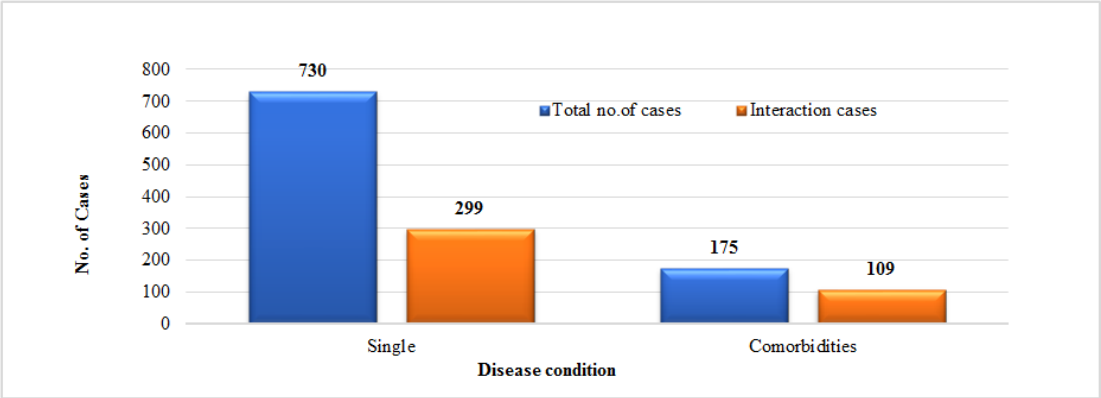

Fig-3: Diagnosis condition versus number of cases

Analysis on number of medications prescribed & risk of DDIs

Taking in to account the number of drugs the patients received, 77% of the patients in our analysis received 5-8 drugs per prescription, followed by 15.5% and 7.5% in ≥ 9 drugs and 2-4 drugs per prescription respectively.

System wise categorization of diseases with DDIs

Out of 408 cases, neurological diseases show highest number of drug-drug interaction cases i.e., 21% as shown in figure 6, and the remaining as followed by 14.4% nephrological diseases, 13.2% gastroenterological diseases, 12.9% co-morbidities, 12.5% cardiac diseases, 9.5% hematological diseases,

6.7% other diseases, 4.1% hepatic diseases and 0.7% respiratory diseases.

Categorization of DDIs by severity

Taking into the severity classification of DDIs, the severity of the drug-drug interactions is high in moderate type of interactions found in 378 cases (44.6%) (n=848) followed by major interactions in 326 cases (38.4%), minor interactions in 141 cases (16.6%) and contraindicated interactions in 3 (0.4%) in severity respectively. Every DDIs has its onset of action, as was drug onset of action. Based on the onset of action, among 848 interactions in 408 cases 47.9% of the DDIs were not specified, 37.4% delayed and 14.7% rapid DDIs.

All the interaction has some ADRs, side effects, and/or synergistic effects; these are depending on the mechanism of the DDIs, Where the drug interaction changes PK or PD activity of active compound. In this study the mechanisms of the reported DDIs mostly found to be Pharmacodynamic that was 53.1%, followed by Pharmacokinetic 33.4% and unknown 13.5%. The documentation of drug-drug interactions, in which 54.6% DDIs were having Fair documentation, followed by 29.2% Good and 16.2 % Excellent.

Prevalence of most commonly interacting drugs

Out of all 408 interaction cases, 848 interactions were found. Most common interacting pairs were Aspirin+ Clopidogrel with the prevalence of 10.81%, followed by Atorvastatin + Clopidogrel with prevalence of 9.03%. The prevalence of all the identified most common interacting pairs, their frequency, prevalence, severity and Drug interaction probability ratings are all mentioned (Table 3).

Table-3: Most prevalent drug-drug interactions in the study prescriptions.

Interaction	Frequency	Prevalence (%)	Severity	DIPS
Aspirin+Clopidogrel	91	10.81	Major	Probable
Atorvastatin +Clopidogrel	76	9.03	Moderate	Probable
Furosemide+Theophylline	58	6.89	Minor	Probable
Ciprofloxacin+Metronidazole	51	6.06	Major	Probable
Iron Folic Acid +Pantoprazole	44	5.23	Moderate	Possible
Metronidazole+Ondansetron	44	5.23	Major	Doubtful
Ciprofloxacin +Ondansetron	43	5.11	Major	Probable
Aspirin+Telmisatron	36	4.28	Moderate	Possible
Aspirin+Furosemide	29	3.44	Moderate	Probable
Aspirin+Amlodipine	25	2.97	Moderate	Possible
Amlodipine+Clopidogrel	23	2.73	Major	Possible
Furosemide+Hydrocortisone	22	2.61	Moderate	Possible
Aspirin+Metoprolol	19	2.26	Moderate	Probable
Ranitidine+Theophylline	19	2.26	Minor	Possible
Phenytoin+Ranitidine	12	1.43	Minor	Possible
Acetaminophen+Phenytoin	10	1.19	Moderate	Probable
Aspirin+Ranitidine	10	1.19	Minor	Probable
Diazepam +Phenytoin	10	1.19	Major	Probable

DIPS: Drug Interaction Probability Scale, N: number of cases

Among 408 cases 5% of the cases were observed interactions, 95% of suspected interaction prescriptions. The observed DDIs were treated as showed & the most common DDIs necessary action that was taken to prevent the toxic outcome (Table 4).

Table-4: Commonly observed DDIs and necessary action that was taken to prevent the toxic outcome

Observed DDI	Anticipated Outcome	Action that was taken
Aspirin – Clopidogrel	Increased GI bleeding	stopped combination and used either of the one
Theophylline – Ranitidine	Theophylline toxicity (nausea, vomitings, palpitations, seizures)	stopped ranitidine and started Pantoprazole
Ciprofloxacin – Metronidazole	Raised risk of QT interval prolongation and arrhythmias	stopped combination and used either of the one
Theophylline – Albendazole	Theophylline toxicity (nausea, vomitings, palpitations, seizures)	Albendazole stopped

STATISTICAL ANALYSIS

Statistics were conducted using IBM SPSS for windows, version 25 software [13], different types of statistical tools were used for analysis of descriptive data, along with regression analysis to evaluate the association of DDIs with predictive factors. The descriptive data of demographics were reported in

standard deviation and percentage. Our study hypothesis was, there is a significant relation between the number of drugs prescribed per prescription and the drug interaction at the level of 95% CI ($p \leq 0.05$). The other hypothesis were Predictive factors such as gender, age and length of hospital stay also have significant relation (figure 5) with drug interaction at the level of 95% CI ($p \leq 0.05$).

Table-5: Predictors of DDIs variables descriptive data

Variable	Total no. of cases (n=905)	Interaction cases (n=408)	Avg.	Stdv.	P (≤0.05)
No. of drugs per prescription					
2-4	171	31	6.106	1.9	0.00
5-8	645	314			
≥9	89	63			
Age group					
18-26	101	28	47.19	16.076	0.00
27-35	126	38			
36-44	141	55			
45-53	188	111			
54-62	169	81			
63-71	180	95			
Length of hospital stay					
1 to 2	0	0	5.25	1.19	0.00
3 to 5	573	204			
6 to 8	326	200			
≥9	6	4			

Avg: mean of total cases, Stdv: standard deviation.

DISCUSSION

Prevalence of polypharmacy was grater in number to treat a single disease condition or co-morbid disease. That may result in the emergence of Drug-drug interactions, adverse drug effects, non-adherence and poor quality of life outcomes. The prevalence of the DDIs was found to be 45% in this study.

Most of the studies are reposted that DDIs were reported in elderly age groups, Jyothi *et al.* study results shown that 23.6% of cases seen in 51-60 years age group. Similarly, in this study most of the patient comes under the age group 45-53 years and the mean age was 47.19 ± 16 years Bajracharya, *et al*. has reported in their study that the average age 45.7 ± 19 [14, 15].

The minimum and maximum prescription drugs were found to be 2 &17, and the mean number of drugs per prescription was 6.1± 1.9 drugs. In our study the potency of DDIs is started to be 49% to 70.78% when patients taking more than 5 drugs, compared to 2-4 (18.12%) medications. Shahabudin Soherwardi *et al*., study results that the risk of potential drug interactions raises from 39% to 100% when patients take more than six medications compared to 2-3 medications [16].

Of our study the average length of hospital stays 5.6±1.5 days and the DDIs were higher in the nature. Khan *et al*. The average length of the hospital stay is found to be 4.8±2.7 days according to Khan *et al*. study [17].

The severity-rated DDIs in our study showed that most interactions were moderate (45%), followed by large 38% and minor 17%. This trend is similar to that in another work by Vijay Kulkarni *et al*. moderate 70%, minor 28%, and major 2% [18].

Many researchers worked on the DDIs mechanisms, of our study 53.1% prescriptions have pharmacodynamic interactions while 33.4% pharmacokinetic interactions and 13.5% of the interaction mechanism was unknown, as was Teshager Aklilu Yesuf *et al*., study 53.4% of the potential interactions were the pharmacodynamic while 29.3% were pharmacokinetic mechanism [19].

In our study, 54.61% DDIs show fair documentation, which is similar to the work of Faisal Shakeel *et al*., 38.5% fair, 49.2% DDIs of good and 12.3% DDIs of excellent documentation of the DDIs, followed by our study 29.24% good, 16.15% excellent Documentation [20].

Only a few studies on system-related interactions are carried out and internal ranks are assigned, as reported by Ahmadizar F *et al*., study results show that most of the identified interactions are at the top of the list in cardiology and internists, while dermatologists ranked the lowest. In our study, neurology took first place on the list, while pulmonology took the lowest place [21].

Maximum studies explored the most collective interacting pairs, and stated different results. This is to be predictable due to the differences in the medication accessibility and medical practice of each institute. Of top 20 most collective interacting pairs we identified, Aspirin was responsible for five. Rawabi Aljadani *et al*. study results shown that in top 20 known common interacting pairs Atorvastatin was ranked top, it is responsible for four interactions, as was aspirin [22].

As per the study of G. Murtaza *et al.* there is association with old age, polypharmacy and increased lengths of hospital stay with DDIs, as per our study we analyzed the significance level at 95% CI that results a correlation was observed between the polypharmacy and DDIs (r:0.394, p <0.05). Similar outcomes were seen in other studies; so, polypharmacy is at increased risk of PDDIs. A direct correlation was also observed between the Predictive factors such as sex, age and length of hospital visit and DDIs (r: 0.451, p <0.05). Similar findings were seen in other studies; so, the predictive factors increase the risk of DDIs [23].

CONCLUSION

Most of the studies conclude that there is a percentage of DDIs, but few studies have described whether the interaction was observed or suspected in prescription. By our study we conclude that, there were so many interactions in the prescription but we observed less percentage of the DDIs and the remain are suspected interaction, which means the prescriptions have the interacting drugs but those interactions were not observed, because, in our study most of the interactions onset of action is not specified, and some of the interaction onset is delayed, few of the interaction onset is rapid. Most of the patients are vulnerable to DDIs due polypharmacy and Co-morbidities. Age, gender, length of stay, and other patient characteristics, are known to be as the possible predictors of DDIs. At the end of the study concludes, these predictors have greater significant levels on DDIs. This study shows that DDIs are one of most important issues. This may contribute to the safe and effective use of medication in our hospital and also fosters the possible role of the pharmacist in regularly monitoring patients for the use of various medications.

LIMITATIONS

There are some limitations in this study. The first limitation was no log relation with the patient to monitor delayed interactions and unknown on set of time. The second limitation was, interacting pair, Aspiring + Clopidogrel has an interaction and also synergetic effect, most of the prescribers are prescribing this combination and some companies are manufacturing combination in a single dose. In this type of situation, the distinguish of the interaction is difficult.

Conflict of interest

The authors don't have any conflicts.

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REFERENCE

1. Chavda, N. B., Solanky, P. P., Baria, H., Naik, R., & Bharti, K. (2015). Study of potential drug–drug interaction between prescribed drugs in patients attending outpatient department of medicine at tertiary-care hospital in south Gujarat region. *National Journal of Physiology, Pharmacy and Pharmacology*, *5*(3), 236-242.
2. George, G. K., Sundaran, S., Cp, A. A., & Km, M. (2018). Thansiya Ph, Babu G. Study of drug-drug interaction in the inpatients of a tertiary care hospital at calicut. *Asian J Pharm Clin Res*, *11*, 162-4.
3. Schalekamp, T. (1997). Omgaan met geneesmiddeleninteracties. *Geneesmiddelenbulletin*, 31; 87-94.
4. John, N. N., Udupi, R. H., & Binu, K. M. (2012). Incidence of polypharmacy induced drug interaction in a tertiary care hospital. *International Journal of Pharmaceutical Sciences and Research*, *3*(7), 2119.
5. Soherwardi, S., Chogtu, B., & Faizal, P. (2012). Surveillance of the Potential Drug-Drug Interactions in the Medicine Department of a Tertiary Care Hospital. *Journal of Clinical & Diagnostic Research*, *6*(7).
6. Ruiz, B., García, M., Aguirre, U., & Aguirre, C. (2008). Factors predicting hospital readmissions related to adverse drug reactions. *European journal of clinical pharmacology*, *64*(7), 715-722.
7. Tripathi, K.D. (2013). Essentials of Medical Pharmacology. 7th Edi. *New Delhi: Jaypee Brothers Medical Publishers*, 928–929.
8. Nikolic, B., Jankovic, S., Stojanov, O., & Popovic, J. (2014). Prevalence and predictors of potential drug-drug interactions. *Open Medicine*, *9*(2), 348-356.
9. Marchianti, A. C. N., Prameswari, M. C., Sakinah, E. N., & Ulfa, E. U. (2019). The enhancement of collagen synthesis process on diabetic wound by Merremia mammosa (Lour.) extract fraction.

10. IBM Micromedex ® for system https://www.micromedexsolutions.com/micromedex.
11. Horn, J. R., Hansten, P. D., & Chan, L. N. (2007). Proposal for a new tool to evaluate drug interaction cases. *Annals of Pharmacotherapy*, *41*(4), 674-680.
12. Imran, M., Najmi, A. K., Rashid, M. F., Tabrez, S., & Shah, M. A. (2013). Clinical research regulation in India-history, development, initiatives, challenges and controversies: Still long way to go. *Journal of pharmacy & bioallied sciences*, *5*(1), 2.
13. IBM® SPSS® Statistics for windows, version 25 http://www.ibm.com/software/analytics/spss/support/clientcare.html. 17 June 2018.
14. Jyothi, N. V., Bharathi, D. R., & Prakruthi, G. M. (2018). Evaluation of drug-drug interactions in patients of general medicine, ICU and emergency departments at a tertiary care hospital. *Int J Curr Pharm Res*, *10*(3), 68-71.
15. Bajracharya, N., Swaroop, A. M., Rajalekshmi, S. G., Viswam, S. K., & Maheswari, E. (2018). Incidence of drug-drug interactions among patients admitted to the department of general medicine in a tertiary care hospital. *Journal of Young Pharmacists*, *10*(4), 450.
16. Soherwardi, S., Chogtu, B., & Faizal, P. (2012). Surveillance of the Potential Drug-Drug Interactions in the Medicine Department of a Tertiary Care Hospital. *Journal of Clinical & Diagnostic Research*, *6*(7).
17. Khan, M. Z., Sridhar, S. B., & Gupta, P. K. (2019). Assessment of potential drug–Drug interactions in hospitalized cardiac patients of a secondary care hospital in the United Arab Emirates. *Journal of research in pharmacy practice*, *8*(1), 20.
18. Kulkarni, V., Bora, S. S., Sirisha, S., Saji, M., & Sundaran, S. (2013). A study on drug–drug interactions through prescription analysis in a South Indian teaching hospital. *Therapeutic advances in drug safety*, *4*(4), 141-146.
19. Yesuf, T. A., Belay, A. Z., Sisay, E. A., & Gebreamlak, Z. B. (2017). Prevalence and Clinical Significance of Potential Drug-Drug Interactions at Ayder Referral Hospital, Northern Ethiopia. *J Dev Drugs*, *6*(3), 10-4172.
20. Shakeel, F., Aamir, M., Khan, A. F., Khan, T. N., & Khan, S. (2018). Epidemiology of potential drug-drug interactions in elderly population admitted to critical care units of Peshawar, Pakistan. *BMC Pharmacology and Toxicology*, *19*(1), 1-6.
21. Ahmadizar, F., Soleymani, F., & Abdollahi, M. (2011). Study of drug-drug interactions in prescriptions of general practitioners and specialists in Iran 2007-2009. *Iranian journal of pharmaceutical research: IJPR*, *10*(4), 921.
22. Aljadani, R., & Aseeri, M. (2018). Prevalence of drug–drug interactions in geriatric patients at an ambulatory care pharmacy in a tertiary care teaching hospital. *BMC research notes*, *11*(1), 1-7.
23. Murtaza, G., Khan, M. Y. G., Azhar, S., Khan, S. A., & Khan, T. M. (2016). Assessment of potential drug–drug interactions and its associated factors in the hospitalized cardiac patients. *Saudi Pharmaceutical Journal*, *24*(2), 220-225.