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Research Article

PREVALENCE OF DRUG INTERACTIONS AND ADVERSE DRUG REACTIONS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

In healthcare delivery system, medicines play a key role in reducing patient's suffering. Nonetheless, irrational use of medicines remains a major issue facing most health systems across the world. This might eventually lead to drug interactions and adverse drug reactions (ADRs). Hence a study was planned with an aim to evaluate the prevalence of drug interactions and adverse drug reactions in a tertiary care hospital. A total of 500 patients were selected by convenience sampling method. Complete case records of all the 500 subjects were collected. 26.32% (n = 15) ADRs are seen in the age group of 51-60 years. 70.18% (n = 40) of ADRs are seen in males. Irrational prescribing is seen in 30.2%. Most of the (Potential Drug Drug Interactions) PDDIs are due to the combined use of aspirin and clopidogrel (n = 76). Hence, by evidence based practice and rational drug use guidelines, the adverse drug effects can be minimized. Also, by minimizing polypharmacy the number of ADRs can be reduced, thereby decreasing the cost of health care.

Keywords: Irrational prescriptions, drug interactions, adverse drug reactions, polypharmacy, PDDIs, ADDIs

INTRODUCTION

One of the important fundamental human rights is access to health care. It is a worldwide concern for healthcare policy makers, professionals and the public regarding the medication errors occurring in hospitals. In healthcare delivery system, medicines play a key role in reducing patient's suffering. In order to promote rationale drug use, proper policies along with good team work between professionals, patients and community is needed.[1] "Patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community" (WHO, 1985). Irrational prescribing refers to prescribing that fails to conform to good standards of treatment.[2] There is increased risk of unsafe treatment, drug interactions, antimicrobial resistance and cost of treatment due to irrational drug use.[3]

Concomitant use of multiple drugs is often indicated in the management of diseases. Such concomitant use of multiple drugs has been defined as "polypharmacy." A commonly applied definition of poly pharmacy is "the concomitant use of five or more drugs." Polypharmacy often results in heightened risk of drug-related problems. Drug-Drug Interaction (DDI) is said to occur when two or more drugs interact in such a manner that efficacy or toxicity of one or more of the drugs is altered. DDIs are considered as preventable medication-related problems. The topic of DDI has received a great deal of recent attention from the regulatory, scientific, and health care communities worldwide. A large number of drugs are introduced every year, and new interactions between medications are increasingly reported. Drug interactions that cause important changes in the action of a drug are of the greatest concern. These may sometimes land up in adverse drug reactions.[4,5]

Adverse Drug Reactions (ADRs) involving prescribed drugs have generated much attention over the years. Some researchers claim that ADRs increase hospitalization cost. Karch and Lasagna, in 1975, defined an ADR as "any response to a drug that is noxious and unintended and that occurs at doses used in man for prophylaxis, diagnosis or therapy, excluding failure to accomplish the intended purpose".[6] It was estimated that the incidence of adverse drug events (ADEs) is to be 6.5 per hundred admissions in a U.S. study conducted in two academic hospitals.[7] Considering all these issues, a study was planned with an aim to evaluate the prevalence of irrational prescriptions, drug interactions and adverse drug reactions in a tertiary care hospital.

MATERIALS AND METHODS

Sample selection

A total of 500 patients were selected by convenience sampling method from a tertiary care hospital. Patients of all age groups, having complete case notes and consent form were included in the study. Patients with incomplete case notes and not willing to participate in the study were excluded. All procedures performed in human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was started after obtaining clearance from institutional ethical committee. Informed consent was obtained from all individual participants included in the study.

Identification of Irrational prescriptions, Drug interactions and ADRs

Complete case records of all the 500 subjects were collected. Information regarding age, gender, diagnosis, number of drugs, laboratory reports and any abnormal signs and symptoms were recorded. Later the data was analysed for Potential Drug-Drug Interactions (PDDIs), Actual Drug-Drug Interactions (ADDIs) and Adverse Drug Reactions (ADRs). Based on the diagnosis and drugs prescribed for the patients irrational prescriptions were identified. The data was analysed using SPSS-18 version. Chi-square test, Pearson correlation test were used. Graphs were drawn in Prism graph pad 8.

RESULTS

Among the total sample (n = 500) included in the study 45% (n = 225) are males and 55% (n = 275) are females. According to various age groups included in the study, the sample can be categorized as; 27 patients from 11-20 years age group, 50 patients from 21-30 years age group, 69 patients from 31-40 years age group, 101 patients from 41-50 years age group, 108 patients from 51-60 years age group, 83 patients from 61-70 years age group, 49 patients from 71-80 years age group and 13 patients from 81-90 years age group.

Among the total sample 151 (30.2%) irrational prescriptions are found and 349 (69.8%) are rationale. Average drugs in irrational prescription are 13.43 where as it is 6.41 in rational prescriptions. Average number of PDDIs is found to be 3.89 in irrational prescriptions whereas it is only 0.87 in rational prescriptions. Average number of ADDIs is 0.6 in irrational prescriptions where as it is 0.014 in rational prescriptions. The difference between all the variables is highly statistically significant (Table 1).

Among the study population, a total of 893 Potential Drug-Drug Interactions (PDDIs) are noted, which contribute to an average of 1.8 PDDIs per person. Among these 893 PDDIs, 100 Actual Drug-Drug Interactions (ADDIs) are identified, making an average of 0.2 ADDIs per person. A total of 57 Adverse Drug Reactions (ADRs) are identified which make an average of 0.1 ADRs/person.

26.32% (n = 15) ADRs are seen in the age group of 51-60 years, 24.56% (n = 14) ADRs in 41-50 years, 14.04% (n = 8) ADRs in 61-70 years, 10.53% (n = 6) ADRs in 11-20 years, 8.77% (n = 5) ADRs in 21-30 years and 31-40 years, 5.26% (n = 3) ADRs in 71-80 years and 1.75% (n = 1) ADRs are seen in the age group of 81-90 years. (Graph 1) Among the total reported ADRs 70.18% (n = 40) are seen in males and 29.82% (n = 17) are seen in females. (Graph 2)

Among the ADRs, increased bleeding was reported by 10 patients, followed by GI bleeding in 6 patients, abdominal pain and nausea by 4 patients each. Anaphylaxis, broncho spasm, constipation, gingival enlargement, headache, hypokalaemia, renal failure and vomiting are reported by 2 patients each. Angioedema, bloating, oedema, diarrhoea, dizziness, erythema, hypersensitivity, hypoglycaemia, lactic acidosis, osteoporosis, palpitation, peptic ulcer, rashes, sinus bradycardia, tachycardia, vision impairment and xerostomia are reported by one patient each. (Table 2) Among the drugs most of the ADRs are caused due to Aspirin (n = 11) followed by clopidogrel (n = 5), diclofenac (n = 4), ferrous gluconate (n = 4), amoxicillin (n = 2), ceftriaxone (n = 2), digoxin (n = 2), furosemide (n = 2), ibuprofen (n = 2), moxifloxacin (n = 2), phenytoin (n = 2). (Table 3)

Most of the PDDIs are due to the combined use of aspirin and clopidogrel (n = 76), followed by ondansetron and tramadol (n = 37), aspirin and furosemide (n = 35), clopidogrel and heparin (n = 35), aspirin and heparin (n = 26), atorvastatin and clopidogrel (n = 21), aspirin and torsemide (n = 17), ondansetron and metronidazole (n = 17), azithromycin and ondasetron (n = 15), salbutamol and furosemide (n = 13), Enoxaparin and clopidogrel (n = 13), aspirin and insulin (n = 12), levofloxacin and ondansetron (n = 12), amlodipine and clopidogrel (n = 11), pantoprazol and levothyroxine (n = 11), insulin and levofloxacin (n = 10) and other combinations have shown each less than 10 PDDIs. (Table 4)

There is positive association between number of drugs and PDDIs (0.787). As number of drugs increased by 0.787 units there is an increase in the number of PDDIs occurring in a patient by 1 unit. This association is statistically significant (P = 0.0001). There is positive association between no of drugs and ADDIs (0.453). As number of drugs increased by 0.453 units there is an increase in the number of ADDIs occurring in a patient by 1 unit. This association is statistically significant (P = 0.0001). There is positive association between no of drugs and ADRs (0.206). As number of drugs increased by 0.787 units there is an increase in the number of ADRs occurring in a patient by 1 unit. This association is statistically significant (P = 0.0001). There is positive association between PDDIs and ADDIs (0.533). As number of PDDIs increased by 0.533 units there is an increase in the number of ADDIs occurring in a patient by 1 unit. This association is statistically significant (P = 0.0001). There is positive association between PDDIs and ADRs (0.156). As number of PDDIs increased by 0.156 units there is an increase in the number of ADRs occurring in a patient by 1 unit. This association is statistically significant (P = 0.0001). There is positive association between age and number of drugs (0.274). As age increased by 0.274 units there is an increase in the number of drugs given to a patient by 1 unit. This association is statistically significant (P = 0.0001). There is positive association between age and PDDIs (0.266). As age increased by 0.266 units there is an increase in the number of PDDIs occurring in a patient by 1 unit. This association is statistically significant (P = 0.0001). There is positive association between age and ADDIs (0.199). As age increased by 0.199 units there is an increase in the number of ADDIs occurring in a patient by 1 unit. This association is statistically significant (P = 0.0001). There is positive association between ADDIs and ADRs (0.114). As the number of ADDIs increased by 0.114 units there is an increase in the number of ADDIs occurring in a patient by 1 unit. This association is statistically significant (P = 0.011). (Table 5)

DISCUSSION

A total of 500 sample of 11-90 years were included in the study of which 45% (n = 225) were males and 55% (n = 275) were females. In the present study prevalence of ADRs were observed in 57 patients (11.4%), whereas in the study conducted by Gor AP *et al*. (2008) the prevalence was 3%.[8] Prevalence of ADRs was higher in males 70.18% (n = 40) than females 29.82% (n = 17) in the present study. This was in accordance with the study conducted by Shamna M *et al*. (2013) where it was 53.06% in males and 46.93% in females but in contrast the study conducted by Lihite RJ *et al*. (2017) has shown that prevalence of ADRs was higher in females 53.8% than males 46.1%.[3,9]

Table 1: Comparison of variables between rational and irrational prescriptions

Variable	Irrational	Rational	Significance
Average number of drugs per prescription	13.43	6.41	0.0001(HS)
Average number of PDDIs	3.89	0.87	0.0001(HS)
Average number of ADDIs	0.6	0.014	0.0001(HS)

*HS-Highly statistically significant

Table 2: Depicts the list of ADRs in the study population

ADR	Number	ADR	Number
Bleeding	10	Diarrhoea	1
GI Bleeding	6	Dizziness	1
Abdominal pain	4	Erythema	1
Nausea	4	Hypersensitivity	1
Anaphylaxis	2	Hypoglycaemia	1
Bronchospasm	2	Lactic acidosis	1
Constipation	2	Osteoporosis	1
Gingival enlargement	2	Palpitation	1
Headache	2	Peptic ulcer	1
Hypokalaemia	2	Rashes	1
Renal failure	2	Sinus bradycardia	1
Vomiting	2	Tachycardia	1
Angioedema	1	Vision impairment	1
Bloating	1	Xerostomia	1
Oedema	1		

Table 3: Number of ADRs caused by drugs

Drug	Number of ADRs caused	Drug	Number of ADRs caused
Aspirin	11	Clonidine	1
Clopidogrel	5	Desferrioxamine	1
Diclofenac	4	Escitalopram	1
Ferrous gluconate	4	Glimepiride	1
Amoxicillin	2	Hydroxychloroquine	1
Ceftriaxone	2	Lactulose	1
Digoxin	2	Levothyroxine	1
Furosemide	2	Metformin	1
Ibuprofen	2	Oestrogen	1
Moxifloxacin	2	Ofloxacin	1
Phenytoin	2	Orlistat	1
Aliskiren	1	Oseltamivir	1
Amlodipine	1	Prednisolone	1
Azithromycin	1	Propranolol	1
Chloroquine	1	Salbutamol	1

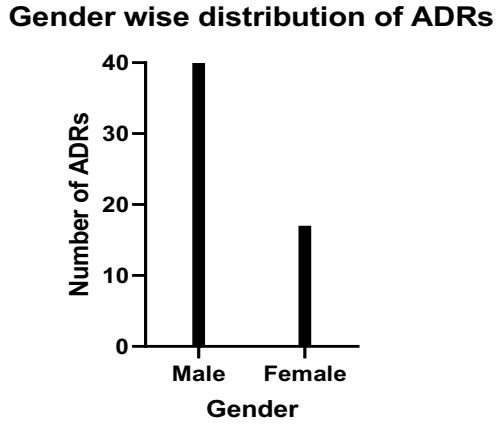
Table 4: Frequency of PDDIs caused by drug combinations

Drug combination	Frequency of PDDIs	Drug combination	Frequency of PDDIs
Aspirin + Clopidogrel	76	Nitroglycerin + Heparin	9
Ondansetron + Tramadol	37	Salbutamol + Torsemide	8
Aspirin + Furosemide	35	Aspirin + Metoprolol	8
Clopidogrel + Heparin	35	Aspirin + Metformin	7
Aspirin + Heparin	26	Aspirin + Spironolactone	7
Atorvastatin + Clopidogrel	21	Ciprofloxacin + Insulin	7
Aspirin + Torsemide	17	Ciprofloxacin + Ondansetron	7
Ondansetron + Metronidazole	17	Hydrocortisone + Furosemide	7
Azithromycin + Ondansetron	15	Insulin + Metformin	7
Salbutamol + Furosemide	13	Nitroglycerin + Aspirin	7
Enoxaparin + Clopidogrel	13	Ranitidine + Aspirin	7
Aspirin + Insulin	12	Acetaminophen + Phenytoin	6
Levofloxacin + Ondansetron	12	Ceftriaxone + Calcium gluconate	6
Amlodipine + Clopidogrel	11	Clopidogrel + Torsemide	6
Pantoprazole + Levothyroxine	11	Fentanyl + Ondansetron	6
Insulin + Levofloxacin	10	Clonazepam + Tramadol	5
Atorvastatin + Azithromycin	9	Ondansetron + Domperidone	5
Azithromycin + Levofloxacin	9	Aspirin + Levofloxacin	5
Hydrocortisone + Aspirin	9		

Table 5: Correlation between various study variables

		No of drugs	PDDIs	Age	ADDIs	ADRs
No of drugs	Pearson Correlation	1	0.787**	0.274**	0.453**	0.206**
	Sig. (2-tailed)		0.0001	0.0001	0.0001	0.0001
	N	500	500	500	500	500
PDDIs	Pearson Correlation	0.787**	1	0.266**	0.533**	0.156**
	Sig. (2-tailed)	0.0001		0.0001	0.0001	0.0001
	N	500	500	500	500	500
Age	Pearson Correlation	0.274**	0.266**	1	0.199**	0.052
	Sig. (2-tailed)	0.0001	0.0001		0.0001	0.242
	N	500	500	500	500	500
ADDIs	Pearson Correlation	0.453**	0.533**	0.199**	1	0.114*
	Sig. (2-tailed)	0.0001	0.000	0.000		0.011
	N	500	500	500	500	500
ADRs	Pearson Correlation	0.206**	0.156**	0.052	0.114*	1
	Sig. (2-tailed)	0.0001	0.0001	0.242	0.011	
	N	500	500	500	500	500

Graph 1: Age wise distribution of ADRs



Graph 2: Gender wise distribution of ADRs

In the present study prevalence of ADRs was higher in the age group of 51-60 years (26.32%), whereas the study conducted by Lihite RJ *et al*. (2017) has shown highest prevalence of 37.4% in the age group of 21-30 years.[9] The study conducted by Shamna M *et al*. (2013) has shown highest prevalence of 44.89% in geriatric patients.[3] In the current study the most common ADRs observed were related to gastrointestinal tract 35.09%. This was in accordance with the study conducted by Gor AP *et al*. (2008) where most ADRs were observed related to gastrointestinal tract 66.69%.[8] In contrast in the study conducted by Lihite RJ *et al*. (2017) most ADRs were observed related to skin 63.52%.[9] In present study most common drugs causing ADRs were NSAIDs 29.82%. In contrast the study conducted by Gor AP *et al*. (2008) has shown penicillin related drugs as most common drug causing ADRs 22.22%.[8]

Total PDDI pairs found in the present study were 395 (79%). Among them 221 (55.94%) were seen among males and 174 (44.09%) among females. According to the study conducted by Kafeel H *et al* (2014) the prevalence of PDDIs was 42.96% in females and 34.68% in males.[10] Akshay K *et al*. (2017), in their study observed that ranolazine and phenytoin were the most common cause of PDDIs.[5] In the present study there was a significant association between Poly pharmacy and PDDIs (P = 0.0001), this was in accordance with the study conducted by Kafeel H *et al* (2014) where the P < 0.005.[10] In the current study there was a significant association between age of the patient and the occurrence of PDDIs (P = 0.0001) which was in accordance with the study conducted by Kafeel H *et al* (2014) where the P < 0.005.[10] In the present study there was no significant association between gender of the patient and the occurrence of PDDIs (P = 0.090), which was in contrast to the study conducted by Kafeel H *et al* (2014) where the P < 0.005.[10]

In the present study out of 500 a total of 480 (96.2%) prescriptions were found to have poly pharmacy. The study conducted by Kafeel H *et al* (2014) has shown the prevalence of polypharmacy as 77.7%.[10] In contrast the study conducted by Akshay K *et al*. (2017) had shown the prevalence of polypharmacy as 13.85%. 30.2% (n = 151) of the prescriptions in the current study had shown irrational prescriptions, the main reasons being polypharmacy and antibiotic abuse.[5] Lukali V *et al* (2015) and Patel V *et al*. (2005) found that the prevalence of irrational prescriptions as 51.4% and 80% respectively.[11,12]

CONCLUSION

As the number of drugs used by the patient increase, there is higher risk of PDDIs and ADDIs. The number of ADRs increases with age and the number of drugs prescribed. Hence, by minimizing polypharmacy the number of ADRs can be reduced, thereby decreasing the cost of health care. Irrational prescribing is one of the leading causes of morbidity and mortality. The main reason of this being irrational use of antibiotics, NSAIDs and PPIs. Hence, by evidence based practice and rational drug use guidelines, the adverse drug effects can be minimized.

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