Assessment of Drug-Related Problems among Inpatients in a Tertiary Care Hospital of Eastern Nepal

Rashmi Adhikari[1], Prasanna Dahal[1*], Sitaram Khadka[2], Shyam Kumar Mallik[1], Kadir Alam[3]

[1]Department of Pharmacy, Purbanchal University College of Medical and Allied Sciences, Gothgaun, Morang
[2]Department of Pharmacy, Shree Birendra Hospital; Nepalese Army Institute of Health Sciences, Kathmandu
[3]Department of Clinical Pharmacology and Therapeutics, BP Koirala Institute of Health Sciences, Dharan
Corresponding Author: Dr Prasanna Dahal; Email: drprasannadahal@gmail.com

ABSTRACT

Background: Drug-related Problems are major safety concerns in hospitalized patients; failure to prevent those medications related errors may lead to therapeutic failure, adverse effects, and poor therapeutic outcomes. This study aims to assess drug-related problems in the medicine ward of a tertiary care hospital in Eastern Nepal.

Methodology: Prospective observational study was conducted from March to August 2019. Descriptive analysis was performed, and Bivariate analysis using chi-square was used to test the association between demographic characteristics and drug-related problems.

Results: 365 patients were selected, of which 96 patients had drug-related problems. A total of 127 drug-related problems were documented. The most common drug-related problems were drug and therapeutic duplication 31(24.4%), a drug prescribed but no clear indication 22(17.3%), potential ineffective therapy 16(12.6%), inappropriate duration 11(8.7%), and adverse drug reaction 10(7.8%). The majority of recommendations provided by the pharmacist were drug discontinuation 57(44.9%), followed by drug change 16(12.6%), and the need for antibiotic susceptibility testing 14(11%). Antimicrobials 75(59.1%) was the most frequent drug class involved in drug-related problems followed by Corticosteroids 12(9.4%), and non-steroidal anti-inflammatory drugs 8(6.3%). A significant association with drug-related problems occurrences was found between age groups, length of hospital stays, and polypharmacy which was significant at p<0.05

Conclusion: Nearly one-fourth of hospitalized inpatients had drug-related problems. Drug and therapeutic duplication were the most common drug-related problems followed by a drug prescribed without clear indication, potential ineffective therapy, and inappropriate duration. The pharmacist plays a crucial role in identifying and resolving drug-related problems during inpatients care.

Keywords: Pharmacy practice, inpatients care, Pharmacist intervention, drug-related problems, Drug therapy review.

BACKGROUND

Drug-related problems (DRPs) are defined as "events or circumstances involving drug therapy that actually or potentially interfere with desired health outcomes".[1] DRPs include medication errors namely prescribing errors, transcription/interpretation errors, dispensing errors, administration errors, and adverse drug reactions (ADRs).[2] DRPs are relatively common in hospital inpatients where multiple changes in patient's medication regimens occur which may be accompanied by poor patient education and sometimes due to inadequate information on medicine-related aspects (pharmacokinetics and pharmacodynamics) in health professionals.[3]

These DRPs may reduce therapeutic outcomes, increase healthcare costs and even increase the risk of morbidity and mortality.[4,5] However, studies show that the majority of DRPs are often preventable, and pharmaceutical care services can reduce the number of medication errors, ADRs, the cost of care and improve overall outcomes with no evidence of harm.[6,7]

Research conducted in various developed and developing countries has reported that the participation of pharmacists in the healthcare team had significantly contributed to identifying and resolving DRPs.[8-15]However, In Nepal, the concept of clinical pharmacists' participation has not been effectively implemented. Although at least one clinical pharmacist's requirement for hospitals with ≥ 50 beds is laid down by Hospital Pharmacy Guidelines 2072 BS [16], its effective implementation is still a far cry. Thus, this study was conducted to assess the influence of pharmacist participation in assessing drug-related problems among inpatients in a tertiary hospital of Eastern, Nepal.

MATERIALS AND METHODS

The prospective observational study was conducted at 100-bedded tertiary care hospital located in the urban area of Jhapa district, Eastern Nepal, from March 2019 till August 2019. Inpatients of either sex, of any age, admitted to the hospital and undergoing treatment on the medicine ward of the hospital were selected using random sampling techniques. For patients undergoing treatment less than one day of hospital stay, the patients who left against medical advice and referred cases were excluded from the study. Selected inpatients were screened and reviewed for the DRPs.

The sample size of 345 was estimated at a 95% confidence interval and 5% margin of error using a prevalence-based estimate calculator.[17] The prevalence (p=0.66) value is taken from Peterson et al., a study in Northern Sweden, due to scare of research in our country.[15] However, a total of 365 (5% additional) patients were followed during the study. Modified Williams and Peterson et al., a classification system was adopted to classify DRPs.[18] The key points for evaluation were drug and therapeutic duplication, a drug prescribed without clear indication, inappropriate dosage forms, potential ineffective therapy, drug selection, drug dosage issues, drug allergies, ADRs, drug-drug interactions, inappropriate duration, monitoring needs, etc. These were recorded referencing standard textbooks such as British National Formulary (BNF), Pharmacotherapy; a pathophysiologic approach by DiPirio et al, published journals, and standard treatment guidelines (STGs).[19-22]In case of suspected DRPs, attending physicians were consulted for ethical reasons. The conformity and reliability of each DRPs and its clinical significance were assessed by independent clinical pharmacist

and physician and was recorded in DRPs documentation form. Based on expected outcomes of problems, the clinical significance of DRPs was classified into minor, moderate, and major significance. Finally, physicians' response to particular interventions was also noted during follow-up. Descriptive analysis was performed, and the association between demographic characteristics and DRPs were analyzed using the chi-square test. P-value ≤0.05 was considered statistically significant. The Ethical approval to conduct this study was obtained from the Nepal Health Research Council (ref no: 2926; reg no.122/2019). Institutional permission was obtained before conducting the study. Patients were informed regarding the purpose of the investigation, and verbal consent was taken from the patients.

RESULTS

In this study, 365 patients were followed, out of which 220 (60.3%) were females, and 145 (39.7%) were males. The median age of patients was 36 years (IQR 32 years). The average length of hospital stay of the patients in the medical ward was 3.39 (±0.942) days. 63.3% of patients had one or more co-morbidity. Most of the patients (91.2%) had stayed in the hospital for 3-6 days. Only 2.5% of patients were prescribed less than five drugs during their in-patient days (Table 1).

Table 1: Patient's characteristics (N=365)

Characteristics	Category	Frequency (n)	Percentage (%)
Gender	Male	145	39.7
	Female	220	60.3
Age group (Years)	1-20	49	13.4
	21-40	159	43.6
	41-60	81	22.2
	>60	76	20.8
Hospital stays (days)	< 3	27	7.4
	3-6	333	91.2
	≥7	5	1.4
Number of diseases	1	134	36.7
	2	170	44.4
	≥3	61	18.9
Number of drugs prescribed	< 5	9	2.5
	5-9	229	62.7
	≥ 10	127	34.8

Drug-related problems (DRPs)

Out of 365 patients, 96 (23.6%) patients had drug-related problems (DRPs). A total of 127 DRPs were identified from 96 patients, among which drug and therapeutic duplication was the most common drug therapy problem recorded 31(24.4%). The second most common DRPs was drug prescribed but no clear indication 22(17.3%), followed by potential ineffective therapy 16(12.6%), inappropriate duration 11(8.7%), and adverse drug reactions 10 (7.9%) as shown in Table 2. Antimicrobials 75(59.1%) were the most frequently involved class in DRPs, followed by corticosteroids 12(9.4%) and non-steroidal anti-inflammatory drugs (NSAIDs) 8(6.3%) (Table 3).

Table 2: Types of DRPs identified (N=127).

Types of DRPs	Frequency (n)	Percentage
Drug and therapeutic duplication	31	24.4%
Drug prescribed but no clear indication	22	17.3%
Potential ineffective therapy	16	12.6%
Inappropriate duration	11	8.7%
Adverse drug reaction	10	7.9%
Inappropriate drug selection	6	4.7%
Drug interaction	6	4.7 %
Laboratory monitoring needed	5	3.9%
Inappropriate dosage schedule	4	3.1%
Non-laboratory monitoring	4	3.1%
Contraindication apparent	3	2.4%
No drug prescribed but clear indication	3	2.4%
Non-adherence to medication	3	2.4%
Inappropriate dosage forms	1	0.8%
Low dose	1	0.8%
Incorrect or unclear dosing instruction	1	0.8%

Table 3: Classes of drugs involved in DRPs (N=127).

Class of Drugs involved in DRP	n (%)
Antimicrobials	75 (59.1)
Corticosteroids	12 (9.5)
NSAIDs	8 (6.3)
β-2 sympathomimetic	5 (3.9)
Diuretics	5 (3.9)
Anti-Hypertensive	5 (3.9)
Anticholinergics	4 (3.1)
Insulin and oral hypoglycemic	5 (3.9)
CNS drugs	3 (2.4)
Antianemics	2 (1.6)
Antiemetics	1 (0.8)
Electrolytes supplements	2 (1.6)

Significance of DRPs

Among 127 DRPs identified, 21(16.5 %) of the DRPs were minor, indicating problems requiring minimal changes to therapy and optimization of treatment, but are not likely to prolong hospital stay, resource utilization, or clinical outcome. Whereas 83(65.4 %) were of moderate significance, which involves problems requiring improvements for enhancing the efficacy of drug therapy, resulting in small reductions in patient morbidity or treatment costs and 23 (18.1%)

were categorized as of major significance representing problems requiring action, to prevent or resolve very serious DRPs, which possess a significant reduction in length of hospital stay and morbidity (Figure 1).
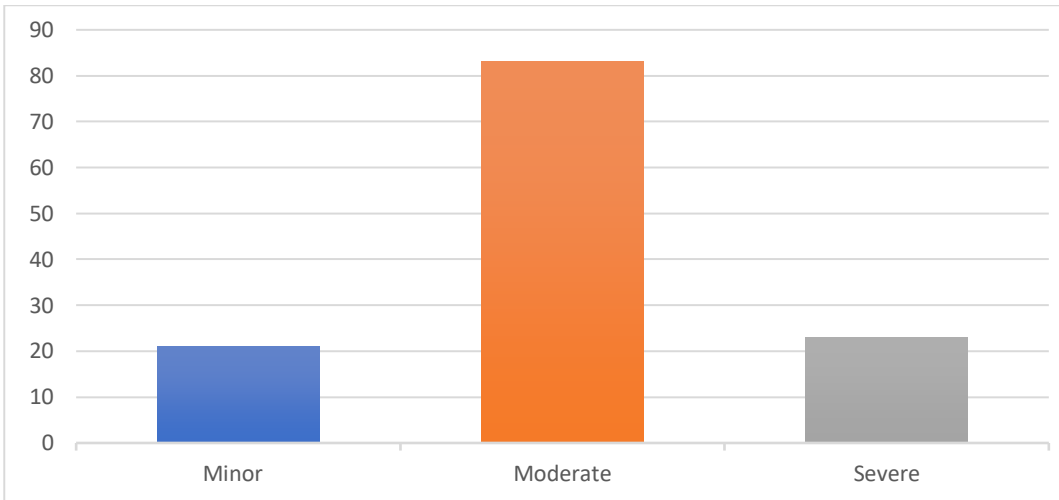

Figure 1: A clinical significance level of DRPs (N=127).
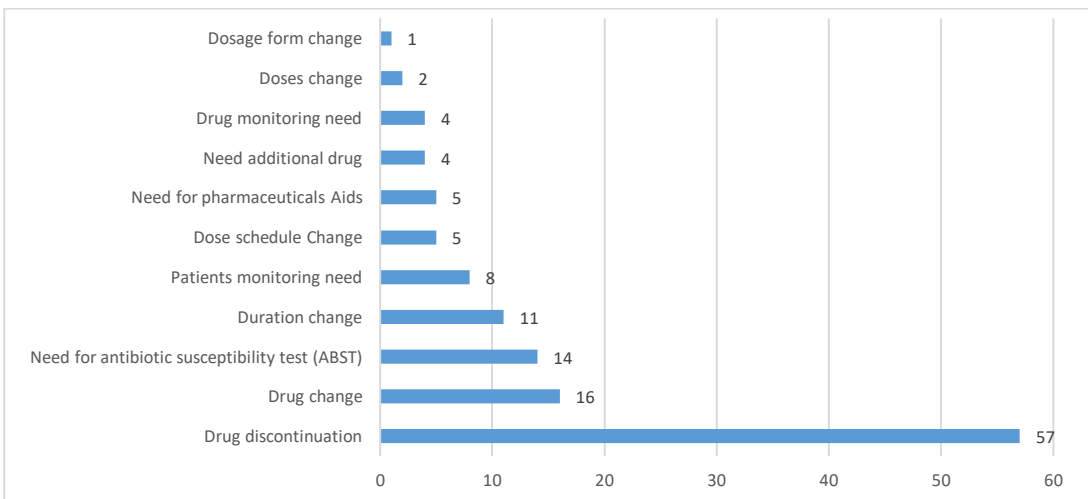
Figure 2: Types of Recommendations provided (N=127).

Pharmacist intervention

In our study, drug discontinuation 57(44.9%) was the most common recommendation provided, followed by drug change 16(12.6%), the need for antibiotic susceptibility test 14(11%), and duration change 11 (8.7%). The details of other recommendations provided are given in figure 2. Further, 96 (75.6%) recommendation provided by the clinical pharmacist was accepted by the attending physician and therapy was changed, while in 31(24.4%) cases recommendation was accepted but the therapy was not changed (Figure 3).

Figure 3: Results of pharmacist intervention

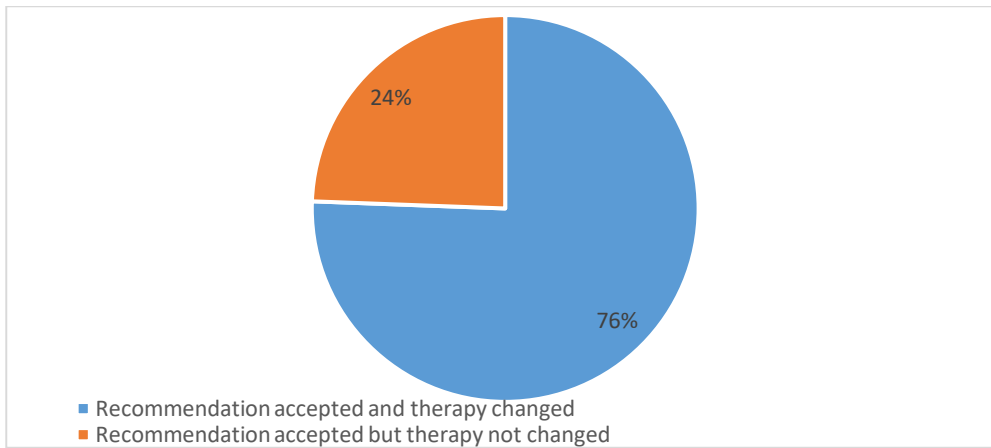**Association between Patient's characteristics and Drug-Related Problems**

The majority of patients, 37(38.5%) of those who had DRPs, were aged 21-40 years, followed by the age group greater than 60 years 30(31.3%). A significant association with DRP occurrences was found between age groups (p=0.032), length of hospital stay (p=0.010), and polypharmacy (p<0.001) (Table 4).

Table 4: Association between patient's characteristics and Drug-Related Problems (N=365).

Patients Characteristics	Category	DRP Present n (%)	DRP Absent n (%)	Total	P value*
Gender	Male	58 (15.9)	87 (23.8)	145 (39.7)	0.973
	Female	38(10.4)	182 (49.9)	220 (60.3)	
Age Group	1-20	12(32.9)	37 (10.1)	49 (13.4)	
	21-40	37(10.1)	122 (33.4)	159 (43.6)	0.032*
	41-60	17(4.7)	64 (17.5)	81(22.2)	
	>60	30(31.3)	46(12.6)	76 (20.8)	
Length of Hospital Stay	< 3	4 (1.1)	23 (6.3)	27 (7.4)	0.010*
	3-6	88(24.1)	245 (6.7)	333 (91.2)	
	≥7	4(1.1)	1 (0.2)	5 (1.3)	
Number of Disease	1	38(10.4)	96 (26.3)	134 (36.7)	0.124
	2	37 (10.1)	133 (36.4)	170 (46.5)	
	≥3	21(5.8)	40 (10.1)	61 (18.9)	
Number of Drug prescribed	< 5	2 (0.5)	7 (2)	9 (2.5)	<0.001**
	5-9	38(10.4)	191 (52.3)	229 (62.7)	
	≥ 10	56(15.3)	71 (19.5)	127 (34.8)	

chi-square test (X2) performed, P-value *indicates statistically significant, **indicates a highly significant association,

DISCUSSION

In our study, a total of 127 DRPs were identified among which drug and therapeutic duplication 31 (24.4%) were most commonly reported DRPs followed by a drug prescribed without clear indication 22 (17.3%) and potential ineffective therapy 16 (12.6%). This finding was somewhat similar to a study conducted by Alagiriswamy et al.,[23] in an Indian teaching hospital where drug use without indication (18%) was the most prevalent DRPs followed by improper drug selection (14%). A study conducted by Abunahlah et al., [12] in Turkish hospital found that drug selection, dose selection, and medication procedures errors were the most common drug cause of DRPs. Similarly, findings from a Naïve hospital of Northern Sweden disclosed inappropriate drug use and interaction as leading issues of DRPs.[15] Our study identified simultaneous use of drugs of identical therapeutic categories mainly NSAIDs, antibiotics, and steroid use, as main contributors for drugs and therapeutic duplication. Similarly, antibacterial agents in generalized anxiety disorder, dengue fever, viral diseases represented examples of prescribing drugs without clear indication. Likewise, cases of ineffective therapy were reported in prescriptions containing resistant antibiotics used, as demonstrated by a culture report. Insufficient antibiotic duration and switching of antibiotics in the course without clear indications were reported as the use of drugs for the inappropriate duration. The drug allergies or adverse drug reactions and drug-drug interactions corresponded to 10 (7.9%) and 6 (4.7%) in our study. Some similar studies on oncology and pediatric unit have reported adverse drug reactions and drug interaction as major contributing factors for DRPs.[24,25] In our study, several cases of the ADRs such as; hypersensitivity reactions after antibiotics (cefixime), analgesics (paracetamol), and corticosteroids administration were documented. Similarly, drug-induced orthostatic hypotension, electrolyte imbalance, headache, diarrhea, and vomiting were also reported which were later resolved after drug discontinuation.

In this study, antimicrobials 75 (59.1%), corticosteroids 12 (9.5%), and NSAIDs 8 (6.3%) were reported as the common drug classes involved in DRPs. These findings were in line with finding obtained by Ayalew et al.,[10] and Belayneh et al.,[26] in Ethiopia, and Mohammed et al.,[27] in India where antimicrobial, corticosteroid, and NSAIDs were the most popular drugs involved for DRPs. The trend of empirical therapy, prevalent cases of infectious disease, delay in laboratory reports, and patients' non-compliance might add as contributing factors in such cases.

Drug discontinuation was the most common recommendation of our study accounting for 44.9% of DRPs followed by drug substitution 12.6%, which coincides with the findings of a study conducted in a tertiary hospital in Southern India [13], Belgian [8], Northern Sweden [10,] and southwest Ethiopia [28] where discontinuation of drug therapy was the most common recommendation provided. Drug discontinuation was recommended in noted cases of drug or therapeutic duplication showing no convincing benefits, a drug prescribed without clear indication, potential ineffective therapy, drug allergies or ADR, and clinically significant drug interactions. Whereas, drug substitution 16 (12.59%) or the need for antibiotic susceptibility test 14 (11.02%) were mostly suggested in cases of inappropriate drug selection and potentially ineffective therapy. Drug monitoring was found essential in a situation where drugs with

hypoglycemic and hypotensive potentials were used in susceptible patients.

In this study, the majority of DRPs recognized were of moderate clinical significances 83(65.4%), followed by major 23(18.1%) and minor 21(16.5%) natures. This finding coincides with the observation carried out in several studies in different countries where the DRPs of moderate and major clinical significances were mostly observed.[6,13,28,29] High patient load, empirical practice, unavailability of clinical pharmacists at the bedside might be responsible for such DRPs. In our study, 96 (75.6%) of pharmacists' recommendations were preceded by the changes in therapy during follow-up. This shows that pharmacist intervention was clinically relevant and helpful in solving the DRPs. Besides, reflects the substantial contribution of pharmacists to assist in reducing the incidence of drug-related issues and improved pharmacotherapy for the patient.

In our study, the incidence of DRPs among hospitalized patients was significantly associated with increasing age groups, hospital stay duration, and poly-pharmacy (p<0.05). These findings were in line with the results of many similar studies.[10,12,15] Studies have shown that polypharmacy increases the risk of ADR, drug interaction. Similarly, the comparatively deteriorated pharmacokinetic and pharmacodynamics parameters due to alteration in hepatic and renal functions and other physiological characteristics in the elderly and those with co-morbidities may be responsible for the higher incidence of DRPs.[30,31]

In our study, DRPs were demonstrated in 26.30% of patients. This finding was higher than that obtained in similar studies conducted by Satish et al (19.6%) [13] and Alagiriswamy et al., (7.9%) [23] in India. However, it is quite low as compared to the findings of Northern Sweden (66%) [15], Ethiopia (52%)[10], Turkey (80%).[12] Since we did not report DRPs that were not committed by both pharmacist and physician, therefore, may predispose to lower reporting of DRPs in our study. Furthermore, the study was carried in a single hospital therefore the findings may not be generalizable in context to hospitals of the entire province or the country as a whole.

CONCLUSION

Nearly one-fourth of hospitalized inpatients had DRPs. Drug and therapeutic duplication were the most common DRPs followed by a drug prescribed without clear indication, potential ineffective therapy, and inappropriate duration. The incidence of DRPs among hospitalized patients was found significantly associated with increased age, greater hospitalized days, and polypharmacy. The study recommends that incorporating pharmacists in the care of hospital inpatients play a crucial role in minimizing DRPs and optimizing drug therapy outcomes.

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