Research Article

Impact of drug-related problems and clinical pharmacist interventions on therapeutic outcomes of the patients admitted to a tertiary care hospital

Siddaruda M Biradar[1], Pathi Indu[1], Manjunatha Rao G[1], Kalyane N V[1], Anand P Ambali[2], Akram Naikwadi[2], Pournamy[1], Neeraja Nayakavadia[1], Prudvi C[1]

[1]Department of Pharmacy Practice, BLDEA's S. S. M. College of Pharmacy and Research Centre, Vijaypur, Karnataka, India, [2]Department of Medicine, Shri B. M. Patil Medical College Hospital and Research Centre, Vijaypur, Karnataka, India

Correspondence to: Siddaruda M Biradar, E-mail: smbiradar@rediffmail.com

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ABSTRACT

Background: A drug-related problems (DRPs) are defined as an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes. The DRPs can occur at any level of its usage. **Objective:** The aim of the study was to find out the DRPs and pharmacist intervention on therapeutic outcome of the patients. **Materials and Methods:** A prospective and observational study was conducted over a period of 6-month. The data collected from each patient were documented in a patient data collection form. DRPs and interactions were analyzed using the Micromedex online database and Stockley's Drug-Drug Interactions text book. **Results:** Out of 120 patients, 32 males and 19 females were identified with DRPs. The maximum subjects 24 were found between the age group 26-35 and minimum subjects 13 were found in the age group >65 years. Most of the comorbidities were observed in hypertensive patients 15 and diabetes 12. 42 risk factors were observed like smoking 19, tobacco chewing 05, and alcohol 18.137 DRPs were have been identified in which most of them accounted for drug interactions 119, adverse drug reactions (ADRs) 11, untreated indication 05, drug use without indication 02. DRPs were more observed in subjects with anemia 17 and gastrointestinal 15.119 drug interactions have been identified in which major 26, moderate 71, and minor 22. Most of the ADRs are caused due to antiviral drugs such as zidovudine and tenofovir followed by fluoroquinolones, ofloxacin, and levofloxacin. Clinical pharmacist's interventions were recommended which include drug replacement 03, drug discontinuation 03, and frequency changes 01. **Conclusion**: The study concludes that involvement of clinical pharmacist services in patient care can significantly help to identify, resolve, and prevent the DRPs in the hospital thereby enhance the patient compliance.

KEY WORDS: Drug-related Problems; Clinical Pharmacist Intervention; Therapeutic Outcome

INTRODUCTION

Clinical pharmacy practice is concerned with the promotion of effective, safe, and economic drug therapy. Pharmacy practice is broad term which includes clinical pharmacy and other patient care related activities performed by pharmacists in the hospital and community settings.[1] These include dispensing and drug distribution, drug information, health promotions, patient counseling, pharmacovigilance, medication reviews, academic detailing, and sterile and nonsterile manufacturing.[1] The drug-related problems (DRPs) are defined as an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes.[2] Patient safety is one of the most important aspects of health care system. Medicines can cure illness and at the same time harm the patient if not appropriately used.

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Hence every patient must receive the right medication, in the right amount and at the right time.[3]

DRPs include both actual and potential problems. An actual problem has resulted in clinical manifestations (e.g., a drug-related rash, an adverse drug reactions [ADR]), or therapy failure due to incorrect dosage. A potential problem is not manifest, but if left unresolved, it may lead to drug-related harm to the patient.[4] DRPs are frequent in hospitalization where multiple changes in patient's medication regimens and lack of continuity of care may be accompanied. Problems associated with drug use are many and includes inappropriate medication prescribing, discrepancies between prescribed and actual regimens, poor adherence, drug interactions, inappropriate use, patients monitoring, and inadequate surveillance for adverse effects. DRPs may lead to reduced quality of life, increase hospital stay, overall increase health cost and even increase risk of morbidity and mortality.[2] Studies on the prevalence of DRPs in hospitals and a closer characterization of all DRPs are lacking and the beside clinical approach evaluation of DRPs are applied.[5] Classification of DRPs can serve as a cynosure for establishing a systematic process for pharmacists to put in appreciably to positive patient outcomes.[6] Many ways of classifications are available to code DRPs but all those classifications have not been tested for validity and reproducibility. DRPs can be classified as per different classification systems. These include the American Society of Hospital Pharmacists System, Cipolle et al., Granada consensus, Hepler/Strand, Pharmaceutical Care Network Europe (PCNE) classification, problem-intervention documentation (PI-oc), and Westerlund classification.[2] Among all classifications, the most commonly tested were PCNE and Charles and Linda. PCNE basically has 4 primary domains for problems, 8 primary domains for causes, 5 primary domains for interventions, and 4 primary domains for outcome of intervention (PCNE, 1999).[6] Similarly, the most commonly tested was Charles and Linda (1990), according to them DRPs were categories into eight segments such as untreated indication, improper drug selection, subtherapeutic dose, failure to receive drugs, over dosage, ADR, drug interaction, and drug use without indication.[7,8] In this approach, problems and causes were not separated.[7,8] If one or more problems are identified, these should be brought to the notice of the concerned physician. Pharmacist should seek corrective measures on a priority basis so that major problems requiring urgent action are addressed before more minor problems. While seeking corrective measures, pharmacists may suggest/recommend suitable corrective strategies with justifications. Identification of DRPs involves the systematic review of each drug order on the patient's medication chart for its appropriateness.[8]

MATERIALS AND METHODS

Study Design and Setting

A prospective observational study was conducted over a period of 6-month in the Department of Medicine of a Shri B. M. Patil Medical College Hospital and research Centre. Hospital provides primary and specialized health-care facilities to people in and around Vijaypur district. The inclusion criteria for the study were all the patients admitted to a general medicine ward and dermatology, patients of either sex, age >18 years, patients receiving oral/parenteral drug therapy, and patients who were willing to participate were included in this study. The patients with pregnant and lactating women, unconscious, and coma patients were excluded from the study.

Source of Data

Patient case file consisting of demographic and medication details, patient interview, Truven Micromedex online database, and Stockley's Drug-Drug Interactions text book were utilized for the study. The study was well before approved by Institutional Ethics Committee (IEC/BLDCOP/2015-16/02).

Data Collection

Data from each patient were collected by either interview or patient case file or both of the above. The data collected from each patient were documented in a patient data collection form. Data regarding drug interactions collected from Micromedex online database and Stockley's Drug-Drug Interactions text book.

RESULTS

Out of 120 patients, males were 70 (58.4%) and females were 50 (41.6%) (Table 1). The maximum DRP patients, 24 (20%) were found between the age group of 26-35 and minimum subjects 13 (10.8%) were found in the age of group >65 years (Table 2).

In this study, most often comorbid involved was hypertension (HTN) (15 [12.5%]) followed by diabetes (12 [10%]) in the selected patients (Table 3), 42 risk factors were observed such as smoking 19 (15.8%), tobacco chewing 05 (4.1%), and alcohol 18 (15%) (Table 4).

Most number of drugs prescribed were proton pump inhibitors (PPIs) 94 (78.3%), followed by cephalosporins 59 (49%), and NSAIDs 55 (45.8%) (Table 5). On admission, the maximum number of patients 62 (51.6%) prescribed with 5-8 types of medication and least number of patients 3 (2.5%) were prescribed with 13-16 medications (Table 6).

A total number of DRPs identified were 137, in which most of them accounted for drug interactions 119 (86.8%), ADRs 11 (8%), untreated indication 05 (3.6%), and drug use without indication was 02 (1.4%) (Table 7). Among 120 patients, males with DRPs were 32 (45.7%) and without DRPs were 38 (58.2%) whereas Females with DRPs were 19 (38%) and without DRPs were 31 (62%) (Table 8).

Table 1: Gender differences

Gender	Number of patients (%)
Male	70 (58.4)
Female	50 (41.6)
Total	120

Table 2: Age distribution

Age group (in years)	*n* (%)		
	Male	Female	Total
18-25	8 (11.4)	13 (26)	21 (17.5)
26-35	17 (24.2)	7 (14)	24 (20)
36-45	13 (18.5)	6 (12)	19 (15.8)
46-55	13 (18.5)	10 (20)	23 (19.3)
56-65	9 (12.8)	11 (22)	20 (16.6)
>65	10 (10.8)	3 (26)	13 (10.8)
Total	70	50	120

Table 3: Comorbidities

Comorbidity	Male (%)	Female (%)	Total (%)
HTN	11 (15.7)	4 (08)	15 (12.5)
Diabetes	11 (15.7)	1 (02)	12 (10)
Asthma	2 (2.8)	1 (02)	03 (2.5)
RVD	7 (10)	4 (08)	11 (9.1)
COPD	3 (4.2)	1 (02)	04 (3.3)
Seizures	2 (2.8)	0 (00)	02 (1.6)
Parkinson's	2 (2.8)	0 (00)	02 (1.6)
TB	2 (2.8)	1 (02)	03 (2.5)
Jaundice	2 (2.8)	0 (00)	02 (1.6)
Total	42 (59.6)	12 (24)	54 (45)

HTN: Hypertension, COPD: Chronic obstructive pulmonary disease

Table 4: Risk factors involved in the patients

Risk factor	Male (%)	Female (%)	Total (%)
Smoking	19 (27.1)	0 (0)	19 (5.8)
Tobacco	3 (4.2)	2 (4)	05 (4.1)
Alcohol	17 (24.2)	1 (2)	18 (15)
Total	39	03	42

DRPs were more commonly observed in subjects with anemia 17 (12.4%) followed by gastrointestinal (GI) 15 (10.9%), chronic obstructive pulmonary disease 13 (8.5%), tuberculosis 12 (7.8%), and HTN 12 (8.7%) (Table 9). Most of the ADRs were caused due to antiviral drugs such as zidovudine-neutropenia, anemia, and tenofovir - vomiting followed by fluoroquinolones such as ofloxacin - fever and levofloxacin-skin rashes (Table 10). Some of the clinical pharmacist's interventions were recommended which includes drug replacement 03 (42.8%), drug discontinuation 03 (42.8%), and frequency changes 01 (14.2%) (Table 11).

Table 5: Pharmacological classifications of prescribed drugs

Pharmacological classification	Number of patients (%)
Cephalosporins	59 (49)
Fluoroquinolones	18 (15)
ACE inhibitors	18 (15)
Calcium channel blockers	13 (10.8)
Diuretics	19 (15.8)
NSAIDs	55 (45.8)
PPI	94 (78.3)
H2 blockers	11 (9.1)
Insulin	11 (9.1)
Biguanides	09 (7.5)
ART	07 (5.8)
Beta blockers	13 (10.8)
Bronchodilators	25 (20.8)
Vitamin supplements	42 (35)
Antitubercular drugs	07 (5.8)
Antiemetics	30 (25)
Antihistamines	09 (7.5)
Corticosteroids	24 (20)
Sulphonamides	06 (05)
Beta-lactams	16 (13.3)
Antacids	06 (05)
Benzodiazepines	16 (13.3)
Antiplatelets	08 (6.6)
Tetracyclines	08 (6.6)
Anticonvulsions	04 (3.3)
Anti-Parkinson's	05 (4.1)
Nitrates	06 (05)
Antifungal	07 (5.8)
Analgesics	11 (9.1)
ARB inhibitors	06 (05)
Antiprotozoal	11 (9.1)
HMG coA reductase inhibitors	09 (7.5)
Antimalarials	04 (3.3)
Anticoagulants	05 (4.1)
Aminoglycosides	08 (6.6)
Antithrombolytics	03 (2.5)
Laxatives	03 (2.5)
Anthelmintics	03 (2.5)
SSRI	01 (0.83)
Liver enzymes	09 (7.5)

PPI: Proton pump inhibitors, NSAIDs: Nonsteroidal anti-inflammatory drugs, ARB: Angiotensin II receptor blocker, ACE: Angiotensin-converting-enzyme

DISCUSSION

This study was carried out to assess the impact of DRPs and clinical pharmacist interventions on therapeutic outcomes of

Table 6: Number of medications received on admission, where (n=120)

No of medications	Number of patients (%)
1-4	42 (35)
5-8	62 (51.6)
9-12	13 (10.8)
13-16	3 (2.5)
17-20	0 (0)
Above 20	0 (0)
Total	120

Table 7: Types of DRPs identified

Types of DRPs	Number of DRPs (%)
Drug interactions	119 (86.8)
ADR	11 (8)
Untreated Indication	05 (3.6)
Drug use without indication	02 (1.4)
Failure to receive drugs	00 (00)
Improper drug selection	00 (00)
Subtherapeutic dose	00 (00)
Over dosage	00 (00)
Total	137

DRP: Drug-related problems, ADRs: Adverse drug reactions

Table 8: DRPs according to gender

DRP	Male (%)	Female (%)	Total (%)
With DRPs	32 (45.7)	19 (38)	51 (42.5)
Without DRPs	38 (54.2)	31 (62)	69 (55.7)
Total	70	50	120

DRP: Drug-related problems

the patients admitted to a tertiary care hospital. The patients included in this study were 120, after fulfillment of inclusion, and exclusion criteria. Among the study population (120), the incidence of DRPs was higher in males in comparison with the females which is contrast to a study conducted by Kumar et al., Assessment of clinical pharmacist intervention in tertiary care teaching hospital of southern India, and Alagiriswami et al., a study of clinical pharmacist initiated changes in drug therapy in a teaching hospital[2,5] which shows that males are more subjected to DRPs than females the factor might have involved were lifestyle modification and habits. Most of the patients were between the age group of 26-35 years with incidence of 24 followed by, 46-55 (23) years and 18-25 (21) years, the data indicate that the prevalence of the DRPs were higher with young and middle-aged people in comparison with old age >65 (13), which is similar to a study conducted by Areif et al.,[9] Clinical pharmacist role in management of Asthma in Tertiary Care Hospital. It implies that DRPs were might not be because of age related, the other factor might have contributed were risk factors, multi drug regimen, and comorbidity of the patients.

Table 9: DRPs according to disease

Disease	Number of patients	Number of DRPs	%
Hypertension	03	12	8.7
Diabetes	03	08	5.2
Asthma	02	09	7.2
RVD	03	08	5.8
COPD	02	13	8.5
Seizures	02	04	2.6
Parkinson's	03	09	5.9
TB	04	12	7.8
Liver diseases	04	11	7.2
Anemia	09	17	12.4
Malaria	02	03	1.9
DVT	01	01	0.7
GI	06	15	10.9
UTI	01	02	1.4
CVS	04	07	4.6
Cerebral ataxia	01	01	0.65
Pneumonia	01	01	0.65
Total	51	137	

COPD: Chronic obstructive pulmonary disease, TB: Tuberculosis, DRPs: Drug-related problems, RVD: Right ventricular dysfunction, UTI: Urinary tract infection, DVT: Deep venous thrombosis, CVS: Cardio vascular system, GI: Gastrointestinal

Table 10: Classes of drugs involved in causing ADRs

Class	Drug	Frequency
Antiviral drugs	Zidovudine	02
	Tenofovir	01
Topical corticosteroid	Desonide	01
Fluoroquinolones	Ofloxacin	02
	levofloxacin	01
Antimalarial	Chloroquine	01
Anti-TB	Ethambutol	01
Thrombolytic	Streptokinase	01
Adrenergic	Noradrenaline	01
Total		11

TB: Tuberculosis, ADRs: Adverse drug reactions

Majority of patients have comorbidities such as HTN and diabetes, and received 5-8 medications on their admission, which is in contrast to a study conducted by Mandavi et al.; ADR and their risk factors among Indian ambulatory patients,[10] which shows that more number of patients were having comorbidities such as HTN (64.8%) and diabetes (36%) thus increasing the likelihood of developing DRPs. The maximum numbers of DRPs were found in patients with anemia followed by GI and HTN which may be due to the usage of multiple drug regimens and disease related factors. 42 patients were identified with risk factors (smoking, tobacco chewing, and alcohol), out of which more were male

Table 11: Types of clinical pharmacist's interventions recommended

Type of recommendation	Number (%)
Frequency changes	01 (14.2)
Drug replacement	03 (42.8)
Drug discontinuation	03 (42.8)
Drug monitoring	00 (00)
Dose adjustment	00 (00)
Total	07

patients, most of the times males were exposed to smoking followed by tobacco chewing and alcohol, whereas female patients were restricted to tobacco chewing & alcohol only. Which closely relates to a study conducted by Areif et al., Clinical pharmacist role in management of Asthma in Tertiary Care Hospital,[9] where most patients were exposed to smoking 7 (19.44%) and alcohol 4 (11.11%). Which illustrates that risk factor is also one of the significant factors for triggering DRP. PPIs and Cephalosporins were the most commonly prescribed drugs in this study, as these drugs are commonly prescribed for prophylaxis. Other major classes of drugs prescribed were NSAIDs and vitamin supplements, this is in contrast to a study conducted by Kumar et al., Assessment of clinical pharmacist intervention in tertiary care teaching hospital of southern India,[2] where most commonly prescribed drugs were antibiotics-cephalosporins, PPIs, and NSAIDs which have resulted in drug or therapeutic duplication.

A total of 137 DRPs were identified in this study where their occurrence is more in males than in females. DRPs were such as untreated indication, ADR, drug interactions, failure to receive drugs, and drug use without indication. The most often encountered DRP was drug-drug interaction, which is similar to a study conducted by Celin et al. Assessment of DRPs in stroke patients admitted to south Indian tertiary care teaching hospital,[11] where most commonly found DRP was drug interactions, i.e. 20 (25.0%). It may be due to multiple drug regimens with many more comorbid conditions of a patient. The predominant type of DRP was drug interaction which incorporates DDI and DFI, drug interaction between theophylline and levofloxacin is commonly observed in the study subjects. This was because both the drugs were prescribed frequently in lower respiratory tract infections. Interaction between alprazolam and grape juice is the second most common drug interaction occurred due to lack of patient's knowledge. These occurrences of drug interactions may be related with lack of physician knowledge about drug pharmacodynamics/pharmacokinetic properties, lack of patient medication and medical determination, etc. ADR accounted for the second most cause of the DRP in the study, which is in contrast to a study conducted by Celin et al. Assessment of DRPs in stroke patients admitted to south Indian tertiary care teaching hospital,[11] where number of ADRs found were 12 (15%). ADR causing drugs such as zidovudine, tenofovir (antivirals) caused neutropenia, and vomiting in the study subjects whereas ofloxacin, levofloxacin (fluoroquinolones) caused fever, and skin rashes contributing for most of the ADRs in the study. Other ADR like blurred vision was observed with ethambutol. Other DRPs like untreated indication (5) was observed in few study subjects and these include vomiting, breathlessness, swelling of both upper limbs, and hypokalemia this may be due to the physician improper care. Types of other DRPs had minority occurrence in the study which involves patients with drug use without indication was observed in few subjects like sucralfate was used in the patient with nonalcoholic steatohepatitis and ondansetron was used in the patient with anemia. The clinical pharmacist's interventions such as drug discontinuation, drug replacement, and frequency changes were recommended in the management of DRPs. Drugs such as desonide, streptokinase, and noradrenaline were discontinued due to their ADRs. Whereas some of drugs such as tenofovir replaced with efavirenz due to vomiting as an ADR and ondansetron was prescribed to treat vomiting. Zidovudine replaced with efavirenz+tenofovir+emtricitabine (antiviral combination therapy) due to anemia as ADR and folic acid and vitamin B complex supplements were given to treat anemia. Ofloxacin was replaced by ceftriaxone due to the ADR - fever and paracetamol was prescribed to relieve fever. Concurrent use of Pantaprazole and iron supplements administration frequency was changed, as iron supplements are not well absorbed in the low acidic medium.

This study clearly indicates that the type of DRP occurred with respect to risk factors, age, sex, comorbidity, and class of drugs involved. The positive outcome of the study demonstrates that the importance of the clinical pharmacist in betterment of the patient compliance by resolving the DRPs and most of study finding are comparable with previous studies. The limitations of the study are conducted in small group of patients and some of study findings are varies in comparison with previous studies in some aspects.

CONCLUSION

Under conclusion part, the multiple drug regimens, comorbidities, patient's age and underlying disease have been found to be major cause of DRPs in this study. The study recommends that the proper involvement of clinical pharmacist services in patient care can significantly help to identify, resolve, and prevent the DRPs in the hospital stay, thereby enhancing the patient therapeutic outcomes. Hence awareness should be increased among all health-care professionals about the importance of clinical pharmacist in minimizing the DRPs.[12]

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