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IDENTIFICATION AND EVALUATION OF DRUG RELATED PROBLEMS IN INTENSIVE CARE UNITS AND EMERGENCY WARD OF A TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Objective: To identify and assess the drug related problems in Intensive Care Units and Emergency Wards of a tertiary care teaching hospital. Methods: This was a prospective observational study in which all patients above 18 years of age admitted to ICU's and emergency ward were considered in inclusion criteria. Exclusion criteria involved patients not willing to participate and poisoning related cases. After the initial visit the patients' case sheets were followed and the collected data was analyzed for possible Drug Related Problems. Results: In this study 160 cases were analyzed for DRPs. In terms of DRP, 146 cases were identified with DRP and 14 cases without DRPs. Major poly-pharmacy was common in the hospitalized patients as 69.4% of patients were given more than 10 drugs during the hospital stay. Drug-Drug interactions (64.47%) were the top ranking DRP followed by Drug Choice Problems (30.19%), Dosing Problems (3.77%) and ADRs (1.57%). The most common class of drugs involved in DRPs was Loop Diuretics. Azithromycin and Ondansetron was the most common drugs that interacted with each other. Potentially inappropriate drugs for geriatrics include Acetaminophen (9), Tramadol (7). Y-site drug incompatibility was 13.9%. There was an association between age, poly-pharmacy, co-morbidities and length of hospital stay with DRPs. Conclusion: Considering the results and conclusions, this study shows the significance of the need for clinical pharmacy services for better management of disease in order to reduce DRPs and improve quality of life.

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INTRODUCTION

Emergency department as well as the Intensive Care Unit of a hospital handle patients on acute and life threatening conditions who present themselves without prior appointment and broad spectrum treatments are rendered usually without proper history of these patients.[1] Complex pharmacotherapy, simultaneous use of drugs in critically ill patients in ICU often require close monitoring as their safety is of paramount importance.[2] In addition to multiple drugs therapy, patients in the ICU presented a risk due to the severity of disease and organ failure.[3] The widespread use of broad spectrum antibiotics has lead to the emergence of several resistant strains of microbes.[4]

According to Pharmaceutical Care Network Europe Foundation (PCNE) Drug-Related Problems are defined as "A Drug-Related Problem is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes".[5]

DRP's can lead to patient's morbidity, mortality, extra hospitalization and decreased quality of life.[6] A literature search showed that most of one out of 3 hospital admissions were caused by drug related problems.[7]

DRP can be manifested in several ways. DRPs may arise at all stages of the medication process from prescription to follow-up of treatment. Most of the problem usually occurs on administration, dispensing and during the patient's use of a medicinal product, but the lack of proper follow-up and reassessment of medical treatment by the physician is also a major problem. DRPs occur more frequently in hospitalized patients where multiple changes are being made in patient's medication regimens, and lack of continuity of care may be accompanied. [8]

World Health Organization (WHO) defines ADRs as any response to a drug which is noxious, unintended and which occur at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases, or for the modification of physiological function. [8]

Classification of drug related problems:

The various classification systems of drug related problems are as follows:
ABC system
ASHP classification
Cipolle et al.
Granada consensus
Hanlon
Hepler/Strand
Krska et al.
Mackie
PAS
PCNE Classification
PI-doc
SHB-SEP
Westerlund classification.[7]

Among classifications which are continuously tested is Pharmaceutical Care Network Europe Classification (PCNE) classification. Its basic classification has 4 primary domains for problems, 8 primary domains for causes, 5 primary domains for interventions, and 4 primary domains for outcome of intervention. [8]

Risk factors of Drug Related Problems

The patients most likely to experience ICU complications are at the extremes of age, the sick and patients with two or more organ system failure. Length of stay, gender, altered renal and hepatic functions and drug exposure are other important factors affecting ADEs. [9]

Poly-pharmacy:

Daily consumption of 5 or more medications can be defined as poly-pharmacy. Formulations of one drug administered through different routes were considered as separate items. If a drug has more than one active ingredient in it like in case of a combination drug, then it was regarded as a single item. [10]

Age:

Among the risk factors, advanced age has been associated with substantial increased risk of acquiring ADR. A sevenfold increase in occurrence of ADRs from 3% to 21% has been shown to occur between patients aged 20–30 years and 60–70 years. Hence, poly-pharmacy along with old age could be considered a potent combination for ADRs to take place. [10]

Although the elderly represent 12–14% of the population, they consume over one-third of prescription drugs. [11]
Elderly patients experience higher incidence of ADEs because they are exposed to a greater number of medications, making them vulnerable to medication errors and drug interactions. The low therapeutic index of certain drugs narrows their safety margin in critically ill patients owing to altered pharmacodynamics and pharmacokinetic secondary to illness which may predispose to drug toxicity. [9]

Co-Morbidities:

Drug-related morbidities are a significant healthcare problem, and a great proportion are preventable. [12] DRPs were common among renal impaired patients due to co-morbid medical conditions, as most of them were receiving multiple medications which require dosage adjustment and routine monitoring. [13] Therefore, in patients with renal impairment, dosage adjustment and close monitoring of renal function are crucial in order to reduce drug toxicity or sub therapeutic effect. [13]

Duration of Stay:

The patients who were admitted for 5–10 days were found to have the highest number of DRPs compared to the patients with length of stay <4 days.[14] Another study on hospitalized cancer patients also found a correlation between duration of hospital stay (≥ 6 days) and potential interactions. [13]

Classification of DRPs:

- Adverse drug reactions
- Drug - Drug interactions
- Therapeutic duplication.
- Treatment without indication
- Inappropriate drug
- Untreated indication
- Low dose
- High dose
- Contraindication
- Duration of therapy

Identifying and resolving the drug related problems is an important tool and core component of pharmaceutical care practice which tends to improves the patient's safety, clinical outcomes and rationalize drug use in patients with cost economic and holistic driven approach.[6] Therefore, the pharmacist is pivotal to the identification, prevention and resolution of DRP. Significant reduction in the number of medication prescribing and administration errors has been achieved through this approach. [1]

Hence this project was designed to identify and evaluate DRPs in the Emergency and Intensive Care Unit of a tertiary care teaching hospital. This in turn provide a channel for improving the quality of care for patients admitted in the hospital.

METHODOLOGY

The prospective observational study was conducted in the Medicine and Emergency departments of a tertiary care teaching hospital at Davangere for a period of six months with a sample size of 160 patients. The inclusion criteria involved all patients above 18 years of age admitted to Intensive Care Units (MICU, NSICU, and RSICU) and Emergency ward. Exclusion criteria involved patients who are treated from outpatient department without requiring hospital stay, patients who are not willing to give informed consent to participate in the study, poisoning related cases and patients with missing and insufficient data. Data will be collected from Medicine case sheets of inpatients who are admitted in the Intensive Care Units and Emergency ward. The ethical clearance for the study was obtained from Institutional Ethical Committee, Davangere.

The first phase of the study included preparation of a data collection form which contain details of patient characteristics, physical examination, laboratory result, current medication, co-morbidities, length of hospitalization and relevant previous medical and medication histories. In the second phase, the collected data from the patient profile was categorized, assessed and analyzed for identifying the most common drugs and drug classes involved in drug related problems and evaluating the drug related problems. A suitably relevant patient data collection form was developed. The collected data was documented in a predesigned data collection form. A computerized database was created by using Microsoft Excel Sheet and all details of the patients and DRPs identified was enrolled into it. The collected data was analyzed by applying suitable statistical method. All extracted data were pooled and analyzed using the statistical package for the social sciences (SPSS) software version 22.0 (IBM). Continuous data were tested for normality. A normally distributed data was expressed as mean ± standard deviation. For categorical variables, the chi-square test was used to determine the association of patient's characteristics and other variables. The t-test was used to compare mean between groups for continuous data. The statistical significance was assumed at $p<0.05$ in this study. The summarized findings were rearranged and tabulated in a graphical or table form.

RESULTS

Details of the gender of the patients (n=160)

A total of 160 patients case sheet were analyzed during the study period out of which 60.6% were males and the rest 39.4% were females.

Table 1: Gender wise distribution of patients.

Gender	No of Patients (n=160)	Percentage (%)
Male	97	60.6
Female	63	39.4
Total	160	100.0

Details of age group of the patients

Out of 160 patients enrolled, subjects under the age group of 40-60 years were majority with 66 patients (41.25%) followed by age group 60 and above consisting of 58 patients (36.25%) and remaining belonging to the age group 19-40 years with 36 patients (22.5%).

Table 2: Distribution of cases with respect to age group.

Age (years)	No of Patients (n=160)	Percentage (%)
19-40	36	22.5
40-60	66	41.25
≥60	58	36.25
Total	160	100.0

Details of Length of hospital stay

Table 3 shows the details of Length of hospitalization of patients during the study period. By analyzing the data, we found that 77 patients (48.1%) stayed for 6-9 days, which was majority followed by 63 patients (39.4%) who stayed for 2-5 days and the remaining 20 patients (12.5%) stayed for more than 9 days.

Table 3: Distribution of Length of Hospitalization.

Length of Hospital Stay (days)	No of Patients (n=160)	Percentage (%)
2-5	63	39.4
6-9	77	48.1
>9	20	12.5
Total	160	100.0

Details of Co-morbidity of patients

The patients were categorized based on co- morbidities present to them. The maximum number of patients had co-morbidities ranging 1-3 consisting of 122 patients (76.2%).

Table 4: Distribution of co-morbidities.

Co-Morbidities	No of Patients (n=160)	Percentage (%)
0	27	16.9
1-3	122	76.2
≥4	11	6.9
Total	160	100.0

Details of Poly-pharmacy

Table 5 shows the distribution of drugs prescribed per prescription. Out of 160 cases, 111 cases (69.4%) were observed with major poly-pharmacy (≥10 drugs) and 49 cases (30.6%) were observed with minor poly-pharmacy (<10 drugs).

Table 5: Distribution of drugs prescribed per prescription.

Poly-pharmacy	No of Patients (n=160)	Percentage (%)
Major	111	69.4
Minor	49	30.6
Total	160	100.0

Average number of drugs prescribed

Total number of drugs prescribed for patients during hospitalization was 2007 drugs.
The average no of drugs prescribed per patient was found to be 12.54.

Table 6: Average number of drugs prescribed during hospitalization.

Number of drug prescribed	Mean ± SD
Hospitalization (2007 drugs)	12.54 ± 5.02

Distribution of Cases with and without DRP's

Out of 160 cases, 146 cases (91.2%) were identified with DRPs and 14 cases (8.8%) without DRPs. Among 146 cases identified with DRPs 86 patients (88.7%) were males and 60 patients (95.2%) were females.

Table7: Distribution of Cases with and without DRP's.

DRP	Gender Male	Female	Total (n=160)
Case with DRPs	86	60	146
	88.7%	95.2%	91.2%
Case without DRPs	11	3	14
	11.3%	4.8%	8.8%
Total	97	63	160
	100.0%	100.0%	100.0%

Types of Drug Related Problem

A total of 636 drug related problems were obtained from 146 cases. 410 possible Drug–Drug Interactions (64.47%) were found which was the top ranking Drug related problem followed by 192 Drug Choice problems (30.19%), 24 Dosing Problems (3.77%) and 10 ADRs (1.57%).

Table 8: Categorization of Types of Drug Related Problems.

Type of DRP	No of DRP (n=636)	Percentage (%)
ADR	10	1.57
Drug-Drug Interactions	410	64.47
Drug Choice Problems	192	30.19
Dosing Problems	24	3.77
Total	636	100.00

Types of Drug-Drug Interactions

The identified possible drug–drug interactions were analyzed as major, moderate and minor. A total of 410 drug-drug interactions were obtained from 146 cases. Out of these 54 drug-drug interactions (13.17%) were of major severity, 211 drug-drug interactions (51.46%) were of moderate severity which was found to be the highest in number followed by 145 drug-drug interactions (35.37%) which were of minor severity.

Table 9: Distribution of Drug-Drug interactions according to degree of severity.

Type of Drug-Drug Interactions	No of Drug-Drug Interactions (n=410)	Percentage (%)
Major	54	13.17
Moderate	211	51.46
Minor	145	35.37
Total	410	100.00

Details of potential Drug-Drug Interactions:

As per our study potential Drug-Drug Interaction were frequently observed with the combination of following drugs: Azithromycin + Ondansetron in 6 patients (11.11%) and Ofloxacin + Ondansetron in 6 patients (11.11%) followed by Levofloxacin+ Ondansetron in 3 patients (5.56%) and Ondansetron + Ivabradine in 2 patients (3.70%).

Table 10: Potential drug- drug interactions (n = 54).

Sl No	Interacting Drugs	Effect	Severity	No. of Patients (%)
1	Azithromycin + Ondansetron	Both Increase Qt_c Interval	Major	6 (11.11%)
2	Ofloxacin + Ondansetron	Both Increase Qt_c Interval	Major	6 (11.11%)
3	Levofloxacin + Ondansetron	Both Increase Qt_c Interval	Major	3 (5.56%)
4	Ondansetron + Ivabradine	Both Increase Qt_c Interval	Major	2 (3.70%)
5	Furosemide + Amikacin	Both together cause ototoxicity and nephrotoxicity	Major	2 (3.70%)
6	Tramadol + Levofloxacin	Both together cause seizure	Major	2 (3.70%)
7	Fluconazole + Ondansetron	Both Increase Qt_c Interval	Major	2 (3.70%)
8	Haloperidol + Ondansetron	Both Increase Qt_c Interval	Major	2 (3.70%)
9	Octreotide + Ondansetron	Both Increase Qt_c Interval	Major	2 (3.70%)
10	Moxifloxacin + Ondansetron	Both Increase Qt_c Interval	Major	2 (3.70%)
11	Dextromethorphan+ Linezolid	Both increases serotonin syndrome	Major	1 (1.85%)
12	Chlorpheniramine + KCL	Gastric irritation of Potassium	Major	1 (1.85%)
13	Escitalopram + Sertraline	Both increases serotonin level	Major	1 (1.85%)
14	Digoxin + Amiodarone	Increase serum concentration of Digoxin	Major	1 (1.85%)
15	Amikacin + Vecuronium bromide	Increases adverse effects of Vecuronium bromide	Major	1 (1.85%)
16	Ceftriaxone + Furosemide	Both together cause nephrotoxicity	Major	1 (1.85%)
17	Moxifloxacin + Deflazacort	Both together cause tendon rupture	Major	1 (1.85%)
18	Clonidine + Tramadol	Increases depressant effect of Tramadol	Major	1 (1.85%)
19	Piperacillin + Enoxaparin	Increases anticoagulation effect of Enoxaparin	Major	1 (1.85%)
20	Hyoscine + Tramadol	Increases depressant effect of Tramadol	Major	1 (1.85%)
21	Ceftriaxone+ Heparin	Increases anticoagulation effect of Heparin	Major	1 (1.85%)
22	Ondansetron + Mirtazapine	Both increases serotonin syndrome	Major	1 (1.85%)
23	Enalapril + Pregabalin	Both together can cause angioedema of face, mouth and neck	Major	1 (1.85%)
24	Artesunate + Ondansetron	Both increase Qt_c interval	Major	1 (1.85%)
25	Phenytoin + Tolvaptan	Decreases level of Tolvaptan	Major	1 (1.85%)
26	Labetalol + Oxymetazoline	Both together increases hypertension	Major	1 (1.85%)
27	Clonidine + Metoprolol	Both enhances sinus node dysfunction, rebound hypertensive effect, causing bradycardia	Major	1 (1.85%)
28	Calcium Gluconate + Doxycycline	Both causes inhibition of GI absorption of each other drug	Major	1 (1.85%)
29	Clopidogrel + Pantoprazole	Decreases effect of Clopidogrel	Major	1 (1.85%)
30	Levothyroxine + Heparin	Increases the effect of Heparin	Major	1 (1.85%)
31	Spironolactone + KCL	Both increases serum Potassium level	Major	1 (1.85%)
32	Moxifloxacin+ Clarithromycin	Both increase Qt_c interval	Major	1 (1.85%)
33	Clarithromycin+ Ondansetron	Both increase Qt_c interval	Major	1 (1.85%)
34	Amitriptyline + Ondansetron	Both increase Qt_c interval	Major	1 (1.85%)
35	Fluconazole + Haloperidol	Both increase Qt_c interval	Major	1 (1.85%)

Types of Drug Choice problems

A total of 192 drug choice problems were obtained from 146 cases. Out of these, 65 Drug Choice Problems (33.85%) were of Inappropriate Drug followed by 59 Drug Choice Problems (30.73%) belonging to Duplication of therapeutic group, 48 Drug Choice Problems (25%) belonging to Untreated Condition, 12 Drug Choice Problems (6.25%) belonging to Contraindication, and remaining 8 Drug Choice Problems (4.17%) belonging to Treatment Without Indication.

Table 11: Types of Drug Choice Problems.

Types of Drug Choice Problems	No of Drug Choice Problems (n=192)	Percentage (%)
Inappropriate Drug	65	33.85
Duplication of therapeutic group	59	30.73
Contraindications	12	6.25
Treatment Without Indication	8	4.17
Untreated Condition	48	25.00
Total	192	100.00

Types of Dosing Problems

A total of 24 Dosing problems were identified. Out of 24 Dosing Problems, 16 Dosing Problems (66.67%) were of High dose which was more prominent followed by 7 Dosing Problems (29.17%) belonging to change in Duration of treatment and 2 Dosing Problems (8.33%) belonging to Low dose.

Table 12: Categorization of Dosing Problems.

Type of Dosing Problems	No of Dosing Problems (n=24)	Percentage (%)
High Dose	16	66.67
Low Dose	2	8.33
Duration of Treatment	7	29.17
Total	24	100.00

Details of suspected ADR's

Among 10 ADR's, most frequent ADR was found to be caused by ARB/Hydrochlorothiazide which was identified in 2 patients followed by 2 different NSAIDs, calcium channel blocker, antiplatelet, blood components, antipsychotic, immunosuppressant and volume expanders in each patient.

Table 13: Identified cases of suspected Adverse Drug Reactions:

Class	Drug	ADR	No of Patients (n=10)	Percentage (%)
NSAID	Acetaminophen	Gastritis	1	10.00
	Diclofenac	Breathlessness	1	10.00
Calcium Channel Blocker	Amlodipine	Pedal Edema	1	10.00
Antiplatelet	Clopidogrel	Haematuria	1	10.00
Blood Components	FFP	Plasma Transfusion Reaction	1	10.00
Antipsychotic	Haloperidol	Tardive Dyskinesia, Tremor, Dystonia	1	10.00
Immuno-suppressant	Azathioprine	Drug induced Thrombocytopenic Purpura	1	10.00
Volume Expanders	IV Albumin	Hypotension, Tingling Sensation	1	10.00
ARB / Thiazide Diuretic	Telmisartan+ Hydrochlorothiazide	Hyponatraemia	2	20.00
	Total		10	100.00

Drugs and drug classes involved in the DRPs

A total of 139 drugs were involved in different types of DRPs. Among these the most commonly involved drugs in the DRPs along with their frequency were Furosemide (41), Ondansetron (40), Pantoprazole (25), Piperacillin+Tazobactum (23), Ceftriaxone (23), Amlodipine (19), Albuterol (17), Tramadol (17), Hydrocortisone (16), Doxycycline (15), Acetaminophen (13), Azithromycin (13), Spironolactone (13), Aspirin (13), Dexamethasone (12). Table 14 shows that Loop diuretics was the most common drug class involved in the DRPs followed by 5-HT3 Receptor Antagonist, Proton-Pump Inhibitor, Penicillin, Cephalosporin, Calcium-channel blocker, Beta 2 agonist, NSAIDs, Corticosteroids, Tetracycline, Macrolide antibiotic, Potassium sparing diuretic.

Table 14: Most common drug and drug classes involved in DRP.

Drug	Drug class	No. of drugs	Percentage (%)
Furosemide	Loop Diuretics	41	6.50
Ondansetron	5-HT3 receptor antagonist	40	6.34
Pantoprazole	Proton pump inhibitor	25	3.96
Piperacillin+Tazobactum	Penicillin	23	3.65
Ceftriaxone	Cephalosporin	23	3.65
Amlodipine	Calcium channel blocker	19	3.01
Albuterol	Beta 2 agonist	17	2.69
Tramadol	NSAIDs	17	2.69
Hydrocortisone	Corticosteroid	16	2.54
Doxycycline	Tetracycline	15	2.38
Acetaminophen	NSAIDs	13	2.06
Azithromycin	Macrolide antibiotic	13	2.06
Spironolactone	Potassium sparing diuretic	13	2.06
Aspirin	NSAIDs	13	2.06
Dexamethasone	Corticosteroids	12	1.90

Beers Assessment

Using the modified Beers Criteria to evaluate inappropriate use of therapeutic agents among the elderly patients

Table 15: Potentially inappropriate drugs prescribed as per Beers Criteria, 2015.

Drugs	Frequency	Concern
BENZODIAZEPINES		
• Lorazepam	1	Older adults have increased sensitivity to benzodiazepines and decreased metabolism. In general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults.
ANTIPSYCHOTICS		
• Haloperidol	1	When given with ≥2 other CNS active drugs, may increase risk of falls, ataxia, and impaired psychomotor function. May exacerbate or cause SIADH or hypernatremia; monitor sodium level closely when starting or changing dosages in older adults.
ANTICHOLINERGICS		
First generation antihistamines		
• Chlorpheniramine	2	
• Promethazine	1	
Third generation antihistamines		Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; risk of confusion, dry mouth, constipation, and other anticholinergic effects or toxicity.
• Levocetrizine	1	
Antispasmodics		
• Hyoscyamine	2	When given with other anticholinergic drugs, may increase risk of cognitive decline.
• Ipratropium bromide	1	
Antimuscarinics		
• Darifenacin	1	
• Flavoxate	1	
ALPHA-1 BLOCKER		
• Prazosin	1	
• Silodosin	1	High risk of orthostatic hypotension or bradycardia
CALCIUM CHANNEL BLOCKER		
• Nifedipine	1	Potential for hypotension, risk of precipitating myocardial ischemia
NSAIDs(non-COX and COX-selective, oral and parenteral)		Increased risk of gastrointestinal bleeding or peptic ulcer disease in higher-risk groups, including those aged >75 or taking oral or parenteral Corticosteroids, Anticoagulants or Antiplatelet agents.
• Aspirin	2	
• Mefenamic Acid	1	
• Acetaminophen	9	In case of elderly patients with heart failure, may promote fluid retention and exacerbate heart failure.
• Aceclofenac	2	

		In case of Chronic kidney disease Stages IV or less, may increase risk of acute kidney injury and further decline of renal function
OPIOID ANALGESIC		
• Tramadol	7	Along with the above mentioned effects, Tramadol may cause CNS adverse effects. When given with ≥2 other CNS active drugs, may increase risk of falls
DIURETICS		
Potassium sparing diuretic		May exacerbate hypernatremia; monitor sodium level closely when starting or changing dosages in older adults. Cause increased potassium at creatinine clearance <30mL/min
• Spironolactone	3	
HYPOGLYCEMIC AGENTS		
• Insulin	6	Higher risk of hypoglycaemia without improvement in hyperglycaemia management regardless of care setting.
Sulphonylureas, long duration		Higher risk of severe prolonged hypoglycaemia in older adults.
• Glyburide	2	
GASTROINTESTINAL		
• Metoclopramide	5	Can cause extrapyramidal effects, including tardive dyskinesia; risk may be greater in frail older adults. Mental status changes when creatinine clearance <50mL/min
• Ranitidine	1	
CORTICOSTEROIDS ORAL OR PARENTRAL		
• Dexamethasone	3	Increased risk of peptic ulcer disease or gastrointestinal bleeding when given with NSAIDs
• Deflazacort	1	
• Methylprednisolone	2	
• Hydrocortisone	2	
• Budesonide	1	

POTENTIAL RISKS OF DRUG INCOMPATIBILITY BASED ON Y-SITE DRUG COMPATIBILITY CHART IN ICU

A total of 89 (13.9%) Y-site drug incompatibilities based on Thames Valley Y-Site Intravenous Drugs Compatibility Chart were detected among DRPs. This investigation only addresses the risk of the incompatibility of drug pairs and is not based on whether the patient was actually harmed.

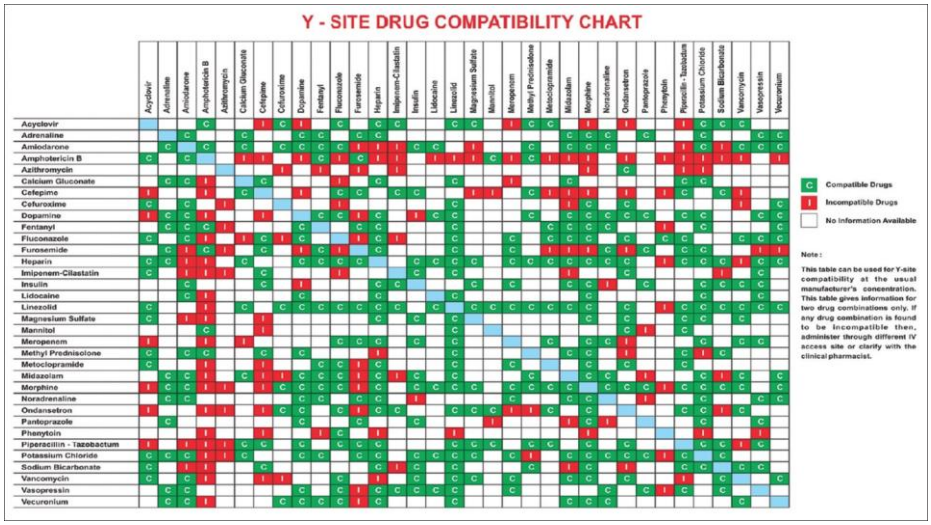

Figure1.

A total of 89 Y-site drug incompatibilities (55.6%) were detected .This investigation only address the risk of the incompatibility of drug pairs and is not based on whether the patient was actually harmed.

Types of Pharmacist care Intervention

Interventions were provided for 146 cases, of which suggestion accepted therapy not changed were found to be predominant which occurred for 60 cases (41.10%) followed by suggestion accepted therapy changed for 51 cases (34.93%), neither suggestion accepted nor therapy changed for 35 cases (23.97%).

Table 16: Acceptance of recommendation according to drug involved in DRP.

Acceptance of interaction	No. of cases (n=146)	Percentage%
Suggestion accepted therapy changed	51	34.93
Suggestion accepted but therapy not changed	60	41.10
Neither suggestion accepted nor therapy changed	35	23.97
Total	146	100.00

Predictors of occurrence of DRPs

The identification of risk factors for DRPs may be useful in finding patients at risk. These patients can then be given special attention, with the hope of avoiding DRPs. Gender, age, length of hospital stay, number of drugs, number of co-morbidities were analyzed to determine whether they could predict the occurrence of DRPs or not. Number of drugs was shown to be a risk factor for the occurrence of DRPs while gender, length of hospital stay, age and number of co-morbidities were not. As shown in table 17.2, Patients belonging to the group of major poly-pharmacy are 5.3 times more likely to develop drug related problem as compared to patients belonging to the group of minor poly-pharmacy.

Table 17.1: Associated factors for the occurrence of DRP's.

Variables	Category	DRP(YES/NO) Yes	No	Total	p value
Gender	Male	86	11	97	0.150
	Female	60	3	63	
Age	<60	92	10	102	0.532
	≥60	54	4	58	
Length of Hospital Stay (in days)	2-5	58	5	63	0.246
	6-9	68	9	77	
	>9	20	0	20	
No. of Drugs	<10	39	9	48	0.003**
	≥10	107	5	112	
Co-morbidity	0	22	5	27	0.138
	1-3	114	8	122	
	≥4	10	1	11	
Total		146	14	160	

Table 17.2: Influence of number of drugs as a risk factor for occurrence of DRPs.

Variable	Category	DRP Yes	No	Total	Odds ratio (95% CI)	P value
No. of Drugs	<10	39	9	48	1.0	
	≥10	107	5	112	5.29 (1.43-19.65)	0.013*

Comparison between parameters and classification of DRP's

Certain factors were found to have a statistically significant association with the domains of DRP's.

Adverse Drug Reaction

None of the parameter had a positive result of ADR.

Table 18: Comparison of factors and occurrence of Adverse Drug Reactions.

Factors		ADR reaction Yes	No	Total	p value
Gender	Male	5	92	97	0.478
	Female	5	58	63	
Elderly	Yes	5	53	58	0.350
	No	5	97	102	
Length of Hospital Stay (in days)	2-5	5	58	63	0.777
	6-9	4	73	77	
	>9	1	19	20	
Co-morbidity	0	1	26	27	0.220
	1-3	7	115	122	
	≥4	2	9	11	
Poly-pharmacy	Major	8	103	111	0.452
	Minor	2	47	49	
Total		10	150	160	

Drug-Drug Interactions

The parameter poly-pharmacy had a positive result of Drug-Drug Interactions ($p<0.000$). Also there was a significant association between Length of Hospital Stay and Drug-Drug Interactions.

Table 19: Comparison of factors and occurrence of Drug-Drug Interactions.

Factors		Drug-Drug Interactions Yes	No	Total	p value
Gender	Male	75	22	97	0.189
	Female	54	9	63	
Elderly	Yes	45	13	58	0.538
	No	84	18	102	
Length of Hospital Stay (in days)	2-5	47	16	63	0.044*
	6-9	62	15	77	
	>9	20	0	20	
Co-morbidity	0	20	7	27	0.471
	1-3	99	23	122	
	≥4	10	1	11	
Poly-pharmacy	Major	98	13	111	0.000**
	Minor	31	18	49	
Total		129	31	160	

Drug Choice Problems

The factor elderly had a positive statistical association with Drug Choice Problems ($p<0.000$).

Table 20: Comparison of factors and occurrence of Drug Choice Problems.

Factors		Drug Choice Problems Yes	No	Total	p value
Gender	Male	62	35	97	0.209
	Female	34	29	63	
Elderly	Yes	45	13	58	0.000**
	No	51	51	102	
Length of Hospital stay (in days)	2-5	37	26	63	0.881
	6-9	46	31	77	
	>9	13	7	20	
Co-morbidity	0	16	11	27	0.967
	1-3	73	49	122	
	≥4	7	4	11	
Poly-pharmacy	Major	71	40	111	0.123
	Minor	25	24	49	
Total		**96**	**64**	**160**	

Dosing Problems

Co-morbidities had a positive statistical association with Dosing Problems.

Table 21: Comparison of factors and occurrence of Dosing Problems.

Factors		Dosing Problems		Total	p value
		Yes	No		
Gender	Male	14	83	97	0.979
	Female	9	54	63	
Elderly	Yes	10	48	58	0.436
	No	13	89	102	
Length of hospital stay (in days)	2-5	6	57	63	0.209
	6-9	12	65	77	
	>9	5	15	20	
Co-morbidity	0	0	27	27	0.040*
	1-3	20	102	122	
	≥4	3	8	11	
Poly-pharmacy	Major	18	93	111	0.318
	Minor	5	44	49	
Total		**23**	**137**	**160**	

Comparison of with & without DRPs in relation to other variables

Mean number of drugs with DRP was 12.84 and without DRP was 9.43. There is a mean difference between two groups and this difference is statistically significant ($p<0.014$). Higher the number of drugs, chances of occurrence of DRPs was more. For other variables there is no mean difference.

Table 22: Comparison of with & without DRPs in relation to other variables.

Variables	DRPs		t value	p value
	Yes(n=146)	No(n=14)		
Age (in years)	52.83±16.89	47.93±18.51	0.953	0.355
Length of hospital stay (in days)	6.74±2.73	5.79±1.81	1.791	0.089
No. of comorbidities	1.47±1.10	1.14±1.29	0.923	0.371
No. of drugs	12.84±4.99	9.43±4.40	2.741	0.014

DISCUSSION

During this study period, a total of 160 cases were enrolled and the types of Drug related problems were identified and evaluated.

In this study, out of 160 patients 97 patients (60.6%) were males and 63 patients (39.4%) were females. This study revealed a male predominance over female which is similar to a study conducted by Dinesh R et al [5] and Sathish BP et al. [15]

The present study revealed that the patients belonging to the age group 40-60 years were more predominant which is in compliance with study conducted by Javedh Shareef et al. [16]

In this study, majority of the patients have co-morbidities between 1 to 3 followed by patient having co- morbidity more than or equal to 4 which was found to be similar to the study conducted by Javedh Shareef et al. [16]

Major poly-pharmacy was common in the hospitalized patients as 69.4% of the study patients were given more than 10 drugs during the hospital stay when compared to that of minor poly-pharmacy. This observation is contrast with the study conducted by Ramya Movva et al. [14]

Total number of drugs prescribed for patients during hospitalization was 2007 drugs.

The average number of drugs prescribed per patient was found to be 12.54. This result was observed in concordance with the study conducted by Rijo Mary George et al. [17]

Drug interactions (64.47%) were the predominantly occurring drug related problem followed by Drug Choice Problems (30.19%), Dosing Problems (3.77%) and ADR (1.57%). The finding were similar to study conducted by Sarfaraz Mohammed et al. [8]

A total of 410 drug interactions were observed in 146 cases. The majority of drug interactions were of moderate severity (51.46%) followed by interactions of minor severity (35.37%) and then major severity (13.17%). This coincides with the study conducted by A. Chandrakanth et al. [18]

The present study examined and categorized Drug Choice Problems into Inappropriate Drugs, Duplication of therapeutic group, Contraindications, Untreated Condition and Treatment without Indication. The most common drug choice problem identified was Inappropriate Drug with a number of 65 (33.85%) followed by 59 Duplications of therapeutic group (30.73%), 48 Untreated Conditions (25.00%), 12 Contraindications (6.25%) and 8 Treatments without Indication (4.17%). This result is in contrast with the study conducted by Hasniza Zaman Huri et al. [13]

Dosing Problems were categorized into Low dose, High dose and change in Duration of treatment. High doses were found to be more with a number of 16 (66.67%) followed by 7 Changes in the Duration of treatment (29.17%) and 2 Low doses (8.33%). This result is supported by the study conducted by Hasniza Zaman Huri et al. [19]

The most frequent ADR was caused by the drug class ARB/ Thiazide diuretic resulting in 2 ADRs (20.00%).This was in contrast with the result obtained by study conducted by Dinesh R et al. [5]

In the present study, the therapeutic agents most commonly involved in DRPs include Furosemide (41), Pantoprazole (40), Ondansetron (25), Piperacillin+Tazobactum (23), Ceftriaxone (23) which is contrasted with the study conducted by Jainaf Nachiya et al.[20]

The most frequent intervention provided by pharmacist was suggestion accepted, but therapy not changed (41.10%). The observation correlates with study conducted by A. Chandrakanth et al. [18]

Potentially inappropriate drug use in the elderly was assessed by Beers criteria which comprises a list of medications that pose potential risks outweighing potential benefits. A total of 26 drugs from Beers criteria were found to have been used inappropriately. Among which use of Acetaminophen was most common and showed the potential risk of GI bleeding followed by Tramadol which showed the potential risk of CNS adverse effects followed by Insulin which showed the potential risk of hypoglycaemia. This result obtained was contrasted to the study conducted Ogbonna B.O et al. [21]

Drug incompatibility is also considered likely to harm the patients. As a result of incompatibility, the drug either loses its efficacy or precipitates. In this study 13.9% Y-site drug incompatibilities were found which was found similar to study conducted by Mohamed Hisham et al. [24]

In the attempt to identify the risk factors associated with the occurrence of DRPs, the study showed that poly-pharmacy is an important risk factor for DRPs, whereas gender, age, length of hospital stay, and number of comorbidities did not have significant association with the occurrence of DRPs. This study is similar with the study conducted by Mohammed Biset et al. [22]

Comparison between factors and occurrence of DRPs were identified. Age had a positive statistical association with Drug Choice problem ($p< 0.002$). Comorbidity had a positive statistical association with Dosing problem ($p<0.040$). This observation is supported with the study conducted by Hasniza Zaman Huri et al. [23]

Comparison between patient with & without DRPs in relation to other variables was observed. Mean number of drugs with DRP was 12.84 and without DRP was 9.43. There is a mean difference between two groups and this difference is statistically significant. Higher the number of drugs, chances of occurrence of DRPs was more. For other variable there is no mean difference.

CONCLUSION

Out of 160 patients, 146 DRPs were identified among which Drug-Drug Interactions (410) were the most prominent DRP followed by Drug Choice Problems (192), Dosing Problems (24) and ADRs (10). ARB/Thiazide Diuretic was the drug that caused ADR frequently. The most common drugs involved in Drug-Drug Interactions was Azithromycin + Ondansetron (6), Ofloxacin + Ondansetron (6), Levofloxacin + Ondansetron (3), Ondansetron + Ivabradine (2). The most common drugs involved in the DRPs were Furosemide, Ondansetron, Pantoprazole, Piperacillin + Tazobactum and Ceftriaxone. The potentially inappropriate drugs prescribed for elderly patients were assessed as per Beers criteria. A total of 26 drugs from Beers criteria were found to have been used inappropriately. Among which, use of Acetaminophen was found to be the most common drug which presented potential risk of GI bleeding. Y-site drug incompatibility was found to be 13.9%. In our study there is a significant association between poly-pharmacy and DRP. Suggestion accepted but therapy not changed was more (41.10%) followed by suggestion accepted, therapy changed (34.93%) and neither suggestion accepted nor therapy changed (23.97%).In future, further research could be conducted based on this study.

LIST OF ABBREVIATIONS

ADR	:	Adverse Drug Reaction
DRPs	:	Drug Related Problems
NSAIDs	:	Non Steroid Anti- Inflammatory Drugs
PCNE	:	Pharmaceutical Care Network Europe
SD	:	Standard Deviation
T2DM	:	Type 2 Diabetic Mellitus
AMC	:	Adverse Drug Reaction Monitoring Centre
ICU	:	Intensive Care Unit
MICU	:	Medicine Intensive Care Unit
NSICU	:	Neurosurgery Intensive Care Unit
RSICU	:	Respiratory Intensive Care Unit
WHO	:	World Health Organisation
ASHP	:	American Society of Health-System Pharmacists
PAS	:	Problem Assessment Solutions
PI-Doc	:	Problem- Intervention- Documentation
ADE	:	Adverse Drug Events
TWI	:	Treatment Without Indication
UI	:	Untreated Indication
GI	:	Gastrointestinal Bleeding
CNS	:	Central Nervous System
ARB	:	Angiotensin II Receptor Blocker

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CONFLICT OF INTEREST

There is no conflict of interest among the authors.

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