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Original Research

Pattern of drug therapy related problems encountered by clinical pharmacists in a critical care setting in Nepal

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Abstract

Background: Most hospitalized patients experience Drug Therapy-Related Problems (DTRPs) resulting in morbidity, mortality, and an increase in the cost of treatment. DTRPs are an important issue and a serious yet preventable problem. **Objective:** To identify DTRPs in the department of critical care medicine of a tertiary care center in Nepal. **Methods:** This was a cross-sectional study carried out at the department of critical care medicine in a tertiary care hospital in Kathmandu, Nepal from August to November 2021. All the patients admitted to ICU/ high care unit (HCU) for more than 48 hours during the study period were recruited in this study. Two clinical pharmacists visited the ICU/ HCU daily to identify any drug therapy-related problems. The Pharmaceutical Care Network Europe (PCNE) Classification system version 9.1 was referred for the classification of identified DTRPs. Descriptive statistics were applied for demographic variables. The Chi-square test was used for categorical variables. Pearson correlation was used to study the relationship between patient variables and the number and types of DTRPs. **Results:** DTRPs were identified in 74.2% (n=89) of patients. More than one DTRP was identified in 38.5% of patients. The identified DTRPs were primarily classified into two sections: Problems and Causes. A total of 106 problems were identified among which unnecessary drug treatment (40.5%, n=43) was the most common problem. For the causes: total of 137 were identified, out of which the drug and dose selection accounted for 44.5 and 16.8%, respectively. The average DTRP per patient was 1.5± 0.7. Antibiotics 30 (22%) and multivitamins, 10 (7%) were the maximal involved in DTRPs. More DTRPs were observed in male patients (n=60, 80%). The association between dose selection and gender was significant. Drug selection issues were observed more in patients prescribed multiple drugs and with a shorter hospital stay. **Conclusion:** Most DTRPs identified in the study were those that could be prevented. More focus is needed on antibiotic usage in the ICU and special monitoring measures are needed for vulnerable patient groups such as the elderly. Inclusion of more clinical pharmacists can help to identify and mitigate DTRPs.

Keywords: drug therapy, problems, intensive care unit, Nepal

INTRODUCTION

Medicines (drugs) can be used for curing, preventing, and diagnosing diseases. They can also cause a threat to life if used inappropriately and lead to increased morbidity and mortality.[1] Drug-Therapy Related Problems (DTRPs) can be defined as an 'event or condition involving drug therapy that actually or potentially interferes with desired health outcomes'.[2] It includes medication errors, adverse drug reactions, and other issues such as drug interaction, drug selection, etc. Most hospitalized patients have drug-related problems resulting in morbidity, mortality, and an increase in the cost of treatment.[3,4] DTRPs can be considered as an important issue and are a serious yet preventable problem.[5-7]

Various classifications of DTRPs can be found in the literature.[8] The widely accepted Pharmaceutical Care Network Europe Foundation (PCNE) classification has divided drug-related problems into the problem and cause with a total of 12 domains. The PCNE classification has unique characteristics such as coding for the problem, classification of the actual or suspected cause of the problem, and intervention required to address the problem and its outcome. In the problem, the six domains are: adverse reaction, drug choice problem, dosing problem, drug use problem, interaction, and others. Similarly, under cause, the six domains are: drug/dose selection, drug use process, information, patient /psychological, logistics, and others.[2]

Owing to disease severity, complex treatment, acute organ dysfunction, and other co-morbidities, critically ill patients are more prone to DTRPs.[9] DTRPs can interfere with achieving optimal patient outcomes and clinical pharmacists (CP) can contribute to rational drug use by identifying and managing DRPs. Care of critically ill patients requires a multidisciplinary team approach with pharmacists being an important part of the team. In recent years, the role of the pharmacist in the intensive care unit (ICU) has been linked to better patient outcomes.[10-12] Various studies have shown that clinical pharmacists are in a

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better position to identify and resolve DTRPs.[13-15]

A study from Nepal showed the prevalence of medical error as 13.3%, the majority of which were avoidable.[16] Another study conducted by Garrouste-Orgeas *et al* involving 70 ICUs showed the rate of medical error as 2.1/1000 patient days and 26.8% of patients experienced at least 1 medical error.[9]

Nepal is a low-income developing country in South Asia. The common causes of DTRPs reported from Nepal are medication errors,[16-19] lack of drug information,[20] ADRs[21] drug-drug interactions[22-24] poor patient counseling services,[25] etc. DTRPs have led to irrational medicine use and are undoubtedly contributing to compromised patient safety and therapeutic failure.[3] The role of pharmacist in direct patient care including identification of DTRPs is still unrecognized in many hospitals.[26] Some earlier studies done in the intensive care unit of hospitals in Nepal have mainly focused on drug utilization, ADRs, and drug-drug interactions.[15,22,24] This will be the very first study in Nepal that will focus on broad DTRPs as per the classification of PCNE and will highlight the role of the pharmacist in identifying DTRPs in clinical settings. This study willadvocate for a multi-team approach for the minimization of drug-related problems.

The objective of the study

To identify drug therapy-related problems (DTRPs) in the department of critical care medicine in a tertiary care center in Nepal.

Ethics approval

The study was approved by the Institutional Review Committee (IRC) of Grande International Hospital, Nepal, and an official letter was obtained to start the study (Ref: 08/2021).

METHODS

Study design

This was a cross-sectional study carried out at the department of critical care medicine of a tertiary care hospital in Kathmandu, Nepal.

Study setting

The hospital has 20 intensive care beds and 10 high care beds managed by the Department of Critical Care Medicine.

Study subjects

All the patients admitted to ICU/ High Care Unit (HCU)for more than 48 hours during the period from August to November 2021were included in this study. A total of 120 patients were enrolled. Few of the patients were missed due to lack of follow-up, change in duty shifts, and public holidays.

Method of data collection

During the study period, two clinical pharmacists visited the ICU/ HCU daily to review the medication charts, laboratory investigation, and clinical notes of the patients to identify any DTRPs. The parts of the ICU/HCU were divided among the pharmacists so that the data collected did not duplicate each other. Information such as age, gender, comorbidity, length of stay, medication history, diagnosis, laboratory investigations, and medications used were recorded in a self-designed data collection form (Appendix I). The patients were followed up daily until their discharge or transfer from the ICU/HCU.

Identification of DTRPs

After the data collection, all the data were reviewed and discussed with the team to confirm the identified DTRPs. The appropriateness of drug choice and dosing were checked by comparing them with local and international treatment guidelines such as IDSA (Infectious Disease Society of America), WHO (World Health Organization), American Heart Association/ American College of Cardiology, Clinical Practice Guidelines, and also pharmacotherapy textbooks. UpToDate was used as an evidence-based source for evaluating the dosing and treatment pattern of drugs. Drug interactions were evaluated using the Medscape database, the easy availability, accessibility, and quick provision of medical information make it a good option for all healthcare professionals (HCPs). Thus, we preferred to use it in our study. Only significant and serious interactions found using this database were considered as DTRPs. Adverse drug reactions were suspected based on relevant laboratory investigations and in consultation with treating physicians. When the adverse drug reactions were observed, the date, the onset of the reaction, and the time of administration of the suspected drug were noted. The causal relationship between the suspected drug and the onset of the reaction was then identified and discussed with the HCPs to confirm the observed ADRs. All the identified DTRPs were then entered into an excel file for analysis.

Data analysis

The Pharmaceutical Care Network Europe (PCNE) Classification system version 9.1 was referred to for the classification of identified DTRPs as a problem, and cause for this study. The basic category has three primary domains for problems, further divided into six subdomains, and nine primary domains for causes which are further divided into 38 subdomains. A problem was defined as an expected or unexpected event/ circumstance that actually or might lead to t wrong drug therapy. Each problem or potential problem has a cause. There may be one or more causes for a single problem.

Descriptive statistics were applied for demographic variables. The Chi-square test was used for categorical variables. A confidence interval of 95% and *p-value* <0.05 were considered significant. Pearson correlation was used to study the relationship between patient variables and the number and types of DTRPs. The SPSS version 26.0 for Windows was employed for all statistical analyses.

Pilot study

A pilot study was conducted in which 6 (54.5%) patients out of 11 were identified to have DTRPs. No clear indication for the drug was observed in 22% followed by patients unable to take medicine as directed. Aspirin, voriconazole, and azithromycin were the drugs most involved in DTRPs.

RESULTS

A total of 120 patients were included in the study. Table 1 shows the demographic details of the patients.

Table 1. Demographic and health related details of study population

Variables	Frequency(N=120)
Gender Male Female	 77(64.2%) 43(35.8%)
Co morbidity Nil 1 ≥2	 27(22.5%) 30(25%) 63(52.5%)
Age group (in years) 17-30 31-45 46-64 >64	 19(15.8%) 17(14.2%) 40(33.3%) 44(36.7%)
Length of stay (days) <5 5-10 >10 Average length ICU stay(d)	 54(45%) 41(34.2%) 25(20.8%) 6.7±5.1
Number of medicines 6-10 11-15 >=16 Average number of medicines per prescription(N)	 30(25%) 44(36.7%) 46(38.3%) 15.5±6.6

The average DTRP per patient was 1.5± 0.7.

PCNE classification of problem and causes of DTRPs

DTRPs were identified in 74.2% (n=89) of patients. More than one DTRP was identified in 38.5%. The identified DTRPs were primarily classified into two sections: Problem and Causes. In the problem domain, a total of 106 problems were identified among which unnecessary drug treatment (40.5%, n=43) was the most common problem to be identified. Regarding the cause domain, a total of 137 causes was identified among which drug selection accounted for 44·5% of total causes followed by dose selection (16.8%) and drug use process (9·5%). Table 2 shows the number of problems and causes of DTRPs as per PCNE classification. Table 3 lists some of the commonly encountered DTRPs.

Drug class and individual drugs responsible for causing DTRPs (n=55)

The common drug class responsible for DTRPs were antibiotics (Figure 1) and the individual drug responsible was vitamin supplement. (Table 4)

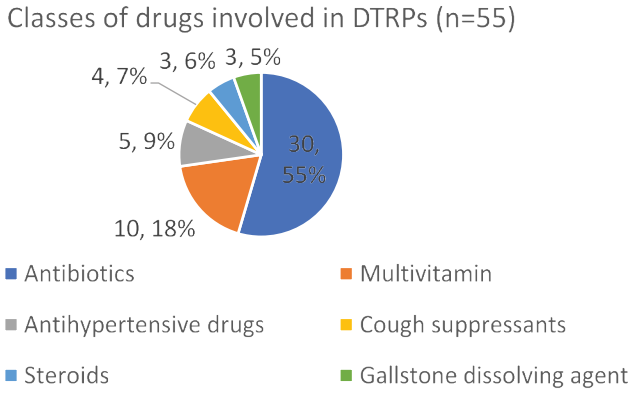

Figure 1. Classes of drugs involved in DTRPs (n=55)

The correlation between variables (Pearson correlation) and the level of association among causes of DTRPs

Correlations were seen between the cause of DTRPs and age, hospital stay, co morbidities, and previous medication use. Similarly, correlation existed among the number of DTRPs and age, the number of drugs, and comorbidities. Table 5 shows the correlation between patient variables and DTRPs. The correlation between variables (Pearson correlation) and the level of association among causes of DTRPs was calculated.

DTRPs were observed more in male patients (n=60,80%). The association between dose selection and gender was significant. Drug selection issues were more observed in patients prescribed multiple drugs and with a shorter hospital stay (Table 6).

DISCUSSION

In this study, DTRPs were identified in 74.2% (n=89) of patients.

Table 2: PCNE classification of problem and causes of DTRPs

DTRP pattern		n	%
	Patients with DRP (n, %)	91	75.8
	DTRPs	137	
	DTRPs per patient	1.5	
PRIMARY DOMAIN	PROBLEM		
1. Treatment effectiveness	P 1.1 No effect of drug treatment despite correct use	5	4.70
	P 1.2 Effect of drug treatment not optimal	12	11.30
	P 1.3 Untreated symptoms or indication	8	7.50
2. Treatment safety	P 2.1 Adverse drug event (possibly) occurring	10	9.40
3.Other	P 3.1 Unnecessary drug treatment	43	40.60
	P 3.2 Unclear problem	28	26.40

	CAUSE		
1. Drug selection	C 1.1 Inappropriate drug according to guidelines/formulary	10	7.30
	C 1.2 No indication for drug	25	18.20
	C 1.3 Inappropriate combination of drugs	2	1.40
	C 1.4 Inappropriate duplication of therapeutic group or active ingredient	11	8.02
	C 1.5 No or incomplete drug treatment in spite of existing indication	7	5.10
	C 1.6 Too many different drugs/active ingredients prescribed for indication	6	4.30
2. Drug form	C 2.1 Inappropriate drug form/formulation (for this patient)	3	2.2
3.Dose selection	C 3.1Drug dose too low	6	4.3
	C 3.2 Drug dose of a single active ingredient too high	9	6.6
	C 3.3 Dosage regimen not frequent enough	3	2.20
	C 3.4 Dosage regimen too frequent	4	2.90
	C 3.5 Dose timing instructions wrong, unclear or missing	1	0.70
4. Treatment duration	C 4.2 Duration of treatment too long	8	5.80
5. Dispensing	C 5.1 Prescribed drug not available	12	8.70
6.Drug use process	C 6.1 Inappropriate timing of administration or dosing intervals by a health professional	5	3.60
	C 6.2 Drug under-administered by a health professional	1	0.70
	C 6.3 Drug over administered by a heath professional	6	4.40
	C 6.4 Drug not administered at all by a heath professional	1	0.70
7.Patient related	C 7.1 Patient intentionally uses/takes less drug than prescribed or does not take the drug at all for whatever reason	2	1.50
	C 7.9 Patient physically unable to use drug/form as directed.	2	1.50
8. Patient transfer related	C 8.1 Medication reconciliation problem	3	2.20
9. Others	C 9.1 No or inappropriate outcome monitoring(incl.TDM)	1	0.70
	C 9.3 No obvious cause	9	6.6
	Total	**137**	

Table 3. Examples of few of the DTRPs identified by the CPs

Primary domain	**Code as per PCNE**	**Cause**	**Examples of patients identified with specified DTRP**	**Comments**
Drug selection	C1.2	No indication for drug	*Case 1:* A male patient in his mid-40 was admitted with altered sensorium for 14 days. He is a known case of chronic liver disease and diabetes mellitus. He had ascites for 1 year and came to his hospital on request from another hospital. During the course of his treatment, he was prescribed ursodeoxycholic acid which shows no benefit. *Case 2:* A 63-year female patient was admitted with post-COVID-19 pneumonia, hospital-acquired pneumonia, and septic shock. She is a known case of rheumatoid arthritis. She was prescribed calcium 500 mg Q12 H for no clear reason as her calcium level was within normal range. Regular prescribing of thiamine and multivitamin to patients without any indication was also common.	The use of medication like ursodeoxycholic acid and multivitamins were common as seen to be frequently prescribed though not recommended in most cases.
Dispensing	C5.1	Prescribed drug not available	*Case 1:* A 30 yrs. male admitted for a road traffic accident had blunt abdominal trauma (after embolization of right hepatic artery), soft tissue injury was initially required to cover for MSSA as post-surgical prophylaxis but drug unavailability lead to choosing some fewer effective drugs. Other patients with similar medical conditions faced problems due to drug unavailability. Unavailability of the drug is a DTRP.	The unavailability of recommended treatment options for methicillin sensitive staphylococcus aureus (MSSA) infection such as oxacillin, nafcillin (unregistered products), cefazolin (shortage product) forced to prescribe other less effective agents. Similarly, shortage of thiamine injection cause problem in management of alcohol use disorder particularly in suspicion of Wernicke's encephalopathy.

Drug selection	C1.4	Inappropriate duplication of therapeutic group or active ingredient	*Case 1*: 39 yrs. male admitted for acute febrile illness with Acute Kidney Injury was prescribed doxycycline and azithromycin both at the same time for atypical coverage. Both antibiotics show a similar spectrum so the use of both at the same time causes duplication of the therapeutic group. *Case 2:*42 yrs. male admitted for severe pancreatitis was prescribed imipenum+cilastin with suspicion of infected necrotizing pancreatitis, in addition to this metronidazole was added for anaerobic coverage. As per international guidelines, imipenem+cilastin itself provides excellent anaerobic coverage so the addition of metronidazole is a duplication of antibiotics coverage.	Duplication of therapeutic group has occurred in some cases. Combined prescribing of azithromycin with doxycycline for atypical coverage and metronidazole with carbapenem for anaerobic coverage have been observed.
Drug selection	C1.1	Inappropriate drug according to guidelines/ formulary	*Case 1:* A 48 yrs. male referred from other hospital with known case of hypertension and diabetes mellitus II was admitted with left posterior circulation secondary to occlusion to the left superior cerebellar basilar artery (post-status tracheostomy), bacteremia (Acinetobacter), and acute kidney injury later developed urinary tract infection (UTI). He was initially prescribed with nitrofurantoin for UTI.	UTI in male by virtue should be treated as complicated UTI and antimicrobial selected to treat such patients should penetrate prostrate sufficiently. As the patient is in the intensive care unit and critically ill, the choice of antibiotic (nitrofurantoin) may not be appropriate for complicated UTI.
Dose selection	C3.2	Drug dose of a single active ingredient too high	*Case 1:* A 45 yrs. patient admitted with severe COVID-19, bilateral hospital acquired pneumonia with methicillin resistance staphylococcus aureus (MRSA)), type 2 respiratory failure was prescribed dexamethasone 20 mg Q 24 H for 8 days whereas recommended dose is 6 mg Q 24 H. *Case 2:* 52 yrs. female was admitted with severe COVID-19 pneumonia and had a severe dry cough so she was prescribed codeine and dextromethorphan (160 mg/day). It exceeds recommended dose (120 mg/day).	Dose of some medicines like dexamethasone and dextromethorphan has exceed maximum recommended daily dose.
Treatment duration	C4.2	Duration of treatment too long	*Case 1:* A 64 yrs. an old patient was admitted for stroke and was prescribed the antibiotic ceftriaxone as prophylaxis for minor abrasions (no sign of infection) for more than 5 days. *Case 2:* A 46 yrs. old patient admitted for a suicidal attempt by ingesting toilet cleaner (Harpic) was prescribed antibiotic piperacillin-tazobactam with suspicion of pneumonia (high procalcitonin level: 41) was continued for 14 days despite clinical improvement and procalcitonin fallen by more than 80%.	Antibiotics were prescribed for more than recommended days.
Drug selection	C1.5	No or incomplete drug treatment in spite of existing indication	Case 1: 36 yrs. male admitted with conditions like seizures, leptospirosis, acute kidney injury and anxiety disorder was acutely ill but not prescribed DVT prophylaxis despite being medically restricted and correction of thrombocytopenia.	Venous thrombosis (VTE) prophylaxis was not prescribed in medically restricted acutely ill patients despite no contraindication to anticoagulants. Administration of heparin or anticoagulants prevent the incidence of deep vein thrombosis or pulmonary embolism in hospitalized patients.
Dose selection	C1.6	Too many different drugs/active ingredients prescribed for indication	*Case 1:* A 40 yrs. female was admitted for recurrent focal seizure (known case of mixed connective tissue disorder) and was treated with different medicines. She presented with symptoms of vomiting and diarrhea for which rifaximin, azithromycin, and metronidazole were prescribed. She was additionally prescribed vitamin D, zinc, phosphorus, thiamine, and methylcobalamin supplements. *Case 2:* A 35 yrs. male presented with cough and fever for 10 days and was helirescued with COVID-19. He was prescribed a number of antibiotics (piperacillin-tazobactam, meropenem, polymyxin B, ampicillin/sulbactam, cefoperazone-sulbactam, fosfomycin,, amikacin, tigecycline, cotrimoxazole,) with no benefit of one over the other. The patient did not survive.	Too many antibiotics were prescribed one after another empirically for suspected infection owing to patient's critical condition.

Dose selection	C3.1	Drug dose too low	*Case 1:* A 51 yrs. female was treated for Upper Gastrointestinal bleeding (esophageal varices), Chronic Liver Disease, Hepatic encephalopathy grade IV, Acute Kidney Injury, and Hepatorenal syndrome (HRS) were intubated after 3 days of her admission. She was given 20 gm albumin whereas the dose for HRS is 1 g/kg (pt weight 55kg) followed by 20-40 gm per day. Case 2: A 64 yrs. Female with uncontrolled diabetes mellitus 2 was treated for Tuberculosis (TB) meningitis and was not given the recommended dose of steroid dexamethasone i.e. 0.4 mg//kg for the first week. She was prescribed only given 24 mg/day (patient weight:75 kg) and doses of antimicrobials pyrazinamide and ethambutol were only prescribed 3 times a week despite normal renal function. Another case of chronic liver disease (64 yrs. female) with peritoneal TB was also prescribed a low dose of ethambutol and pyrazinamide.	Dose of medicines like dexamethasone and antitubercular agents were prescribed low than standard dose.
Drug use process	C6.3	Drug over administered by a heath professional	*Case 1:* A 70 yrs. the male was admitted for a road traffic accident had multiple fractures and complained of pain was prescribed fentanyl (IV) 74 mcg/hr. infusion in addition to fentanyl (IV) 50 mcg in between when needed and fentanyl patch 50 mcg. After a few hours, the patient was unresponsive (Heart Rate-160 beats per min/Blood pressure-.170/67mm hg. Fentanyl infusion was then stopped and the fentanyl patch was removed). He was given the opioid antidote naloxone and the patient regain consciousness.	Over prescribing of opioid has occurred which was reversed using antidote.

Table 5. Correlation between patient variables and DTRPs

Variables	**DTRPs**		**Number of DTRPs**	
	R	**p value**	**R**	**p value**
Age	-0.21	**0.02***	-0.18	**0.039***
Gender	-0.103	0.261	-0.044	0.635
Hospital stay	0.202	**0.026***	-0.054	0.557
Number of drugs	0.107	0.244	0.242	**0.007***
Co morbidities	-0.212	**0.019***	-0.196	**0.031***
Renal function	-0.122	0.183	-0.015	0.867
DM II	-0.086	0.351	-0.116	0.208

R=relation coefficient
*correlation significant at 0.05 level (two tail)

Table 4. Individual drugs responsible for DTRPs (Top ten only)

Drug name	**n**
Vitamin B-complex *	10
Azithromycin	9
Doxycycline	9
Cefazolin	5
Piperacillin-tazobactam	4
Metronidazole	4
Dexamethasone	4
Dextromethorphan	4
Prazosin	3
Ursodeoxycholic acid	3

*It includes vitamin preparations such as Fortiplex and Polybion

Table 6. Differences in main causes of DTRPs among different patient subgroups

FACTORS	**n**	**Number of DRPs**		**Drug selection**		**Dose selection**		**Drug use process**	
Gender		N	p value	n	P	n	P	N	p
Male	77	62	0.956	41	0.278	10	**0.039**	10	0.32
Female	43	29		19		13		3	
Geriatric									
yes	44	30	0.104	14	0.006	8	0.89	7	0.438
No	76	61		46		15		6	
Hospital stay									
<=5 days	67	48	0.856	44	0.722	12	0.617	9	0.853
>5 days	53	43		16		11		4	

Renal impairment									
yes	15	9	0.520	4	0.145	0	0.05	3	0.222
No	105	81		56		23		10	
DM									
yes	42	29	0.429	12	**0.012**	8	0.882	4	0.735
No	78	61		48		15		9	

Note: Bold values indicate a statistical significance

This is comparable to 73.9% and 71.5% reported from in similar studies that were carried out in Thailand[27] and Turkish respectively.[28] The average DTRP experienced per patient in the present study was 1.5± 0.7 and similar to that of DTRPs reported in a Turkish Hospital's ICU (1.36).[28] In general, ICU patients experience more DTRPs[9] and hence more stringent measures are needed to minimize the occurrence of DTPRs in ICUs than in the rest of the hospital. Like any healthcare facility, ICU drug use can be improved with proper drug selection, drug use, monitoring, and patient education. Most of these can be achieved by appointing clinical pharmacists in ICUs to identify and mitigate DTRPs. Though this has been a recent approach in many countries, the concept of clinical pharmacy is not well-established in Nepal. A non-randomized study from Turkey that assessed the impact of CPs contribution in reducing ICU DTRPs during which CPs intervened on DTRPs by interrupting/discontinuing the drug (28.02%), dose alteration (25.27%), modifying instructions for use (20.32%), and imitating treatment with a new drug (15.93%).[29] Multiple studies worldwide reported positive outcomes with CPs intervention.[7,10-13] The hospital in which the study was conducted had clinical pharmacists in the ICU and mitigated the DTRPs reported in the study. Though this has been a recent approach in many countries, the concept of clinical pharmacy is not well-established in Nepal. It is worth mentioning that Pharmaceutical care services are not well established in Nepal. Various challenges have been reported in practicing pharmaceutical care in Nepalese Hospitals.[30] Hence policy-level and institution-level initiatives are needed to minimize DTRP occurrence in the hospitals in the country.

A deeper assessment of the types of DTRPs showed unnecessary drug treatment accounted for highest number (40.5%) of DTRPs. An analysis of causes behind DTRPs showed drug selection problems being the most typical cause accounting for 44.5% of total reasons followed by dose selection (16.8%) and drug use process (9.5%). In the Turkish study, the common DTRPs were potential DDIs (31.76%), wrong dose (12.44%), and errors in dose timing (9.24%).[28] In the Thai study, the common DTRPs were wrong dose (27.7%), selection of ineffective drug (17.2%), need for additional drug therapy (15.3%), use of unnecessary medicines (14.6%), and ADRs (9.7%).[27] A broader look at these DTRPs shows that in most cases the pattern of DTRPs is nearly the same and hence focus should be on measures to deal with the DTRPs than the identification of the types. It is worth recommending future research to focus on novel initiatives to prevent DTRPs.

The findings of the study show that a good percentage of DTRPs can be prevented by proper selection and rational use of a few drugs such as vitamin supplements and antimicrobials (azithromycin, doxycycline, cefazolin, piperacillin-tazobactam, and Metronidazole) (Table 4). An in-depth assessment shows antibiotics are the major culprits for DTRPs (Figure 1) and hence serious measures are needed to develop and implement antibiotic prescribing guidelines. Our findings agree with another study wherein antibiotics accounted for 62.2% of the DTRPs.[31] Multiple studies have previously reported irrational use of antibiotics in Nepal.[32-35] In line with previous studies, the present study also reported antibiotics as the major group of medicines contributing to DTRPs. Multiple previous studies have analyzed antibiotic use in hospitals and the prevalence of antimicrobial resistance.[35-39] A probable reason for antibiotics contributing to more DTRPs could be due to the fact that often multiple antibiotics are used in patients in previous hospitals prior to visiting the current one due to which physicians may be forced to use a higher generation antibiotic. Further, there is a lack of a system for maintaining antibiograms for hospitals linked to poor data management and retrieval.

In this research, correlations were seen between the cause of DTRPs and age, hospital stay, co-morbidities, and previous medication use (Table 5). In a multicenter study from the UK, authors performed logistic regression to explore if clinical demographics predicted a clinically significant medication-related problem and authors found hospital length of stay, and number of ICU discharge medications, had significant associations with DTRPs.[40] Findings suggest the need for measures to monitor vulnerable patient populations (such as elderly, patients with an increased length of ICU stay, multiple medications etc.) who are more likely to experience DTRPs.

LIMITATIONS

The DTRPs were identified by CPs but not verified by the treating physicians. This could have probably led to an over-reporting of DTRPs. The ICU studied in this research is from a single multispecialty referral hospital hence the pattern may not be generalized to all hospitals in the country. The COVID-19 pandemic could have probably influenced the overuse of antibiotics and aggressive treatment of patients with any respiratory symptom contributing to a greater number of DTRPs.

RECOMMENDATIONS

A high occurrence of DTRPs suggest the need for initiatives to minimize their occurrence. Since the CPs (researchers in this

study) were able to identify the DTRPs, it is justifiable to add more CPs in the ICUs which could probably help minimize the DTRP burden. Implementation of standard treatment guidelines, and antimicrobial stewardship programs can be beneficial in minimizing DTRPs.

CONCLUSIONS

A high prevalence of easily identifiable DTRPs were observed in this study. Identification of DTRPs is the initial step towards DTRPs mitigation. Most DTRPs identified in the study are easily preventable ones with changes in the drug use process. More focus is needed on antibiotic usage in the ICU and special monitoring measures are needed for vulnerable patient groups such as the elderly and patients with an extended duration of hospital stay. A close stewardship in medicine use process program and adding more clinical pharmacists can help identify and mitigate DTRPs.

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CONSENT

I have read and agree to the privacy policy.

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ANNEXURE 1

Data collection tool

Patient ID	
Age	
Gender	
Length of stay	
History of present illness	
Past Medical condition	
Medication history	
Presenting symptoms	
Laboratory investigation	
Provisional diagnosis	
Final diagnosis	

Drug used with dose and duration

S.No	Name of Medicine dose	Morning	Afternoon	Evening	Night	Duration

Discharge/transfer Medications (generic name, dose, duration)

S.No	Medicine Name and Dose	Duration

Suspected ADR(YES/No)
If yes, elaborate……..

Drug therapy related problems (DTRPs)

Tick the appropriate box:

PRIMARY DOMAIN	PROBLEM	n	%
1.Treatment effectiveness	P1.1 No effect of drug treatment despite correct use		
	P1.2 Effect of drug treatment not optimal		
	P1.3 Untreated symptoms or indication		
2. Treatment safety	P2.1 Adverse drug event (possibly) occurring		
3. Other	P3.1 Unnecessary drug treatment		
	P3.2 Unclear problem		
	CAUSE		

1. Drug selection	C1.1 Inappropriate drug according to guidelines/formulary		
	C1.2 No indication for drug		
	C1.3 Inappropriate combination of drugs		
	C1.4 Inappropriate duplication of therapeutic group or active ingredient		
	C1.5 No or incomplete drug treatment in spite of existing indication		
	C1.6 Too many different drugs/active ingredients prescribed for indication		
2. Drug form	C2.1 Inappropriate drug form/formulation(for this patient)		
3. Dose selection	C3.1Drug dose too low		
	C3.2 Drug dose of a single active ingredient too high		
	C3.3 Dosage regimen not frequent enough		
	C3.4 Dosage regimen too frequent		
	C3.5 Dose timing instructions wrong, unclear or missing		
	C4.1 Duration of treatment too short		
4. Treatment duration	C4.2 Duration of treatment too long		
5. Dispensing	C5.1 Prescribed drug not available		
	C5.2 Necessary information not provided or incorrect advice provided		
	C5.3 Wrong drug, strength or dosage advised (OTC)		
	C5.4 Wrong drug or strength dispensed		
6. Drug use process	C6.1 Inappropriate timing of administration or dosing intervals by a health professional		
	C6.2 Drug under-administered by a health professional		
	C6.3 Drug over administered by a heath professional		
	C6.4 Drug not administered at all by a heath professional		
	C6.5 Wrong drug administered by a health professional		
	C6.6 Drug administered via wrong route by a health professional		
7. Patient related	C7.1 Patient intentionally uses/takes less drug than prescribed or does not take the drug at all for whatever reason		
	C7.2 Patient uses/takes more drug than prescribed		
	C7.3 Patient abuses drug (unregulated overuse)		
	C7.4 Patient decides to use unnecessary drug		
	C7.5 Patient takes food that interacts		
	C7.6 Patient stores drug inappropriately		
	C7.7 Inappropriate timing or dosing intervals		
	C7.8 Patient unintentionally administers/uses the drug in a wrong way		
	C7.9 Patient physically unable to use drug/form as directed.		
	C7.10 Patient unable to understand instructions properly		
8. Patient transfer related	C8.1 Medication reconciliation problem		
9.Others	C9.1 No or inappropriate outcome monitoring(incl.TDM)		
	C9.2 Other cause; specify		
	C9.3 No obvious cause		
	Total		