Identifying Drug Related Problems in department of nephrology at a rural set up

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ABSTRACT: Background and purpose: Drug Related Problem is defined as an extent or circumstance involving drug treatment that actually or potentially interferes with the patient experiencing an optimum outcome of medical care. Drug Related Problems are of two types actual DRP and Potential DRP. Clinical pharmacist has a significant role in identification, prevention and management of the drug related problem.

Materials and methods: A total of 184 patients visiting nephrology department were enrolled in this prospective study for a period of 6 months in Warangal region.

Results: Of 184 patients, 94.5 %, 2 %, 1.2 %, 1.07 %, 0.3 % and 0.17 % were drug drug interaction, adverse reaction and treatment effectiveness, non adherence, medication error and over dose and contraindication respectively.

Conclusion: Anti-hypertensive drugs, antibiotics are the major class of drugs which cause DRPs. Drug interactions, non-adherence and ADRs are most frequently observed DRPs.

Key Words: Drug Related Problem, Adverse Drug Reaction

INTRODUCTION
Drug Related Problem (DRP) is defined as an extent or circumstance involving drug treatment that actually or potentially interferes with the patient experiencing an optimum outcome of medical care [1]. DRPs can increase the carrying cost and also can block the attained of the therapy purposed [2]. One of the factors for identifying DRPs is use of electronic prescription and for improving the drug safety [3]. The core process of pharmaceutical care is identification, prevention and solution of DRPs [4]. The purpose of identifying DRPs is to realize the best possible outcomes from drug therapy and help to the patients achieve their goals of therapy [5]. Therefore, through knowledge of DRPs may benefit health care professionals including pharmacists to identify DRPs, resolve actual DRPs and prevent potential DRPs in order to optimise patients’ outcomes [6], 50-80 % of the drug related problems can be prevented by pharmacist intervention [7]. There are two types of DRPs: Actual DRP and potential DRP.

Actual DRP: An actual drug related problem is defined as an event which is already seen in patients due to the drugs which are administered without involvement of pharmacist.

Potential DRP: Potential drug related problem is defined as an event that occurs in the absence of pharmacist intervention.

The most important drug related problems include adverse drug reactions (ADRs), drug interactions (DIs) and therapeutic failure [8].

Types of drug related problems:
HELPER AND STRANDS classified the DRPs into 8 categories: [9]
i. Adverse drug reaction (ADR)
ii. Drug interaction (DI)
iii. Failure to receive drug
iv. Sub therapeutic dosage
v. Over dosage
vi. Indication without drug therapy
vii. Drug use without indication
viii. Inappropriate drug selection

i. Adverse drug reaction (ADR):
According to WHO an adverse drug reaction (ADR) is defined as a response to a drug which is noxious and unintended and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy for a disease and for the modification of function excluding failure to accomplish the intended purpose. Drug
administration either alone or combination can leads to ADR. When the number of medications administered increases the frequency of ADR increases [10]. ADRs are major cause for morbidity and it accounts mostly 5% of hospitalised patients all over the world. ADRs are 4th leading cause of death in pulmonary disease, diabetes mellitus, AIDS, pneumonia and automobile death conditions [10]. Ex: theophylline induced anxiety and seizure [10]; methylxanthines induced hypokalaemia [11].

**ii. Drug interactions (DIs):**

**Drug-drug interaction:**

Drug-drug interaction can be defined as a change in a drugs effect on the body when the drug is taken together with a second drug [12]. A drug-drug interaction can delay, decrease, or enhance absorption of either drug. This can decrease or increase the action of either or both drugs or cause adverse effects [11]. More number of drugs prescribed in elderly is more prone to drug-drug interactions. Patient factors, prescriber factors, and communication between health professional and patient are the patient’s risk factors for drug-drug interactions [13]. Interactions can be prevented by avoiding multiple drug treatment and potential benefits of drug combination [13]. Ex: combination of linezolid and theophylline, linezolid may enhance the hypertensive effect of sympathomimetic [11], combination of amlodipine and labetalol cause bradycardia [12].

Drug-drug interactions include Pharmacokinetic interactions and pharmacodynamic interactions. Pharmacodynamic interactions are mainly synergism, antagonism and additive effect; synergistic is one of the most pharmacodynamic interactions [14]. Ex: efficacy of inhaled corticosteroids might be reduced in patients with asthma and COPD. Higher doses of inhaled corticosteroids are required in patients with asthma who smokes [15]. Pharmacokinetic type of interaction which affects the drug absorption, distribution, metabolism and elimination. The most pharmacokinetic interaction is metabolism [14]. Ex: smoking and theophylline; theophylline has a narrow therapeutic window dose adjustment is done in the smoking patients [15].

**Drug-food interaction:**

Drug-food interactions occur when food and medicine interfere with one another. Interactions can happen both prescription and over the counter medicines. These include antacids, vitamins and iron pills [16]. Interaction between food and drugs can produce negative effects in safety and efficacy of drug therapy and nutritional therapy. They may increase or decrease the drug effect. Taking one hour before or 2 hours after eating interactions can be avoided [14]. Ex: while taking ACE inhibitors potassium containing foods are avoided like banana, sweet potato etc.. [16].

**Drug-disease interaction:**

Drug-disease interaction is an event in which a drug intended for therapeutic use causes some harmful effect in a patient because of disease or condition that the patient has. There are some diseases that alter the body ability to metabolize or breakdown, a drug so that it can have the intended effect [17]. These interactions can occur in any age group people but more common in elderly people and who are having a greater number of diseases. For example, beta blockers are taken for hypertension can worsen the asthma [18].

**iii. Failure to receive drug:**

Failure to receive drug is defined as a deviation from the prescribed medications because of a choice, non-comprehension or forgetfulness [19]. Ex: Iron preparations, multivitamins, paracetamol, phenytoin [7].

**iv. Sub therapeutic dosage:**

It can be defined as if the prescribed dose was less than recommended dose [19]. Ex: according to indication or guidelines; budesonide inhaler-pregabalin [20], amoxicillin-calcium [19], telmisartan-metoprolol [7].

**V. over dosage:**

Over dosage can be defined as if the prescribed dose was too high in relation to the patient’s renal function, liver function or age; Ex: Gabapentin and allopurinol dose was not adjusted in renal function patients.

**VI. Indication without drug therapy:**

If a patient had an unnecessary drug therapy this was classified as indication without drug therapy [19]. Ex: calcium and vitamin D, omeprazole, potassium, prednisolone [20].

**VII. Drug use without indication:**

Inappropriate drug use according to explicit Swedish criteria and inappropriate drugs according to renal function or disease were classified as inappropriate or ineffective drug. Ex: antidiabetic agents like Metformin and Glibenclamide [19].
VIII. Medication error:
The National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) defines a "medication error" as "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer". Types of Medication Error include prescription error, dispensing error and administration error.

MATERIALS AND METHODS
A total of 184 patients attending nephrology department were subjected to prospective study for a period of 6 months in Warangal region at SVR Hospital, Hanumakonda after obtaining approval from Institutional Ethics Committee. Every individual patient was approached before and after consultation with the Clinician. Nature and purpose of the study have been explained to every individual person and informed consent was obtained. Patients prescribed with more than one drug were included in the study. Information was collected from the case sheets, patients and their care givers.

RESULTS

Table 1: Types of drug related problems and percentage of drug related problem

<table>
<thead>
<tr>
<th>Drug related problems</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug drug interaction</td>
<td>94.5 %</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>2 %</td>
</tr>
<tr>
<td>Treatment effectiveness</td>
<td>2 %</td>
</tr>
<tr>
<td>Non adherence</td>
<td>1.2 %</td>
</tr>
<tr>
<td>Therapeutic duplication</td>
<td>1.07 %</td>
</tr>
<tr>
<td>Medication error</td>
<td>0.3 %</td>
</tr>
<tr>
<td>Over dose</td>
<td>0.3 %</td>
</tr>
<tr>
<td>Contraindication</td>
<td>0.17 %</td>
</tr>
</tbody>
</table>

Table 2: percentage of drug related problems in male and female patients

<table>
<thead>
<tr>
<th>Drug related problems</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug drug interaction</td>
<td>61 %</td>
<td>39 %</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>66.6%</td>
<td>33.3%</td>
</tr>
<tr>
<td>Treatment effectiveness</td>
<td>67 %</td>
<td>33 %</td>
</tr>
<tr>
<td>Non adherence</td>
<td>50 %</td>
<td>50 %</td>
</tr>
<tr>
<td>Therapeutic duplication</td>
<td>100%</td>
<td>0 %</td>
</tr>
<tr>
<td>Medication error</td>
<td>100%</td>
<td>0 %</td>
</tr>
<tr>
<td>Over dose</td>
<td>100%</td>
<td>0 %</td>
</tr>
<tr>
<td>Contraindication</td>
<td>100%</td>
<td>0 %</td>
</tr>
</tbody>
</table>

Table 3: Drug related problems Vs Patient age group

<table>
<thead>
<tr>
<th>Drug related problems</th>
<th>Age group (in years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug drug interaction</td>
<td>31-40</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>21-30</td>
</tr>
<tr>
<td>Treatment effectiveness</td>
<td>61-70</td>
</tr>
<tr>
<td>Non adherence</td>
<td>21-30</td>
</tr>
<tr>
<td>Therapeutic duplication</td>
<td>41-50</td>
</tr>
<tr>
<td>Medication error</td>
<td>61-70</td>
</tr>
<tr>
<td>Over dose</td>
<td>51-60</td>
</tr>
<tr>
<td>Contraindication</td>
<td>61-70</td>
</tr>
</tbody>
</table>

DISCUSSION
Among 184 patients, drug-drug interactions accounted for 94.5 %, adverse drug reactions accounted for 2 %, non-adherence 1.2 %, therapeutic duplication 1.2 %, treatment effectiveness 0.5 %, medication errors 0.3 % and over dose 0.3 %. Of 184 patients, 64.1 % were male and 35.8 % were female. Most of the patients had 6-7 drugs prescribed in this department.

Drug Interactions:
According to our study, 94.5 % DRPs were drug-drug interactions and they were observed more in male patients (61 %) compared to female (39 %). Similar observations were made by Sibi C Chacko et al., 2016.
Hospitalized patients with severe illness were more prone to drug interactions due to presence of more than one comorbid condition demanding a greater number of drugs. In our study, hypertensive patients were found to have more number of drug interactions. Drug-drug interactions were observed more in patients above 50 years of age, which is similar to the findings of Enugu Adana Onyedikachi et al., 2017 [21]. Contrast to our study Maxwell O Adibe et al., 2017 [22] observed 36.7 % drug interactions. Drug interactions in our study were observed more with concomitant use of metoprolol with prazosin, metolazone with torsemide and calcium with ferrous fumarate.

Adverse drug reactions & treatment effectiveness:
In our study, 2 % adverse drug reactions were observed of which 60 % were male & 40 % were female patients, which are found to be similar to the study conducted by Aster Wakjira Garedow et al., 2016 [23]. The failure of treatment effectiveness is observed in 0.5 % patients among which 66.6 % were male and 33.3 % were female which is in contrast to the findings of Hesty U.Ramadaniati et al., 2016[6] wherein they observed 47.1 % ADRs and 28.7 % failure of treatment. The less number of ADRs and failure of treatment effectiveness could be due to rational use of the drugs.

Medication error & over dose:
According to our study, 0.3 % male patients were identified with medication error and drug over dose. A Study conducted by Ghazal vessal 2010 [24] observed 16 % medication error and 12.8 % drug over dose in 76 patients. In our study, less number of medication error and over dose were due to constant monitoring of patient's condition by clinician regularly during clinical rounds. It may also be attributed to active participation of other healthcare professionals in monitoring patients.

Contraindications:
In our study 0.17 % male patients were found to be prescribed with contraindicated drugs. In contrast to our study higher percentage (14 %) contraindications were observed by Adel Yousess et al., 2015 [25] despite using health information technology adopting system like CDSS, which is designed to support physician and other healthcare professionals in clinical decision making. Where as in our study, without implementing of following CDSS, contraindications were observed in small number of patients which reflects team work of all health care professionals and sound clinical knowledge of physician regarding drug combinations used in comorbid conditions and chronic conditions.

Non-adherence:
Of 1.2 % non-adherence patients, 67 % were male and 33 % female which is similar to the study conducted by Savitha R S et al., 2020 [26]. The less incidence of non-adherence may be due to elder patients being regular with their hospital visits, religious intake of drugs without failure. Another reason could be rational drug therapy and as most of the patients were hospitalized, medication therapy management was done properly. In contrast, Shiva Kala et al., 2019 [27] observed non-adherence in greater number of patients due to forgetfulness and high cost of medications.

Therapeutic duplication:
In our study, 1.07 % were therapeutic duplication 50 % were male and 50 % were female patients. Similar study was conducted by Vishwam K Subeesh et al 2016 [28] observed 4.4 % therapeutic duplications. The occurrence of therapeutic duplication may be due to not discontinuing previous medication before initiation of new therapy.

CONCLUSION
In our study, DRPs such as drug-drug interactions, adverse drug reactions, non-adherence, treatment effectiveness, therapeutic duplication, medication error, over dose were observed. Polypharmacy, multiple co-morbid conditions, age, lack of awareness and irrational use of drugs were the major risk factors for DRPs. Anti-hypertensive drugs, antibiotics are the major class of drugs which cause DRPs. Drug interactions, non-adherence and ADRs are most frequently observed DRPs. Clinical pharmacist has important role in management of treatment, patient counseling, creating awareness of disease and drug and thus help in early detection of DRPs so that overall treatment cost can be reduced and patients can be benefited with maximum therapeutic outcome.

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