Assessment of Drug Related Problems in Medical Wards of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

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This is to certify that the thesis prepared by Mohammed Biset entitled 'assessment of drug related problems in medical wards of Tikur Anbessa Specialized Hospital' and submitted in partial fulfillment of the requirements for the degree of master of Pharmacy in pharmacy practice complies with respect to originality and quality.

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Abstract

Assessment of drug related problems in medical wards of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

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Drug related problems are common in hospitalized patients. Ten to thirty percent of hospital admissions are thought to be directly related to drug related problems. Drug related problems may lead to reduced quality of life, increase hospital stay, increase overall health care cost and even increase the risk of morbidity and mortality. Data regarding drug related problems in inpatient settings in Ethiopia is limited. This study was aimed to assess drug related problems in the internal medicine wards of Tikur Anbessa Specialized Hospital. A prospective cross sectional study was conducted on 225 patients admitted in medical wards of TASH. Drug related problems were identified through review of patients' medical charts. In addition to this, discussion with patients and physicians was conducted to get supplementary information and clarification on some patient's medical information. Data regarding patient characteristics, medications, diagnosis, length of hospitalization, investigation and laboratory results were collected. Epi Info 7 was used for data entry and data was analyzed using SPSS version 21. Descriptive statistics, cross-tabs, binary and multiple logistic regressions were utilized. $P < 0.05$ was used to declare association. Drug risk ratio was used to identify drugs that were prone to create DRP. DRP was found in 52 % of study subjects. Drug interaction (48 % of all DRPs) was the top ranking DRP followed by ADR (23%). Antibiotics were common to be involved in DRP followed by GI medicines, CNS drugs and medicines affecting the blood. Cimetidine, tramadol, heparin and warfarin were the top ranking drugs involved in DRP. Gentamycin, warfarin, nifedipin, cimetidine, simvastatin, prednisolone, digoxin and pethidine were drugs with the highest drug risk ratio. The number of drugs taken by the patient per day is an important risk factor for DRPs. There was no significant association between occurrence of DRP and sex, age, hospital stay and number of co-morbidity in the study subjects.

Key words: Drug related problem, Tikur Anbessa Specialized Hospital, Medical wards

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List of abbreviations and acronyms

ACEI	Angeostensin Converting Enzyme Inhibitor
ADR	Adverse Drug Reaction
Anti TB	Anti-tuberclosis
ASA	Acetyl Salicylic Acid
AV block	Atrioventricular block
DRPs	Drug Related Problems
DM	Diabetes Mellitus
DVT	Deep Vein Thrombosis
GI	Gastro-intestinal
ICU	Intensive Care Unit
INR	International Normalized Ratio
KCl	Potassium Chloride
MEs	Medication Errors
NSAIDs	Non Steroidal Anti-inflammatory Drugs
PCP	Pneumocystis Carinii Pneumonia
SCr	Serum Creatinin
TASH	Tikur Anbessa Specialized Hospital

1. Introduction

1.1 Back ground

In the case of most diseases drug therapy will enhance health-related quality of life. However, inappropriate use of drugs may be harmful and lead to drug therapy problems (Fita et al. 2008). In order to achieve a quality health care service inappropriate use of drugs that potentially lead to problems should be identified and corrected. The philosophy of optimizing the outcomes of pharmacotherapy and pharmaceutical care lead to the concept of drug related problems or DRPs, indicating some problem in the pharmacotherapy of the patient (Vanmil et al. 2004). Drug-related problems (DRPs) therefore are defined as 'events or circumstances involving drug therapy that actually or potentially interfere with desired health outcomes (*PCNE Classification V 6.20,* 2010). An actual problem has resulted in clinical manifestations like adverse drug reaction or therapy failure. A potential problem is not manifest, but if left unresolved, it may lead to drug-related harm to the patient (Satish et al. 2013).

An infinite number of drug therapy problems exist because of the rapidly expanding array of drug products available, the growing number of diseases being recognized & diagnosed, and the growing number of patients entering the health care system. All patient problems involving medications can be categorized into one of the seven types of drug related problems. These include unnecessary drug therapy, need for additional drug therapy, ineffective drug, dosage too low, adverse drug reaction, dosage too high and noncompliance (Cipolle et al. 2004).

It would be much better to prevent drug related problems than to correct them. But this is not always possible because of the complexity of pharmacotherapy, lack of training and knowledge of health care providers and the behavior of medicine users (Bergkvist et al. 2011). Also, some pharmacotherapy problems are the result of an unexpected reaction of the individual, like allergies, and cannot always be predicted (Foppe. 2005). Therefore, even if one could analyze the medication and patient related factors during a medication review before a medicine is handed over to the patient, the evaluation of pharmacotherapy after it has been initiated still remains necessary to detect DRPs and optimize outcomes.

1.2 Statement of the problem

Although medications play an important role in the cure, palliation and prevention of disease, they also expose patients to drug-related problems (Gillespie et al. 2009). Drug-related problems (DRPs) are a major safety issue for hospitalized patients (Lampert et al. 2008). Drug related problems may lead to reduced quality of life, increased hospital stay, increased overall health care cost and even increases risk of morbidity and mortality (Satish et al. 2013). More people die of inappropriate drug treatment than from breast cancer, AIDS and traffic accidents all together (Kohn et al. 1999). An Institute of Medicine report estimated that between 44,000 and 98,000 people in U.S hospitals die each year because of medical errors (Institute of Medicine, 1999). It is estimated that the annual cost of drug-related morbidity and mortality is nearly $ 177 billion in the United States. Twice as much money is used to solve drug related problems and adverse drug events than on the drug themselves (Ernst & Grizzle. 2000).

Hospitalized patients are more likely exposed to poly pharmacy. This in turn is a concern for potential drug related problems (Winterstein et al. 2002). Some of the DRPs exist at the time of admission to hospital, while others arise during hospital management. On average 2.6 DRPs occur per patient in internal medicine wards in Norway and the presence of DRPs increased approximately linearly with the number of drugs used (Krahenbuhl et al. 2007). At least 22% of the discharged patients in Spain experience real or potential DRPs (Lỏpez et al. 2010).

In one of the studies in Jimma University Specialized Hospital, Ethiopia, drug related problems were identified in 73.5 % of study subjects. In the United States healthcare system, drug related problems (DRP) are implicated in 16.1% of internal medicine ward hospital admissions, of which 58.9% could definitely or possibly be avoided (Lagnaoui et al. 2000). Overall, 10 to 30% of hospital admissions are thought to be directly related to drug related problems (DRPs) (Krahenbuhl et al. 2007).

1.3 million People are injured each year due to medication errors (Rao et al. 2007). In an Australian study of 28 hospitals, ADEs occurred in 16.6% of admissions, resulting in permanent disability in 13.7% of patients and death in 4.9% (Bosma et al. 2007). Various studies state that the majority of DRPs could have been avoided, reporting a preventability of about 70% (Gillespie et al. 2009; Langebrake et al. 2010).

Several studies conducted in different countries showed a high incidence of drug related problems among hospitalized patients (Krahenbuhl et al. 2007; Bosma et al. 2007; Langebrake et al. 2010; Bruno et al. 2008). But studies related to drug therapy problems are limited in Ethiopia and so this study will add information regarding DRPs in Ethiopian tertiary care hospital settings. In addition, the paper may be useful to other researchers as a reference material while conducting further studies on related topics. Identification and intervention on actual and potential DRPs, along with awareness of drugs carrying a high risk for DRPs, are important elements of drug therapy and may contribute to diminishing drug related morbidity and mortality. The findings of this study might also help in influencing the development of appropriate policies, plans and intervention programmes for the prevention and management of drug therapy problems. This in turn, might improve the quality of care for patients admitted in hospitals.

1.3 Literature review

1.3.1 Prevalence of drug related problems

The prevalence of drug related problems varies through different studies. Some reported higher figures with a prevalence of more than 70 % (Annemie et al. 2013; Trine et al. 2013; Tigabu et al. 2014; Fita et al. 2008; Blix. 2007; Bertrand et al. 2013), while others reported a relatively lower frequency (less than 30 %) (Gopal et al. *2011;* Satish et al. *2013;* Al-Hajje. 2012; Mekonnen et al. 2013).

A study in Jimma Ethiopia by Tigabu et al (2014) found that 73.5% of patients in the internal medicine wards of jimma university specialized hospital had one or more DRPs. Among 257 patients involved in the study a total of 316 DRPs were identified in 189 patients making the average number of DRPs 1.2 per patient. A single DRP was identified in 97 (37.7%) of patients while 92 patients had 2 or more DRPs. From the six classes of DRPs addressed by the study, 103 (32.6%) cases were related to untreated indication or need for additional drug therapy, and 49 (15.5%) cases were related to high medication dosage. Unnecessary drug therapy in 49 (15.5%) cases, low medication dosage in 44 (13.9%) cases, and ineffective drug therapy in 42 (13.3%) cases were the other classes of problems identified. Noncompliance in 31 (9.8%) cases was the least prevalent DRP (Tigabu et al. 2014).

Another study at three Danish hospitals had identified drug-related problems in 85 % of the patients. The most frequent types of interventions given by clinical pharmacists were ‘changed drug’, ‘drug stopped’, ‘prescriber informed’, ‘changed dose’ and ‘drug started’ (Trine et al. 2013). Similarly a study done in Norway showed 81% of the patients had DRPs and an average of 2.1 clinically relevant DRPs was recorded per patient. The DRPs most frequently recorded were dose-related problems (35.1% of the patients) followed by need for laboratory tests (21.6%), non-optimal drugs (21.4%), need for additional drugs (19.7%) and unnecessary drugs (16.7%) (Blix et al. 2004).

A prospective study done by Bertrand G et.al indicated 383 DRPs were identified from 145 patients, with a mean of 2.6 DRPs per patient. The most frequently identified DRPs were: drug interactions (21%), untreated indications (18%), over dosage (16%) and drug used without a valid indication (10%) (Bertrand G et al. 2013). A report from a sample of elderly patients who received pharmaceutical care for one year at the University of Minnesota had revealed that need for additional drug therapy was the most common DRP identified, followed by low dosage accounting for 32% and 23% respectively (Rao et al. 2007).

The result of a study in Indonesia showed that drug related problems occurred in 79.1 % of patients. The most commonly presented problems were drug use without indication/ unnecessary drug therapy and wrong drug. The causes of unnecessary drug therapy were either the absence of any medical indication for drug therapy or non drug therapy being more appropriate for the medical condition. Some causes of wrong drug use were 'more effective drug available', 'potentially inappropriate for elderly patients' and 'contraindication in geriatric patient'. Inappropriate dose of some drugs (dosage too high) were largely caused by non-adjusted dosage for patients with renal impairment (Fita et al. 2008).

According to a retrospective study done in Malaysia the frequency of DRP occurrence was very high in patients with type 2 diabetes mellitus and hypertension. That study showed 90.5% had at least one DRP, averaging 1.9 ± 1.2 problems per patient. The most common DRPs encountered were insufficient awareness of health and diseases (26%), drug choice problems (23%), dosing problems (16%) and drug interactions (16%) (Zaman et al. 2013).

In the study conducted on 115 patients admitted in general medicine wards of a tertiary care teaching hospital in South India, to identify drug related problems and resolve them by providing pharmaceutical care, 60 drug related problems/ pharmaceutical care issues were identified and tabulated. Lack of understanding of the therapy by 33 patients (28.7%) was the major pharmaceutical care issue identified and this was addressed by patient education. This was followed by presence of drug–drug interactions in 11 prescriptions (9.6%). Eleven patients (9.6 %) failed to adhere to the therapy on economic grounds. Of these 11 patients, 7 patients had upper respiratory tract infections and were prescribed with expensive antibiotics. Suggestion was

made by the clinical pharmacist at the prescriber level to substitute by a cheaper but equally efficacious alternative, thereby ensuring patient compliance to the full course of antibiotic therapy and the patients were switched over to less costly antibiotics that were affordable to them. Three patients (2.61%) had medical conditions for which there was no medication prescribed. The pharmacist's intervention was made at the prescriber level and the patients were given the required medications (Gopal et al. *2011*).

In a study done to identify drug related problems in the Grenoble university hospital, France, the most commonly identified DRPs were non-conformity to guidelines or contra-indication (29.5%) followed by improper administration (19.6%), drug interaction (16.7%) and over dosage (12.8%) (bedouch et al. 2009). In a study at Ghent university hospital, Belgium, the most common drug-related problems were incorrect dose (31%), drug–drug interaction (20%), and adverse drug reaction (15%). For these DRPs the most common types of recommendations were adapting the dose (35%), and stopping or changing a drug (15%) (Annemie. 2013).

A relatively lower prevalence of DRP was seen in a study conducted at university hospital of Beirut, Lebanon. According to the study among 572 patients hospitalized during the 6-month study period in the internal medicine wards 90 (15.7%) patients developed DRPs. The most commonly identified drug-related problems were drug interactions (37%), over dosage (28%), non-conformity to guidelines or contra-indications (23%), under dosage (10%) and improper administration (2%). The clinical pharmacist's interventions consisted of dose adjustment (38%), addition of drugs (31%), changes in drugs (29%) and optimization of administration (2%) (Al-Hajje. 2012).

In another prospective, observational and interventional study carried out to assess clinical pharmacist intervention on drug related problems in internal medicine wards of a tertiary care hospital in Southern India 20.4 % of patients were intervened for having one or more drug related problems. In the study a total of 71 drug related problems were identified from 49 patients intervened during the study period, in which, 1 DRP was found in 33 (67.4%) patients, 2 DRPS in 12 (24.5%) patients and 3 DRPs in 4 (8.2%) patients. Most of the DRPs observed in the study resulted from inappropriate drug dosing (25.4%) followed by drug selection (23.9%), drug

interaction (21.1) and ADR (12.7). Majority of the clinical pharmacist recommendations were on drug discontinuation (29.6%) and drug dose change (22.5%) (Satish. *2013*).

One hundred forty nine drug related interventions conducted for 48 patients (16% of study subjects) were documented in a study in Jimma, Ethiopia by Mekonen et al (2013) The most frequent DRPs underlying interventions were unnecessary drug therapy, 36(24.2%); need for additional drug therapy, 34(22.8%) and noncompliance, 29(19.5%). The most frequent intervention type was change of dosage/instruction for use, 23(15.4%). For 17 of the subjects, a medical condition indicated the need for initiation of drug therapy, with 12 (35.3%) requiring preventive drug therapy to prevent development of a new condition. Among cases with non compliance 18 (62.1%) were due to unavailability of drug product and 9 (31%) were due to the patient preference not to take the medications (Mekonnen et al. 2013).

In the study designed to compare between two groups of patients, those receiving care from a rounding team of physicians, nurses, and clinical pharmacists (study or intervention group with 51 patient); and those receiving care from a rounding team of physicians and nurses, but without any pharmacist) (control group with 49 patient), 77 drug interventions were provided by the clinical pharmacists during rounding process for patients of the study group. The most common intervention was recommending dosage or frequency of medication (32.4%), followed by addition of medication (19.5%). Some examples of the interventions given by clinical pharmacists were decreasing antihypertensive drugs dose, laboratory monitoring of anticoagulant agents, change NSAIDs to less GI disturbing analgesics, avoiding potassium level disturbance, and select the most appropriate drug within the same group (Mshiemish. 2011).

A cross-sectional interventional study conducted in internal medicine wards of a teaching hospital in Iran indicated 262 errors were detected from 132 patients (1.98 per patient). Wrong frequency 71 (27%), forgetting to order 37 (14.1%), wrong selection 33 (12.5%), drug interactions 26 (9.9%), forgetting to discontinue 25 (9.5%) and inappropriate dose adjustment in renal impairment 25 (9.5%) were the most common types of errors (Mohammad et al. 2013).

1.3.2 Drugs associated with DRPs

A hospital based cross-sectional study conducted in Jimma University Specialized Hospital identified antimicrobials, ACEI, vitamins & minerals and beta blockers as the common drug classes that were involved in DRPs. Vitamins and minerals were common among the need for additional drug therapy and antimicrobials among all other DRPs (Tigabu et al. 2014).

According to the study at a Danish hospital the drugs with highest risk ratio in causing DRP were warfarin, digoxin and prednisolone. The drug groups causing most DRPs were antithrombotic agents, NSAIDs, opioids and ACE inhibitors (Blix H, et al 2004). The study in Beirut, Lebanon reported cardiovascular drugs were the most frequently implicated drug classes in DRPs (44%), followed by anticoagulants (17%) and corticosteroids (14%) (Al-Hajje. 2012). Similarly in the Grenoble University Hospital DRPs appeared most frequently for cardiovascular drugs, central nervous system drugs, and gastrointestinal agents (Annemie et al. 2013).

In the Indonesian study agents most commonly associated with no medical indication were ranitidine and antibiotics. In some cases, ranitidine was prescribed to prevent side effect/prophylactic therapy/ in patient who were given low dose aspirin and without a history of peptic ulcer disease. Unnecessary drug therapy also was caused by no medical indication for antibiotic prescribing. Some agents most commonly associated with potentially inappropriate for elderly patient were diazepam and paraffin liq (laxative) (Fita et al. 2008).

The Iranian study showed cardiovascular medications were the class with the highest encountered errors 83 (31.6%), after which gastrointestinal agents 41 (15.6%) had the highest rank. Hormonal medications were the class with the lowest frequency of error. The most prevalent types of errors in cardiovascular agents were wrong frequency 38 (46%) and wrong selection 13 (15.6%). The most common types of medication errors in gastrointestinal drugs were forget to order 19 (46.3%) and wrong frequency 11 (26.8%). The frequently occurred errors in respiratory drugs were related to forget to discontinue and forget to order. The most prevalent errors related to central nervous system agents were wrong selection followed by under dose. Fifty percent of identified interactions were related to interaction between ciprofloxacin and calcium and the second important one was the interaction between omeprazole and clopidogrel 4

(15.3%). The main error in dose adjustment was associated with wrong glomerular filtration rate (GFR) calculation based on Cockcroft- Gault formula including inappropriate dose adjustment for metformin 4 (16%) and antibiotics 4 (16%) (Mohammad et al. 2013).

A retrospective cross-sectional study performed in an acute-care hospital in Singapore showed the drugs most implicated in DRPs were B-blockers (atenolol and propranolol), NSAIDs (aspirin, ketoprofen, diclofenac, and mefenamic acid), and angiotensin converting enzyme (ACE) inhibitors. (Yvonne, et al, 2005). Aspirin, clopidogrel, simvastatin, amlodipine and metformin were the most implicated drugs for DRPs in type 2 DM patients with hypertension (Matsoso. 2009). Common drug-drug interactions identified in the southern Indian study involve drug interaction between digoxin and amiodarone, digoxin with calcium channel blockers, diuretics and corticosteroids; drug interaction with sucralfate. (Satish et al. *2013*)

The study conducted in the Grenoble University Hospital, France reported that 429 different drugs were associated with DRPs. Cardiovascular drugs were the most frequently implicated agents (22.2%), followed by anti-infective (13.3%), analgesic／anti-inflammatory drugs (11.3%), gastrointestinal drugs (11.2%), psychotropic drugs (9.6%) and antithrombotic agents (6.3%) (Bosma et al. 2007). Similar result was also found in a study done at jimma university specialized hospital to assess medication prescribing errors. According to the study antibiotics (32.5%) and cardiovascular drugs (26.3%) were the most common categories of drugs associated with prescribing errors followed by analgesic/antipyretics (9.6%). Taking specific drugs into consideration, diclofenac (7.7%), ceftriaxone (7.2%), and furosemide (6.2%) were the three drugs most commonly associated with prescribing error (Agalu et al. 2011).

According to the study in Jimma iron, calcium, vitamins and other supplements were the most frequent 30 (20.1%) drugs involved in DRPs, followed by antibiotics 22 (14.8%). The frequencies of classes of drugs with each particular drug therapy problem demonstrated; the most predominant were antibiotics as ‘unnecessary drug therapy’ and ‘adverse drug reaction’ categories; digoxin from the ‘ineffective drug therapy’ category; iron, calcium, vitamins and other supplements from the ‘needs additional drug therapy’ and ‘dosage too low’ categories and anticoagulants, anti-hyper lipidemics from the ‘dosage too high’ and ‘noncompliance’ categories. (Mekonnen et al. 2013)

The study at the University of Minnesota reported hypertension, DM, arthritis, chronic heart disease (CHD) and osteoporosis were the most common medical conditions requiring additional drug therapy. The majority (59%) of these were indicated to prevent the onset of a new medical condition. The addition of daily aspirin (11%) to prevent myocardial infarction and/or stroke in patients with diabetes, ischemic heart disease or hypertension and the addition of calcium supplements to prevent osteoporosis (9%) were both common (Rao et al. 2007).

A study done by Bertrand G et al indicated the most frequently involved drugs or drug classes in DRP were tramadol, antidepressants and acenocoumarol for drug interactions; calcium-vitamin D, statins and aspirin for untreated indications; proton pump inhibitors and paracetamol for over dosage; proton pump inhibitors and aspirin for drug used without a valid indication (Bertrand et al. 2013).

1.3.3 Predictors of DRP occurrence

According to the study in Jimma done by Tigabu B et al independent factors which predicted the occurrence of DRPs in the study population were sex, age, poly-pharmacy, and clinically significant potential drug-drug interactions. From all covariates studied, females were 1.95 times more likely to have DRPs than males. Patients, who took ≥ 5 drugs/day on average, were 5.23 times more likely to have DRPs than patients who took < 5 drugs/day on average. The odds of DRPs were 15.5 times higher among patients who had clinically significant potential drug - drug interaction in drug therapy regimen compared to patients who did not have (Tigabu et al. 2014).

The Danish study showed that the number of drugs at admission and the number of clinical/pharmacological risk factors were both independent risk factors for the occurrence of DRPs, whereas age and gender were not (Blix et al. 2004). According to the study done by Tigabu et.al in jimma Patients who took five or more drugs per day on average were 5.96 times more likely to have unnecessary drug therapy than patients who took less than five drugs per day on average. (Tigabu et al. 2013)

In a retrospective cross-sectional study performed in an acute-care hospital in Singapore no statistical correlations were observed between age and gender with developing DRPs. An increased number of medications was associated with higher risk for patients with DRPs on admission, but not for inpatients with DRPs. Results from patients with ADRs showed that the relative risk (RR) of geriatrics prescribed poly-pharmacy and major poly-pharmacy (10 and more drugs) were 1.01 and 1.23, respectively. Female patients had a RR of 0.79 compared with male patients in developing ADRs (Yvonne et al. 2005). According to the southern Indian study drug related problems were more commonly seen in patients aged above 60 years (53.10 %) (Satish et al. *2013*).

2. Objectives

2.1 General objective

To asses drug related problems in medical wards of Tikur Anbessa Specialized Hospital.

2.2 Specific objectives

- ✓ To determine the prevalence of drug related problems
- ✓ To identify the most common drugs and drug classes involved in drug related problems
- ✓ To identify predictors of occurrence of drug related problems.

3. Methods

3.1 Study area and period

The study was conducted in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. Tikur Anbessa Specialized Hospital is the largest teaching institution among federally established teaching hospitals in Ethiopia. The hospital has more than 600 beds and gives diagnostic and treatment service for about 370,000-400,000 patients per year (*Seattle Alliance Outreach*, 2014). The study was conducted in the medical wards of the Hospital in a 3 months period from March 15, 2014 to June 15, 2014. These wards have an average of 510 new admissions per 3 months period.

3.2 Study design

A prospective cross-sectional study design was used to asses drug related problems in the medical wards of Tikur Anbessa Specialized Hospital.

3.3 Population

3.3.1 Source population

All patients admitted to Tikur Anbessa Specialized Hospital, medical wards were taken as the source population.

3.3.2 Study population

The study population was all in-patients in the medical wards of Tikur Anbessa Specialized Hospital who were admitted between March 15 and June 15, 2014.

3.3.3 Sample population

All in-patients in the medical wards of Tikur Anbessa Specialized Hospital who were admitted between March 15 and June 15, 2014 and satisfied the inclusion criteria were candidates as a subject for the study.

3.3.4 Inclusion and exclusion criteria

Inclusion criterias were

- ✓ Patients admitted to the non ICU unit of medical wards
- ✓ Patients with more than 48 hours of length of stay

Exclusion criterias were

- ✓ Refusal to participate
- ✓ Patient re-admitted during the study period

3.4 Sample size and sampling technique

Sample size was computed based on single population proportion formula by using the following assumption. The proportion (P) of drug related problems (DRPs) in this group is taken as 50% to get possible minimum large sample size.

$$n = \frac{Z_{\frac{\alpha}{2}}^{2} P (1 - P)}{d^{2}}$$

Where: Proportion of drug related problems (p) = 50 %

Confidence level of 95 % chosen

Margin of error (d) = 5%

n = 385

Total population of patients in 3 months (N) = 510

$$\text{Corrected sample size} = \frac{n \times N}{n + N}$$

By using the correction formula the sample size will be 219 from 510 study populations. Based on this 225 patients were included in the study. The subjects were chosen by using simple random sampling method.

3.5 Variables

3.5.1 Dependent variables

- Drug related problems

3.5.2 Independent variables

- Age
- Sex
- Co-morbidity
- Length of hospitalization
- Number of drugs
- Drug type
- Disease type

3.6 Data collection procedure

Relevant information about each patient like patient characteristics, physical examination, laboratory results, current medications, co-morbidities, length of hospitalization, relevant previous medical and medication histories were recorded using data abstraction format (annex I) through reviewing patients' medical chart. Supplementary information and clarifications on some patient's medical information were obtained through discussion with the patient and the physician. With the data collected, the principal investigator had evaluated appropriateness of medical therapy using various references like Medscape, Up-to-date, Epocratus and Micromedex. Medscape drug interaction checker was used to identify drug-drug interactions. Identified DRPs were recorded and classified using DRP registration format (taken from Cipolle et al. 2004 with modification). Drugs involved in DRPs were also recorded. Then the possible intervention measures were proposed and communicated to either the internist/resident/senior physician or the patient in order to resolve or prevent DRPs.

3.7 Data quality assurance

In order to assure its quality, data was collected by two pharmacists who had basic knowledge on pharmaceutical care services; the data collectors were trained for 2 days on the documentation of drug therapy problems and techniques of data collection; the principal investigator had supervised the data collection process and the principal investigator had reviewed all filled DRP registration formats and data abstraction formats.

3.8 Data analysis

Data was checked for its completeness every day. It was edited, cleaned and analyzed. The collected data was entered into a computer using Epi Info 7 soft ware and analyzed using SPSS version 21. Cross tabulation was used in bivariate analysis. A test of association was done using binary and multiple logistic regressions. P value < 0.05 was considered significant. Drug risk ratio (frequency of involvement in DRP divided by frequency of prescription) was used to identify drugs that were prone to create DRP. Descriptive statistics was used to characterize drug related problems. Results of the study were organized in the form of frequencies and percentages. The data was summarized and described using tables and figures.

3.9 Ethical considerations

Letter of ethical clearance was obtained from the ethical review committee of school of pharmacy, Addis Ababa University. Letter for cooperation from department of internal medicine was taken. Verbal consent from a patient was requested to extract data from patents' medical charts. Privacy and confidentiality was ensured during patient interview and review of patient charts. Thus, name and address of the patient was not recorded in the DRP registration and data abstraction formats.

3.10 Operational definitions

Adverse drug reaction - any noxious, unintended, and undesired effect of a drug, which occurs at doses used in humans for prophylaxis, diagnosis or therapy.

Drug-related problem - an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes.

Hospital stay – the time gap spent by the patient in the hospital from his/her admission till the date the data was taken.

Medication error- 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.

Pharmaceutical care - the process through which a pharmacist cooperates with a patient and other professionals in designing, implementing and monitoring a therapeutic plan that will produce specific therapeutic outcomes for the patient.

Poly-pharmacy - the daily consumption of 5 or more medications. Different strengths of the same drug were counted as one item. However, formulations of one drug requiring different routes of administration were regarded as separate items. Combination drug, that is a drug with more than one active ingredient in it, was regarded as a single item.

4. Result

4.1 Demographic details and characteristics of patients

A total of 225 patients were included in the study, of which 114 (50.7%) were males and 111 (49.3) were females. The mean age was 39.1years with the maximum number of patients being in the age group of 25 to 39 years. Majority of patients 122 (54.2%) were found to have 1-2 co-morbidities followed by 3-4 co-morbid illnesses 75 (33.3%). Only18 (8%) of the study subjects were without any co-morbid condition. A total of 1729 medications were prescribed. Average number of drugs per day for a patient was 7.7. Majority of the study subjects (49.8%) received 5 to 9 drugs per day. The details of patients demographic characteristics along with other factors that may influence DRPs like number of co-morbidity, length of hospital stay, and average number of drugs received per day are shown in Table 1.

Table 1: Demographic details and characteristics of the study subjects, TASH, Ethiopia, 2014

Demographics and characteristics of patients	**Category**	**Number (%)**	**Mean ± SD**	**Range**
Sex	Male	114 (50.7)		
	Female	111 (49.3)		
Age group	14-24	52 (23.1)	39.1± 17.9	14 - 85
	25-39	77 (34.2)		
	40-64	63 (28.0)		
	≥65	33 (14.7)		
Hospital stay	< 7 days	83 (36.9)	10.8 ± 7.4	3 - 49
	≥ 7 days	142 (63.1)		
Number of co-morbidity	0	18 (8.0)	2.2 ± 1.4	1 - 8
	1-2	122 (54.2)		
	3-4	75 (33.3)		
	≥5	10 (4.4)		
Average number of drugs received/day	<5	51 (22.7)	7.7 ± 3.7	1- 15
	5-9	112 (49.8)		
	≥10	62 (27.6)		

As indicated in figure 1 the disease distribution of the study subjects showed a higher incidence of infections (37.9%) followed by cardiovascular diseases (21.1%), malignancies (8.1%), electrolyte abnormalities (7.5%), GI disorders (4.2%), kidney disease (3.6%), respiratory disorders (3.3%), endocrine disorders (2.5%), psychiatric disorders (2.3%) and others (9.5%).

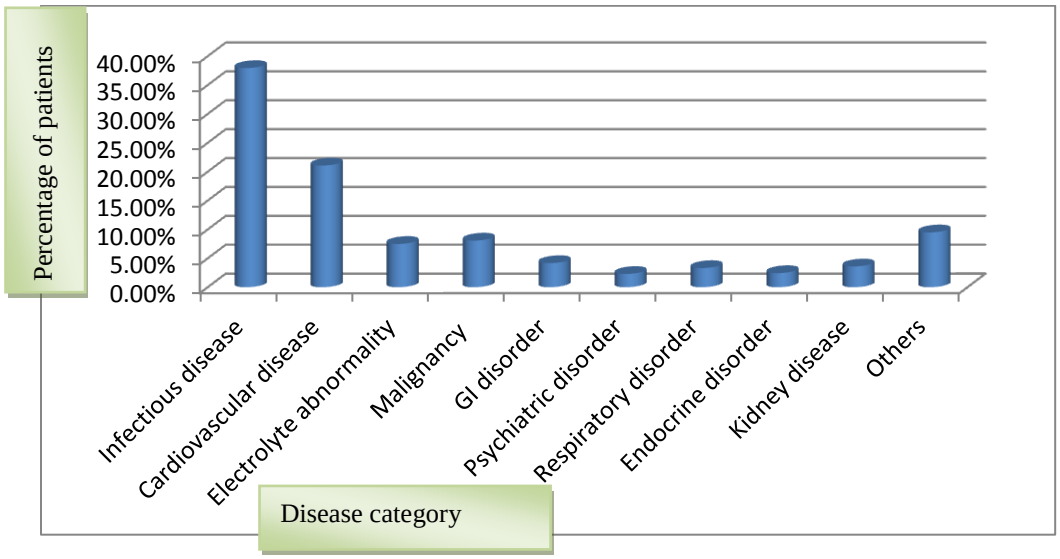

Fig. 1 Disease distribution of the study subjects, TASH, Ethiopia, 2014

Commonly prescribed drug classes in the study subjects were anti-infectives (629), CNS drugs (294), GI medicine (244), cardiovascular drugs (171), medicines affecting the blood (142), drugs used for endocrine disorder (109), vitamins & electrolytes (89) and cancer chemotherapy (52). As shown in fig 2 the most frequently prescribed specific drugs were ceftriaxon 101(44.9%), cimetidine 90(40.0%), tramadol 83(36.9%), heparin 71(31.5%), frusemide 66(29.3%) and paracetamol 57(25.3%)

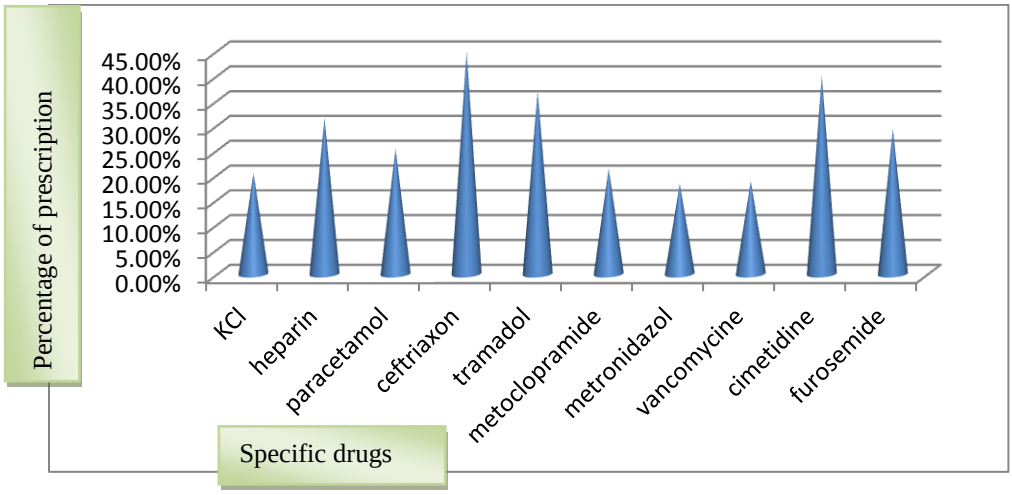

Fig 2 Top ten frequently prescribed drugs in the study subjects, TASH, Ethiopia, 2014

4.2 Prevalence of drug related Problems

DRPs were found in 52 % of the study subjects. A total of 152 drug related problems were identified from 117 patients during the study period, in which, 1 DRP was identified in 82 (70.1%) patients, 2 DRPS in 31(26.5) patients and more than 2 DRPs in 4 (3.4%) patients. Average number of DRP per patient is 0.68.

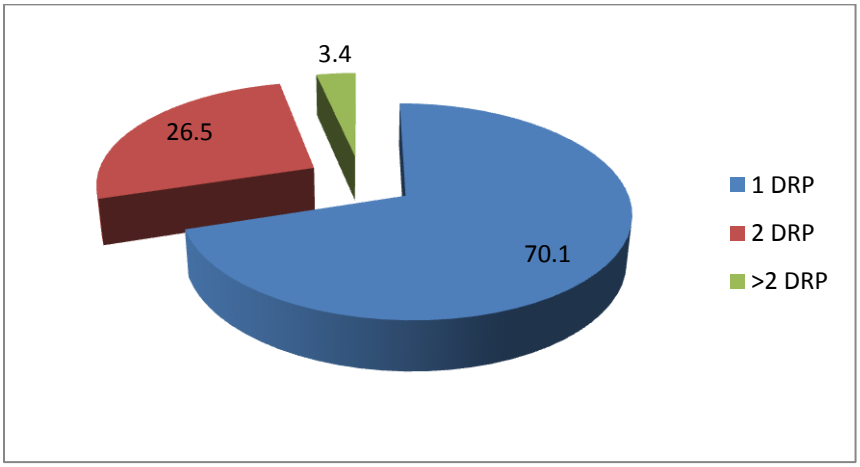

Fig 3 Number of drug related problems per patient, TASH, Ethiopia, 2014

Drug interaction was the top ranking drug related problem (48 % of all DRPs) followed by ADR (23%), need for additional drug therapy (11.2%), inappropriate dose (10.5%), unnecessary drug therapy (4.6%) and ineffective drug (2.6%). Of the 17 DRPs classified as need for additional drug therapy, 9 (52.9%) were because of untreated medical condition, 7 (41.2%) were due to need for prophylaxis therapy to reduce the risk of developing a new condition. The type and number of drug related problems identified were characterized as shown in table 2.

Table 2: Types of drug related Problems identified, TASH, Ethiopia, 2014

DRP		No. of DRPs	Total	(%)
Drug interaction			73	48.0
Adverse drug reaction			35	23.0
Need for additional drug therapy	Untreated medical condition	9		
	Need for prophylaxis therapy	7	17	11.8
	Need for additive / synergetic effect	1		
Inappropriate dose	Low dose	6		
	High dose	2	16	10.5
	Inappropriate frequency	8		
Unnecessary drug therapy	No indication	3		
	Duplication	4	7	4.6
Ineffective drug	Not the most effective	1		
	Refractory to the drug therapy	2	4	2.6
	Inappropriate dosage form	1		
Total			152	100

4.3 Drugs and drug classes involved in drug related problems (DRPs)

As indicated in figure 4 Anti-infectious agents were the most common drug class involved in DRP followed by GI medicines, CNS drugs and medicines affecting the blood. Cimetidine, tramadol, heparin, and warfarin were the top ranking drugs involved in DRP.

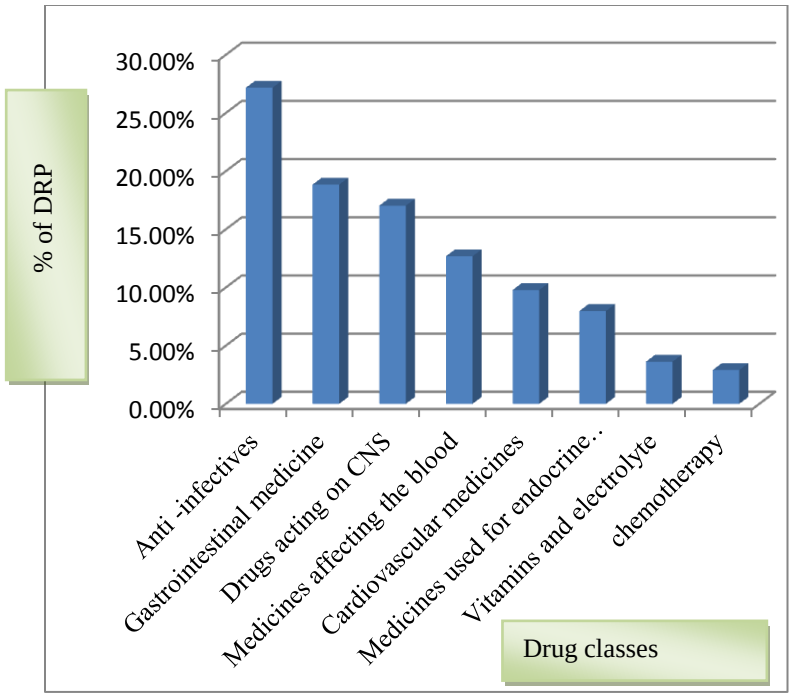

Fig 4 Common drug classes involved in drug related problems, TASH, Ethiopia, 2014

Hypokalemia was common among the untreated medical conditions. Patients in need of prophylaxis therapy are those who should had been given GI prophylaxis for stress ulcer, co-trimoxazole for PCP, pyridoxine for TB patients who were at risk of isoniazid induced neuropathy and anticonvulsants for brain abscess. ADR was commonly seen in drugs given for treating DVT, TB and hematologic malignancy. Among these drugs warfarin, anti-cancer chemotherapy, anti TB and co-trimoxazole were commonly involved in ADR. The most frequent drug interaction was between cimetidine and opioids/steroids followed by ceftriaxon and heparin /warfarin; azithromycine and digoxin; fluconazole and ondansetron. The frequencies of classes of drugs with each particular DRP demonstrated that the most predominant drug categories were GI medicines in ‘drug interaction’ and ‘unnecessary drug therapy’; anti-infectives in ADR, ‘ineffective drug’ and ‘inappropriate dose’; vitamins and electrolytes in ‘need for additional drug therapy’. Table 3 shows drug classes involved in specific type of DRPs.

Table 3 Drug classes involved in specific type of drug related problems, TASH, Ethiopia, 2014

Drug class	DI	ADR	Unnecessary -drug therapy	Need additional drug therapy	Ineffective drug	Inappropriate dose
GI medicine	47	0	3	3	0	1
Anti-infectives	38	12	1	2	3	9
CNS drugs	29	4	1	3	0	1
Vitamin & electrolyte	0	0	1	8	0	1
CV drugs	28	2	0	1	1	3
Medicines affecting -the blood	38	7	0	0	0	0
Medicines used for -endocrine disorder	15	3	1	0	0	0
Cancer chemotherapy	9	5	0	0	0	3

A total of 64 drugs were involved in different types of DRPs. Among these the most frequently involved drugs in DRPs were cimetidine (36), tramadol (20), heparin (18), warfarin (16), ceftriaxon (12), prednisolone (11) and cotrimoxazol (10). Gentamycin, warfarin, nifedipine, cimetidine, simvastatin, prednisolone, digoxin and pethidine were drugs with the highest drug risk ratio. All of these drugs had a risk ratio of above 0.33 which indicates that DRP may occur in more than one third of the times these drugs are used. Cimetidine is one of the commonly used drugs with a higher drug risk ratio. In the contrary ceftriaxon is the most frequently used drug with the lowest drug risk ratio. Fig 5 shows frequency of commonly used drugs which were involved in DRP and their drug risk ratio.

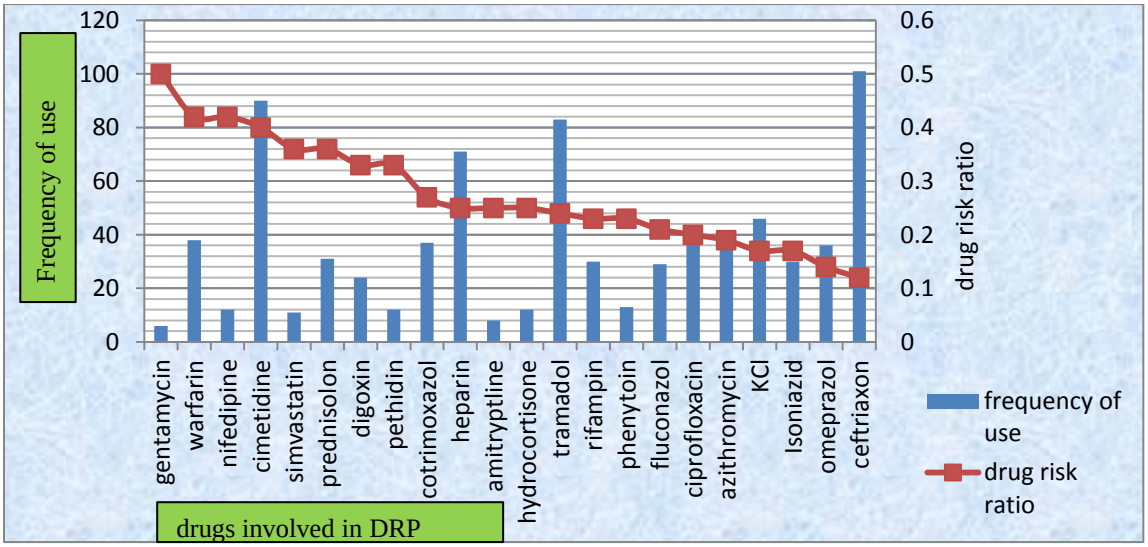

Fig 5 Frequency of commonly used drugs which were involved in drug related problems and their drug risk ratio, TASH, Ethiopia, 2014

4.5 Interventions for drug related problems

Appropriate intervention measures were taken to correct the identified DRPs. For the majority of DRPs (66.3%) interventions were given by principal investigator. There are also DRPs that were intervened by physicians. The most commonly applied intervention was informing the physicians to monitor for the adverse effect of a drug which may occur due to a potential drug - drug interaction or potential ADR because of risk factors in a patient like renal failure, history of allergy and co-morbidity. As shown below in figure 5 the rest of the interventions were to discontinue the drug, to change the frequency of administration, to do laboratory monitoring, to change the dose, to change the drug, to monitor for the drug's effectiveness, to treat the adverse effect or change the route of administration.

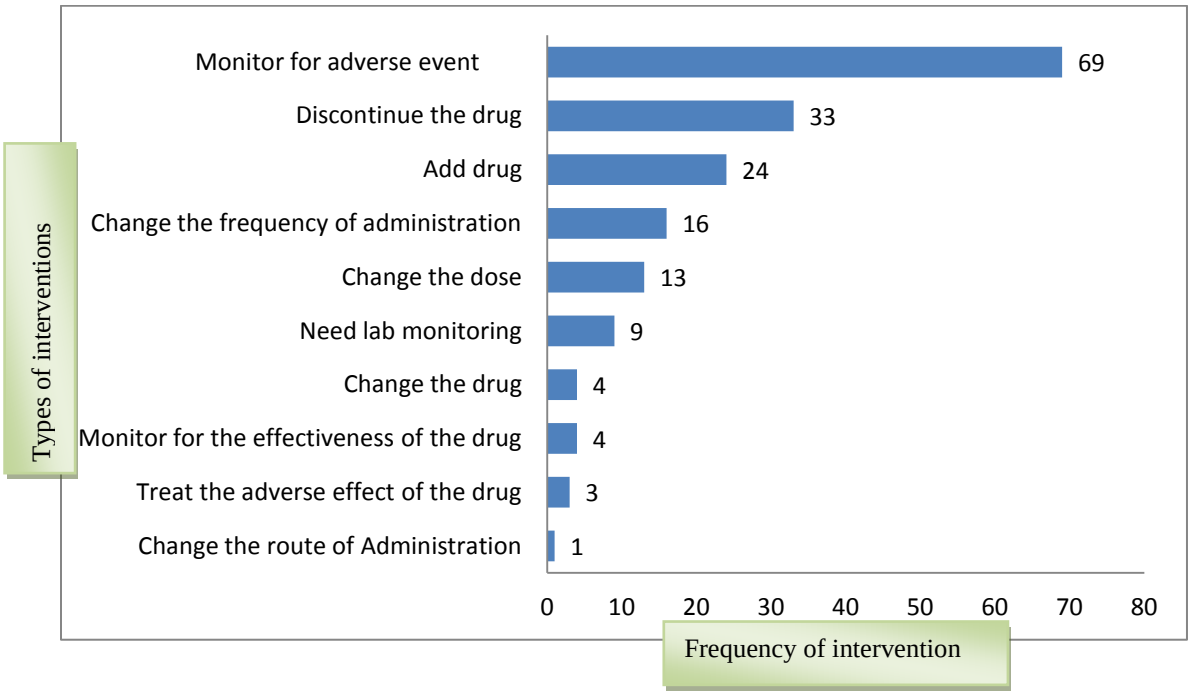

Fig 6 Types of interventions for drug related problems, TASH, Ethiopia, 2014

4.5 Predictors of occurrence of drug related problems

The identification of risk factors for DRPs may be helpful in finding patients at risk. These patients can then be given special attention, with the hope of avoiding overt DRPs. Sex, age, average number of drugs/day, length of hospital stay and number of co morbidities were analysed to determine whether they could predict the occurrence of DRPs or not. The average number of drugs taken by the patient/day was shown to be a risk factor for the occurrence of DRPs while age, sex, length of hospital stay and number of co-morbidities were not. As shown in table 4 Patients who took an average of 5-9 drugs per day (minor poly pharmacy) are 2 times more likely to develop drug related problem as compared to patients who took less than 5 drugs per day while those taking more than 10 drugs per day (major poly pharmacy) are 3.1 times more prone in developing DRP.

Table 4: Predictors of occurrence of drug‑related problems in the study subjects, TASH, Ethiopia, 2014

Variable	category	Drug‑related problems (%)		COR (95% CI)	AOR (95% CI)	p value
		No	Yes			
Sex	Female	55(50.9)	56(47.9)	1.00	1.00	
	Male	53(49.1)	61(52.1)	1.13(0.670-1.908)	1.07 (0.63-1.83)	0.798
Age	14-24	27(25.0)	25(21.4)	1.00	1.00	
	25-39	36(33.3)	41(35.0)	1.23 (0.608-2.488)	1.69 (0.69-4.09)	0.245
	40-64	31(28.7)	32(27.4)	1.12 (0.535-2.324)	1.39 (0.59-3.24)	0.447
	≥ 65	14(13.0)	19(16.2)	1.47 (0.609-3.530)	1.56 (0.64-3.84)	0.331
Hospital stay	<7 days	45(41.7)	38(32.5)	1.00	1.00	
	≥7 days	63(58.3)	79(67.5)	1.49 (0.862-2.559)	1.28 (0.73-2.24)	0.392
Number of co-morbidity	0	9(8.3)	9(7.7)	1.00	1.00	
	1-2	63(58.3)	59(50.4)	0.937 (0.348-2.520)	1.71 (0.35-8.36)	0.505
	3-4	30(27.8)	45(38.5)	1.500 (0.534-4.214)	2.32 (0.60-8.99)	0.220
	≥ 5	6(5.6)	4(3.4)	0.667 (0.139-3.194)	1.52 (0.41-5.71)	0.535
Number of drug	<5	33(30.6)	18(15.4)	1.00	1.00	
	5-9	53(49.1)	59(50.4)	2.041(1.030-4.043)	2.02 (1.14-3.31)	0.012
	≥10	22(20.4)	40(34.2)	3.333(1.536-7.235)	3.13 (1.43-6.89)	0.004

4.6 Examples of drug related problems identified in the study subjects

Some examples of drug related problems identified in the study subjects are described in table 5

Table 5: Examples of drug related problems identified in the study subjects, TASH, Ethiopia, 2014

Sr. No.	Description of the drug related problem	Intervention done
1	An 80 year old male patient with serum creatinin of 1.73 was on metformin. But metformin is contraindicated if Sr.Cr. > 1.5 for male and >1.4 in female because of the risk of lactic acidosis which is 50 % lethal.	Metformin was discontinued
2	Coartem (artemether – lumefantrine) was prescribed as 4/4/2 for a 19 years old patient with malaria.	the dose was changed to 4 tab po Bid for 3 days
3	A patient on KCl was taking it after the serum potassium was corrected.	KCl was discontinued
4	Patient was taking multiple drugs which have serious drug – drug interaction with warfarin like cotrimoxazole, cimetidine and ceftriaxon. But the patient had only a single INR measurement in his stay.	Monitoring INR and for signs symptoms of bleeding was considered
5	The dose of atenolol and metronidazol was not adjested for a patient whose CrCl is 2.9 ml/min (SrCr = 30) Maximum dose of atenolol for a patient with CrCl <15 is 25 mg po/d. The dose of metronidazol For CrCl < 10 is 250 mg tid	atenolol dose was changed to 25 mg po/d rather than 50 mg po bid metronidazol dose was reduced to 250 mg iv tid instead of 500 mg iv tid.
6	HIV patient on anti TB treatment was not on pyridoxine prophylaxis for neuropathy. He is at risk of developing INH induced neuropathy because of immune-suppression (CD4=125)	prophylaxis dose of pyridoxine (50 mg po/d) was started
7	A patient who had a history of allergy to cotrimoxazol was given the medicine.	Reminded to closely watch the patient for sever drug allergy.
8	Patient developed hepatotoxicity from anti TB medication	Rifampine and INH were changed by streptomycin

9	An old patient was given amlodipine 20 mg po/d for treating his hypertension. But the dose of amlodipine should not be > 10 mg/d for older patients	the dose of amlodipine was reduced to 10 mg po/d
10	Vancomycin induced nephrotoxicity	vancomycin was discontinued
11	Serious drug-drug interaction between paracetamol and rifampine. Rifampin increases acetaminophen toxicity	Patient was told to take paracetamol not more than 4 tab/d
12	A patient taking Phenobarbital for treating epilepsy developed megaloblastic anemia secondary to Phenobarbital toxicity	Tapering of Phenobarbital was started and replaced with safer alternative
13	High WBC count and persistent anemia were seen for 2 weeks regardless of conventional dose of chlorambucil (4 mg po/d) and prednisolon (3o mg po/d) given to treat CLL	the dose of chlorambucil and prednisolon was increase to 6 mg and 50 mg respectively
14	A patient at risk of developing stress ulcer (platlet count < 50,000) was not given GI prophylaxis	stress ulcer prophylaxis (cimetidine) was started
15	A 27 year old female patient who was on anti TB was using oral contraceptive for birth control. Rifampine decreases effectiveness of oral contraceptive.	Patient was told to use additional birth control methods.
16	A patient at risk of GI ulcer was taking diclofenac for treating her fever	Diclofenac was changed to paracetamol because paracetamol is safer than diclofenac for patients who are at risk of ulcer
17	Incorrect dosing frequency of azithromycin for a patient with community acquired pneumonia. (500 mg po tid)	Azithromycine dosing was changed to 500 mg po qd

5. Discussion

The goal of drug therapy is to achieve defined therapeutic outcomes and improve the patient's quality of life while minimizing patient risk. But inappropriate use of drugs during disease management may lead to drug therapy problems. Identification of common types of DRPs and common drugs involved in DRP is an important component of drug therapy and contributes to reduction of drug related morbidity and mortality. Majority of studies conducted at different countries and various groups of patients showed higher prevalence of drug related problems and indicated different drugs and drug classes involved in DRP. This study was carried out to asses DRPs in medical inpatients in one of a tertiary care teaching hospital in Ethiopia.

This study showed that 52% of patients admitted to the medical wards of TASH within the study period had DRPs. This result is lower than what was found in Jimma, Ethiopia (73.5 %) (Tigabu et al. 2014). The lower rate of DRP in this study as compared to what was done in Jimma might be because of the presence of more senior staffs and sub specialists in Tikur Anbessa Specialized Hospital than Jimma University Specialized Hospital or it may be because the data collection of the study in Jimma was conducted at 2011 when clinical pharmacists were not involved in the ward based activities. The study in Malaysia also found a prevalence of 90.5 %. The lower prevalence of DRPs in my study as compared to the Malaysian study might be because the Malaysian study was done on patients with type 2 diabetes mellitus and hypertension. These patients have a higher probability to develop DRP since patients with diabetes and hypertension are more prone to receive more drugs and to develop more complications.

The most frequently encountered drug related problems in the present study were drug interaction, ADR, need for additional drug therapy and inappropriate dose. Similarly the study done at Ghent University Hospital in Belgium showed drug interaction and ADR were among the top ranking types of DRPs (Annemie. 2013).

In this study drug interaction was the number one frequently encountered DRP. In line with this the studies done at the acute care hospital of Singapore (Yvonne et al. 2005) and University Hospital of Beirut, Lebanon (Al-Hajje et al. 2012) showed drug - drug interaction was the most frequently encountered DRP. The study in Iran also showed among medication errors in internal medicine ward drug interactions were commonly seen and unfortunately most of the time physicians don't take these interactions seriously (Mohammad et al. 2013).

Drug interaction is a major factor that might cause ADR, therapeutic failure and drug related harm to patients (Veggeland et al. 2008). Even though the majority of drug interactions in my study were only potential drug interactions there are some interactions that had resulted in significant adverse events like bleeding, raised INR, hypoglycemia and constipation. The most common intervention measure given for this class of DRP in my study was informing the physician orally to monitor the patient for serious adverse events. In addition monitoring for the effectiveness of some drugs and limiting the daily dose of a drug (e.g. Paracetamol dose not > 2 g /d when given with imatinib or rifampin) were taken as intervention measures.

Drug-pairs that could give rise to potentially severe interactions were identified. The judgment here is based on theoretical consideration. In clinical practice, some of these combinations may still be used, but the patient should be closely monitored for manifestations such as lack of therapeutic efficacy or toxicity, especially for drugs whose therapeutic effects may be diminished or augmented when used in those combinations. As drug interactions can affect patient's clinical outcome, quality of life, as well as contribute to unnecessary health care cost, the high prevalence rate (48% of all the DRPs) in this study would make this an important area requiring future pharmacists to focus on reviewing patients' medication charts and checking for potential drug-drug interactions.

The second most common drug related problem identified in this study was ADR (23.03%). This was in close proximity with the result of Harvard Medical Practice Study showing up to 20% of hospitalized patients experiencing at least one ADR during their hospital stay (Brennan. 2011). Some of the adverse drug events identified in this study were bleeding / increased INR due to warfarin; hepatotoxicity due to anti TB, Propylthiouracil & chemotherapy; allergic reaction due to cotrimoxazole, vancomycin and frusemide; gastritis due to ASA, cotrimoxazole & anti TB;

nephrotoxicity due to vancomycin & tenofovir; AV block due to digoxin and megaloblastic anaemia due to Phenobarbital.

Many of the drugs that had caused ADR like vancomycin, hydroxyurea, frusemide, tenofovir and ASA were discontinued immediately, while others like Phenobarbital were tapered gradually. Anti TB drugs like rifampin, isoniazid and pyrazinamide were changed with a safer alternative. Drugs which are contraindicated for some type of patients like metformin for patients with SCr > 1.5/1.4 mg/dl and heparin for patients who have active bleeding were discontinued because of potential ADR. Drugs were also added to treat some ADRs for example pyridoxine to treat isoniazid induced neuropathy; bisacodyl or other laxatives to treat opioid induced constipation and dextrose for insulin induced hypoglycaemia.

Among patients who needed additional drug therapy 29.4% were those who needed KCl for treating hypokalemia and those who needed stress ulcer prophylaxis. There were also patients who needed pyridoxine, cotrimoxazole and anticonvulsants as prophylaxis for neuropathy, PCP, and seizure respectively. Ineffective drug use (2.6%) was less frequently occurring DRP in this study. This result is in close agreement with a study in Jimma which showed ineffective drug therapy (2.7%) as the less frequently occurring DRP among all the DRPs identified (Mekonnen et al. 2013).

In this study anti-infectives, GI medicines and CNS drugs were common drug classes involved in DRP. The 2 studies on DRPs at Jimma university specialized hospital, Ethiopia found antimicrobials were the top ranking drug classes involved in drug related problems (Tigabu B et al. 2014, Mekonnen A et al. 2013). Another study in France indicated anti-infective and CNS drugs were from the top 3 drug classes involved in DRP (Bosma et al, 2007). The study in Belgium also indicated GI medicines and CNS drugs were among the frequently involved drug classes in DRPs (Annemie. 2013). In the present study the higher interaction rate of cimetidine with a number of drugs like morphine, tramadol, codein, predinisonole, warfarin, digoxin and others makes GI medicines among the commonly involved drug classes in DRP. In close agreement with my study the study in Iran also found gastrointestinal agents (15.6%) as the second common drug classes involved in DRP (Mohammad et al. 2013).

The frequencies of classes of drugs with each particular DRP demonstrated that the most predominant drug categories were GI medicines in 'drug interaction' and 'unnecessary drug therapy'; anti-infectives in ADR, 'ineffective drug' and 'inappropriate dose'; vitamins and electrolytes in 'need for additional drug therapy'. The study in Jimma similarly showed predominant drug classes involved in DRP were antibiotics for ADR & iron, calcium, vitamins and other supplements for 'need for additional drug therapy'(Mekonnen et al. 2013). Tigabu's study also indicated antimicrobials were commonly involved in inappropriate dose and ineffective drug therapy and vitamins & minerals in need for additional drug therapy (Tigabu et al. 2014).

It is necessary to be aware of those drugs with the highest drug risk ratio (high rate of causing DRP) since these are drugs most frequently expose the patient to DRP when taking them. In this study gentamycin, warfarin, nifedipin, cimetidine, simvastatin, prednisolone, digoxin and pethidine were drugs with the highest drug risk ratio. Similarly the study in Norway mentions warfarin, prednisolone and digoxin among drugs with high risk ratio (Blix, 2007).

Cimetidine was one of the frequently prescribed drugs in internal medicine ward. It has a higher drug risk ratio because of its frequent involvement in interaction with various drugs like tramadol, prednisolone, dexamethason, warfarin, fluconazole, cotrimoxazole, pethidine, hydrocortisone, diazepam, codeine, nimodipine, simvastatin and digoxin. The mechanism of interaction of cimetidine with these drugs was either by inhibiting CYP 450 enzyme or by increasing gastric PH. Involving in drug interaction was also a very common reason in being a high risk drug for digoxin, pethidine and simvastatin. Gentamycin was found to cause nephrotoxicity because of its interaction with furosemide. In 42 % of patients who took warfarin there was either an actual ADR (bleeding) or raised INR, or serious drug interaction with other drugs like cimetidine, ceftriaxon, cotrimoxazole, heparin, ciprofloxacin, ASA, fluconazole, and azithromycin. Nifedipine was involved in low dose and drug interaction with phenytoin and simvastatin.

In the attempt to identify risk factors, the result of this study supported published findings that the number of drugs taken by a patient is an important risk factor for DRPs but sex and age did not have significant correlation with the occurrence of DRP. Number of medications used was found to be a risk factor for increasing DRPs by a number of studies (Strand L et al. 1990; Blix et al. 2004; Aburuz et al. 2011; Christian et al. 2013). However, sex and age were not found to affect DRPs (Blix et al. 2004; Aburuz et al. 2011; Nascimento et al. 2009). A study in Singapore similarly showed increasing number of drugs as a risk factor for DRP and the absence of statistically significant correlation between age and sex with the likelihood of developing DRP (Yvonne. 2005). In my study length of hospital stay and number of co-morbidity were not found to significantly affect the occurrence of DRP. Similarly the study in Jimma by Tigabu et al did not show significant association between likelihood of DRP occurrence and length of hospital stay or number of co-morbidity (Tigabu et al. 2014).

5.1 Limitation of the study

- ✓ Drug therapy problems related to adherence to the prescribed medications were not studied.
- ✓ The study did not show the overall prevalence of DRPs for a patient in his/her hospital stay (admission to discharge) rather it shows DRPs up to some cross-section of time after his or her admission.
- ✓ The intervention given for the identified DRPs may to some extent affect the prevalence of DRPs in the study subjects.
- ✓ DRPs related to medication administration were not addressed in the study.
- ✓ The result of the study may not be generalized to all hospitals because it was single centered study conducted in a hospital serving referred patients who have severe illnesses and more co morbidities.

6. Conclusion

Drug‑related problems are common among medical ward patients. Drug interaction was the top ranking DRP followed by ADR, need for additional drug therapy, inappropriate dose, unnecessary drug therapy and ineffective drug. The most common drug classes involved in DRP were anti-infectives, GI medicines, CNS drugs and medicines affecting the blood. Gentamycin, warfarin, nifedipin, cimetidine, simvastatin, prednisolone, digoxin and petidine were drugs with the highest drug risk ratio. Common types of interventions done for the DRPs were monitoring for potential ADR, drug discontinuation, addition of drug and changing the frequency of administration. There was a stronger association between number of drugs taken by the patient and DRP occurrence.

7. Recommendation

Based on the findings of this study, the following recommendations are suggested

- ✓ The health sector policy makers should continue to include clinical pharmacists in the hospital. The role of clinical pharmacists should also be geared to identify, solve, and prevent DRPs rather than overlapping on the already existing dispensing pharmacists.
- ✓ The hospital administrators should try their best to introduce computerized physician order entry (CPOE) system software to decrease medication errors. Computerized physician ordering programs can alert clinicians to potential problems (e.g., allergy, need for reduced dosage in patients with impaired renal function, drug-drug interactions).
- ✓ Clinicians should monitor patients for signs of adverse drug effects, including doing laboratory tests as necessary.
- ✓ Consider age-related changes in pharmacokinetics or pharmacodynamics and their effect on dosing requirements
- ✓ Check for potential drug-disease and drug-drug interactions before starting a new drug
- ✓ Choose the safest possible alternative
- ✓ Further studies with a follow up of patients till discharge are required.

References

Aburuz S, Bulatova N, Yousef A, Al‐Ghazawi M, Alawwa A and Al‐Saleh A, 2011, Comprehensive assessment of treatment related problems in hospitalized internal medicine patients in Jordan, Int J Clin Pharm;33:501‐11.

Agalu A, Ayele Y, Bedada W and Woldie M, 2011, Medication prescribing errors in the intensive care unit of Jimma University Specialized Hospital, Southwest Ethiopia, J Multidiscip Health; 4: 377–382

Al-Hajje A, Atoui F, Awada S, Rachidi S, Zein S and Salameh P, 2012, Drug-related problems identified by clinical pharmacist's students and pharmacist's interventions, Ann Pharm Fr, doi:10.1016/j.pharma.2012.02.004

Annemie S, Hugo R, Peter D, 2013, Evaluation of clinical pharmacist recommendations in the geriatric ward of a Belgian university hospital, Clinical Interventions in Aging; 8:703–709

Bandolier extra, 2002, Adverse drug reactions in hospital patients, a systematic review of the prospective and retrospective studies, www.ebandolier.com.

Bedouch P, Allenet B, Grass A. et al. 2009, Drug-related problems in medical wards with a computerized physician order entry system, Journal of Clinical Pharmacy and Therapeutics; 34, 187–195

Bergkvist C, Holmbjer L, Midlöv P, et al. 2011, The process of identifying, solving and preventing drug related problems in the LIMM-study, Int J Clin Pharm; 33(6):1010-1018

Bertrand G, Caroline S, Arnaud P, et al. 2013, Drug-related problems in a general internal medicine service, Allgemeine Innere Medizin; 10:17-23

Blix H, 2007, Drug-related problems in hospitalised patients, Norway, Br J Clin Pharmacol; 63:187–95

Blix H, Viktil K, Reikvam A, et.al. 2004, The majority of hospitalised patients have drug-related problems: results from a prospective study in general hospitals, Eur J Clin Pharmacol; 60(9):651-8.

Bosma L, Jansman F, Franken A, Harting J, Vanden B, 2007, Evaluation of Pharmacist clinical intervention in Dutch hospital setting, Pharm World Sci; 30(1): 31-38.

Brennan TA, Leape LL, Laird NM, et al. 2011, Incidence of adverse drug events and negligence in hospitalized patients: results of Harvard Medical Practice Study I, N Engl J Med; 324:370–6.

Bruno C, Ornella C, Francoois-Xavier R, 2008, Assessment of Clinical Pharmacists Interventions in French Hospitals: Result of Multicenter Study, Ann. Pharmacother; 42(7):1095-1103.

Cipolle R, Strand L, Morley P, 2004, Pharmaceutical care practice: the clinicians guide, New York: McGraw Hill.

Ernest F, Grizzle A, 2001, drug related morbidity and mortality: updating the cost of illness model J Am. Pharm Assoc (Wash); 41:192-199

Foppe V, 2005, Drug-related problems: a cornerstone for pharmaceutical care, Journal of the Malta College of Pharmacy Practice; 10:5-8

Fita R, Syed A, dewa P, Wasilah R, 2008, involvement of ward pharmacist during theraputic process in hospitalized geriatric patients in dr. sarjito hospital, yogyakarta, indonesia

Gillespie U, Alassaad A, Henrohn et al. 2009, A comprehensive pharmacist intervention to reduce morbidity in patients 80 years or older: A randomized controlled trial, Arch Intern Med; 169(9):894-900.

Gopal K, Vasantha J, Vanitha R, et.al. 2011, Pharmaceutical care in the general medicine ward of a tertiary care hospital in South India, Journal of Pharmacy Research; 4(5), 1467-1469

Kohl L, Corrigan J and Donaldson M (Eds) committee on quality of health care in America, institute of medicine, 1999, to err is human: building a safer health system, Washington, DC: National Acadamy Press

Krahenbuhl M, Schlienger R, Lampert M, Haschke M, Drewe J, Krahenbuhl S, 2007, Drug-related problems in hospitals: a review of the recent literature. Drug Saf; 30(5):379-407.

Lagnaoui R, Moore N, Fach J, Longy-Boursier M, Begaud B, 2000, Adverse drug reactions in a department of systemic diseases-oriented internal medicine: prevalence, incidence, direct costs and avoidability, Eur J Clin Pharmacol;56(2):181-6.

Lampert M, et al. 2008, Drug-related problems: evaluation of a classification system in the daily practice of a Swiss university hospital, Pharmacy world science; 30:768-776.

Langebrake C, Hilgarth H. 2010, Clinical Pharmacist intervention in German University Hospital, Pharm World Sci; 32:194-199.

Lǒpez A, et al. 2010, Drug related problems at discharge programme consultenos. International journal of pharmacy practice;18:297-304.

Matsoso M, 2009, Future vision and challenges for hospital pharmacy, Am J Health-Syst Pharm; 66:(3) 9-12.

Mekonnen A, Yesuf E, Odegard P, Wega S, 2013, Implementing ward based clinical pharmacy services in an Ethiopian University Hospital, Pharmacy Practice;11(1):51-57.

Mohammad A, Azita H, Azadeh E, Zahra S, 2013, Detection and Management of Medication Errors in Internal Wards of A Teaching Hospital by Clinical Pharmacists, Acta Medica Iranica; 51(7): 482-486.

Mshiemish B, 2011, Role of the Clinical Pharmacist in Reducing Preventable Adverse Drug Events, Iraqi J Pharm Sci; 20(2): 85-90

Nascimento Y, Carvalho W, Acurcio F, 2009, Drug related problems observed in a pharmaceutical care service, Belo Horizonte, Brazil, Braz J Pharm Sci;45:321‑30.

Nickel C, Juliane M, Anna S, Silke M, Arno P, Michael B et al, 2013, Drug - related emergency department visits by elderly patients presenting with non-specific complaints, Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine; 21(15):1-9

Pharmaceutical Care Network Europe Foundation, 2010, classification for drug related problems revised V 6.20. Page 2

Rao D, Gilbert A, Strand L, Cipolle R, 2007, Drug therapy problems found in ambulatory patient populations in Minnesota and South Australia, Pharm World Sci; 29:647–654.

Satish K, Prasanna D, Rajesh V, Prashant C, 2013, Assessment of clinical pharmacist intervention in tertiary care teaching hospital of southern india, asian j pharm clin res;6 (2): 258-261

Seattle Alliance Outreach, 2014, http://www.ethiomedic.com/index.php/healthcare-facilities/69-hospitals-in-addis-ababa/84-black- lion-specialised-hospital.html

Strand L, Morley P, Cipolle R, Ramsey R, Lamsam G, 1990, Drug‑related problems: Their structure and function, DICP;24:1093‑7.

Tigabu B, Daba D, Habte B, 2013, Factors associated with unnecessary drug therapy and inappropriate dosage in jimma university specialised hospital, South west Ethiopia, World J Pharm Sci; 1(4): 93-98

Tigabu B, Daba D, Habte B, 2014, Drug-related problems among medical ward patients in Jimma University specialized hospital, Southwest Ethiopia, J Res Pharm Pract;3:1-5.

Trine R, Stig E, Mette R, Per H, 2013, Clinical pharmacist service in the acute ward, Int J Clin Pharm;12(3):1-15

Vanmil J, Schulz M, Tromp T, 2004, Pharmaceutical care, European developments in concepts, implementation, teaching and research: a review, Pharm World Sci; 26:303-11.

Winterstein A, Sauer B, Hepler C, Poole C, 2002, Preventable drug-related hospital admissions. Ann Pharmacother; 36(7-8):1238-48.

Yvonne K, Fatimah B, Shu C, 2005, Drug-related problems in hospitalized patients on polypharmacy: the influence of age and gender. Therapeutics and Clinical Risk Management: 1(1) 39–48

Zaman H and Fun W, 2013, Drug related problems in type 2 diabetes patients with hypertension: a cross-sectional retrospective study, BMC Endocrine Disorders; 13:2

Annex I

Data abstraction format

Ward _____ chart code _____ diagnosis _____
_____
_____
_____

Patient Name (initials) _____ card no. _____ Age (yrs) _____ Sex _____

Wt. (kg) ____ if female Pregnancy Status: _____Date of admission _____ Date the data taken _____

sr. no.	Disease condition	Treatment	Dosage regimen	Length of therapy	Comment (DRP)
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					

Pertinent lab values and investigations

_____
_____
_____
_____
_____
_____

Drug interaction

1. Is there any drug interaction yes …… no ……..
2. If drug interaction is there Specify it

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

ADR

1. Is there any adverse drug reaction yes …… no. ……..
2. If yes specify the ADR

_____

_____

_____

_____

_____

_____

_____

Relevant Patient medical and medication history

Annex II

DRP registration format

TYPE OF PROBLEM

Drug therapy problem 1: Unnecessary drug therapy

- There is no valid medical indication for the drug therapy at this time
- Multiple drug products are being used for a condition that requires single drug therapy
- The medical condition is more appropriately treated with nondrug therapy
- Drug therapy is being taken to treat an avoidable adverse reaction associated with another medication
- Drug abuse, alcohol use, or smoking is causing the problem

Drug Therapy Problem 2: Needs Additional Drug Therapy

- A medical condition requires the initiation of drug therapy.
- Preventive drug therapy is required to reduce the risk of developing a new condition
- A medical condition requires additional pharmacotherapy to attain synergistic or additive effects

Drug Therapy Problem 3: Ineffective Drug

- The drug product is not the most effective for the indication being treated
- The medical condition is refractory to the drug product
- The dosage form of the drug product is inappropriate
- The drug is not effective for the medical problem

Drug therapy problem 4: inappropriate dose

- The dose is too low to produce the desired response.
- The dosage interval is too infrequent to produce the desired response.
- The duration of drug therapy is too short to produce the desired response
- Dose is too high
- The dosing frequency is too short
- The duration of drug therapy is too long

Drug Therapy Problem 5: Adverse Drug Reaction

 The drug product causes an undesirable reaction that is not dose-related

 A safer drug product is required due to risk factors

 A drug interaction causes an undesirable reaction that is not dose-related

 The dosage regimen was administered or changed too rapidly

 The drug product causes an allergic reaction

 The drug product is contraindicated due to risk factors

Drug Therapy Problem 6: Drug interaction

Annex III:

Consent Form

Addis Ababa University

School of Pharmacy

Department of pharmacology and clinical pharmacy

Prospective cross-sectional study on assessment of drug related problems in medical wards of Tikur Anbessa Specialized Hospital

Greeting:

Hello, My name is_____. I am here today to collect data to asses drug related problems in medical wards of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. The study is being conducted by Mr. Mohammed Biset from Addis Ababa University, school of Pharmacy, department of clinical pharmacy and pharmacology, post graduate program.

The objective of this study is

- ✓ To determine the prevalence of drug related problems
- ✓ To identify the most common drugs and drug classes involved in drug related problems
- ✓ To identify predictors of occurrence of drug related problems.

This is prospective cross-sectional study so I request you to take part in this study. Your cooperation and willingness is greatly helpful in assessing drug therapy problems in Tikur Anbessa Specialized Hospital. The study will be conducted through recording medical findings from your medical chart and interviewing (if needed). Intervention will be given to correct any drug related problem as fast as possible.

Your name will not be written in this form and will never be used in connection with any information we take from the chart and you tell us. There is no possible risk associated with participating in this study except the time spent to deliver information for us. All information taken from your medical chart or given by you will be kept strictly confidential. Your participation is voluntary and you are not obligated to participate in the study. If you feel discomfort with the study, it is your right to drop it. If you have questions regarding this study or would like to be informed of the results after its completion, please feel free to contact the principal investigator.

Address of the principal investigator:

Mohammed Biset

Cell phone: +251- 939496171

E-mail: mb6767@gmail.com

Are you willing to participate in this study?

1. Yes - …….. Continue

2. No - …… Skip to the next participant