Medication Dosing Error and Contributing Factors among admitted patients with Renal Impairment in Jimma University Specialized Hospital, Southwest Ethiopia

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Abstract

Background*:* Medication dosing errors are among the frequently encountered medication problems in patients with renal impairment. Dose adjustment becomes very important when dealing with medications with potential nephrotoxicity and/or elimination through renal excretion or metabolism.

Objective*:* The aim of this study was to assess the medication dosing errors with drugs of potential nephrotoxicity and/or elimination through renal excretion or metabolism and contributing factors among admitted patients with renal impairment in Jimma University Specialized Hospital.

Methodology*:* A cross-sectional quantitative study was carried out at pediatrics, surgical and medical wards of Jimma University Specialized Hospital from February 7 to April 10, 2011. Patients' clinical, laboratory findings and medications prescribed to patients with renal impairment were abstracted from their medical cards using pretested data abstraction format. Calculated creatinine clearance $\leq$ 50 ml/min was considered for selection of patients with renal impairment. Appropriateness of dosing was evaluated based on standard drug treatment guidelines. Subjective data were also collected from prescribers in the selected wards using self administered questionnaire to assess contributing factors for medication dosing error. The data obtained was analyzed using SPSS version 16.0. Descriptive statistics and logistic regression were undertaken to assess medication dosing errors and their contributing factors. The significance level for the analysis was 0.05.

Results: A total of 86 patients with calculated creatinine clearance $\leq$50 ml/min were included in the study. They were prescribed a total of 406 lines of prescription, of which 371(91.38%) were medications with potential nephrotoxicity and/or elimination through renal excretion or metabolism from which 85 (22.91%) lines of prescriptions were inappropriately dosed. Moreover, 52(60.5%) of the patients had at least one medication dosing error. Forty seven (55.29%) of the 85 dosing errors were associated with increase or decrease in frequency of the drug regimen; the rest being associated with dose or both dose and frequency errors. The most inappropriately dosed medications were furosemide, diclofenac, salbutamol, amlodipine and digoxin. Sex of the patient, hospital stay, and complexity of the regimen were significantly associated with the medication dosing error.

Conclusion and recommendation: In our present study, medication dosing errors were prevalent (22.91%) among admitted patients with renal impairment. Errors were mainly associated with dosage frequency of cardiovascular drugs such as furosemide, amlodipine and digoxin. Continued medical education in the field of clinical pharmacokinetics and renal drug dosing is required.

Key words*:* Dosing error, renal impairment, nephrotoxic and/or elimination through renal excretion or metabolism, contributing factors.

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List of abbreviations

ACE: Angiotensin Converting Enzyme

ADE: Adverse drug events

AOR: Adjusted Odds Ratio
ARF: Acute Renal Failure

BMI: Body Mass Index

BUN: Blood Urea Nitrogen

CI: Confidence Interval

CKD: Chronic Kidney Disease

COR: Crude Odds Ratio
CrCl: Creatinine Clearance

ERB: Ethical review Board
GFR: Glomerular Filtration Rate

GP: General Practitioner

HO: Health Officer

ICU: Intensive Care Unit

JU: Jimma University

JUSH: Jimma University Specialized Hospital

KDOQI: Kidney Dialysis Outcomes Quality Initiative

MDE: Medication Dosing Errors

MDRD: Modification of Diet in Renal Disease

NSAIDs: Non-steroidal Anti-inflammatory Drugs

SCr: Serum Creatinine

SPSS: Statistical Package for Social Sciences

TEM: Nephrotoxic and/or eliminated through renal Excretion or Metabolism

UK: United Kingdom

Operational definitions

Medication dosing error: Commission of errors when dose ordered renally impaired patients is high or low; dosage information is omitted; dose is missing; dosage frequency is incorrect.

Renal impairment: The stage of Stage of kidney damage at which the creatinine clearance is less than or equals to 50ml/min.

Renal drug dosing: Administering (dosing) of adjusted amount (dose) of a drug according to the level of kidney function

Appropriately dosed drugs: Drugs whose doses are adjusted in line with the dosing protocol of *Drug Prescribing in Renal Impairment*

Complex regimen: A drug regimen administered three times and above per day and/or three or more drugs per order.

Line of prescription: Individual drug regimen that is written on the medical card. If a given drug regimen is written more than once, it is considered as multiple lines of prescriptions

1. Introduction

The kidney is an important organ in excretion of metabolic waste products, foreign chemicals and drugs, regulation of water and electrolyte balances, regulation of arterial pressure, regulation of acid-base balance, secretion, metabolism, and excretion of hormones, and gluconeogenesis. These functions are commonly measured by glomerular filtration rate (GFR) (Guyton, *et al.*, 2006*;* schonder, 2008).

Inability of the kidney to accomplish the aforementioned functions is termed as renal impairment (failure). Renal impairment is a major public health problem amenable to treatment and prevention. It is generally classified as acute or chronic renal failure. Acute renal failure (ARF) is characterized by a rapid decline in glomerular filtration rate over hours to days. Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function, and a progressive decline in glomerular filtration rate over months to years. According to recent guidelines of the National Kidney Foundation [Kidney Dialysis Outcomes Quality Initiative (KDOQI), CKD is staged based on the GFR (ml/min/1.73 m^2) as stage 0 (>90), 1($\geq$90), 2(60-89), 3(30-59), 4(15-29) and 5(<15) (Basta, *et al.*, 2000*;* Rakel, *et al., 2008;* Skorecki, *et al.*, 2008).

Impairment or degeneration of kidney function affects the pharmacokinetics of drugs. This progressive loss of kidney function leads to impaired renal excretion of numerous drugs and their metabolites resulting in a longer elimination half-life of the administered drugs and their active and toxic metabolites. In addition to changing renal elimination directly, uremia can affect drug pharmacokinetics in unexpected ways. For example, declining renal function leads to disturbances in electrolyte and fluid balance, resulting in physiologic and metabolic changes that may alter the pharmacokinetics(such as drug distribution and elimination) and pharmacodynamics (such as changes in drug sensitivity at the receptor site) of a drug (Dowling, 2002*;* Shargel, *et al.*, 2004).

Therefore, uremic patients have special dosing considerations to account for such pharmacokinetic and pharmacodynamic alterations (Shargel, *et al.*, 2004). The proper dosing of medications for patients with renal impairment can maximize therapeutic efficacy, minimize

toxicity and cost (Hug, *et al.,* 2009). Dose adjustment becomes very important when dealing with medications with potential nephrotoxicity and/or elimination through renal excretion or metabolism designated as TEM medications because of high prevalence of renal impairment and large number of drugs with renal elimination and/or potential nephrotoxicity (Salomon, *et al.,* 2003*;* Sweileh, *et al.,* 2007).

Even though the GFR is reasonably good estimate of overall kidney function, these standard methods of GFR determination are not typically used in clinical practice because the filtration markers (like inulin) are, to varying degrees, costly and cumbersome and may involve radioactivity which necessitates special handling and disposal measures. Therefore, calculated creatinine clearance (CrCl) based on serum creatinine concentration is the most convenient method to estimate GFR as it requires only a single blood sample (Verbeeck, *et al.,* 2009). The normal estimated ranges of SCr are female (0.6–1.2 mg/dL), male (0.8–1.4 mg/dL), and children (0.2–1.0 mg/dL) (Wilson, 2008). The Cockroft-Gault equation is still most often used for estimating GFR in pharmacokinetic studies and for drug dosage adjustment, although some studies have shown the Modification of Diet in Renal Disease (MDRD) study equations to be more accurate for estimating GFR (Melloni, *et al.,* 2008*;* Verbeeck, *et al.,* 2009).

The design of the optimal dosage regimen for patients with renal impairment is dependent on the availability of an accurate characterization of the relationship between the pharmacokinetic parameters of the drug and renal function, and an accurate assessment of the patient's renal function. Most dosage-adjustment guidelines have proposed the use of a fixed dose or interval for patients with broad ranges of renal function. Although several methods have been proposed to attain the desired average steady-state concentration profile, the principal choices are to decrease the dose or prolong the dosing interval. Otherwise, the dose and dosing interval may both need to be changed to allow the administration of a clinically feasible dose or a practical dosing interval *(*Matzke, *et al.,* 2008).

Renal clearance status is especially important for some drugs where the gap between efficacy and toxicity is narrow. Doses of these drugs need careful adjustment if they are prescribed for patients with impaired renal function. Some drugs also have the potential to cause renal toxicity.

This is particularly likely to occur in patients who already have some degree of renal impairment, although other factors can increase the risk (Faull & Lee, 2007). These all issues are the results of the interplays of patient, prescriber and environment factors (Bradley, 1992).

In summary, responses to drug therapy in patients with renal impairment are markedly heterogeneous and require thoughtful dosing considerations and ongoing evaluation by prescribing physicians. Although reductions in glomerular filtration rates can be factored mathematically into dosage adjustment strategies, this merely represents the initial step and one of many pharmacokinetic and metabolic principles to be considered. Dosing information must be applied to individual patients in a prudent manner, taking into account specific alterations in drug handling induced by the degree of renal impairment and any other concurrent conditions (Swan, *et al.*, 1992).

2. Statement of the problem

Medication errors are among the most common types of medical errors, medication dosing errors (MDEs) being the most common which ultimately determine the amount of drug available to elicit its therapeutic and/or toxic effect. The outcome of these errors could range from minimal (or no) patient harm to life-threatening risk. Studies have shown that 26–42% of adverse drug events (ADEs) are preventable and these preventable ADEs are mainly caused by prescribing and transcribing errors. Adverse events within the hospital lead to morbidity and mortality in up to 6.5% of hospital admissions and are mainly attributed to medication errors and ADEs (Vessal, 2010).

Likewise, from a national study in Australia, medication dosing errors result in around 3% of all hospital admissions, and up to 30% for those above 75 years of age. Three quarters of these errors are potentially preventable (Runchiman, *et al.,* 2003*).* Close to 20% of patients consulted physicians because of an adverse drug event in France (Queneau, *et al.,* 2005*)*, and more than 12% of admissions being associated with adverse drug reactions in Greece which are expected to occur more commonly with age and the number of drugs taken (Alexopoulou, *et al.,* 2008*).*

Between 44,000 and 98,000 Americans die each year because of medication errors and about 1 million people are injured (Hug, *et al.,* 2009). In contrast, in the Netherlands, adverse drug reactions due to medication dosing errors resulted in more than 12,000 patients being hospitalized in a year; bleeding, low blood sugars levels and fever being the most common types. Of these, 6% were found to be fatal and greater risk is associated with older age and female gender (van der Hooft, *et al.,* 2006*).*

In a study conducted in UK, potentially serious error occurred in 0.4% (95% CI 0.3 to 0.5). Most of the errors (54%) were associated with choice of dose. Error rates were significantly different for different stages of patient stay ($p<0.0001$) with a higher error rate for medication orders written during the inpatient stay than for those written on admission or discharge. While the majority of all errors (61%) originated in medication order writing, most serious errors (58%) originated in the prescribing decision (Dean, *et al.,* 2002a).

Medication dosing errors, especially in patients with reduced creatinine clearance, are harmful and costly. In a review to assess compliance with dosing guidelines in patients with chronic kidney disease, the non-compliance rate in hospitals ranged from 19% to 67% (Hassan, *et al.,* 2009). Adverse drug events can prolong the length of stay and increase costs in patients with reduced creatinine clearance. The cost of drug-related morbidity and mortality has been estimated to be 76.6 billion dollar per year in the United States (Hug, *et al.,* 2009*;* Vessal, 2010).

Despite the importance of dose adjustment among patients with renal impairment, such adjustments were rarely made in France. Thirty four percent of the prescriptions of TEM medications were inappropriate and 75% of the order sheets contained at least one inappropriate prescription. A major reason for such medication dosing error was the underestimation of potential adverse consequences (Salomon, *et al.,* 2003*).*

In the Jimma University Specialized Hospital (JUSH), there is no published work on medication dosing error; and hence, there is lack of information on dosage adjustment pattern among patients with renal impairment. There is no local renal drug dosing guideline in the hospital and the usual trend of dose adjustment, even for any other disease states, is escalation or tapering of dosage without explicit consideration of the objective level of renal function and looking for clinical deterioration or improvement. This is not only the issue of JUSH but also the whole Ethiopia too as there are limited researches conducted regarding drug dosage pattern in patients with renal impairment in the country.

3. Literature Review

Medication dosing errors were present during ancient times and patients ultimately suffer and die without good medical care. In a study performed in a 15-bed nephrology ward of a university hospital in Shiraz, Seventy six patient charts were reviewed during the 4-month period. A total of 818 medications were ordered in these patients. Eighty six prescribing errors were detected in 46 hospital admissions. Different types of prescribing errors and their frequencies were as follows: wrong frequency (37.2%), wrong drug selection (19.8%), overdose (12.8%), failure to discontinue (10.5%), and failure to order (7 %), under-dose (3.5%), wrong time (3.5%), monitoring (3.5%), wrong route (1.2%), and drug interaction (1.2 %). The attending physician agreed to 96.5% of the prescription errors detected, and interventions were made. Although 89.5% of the detected errors caused no harm, 4(4.7%) of the errors increased the need for monitoring, 2 (2.3%) increased length of stay, and 2 (2.3%) led to permanent patient harm (Vessal, 2010).

In an interventional study conducted at the general internal service of the university hospital of Basel, doses were adjusted to individual renal function in only 33% of renally eliminated drugs. In contrast, in the interventional group, 81% of all doses which required adjustment were correct ($p<0.001$ versus control). In patients receiving doses that have not been adjusted to the degree of renal impairment, the dose was always too high. Drugs often prescribed in doses which were too high included digoxin, amoxicillin, ciprofloxacin, flucloxacillin, norfloxacin, atenolol, sotalol, enalapril, ranitidine, fluconazole, and acyclovir (Falconnier, *et al.*, 2001).

Two hundred and two order sheets were completed for 164 patients from *Hopital pitie Salpetriere (Assistance publique, Hopitau de Paris, Paris, France)* by a prospective descriptive method. It was totaled 1469 lines of prescription, 85% of which were TEM medications, with guidelines for dosage adjustment for 886(71%) of them. Of these 886 prescriptions, 34%were inappropriate, 14% being contraindicated and 20% indicating inappropriate dosage with regard to the patient's renal function status. Among the 202 order sheets, 75% included at least one inappropriate prescription. Sixty three percent included at least one prescription with potentially adverse consequences, 3% of these having potentially fatal and sever consequences (Salomon, *et al.*, 2003).

Medication charts of eligible patients were reviewed in The Princess Alexandra Hospital of 480 beds. Of the total of 248 prescriptions, 111 (44.8%) were found to have inappropriately high doses. For 26 prescriptions (23.4%) there was an appropriate dose reduction in hospital. Seventy three (29.3%) prescriptions were continued at an inappropriately high dose. Of 22 admission prescriptions for metformin the dose was excessive in 17 (77.3%). The dose was reduced in only five of these instances in hospital (31%). Apart from metformin, the percentage of prescriptions with an inappropriately high dose ranged from 12% for ciprofloxacin to 66.7% of atenolol. Only 34 prescriptions for the target drugs were initiated in hospital, of which 17 were for ACE inhibitors, 7 were for atenolol and 8 were for ciprofloxacin. Most patients (88.2%) were commenced in hospital on an appropriate dose (Pillans, *et al.,* 2003).

In a cross-sectional study of a group of hospitalized patients was carried out at Al-Watni governmental hospital, Nablus, Palestine, a total of 78 patients had been calculated creatinine clearance $\leq$59 ml/min. Those patients were prescribed a total of 1001 lines of prescription medication. Dosage adjustment was necessary for 193 TEM medications. Analysis of TEM medications with guidelines for adjustment indicated that 142(73.58%) were found to be inappropriate and 51(26.42%) were found to be appropriate. The most common inappropriate medications were ranitidine, antibiotics, and digoxin. Approximately 77.5% of the unadjusted medications were prescribed during hospitalization (Sweileh, *et al.*, 2007).

In terms of the components of the prescribing process, most of the errors concerned selection of the drug dose. Potentially serious errors occurred mainly in deciding whether or not drug treatment is required and in selection of the drug dose. The error rates varied greatly between wards and the amount of time spent on the ward (Dean, *et al.*, 2002a).

Factors that contribute for medication dosing errors are typically divided in to two sub groups: those caused by systems error and those caused by individual health care professional issues (figure 1). Another issue that is worthy of examination in the context of contributing factor is that of incident reporting. With regard to systems, as hospitals are complex systems comprising both human and technological aspects, may be thought of as comprising of components that

include design, equipment procedures, operators, supplies and environments, the medication process itself within which errors may occur. The professional issue that affect individual professional's practice are varied and multi-factorial which is frequently linked to specific professional traits, focusing on individual practitioner's attributes, skill levels and competencies including understanding of how errors occur, failure to adhere policy and procedure documents, distractions, lack of knowledge about medications, dosage calculation, and workload. In terms of reporting medication dosing error, vast majority of accidents are not reported and near-miss accidents are almost never reported due to fear of consequences of reporting because of disciplinary and professional ramification and the format of the forms, many of which are structured in such a way that systems issues are not identified (McBride-Henry and Foureur, 2005) .

In a prospective study conducted in UK teaching hospital, factors underlying medication errors were categorized using *Reason's model of accident causation*. Therefore, the factors are categorized, with increasing proximity to the erroneous event, as latent conditions (such as organization process), error provoking conditions (such as environmental or individual factors that affects performance at the time of the error) and active failures (such as errors due to slips, lapses, mistakes and violations. Among active failures, the study results revealed that Skill-based slips or lapses were most frequent (25, 57%), though rule-based mistakes (17, 39%) and violations (2, 4%) and doctors often mentioned that they were busy (31, 70%), or had been interrupted during routine tasks (13, 30%); Slips were more frequent than lapses (23 *vs* two). All the mistakes noted were rule-based. A common cause of such mistakes was the absence of knowledge of a relevant rule (6, 35%) and other mistakes included application of the wrong rule (5, 29%). Two violations were made, both of which involved doctors not adequately checking the doses of prescriptions written by final-year medical students, despite being aware that, according to hospital policy, the entire prescription should be checked. Regarding error-provoking conditions, doctors often cited multiple factors as having contributed to their error: the most frequent concerned the work environment, individual factors, and the working of the team. In 31 instances workload was thought by the interviewee to have contributed to the error, in 13 the physical environment was cited, and in 15 staffing was mentioned, including 12 instances in which difficulties arose from having to attend to another doctor's patient. As part of latent conditions, many doctors did not seem to consider the task of prescribing drugs important. The

act of prescribing was often embodied in a drug's name (like "put them on verapamil"), and the details of dose, form, frequency, route, and duration left to the house officer to complete (Dean, *et al.*, 2002b)

Systematic review of seventeen papers reporting 16 studies, selected from 1268 papers identified by the search, was conducted. Studies from the US and UK in university-affiliated hospitals predominated (10/16, 62%). The definition of prescribing error varied widely and the included studies were highly heterogenous. Causes were grouped according to *Reason's model of accident causation.* The active failure most frequently cited was a mistake due to inadequate knowledge of the drug or the patient. Skills-based slips and memory lapses were also common. Where error-provoking conditions were reported, there was at least one per error. These included lack of training or experience, fatigue, stress, high workload for the prescriber and inadequate communication between health care professionals. Latent conditions included reluctance to question senior colleagues and inadequate provision of training (Tully, *et al.*, 2009).

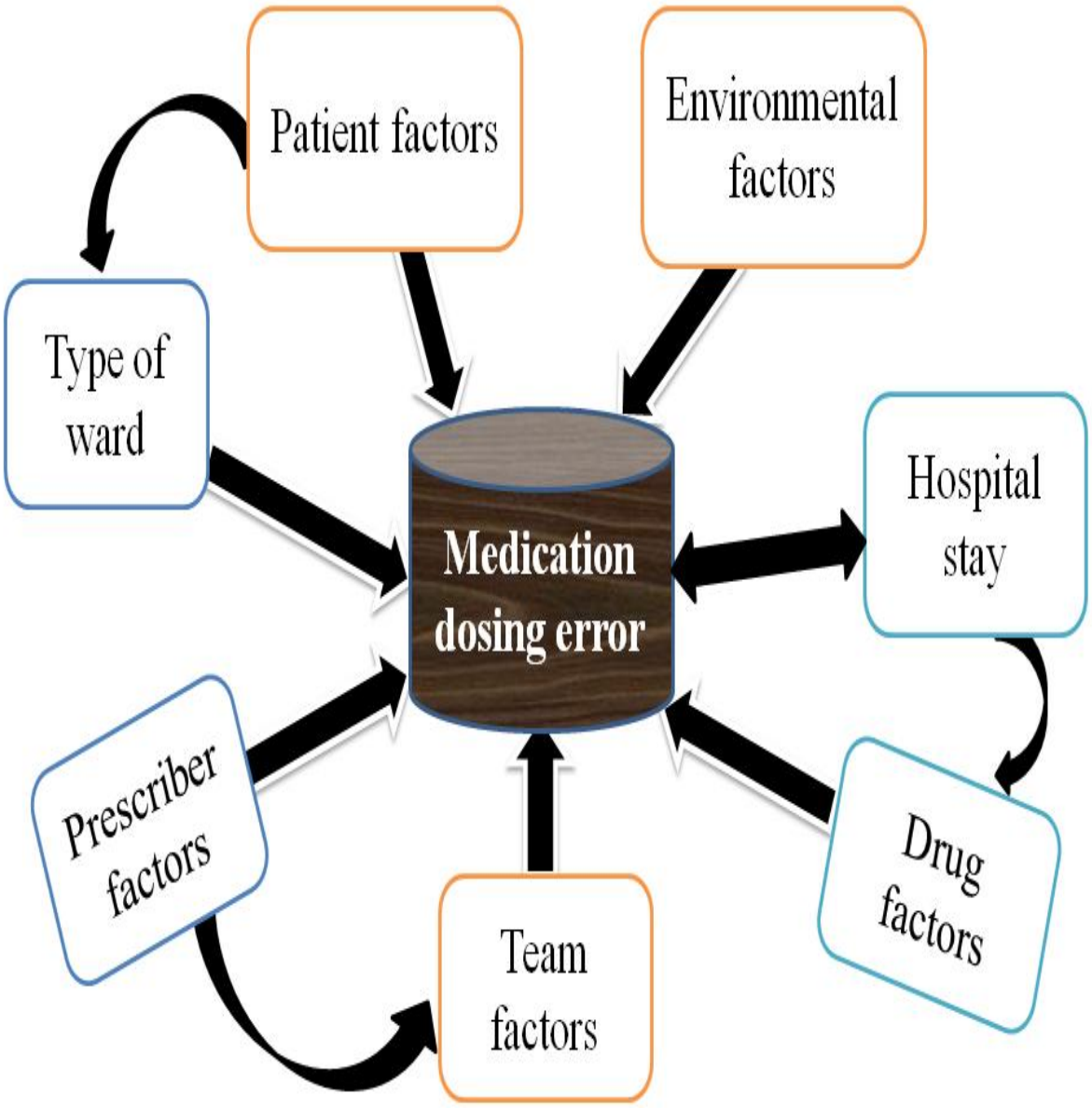

Figure 1: Conceptual framework of medication dosing error and contributing factors (Tully, *et al.*, 2009)

4. Significance of the study

The "standard" dose of a drug is based on average ability to absorb, distribute, and eliminate the drug. This dose will not usually be suitable for every patient. Several physiologic processes (e. g, maturation of organ function in infants) and pathologic processes (example, heart failure, and renal impairment) dictate dosage adjustment in individual patients. These processes modify specific pharmacokinetic parameters and drug sensitivity.

Therefore, this study assessed the appropriateness of the current dosing practice that is being followed in the study setup. It also provides pertinent finding related to the extent of medication dosing errors and the study output helps to point out how the drug regimens should be adjusted during prescribing drugs for patients with renal impairment with the ultimate goal of preventing over and under dosage of TEM medication and subsequent mortality and morbidity. Moreover, the study output would serve as baseline information for other interventional studies and serve as an input in the management of patients prescribed with TEM medications.

5. Objectives of the study

5.1. General objective

The aim of the study was to assess medication dosing errors of TEM medications and contributing factors among admitted patients with renal impairment in Jimma University Specialized Hospital

5.2. Specific objectives

- To determine the prevalence of TEM medications dosing error among admitted patients with renal impairment
- To assess the pattern of inappropriate dosing practice of TEM medications among admitted patients with renal impairment
- To assess the contributing factors for inappropriate dosing of TEM medications in admitted patients with renal impairment

6. Participants and methods

6.1. Study area and period

The study was conducted in Jimma University Specialized Hospital (JUSH) from February 7 to April 10, 2011. JUSH is found in Jimma town which is located in Jimma Zone, Oromia region. Jimma town is situated at about 352 km southwest of the capital of Ethiopia, Addis Ababa. The population of the Jimma zone is 2,495,795, of which male represents 1,255,130 and female represents 1,240,665 (Central Statistics Agency, 2008).

Description of the study setup

JUSH is the only referral hospital in south west Ethiopia where multidisciplinary team of professionals provide health care services to about 10 million peoples (Worku *et al.*, 2010). The hospital provides inpatient services with around 450 beds in six clinical wards (Internal medicine, surgery, gynecology and obstetrics, pediatrics, psychiatry and ophthalmology) and outpatient services in the chronic illness follow up clinics (diabetes, cardiovascular, asthma, epilepsy, tuberculosis and HIV), dermatology, dentistry and other outpatient departments. Currently, there are a total of around 558 staffs comprising of 27 specialist medical doctors, 66 general practitioners, 191 nurses, 12 anesthetists, 13 pharmacy professionals, 21 medical laboratory professionals and other medical and administrative staffs (Ethiopian health sector, 2010).

6.2. Study design

A prospective cross-sectional quantitative study was conducted.

6.3. Population

6.3.1. Source population

All patients with renal impairment who were admitted to the inpatient wards of JUSH and all prescribers of JUSH

6.3.2. Study population

All patients with renal impairment who were admitted to the pediatrics, medical and surgical wards of JUSH and prescribers available at pediatrics, medical and surgical wards of JUSH

during the study period. The rationale why these wards were selected was the feasibility of the data collection process and the cost of undertaking the study. For example, patients in ICU were mostly bed ridden; and hence, measuring their weights and heights was impossible.

Inclusion criteria for patients

- Patients whose latest measured serum creatinine level >1.2 mg/dL available
- Patients who stayed in the selected admission wards for ≥24 hours.
- Patients who were receiving at least one medication
- Patients who were greater than one year of age
- Patients whose calculated creatinine clearance ≤50 ml/min

The reason why patients with serum creatinine >1.2 mg/dl as a cutoff point was that SCr=1.2 mg/dl ((1.0+1.2+1.4)/3) was found to be the average upper limit for all patient groups (Wilson, 2008). Patients who were admitted for at least 24 hours were included because most patients collect their laboratory results during their first day of admission.

Inclusion criteria for Prescribers

- Prescribers who were in charge of the pediatrics, medical and surgical wards of JUSH during the study period.

Patient exclusion criteria

- Pregnant women
- patients less than one year of age

The basic rationale for exclusion of pregnant women and patients less than one year of age was the rapid variability of glomerular filtration rate in these patient groups.

6.4. Sampling technique

After patients were identified using the other aforementioned inclusion criteria, creatinine clearance was calculated using Cockroft-Gault equation (Shargel, *et al.*, 2004). Calculated creatinine clearance ≤50 ml/min was considered for renal impairment.

Adult

Male

$$CrCl = \frac{(140\text{-age (yrs)}) \times \text{weight (kg)}}{72 \times \text{serum creatinine (mg/dl)}}$$

Female

$$CrCl = \frac{(140\text{-age (yrs)}) \times \text{weight (kg)}}{72 \times \text{serum creatinine (mg/dl)}} \times 0.90$$

Children:

$$CrCl = \frac{0.55 \times \text{body length (cm)}}{\text{Serum creatinine (mg/dl)}}$$

When the patient's BMI $\geq$25, ideal body weight (IBW) was calculated and used if the difference between actual body weight and ideal body weight is greater than 20% of the ideal body weight.

IBW for male = 50kg + (2.3kg x number of inches over 5 feet)

IBW for female = 45.5kg + (2.3kg x number of inches over 5 feet)

All patients who were available in the pediatrics, medical and surgical wards of JUSH during the study period and fulfilled all the above inclusion criteria were included. On the other hand, prescribers in charge of pediatrics, medical and surgical wards of JUSH during the study period were included (figure 2).

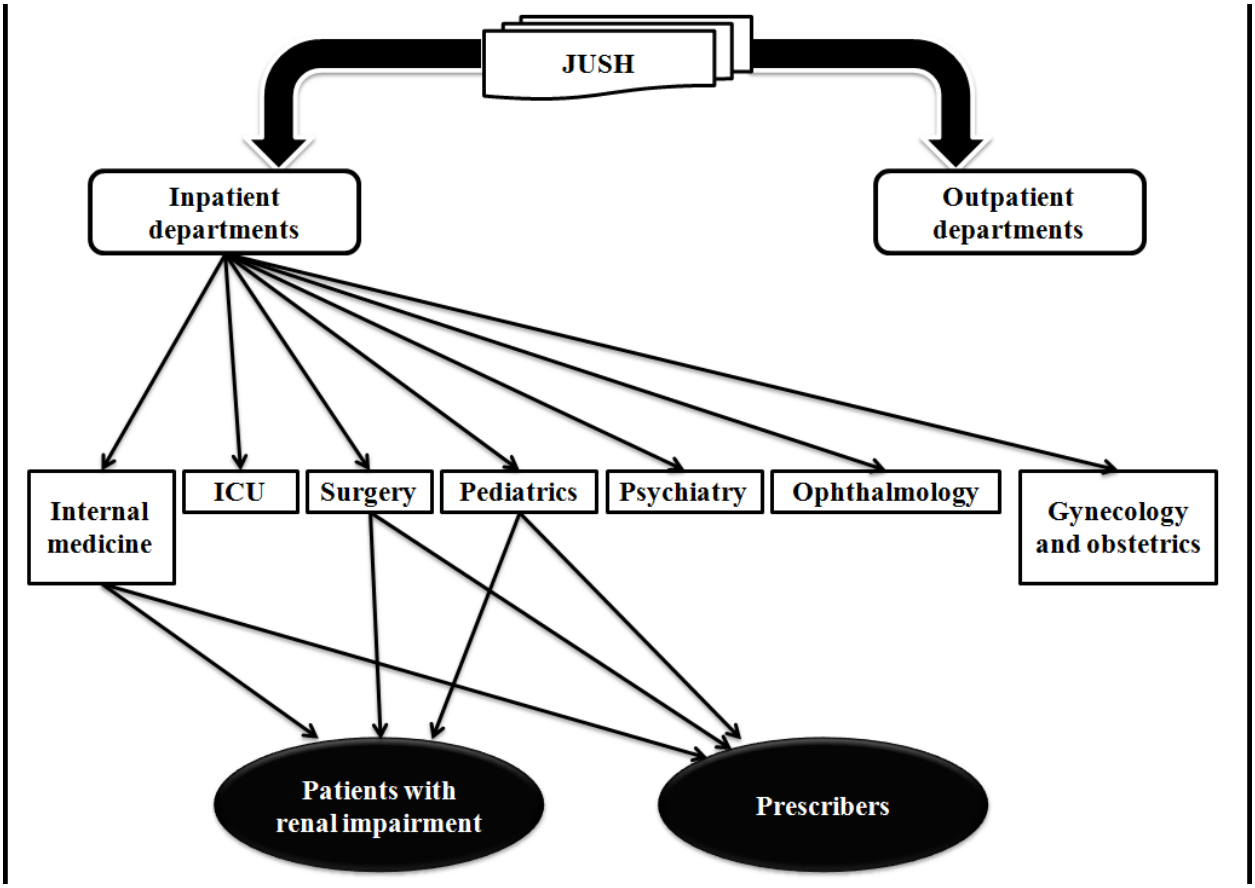

Figure 2: Structural framework of inpatient wards and study setups from which patient participants and prescribers were selected

6.5. Study variables

6.5.1. Independent variables

- Patient factors (Age, Sex, Complexity of the clinical condition, Language and communication, Uncooperativeness, CrCl, BMI, Comorbidity)
- Individual prescriber factors (Physical health, Mental health, Skills and knowledge)
- Working environment (physical environment, Staffing, Work overload)
- Medical Team factors (Communication, Supervision, Responsibility)
- Type of ward
- Complexity of drug regimens
- Amount of time of stay in the ward

6.5.2 Dependent variable

- TEM medication dosing error

6.6. Data collection tools and Method

Separate data abstraction format and semi structured questionnaire were used. Patient data were collected by abstracting relevant information including renal function test, medication regimen prescribed, co-morbidities of the patients, and prescriber's qualification from medical cards of study participants, and direct measurement of unrecorded parameters including weight and height. Self administered semi structured questionnaire was used to collect data regarding clinicians' prescribing practice of TEM medications and perceived contributing factors for TEM medication dosing errors among patients with renal impairment.

6.7. Training of data collectors

Three BSc nurses were recruited for data abstraction from medical cards and measurement of pertinent patient parameters. The data collectors were given training for one day on how to identify the right patient, approach the patient, fill the data abstraction form and measure unrecorded parameters that are pertinent to the study. They were also well introduced on the issues of consent process and confidentiality. For ease of communication during the data collection process, data collectors involved in clerking of patients were chosen such that they are speakers of the native regional language (Afaan Oromoo). The data from prescribers working at the pediatrics, surgery and medical wards of JUSH were collected by the principal investigator.

6.8. Pretest

A pretest was conducted on five patients selected purposively in Medical ward B of JUSH in order to assess the validity and repeatability of the data collection instrument, highlight problems associated with the data collection tools, check the data collectors' performance and ensure standardization of techniques, highlight other problems related to the design, such as problems in finding enough cases based on the case definition criteria.

6.9. Data quality management

Monitoring of the data collectors by regular supervision and spot checking was done daily by the principal investigator for early detection of incomplete and inconsistent data and cross check with the patients' medical card for timely correction. Data collectors were trained theoretically

and practically on how to conduct the data collection. Pretest was also done and the data collection tools were validated.

6.10. Data processing and analysis

The data were cleaned, coded, entered and analyzed using SPSS version 16.0 for windows. Questionnaires with incomplete data were excluded out from analysis. Descriptive statistics was run to determine demographic characteristics of the patients, TEM medication dosing error, and co-morbid conditions. The data were also subjected to logistic regression to figure out contributing factors of TEM medication dosing error. P value less than 0.05 was considered significant for the analysis. Data from prescribers were also analyzed descriptively

6.11. Ethical considerations

The study was conducted after ethical clearance was granted from the Ethics Review Board (ERB) of the College of Public Health and Medical Sciences, Jimma University (Ref. No.: RPGC/173/2011). Permission was also obtained from the clinical director of JUSH. An informed verbal consent was obtained from the individual participants and/or guardians of children. The patients or guardians of children were explained about the aims and reasons for conducting the study, how their involvement contributes to the outcome of the study, and what their rights are within the study. Accordingly, the right of the patient not to participate or to withdraw at any time from the study was respected. They were informed that their refusal or withdrawal do not affect the quality of care they receive. They were also explained about the expected benefits of the study and the probable injuries or incidences that might occur to them in the study.

During the investigation, all patient records were kept confidential (except for those involved in the study) such that each patient was identified only by code. Neither their name nor residential address was recorded.

6.12. Limitations of the study

Most senior clinicians' recommendations were transferred verbally and hence, all the prescription written by medical interns and/or residents might not been of their own. In addition, as the study was a cross-sectional study, the pattern of drug therapy like escalation or tapering of dosage could not be ascertained and all the prescriptions were considered as a maintenance dosage. Likewise, the cause-effect relationships of factors could not be established.

7. Result

A total of 120 admitted patients with recorded SCr >1.2mg/dl and fulfilling all other inclusion criteria, were identified from the three inpatient wards, medical, surgical and pediatrics. 86 patients, represented by 38(44.2%) males and 48(55.8%) females, were identified to have a calculated CrCl $\leq$50ml/min and included in the study. The age range of the majority (57%) of the patients was 18-50 with mean age of 44 years. Fifty two patient accounting 60.5% had a calculated Creatinine clearance ranging from 30 to 50 with body mass index of 18.5-25 $kg/m^2$and hospital stay less than 7 days. The average serum creatinine of the patients was 2.46 mg/dl. Moreover, most 75(87.2%) of these admitted patients were from medical wards (table 1).

Table 1: Demographic characteristics of patients with renal impairment in JUSH, February-March, 2011

Demographic variables		**Frequency**	**Percent**
Age (years)	<18	4	4.7
	18-50	49	57.0
	>50	33	38.4
Sex	Male	38	44.2
	Female	48	55.8
Creatinine clearance (ml/min)	<10	5	5.8
	10-29	29	33.7
	30-50	52	60.5
Body mass index (kg/m2)	<18.5	28	32.6
	18.5-25	50	58.1
	>25	8	9.3
Ward of admission of the patient	Medical	75	87.2
	Surgical	7	8.1
	Pediatrics	4	4.7
Hospital stay of the patient	≤7 days	52	60.5
	>7days	34	39.5

Regarding the co-morbidity conditions, it was found that, 55 of the studied admitted patients accounting for 63.95%, were co-morbid with cardiovascular diseases such as heart failure, hypertension, ischemic heart disease and venous thrombo-embolism. Infectious diseases were the second commonly observed co morbid conditions among the admitted patients accounting for 53.33% (table 2).

Table 2: Co-morbid conditions among patients with renal impairment in JUSH, February-March, 2011

Disease category	Number	Percent
CVS diseases	55	63.95
Infectious diseases	45	52.33
Hematologic diseases	13	15.12
GUS diseases	12	13.95
GIT diseases	7	8.14
Respiratory diseases	7	8.14
CNS diseases	6	6.98
Other s[£]	11	12.79

[£] = tumor, malnutrition, hypothyroidism, diabetes mellitus, liver disease

In the current study, a total of 406 lines of prescriptions were prescribed to the studied patients from which 371(91.38%) lines of prescriptions were TEM medications with specific dosing guideline according to the guideline '*Drug Prescribing in Renal Failure'* (figure 3). The average number of drugs prescribed per individual admitted patient was 4.72 and the average number of TEM medications per patient was 4.31. Fifty two (60.5%) of the patients were prescribed at least one medication with dosing error (figure 4)

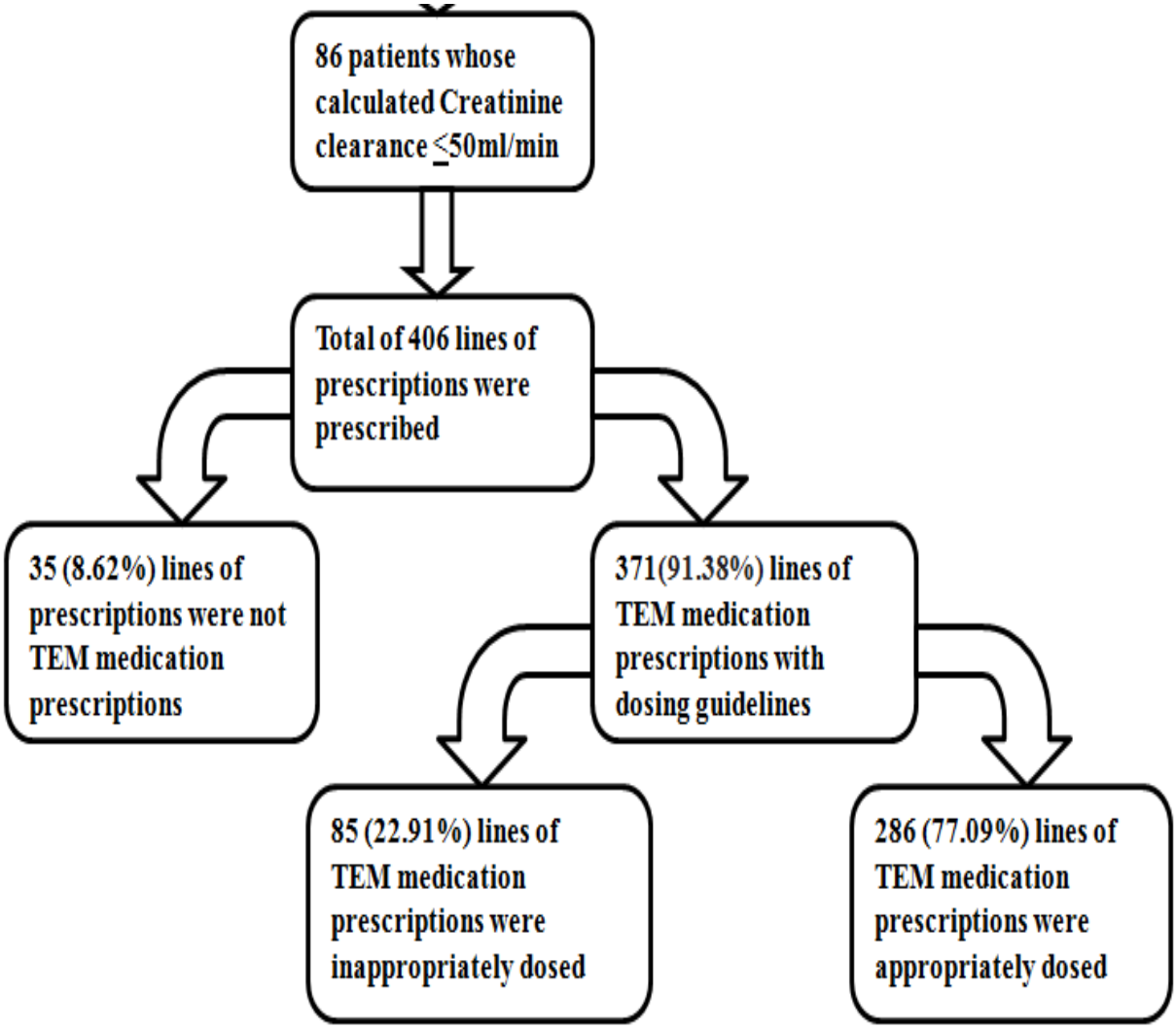

Figure 3: Appropriateness of prescriptions among patients with renal impairment in JUSH, February-March, 2011 (Salomon, *et al.*, 2003)

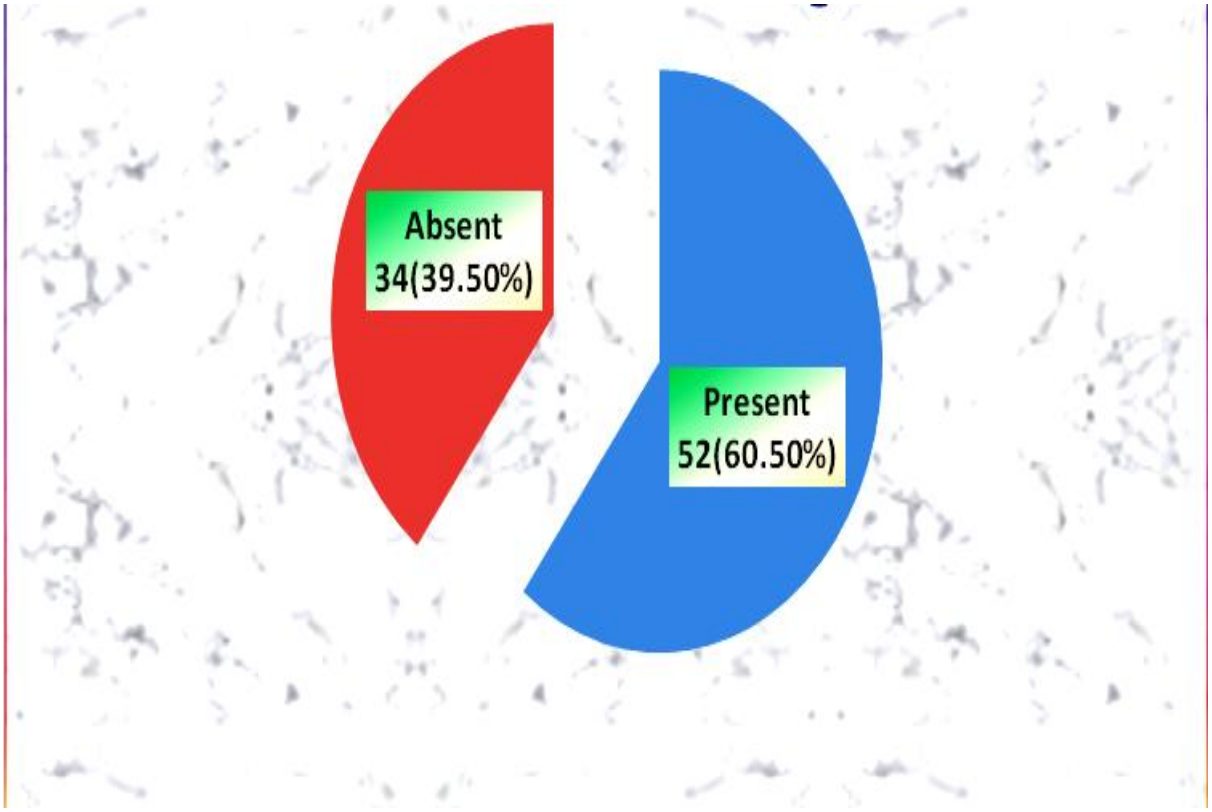

Figure 4: Profile of TEM medication dosing errors in patients with renal impairment in JUSH, February-March, 2011

Regarding medication dosing, out of the 371 TEM medications, 85 of them were wrongly prescribed making the overall medication dosing error to be 22.91% and the approximate average incidence of medication dosing error per individual patient to be 1. Forty seven (55.29%) of these errors, were errors associated with increase (45.88%) or decrease (9.41%) in frequency of the dosage schedule, 27(31.77%) were associated with dose errors and 11(12.94%) lines of prescriptions contained errors associated with both dose and frequency. Moreover, almost all prescriptions were lacking the required dosage forms (table 3).

Table 3: Pattern of TEM medication dosing errors in patients with renal impairment in JUSH, February-March, 2011

Type of error		**Number**	**Percent**
Dose error	Lower	10	11.76
	Higher	14	16.47
	Omission	3	3.57
Frequency error	Decreased	8	9.41
	Increased	39	45.88
Both dose and frequency error		11	12.94
Total		85	100

Medication dosing errors were frequently observed for drugs including, furosemide (16, 18.82%), diclofenac (9, 10.59%), amlodipine (9, 10.59%), salbutamol (9, 10.59%), and digoxin (7, 8.24%). Based on pharmacologic classification, diuretics (21, 24.70%) and calcium channel blockers (11, 12.94%) were observed to be associated with TEM medication dosing errors. Seventy (82.35%), 7 (8.23%), and 8 (9.41%) of the medication dosing errors were committed in medical, pediatrics and surgical wards of JUSH respectively (table 4).

Table 4: TEM medication dosing error incidences in different wards of JUSH, February-March, 2011

Drug	Ward			Total	Percent
	Medical	Pediatrics	Surgery		
Furosemide	13	3	0	16	18.82
Diclofenac	6	0	3	9	10.59
Amlodipine	9	0	0	9	10.59
Salbutamol	9	0	0	9	10.59
Digoxin	7	0	0	7	8.24
Spironolactone	5	0	0	5	5.88
Atenolol	4	0	0	4	4.71
Pethidine	2	0	1	3	3.53
Chloramphenichol	1	0	2	3	3.53
Captopril	3	0	0	3	3.53
Nifedipine	0	1	1	2	2.35
Hydrocortisone	2	0	0	2	2.35
Gentamicin	0	1	1	2	2.35
Ampicillin	0	1	0	1	1.18
Metronidazole	0	1	0	1	1.18
Fluconazole	1	0	0	1	1.18
Omeprazole	1	0	0	1	1.18
Methyldopa	1	0	0	1	1.18
Dexamethasone	1	0	0	1	1.18
Prednisolone	1	0	0	1	1.18
Phenobarbitone	1	0	0	1	1.18
Phenytoin	1	0	0	1	1.18
Acyclovir	1	0	0	1	1.18
Metoprolol	1	0	0	1	1.18
Total	70	7	8	85	100.0

Among variables tested for association using binary logistic regression, sex of the patient (COR=2.800, 95% C.I=1.119-7.007), length of hospital stay (COR=4.166, 95% C.I=1.543-11.250), and complexity of the regimen (COR=.156, 95% C.I=.055-.441) were found to be significantly associated with the commission of TEM medication dosing error. Complexity of the drug regimen was found to be the predictor variable that affects TEM medication dosing error. The odds of receiving inappropriately dosed TEM medication was 80.5% times (AOR=.195, 95% C.I=.063-.604) lesser in patients who receive simple medications as those who take complex medications (table 5).

Table 5: Association of factors affecting TEM medication dosing error in patients with renal impairment in JUSH, February-March, 2011

Variables		TEM medication dosing errors		♈COR(95.0% ♌CI)	♉AOR (95.0% CI)
		Present	Absent		
Age (years)	≤50	29	24	1.000	
	>50	23	10	1.903(.760-4.769)	
Sex	Male	28	10	2.800 (1.119-7.007)*	2.463 (.880-6.892)
	Female	24	24	1.000	1.000
Weight (kg)				.993 (.955-1.032)	
Height(cm)				.997 (.968-1.027)	
Serum creatinine (mg/dl)				1.011 (.817-1.253)	
Hospital stay	≤ 7days	25	27	1.000	1.000
	>7 days	27	7	4.166 (1.543-11.250) *	2.249 (.757-6.678)
Complexity of the regimen	Simple	7	17	.156 (.055-.441) *	.195 (.063-.604)*
	Complex	45	17	1.000	1.000
Prescriber qualification	Medical intern	29	15	1.000	
	Resident	23	18	.661 (.275-1.589)	
CVS disease	No	20	11	1.307 (.526-3.247)	
	yes	32	23	1.000	
Infectious disease	No	25	16	1.042 (.438-2.476)	
	Yes	27	18	1.000	
Hematologic disease	No	47	26	1.000	
	Yes	5	8	.346 (.103-1.166)	

♌CI: Confidence Interval; ♈COR=Crude Odds Ratio; ♉AOR= Adjusted Odds Ratio; * =statistically significant at p-value < 0.05

On the other hand, a total of 68 prescribers were selected from the medical, pediatrics and surgery wards of JUSH to collect additional information on prescribers' medication dosing practice and contributing factors for TEM medication dosing errors. Among those prescribers, 41(60.3%), 17(25%) and 10(14.7%) were medical interns, residents and senior clinicians respectively. Only around one-third (24, 36.4%) of them were prescribers with an experience of greater than one year.

Forty one, accounting 60.3% of the prescribers, were not considering renal function test before prescribing drugs and 39(57.4%) were considering dosage adjustment when renal function was low. But, only 10(24.4%) of prescribers were using creatinine clearance for renal function estimation while 20(48.8%) were using serum creatinine for estimation of renal function. National standard treatment guidelines were the most referred by medical interns as a guideline for TEM medication dosing while standard textbooks (like *Harrison's Principles of Internal Medicine)* and *Uptodate® software* were the most consulted references by senior clinicians and residents. Aminoglycoside antibiotics (33), NSAIDs (18), and ACE inhibitors (17) were most commonly considered drug classes for dosage adjustment by the prescribers (table 6).

Table 6: Clinical practices of the prescribers among patients with renal impairment in JUSH, February-March, 2011

Clinical practice		**Number**	**Percent**
Consider renal function test during medication dosing	Yes	27	39.7
	No	41	60.3
Parameter of renal function estimation	Serum creatinine (SCr)	20	48.8
	Creatinine Clearance(CrCl)	10	24.4
	BUN/SCr ratio	10	24.4
	Urine output	1	2.4
Consider dose adjustment before prescribing	Yes	39	57.4
	No	29	42.6

Among the classes of perceived factors that contribute for TEM medication dosing errors, environmental factors (52, 76.5%) and team factors (51, 75%) were found to contribute a major part. The other classes of contributing factors were patient conditions (49, 72.06%), prescriber conditions (48, 70.59%) and latent conditions (43, 63.23%) (figure 5).

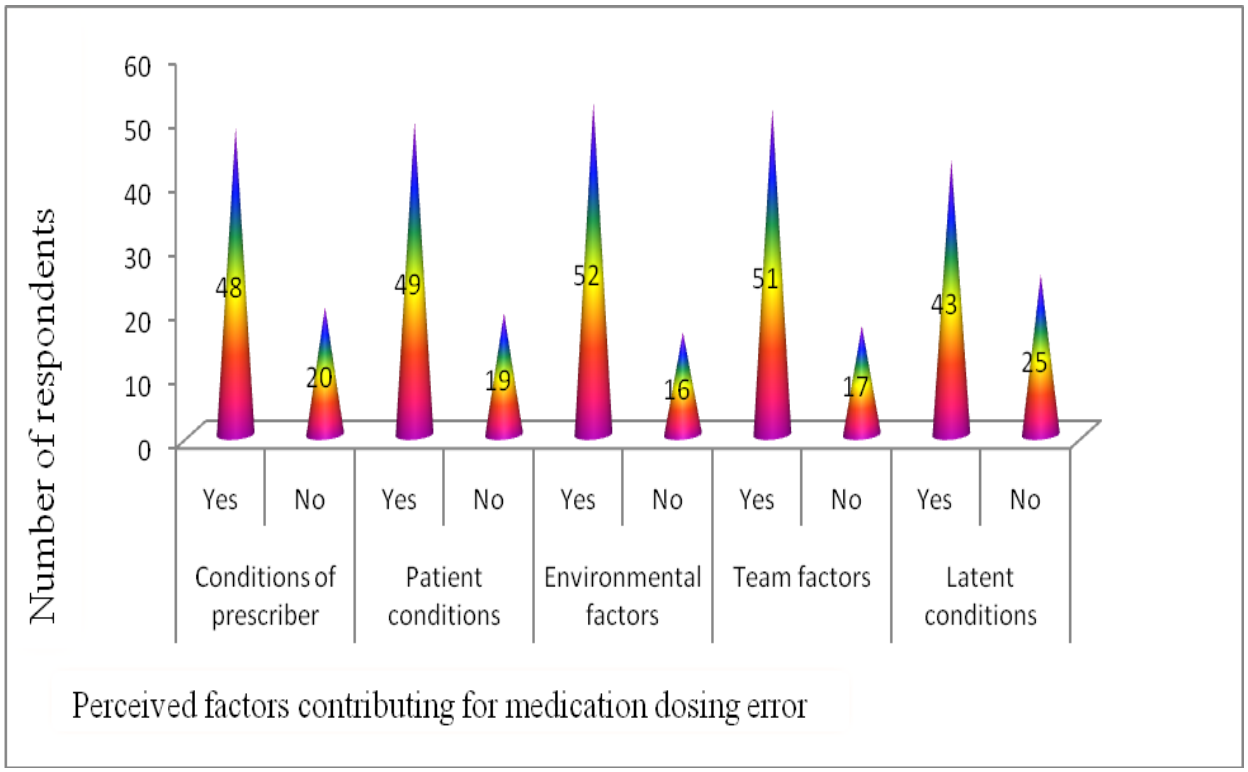

Figure 5: Distribution of perceived conditions that contribute for TEM medication dosing in patients with renal impairment in JUSH, February-March, 2011

Furthermore, lack of appropriate dosage forms and less nephrotoxic alternatives (51), lack of well established guidelines for drug dosing in renal impairment (50), and absence of clinical pharmacists or drug experts in the medical team (49) were known to be the most commonly perceived factors to contribute for medication dosing errors (table 7).

Table 7: Profile of specific conditions perceived to contribute for TEM medication dosing errors in patients with renal impairment in JUSH, February-March, 2011

Perceived conditions		Number of respondents
Conditions of the prescriber	Lack of adequate Knowledge and/or Experience	43
	Underestimation of potential adverse consequences	38
	Inappropriate dosage calculation	32
	Sleep abnormality	28
	Tiredness	26
	Low morale or motivation	23
	Stress	19
	Depression	18
	Being Unwell	11
	Hungriness	10
Patient conditions	Complexity of clinical condition	47
	Uncooperativeness	19
	Language and communication	17
Team factors	Absence of clinical pharmacists or drug experts	49
	Lack of communication	33
	Overlapping responsibility	20
	Poor supervision	17

Table7: cont'd

Environmental factors	Lack of appropriate dosage forms and less nephrotoxic alternatives	51
	Lack of well established guidelines for drug dosing in renal impairment	50
	Lack of objective drug information service	45
	Lack of routine laboratory tests.	42
	Heavy work load	40
	Inadequate staff	23
	Dealing with patients other than your own	19
	Environmental distraction	18
	New or locum staff	16
Latent conditions	Lack of training	41
	Poor data storing system	39
	Lack of feedback systems	37
	Pharmacy systems separate from clinical service	37
	Low self-awareness of making errors	28
	Culture within team (lack or reluctance of questioning seniors)	26
	Not teaching about dose in medical schools	23
	Not seeing transcription as prescribing	20
	Not considering the task of prescribing drugs important	19

8. Discussion

Medication dosing errors are the frequently encountered medication problems in patients with renal impairment as these patients often have alteration in pharmacokinetic parameters such as drug bioavailability, protein binding, biotransformation, volume of distribution, and renal excretion (Pillans, *et al.*, 2003; Vessal, 2010). Though medication dose adjustment is a critical measure to avoid the risk of drug toxicity among patients with reduced renal function, such measure was found to be rarely practiced in the current study setup.

In the current study, patients with renal impairment were selected based on the levels of their serum creatinine as these values were available in the patients' medical cards of the study setup as opposed to creatinine clearances which were unavailable. Thus, it was found that serum creatinine value is the only laboratory data available for the physician in the patients' medical cards. However, for the purpose of this work, body weight and height were measured and CrCl value was calculated by the research team for each admitted patient. The choice of serum creatinine level>1.2 mg/dl as a cutoff point in our study in pre selection rather than creatinine clearance was based on two reasons: first, SCr value of 1.2 mg/dl is considered the upper normal value for SCr in clinical practice and secondly, the serum creatinine (SCr) values mimic the current situation in the hospital.

The mean serum creatinine of the studied admitted renally impaired patients in this work was 2.46 $\pm$ 2.05. Most of the patients were co-morbid with cardiovascular diseases (63.5%) like hypertension, ischemic heart disease, heart failure, and venous thrombo-embolism and infectious diseases (52.33%). Likewise, hypertension (83%) was reported to be the major co-morbid condition among patients studied at university hospital of Shiraz (Vessal, 2010).

The present study results revealed that the prevalence of TEM medication dosing errors to be 22.91%. In comparison, a study performed on 164 patients from *Hopital pitie Salpetriere (Assistance publique, Hopitau de Paris, Paris,* France*)* by a prospective descriptive method depicted that 34% of medications were inappropriate among 886 prescriptions of TEM medications (Salomon, *et al.*, 2003), 44.8% of TEM medications were found to be inappropriately dosed in The Princess Alexandra Hospital, Australia (Pillans, *et al.*, 2003), and

73.58% of the TEM medication prescriptions were found to be inappropriate in a cross-sectional study of a group of hospitalized patients carried out at Al-Watni governmental hospital, Nablus, Palestine (Sweileh, *et al.,* 2007). However, the TEM medication dosing error recorded in the present study was found to be higher than the result of study performed in a 15-bed nephrology ward of a university hospital in Shiraz (10.5%) (Vessal, 2010).

It was also noted from the present study that, 60.5% of the admitted patients had at least one TEM medication dosing error in their medications prescribed during their hospital stay. This study result was almost similar with the study result of university hospital in Shiraz (60.5%) (Vessal, 2010). But, relatively higher rate of incidence of TEM medication dosing error was reported in Palestine (80.77%) (Sweileh, *et al.,* 2007).

There was also approximately one TEM medication dosing error observed per individual patient which was relatively lower compared to the result in Palestine where 2.6, 2.5, and 1.5 inappropriately dosed TEM medications per patient with stage V, IV, and III renal impairment respectively were reported (Sweileh, *et al.,* 2007). This could be due to the difference in the number of medications prescribed per patient (4.72 medications and 4.31 TEM medications per patient in our study versus 12.83 medications and 9.9 TEM medications per patient in Palestine).

It was revealed that, the most common drugs associated with TEM medication dosing errors in this work were furosemide, amlodipine and digoxin which were meant to treat the co morbid cardiovascular disorders. High dosing errors have also been recorded for Salbutamol and diclofenac. Nearly Similar rate of dosing error with digoxin was reported in Palestine. On the contrary, dosing errors associated with such drugs as immunosuppressive therapies and antibiotics (in Shiraz) and ranitidine and antibiotics (in Palestine) were not observed in the current study. The discrepancy between the specific category of drugs might be related with the availability of the drugs and also the medical care delivered (for example, the study area do not have cancer unit and hence, the use of immunosuppressives and chemotherapeutic agents is limited).

Most of TEM medications dosing errors demonstrated in this study were related to inappropriate frequency which contributed for 55.29%. Furosemide, amlodipine and digoxin were known to be

given with wrong frequency. Furosemide was observed to be administered three times per day while the recommended frequency, according to the guideline '*Drug prescribing in renal failure*' (Aronoff *et al.*, 2007), is once or twice per day. Similarly, digoxin was prescribed once daily while every 36 hours being the advised frequency; and amlodipine was administered twice or three times a day while once a day administration being the appropriate frequency (Aronoff *et al.*, 2007). Frequency errors were also reported to be the most common 32(37.2%) errors in a study conducted at university hospital of Shiraz (Vessal, 2010).

In the present study, sex of the patient, hospital stay, and complexity of the regimen were found to be significantly associated with the commission of TEM medication dosing error. Among them, complexity of the drug regimen was found to be the predictor variable which affects medication dosing error; and hence, patients taking drugs three times a day and/or three drugs at a time or more were six times more likely to get inappropriately dosed TEM medications (table 5). Other studies have also demonstrated the association of hospital stay with TEM medication error rates (Dean, *et al.*, 2002a). The association of hospital stay might be related with the increased probability of getting complex regimens. The probable rationale for males being at risk of getting inappropriately dosed TEM medications might be the increased risk of getting cardiovascular diseases (Parker *et al.*, 2008) and subsequent indication of cardiovascular drugs which were the most inappropriately dosed as shown in this study. But, age, sex, SCr, CrCl and stage of renal impairment were tested and found to be not associated with TEM medication dosing error in a study conducted at Palestine (Sweileh, *et al.*, 2007).

As of our study result, the perceived factors for TEM medication dosing error were mainly factors that target to the set up or the working environment; lack of appropriate dosage forms and less nephrotoxic alternatives being the most perceived factor by the prescribers in our study set up (table 7). These findings were supported by a prospective study conducted in UK teaching hospital even though the specific perceived factor reported was heavy workload (Dean, *et al.*, 2002b). On the other hand, underestimation of the potential adverse consequences was the major factor as of the study conducted at France (Salomon, *et al.*, 2003). The discrepancy might be explained by unaffordability of less nephrotoxic alternatives as Ethiopia is a developing country unlike France and United Kingdom. Among conditions of the prescribers that contribute for

TEM medication dosing errors, lack of adequate knowledge and/or experience was most common in our study. Likewise, inadequate knowledge of the drug or the patient was the most common contributing factor for TEM medication dosing error both at UK (Dean, *et al.,* 2002b) and USA(Tully, *et al.,* 2009). But, lack of training was the most common latent condition that contribute for TEM medication dosing error in our study setup unlike reluctance to question senior colleagues in UK (Dean, *et al.,* 2002b) and not considering the task of prescribing drugs important USA(Tully, *et al.,* 2009). This could also be explained by the economic development differences of the countries and our study setup that the cost of training prescribers could have limited their knowledge on TEM medication dosing.

Furthermore, all medical cards of the admitted patients in our study setup contained only the serum creatinine and weight, height and creatinine clearance of the patients were missing. This is in inline with the prescribers' response that 48% of them reported that they use serum creatinine for renal function estimation. This could also have contributed for high rate of medication dosing error in the current study. Using serum creatinine level as a sole indicator of renal function is not recommended since glomerular filtration rate is affected by age, sex, weight and height of a patient though creatinine clearance is also not an accurate parameter in some patient groups like emaciated patients where production of creatinine is compromised (Shargel, *et al.,* 2004). In our study, approximately 21% of the patients with border line SCr (1.2-1.3mg/dl) were having low CrCl suggesting that borderline SCr does not exclude renal impairment.

9. Conclusion

From this study it can be concluded that TEM medication dosing errors were prevalent (22.91%) among admitted patients with renal impairment. Cardiovascular agents including furosemide, amlodipine, and digoxin were the most inappropriately dosed medications. Errors associated with the frequency of the dosage schedule were the commonly encountered errors (55.29%). Most of these dosing errors were made during later times of hospital stay, on male patients, and on patients taking complex drug regimens. On the other hand, lack of appropriate dosage forms and less nephrotoxic alternatives was the most common perceived factor contributing for TEM medication dosing error.

10. Recommendations

Based on the study findings, the researchers like to forward the following recommendations.

- To prescribers:
  - All the patients' medical cards should contain appropriate demographic parameters like height, weight, sex, age and others.
  - Drug dosage adjustments should be made based on creatinine clearance rather than serum creatinine only.
  - Standard guidelines for renal drug dosing like Drug prescribing in renal failure, British national formulary, The American Hospital Formulary System Drug Information, and The Physicians' Desk Reference (PDR) should be used than using textbooks.
- To the hospital and other stakeholders:
  - Due attention should be given to avail different dosage forms and less nephrotoxic alternatives, prepare local renal drug dosing guidelines, train and/or recruit clinical pharmacists or drug experts in the medical team, devise a better data storing system and feedback systems, train professionals on renal drug dosing, integrate pharmacy systems with clinical service, and establish objective drug information service as much as possible.
  - Renal drug dosing information should be considered in the development of strategies to prevent adverse patient outcomes resulting from such errors.
  - Continued medical education in the field of clinical pharmacokinetics is also required for all health practitioners.

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12. Annexes

Annex 1: Data abstraction format from patients' medical card

"Medication Dosing Error and Contributing Factors among admitted patients with Renal Impairment in Jimma University Specialized Hospital, Southwest Ethiopia"

I. Review on General Information

Initials (code) _____

Admission date: _____

Ward of admission: _____

Card number: _____

Bed Number: _____

II. Patient Demography:

Age (yrs): _____

Sex: _____

Weight (kg):_____

Height (cm):_____

BMI (kg/m^2): _____

CrCl (ml/min): _____

Table 8: Data abstraction format from patients' medical card

S. No.	Clinical findings	Laboratory findings	Comorbidity	drug regimen prescribed and modified (drug, dose, dosage form, route, frequency, duration)	Date of order	Prescriber qualification
		CBC: - - - - - - U/A: - - - LFT: - - - - RFT: - - Others:		1st regimen 2nd modified regimen 3rd modified regimen		

Name of **assessor**: _____**Signature**: _____Date:_____

Annex 2: Questionnaire for prescribers

"Medication Dosing Error and Contributing Factors among admitted patients with Renal Impairment in Jimma University Specialized Hospital, Southwest Ethiopia"

***Dear prescriber**: The research team is glad to thank you in advance for your cooperation. We humbly request you to take some time and respond to the following queries. Your participation and genuine information will help the research team to answer the research question effectively. We would like to assure you that all the information would be kept confidential.*

I. General Information

1) Prescriber qualification

i) General Practitioner
ii) Specialist: Specify: _____
iii) Resident: Specify: _____
iv) Medical intern
v) Health officer (HO)
vi) HO intern
vii) Other: specify _____

2) Year of experience: _____

II. Drug dose adjustment practice

1) Do you **frequently** consider renal function test before drug prescribing in the inpatient wards?

i) Yes ii) No

If No, skip to question no. 3

2) What parameter do you **frequently** use for renal function estimation?

i) Serum creatinine
ii) Blood urea nitrogen (BUN)
iii) Creatinine clearance
iv) BUN/SCr ratio
v) Other: specify _____

3) Do you **frequently** consider drug dose adjustment during prescribing in renal impairment?

i) Yes ii) No

If No, skip to question no. 5

4) If Yes:

a) What is your guideline/reference for dosage adjustment in patients with renal impairment?

_____

b) At which level of renal impairment do you consider adjustment of medications?

_____

c) For which **specific** drugs do you commonly consider adjustment in renal impairment? (Mention as much as you recall)

_____

_____

_____

5) Do you think that the **conditions of prescribers** affect drug dosing in renal impairment?

i) Yes ii) No

If **No**, skip to question no. 7

6) If your answer is **yes**, which factor(s) **commonly** affect drug dosing in renal impairment? (Make √ mark)

	Yes	No
Tiredness		
Hungriness		
Being Unwell		
Stress		
Low morale or motivation		
Depression		
Sleep abnormality		
Lack of adequate Knowledge and/or Experience		
Underestimation of potential adverse consequences		
Inappropriate dosage calculation		
Other: specify _____		

7) Do you think **patient conditions** affect your drug dosing in renal impairment?

i) Yes ii) No

If **No**, skip to question no. 9

8) If your answer is **yes**, which factor frequently affects your drug dosing in renal impairment? (Make √ mark)

	Yes	No
Uncooperativeness		
Complex clinical condition		
Language and communication		
Other: specify _____		

9) Do you think that **working environment** affects your drug dosing in renal impairment?

i) Yes ii) No

If No, skip to question no. 11

10) If your answer is **yes**, which working environment factors(s) most commonly affects your drug dosing in renal impairment? (Make √ mark)

	Yes	No
Lack of appropriate dosage forms and less nephrotoxic alternatives		
Heavy work load		
Lack of well established guidelines for drug dosing in renal impairment		
Lack of objective drug information service		
Lack of routine laboratory tests.		
Environmental distraction		
Inadequate staff		
New or locum staff		
Dealing with patients other than your own		
Other: specify_____		

11) Do you think that **team factors** do have an impact on your drug dosing in renal impairment?

i) Yes ii) No

If No, skip to question no. 13

12) If your answer is **yes**, which factor most commonly affects your drug dosing in renal impairment? (Make √ mark)

	Yes	No
Lack of communication		
Poor supervision		
Overlapping responsibility		
Absence of clinical pharmacists or drug experts		
Other: specify _____		

13) Do you think **latent conditions of organizational processes and managerial decisions** affect your drug dosing in renal impairment?

i) Yes

ii) No

14) If your answer is **yes**, which organizational processes and managerial decision factors (s) affect drug dosing in renal impairment? (Make √ mark)

	Yes	No
Not considering the task of prescribing drugs important		
Not seeing transcription as prescribing		
Lack of training		
Low self-awareness of making errors		
Lack of feedback systems		
Poor data storing system		
Pharmacy systems separate from clinical service		
Not teaching about dose in medical schools		
Culture within team (lack or reluctance of questioning seniors)		
Other : specify_____		

Name of data collector: _____Signature:_____ Date: _____

Annex 3: Consent form

"Medication Dosing Error and Contributing Factors among admitted patients with Renal Impairment in Jimma University Specialized Hospital, Southwest Ethiopia"

English Version

Dear participant,

The purpose of this study is to evaluate medication dosing errors and contributing factors among hospitalized patients with renal impairment. The study will be conducted by reviewing your medical chart. Thus, as a randomly selected participant in the study, your chart will be reviewed. Your medical record is intended to abstract clinical, laboratory findings and medications prescribed and will be secured from access to others other than the research team. After the research is over, your medical information abstracted will be discarded.

Your participation in the study is entirely based on your full voluntary consent and you have the right not to participate in the study or to withdraw from the study at any time you feel uncomfortable with study. The output of this research will be greatly helpful to the medical community and subsequently the patients receiving medical care by indicating the actual dosing practices and factors that contribute for inappropriate dosing in patients with renal impairment.

During the investigation, your name, identity and all your other records will be kept confidential. Rather, all records and samples will only be identified by code designation.

Are you willing to participate? Yes _____ No_____

Date of consent: _____

Name of Data collector: _____

Amharic version

ውድ ተሳታፊ:-

የዚህ ጥናት ዋና ዓላማ የመድኃኒት አጠቃቀም እና መንስኤዎቻቸው የኩላሊት በሽታ ባለባቸው ታካሚዎች ምን እንደሚመስል ለማወቅ ነው:: ጥናቱ የሚከናወነው የሕክምና ካርዶን በማሰስ ነው:: ስለዚህ እንደዕድል እንደመመረጥዎ መጠን የሕክምና ካርዶ ይፈተሻል:: ከሕክምና ካርዶም የበሽታው ሁኔታ# የላቦራቶሪ ውጤቶች እና የሚወሰዷቸው መድኃኒቶች ይወሰዳሉ:: መረጃዎቹም ከጥናት ቡድኑ ውጪ ሌላ አካል በማያገኝበት ይቀመጣሉ\ ምስጢራቸውም ይጠበቃል:: ጥናቱ እንደተጠናቀቀ የተሰበሰቡ መረጃዎች ይወገዳሉ::

በጥናቱ መሳተፍ በሙሉ ፈቃደኝነትዎ ስለሆነ የመሳተፍም ሆነ በዬትኛውም ሰዓት ከጥናቱ የማቋረጥ መብትዎ የተጠበቀ ነው:: የጥናቱ ውጤት የሕክምና ማህበረሰብንና የሕክምናው ተጠቃሚዎችን የመድኃኒት አጠቃቀም እና መንስኤዎቻቸውን በመግለጥ አስፈላጊ እርምቶች እንዲደረጉ ይረዳል::

በጥናቱ ወቅት የስምዎ# ማንነትዎ እና ሌሎች መረጃዎች ሚስጢር ይጠበቃል:: ሁሉም መረጃዎችዎና ናሙናዎችዎ በምስጢራዊ ምልክቶች ይወከላሉ::

ፈቃደኛ ነዎት? አዎ_____ አይደለሁም_____

የተዋዋሉበት ቀን_____

የመረጃ ሰብሳቢ ስም _____ ፊርማ _____

Afaan oromoo Version

Kabajamoo hirmaattoota qayyabannaa keenyaa:

Kaayyoon qayyabannaa kanaa madaalli rakko dogoogora dozii qorichaafi haalota dogoogora kanaaf saaxilan namoota dhibee kaleetiin mana yaalaa ciisani irratti gaggeesu dha.

Qayyabannaan kun kan gageefamu galme kessan qayyabachu dhaani. Kanaaf iyyu galmeen kessan hinlaalamaa dhibee isiin himattan, frii laaboorratorii fi qorichii isiniif ajajame ni fudhatama. Odeeefannon kun nama biraatti hinhimamu icciiti dhaan qabama. Eerga qayyabannaan kun dhume booda odeefannoon kun ni gatama.

Qayyabanaa kana irratti kan isiin hirmaattan gutummaa gututti feedhidhaani, yoo kan hin barbaanne ta,e itti hirmaachu dhiisu dandeessu , eerga itti hirmaachu jalqabdan boodas yoo feedhi dhabdani yaroo barbaadanitti kessaa ba'u dandeessu. Friin qayyabannaa kanaa dozii sirriifi haloota dogogora dozii fidaniifi deebi waan laatuufi ogeessotaa fi namoota dhibe kalee qabaniif bu'a guddaa qaba.

Yaroo qayyabannaa kana maqaan kessanii fi odeefannoon biroo galmee keesani irraa fudhatamu kodiin waan barreefamuufi iccitiin isaa eegamaa dha.

Irratti walii hinagaltu ? eeyye _____ lakki _____

Guyyaa itti walii galame_____

Nama waligaltee kana guuchisiise _____Mallatto_____