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**Ministry of Higher Education & Scientific Research**  
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**Bachelor of Pharm.D**

**Evaluation of a Potentially Inappropriate Medications According  
to American Geriatrics Society (AGS) 2019 among Hospitalized  
Patients at University of Science and Technology Hospital in  
Sana'a City, Yemen.**

**Submitted By: Second Batch Clinical Pharmacist (Pharm-D)**

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وَقُلْ لِّلْعَالَمِينَ

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(التوبة آية 105)

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## **DEDICATION**

**We dedicate this research to our families specially our beloved parents who have educated and enabled us to reach this level. Thank you for all the things you have done for us as we have grown up.**

**And we want to dedicate this research to our respected**

**Supervisor Dr. Ali Alyahawi and  
Ass prof Dr. Mokhtar Al-Ghorafi**

**Who supported us in every step of this work. Without them, it could not be possible to complete this project. They made us able to face different challenges and helped us to bring our research to light.**

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## **LIST OF ABBREVIATIONS**

|                    |                                                                                                  |
|--------------------|--------------------------------------------------------------------------------------------------|
| <b>AGS</b>         | <b>American Geriatric Society</b>                                                                |
| <b>PIMs</b>        | <b>Potentially Inappropriate Medications</b>                                                     |
| <b>CYP</b>         | <b>Cytochrome P450</b>                                                                           |
| <b>GFR</b>         | <b>Glomerular filtration rate</b>                                                                |
| <b>MDRD</b>        | <b>Modification of diet in renal disease</b>                                                     |
| <b>Cr.Cl</b>       | <b>Creatinine clearance</b>                                                                      |
| <b>ADRs</b>        | <b>Adverse drug reactions</b>                                                                    |
| <b>GABA</b>        | <b>Gamma-aminobutyric acid</b>                                                                   |
| <b>NSAIDs</b>      | <b>Non-steroidal anti-inflammatory drugs</b>                                                     |
| <b>STOPP/START</b> | <b>Screening tool of older persons prescription / Screening tool to alert to right treatment</b> |
| <b>FORTA</b>       | <b>Fit for the age</b>                                                                           |
| <b>CNS</b>         | <b>Central nervous system</b>                                                                    |
| <b>CVS</b>         | <b>Cardiovascular system</b>                                                                     |
| <b>GI</b>          | <b>Gastrointestinal</b>                                                                          |
| <b>DM</b>          | <b>Diabetes mellitus</b>                                                                         |
| <b>CLD</b>         | <b>Chronic liver disease</b>                                                                     |
| <b>CKD</b>         | <b>Chronic kidney disease</b>                                                                    |
| <b>SIADH</b>       | <b>Syndrome of inappropriate antidiuretic hormone secretion</b>                                  |
| <b>ACEIs</b>       | <b>Angiotensin converting enzyme inhibitors</b>                                                  |
| <b>ARBs</b>        | <b>Angiotensin receptor blockers</b>                                                             |
| <b>Vd</b>          | <b>Volume of distribution</b>                                                                    |
| <b>TCAs</b>        | <b>Tricyclic antidepressants</b>                                                                 |

## **ABSTRACT**

**Background:** The elderly population is growing rapidly worldwide. Many are suffering from multimorbidity which may threaten their lives. Inappropriate prescribing in the elderly can cause substantial morbidity which leads to additional clinical and economic burden to patients and society. Gaining insight into physicians prescribing patterns to recognize prescribing problems is the fundamental first step in trying to improve the quality of prescribing.

**Aims of the study:** To evaluate and determine the potentially inappropriate medications (PIMs) among hospitalized patients in University of Science and Technology Hospital in Sana'a, Yemen. To determine the polypharmacy, as well as the major drug-drug interactions and drug-diseases interactions.

**Materials and Methods:** A retrospective cross-sectional study was conducted on patients' medication admission and discharge in the internal section of University of Science and Technology Hospital in Sana'a Yemen. The sample size was 100 inpatients medical charts of age 65 years and above of both sexes were included in the study. The relevant data was collected from computerized records of the hospital. The potentially inappropriate medications were evaluated and reviewed according to American Geriatrics Society 2019. Collected data was analyzed using descriptive statistics SPSS version 26.

**Results:** A total of 100 in-patient prescriptions were enrolled. 60 (60%) were male patients and 40 (40%) were female. It was showed that the major morbidity pattern was cardiovascular disease 26 (26%). Based on 2019 Beers criteria, among prescribed drugs, the results demonstrated that drugs that generally should be avoided in older adults on admission were (18 drugs) (60%) and (14 drugs) (40%) on discharge. Concerning drugs that should be used with caution, the ratio was (10 drugs and drug classes) (75%) on admission and (7 drugs) (25%) on discharge. Drugs to be avoided or dosage reduced with varying levels of kidney function were (4 drugs) (50%) on admission and (4 drugs ) (50%) discharge. About polypharmacy on admission, the ratio was 39 (39%) of patients had polypharmacy and 33 (33%) on discharge. The results also revealed that 33 (33%) of patients had one major drug-drug interactions on admission and 17 (17%) on discharge, whereas 21 (21%) of patients had more than one major drug-drug interactions on admission and 2 (2%) on discharge. Regarding drug-disease interactions, 4 (4%) of patients had one major drug-disease interaction on admission and discharge.

**Conclusion:** PIMs, Polypharmacy and drugs interactions were higher. There is a need for guidelines for the use of drugs in the elderly in Yemen, and further studies are needed on this issue.

# Chapter 1

## Introduction & Aims of the Study

## **1- Introduction**

The growth of the aging population and increasing lifespan require that health care professionals gain knowledge necessary to meeting the needs of this patient group. Despite the availability and benefit of numerous pharmacotherapies to treat their diseases, older patients commonly experience drug-related problems, resulting in additional morbidities. Therefore, it is essential for clinicians serving older adults across all health care settings to understand the epidemiology of aging, age-related physiological changes, drug-related problems prevalent in the elderly, comprehensive geriatric assessment, and interprofessional approaches to geriatric care. <sup>(1)</sup>

Aging is a normal process whereby the human body declines after peak growth and development. In general, aging results as the body responds to environmental stressors according to the person's health and lifestyle factors together with genetic makeup. If environmental stressors are severe enough or individuals have too small a reserve capacity, aging causes frailty, disability, and increased vulnerability to disease and death. <sup>(2)</sup>

### **1.1 Age - related changes:**

In basic terms, pharmacokinetics is what the body does to the drug, and pharmacodynamics is what the drug does to the body. All four components of pharmacokinetics absorption, distribution, metabolism, and excretion are affected by aging; the most clinically important and consistent is the reduction of renal elimination of drugs. As people age, they can become more frail and are more likely to experience altered and variable drug pharmacokinetics and pharmacodynamics. Even though this alteration is influenced more by a patient's clinical state than their chronological age, the older patient is more likely to be malnourished and suffering from diseases that affect pharmacokinetics and pharmacodynamics. Older adults can develop significant drug-related problems when alterations in pharmacokinetics and pharmacodynamics are not appropriately accounted for in prescribing and monitoring of medications. Clinicians have the responsibility to use pharmacokinetic and pharmacodynamics principles to improve the care of older patients and avoid adverse effects of pharmacotherapy. Due to the multitude of changes described below, many medications used to treat chronic conditions in older adults should be started at 50% of the recommended initial adult dose, and doses titrated slowly. This is a general recommendation to consider when initiating medications such as antihypertensive and antidepressants, but does not apply to the treatment of acute illness (e.g., antibiotics for pneumonia). <sup>(3)</sup>

### 1.1.1 Classification of age in elderly people: <sup>(18)</sup>

1. 65-74 (youngest old)
2. 75-84 (middle old)
3. 85 or more (oldest-old)

**[Table 1] Common Physiologic Changes with Age That May Change Drug Pharmacokinetics**  
(2,4)

| Organ System            | Physiologic Change with Aging                                                                                  | Effect on Pharmacokinetics                                                                                                                                                                                                                                                                              |
|-------------------------|----------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>GI</b>               | ↑ Or no change in stomach pH<br>↓ GI blood flow<br>Slowed gastric emptying<br>Slowed GI transit                | <ul style="list-style-type: none"> <li>• ↓ Absorption of some drugs and nutrients requiring acid environment</li> <li>• Absorption rate may be prolonged</li> </ul>                                                                                                                                     |
| <b>Skin</b>             | Thinning of dermis<br>Loss of subcutaneous fat                                                                 | <ul style="list-style-type: none"> <li>• ↓ Or no change to drug reservoir formation with transdermal formulation</li> </ul>                                                                                                                                                                             |
| <b>Body composition</b> | ↓ Total body water<br>↓ Lean body mass<br>↑ Body fat<br>↓ Or unchanged serum albumin<br>↑ α1-Acid glycoprotein | <ul style="list-style-type: none"> <li>• ↑ Volume of distribution and accumulation of lipid-soluble drugs</li> <li>• ↓ Volume of distribution of water-soluble drugs</li> <li>• ↑ Free fraction of highly protein-bound drugs</li> </ul>                                                                |
| <b>Liver</b>            | ↓ Liver mass<br>↓ Blood flow to the liver<br>↓ Or no change in CYP enzymes                                     | <ul style="list-style-type: none"> <li>• ↓ First-pass extraction and metabolism</li> <li>• ↑ Half-life and</li> <li>• ↓ clearance of drugs with a high first-pass extraction and metabolism</li> <li>• ↓ Or no change in phase I metabolism</li> <li>• No change in phase II drug metabolism</li> </ul> |
| <b>Renal</b>            | ↓ GFR<br>↓ Renal blood flow<br>↓ Tubular secretion<br>↓ Renal mass                                             | <ul style="list-style-type: none"> <li>• ↓ Renal elimination of many medications</li> <li>• ↑ Half-life of renally eliminated drugs and metabolites</li> </ul>                                                                                                                                          |

## **1.2 Pharmacokinetic Changes:**

### **1.2.1 Absorption**

Multiple changes occur throughout the GI tract with aging, but little evidence indicates that drug absorption is significantly altered. The changes include decreases in overall surface of the intestinal epithelium, gastric acid secretion, and splanchnic blood flow. <sup>(3)</sup> Peristalsis is weaker and gastric emptying delayed. These changes slow absorption in the stomach, especially for enteric-coated and delayed-release preparations. Delays in absorption may lead to a longer time required to achieve peak drug effects, but it does not significantly alter the amount of drug absorbed, and drug movement from the GI tract into circulation is not meaningfully changed. <sup>(3,5)</sup> However, relative achlorhydria can decrease the absorption of nutrients such as vitamin B12, calcium, and iron. <sup>(5)</sup>

Aging facilitates atrophy of the epidermis and dermis along with a reduction in barrier function of the skin. Tissue blood perfusion is reduced, leading to decreased or variable rates of transdermal, subcutaneous, and intramuscular drug absorption. <sup>(3)</sup> Therefore, intramuscular injections should generally be avoided in older adults due to unpredictable drug absorption. Additionally, because saliva production decreases with age, medications that need to be absorbed rapidly by the buccal mucosa are absorbed at a slower rate. Yet, for most drugs, absorption is not significantly affected in older patients and the changes described are clinically inconsequential. <sup>(5,6)</sup>

### **1.2.2 Distribution**

The main physiological changes that affect distribution of drugs in older adults are changes in body fat and water, and changes in protein binding. Lean body mass can decrease by 12% to 19% through loss of skeletal muscle in older adults. Thus, blood levels of drugs primarily distributed in muscle increase (e.g., digoxin), presenting a risk for overdose. <sup>(5)</sup>

While lean muscle mass decreases, adipose tissue can increase with aging by 18% to 36% in men and 33% to 45% in women. Therefore, fat-soluble drugs (e.g., diazepam, amitriptyline, amiodarone, valproic acid, and verapamil) have increased volume of distribution (Vd), leading to higher tissue concentrations and prolonged duration of action. Greater Vd leads to increased half-life and time required to reach steady-state serum concentration. <sup>(3,5)</sup>

Total body water decreases by 10% to 15% by age 80. This lowers Vd of hydrophilic drugs (e.g., aspirin, digoxin, morphine, lithium, and ethanol) leading to higher plasma drug concentrations than in younger adults when equal doses are used. Thus lower doses are needed to prevent toxicity. Toxic drug effects may be enhanced when dehydration occurs and when the extracellular space is

reduced by diuretic use. Likewise, plasma albumin concentration decreases by 10% to 20%, although disease and malnutrition contribute more to this decrease than age alone. <sup>(3)</sup> In patients with an acute illness, rapid decreases in serum albumin can increase drug effects. Examples of highly protein-bound drugs include warfarin, phenytoin, and diazepam. <sup>(5)</sup> For most chronic medications, these changes are not clinically important because although the changes affect peak level of a single dose, mean serum concentrations at steady state are not altered unless clearance is affected. <sup>(5)</sup> For highly protein-bound drugs with narrow therapeutic indices (e.g., phenytoin), however, it is important to appropriately interpret serum drug levels in light of the older patient's albumin status. In a malnourished patient with hypoalbuminemia, a higher percentage of the total drug level consists of free drug than in a patient with normal serum albumin. Thus, if a hypoalbuminemic patient has a low total phenytoin level and phenytoin dose is increased, the free phenytoin concentration may rise to a toxic level. <sup>(5)</sup>

### 1.2.3 Metabolism

Drug metabolism is affected by age, acute and chronic diseases, and drug–drug interactions. The liver is the primary site of drug metabolism, which undergoes changes with age; though the decline is not consistent, older patients have decreased metabolism of many drugs. <sup>(3,7)</sup> Liver mass is reduced by 20% to 30% with advancing age, and hepatic blood flow is decreased by as much as 50%. <sup>(6)</sup> These changes can drastically reduce the amount of drug delivered to the liver per unit of time, reduce its metabolism, and increase the half-life. <sup>(5)</sup> Metabolic clearance of some drugs is decreased by 20% to 40% (e.g., amiodarone, amitriptyline, warfarin, and verapamil), but it is unchanged for drugs with a low hepatic extraction. <sup>(5)</sup> Drugs that have high extraction ratios have significant first-pass metabolism, resulting in higher bioavailability for older adults. For example, the effect of morphine is increased due to a decrease in clearance by around 33%. Similar increases in bioavailability can be seen with propranolol, levodopa, calcium channel blockers, tricyclic antidepressants, and statins. Thus, older patients may experience a similar clinical response to that of younger patients using lower doses of these medications. <sup>(5,7)</sup>

The effect of aging on liver enzymes (cytochrome P450 system [CYP450]) may lead to a decreased elimination rate of drugs that undergo oxidative phase I metabolism, but this is controversial. <sup>(3)</sup> Originally, it was thought that the CYP450 system was impaired in older adults, leading to decreased drug clearance and increased serum half-life, but studies have not consistently confirmed this. Thus variations in the CYP450 activity may not be due to aging but to lifestyle (e.g. smoking), illness, or drug interactions. <sup>(5,7)</sup>

A patient's nutritional status plays a role in drug metabolism as well. Frail elderly have a more diminished drug metabolism than those with healthy body weight. <sup>(3,7)</sup>

Aging does not affect drugs that undergo phase II hepatic metabolism, known as conjugation or glucuronidation, but conjugation is reduced with frailty. Temazepam and lorazepam are examples of drugs that undergo phase II metabolism. <sup>(5)</sup>

#### 1.2.4 Elimination

Clinically, the most important pharmacokinetic change in older adults is the decrease in renal drug elimination. <sup>(3)</sup> As people age, renal blood flow, renal mass, glomerular filtration rate, filtration fraction, and tubular secretion decrease. After age 40, there is a decrease in the number of functional glomeruli, and renal blood flow declines by approximately 1% yearly. From age 25 to 85 years, average renal clearance declines by as much as 50% and is independent of the effects of disease. <sup>(3,5)</sup> Still, the impact of age on renal function is variable and not always linear. Clinically significant effects of decreased renal clearance include prolonged drug half-life, increased serum drug level, and increased potential for adverse drug reactions (ADRs). <sup>(3)</sup> Special attention should be given to renally eliminated drugs with a narrow therapeutic index (e.g. digoxin, aminoglycosides).

Monitoring serum concentration and making appropriate dose adjustment for these agents can prevent serious ADR resulting from drug accumulation. <sup>(5)</sup>

It is important to note that despite a dramatic decrease in renal function (creatinine clearance) with aging, serum creatinine may remain fairly unchanged and remain within normal limits. This is because older patients, especially the frail elderly, have decreased muscle mass resulting in less creatinine production for input into circulation. <sup>(3,5)</sup> Because chronic kidney disease can be overlooked if a clinician focuses only on the serum creatinine value, overdose and ADR can occur.

### **1.3 The most common equations are:** <sup>(8)</sup>

**Cockcroft-Gault:**  $\text{CrCl} = [(140 - \text{age}) \times \text{ideal body weight in kg}] / [(72 \times \text{SCr})] \times 0.85$  if female (use actual weight if it is less than ideal body weight)

**MDRD:** Estimated GFR =  $186 \times \text{SCr}^{-1.154} \times \text{age}^{-0.203} \times 1.21$  if black  $\times 0.742$  if female

**CKD-EPI Creatinine Equation 2009a:** CKD-EPI equation expressed as a single equation:  $\text{GFR} = 141 \times \min(\text{SCr}/\kappa, 1) \alpha \times \max(\text{SCr}/\kappa, 1)^{-1.209} \times 0.993^{\text{Age}} \times 1.018$  [if female]  $\times 1.159$  [if African American]

**[Table 2] Chronic kidney disease stages** <sup>(19)</sup>

| stage | descriptor                    | GFR                        |
|-------|-------------------------------|----------------------------|
| 1     | Kidney damage with normal GFR | >90                        |
| 2     | Mild renal dysfunction        | 60-89                      |
| 3     | Moderate dysfunction          | 30-59                      |
| 4     | Severe dysfunction            | 15-29                      |
| 5     | Kidney failure                | < 15 or dialysis dependent |

Drugs eliminated through glomerular filtration must be dosed according to individual estimated renal function. Chronic medication examples can be found in the **2019 American Geriatrics Society (AGS) Beers Criteria.** <sup>(2)</sup>

### **1.4 Pharmacodynamic Changes:**

Pharmacodynamics refers to the actions of a drug at its target site and the body's response to that drug. Compared to pharmacokinetics, there is much less data on age-related pharmacodynamic changes. In general, the pharmacodynamic changes that occur in older adults tend to increase their sensitivity to drug effects. Most pharmacodynamic changes in the elderly are associated with a progressive reduction in homeostatic mechanisms and changes in receptor properties. Although the end result of these changes is an increased sensitivity to the effects of many drugs, a decrease in response can also occur. The changes in the receptor site include alterations in binding affinity of the drug, number or density of active receptors at the target organ, structural features, and postreceptor effects (biochemical processes/signal transmission). These include receptors in the adrenergic, cholinergic, and dopaminergic systems, as well as aminobutyric acid (GABA) and opioid receptors. <sup>(3,6)</sup>

### 1.4.1 Cardiovascular System

Decreased homeostatic mechanisms in older adults increase their susceptibility to orthostatic hypotension when taking drugs that affect the cardiovascular system and lower the arterial blood pressure. This is explained by a decrease in arterial compliance and baroreceptor reflex response, which limits their ability to compensate quickly for postural changes in blood pressure. It has been estimated that 5% to 33% of older adults experience drug-induced orthostasis. Examples, other than typical antihypertensive, that have a higher likelihood of causing orthostatic hypotension in geriatric patients are tricyclic antidepressants, antipsychotics, loop diuretics, direct vasodilators, and opioids. (3,6) Older patients have a decreased  $\alpha$ -adrenergic receptor function, and they are less sensitive to agonist and adrenergic antagonist effects in the cardiovascular system and possibly in the lungs, but their response to agonists and antagonists is unchanged. Increased hypotensive and heart rate response (to a lesser degree) to calcium channel blockers (e.g. verapamil) are reported. Increased risk of developing drug-induced QT prolongation and torsade de pointes is also present. (6) Therefore, clinicians must start medications at low doses and titrate slowly, closely monitoring the patient for any adverse effects.

### 1.4.2 Central Nervous System

Overall, geriatric patients exhibit a greater sensitivity to the effects of drugs that gain access to the CNS, especially anticholinergic medications. In most cases, lower doses result in adequate response, and higher incidence of adverse effects may be seen with standard and high doses. For example, lower doses of opioids provide sufficient pain relief for older patients, whereas conventional doses can cause over sedation and respiratory depression. (3,5) The blood–brain barrier becomes more permeable as people age; thus more medications can cross the barrier and cause CNS adverse effects. Examples of problematic medications include benzodiazepines, antidepressants, antipsychotics, neuroleptics, and antihistamines. There is a decrease in the number of cholinergic neurons as well as nicotinic and muscarinic receptors, decreased choline uptake from the periphery, and increased acetylcholinesterase. (5,6)

Older adults have a decreased ability to compensate for these imbalances of the neurotransmitters, which can lead to movement and memory disorders. Older adults have an increased number of dopamine type 2 receptors, making them more susceptible to delirium from anticholinergic and dopaminergic medications. At the same time, they have a reduced number of dopamine and dopaminergic neurons in the substantia nigra of the brain resulting in higher incidence of extrapyramidal symptoms from antidopaminergic medications (e.g. antipsychotics). (3,6)

### 1.4.3 Fluids and Electrolytes

Fluid and electrolyte homeostatic mechanism is decreased in the older adult population. Older adults experience more severe dehydration with equal amounts of fluid loss compared with younger adults. The multitude of factors involved include decreased thirst and cardiovascular reflexes, decreased fluid intake, decreased ability of the kidneys to concentrate urine, increased atrial natriuretic peptide, decreased aldosterone response to hyperkalemia, and decreased response to antidiuretic hormone.

The result is an increased incidence of hyponatremia, hyperkalemia, and prerenal azotemia, especially when the older patient is taking a diuretic (e.g., hydrochlorothiazide, furosemide). Angiotensin-converting enzyme inhibitors have an increased potential to cause hyperkalemia and acute renal failure in older adults. Thus these agents need to be started with low doses, titrated slowly, and renal function should be monitored frequently. <sup>(3)</sup>

### 1.4.4 Glucose Metabolism

An inverse relationship between glucose tolerance and age has been reported. This is likely due to reduced insulin secretion and sensitivity (greater insulin resistance). Consequently, the incidences of hypoglycemia are increased when using sulfonylureas (e.g., glyburide, glipizide) from age-related impairment to counter-regulate the hypoglycemic response. <sup>(3)</sup>

Due to an impaired autonomic nervous system, older patients may not distinguish symptoms of hypoglycemia such as sweating, palpitations, or tremors. They do experience neurological symptoms of syncope, ataxia, confusion, or seizures.

## **1.5 Drug-Related Risk Assessment for Older Adults** <sup>(2)</sup>

### 1.5.1 Overuse of medications

- a. Unnecessary drugs: Use of more medications than clinically indicated and unneeded therapeutic duplication
- b. Common unnecessary drugs: GI agents, CNS agents, vitamins, minerals
- c. May be caused by
  - i. Prescribing cascade: When a drug is prescribed for treating another drug's adverse effects
  - ii. Several prescribers
  - iii. Care transitions

### 1.5.2 Underuse of medications

- a. Omitted but necessary or indicated drug therapy or inadequate dosing
- b. Commonly underused drugs: Anticoagulants, statins, antihypertensive
- c. Medications considered appropriate according to guidelines may be omitted because prescriber or patient is overly wary of adverse drug effects.

### 1.5.3 Nonadherence

- a. Unintentional nonadherence caused by complex drug regimen
- b. Dementia or other cognitive impairment increases risk.
- c. Cost of medications is another barrier.
- d. Intentional nonadherence because of patient health beliefs or concerns

### 1.5.4 Withdrawal syndromes

- a. Abrupt discontinuation of medication may cause rebound symptoms or delirium.
- b. Common culprits: Antihypertensive, antidepressants, anxiolytics, pain medications

### 1.5.5 Inappropriate medications

- a. Explicit tools commonly used to identify for quality measures; objective statements that do not require clinical judgment for interpretation. Best known is the AGS Beers Criteria for Potentially Inappropriate Medications. Alternative medications to the potentially inappropriate agents listed in this guideline are also available from AGS.
  - i. Evidence-based list of drugs likely to cause problems
  - ii. Adopted by many federal agencies and Part D plans
  - iii. Arranged as drugs and drug classes to avoid, drugs to avoid in certain diseases or conditions, and drugs to be used with caution
  - iv. Examples: Anticholinergics, benzodiazepines, sedative-hypnotics, older antipsychotics, certain opioids or pain medications, hypoglycemics, NSAIDs, and GI drugs
  - v. Another tool popular in European countries is the screening tool of older people's prescriptions and screening tool to alert to right treatment (STOPP/START) criteria.
- b. Implicit tools are patient-centered, take more time to apply; interpretation requires clinical judgment and patient-specific information. Best studied is the Medication Appropriateness Index, also FORTA (fit for the aged) criteria
  - i. 10 questions to ask about each medication regarding indication, effect, dosing, correct directions, practical directions, duration, drug-drug interactions, drug disease interactions, duplication and cost
  - ii. Indication, effectiveness, and correct dosage carry the most weight.

### 1.5.6 Choosing Wisely criteria

- a. 10 things to question in older adults
- b. 7 of the 10 items are drug related.
  - i. Antipsychotics in patients with dementia should be avoided.
  - ii. Target A1C in diabetes management is 7.5% or higher.
  - iii. Avoid benzodiazepines and sedative-hypnotics for insomnia, agitation, or delirium.
  - iv. Do not initiate antimicrobials for bacteriuria without symptoms.
  - v. Assess benefit-risk of cholinesterase inhibitors (CIs).
  - vi. Appetite stimulants are not helpful for anorexia or cachexia.
  - vii. Drug regimen review is necessary with every new prescription.

### **1.6 Beers criteria:**

The United Nation estimated that the population of older adults defined as those age 65 or older. As older adults population is growing, the prevalence of chronic comorbid health conditions secondary to the inevitable nature of ageing expected to increase. This, therefore, is potentially associated with an increase in the use of multiple drugs (polypharmacy) to well manage these comorbidities or to prevent associated complications.

Polypharmacy, often defined as the use of five or more medications, is prevalent in adults ages 65 years and older, with 40% taking 5 to 9 medications and 18% taking 10 or more. <sup>(9)</sup> Polypharmacy can result in inappropriate prescribing of medications, causing adverse drug events (ADEs) (10). Studies have shown that ADEs in older adults can lead to increased emergency department visits and hospitalizations, resulting in increased health care utilization and cost. <sup>(9,11)</sup>

The use of PIMs is commonly evaluated using different scales and criteria such as the Beers criteria, which are a set of explicit criteria to identify PIMs. It was first developed in 1991. In 2011, after Beers death, the American Geriatrics Society (AGS) began to oversee the revisions and updates to the criteria. AGS has provided updates to the criteria every 3 years, starting in 2012. <sup>(14,15)</sup> In January 2019, AGS published the latest update to the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. It is well known that PIMs use among older patients is associated with negative health consequences and can impact patients' quality of life. <sup>(13)</sup>

The definition of a potentially inappropriate medication (PIM) is "a drug in which the risk of an adverse event outweighs its clinical benefit, particularly when there is a safer or more effective alternative therapy for the same disease. It is also consists of three definitions that must be clarified.

Misprescribing, overprescribing and under-prescribing are the main domains of inappropriate prescribing. Misprescribing means prescribing medication that increases the chance of adverse events. overprescribing means prescribing medication in which no indication for that. Under-prescribing means there is an indication for a certain unprescribed drug.<sup>(24)</sup> Older patients are a sensitive population that should be treated carefully with the most appropriate medication. PIMs use increases the risk of hospitalization, drug-related problems and other adverse health outcomes by two to three folds. Factors associated with inappropriate medications use are variable. Females, older age, having multiple prescriber's physicians, and having poor health status are more likely to be associated with PIMs use. Polypharmacy is a major risk factor that increases the probability of PIMs prescribing. One of the risks of polypharmacy is that physicians may recognize adverse drug reactions as a new disease and try to treat it, which is unacceptable.<sup>(24)</sup> Moreover, certain chronic conditions such as diabetes, hypertension, depression, osteoporosis, and dementia have also been associated with a higher risk of PIMs use compared with older adults who don't have these chronic conditions. Moreover, PIMs use is also associated with an increased cost burden on health care system which requires further research to rationalize the use of such medications. It should be noted that there are many factors that make older patients more prone to PIMs. Older patients become more prone to adverse drug reactions from altered pharmacokinetics and pharmacodynamics. Co-morbidity is another risk factor of PIMs use which means having 2 or more diseases. Since the 20th century, the rate of co-morbidities has increased gradually in the geriatric population.<sup>(24)</sup>

One study that done in the college of pharmacy, Al Ain University, at Tawam Hospital, Abu Dhabi, UAE. A total of 502 older patients (51.6% females and 48.4% males) medical charts were reviewed and the most common chronic diseases in that population were diabetes mellitus (46%) and heart diseases (35.5%). The most common PIMs among the study population that should be avoided were quetiapine and sulphonylurea's (glimepiride and glyburide).

Another study that done by Heba Khader<sup>1</sup>, Luai Z. Hasoun<sup>2</sup>, Ahmad Alsayed<sup>2</sup>, Mahmoud Abu-Samak<sup>2</sup>, department of clinical pharmacy and therapeutics. The Hashemite University Amman, Jordan. A total of 386 geriatric patients were participated in this study (43.6% males and 56.4% female) The most common chronic diseases presented in this population were hypertension (78.5%), diabetes mellitus (DM) (60.4%) and dyslipidemia (57.3%). The most common drugs that should be avoided were the prolonged (more than 8 weeks) use of proton pump inhibitors (lansoprazole, pantoprazole, rabeprazole, omeprazole, and esomeprazole) and long-acting sulfonylureas (glimepiride and glyburide).

**1.7 Aims of the study**

The present study was conducted to:

- Evaluate and determine of a potentially inappropriate medications (PIMs) among hospitalized patients in University of Science and Technology Hospital in Sana'a, Yemen.
- Determine the prevalence of polypharmacy.
- Determine the major drug-drug interactions and drug-diseases interactions.



# Chapter 2

## Materials and Methods

## **2- MATERIALS AND METHODS**

### **2.1 | Study area, setting, sample size and inclusion criteria**

The study was conducted in the internal section of University of Science and Technology Hospital in Sana'a Yemen, during a period of one month (Oct 2021). The sample size was 100 inpatients medical chart. All patients were  $\geq 65$  years old of both sexes.

### **2.2 | Study design**

A retrospective cross-sectional study review to discover PIMs across admission and discharged older patients. The patient's medical charts were reviewed to obtain their medication lists. The screening tool was used to obtain **PIMs 2019 Beers criteria**.

❖ **Beers criteria for potentially inappropriate medicine (PIM) Use in Older Adults are an explicit list of PIMs avoided in older adults:**

1. Drugs that generally should be avoided in elderly.
2. Drugs to be avoided in combination with specific comorbidities.
3. Drugs to be used with caution.
4. Drug-drug interactions that should be avoided in elderly.
5. Drugs to be avoided or dosage reduced with varying levels of kidney function.

### **2.3 | Data collection**

The study reviewed patients' medical charts extracted from the electronic health record (EHR) database. to obtain the required data. Collected demographic data include:

(a) Age and gender, (b) the diagnosis (c) creatinine clearance and (d) the list of admission and discharged medications and each medication generic name, dose, frequency, dosage form, duration of medications and route of administration. The selection of these variables is based on previous similar studies. Gender, age, number of medications and number of diseases will be the risk factors that will be assessed for their association with at least one potentially inappropriate medication.

**2.4 | Statistical analysis**

Data was analyzed using statistical package for social science (SPSS) version 26. Categorical variables were presented as frequencies and percentages.

**2.5 | Ethical approval**

The hospital research ethics committee and EIU approved this study.

# Chapter 3

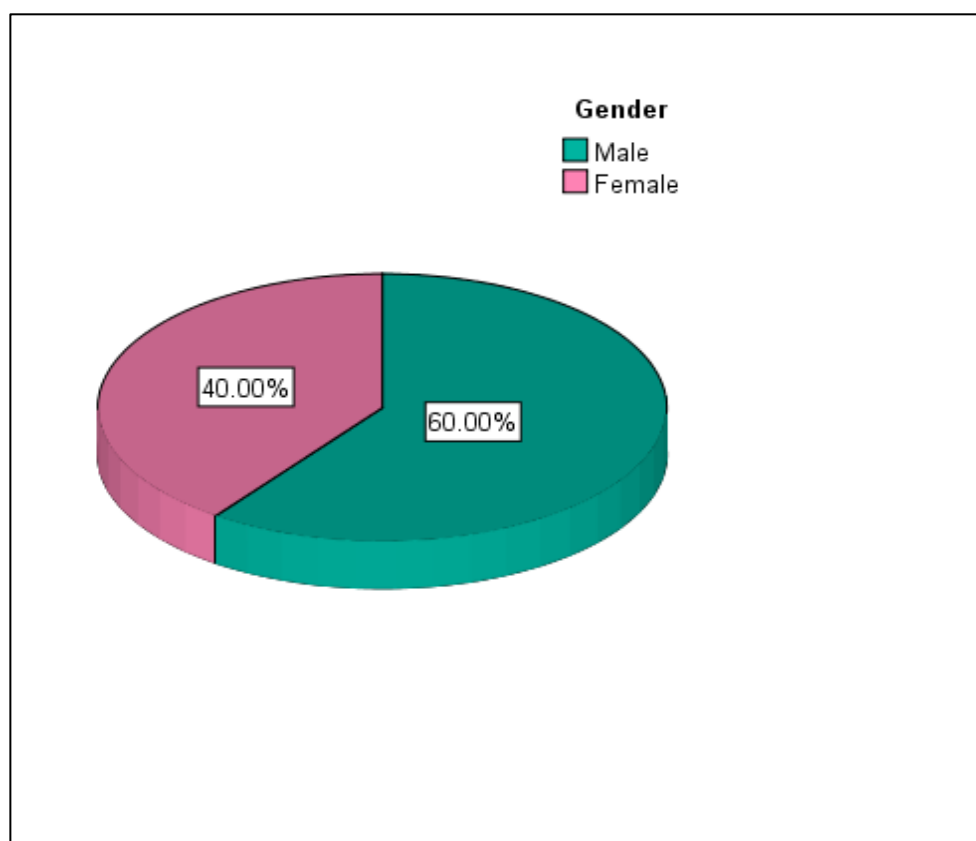
## Results

### 3.1 | Study population characteristics

#### 3.1.1 Gender distribution

During the period of this study a total of 100 in-patients records were reviewed, among which majority were males and the remaining were female. [Table 3]

| [Table 3] Gender distribution |           |             |
|-------------------------------|-----------|-------------|
|                               | Frequency | Percent (%) |
| Male                          | 60        | 60.0%       |
| Female                        | 40        | 40.0%       |
| Total                         | 100       | 100.0%      |

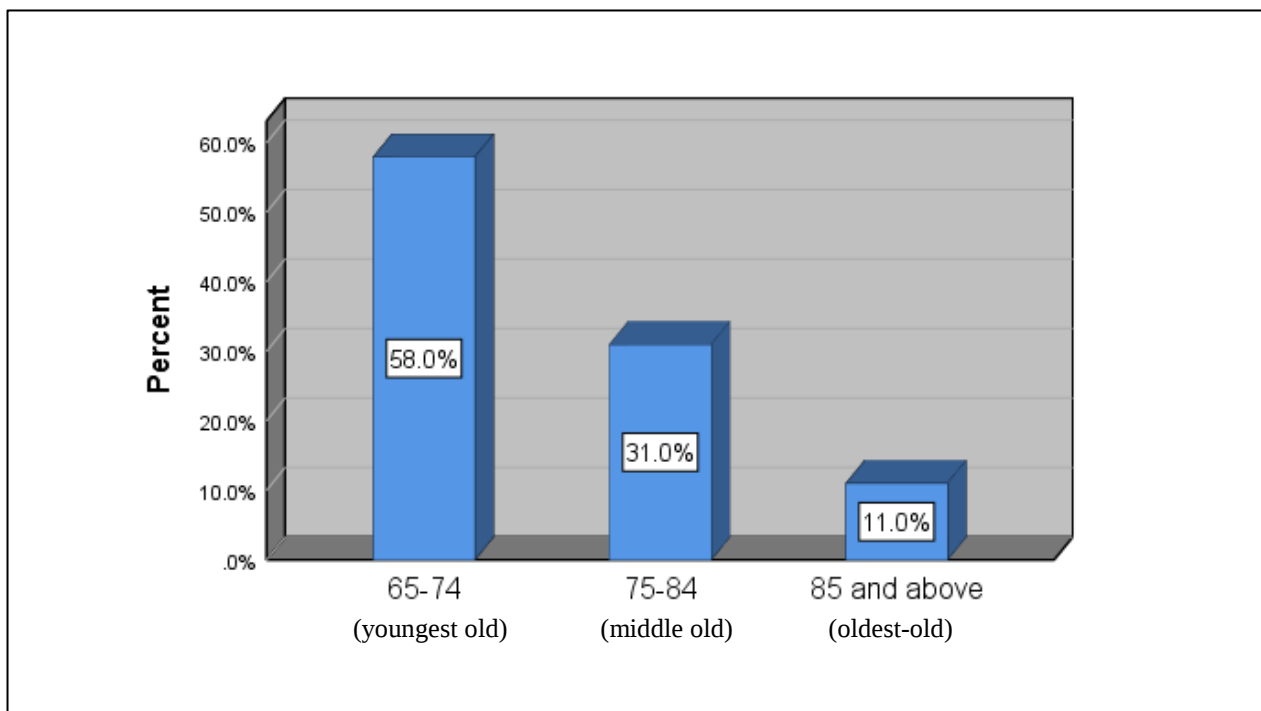


[Figure 1] Gender distribution.

### 3.1.2 Age distribution

It was found that age of the patients involved varied from 65 to 98 years. The age groups were categorized into three: 65-74 years, 75-84 years and 85 years and above. [Table 4]

| [Table 4] Age distribution |           |             |
|----------------------------|-----------|-------------|
|                            | Frequency | Percent (%) |
| 65-74 (youngest old)       | 58        | 58.0%       |
| 75-84 (middle old)         | 31        | 31.0%       |
| 85 and above (oldest-old)  | 11        | 11.0%       |
| Total                      | 100       | 100.0%      |



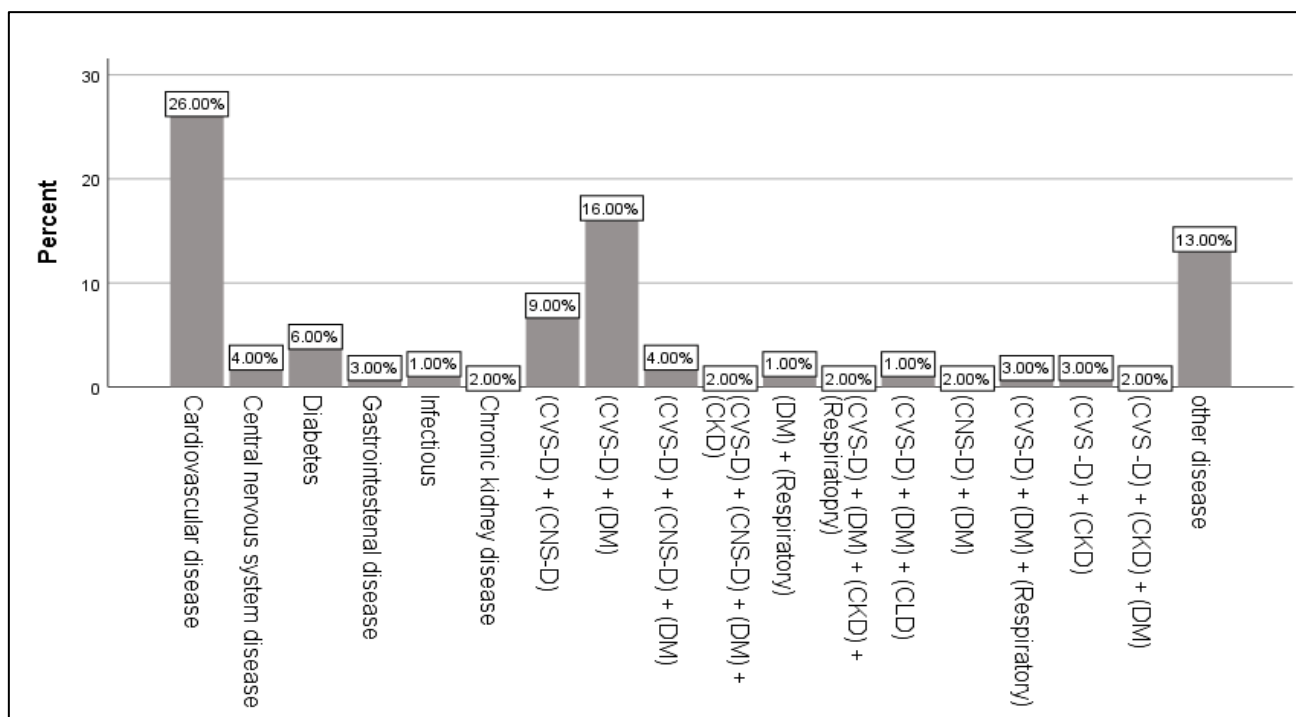
[Figure 2] Age distribution.

### 3.2 | Health conditions of population

#### 3.2.1 Morbidity pattern of the elderly patients

The major morbidity pattern was cardiovascular disease 26%, distributed between hypertension, ischemic heart disease and heart failure which were the most. And 16% of the morbidity included cardiovascular disease with diabetes mellitus together. [Table 5]

| [Table 5] Morbidity pattern of the elderly patients |            |               |
|-----------------------------------------------------|------------|---------------|
|                                                     | Frequency  | Percent (%)   |
| Cardiovascular disease                              | 26         | 26.0%         |
| Central nervous system disease                      | 4          | 4.0%          |
| Diabetes                                            | 6          | 6.0%          |
| Gastrointestinal disease                            | 3          | 3.0%          |
| Infectious                                          | 1          | 1.0%          |
| Chronic kidney disease                              | 2          | 2.0%          |
| (CVS-D) + (CNS-D)                                   | 9          | 9.0%          |
| (CVS-D) + (DM)                                      | 16         | 16.0%         |
| (CVS-D) + (CNS-D) + (DM)                            | 4          | 4.0%          |
| (CVS-D) + (CNS-D) + (DM) + (CKD)                    | 2          | 2.0%          |
| (DM) + (Respiratory)                                | 1          | 1.0%          |
| (CVS-D) + (DM) + (CKD) + (Respiratory)              | 2          | 2.0%          |
| (CVS-D) + (DM) + (CLD)                              | 1          | 1.0%          |
| (CNS-D) + (DM)                                      | 2          | 2.0%          |
| (CVS-D) + (DM) + (Respiratory)                      | 3          | 3.0%          |
| (CVS -D) + (CKD)                                    | 3          | 3.0%          |
| (CVS -D) + (CKD) + (DM)                             | 2          | 2.0%          |
| other disease                                       | 13         | 13.0%         |
| <b>Total</b>                                        | <b>100</b> | <b>100.0%</b> |

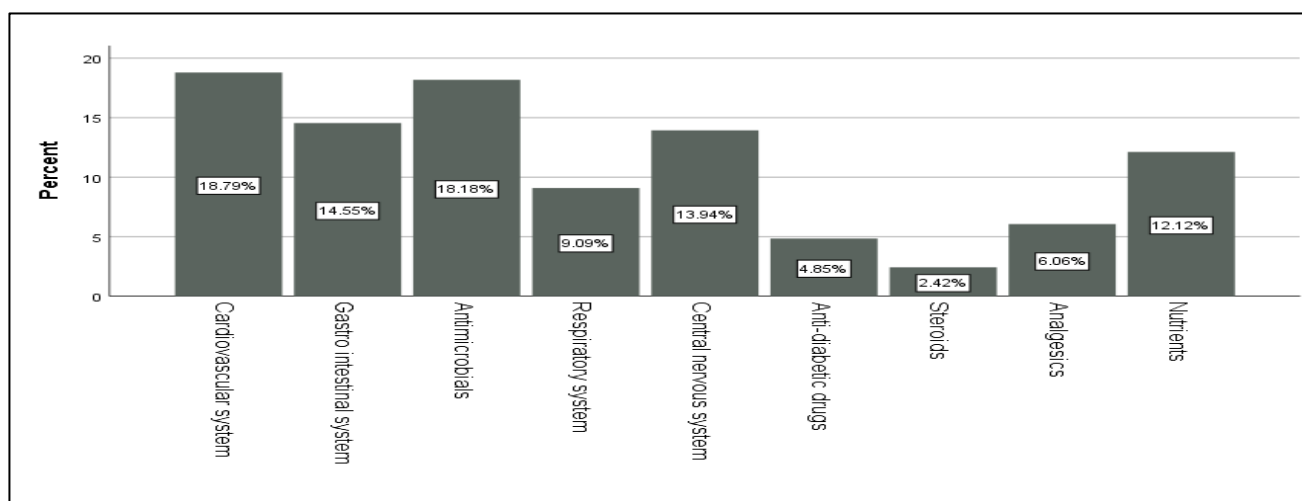


**[Figure 3] Morbidity pattern of the elderly patients.**

### 3.2.2 System-wise drug utilization pattern in elderly patients

A total of 165 drugs were prescribed of which (18.79%) were drugs using for cardiovascular system followed by antimicrobials (18.18%) and (14.55%) used for gastrointestinal system (GI), and the other drugs distributed between other systems as mentioned in [Table 6].

| [Table 6] System-wise drug utilization pattern in elderly patients |            |               |
|--------------------------------------------------------------------|------------|---------------|
|                                                                    | Frequency  | Percent (%)   |
| Cardiovascular system                                              | 31         | 18.8%         |
| Gastro intestinal system                                           | 24         | 14.55%        |
| Antimicrobials                                                     | 30         | 18.2%         |
| Respiratory system                                                 | 15         | 9.1%          |
| Central nervous system                                             | 23         | 13.9%         |
| Anti-diabetic drugs                                                | 8          | 4.8%          |
| Steroids                                                           | 4          | 2.4%          |
| Analgesics                                                         | 10         | 6.1%          |
| Nutrients                                                          | 20         | 12.1%         |
| <b>Total</b>                                                       | <b>165</b> | <b>100.0%</b> |



[Figure 4] System-wise drug utilization pattern in elderly patients.

### 3.3 | Prevalence of PIMs

#### 3.3.1 Drugs that generally should be avoided in older adults

On application of beers criteria, 2019 to all the 100 prescriptions, it had been found that (18 drugs) (60%) out of 165 drugs were drugs that generally should be avoided in older adults on admission and (14 drugs) (40%) on discharge. [\[Table 7\]](#)

| [Table 7] Drugs that generally should be avoided in older adults |           |             |           |             |
|------------------------------------------------------------------|-----------|-------------|-----------|-------------|
|                                                                  | Admission |             | Discharge |             |
| Drug                                                             | Frequency | Percent (%) | Frequency | Percent (%) |
| Atropine                                                         | 2         | 2.3%        | 0         | 0%          |
| Nifedipine                                                       | 5         | 5.8%        | 5         | 13.5%       |
| Amitriptyline                                                    | 1         | 1.2%        | 1         | 2.7%        |
| Glimepride                                                       | 2         | 2.3%        | 2         | 5.4%        |
| Glyburide                                                        | 4         | 4.7%        | 2         | 5.4%        |
| Metoclopramide                                                   | 24        | 27.9%       | 1         | 2.7%        |
| Diclofenac                                                       | 11        | 12.8%       | 3         | 8.1%        |
| Ketoprofen                                                       | 3         | 3.5%        | 1         | 2.7%        |
| Meloxicam                                                        | 1         | 1.2%        | 0         | 0%          |
| Indomethacin                                                     | 1         | 1.2%        | 1         | 2.7%        |
| Digoxin                                                          | 1         | 1.2%        | 1         | 2.7%        |
| Dipyridamole                                                     | 5         | 5.8%        | 4         | 10.8%       |
| Alprazolam                                                       | 1         | 1.2%        | 0         | 0%          |
| Mineral oils                                                     | 5         | 5.8%        | 3         | 8.1%        |
| Chlorzoxazone                                                    | 2         | 2.3%        | 2         | 5.4%        |
| Insulin (sliding)                                                | 11        | 12.8%       | 8         | 21.6%       |
| Hyoscine                                                         | 3         | 3.5%        | 3         | 8.1%        |
| Bromazepam                                                       | 4         | 4.7%        | 0         | 0%          |
| <b>Total</b>                                                     | <b>86</b> | <b>100%</b> | <b>37</b> | <b>100%</b> |

### 3.3.2 Drugs to be used with caution in older adults

For drugs that should be used with caution the number was (10 drugs and drug classes) (75%) that should be used with caution when prescribe to older adults on admission and (7 drugs and drug classes) (25%) on discharge . [Table 8]

| [Table 8] Drugs to be used with caution in older adults |           |             |           |             |
|---------------------------------------------------------|-----------|-------------|-----------|-------------|
|                                                         | Admission |             | Discharge |             |
| Drug                                                    | Frequency | Percent (%) | Frequency | Percent (%) |
| Diuretics                                               | 58        | 54.7%       | 28        | 66.7%       |
| Tramadol                                                | 29        | 27.4%       | 8         | 19.0%       |
| Aspirin (>70 years)                                     | 11        | 10.4%       | 1         | 2.4%        |
| Carbamazepine                                           | 2         | 1.9%        | 2         | 4.8%        |
| Ox carbamazepine                                        | 1         | .9%         | 1         | 2.4%        |
| TCAs                                                    | 1         | .9%         | 0         | 0%          |
| Mirtazapine                                             | 1         | .9%         | 0         | 0%          |
| Escitalopram                                            | 1         | .9%         | 0         | 0%          |
| Sertraline                                              | 1         | .9%         | 1         | 2.4%        |
| Rivaroxaban                                             | 1         | .9%         | 1         | 2.4%        |
| Total                                                   | 106       | 100%        | 42        | 100%        |

### 3.3.3 Drugs to be avoided or dosage reduced with varying levels of kidney function

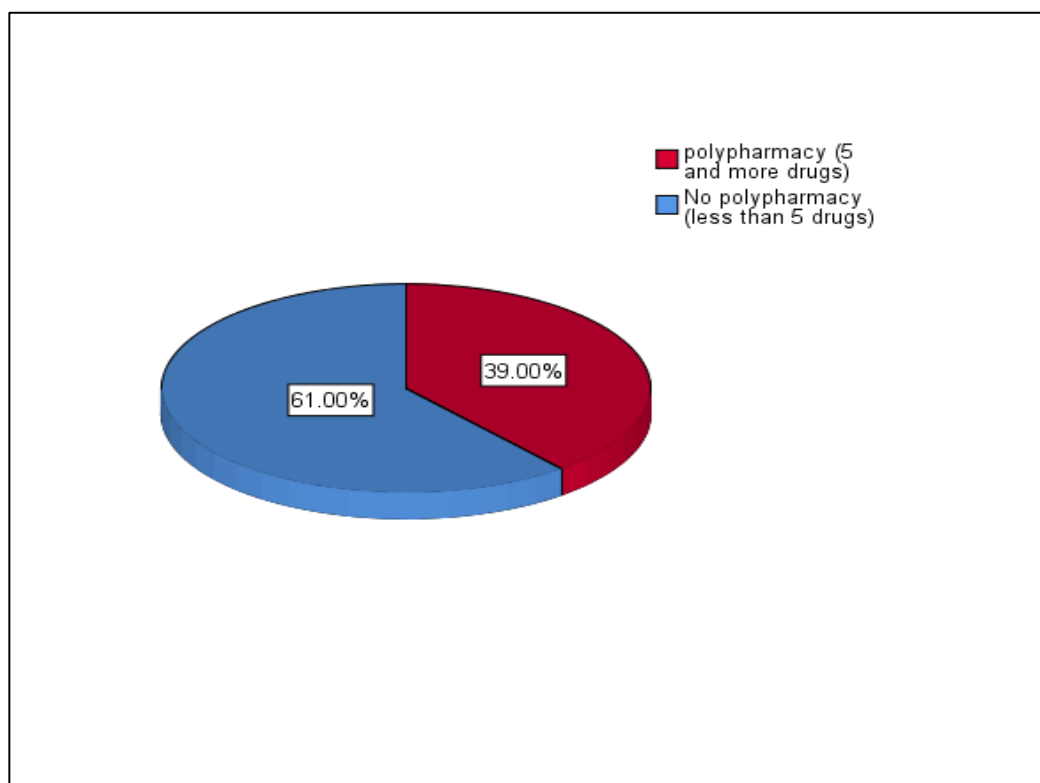
Drugs to be avoided or dosage reduced with varying levels of kidney function out of 165 drugs were (4 drugs) (50%) on admission and on discharge. [\[Table 9\]](#)

| <b>[Table 9] Drugs to be avoided or dosage reduced with varying levels of kidney function in older adults</b> |                  |                    |                  |                    |
|---------------------------------------------------------------------------------------------------------------|------------------|--------------------|------------------|--------------------|
|                                                                                                               | <b>Admission</b> |                    | <b>Discharge</b> |                    |
| <b>Drug</b>                                                                                                   | <b>Frequency</b> | <b>Percent (%)</b> | <b>Frequency</b> | <b>Percent (%)</b> |
| <b>Ciprofloxacin (CrCl&lt;30)</b>                                                                             | <b>3</b>         | <b>30.0%</b>       | <b>2</b>         | <b>28.6%</b>       |
| <b>Tramadol ( CrCl&lt;30)</b>                                                                                 | <b>4</b>         | <b>40.0%</b>       | <b>3</b>         | <b>42.9%</b>       |
| <b>Ranitidine (CrCl&lt;50)</b>                                                                                | <b>1</b>         | <b>10.0%</b>       | <b>1</b>         | <b>14.3%</b>       |
| <b>Enoxaparin (CrCl&lt;30)</b>                                                                                | <b>2</b>         | <b>20.0%</b>       | <b>1</b>         | <b>14.3%</b>       |
| <b>Total</b>                                                                                                  | <b>10</b>        | <b>100%</b>        | <b>7</b>         | <b>100%</b>        |

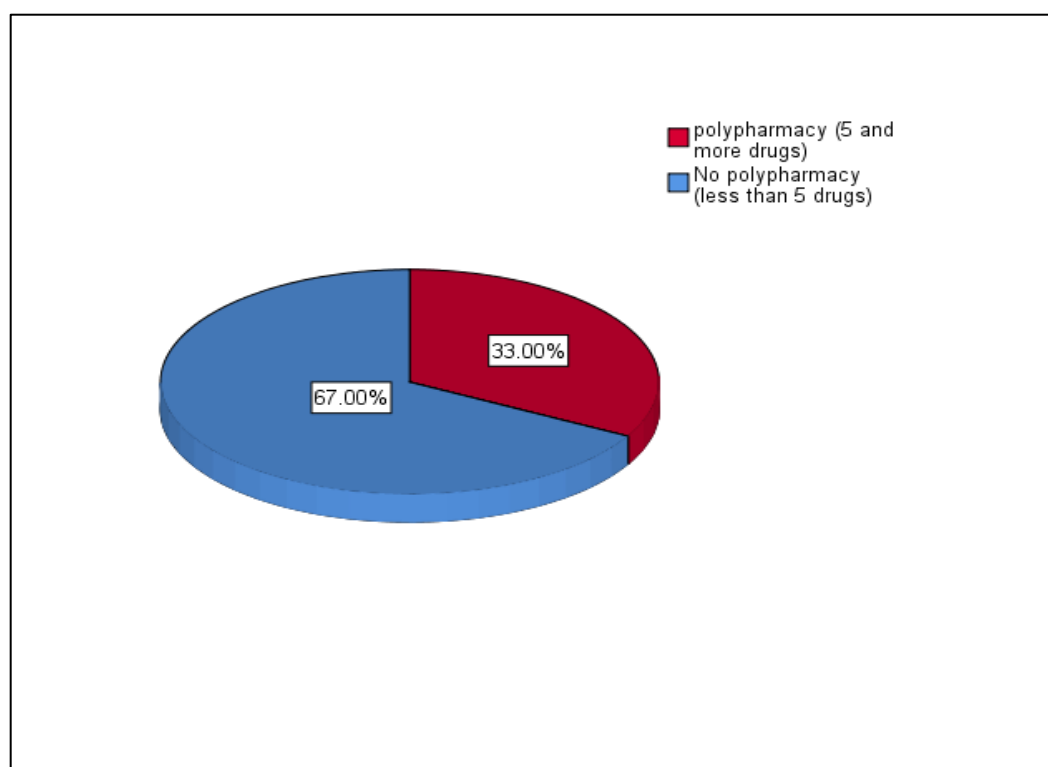
### 3.4 | Prevalence of polypharmacy

For polypharmacy on admission (39%) of patients had polypharmacy and (61%) with no polypharmacy. On discharge the ratio of polypharmacy were (33%) and (67%) had not polypharmacy. [Table 10]

| [Table 10] Prevalence of polypharmacy     |           |             |           |             | P-Value |
|-------------------------------------------|-----------|-------------|-----------|-------------|---------|
|                                           | Admission |             | Discharge |             |         |
|                                           | Frequency | Percent (%) | Frequency | Percent (%) |         |
| Polypharmacy<br>(5 and more<br>drugs)     | 39        | 39.0%       | 33        | 33.0%       | .000    |
| No polypharmacy<br>(less than 5<br>drugs) | 61        | 61.0%       | 67        | 67.0%       |         |
| Total                                     | 100       | 100.0%      | 100       | 100.0%      |         |



**[Figure 5] Polypharmacy on admission.**

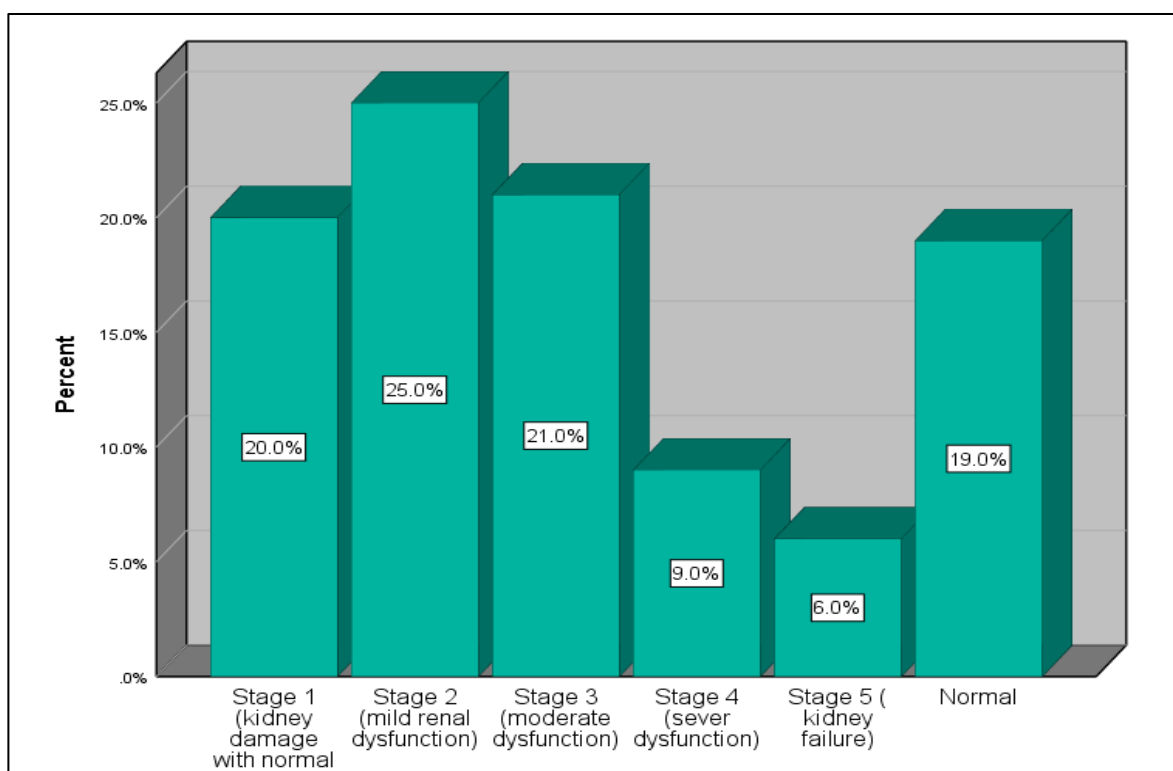


**[Figure 6] Polypharmacy on discharge.**

### 3.5 | Prevalence of chronic kidney disease stages according to GFR. [Table 11]

Based on GFR category 100 inpatients of both sexes were screened for chronic kidney disease stages were as followed:

| [Table 11] Prevalence of chronic kidney disease stages according to GFR |            |               |
|-------------------------------------------------------------------------|------------|---------------|
| Stage                                                                   | Frequency  | Percent (%)   |
| Stage 1 (kidney damage with normal GFR)                                 | 20         | 20.0%         |
| Stage 2 (mild renal dysfunction)                                        | 25         | 25.0%         |
| Stage 3 (moderate dysfunction)                                          | 21         | 21.0%         |
| Stage 4 (sever dysfunction)                                             | 9          | 9.0%          |
| Stage 5 (kidney failure)                                                | 6          | 6.0%          |
| Normal                                                                  | 19         | 19.0%         |
| <b>Total</b>                                                            | <b>100</b> | <b>100.0%</b> |

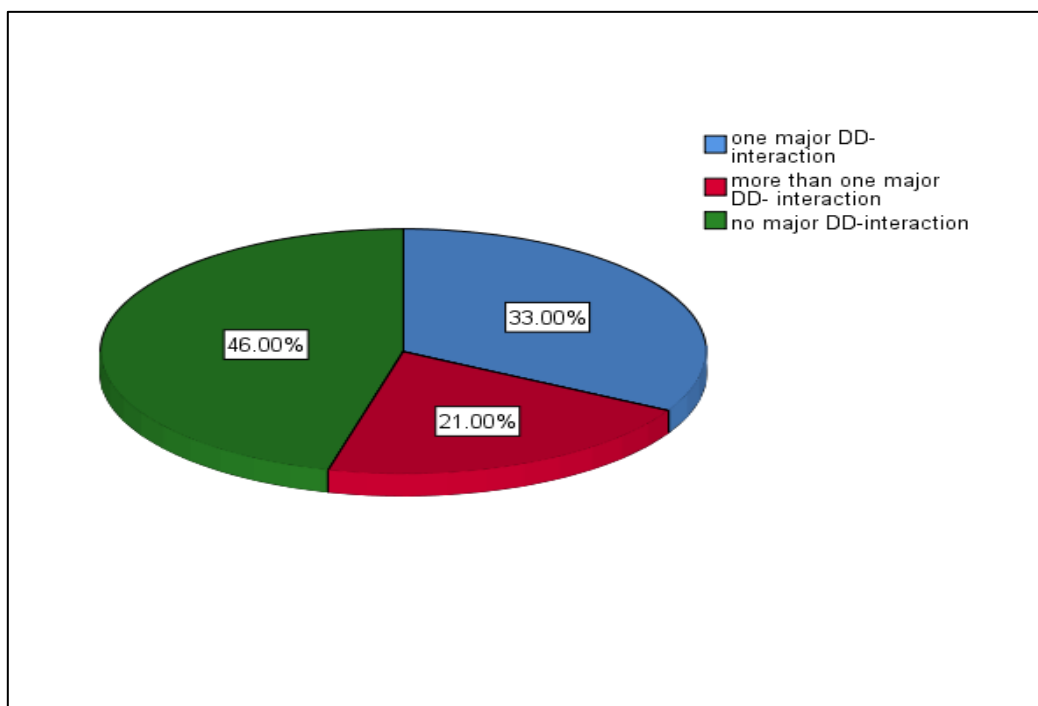


[Figure 7] Prevalence of chronic kidney disease stages according to GFR.

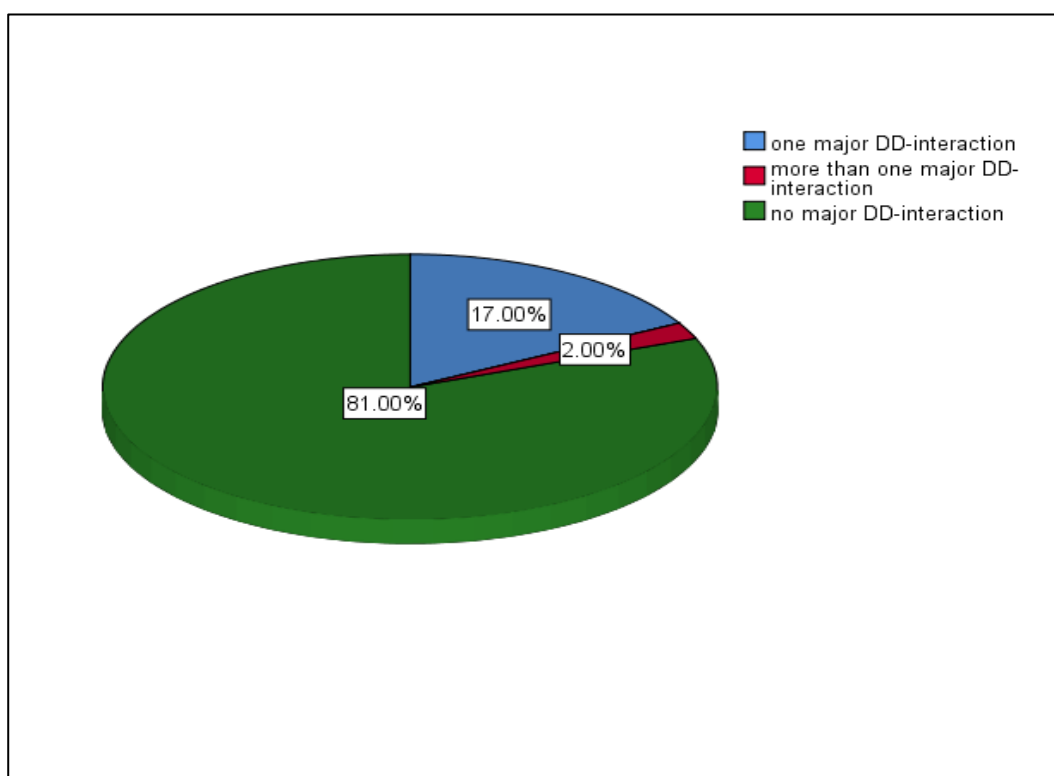
### 3.6 Major Drug - Drug interactions [Table 12]

The results also revealed that 33 (33%) of patients had one major drug-drug interactions on admission and 17 (17%) on discharge.

| [Table 12] Major Drug – Drug interactions    |           |             |           |             | P-Value |
|----------------------------------------------|-----------|-------------|-----------|-------------|---------|
|                                              | Admission |             | Discharge |             |         |
|                                              | Frequency | Percent (%) | Frequency | Percent (%) |         |
| One major Drug – drug interaction            | 33        | 33.0%       | 17        | 17.0%       | .000    |
| More than one major Drug – drug interactions | 21        | 21.0%       | 2         | 2.0%        |         |
| No major Drug – drug interaction             | 46        | 46.0%       | 81        | 81.0%       |         |
| Total                                        | 100       | 100.0%      | 100       | 100.0%      |         |



**[Figure 8] Major drug – drug interactions on admission.**

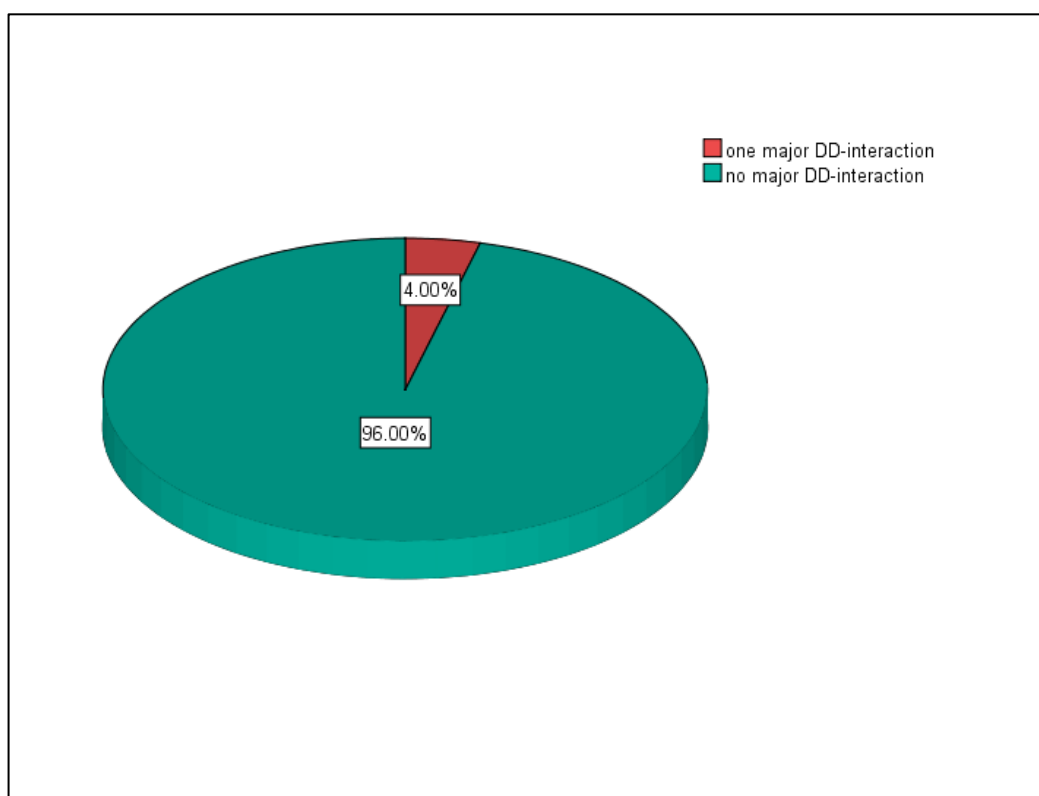


**[Figure 9] Major drug – drug interactions on discharge.**

### 3.7 Drug - disease interactions. [Table 13]

Regarding drug-disease interactions, 4 (4%) of patients had one major drug-disease interaction on admission and discharge.

| [Table 13] Drug - disease interactions      |            |               |            |               |
|---------------------------------------------|------------|---------------|------------|---------------|
|                                             | Admission  |               | Discharge  |               |
|                                             | Frequency  | Percent (%)   | Frequency  | Percent (%)   |
| <b>One major Drug – disease interaction</b> | 4          | 4.0%          | 4          | 4.0%          |
| <b>No major Drug – disease interaction</b>  | 96         | 96.0%         | 96         | 96.0%         |
| <b>Total</b>                                | <b>100</b> | <b>100.05</b> | <b>100</b> | <b>100.0%</b> |



[Figure 10] Drug - disease interactions on admission and discharge.

# Chapter 4

## Discussion

#### **4- Discussion**

This is the first Yemeni study and one of the few international studies that evaluates PIMs use in geriatrics based on the latest version of AGS Beers Criteria (2019 AGS Beers Criteria). Toxic effects of medications and drug-related problems can have profound medical and safety consequences for older adults and economically affect the health-care system. In this study, the presence of certain chronic conditions in older patients predicted the increased chance of PIMs use. The most common morbidity resulting in hospitalization was diabetes, HTN, IHD, HF and CKD. [Table 5] Multiple studies have demonstrated a significant association between PIMs use and CVD, DM, and increase number of chronic diseases. <sup>(20)</sup>

Majority of drugs prescribed to the study population were those acting on cardiovascular system, among the (CVS) drugs, ACEIs, ARBs, CCBs, Diuretics and beta blockers were the most frequently prescribed drugs. Antimicrobials with ceftriaxone and cefuroxime being most commonly used, PPIs and antiemetics were the most (GI) drugs that were prescribed. [Table 6]

The prevalence of PIMs to be avoided for older adults which was (18 drugs), metoclopramide was the most prescribed with a frequency of (24 prescriptions) followed by Diclofenac and insulin sliding scale with frequency of (11 prescriptions) for each one as mentioned in [Table 7].

Atropine has to be avoided in older adults, due to highly anticholinergic and uncertain effectiveness. Nifedipine also should be avoided, because it is known to be potential for hypotension and have risk of precipitating myocardial ischemia. Amitriptyline is highly anticholinergic, cause sedation and orthostatic hypotension.

Glimepiride, glyburide and insulin (sliding scale) are drugs that have been included in updated Beers criteria 2019 as PIMs because they have higher risk of severe prolonged hypoglycemia in older adults. Metoclopramide can cause extrapyramidal effects, including tardive dyskinesia; risk may be greater in frail older adults and with prolonged exposure. The rational of NSAIDS as (Diclofenac, Ketoprofen and meloxicam) to be avoided in older adult is that all increase risk of gastrointestinal bleeding or peptic ulcer disease. For digoxin if used for atrial fibrillation it should not be used for first line because there are safer and more effective alternatives for rate control.

Dipyridamole can cause orthostatic hypotension and mineral oils are potential for aspiration and they should be avoided for those reasons. Chlorzoxazone is muscle relaxant and most muscle relaxant are poorly tolerated by older adults because some have anticholinergic adverse effects, sedation, increased risk of fracture, also Hyoscine cause the same effects. Another drug class that should be avoided in older adults that we found in our study was Benzodiazepine that all of them increase risk of cognitive impairment, delirium, falls and fractures.

For PIMs that's should be used with caution were (10 drugs and drug classes), which diuretics and tramadol had the majority of prescribed drugs as mentioned on [\[Table 8\]](#).

Diuretics and Tramadol may exacerbate or cause SIADH or hyponatremia; monitor sodium level closely when starting or changing dosages in older adults. Aspirin (>70 years) has Risk of major bleeding from aspirin increases markedly in older age. Several studies suggest lack of net benefit when used for primary prevention in older adult with cardiovascular risk factors, but evidence is not conclusive. Aspirin is generally indicated for secondary prevention in older adults with established cardiovascular disease. Rivaroxaban increase risk of GI bleeding so it should be used with caution. Carbamazepine, oxcarbamazepin, TCAs, mirtazapine, Escitalopram and sertraline may exacerbate or cause SIADH or hyponatremia, monitor sodium level closely when starting or changing dosages in older adults is important.

PIMs that's should be avoided or dosage reduced with varying levels of kidney function according to GFR that was calculated using MDRD equation, ciprofloxacin and tramadol had the majority of prescribed drugs as mentioned on [\[Table 9\]](#).

Ciprofloxacin with CrCl <30 mL/min increased risk of CNS effects (e.g., seizures, confusion) and tendon rupture, doses used to treat common infections typically require reduction when CrCl <30 mL/min. Tramadol with CrCl <30 mL/min cause CNS adverse effects, so reduce dose if it is immediate release or avoid when use extended release formulation. Ranitidine is known to cause mental status changes and dose should be reduced when patient CrCl is <30 ml/min.

The most likely factor associated with PIMs use in this study was polypharmacy. We found that 39% of this study population used more than five medications on admission and 33% on discharge. [Table 10] The higher rate of polypharmacy use in our study population can be attributed to the higher rate of multiple chronic conditions (i.e., two or more chronic conditions), in which they may need to take many medications to control their chronic conditions or to prevent complications associated with certain chronic conditions. Specific combination of various drugs in a given patient has the potential to result in an interaction. As number of medications increase the drug-drug interactions will increase.

The overall incidence of drug reactions in geriatric patients is estimated to be at least twice that in the younger population because of errors both in prescription pattern of practitioners and drug usage by the patients. Practitioner errors occur because of lack of knowledge of geriatric clinical pharmacology and not conducting medication review with the patient. Patient errors may result from noncompliance and use of multiple pharmacies. Poor compliance in geriatric patients is due to poor communication with health professionals and decline in cognitive abilities. Other predictors for drug interactions include severity of the diseases being treated, age of the patient, and renal and hepatic dysfunction.

For patients in this study major drug-drug interactions and drug-disease interactions on admission and discharge as mentioned in [Table 12,13]. In drug – drug interactions the majority of interactions found between Cephalosporins (ceftriaxone, cefuroxime) with heparin or enoxaparin that Cephalosporins will increase the levels or effect of heparin by anticoagulation so avoid or use alternative drug. Followed by interactions between fluoroquinolones with ondansetron that both increase QTc interval. Another interaction was between NSAIDs and ACEIs that coadministration may result in a significant decrease in renal function. Sodium bicarbonate with moxifloxacin is another interaction that sodium bicarbonate decrease levels of moxifloxacin by inhibiting GI absorption these interaction applies only to oral form of both agents so avoid or use alternative drug or separate by 2 hours. Omeprazole decreases effects of clopidogrel by affecting hepatic enzyme CYP2C19 metabolism so clopidogrel efficacy may be reduced. More and more drugs interaction had been found in this study and needs more focusing and care when prescribing drugs to patients.

In drug-disease interactions, heart failure with NSAIDs was reported and the rational of that use is potential to promote fluid retention and/or exacerbate heart failure. Also the use of opioid in patients with history of falls or fractures may cause ataxia, impaired psychomotor function, syncope and additional falls so avoid opioids except for pain management in the setting of severe acute pain (e.g., recent fractures or joint replacement).

The role of health care providers should expand in order to take the necessary precautions when managing older patient's conditions to avoid inappropriate medications prescribing, adverse events and other misadventures associated with older patients. Additionally, pharmacists can play a major role in improving the appropriateness of medications use by the recommendation for either medication discontinuation, medication review, the clinical application of tools to assess PIMs such as beers criteria, or other tools to identify older patients at risk of unnecessary use of PIMs.

**Limitations of the study:**

The study is subjected to some limitations. One of the study limitations is that not all medications of Beers criteria are available in the hospital formulary. Also, this study is done over one hospital only, one department and the study duration was short so, the results may be not representative of all geriatrics in Yemen.

This study only used Beer's criteria as the tool for detecting PIMs use. Comparing between Beers criteria and other validated tools such as STOPP/START criteria in detecting PIMs use may be suggested. The reason that STOPP/START criteria was not used in the evaluation is the lack of sufficient information about patient history because of incomplete documentation.

# Chapter 5

## Conclusion & Recommendations

**5.1 Conclusion:**

This study showed a high prevalence of PIMs that should be avoided or used with caution among older patients. Polypharmacy and chronic conditions were predictors for increased use of PIMs among older patients. Increase the knowledge about PIMs and their potential side effects among patients and healthcare providers is warranted.

**5.2 Recommendations:**

According to the results obtained in this work, the following recommendations are proposed:

- Further studies should be done on all departments of Yemen's hospitals.
- Physicians should be aware and given more attention during prescribing of drugs.
- Clinical pharmacists should be present in all branches of the hospitals in order to correct such errors.
- All geriatric's medications should be subjected to Beers criteria to avoid inappropriate use of them.

**Principle investigator statement**

I certify that the information provided in this article is accurate. I have ultimate responsibility for the conduct of the study, the ethical performance, and strict adherence to the study protocol.

**Ethical approval**

The hospital research ethics committee and EIU approved this study.

**Data availability statements**

The data are not publicly available because of ethical restriction as it contains information that could compromise the privacy of patients. As per the ethical approval certificate, the data is the property of hospital.

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## الخلاصة

**المقدمة:** يتزايد عدد المسنين بشكل متسارع في جميع أنحاء العالم، حيث يعاني العديد منهم من أمراض متعددة والتي تشكل تهديداً لحياتهم. يعد استكشاف أنماط الوصفات العلاجية للأطباء للتعرف على مشاكلها هي الخطوة الجوهرية الأولى لتطوير نوعية الوصف.

**أهداف الدراسة:** أجريت هذه الدراسة لتقييم وتحديد الوصفات الطبية الغير ملائمة بين المرضى المرقدين في مستشفى جامعة العلوم والتكنولوجيا صنعاء - اليمن، وتحديد تعدد الادوية لهؤلاء المرضى بالإضافة الى تحديد أهم تداخلات الأدوية مع بعضها وتداخلها مع الأمراض.

**مواد وطرق العمل:** أجريت دراسة رجعية على وصفات الدخول والخروج للمرضى، حيث تضمنت المرضى من عمر ٦٥ عاماً وما فوق ومن كلا الجنسين. وقد جمعت البيانات المتعلقة بالدراسة من سجلات كمبيوتر المستشفى، وتم تقييم ومراجعة احتمالية الوصفات الطبية الغير ملائمة وفقاً للجمعية الأمريكية للمسنين للعام ٢٠١٩ ومن ثم حللت البيانات باستخدام برنامج الإحصاء الوصفي (SPSS) النسخة ٢٦.

**النتائج:** كان إجمالي الوصفات ١٠٠ وصفة طبية ل ١٠٠ مريض في المستشفى خلال شهر اكتوبر لعام ٢٠٢١. ٦٠ وصفة طبية كانت للذكور بما يعادل ٦٠% و ٤٠ للإناث بما يعادل ٤٠%. وقد أظهرت الدراسة بأن نمط الأمراض الأكثر انتشاراً كان مرض الأوعية القلبية بعدد ٢٦ حالة وبما يعادل ٢٦%. وأظهرت نتائج الدراسة التي اعتمدت على معايير بير للعام ٢٠١٩ بأنة من بين الأدوية الموصوفة لكبار السن عدد ١٨ دواء بما يعادل (٦٠%) يجب أن يتم تجنبها في وصفات الدخول و ١٤ دواء بما يعادل (٤٠%) كان يجب تجنبها في وصفات الخروج. وبما يتعلق بالأدوية التي يتم إستخدامها بحذر فإن المعدل كان ١٠ أدوية ومجموعات أدوية في وصفات الدخول بما يعادل (٧٥%) و ٧ في وصفات الخروج بما يعادل (٢٥%). أما الأدوية التي يجب تجنبها او تقليل جرعتها بحسب اختلاف مستويات وظائف الكلى كانت ٤ أدوية بما يعادل (٥٠%) لكل من وصفات الدخول والخروج. وعن تعدد الأدوية فقد وجد بأن ٣٩ مريضاً بما يعادل ٣٩% كانوا يستخدمون أدوية متعددة في وصفات الدخول و ٣٣ مريضاً بما يعادل ٣٣% في وصفات الخروج. كما كشفت النتائج بأن ٣٣ من المرضى ظهرت في وصفات دخولهم تداخل دوائي واحد بمعدل ٣٣% و ١٧ تداخل دوائي واحد في وصفات الخروج بما يعادل ١٧%. بينما لوحظ في وصفات دخول المرضى بأن تداخلات الأدوية فيما بينها والتي شملت أكثر من تداخل واحد كانت ٢١ بما يعادل ٢١%، و ٢ في وصفات خروجهم بما يعادل ٢%. وفيما يتعلق بتداخل الادوية مع الأمراض فقد كانت هناك ٤ تداخلات لأدوية مع الأمراض في كل من وصفات الدخول والخروج أي بما يعادل ٤%.

**الخاتمة:** تعدد الادوية والمخاطر المحتملة للمعالجة الغير ملائمة عالية جداً، لذلك هناك حاجة لدلائل إرشادية لإستخدام الأدوية في كبار السن في اليمن، ودراسات الى حد أبعد فيما يتعلق بهذا الموضوع.

الجمهورية اليمنية  
وزارة التعليم العالي والبحث العلمي  
الجامعة الإماراتية الدولية



كلية الطب والعلوم الصحية  
قسم الصيدلة السريرية  
بكالوريوس دكتور صيدلة

تقييم المخاطر المحتملة للأدوية الغير ملائمة وفقاً للجمعية الأمريكية للمسنين للعام ٢٠١٩م بين  
مرضى مستشفى جامعة العلوم والتكنولوجيا في مدينة صنعاء، اليمن.

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الجامعة الإماراتية الدولية

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