

**Assessment of Inappropriate Prescription via Using
STOPP/START Criteria and Quality of Life in Elderly
Cardiac In-patients in Tertiary Care Hospital Mardan
(MTI)**



M.Phil Thesis

by

ABBAS AHMAD

**Department Of Pharmacy
Faculty of Biological Sciences
Quaid-i-Azam University
Islamabad, Pakistan
2021**

**Assessment of Inappropriate Medication Prescription
via Using START/STOPP Criteria and Quality of Life in
Elderly Cardiac In-patients in Tertiary Care Hospital
Mardan (MTI)**

Thesis submitted by

ABBAS AHMAD

Registration No. 02331713016

to

Department of Pharmacy,

In partial fulfillment of the requirement of

Master of Philosophy

in

Pharmacy (Pharmacy Practice)

Department Of Pharmacy
Faculty of Biological Sciences
Quaid-i-Azam University
Islamabad, Pakistan
2021

AUTHOR'S DECLARATION

I, Abbas Ahmad, hereby state that my M.Phil thesis titled “**Assessment of Inappropriate Prescription via Using START/STOPP Criteria and Quality of Life in Elder Cardiac Inpatients in Tertiary Care Hospital Mardan (MTI)**” submitted to the Department of Pharmacy, Faculty of Biological Sciences, Quaid-i-Azam University Islamabad, Pakistan for the award of degree of Master of Philosophy in Pharmacy (Pharmacy Practice) is the result of research work carried out by me. I further declare that the results presented in this thesis have not been submitted for the award of any other degree from this University or anywhere else in the country/world and the University has right to withdraw my M.Phil degree, If my statement is found incorrect any time, even after my graduation.

ABBAS AHMAD

Date: _____

PLAGIARISM UNDERTAKING

I, Abbas Ahmad, solemnly declare that research work presented in the thesis titled “**Assessment of Inappropriate Medication Prescription via Using START/STOPP Criteria and Quality of Life in Elderly Cardiac In-patients in Tertiary Care Hospital Mardan (MTI)**” is solely my research work with no significant contribution from any other person. Small contribution/help wherever taken has been duly acknowledged and that complete thesis has been written by me.

I understand zero tolerance policy of Quaid-i-Azam University, Islamabad and HEC towards plagiarism. Therefore, I as an author of the above titled dissertation declare that no portion of my thesis is plagiarized and every material used as reference is properly referred/cited.

I undertake that if I am found guilty of committing any formal plagiarism in the above titled thesis even after award of M.Phil degree, the University reserves the right to withdraw/revoke my M.Phil degree and that HEC and University has the right to publish my name on the HEC/University Website on which names of those students are placed who submitted plagiarized thesis.

ABBAS AHMAD

Date: _____

APPROVAL CERTIFICATE

This is to certify that dissertation titled “**Assessment of Inappropriate Prescribing Medications Using START/STOPP Criteria and Quality of Life Among Elderly Cardiac Patients in Tertiary Care Hospital Mardan MMC: A cross sectional study from Mardan KPK, Pakistan**” submitted by **Abbas Ahmad** to the Department of Pharmacy, Faculty of Biological Sciences, Quaid-i-Azam University Islamabad, Pakistan, is accepted in its present form as it is satisfying the dissertation requirements for the Degree of Master of Philosophy in **Pharmacy (Pharmacy Practice)**.

Supervisor

Dr. Hussain Ali
Assistant Professor,
Department of pharmacy,
Quaid-i-Azam University Islamabad

External Examiner

Dr. Touqeer Ahmad
Atta-ur-Rehman School of Applied Biological
Science (ASAB) NUST, Islamabad

Chairperson

Dr. Gul Shahnaz
Department of Pharmacy,
Quaid-i-Azam University Islamabad

Dated: 21-01-2021

DEDICATION

I dedicate this dissertation to my beloved parents

For endless love, encouragement and sincere prayers of their dawn and dusk, that enable me to get such achievement and honor.

**And to my siblings (Sadeeq Akbar, Ilyas Ahmad, M. Yasir Arfat,
Harzat Hamad, Hazrat Talha and Maimona Bibi)**

.Who has been a great source of inspiration, motivation and endless support through this journey

And to all well wishers

TABLE OF CONTENTS

Acknowledgement	I
List of tables.....	II
List of figures.....	III
List of Abbreviations	IV
Abstract	V
1. INTRODUCTION	1
1.1 Background	1
1.2 Potentially inappropriate medications use and elderly population.....	2
1.3 Potentially inappropriate prescribing.....	3
1.4 Consequences of PIM.....	4
1.5 Factors contributing to occurrence of PIM.....	5
1.6 PIM is a major issue with elderly patients.....	6
1.7 Cardiovascular disease status.....	7
1.8 Screening tool for assessment of PIM.....	7
1.8.1 Implicit screening criteria.....	8
1.8.2 Explicit screening criteria.....	8
1.9 STOPP/START Criteria.....	9
1.10 McLeod Criteria.....	10
1.11 ACOVE Criteria.....	11
1.12 Beers Criteria.....	11
1.13 PIM and Quality of Life.....	11
1.14 Rationale of study.....	13
1.15 Aim and objectives.....	14
1.16 Significance of the study.....	15
1.17 Literature review	15

2. RESEARCH METHODOLOGY	19
2.1 Research Methodology.....	19
2.1.1 Study Design	19
2.1.2 Study Settings	19
2.1.3 Sample size and sampling technique	20
2.1.4 Study Participants	20
2.1.5 Inclusion and exclusion criteria	20
2.1.6 Data Collection	21
2.2 Measures	21
2.2.1 Demographic characteristics	21
2.2.2 Socio-economic characteristics	21
2.2.3 Health related Characteristics	21
2.2.4 Disease related Characteristics	21
2.2.5 Health related Quality of Life (HRQoL)	21
2.3 PIM evaluation	22
2.4 Ethics	22
2.5 Statistical analysis	22
3.RESULTS	24
3.1 Socio-demographic and clinical characteristics of patients.....	24
3.2 Socioeconomic Status.....	25
3.4 Disease Related Characteristics.....	25
3.5 Health Related Quality of Life.....	29
3.6 Drug Utilization Pattern of PIM.....	31

3.7 Drug utilization pattern of POs.....	32
3.8 Difference in PIP status by sample characteristics.....	33
3.8 PIPs and Quality of Life.....	34
4. DISCUSSION	36
CONCLUSION	40
REFERENCES	41

ACKNOWLEDGEMENTS

All the praises and thanks to **Almighty Allah** who bestowed His innumerable blessings upon mankind, one of which is knowledge a distinction for mankind. I offer my gratitude to the **Holy Prophet Muhammad** ﷺ who preached us to seek knowledge for the betterment of mankind in particular and other creatures in general.

This dissertation is the end of my journey in obtaining my M.Phil degree. This dissertation has been kept on track and seen through to completion with the support and encouragement of numerous people including my all teachers, friends, colleagues and various institutions.

I would like to thanks my Supervisor Dr. Hussain Ali Assistant Professor Dept. of Pharmacy, QAU Islamabad.

I also like to thanks Dr Gul Majid Khan and all the faculty members for their support.

I would like to extend my deepest thanks to all my academic colleagues, especially M. Saqlain, Sohail Kamran, Shahan Ullah and Zakir Khan who were co-operative in achieving my task directly or indirectly.

Special thanks to my parents and caring family members for their support.

ABBAS AHMAD

List of tables

Table	Title	Page No
1.1	Summary of literature review	18
3.1	Drug Utilization Pattern of PIM	31
3.2	Drug utilization pattern of POs	32
3.3	Difference in PIP status by sample characteristics	33
3.4	PIPs and Quality of Life	34

List of Figures

Figure	Title	Page No
3.1	Socio-demographic and clinical characteristics of patients (age)	24
3.2	Socio-demographic and clinical characteristics of patients (gender)	24
3.3	Socioeconomic Status (income)	25
3.4	Past medical history	25
3.5	Family history	25
3.6	Co-morbidities	26
3.7	Hospital stay days	27
3.8	OTC medications	27
3.9	Number of medications prescribed at ward	28
3.10	Taking medications	28
3.11	Medication procured	28
3.12	Mobility	29
3.13	Self-care	29
3.14	Usual activities	29
3.15	Pain/discomfort	29
3.16	Anxiety/depression	30
3.17	VAS	30

List of Abbreviations

ACOVE	Assessing Care of Vulnerability to Elderly
ADE	Adverse drug events
ADL	Activities of daily living
ADRs	Adverse drug reactions
ATC	Anatomical therapeutic classification
BMC	British medical central
CNS	Central nervous system
CVD	Cardiovascular disease
DRP	Drug related problems
EQ	EuroQoL
EuroQoL	European Quality of Life
GIT	Gastrointestinal tract
HF	Heart failure
HRQoL	Health Related Quality of life
LMICs	Low-middle income countries
MAI	Medication appropriateness index
MI	Myocardial infarction
NORGEF	Norwegian general practice criteria
NSAIDs	Non-steroidal anti-inflammatory drugs

PIM	Potentially inappropriate medication
PIMs	Potentially inappropriate medications
PIMS	Pakistan Institute of Medical sciences
PPI	Proton pump inhibitors
QoL	Quality of life
RCT	Randomized controlled trials
SIADHS	Syndrome of inappropriate antidiuretic hormone
START	Screening Tool to Alert Doctors to Right Treatment
STOPP	Screening Tool of Older Persons Prescriptions
STROBE	Strengthening the Reporting of Observational Studies
SNRI	Selective norepinephrine reuptake inhibitors
SSRI	Selective serotonin reuptake inhibitors
TCA	Tricyclic antidepressants
UN	United nations
US	United states
UK	United kingdom
VAS	Visual analogue scale

ABSTRACT

Background: Within medical field drug utilization research is a recognized area which is a useful tool in accessing variation in prescribing practices and rationalization of medication therapy. It also contribute towards accessing drug utilization and its impact on the community. For health decision makers, drug utilization research has a great value in making drug guidelines and health related policies. The use of drug in any medical condition should be weight against its benefits. Potentially inappropriate prescribing covers, medications use in a condition, in which the adverse drug events outweighs the clinical benefit. The medication regime of such population is very complex and it increases the chances of drug-drug and drug-disease interactions. Such errors in the management of medications, effect badly the patient health, increases hospitalization and mortality. Potentially inappropriate prescribing also increases the chances of adverse drug reactions (ADRs), which in turn enhances the emergency department visits and decreases good health outcomes. START and STOPP are explicate screening tool for the assessment of appropriateness of medication in patient aged about sixty five or above (>65 years). In geriatric pharmacology, 18 experts validated these tools through Delphi consciences process.

The aim of this study was to assess the potentially inappropriate prescribing (PIPs) prevalence amongst the elderly cardiac patients of Pakistan using STOPP/START updated criteria.

Methodology: A single center prospective Cross-sectional study was conducted at Mardan Medical complex, of about 351 in-patients having Cardiovascular disease and aged > 65 years.

Results: A total of three hundarad and fifty one patients were admitted to the medical ward during the stud period. Most of the patient are in 65-74 years age groupe and lesser in the age group i-e above 85 years. Past medical hostory of about 63 patients with hypertension, CAD plus HTN were 26 and 50 with no history. Ten medications were prescribed for 54 aptients and 12 for 24 and 25 medications for two patients. 118 patients have no anxiety and depression, 186 have mild and 47 have severe anxiety and depression. Total PIMs were reported 154 (44.72%) Loop diuretic as first-line treatment for hypertension 50 (14.2) was the most PIM, 30 duplicate medications were prescribed and the use of Spironolactone with K-sparing medications without checking the level of K⁺ frequency were 29. Total PPOs were reported as 154(43.87%). ACEIs with systolic heart failure/coronary artery disease that is 46 (13.1) was omitted, Beta-blocker with ischemic heart disease and Statin therapy with coronary, cerebral or peripheral vascular disease were mostly

omitted. There is significant differences in most of the characteristics that is number of medications ($P=0.021$), hospital stay days (<0.001), gender (0.006) and socioeconomic status have p-value 0.002 . Patient quality of life and PIPs has association in mobility ($p=0.02$) and usual activities ($p=0.043$). there life quality domains are associated with PIPs which means it effect QoL.

Conclusion: The study concluded that the practice of PIPs in elderly cardiac patients was commonly utilized. The common PIM were the use of loop diuretics, duplication of medications, spironolactone with potassium sparing drugs and the most common PPOs were ACEIs, beta-blockers and statins. Higher prevalence rate of PIPs was because of following local and international guidelines. It was also concluded that patients characteristics affect the occurrence of PIPs. Age, socioeconomic status, hospital stay days and medication number are the characteristics that effect PIPs occurrence.

Key words: Potentially inappropriate medications prescribings, potential prescription omission, START/STOPP

1. INTRODUCTION

1.1 Background

Within medical field drug utilization research is a recognized area which is a useful tool in accessing variation in prescribing practices and rationalization of medication therapy (Hekster and Vree, 1986). It also contribute towards accessing drug utilization and its impact on the community. For health decision makers, drug utilization research (DUR) has a great value in making drug guidelines and health related policies (Saqib *et al.*, 2018).

The use of drug in any medical condition should be weight against its benefits (risk to benefit ratio). There are some steps involved in medications use that are:

- Prescribing pattern
- Pharmaceutical dispensing
- Counselling
- Taking medication

Decision at each step is quite critical because it depends upon patient medical condition and preferences of the physician and patient. There is need of research that how all these decisions are making, because mistake at any step may leads to irrational use of drugs and worsening of patient condition (WHO, 2003). Better understanding of patient medical condition and medication pattern would help in rational use of drugs, which may leads to good clinical outcomes and reducing potential risks (Sarwar *et al.*, 2017). Making interventions by educating the health professionals and patients and taking regulatory actions, may improve rational use of medicines and health status.

For the improvement of the community medication use, drug manufacturers, policy makers, health professionals and researchers, health administrators, drug distributers, public and media use the data and findings of drug utilization research. It is also use to ascertain the outputs of the polices and interventions(Laporte *et al.*, 1985; Sarwar *et al.*, 2017).

Most of the chronic disease like hypertension, diabetes etc. effect the health related quality of life. Health related quality of life (HRQoL) is actually considered as an important patients reported

outcomes (PROS). In these chronic disease and co-morbid conditions there is need of medical intervention that may improve life standards and quality as well as safety and efficacy (Beck and Shah, 2012). Health related quality of life also reflect the role of the health care system of a country(Weeda *et al.*, 2019).

Patrick and Erickson (1993) define health-related quality of life (HRQoL) as “*the value assigned to duration of life as modified by the impairments, functional states, perceptions and social opportunities that are influenced by disease, injury, treatment or policy*” (Erickson and Patrick, 1993).

HRQoL emphasis certain aspects that may include physical functioning of the body, mental health, social aspects and overall health of the patient. HRQoL is also used to measure the disabilities associated with the disease and various risk factors affecting it. This outcome report provide a clue to the health care policy makers for amendment in the treatment guidelines, policies, resources and change in the intervention plan to reduce problems in future (Courtney, 2015).

1.2 Potentially inappropriate medications use and elderly population

A person having age 65 or greater is usually considered as elderly person. According to World Health Organization (WHO) the number of elderly population is increasing continuously with time across the world, the proportion of the elderly having age of 65 or more will be two fold (22%) in 2050 as compared to the census of 2015 (12%). This shift will be from 900 million (12%) to two billion (22%). This proportion will 120 million alone in China by 2050. By 2050, about 80% of the all older will be living in the lower or middle class income countries (WHO, 2015). According to the statistics of UN population report, the older people share around the globe will expected to be 21% by 2050 and 77% of all these older people will be living in developing countries (World Population Prospects, 2017).

Being a developing country, Pakistan is at rank 6th amongst the countries with heavy population across the world. The World Factbook states that there are 9.17 million (4.48%) older people living there (The World Factbook, 2017) and this number may escalates to 23.76 million by 2030 and will be expected to reach 43.3 million (Ashiq and Asad, 2017).

Elderly population, because of their age factor experience physical and physiological changes. Because of these changes in their bodies and mental status made them prone to certain chronic conditions. Alteration in pharmacokinetics and pharmacodynamics also occurs with aging. For the management of their chronic and co-morbid condition they use number of medications, over the counter drugs for minor problems and also practice poly pharmacy. All these factors are mostly related to their age which ultimately cause deterioration medication response and cognitive impairment. In short adverse drug reactions chances are increased (Roth *et al.*, 2015; Jastaniah *et al.*, 2018).

Potentially inappropriate medications are frequently used in this elder aged group patients, which increase concern about the consequences of inappropriate medications use during last years. About 74% of residents at nursing homes are exposed to ten or more drugs(Jokanovic *et al.*, 2015).

1.3 Potentially inappropriate prescribing

Inappropriate medication use and polypharmacy are the two major classes of irrational prescribing, which is the prominent issue of elderly patients that leads to higher prevalence of adverse drug events. Potentially inappropriate prescribing covers, medications use in a condition, in which the adverse drug events (ADE) outweighs the clinical benefit, especially when more effective and safe choices are available and omission of medications that are clinically indicated having no contraindication in patients with significant expectancy of life(Beers *et al.*, 1991; Spinewine *et al.*, 2007).

Potentially inappropriate prescribing also includes:

- I. The medication use with high frequency or longer time which is not indicated
- II. The use of drugs having high potential for drug-drug or drug-disease interactions
- III. Duplication of drug class
- IV. The use of potentially effective drug having clear indication of a disease but because of several reasons not prescribed in older patients (Rochon and Gurwitz, 1999).

A drug is considered to be appropriate when there is clear indication that support its use in a specified situation, well accepted by most of the patients and cost-effective. Furthermore

prescription appropriateness in elderly subjects should study the life expectancy individually, avoiding preventive treatment having short life expectancy and promoting drug use having good risk to benefit ratio(Spinewine *et al.*, 2007).

The fundamental component of treating health condition is the proper use of medications. For example in order to control blood pressure of the hypertensive patient and maintaining his quality of life by the use of appropriate antihypertensive. When a drug is wrongly prescribed and used, it may harm the patient physically and physiologically which leads to increase burden of disease i-e tangible and intangible cost and decrease quality of life. The appropriate prescription by a registered practitioner is considered as essential step in the rational drug therapy(Spinewine *et al.*, 2007).

The prescribing appropriateness covers the following three values:

- i. Patient preferences
- ii. Prescriber's technical and scientific rationale
- iii. Interests of the community (Horne *et al.*, 2005)

Determining that what the patient preferences and serving community by a good manner is very hard task because they are influencing by economics, society and family factors. Most of the publications therefore are dedicated to the pharmacological appropriateness and drug causing harm.

1.4 Consequences of PIM

It is very important to monitor potentially inappropriate medication utilization amongst elderly population due to morbidity and mortality linked with poly pharmacy. The medication regime of such population is very complex and it increases the chances of drug-drug and drug-disease interactions(Storms *et al.*, 2017). Such errors in the management of medications, effect badly the patient health, increases hospitalization and mortality(Gallagher *et al.*, 2011). Potentially inappropriate prescribing also increases the chances of adverse drug reactions (ADRs), which in turn enhances the emergency department visits and decreases good health outcomes(Chang and Chan, 2010).

As per Beers criteria PIM utilization is associated with increased drug related problems (DRPs), which ultimately effect the cost and burden of disease as compared to a person having no PIM use(Fick *et al.*, 2008).

According to a study that an individual exposed to PIM use had a higher cost of about \$1237 and consumes \$2.1 on extra prescribed substances as compared to an individual none exposed to PIM. The differences between the controlled and exposed group were calculated was about \$401. So adding on extra substance prescribed affect the cost of health care by \$137. The addition prescription of any medicine affect the total health care cost and burden of therapy is also increases which in turn results in poor outcomes(Heider *et al.*, 2018).

A study reports about association between hospitalization and unplanned medication use in senior citizens of Australia accounts for >30% annually of elderly population (Runciman, Roughead et al. 2003). The consequences of PIP can be significant and one cannot underestimate the psychological, physiological and economic burden brought to the patient, his family and the society. IP is a risk factor harm induced by the drugs and a study showed that the drug induced harm prevalence was 20.4% in patients with inappropriate medication use (Laroache).

Although drug induced harm cannot be fully preventable but it is general understanding that most of the harm induced by drugs can be prevented by proper management. Howard et al. reported that drug related medication admissions were 6.5% and out of those 67% medical admissions were judged as preventable(Howard *et al.*, 2003).

The limitations of the methods by which inappropriate prescribing (IP) are identified and prescribing process is fully defined by a term “potentially inappropriate prescribing” (PIP). PIP consequences in increase in cost of health care (Cahir *et al.*, 2010), decline in the functioning and quality of life of the patient, increase in adverse drug events (ADEs) which leads to increase chances of hospitalization and death (Wahab *et al.*, 2012).

1.5 Factors contributing to occurrence of PIM

There are numbers of factors that contribute to the occurrence of potentially inappropriate prescribing. The most prominent factors are discussed below:

1. Higher morbidity and higher prevalence rate of chronic diseases. Because in chronic diseases management there need taking medication continuously for life time so there may occur chances of over or miss use of drugs which leads to adverse drug events.

2. In elderly patients, comorbidity is a major issue which creates complications for prescriber to prescribe drug having no contraindications and safer than their alternatives. For patient, it is difficult to use medicine properly, because impaired mental condition of elder patient.
3. Higher number of concurrent drug therapies make the patient more susceptible to drug-drug and drug disease interactions(Opondo *et al.*, 2012).
4. Physiological age-related changes alter the pharmacokinetics and pharmacodynamics making patient more prone to side effects and toxicity(Mangoni and Jackson, 2004).
5. The presence of limited group of such patients in a clinical trial.
6. Unawareness of the proper guidelines and improper training of the health professionals also contributes to inappropriate use of medications.
7. Lack of availability of health care resources and research

1.6 PIM is a major issue with elderly patients

Prescribing medication for older age group is quite challenging. Physiological age-related changes alter the pharmacokinetics and pharmacodynamics (Mangoni and Jackson, 2004) potential for poly pharmacy is increased (Reason *et al.*, 2012), evidence regarding safe and effective medicines became limited for old and frail patients (Konrat *et al.*, 2012) and multiple co-morbid conditions affect medication affectivity. These all could result to inappropriate prescribing.

If safe and effective alternatives are there, the use of drugs and combination of drugs should be avoided because it may cause harm more than its benefit (Harrison *et al.*, 2018).

According to World Health Organization (WHO) more than 50% of all medicines are prescribed, sold and dispensed inappropriately. Around half of the patients fail to take and use their medicines appropriately. ADRs in elderly patients are sometimes difficult to be recognized because they are often present with specific symptoms like fatigue, fall and postural hypotension. Two to three times more ADRs are observed in elderly which accounts for 5% -17% of all hospitalizations (Brahma *et al.*, 2013). According to a systemic review ADRs mean prevalence in elderly is 11% and the prevalence of adverse drug reactions that leads to hospital admission is 10%. It is also shown that increase in comorbidities and increase in medication number were significantly associated with a higher risk of ADRs (Alhawassi *et al.*, 2014).

Brahma, Wahlang et al. 2013 estimate that 30%-60% of ADEs could be prevented (Brahma *et al.*, 2013). A study has shown that 45.1% are preventable ADRs which leads to hospitalization (Schmiedl *et al.*, 2018). The prevalence of ADRs in USA and Canada is ranged between 14-37% (Morin *et al.*, 2016) while in Europe it was 23%-43%(Tommelein *et al.*, 2015). The difference between these two continents could be elucidated by drug market differences, prescribing pattern differences and most importantly the tool by which prevalence is measured (Komagamine, 2018).

For safety of elderly patients, appropriate medicines should be prescribed. Amongst the 10 most important causes of death around the globe, adverse drug reactions is included by WHO.

1.7 Cardiovascular disease status

Around the globe, the major contributor to the global burden of disease is the cardiovascular disease. Mortality because of CVD accounts for 31.5% of the total deaths per year. (Benjamin *et al.*, 2017). Benjamin, Blaha et al. reported that in 2013, 12 million deaths (70%) of all CVD deaths mostly occurred low and middle income countries (Benjamin *et al.*, 2017). In geriatric population CVD is increasing and in America the number of CVD patients is about 84.3 million and out of that 43 million are of age 65 years or older than 65 years (Roth *et al.*, 2015). Up to 2030 CVD will be the most foremost cause of deaths around the globe. The number one cause of deaths around the world is the CVDs, people dying of CVDs annually is more than other causes. In 2016, 17.9 million people are estimated to be died because of this disease which is 31% of total deaths per years around the globe

In Pakistan the number of cardiovascular patients is continuously projecting day by day which is major and challenging concern of the health care system of the country (Zubair, Nawaz et al. 2018). Cardiovascular disease death has reached about 200,000 per year which is about 410/100,000 of the population (World Health Organization, Cardiovascular Diseases, August, 2018).

1.8 Screening tool for assessment of PIM

To improve the quality of geriatric medication prescribing, recently various tools are designed and developed, in order to assess the potential inappropriate prescribing. These screening tools are of two categories:

- Explicit criteria
- Implicit criteria

Both categories are based on clinical judgments, expert opinions and consensus method (Spinewine *et al.*, 2007). Explicit criteria in particular use to detect medication appropriateness that either the medication should be given or avoided in a certain medical condition (Mazhar *et al.*, 2018).

1.8.1 Implicit screening criteria

Implicit criteria includes the use of clinical judgments and harm versus benefit in term of patient specific considerations. There needed well trained clinicians having approach to patient clinical data in order to perform medication assessments (Lunde *et al.*, 1979). this criteria is individually applied to each patient and more time is required to perform such assessment.

- It depends upon professional expert judgments
- It is patient specific and focuses on entire patient medication regimen
- Low reliability
- For example: According to Medication Appropriateness Index (MAI) statement-“is there any indication for the drug?”
- Examples of such tools are Lipton criteria, MAI

1.8.2 Explicit screening criteria

Screening of the prescribing appropriateness using explicit criteria as compared to implicit criteria includes the use of list of drugs and disease condition and does not involves much clinical judgments. such list offers a minimum standard which is applicable to most of the patients and one can easily perform with in short time (Spinewine *et al.*, 2007). Because of its easy to use nature, many studies were conducted for the development and application of such criteria.

- It has been developed from literature reviews, expert opinions and Delphi consciences technique.
- There is list of drugs, classes of drugs, drug dosage and the dosage having known cause of harm.
- For example: According to STOPP criteria Beta-blocker in combination with verapamil or diltiazem should be stopped because it increases risk of heart block.

- Examples of such tools are START & STOPP criteria, Beer's criteria, McLeod and PRESCUS

1.9 STOPP/START Criteria

Amongst all explicit criteria, American Beers' criteria is the most popular. Some limitations highlighted in some studies in European context regarding Beers criteria applicability. Because of that in 2008 Gallagher et al. put forward a new set of explicit criteria to check the appropriateness of the medication prescribing. That new tool for screening appropriateness is so called "screening tool of elder persons' prescriptions/ screening tool to alert doctor to right treatment" STOPP/START criteria (Gallagher *et al.*, 2011).

These Europeans criteria are organized in accordance to the physiological system of the patients and in routine practice it is easy to apply. Such criteria is very sensitive in determining potentially inappropriate medications (PIM) and drug induced harm (DIH). It also reports about the issue of under prescribing and omission of potential beneficial medicines (Lam and Cheung, 2012). In various clinical scenarios these criteria are successfully applied.

START and STOPP are explicate screening tool for the assessment of appropriateness of medication in patient aged about sixty five or above (>65 years). In geriatric pharmacology, 18 experts validated these tools through Delphi consciences process (Gallagher *et al.*, 2011). In various countries the lesser the START and mostly the STOPP criteria have been used for the evaluation of the inappropriate prescribing prevalence in health care settings.

In a randomized controlled trials Gallagher et al. reported that the screening of in elderly patients' medications via using START/STOPP criteria provides a feedback to the health care team which is very helpful in improving appropriate prescribing (Gallagher *et al.*, 2011). These tools have many leads over other tools that are as under:

- These tool link evidence- based medication use with a clinical situation.
- The medications list given in the tool for assessment are available and used throughout the European countries.
- These criteria also covers the overuse, misuse and underuse medication events.
- They are comparatively very easy to apply.

According to the tools' creators, the screen criteria application to subjects take few minutes to judge the events of inappropriate prescribing in elderly patients as it provides a comprehensive data about the medications of the patient and co-morbidities. A few studies have evaluated the association between inappropriate prescribing events and clinical outcomes (Hamilton *et al.*, 2011). Hamilton *et al.* compared these both Beers and STOPP criteria as risk factors for serious preventable adverse drug events and concluded that the STOPP criteria are more sensitive to inappropriateness in prescription which results in ADEs than Beers criteria.

For the first time STROP/START criteria was drafted in 2008 in Ireland.

1. STOPP criteria consist of clinically significant 65 indicators for the selection of potentially inappropriate prescribing in older patients.
2. STAR criteria comprises of 22 evidence based indications which reflects potentially prescription omissions. It was the first tool that screen and address the prescribing omission (Gallagher *et al.*, 2008).

These criteria were updated in 2015 containing 34 START and 80 STOPP items arranged in accordance to the physiological order system. The updated version is accompanied by the description that why the prescription is potentially inappropriate and why there is a need of prescription in given condition. These all explanation is evidence based- are according to the articles published and guidelines. The criteria describes the dual nature of the potential inappropriate prescribing (PIP) by including a validated list of potentially inappropriate medications (PIMs) and potentially prescribing omissions (PPOs).

As concerned with cardiovascular disease elderly patients, there are 27 STOPP and 11 START items which are cardioselective in their nature. These criteria contains indications and contraindications for CVDs patients.

1.10 McLeod Criteria

One known explicit criterion is McLeod criteria in Canada. It was developed by a panel of geriatricians and pharmacists in Canada (Elliott and Stehlik, 2013). This criteria specially focuses on the drugs list to shun some medications in a particular condition and not to exceed the duration of certain drugs which may cause harm and ADEs. It also provides a list of best alternatives choices which are safe and addresses disease drug interactions.

1.11 ACOVE Criteria

A suite of minimum standards has been developed by an American research group from the expert views. It intended to improve the quality of life of elderly patients. It also detects the under and misuse of medications by such quality standards.

ACOVE is the abbreviations for Assessing Care of Vulnerable to Elderly. 400 indicators were updated last time for quality of life addressing twenty six clinical situations from which 70 indicators are associated with the use of medications (Wenger *et al.*, 2007).

1.12 Beers Criteria

To identify PIM, the most commonly use criteria was Beers criteria. It was developed by Dr. Mark H. Beers and was so called Beers criteria after his name. it was published in 1991 for the first time(Beers *et al.*, 1991).

Beers criteria was continuously updated with time in order to make it more applicable to modern scenarios. It was revised in 1997, 2003, 2012 and in 2015 (the most updated version). The latest version was made by a panel of expert from different discipline including pharmacist, nurses and physicians(Panel *et al.*, 2015).

This criteria focuses on the detail drug list that should be avoided in any condition or disease, drug dose and duration of drug used should not be exceeded. In Beers explicit criteria 151 drug or drug classes were categorized as PIM and were father more categorized into 5 categories as:

1. Medications or drugs to be avoided
2. Drugs that exacerbate a disease state or any syndrome
3. Kidney functioning based PIM
4. Cautious drugs
5. Drug-drug interactions (Fick *et al.*, 2015)

1.13 PIM and Quality of Life

Quality of life is defined by WHO as “an individual's perception of life in the context of culture and value system in which he or she lives and in relation to his or her goals, expectations, standards, and concerns” (WHO | WHOQOL: Measuring Quality of Life (2014)). Quality of life (QoL) has many

dimensions that covers both negative and positive aspect of life experiences. To know how QoL is affected, various domains of life are assessed that includes patient's individual perceptions, decline in physical activity and performance and other linked factors. It embraced health related quality of life, social and emotional wellbeing (Baernholdt *et al.*, 2012).

Health related quality of life (HRQoL) encompasses physical ability of a person, psychological status, social attachment, beliefs of the person and his relationship with other. HRQoL contains both objective and subjective aspects of different quality of life dimensions as compared to QoL. The scope of QoL is narrowed in the term HRQoL because it made it more relevant to health of the person (Orbell *et al.*, 2013).

To determine that how health condition of a person impact his quality of life, health related quality of life is considered as important tool/indicator of the health of a person (Revicki *et al.*, 2014). And this consideration of quality in elderly population is very important as quality of life is affected by physiological functioning and health status. In elderly these indicators are affected more as compared to other age group population (Vaarama, 2009).

Person of age 65 or more is called elderly. Elderly population are characterized by low physical functioning, higher morbidities, and required more attention for their care, which pose a huge burden on the health care system of a country. It became a tough challenging situation when elderly people are with chronic diseased conditions, the need of medication and decline in their physical and psychological abilities (Milton *et al.*, 2008). The co-morbidities in elderly ultimately increases the number of medication (poly pharmacy) that augments the chances of inappropriate drug prescribing which may leads to increase adverse drug events (ADEs), morbidities and hospital admissions (Liu and Christensen, 2002). There is also intense need of appropriate medication utilization. All these mentioned factor affect the quality of life.

Decreasing in the symptoms and eradication of disease are positive responses to the health care providers but the disease and the drug have certain undesirable and unwanted effect on the patient health that affect the quality of his life (Olsson *et al.*, 2011). The pharmacotherapy should give such that the patient's quality of life restores and less affected by the undesirable effects. To improve the quality of life of elderly population, there must need interventions instead of looking for tradition health outcomes i-e effectiveness and safety (Rich *et al.*, 2016).

In patient reported outcome measures (PROMs), the health related quality are mostly recognized as a key in measuring of successful pharmacotherapy amongst elderly CVD patients (Gjeilo *et al.*, 2018).

It is essential to discover factors that influence the quality of life in elderly patients. Higher exposure to potentially inappropriate medications use was linked with low quality of life (Harrison *et al.*, 2018).

1.14 Rationale of study

A person having age 65 or greater is usually considered as elderly person. According to World Health Organization (WHO) the number of elderly population is increasing continuously with time across the world, the proportion of the elderly having age of 65 or more will be two fold(22%) in 2050 as compared to the census of 2015 (12%). This shift will be from 900 million (12%) to two billion (22%). This proportion will 120 million alone in China by 2050. By 2050, about 80% of the all older will be living in the lower or middle class income countries (WHO, 2015). According to the statistics of UN population report, the older people share around the globe will expected to be 21% by 2050 and 77% of all these older people will be living in developing countries (World Population Prospects, 2017).

Being a developing country, Pakistan is at rank 6th amongst the countries with heavy population across the world. The World Factbook states that there are 9.17 million (4.48%) older people living there (The World Factbook, 2017) and this number may escalates to 23.76 million by 2030 and will be expected to reach 43.3 million (Ashiq *et al.*, 2017).

Around the globe, the major contributor to the global burden of disease is the cardiovascular disease. Mortality because of CVD accounts for 31.5% of the total deaths per year. (Benjamin, Blaha *et al.* 2017). Benjamin, Blaha *et al.* reported that in 2013, 12 million deaths (70%) of all CVD deaths mostly occurred low and middle income countries (Benjamin, Blaha *et al.* 2017). In geriatric population CVD is increasing and in America the number of CVD patients is about 84.3 million and out of that 43 million are of age 65 years or older tah 65 years(Roth *et al.*, 2015). Up to 2030 CVD will be the most foremost case of deaths around the globe. The number one cause of deaths around

the world is the CVDs, people dying of CVDs annually is more than other causes. In 2016, 17.9 million people are estimated to be died because of this disease which is 31% of total deaths per years around the globe

In Pakistan the number of cardiovascular patients is continuously projecting day by day which is major and challenging concern of the health care system of the country (Zubair *et al.*, 2018). Cardiovascular disease death has reached about 200,000 per year which is about 410/100,000 of the population (World Health Organization, Cardiovascular Diseases, August, 2018).

It is very important to monitor potentially inappropriate medication utilization amongst elderly population due to morbidity and mortality linked with poly pharmacy. The medication regime of such population is very complex and it increases the chances of drug-drug and drug-disease interactions (Storms *et al.*, 2017). Such errors in the management of medications, effect badly the patient health, increases hospitalization and mortality (Gallagher *et al.*, 2011). Potentially inappropriate prescribing also increases the chances of adverse drug reactions (ADRs), which in turn enhances the emergency department visits and decreases good health outcomes (Chang and Chan 2010).

Elderly patients with chronic disease having comorbidities along with baseline impairments results in poly pharmacy, that enhance the risk of exposure of elderly cardiac patients to inappropriate medication use. PIM leads to poor QoL. There is scarce evidence on this aspect of older local patients of Pakistan. The research on aspect are also limited. There is need of research in order to fill the space.

1.15 Aim and objectives

The aim of this study was to assess the potentially inappropriate prescribing (PIPs) prevalence amongst the elderly cardiac patients of Pakistan using STOPP/START updated criteria.

There objectives of the study are:

1. To measure PIPs prevalence in elderly cardiac patients.
2. Pattern of use inappropriately prescribed medications.
3. Quality of life of cardiac elderly patients.

4. To investigate an association between PIPs and QoL.

1.16 Significance of the study

Results of the study:

- Enables health care professionals to enhance the evidence-based use of the drugs in elderly cardiac patients.
- Provides approximate idea that how many elderly cardiac patients are exposed to PIPs.
- Provide a view of HRQoL current status of Pakistani elderly patients.
- Determines the risk factors associated with PIPs and QoL.
- Provides data for further investigation.

1.17 Literature review

Various studies has been done for the assessment of prescribing appropriateness using START/STOPP criteria in various health care setting in most of the countries of Europe, America and Asia.

(Barry *et al.*, 2007) The article using START criteria showed that 57.9% in-patients has at least one prescribing omission. It is also reported that medication omission is probably increases with age and female gender. Over the age of 85 years, total 72% of medication omissions were reported in comparison to patient of age between 65 to 74 years (55.2%) and the women were most exposed to inappropriate omissions.

(Ryan *et al.*, 2009) The article identified medication inappropriateness using START/STOPP criteria. It was identified that about 21.4% (248) elderly patients were with at least one PIM and 22.7% patients with PPOs. The prevalence of PIM was associated with medication number and age of patient. It was concluded that prevalence of PIM occurs with increased number of medications prescribed.

(Miquel *et al.*, 2010) This paper tries to detect potentially inappropriate medications prescribing in elderly in health care setting using START/STOOP and Beers criteria. The study founded that

START/STOPP criteria detect 47% while Beers detect 23% inappropriateness in both primary care and nursing homes. The study concludes that START/STOPP criteria detect a greater number of medication inappropriateness as compared to Beers criteria. START criteria also shown various performance in health care areas.

(Kruse *et al.*, 2010) STOPP criteria for inappropriate prescribing has been studied in nursing homes. The results stated that 75.5% Irish resident received at least one PIM and 66% German with to same problem.

(Pyszka *et al.*, 2010) A retrospective study at Veterans Affairs Hospital in USA was performed using START/STOPP screening tool. About 58.6% potentially inappropriate medications and 46.8% medication omissions were detected.

(Lang *et al.*, 2010) The study reported that 77% elderly patients with mental comorbidities were prescribed inappropriately and the inappropriate omissions were 65%. START/STOPP tool were applied in such study. Benzodiazepines and neuroleptics were found the most frequent inappropriate medicines. Medications for cardio vascular disease patients were also assessed for PIP which concluded that there is greater need of health literacy on lively amongst health personals. They also concluded that living in an institution was a common risk factor for PIP.

(Gallagher *et al.*, 2011) A study conducted in 6 European countries, determined that poly pharmacy was major risk factor for potentially inappropriate prescribing in advanced age (>85years) and comorbidity were founded as a risk factor linked to inappropriate medication omissions.

(Gallagher *et al.*, 2011) A randomized controlled trial using START/STOPP criteria for inappropriateness of prescribing in patients aged >65 years. 400 hospitalized random patients were subjected in the study receiving usual drug therapy care as control and screening with STOPP/START, MAI and AOU as intervention group. The results of intervention were effective in ADRs reductions. It were concluded that inappropriateness in the interventional group were significantly low as compared to usual therapy receivers.

(Frankenthal *et al.*, 2014) The study assessed the effect of START/STOPP screening tool for elder patients as medication intervention on economical and clinical outcomes in randomized clinical trials. Patients aged >65 years receiving at least one medication were randomized into two groups. The history of hospitalization and falls and QoL were measured in follow up studies. The study

founded that the number of drugs prescribed after one year were significantly lower than controlled group and the average cost as in intervention group was reduced US\$ 29 per individual per month. The QoL was also improved. It was concluded that STOPP/START intervention significantly reduce medication inappropriateness, economic burden, falls and hospitalizations.

(Castillo-Páramo *et al.*, 2014) This publication reported the detection of inappropriate prescribing using STOPP/START criteria in primary health care setting. A random health records of 272 patients were analyzed use START/STOPP tool and the study founded that per patient the median number of medication was 5 and the PIM prevalence detected by START tool was 37.5% while using START tool prevalence was 45.9%.a significant correlations was found between number of medications and PIM. It was concluded that there was high prevalence of PIM according to START/STOPP criteria and for its prevention intervention has to be done.

(Aziz *et al.*, 2018) this systemic review reports the prevalence of inappropriate prescribing in elderly patients using START/STOPP screening tool. The Beers and START/STOPP criteria are reviewed in the context of previous publications and found that START/STOPP criteria for the uncovering the PIM. It is concluded that these criteria are reliable and validated criteria for uncovering PIP and STOPP criteria predict ADEs and both START/STOPP improves appropriateness of medications and decline ADRs.

(Abegaz *et al.*, 2018) A cross-sectional hospital based study was conducted for the assessment of PIPs and factors associated by the use of START/STOPP criteria. 239 CVD patients were assessed for PIM and a total 221 patients were identified in 147 patients. The prevalence of PIPs was 61.5%. ACEIs are the most frequent PIP medication. Hospital stay, co-morbidities and medication number increases the likely hood of PIPs. It was essential to assess and evaluate medication of in-patients to reduce the PIPs using START/STOPP criteria.

Summary of literature review

Table 1.1

Study	Year	Common PIMs	PIMs %	Common POs	POs %
Barry <i>et al.</i> ,	2007	Not done		ACEIs, statins, warfarin, ASAs, multivitamins	57.9
Gallagher <i>et al.</i> ,	2008	BZDs, PPIs, NSAIDs, ASA	34.5	Not done	
Ryan <i>et al.</i> ,	2009	PPIs TCAs, BZDs, NSAIDs, BBs,	21.4	ASA, calc and vit D suppl, statin	22.7
Lang <i>et al.</i> ,	2010	BZDs, neuroleptics, PPIs, ASA	77	antidepressant, ASA, calc and vit D suppl	65
Kruse <i>et al.</i> ,	2010		66.09(German) 75.65(Irish)	Not done	
Pyszka <i>et al.</i> ,	2010	ASA, NSAIDs, CCBs, digoxin, PPIs	58.6	Statin, ACE-Is, calc and vit D suppl	46.8
Topinková <i>et al.</i> ,	2010	NSAIDs, ASA, neuroleptics, BBs	35.1	ACE-Is, ASA, warfarin, antihypertensive	51.9
Gallagher <i>et al.</i> ,	2011	BZDs, neuroleptics, PPIs, ASA	51.3	Calc and vit D suppl, statin, ACE-Is, antiplatelet	59.4
Liu <i>et al.</i> ,	2011	BZDs, neuroleptics, CCB	41.9		41.9
Castillo-Paramo <i>et al.</i> ,	2014		37.5		45.9
Aziz <i>et al.</i> ,	2018	BZDs, antipsychotics		Statins, CCBs, vit D	
Abegaz <i>et al.</i> ,	2018	ACEIs, aspirin with vit k, statins	48	ACEIs, beta-blockers	52

ACEIs: Angiotensin converting enzyme inhibitor; ASA: Aspirin; BB: beta-blocker; BZD: Benzodiazepine; CCB: Calcium-channel blocker; PIM: Potentially inappropriate medication; PO: Prescribing omission; PPI: Proton pump inhibitor; Suppl: Supplements; Vit: Vitamin.

2. RESEARCH METHODOLOGY

2.1 Research Methodology

This section explains the study design, study settings and duration, sample size, sampling procedure, study participants, inclusion & exclusion criteria, study tools, study variables and detailed data collection procedure. Detail of statistical analysis and procedures, ethical considerations and approvals for conduction of such study are also described.

2.1.1 Study Design

Our study is a prospective, cross-sectional survey-based analysis. Approach followed to gain objectives of the study is quantitative approach. As sectional study design is also a type of observational study design. It is helpful in assessment of epidemiology and frequency of particular diseases and drugs used i.e. pharmacoepidemiology. This study is used for monitoring and evaluation of specific public health issue which will be later on very helpful in making of policies and development of guidelines.

In this study design, a questionnaire is used for the collection of information from study participant for a single time in study duration.

2.1.2 Study Settings

It is a single institutional study involving one tertiary care hospitals, a Government based run hospital. The study was performed for eight months.

The study was performed at the in-patient department of cardiac center in a tertiary care hospital at Mardan, mostly cover upper parts of the KPK. It is a Government based run tertiary care setting and as Pakistan is a developing country where about more than 50% of the population is living at or below the poverty line, the low-cost treatment services attract the bigger pool of patients. Therefore, it is approached by a population more indicative of the country's health status. MMC is one of the country's tertiary care settings which provides services in cardiology as well as other advanced treatment facility not only to the residents of Mardan city but also to people of Buner, Dir, Swat, Nowshera, Swabi and adjoining areas.

Hence, randomly patients are selected from this tertiary care hospital would have minimal chances of significant bias.

2.1.3 Sample size and sampling technique

According to National population survey 2017, the population of Pakistan for the year 2017 is 201,995,540 (Population statistics report, 2017). Previously, there is no data available about accurate prevalence of PIM in elderly cardiac patients. A general and simple formula was used to estimate sample size.

Rao soft sample size calculator was used to guess sample size. The minimum mandatory sample size calculated was 386 based on 95% CI and 5% margin of error.

$$n = N \times \frac{E^2}{(N-1)E^2 + x}$$

Where as

n= sample size.

N= Population size.

E= margin of error.

A random sampling technique was used to attain calculated sample size. Each elder patient visiting the in-patient department of study settings were judged for suitability to be included in study.

2.1.4 Study Participants

The subjects of concentration in our study are elderly in patients with a cardiovascular diseased condition. All elderly patients were asked to participate in study after clarifying purpose and nature of study.

2.1.5 Inclusion and exclusion criteria

Each consented patient was assessed according to predefined inclusion and exclusion criteria as follows;

a. Inclusion criteria

- Patient aged 65 years or older
- Patients had at least one cardiovascular condition.
- Hospitalized patients
- Patients are able to communicate and understand the prescriber advice.

b. Exclusion criteria

- Any patient with incomplete data like wasted medication history or missed serum creatinine level of patients etc .
- Elderly patients with mental impairment.
- Patients who were visiting out-patient clinic due to exacerbation of cardiac illness, acute care, short prognosis and taking palliative care.

2.1.6 Data Collection

A previously validated and complete data collection form developed by Rehan et al was used in present study. The questionnaire used in such study was based on extensive literature review and used to assess drug utilization pattern among elderly patients (Sarwar *et al.*, 2017). To support study outcomes, this pre-validated questionnaire was applied to study participants and reassessed. Data collection form comprised of four parts:

- 1) Demographic characteristics,
- 2) Socio-economic characteristics,
- 3) Health characteristics and
- 4) Disease related characteristics.

A pilot study was also directed among 40 patients. Cronbach's alpha value indicates a high reliability. Data was analyzed using SPSS v 20.

2.2 Measures

2.2.1 Demographic characteristics

Demographic characteristics include gender (Male, Female), age (65-75, 76-85, >85years).

2.2.2 Socio-economic characteristics

Socio-demographic characteristics include annual income (low class (PKR0-25000), middle class (PKR25-50000), and upper class ($\geq 50,000$)). From monthly income we calculated each patient annual income by multiplying monthly income with 12

2.2.3 Health related Characteristics

These characteristics involve assessment of self-reported subjective health (Good, medium and poor), smoking status (yes, no), number of hospital admission days (0-1,2-3, ≥ 3), and OTC medication taking, medication procured or not (1,0).

2.2.4 Disease related Characteristics

These characteristics involve following parameters comorbidities and type of comorbidity (present, absent), number of comorbidities (0,1, ≥ 2) and number of medications prescribed at ward (1-4,5-9, ≥ 10).

2.2.5 Health related Quality of Life (HRQoL)

Numerous tools were established to assess health related quality of life. One of the most frequently used tool is EQ-5D-3L (European Quality of Life scale). EQ-5D is a standardized scale, established by EuroQoL group for calculation of HRQoL. This instrument guesses overall quality of life by a single index value and provides

a brief summary of person health status (Group, 1990). This generic tool assesses health status of the patient into five dimensions (i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Each of five domains further categorized into three levels as no impairment, moderate impairment and extreme impairment.

Visual analogue scale (VAS) is a part of tool which is a 20 centimeter straight calibrated line (ranges from 0 to 100), where 0 indicates worst health and 100 indicates best health state. It is a reliable, validated, easily administrable to the population. The questionnaire is available also in Urdu for the use of local settings of Pakistan. The scale had guaranteed validity, consistency and reliability in number of previous studies (Cronbach's $\alpha=0.65$) (Haq *et al.*, 2012; Saleem *et al.*, 2012).

2.3 PIM evaluation

For the identification of potentially inappropriate prescriptions (PIPs), whole START/STOPP criteria was applied to the medical record of study participants. All the medicines prescribed to patients were assessed to identify the medications that fit to the definition of PIP medication list. Identified PIM were categorized into two categories as 1) PIPs and 2) PIOs. The expert opinions of prescribers and clinical pharmacists were also taken in consideration before getting the final decision.

2.4 Ethics

The study was conducted in accordance with the statement of Helsinki. Study was approved by an Ethical review board of MMC hospital (7388/MTI/MMC). Study protocol was also approved from Ethical review board, Quaid-I-Azam University, Islamabad. Patients were asked to participate in the study and those who granted were explained about the nature of the study and purpose of the study, and patients were formally consented both orally and in writing.

2.4 Statistical analysis

Statistical analysis was done using SPSS version 20 (IBM, Armonk, NY, USA). Due to nonexistence of data on Pakistani population norms, EQ-5D score was calculated by comparing to the values estimated for the general population UK based values printed in 1995 (Dolan *et al.*, 1995). HRQoL domains were categorized into three levels as no problem, moderate problem and severe problem, for analysis in present study. Descriptive statistics included percentages and frequencies for categorical variables and mean (M) and standard deviation (SD) for numerical variables. Chi-square tests and independent t-tests were used to conclude the difference in PIM status by sample features for definite and numerical variables respectively. In order to determine association between QoL and PIM status Kruskal-Wallis tests and Chi square tests were

used depending upon nature of study. Multivariate linear regression analysis and Multivariate binary logistic regression analysis was done to ascertain the factors of PIM use and HRQoL by using variables of $P < 0.05$ in univariate analysis. Results are expressed and accompanied by 95% CIs, and $P < 0.05$ was used for statistical significance.

3. RESULTS

3.1 Socio-demographic and clinical characteristics of patients

A total of three hundred and fifty one patients were admitted to the medical ward during the study period.

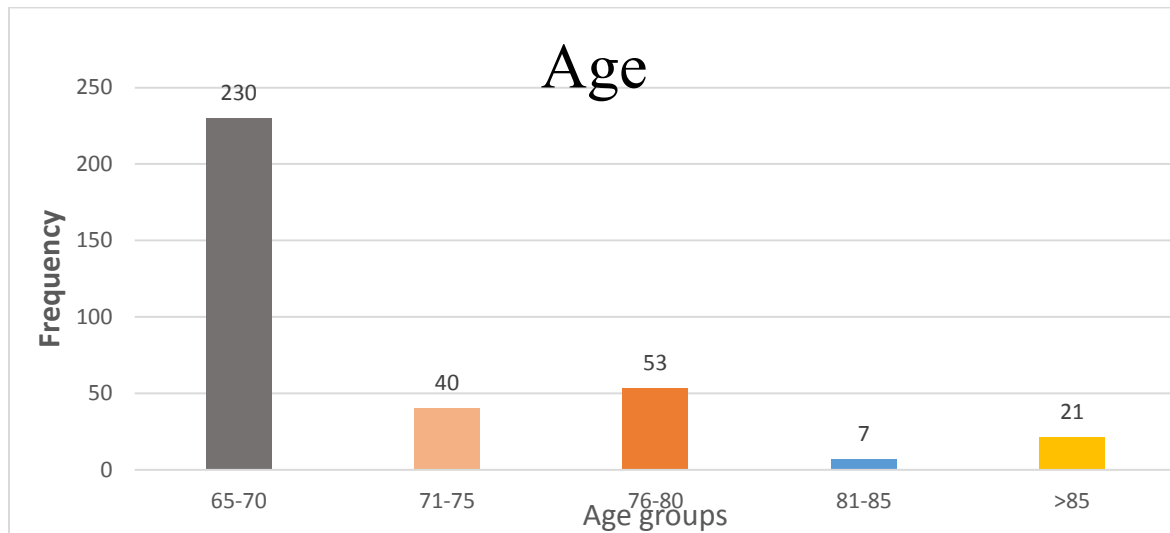


Figure 3.1

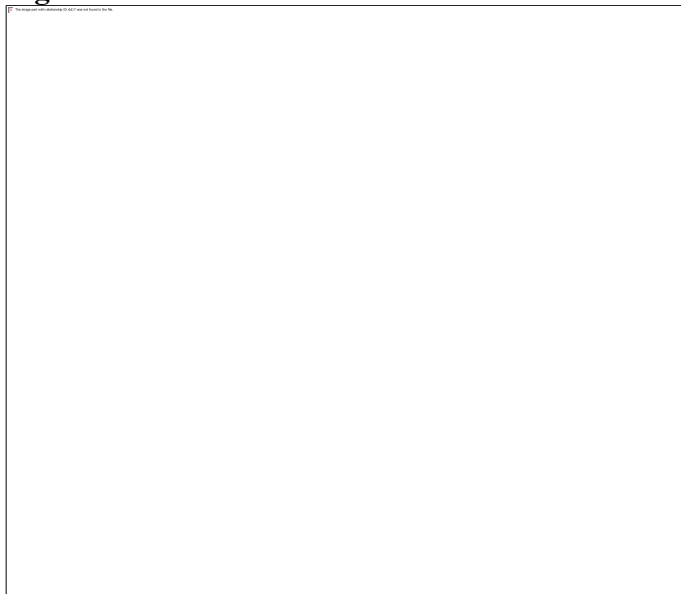


Figure 3.2 Most of the patient are in 65-74 years age group and lesser in the age group i-e above 85 years.

3.2 Socioeconomic Status [N=351]

Annual income

On the basis of annual income there were three categories.

- Low class
- Middle class
- High class

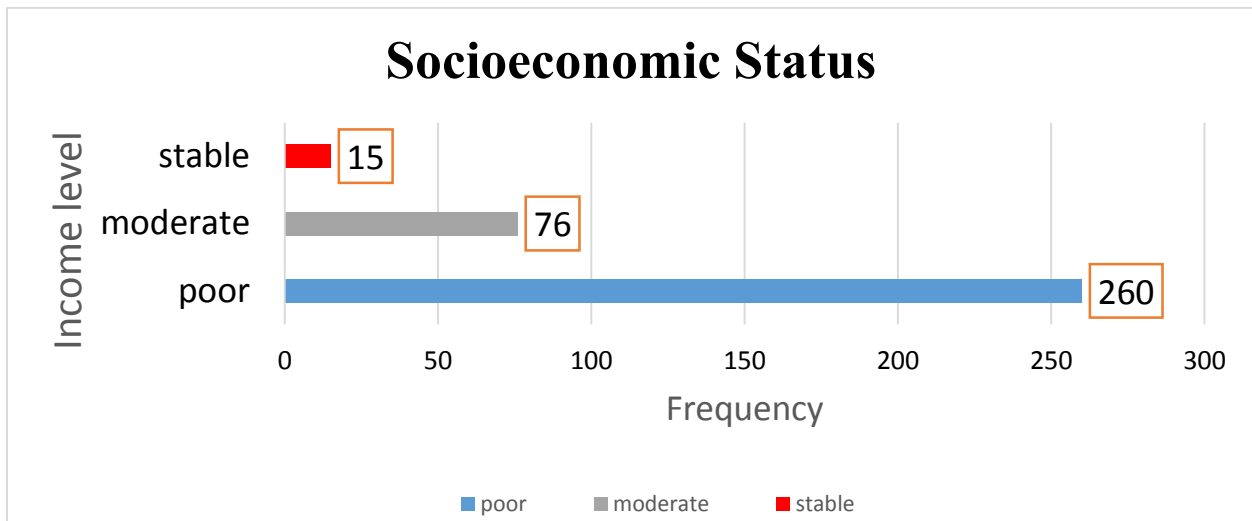


Figure 3.3 Socioeconomic status
Most of the patients (260) were poor.

3.4 Disease Related Characteristics [N=351]

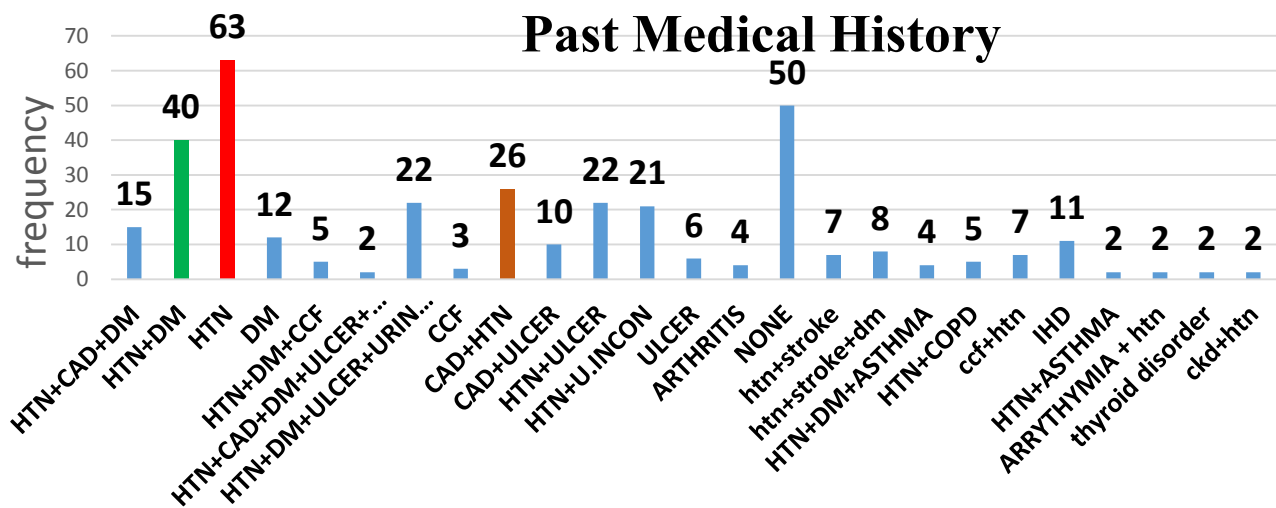


Figure 3.4 Past medical history of about 63 patients with hypertension, CAD plus HTN were 26 and 50 with no history.

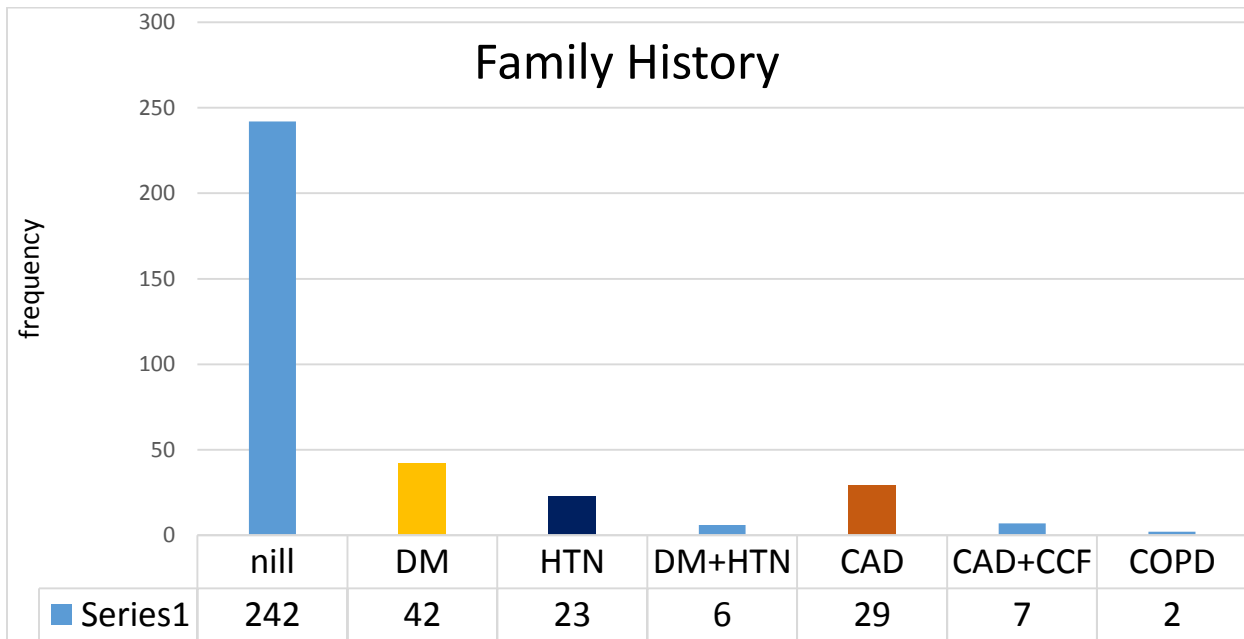


Figure 3.5 242 patients have no family history of cardiac disease. 42 with DM and 29 with CAD.

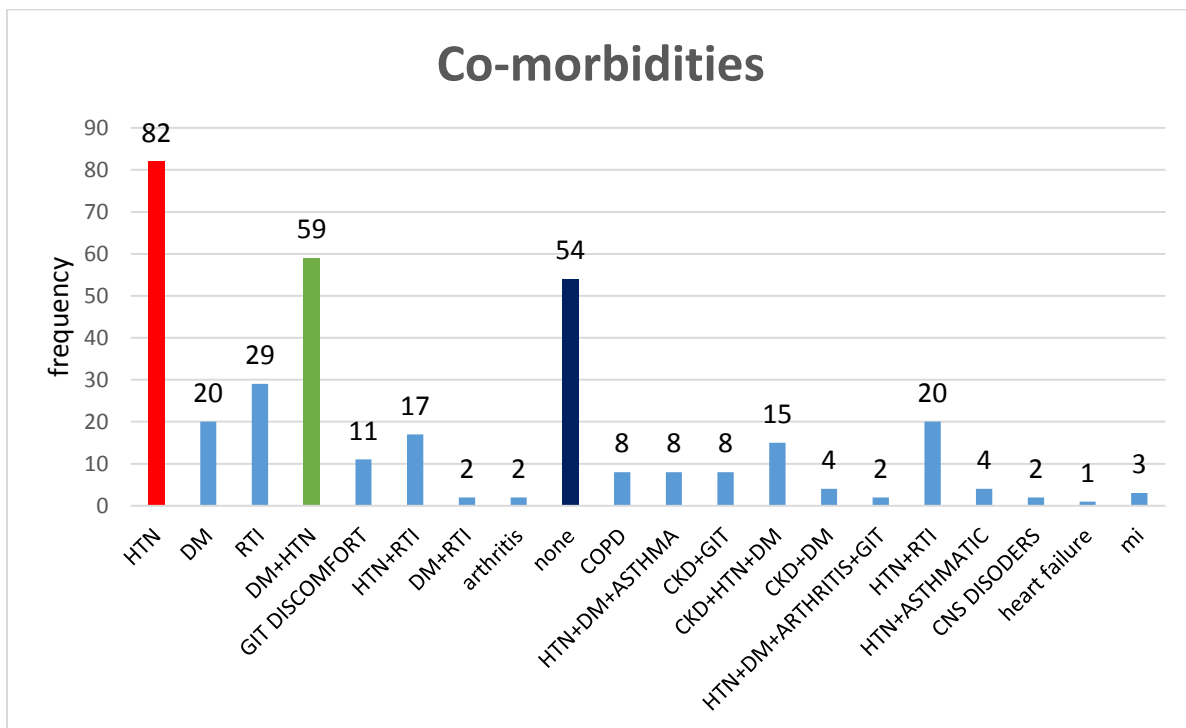


Figure 3.6 Co-morbidities, 82 patients reported having HTN and 59 having HTN and DM

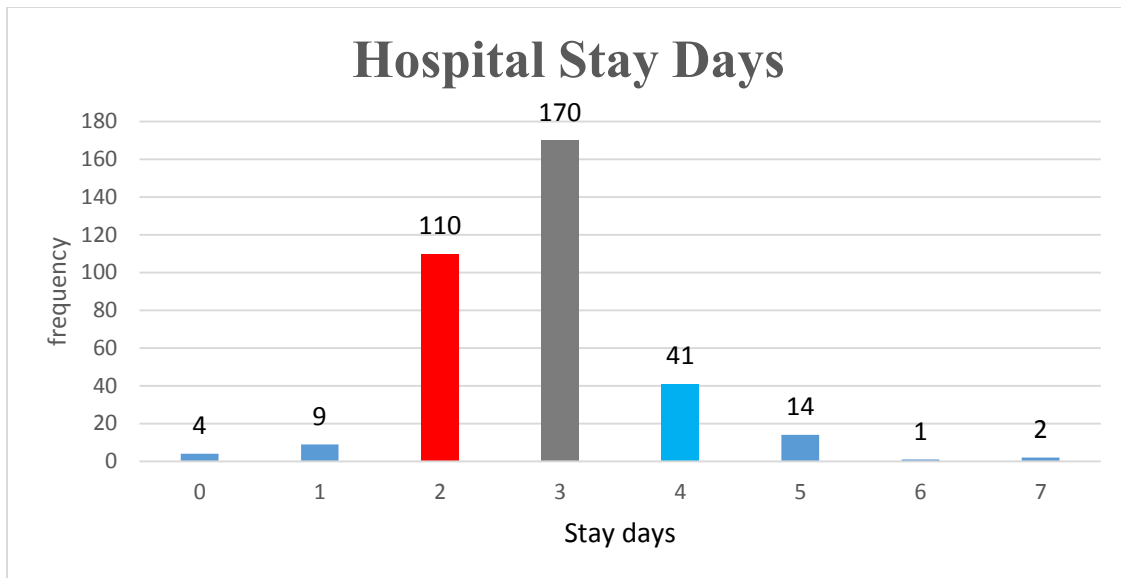


Figure 3.7 170 patients stay at hospital for 3 days and 110 patients for two days. Two patients were hospitalized for 7 days.

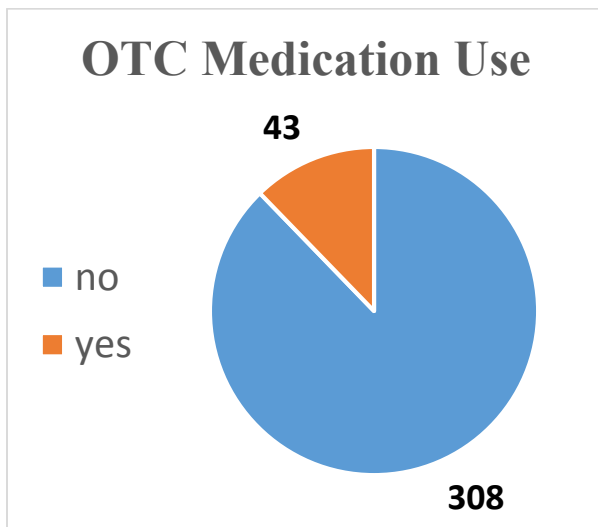


Figure 3.8 43 patients taking over the counter medicines other than prescribed at ward.

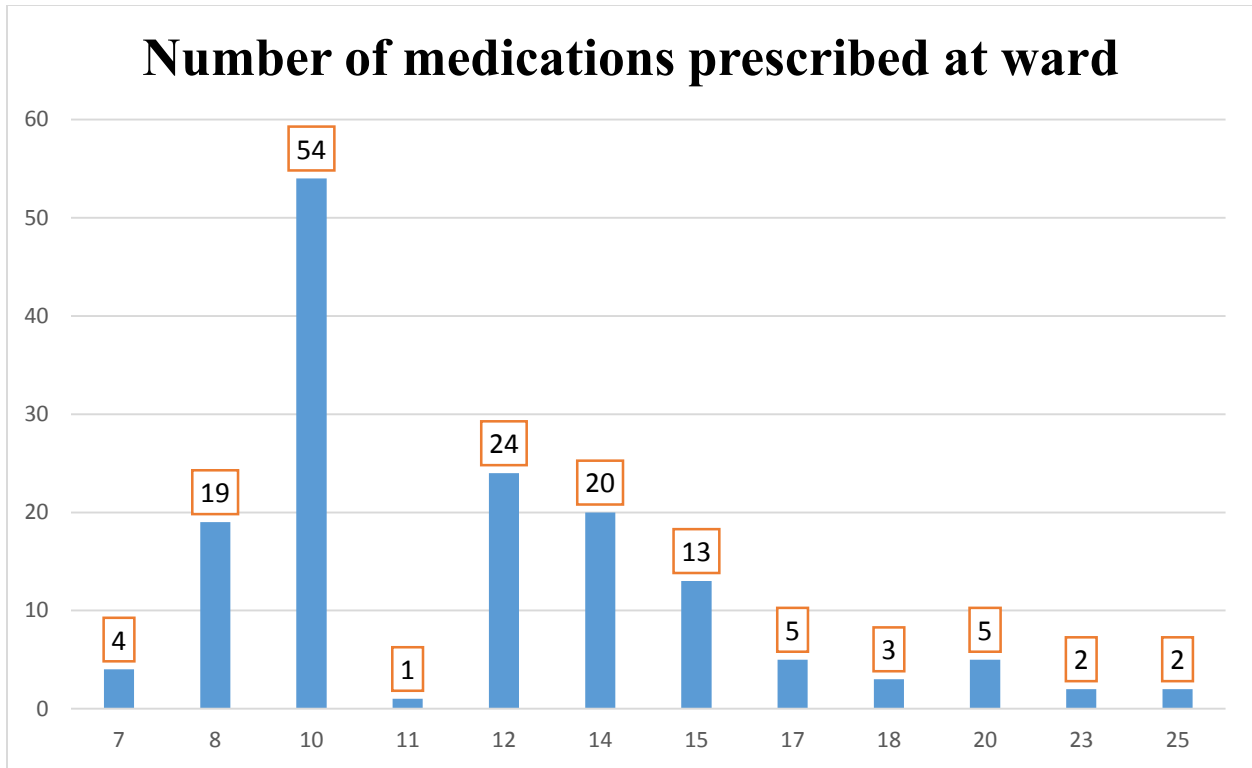


Figure 3.9 Ten medications were prescribed for 54 patients and 12 for 24 and 25 medications for two patients.

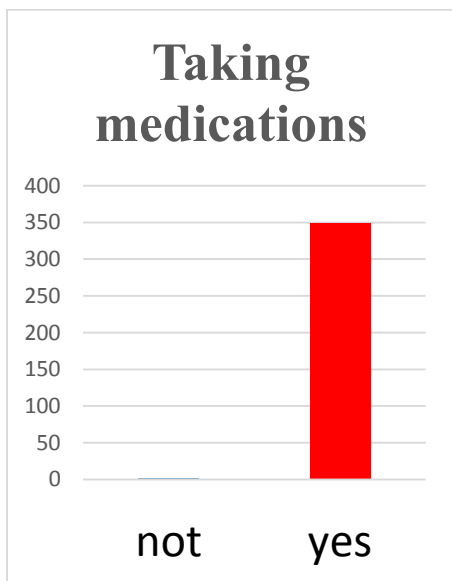


Figure 3.10

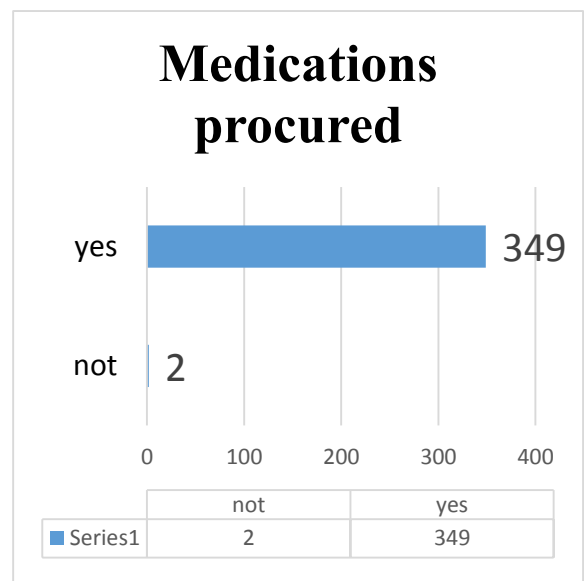


Figure 3.11

Almost all the patients were taking and procured medication properly.

3.5 Health Related Quality of Life

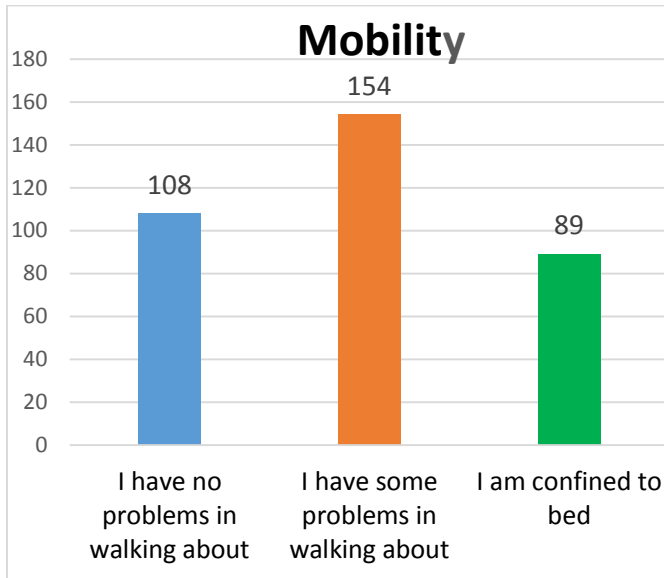


Figure 3.12

154 patients have some problem in walking about and 89 were confined to bed.

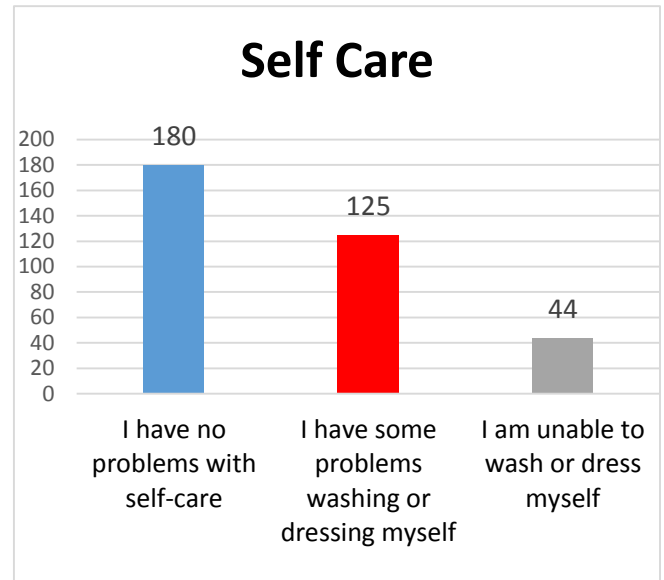


Figure 3.13

180 patients have no problem while 125 have some problem in selfcare and 44 were unable to do so.

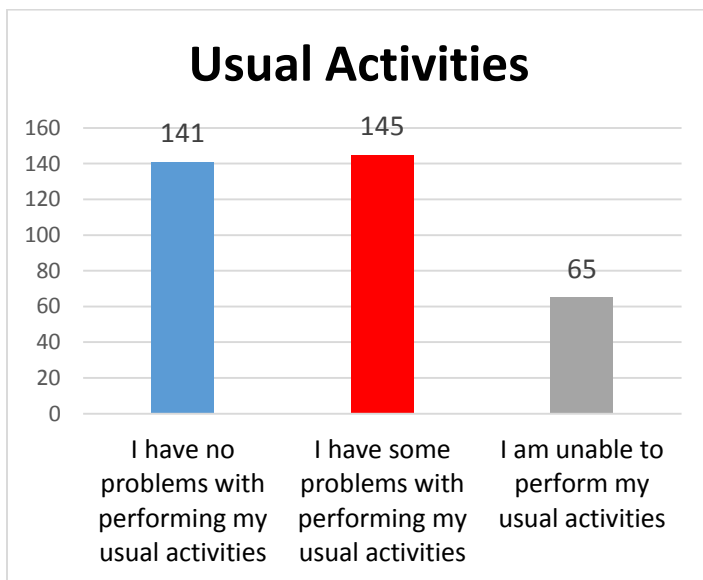


Figure 3.14

141 have no problem with performing daily activities and 65 were unable.

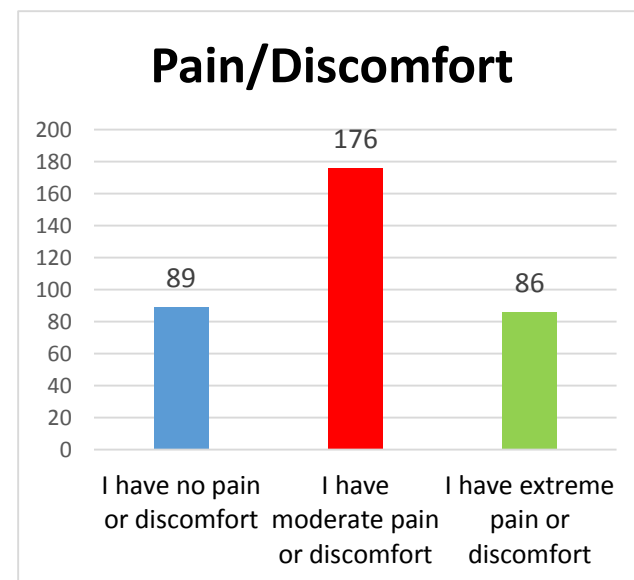


Figure 3.15

176 patients have moderated pain and discomfort.

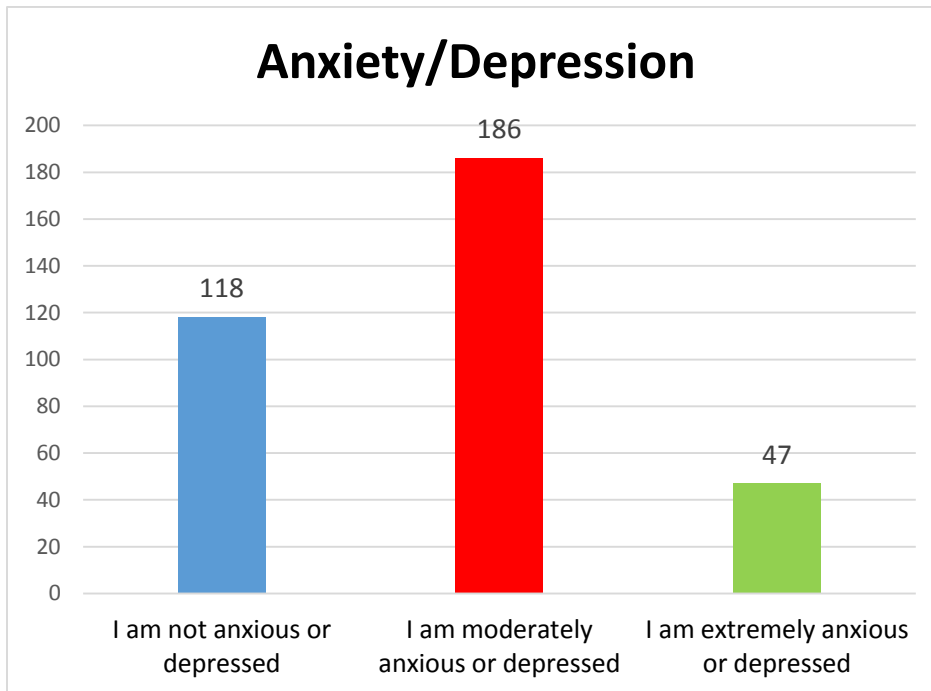


Figure 3.16 118 patients have no anxiety and depression, 186 have mild and 47 have severe anxiety and depression.

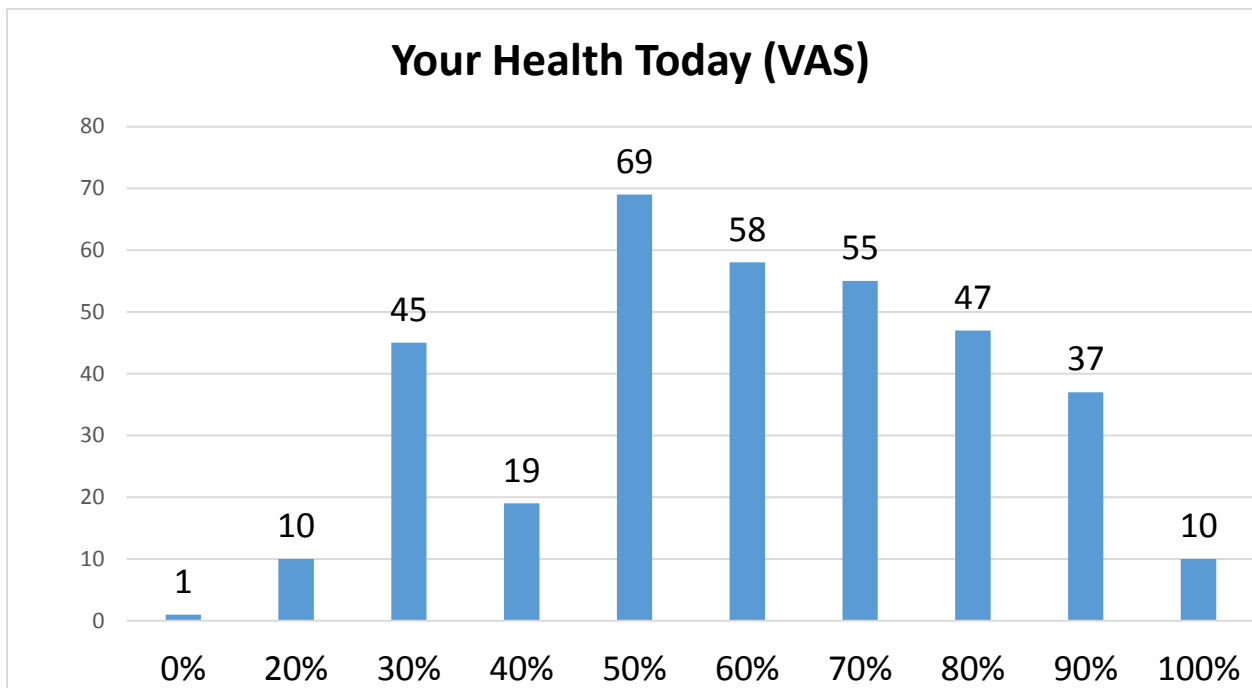


Figure 3.17 The health status move from best to worse (100-0%).

3.6 Drug Utilization Pattern of PIM

Table 3.1

PIMs	Frequency n (%)
Any medication prescribed without any indication	1 (0.5)
Any medication prescribed beyond the recommended duration	0 (0.00)
Any duplicate medication	30 (8.6)
Digoxin for heart failure with normal systolic ventricular function	0 (0.00)
Amiodarone as first line therapy for in SVT	5 (1.4)
verapamil or diltiazem with class three or four heart failure	0 (0.00)
Beta-blocker with verapamil or diltiazem	0 (0.00)
beta blocker with bradycardia	
Loop diuretics with dependent ankle edema	7 (2.0)
Loop diuretic for treatment of hypertension in urinary incontinence	20 (5.7)
Loop diuretic as first-line treatment for hypertension	50 (14.2)
Thiazide diuretic with current electrolyte imbalance	0 (0.00)
Aspirin in peptic ulcer patients without anti-acid	8 (2.3)
Spironolactone with K-sparing medications without checking the level of K ⁺	29 (8.3)
Aspirin with VKA in patients with chronic atrial fibrillation	2 (0.6)
ACEIs or Angiotensin Receptor Blockers in patients with hyper-Kalema.	5 (1.4)
Total PIMs	157(44.72)

Total PIMs were reported 154 (44.72%)

Loop diuretic as first-line treatment for hypertension 50 (14.2) was the most PIM, 30 duplicate medications were prescribed and the use of Spironolactone with K-sparing medications without checking the level of K⁺ frequency were 29.

3.7 Drug utilization pattern of POs

Table 3.2

PPOs	Frequency n%
VKA or direct thrombin inhibitors in the presence of chronic AF	2(0.6)
ACEIs with systolic heart failure/coronary artery disease	46 (13.1)
Aspirin in the presence of chronic atrial fibrillation.	2 (0.6)
Antiplatelet to coronary, cerebral or peripheral vascular disease.	7 (2.0)
Antihypertensive therapy where BP> 160/90mmHg	7 (2.0)
Statin therapy with coronary, cerebral or peripheral vascular disease	33 (9.4)
Beta-blocker with ischemic heart disease	39 (11.1)
Appropriate beta-blocker with stable systolic heart failure	4 (1.1)
Long term aspirin at dose >160mg/day	0 (0.0)
NSAIDS with antiplatelets without PPIs prophylaxis	5 (1.4)
Centrally acting Antihistamines	0 (0.0)
Total PPOs	154 (43.87)

Total PPOs were reported as 154(43.87%).

ACEIs with systolic heart failure/coronary artery disease that is 46 (13.1) was omitted, Beta-blocker with ischemic heart disease and Statin therapy with coronary, cerebral or peripheral vascular disease were mostly omitted.

3.8 Difference in PIP status by sample characteristics

Table 3.3

Characteristics	N	Number of PIPs Mean \pm SD	CI	P
Gender				0.006
Male	213	4.53 \pm 0.98	4.33-4.72	
Female	138	4.10 \pm 0.13	3.76-4.35	
Socio-economic status				0.010
Poor	260	4.32 \pm 0.11	4.08-4.55	
Moderate	76	4.41 \pm 0.21	3.98-4.84	
Stable	15	5.20 \pm 0.46	4.14-6.26	
Age (years)				0.445
65-70	230	4.40 \pm 0.09	4.22-4.58	
71-75	40	4.17 \pm 0.32	3.51-4.85	
76-80	53	4.20 \pm 0.17	3.85-4.55	
81-85	7	4.85 \pm 1.22	0.10-7.90	
>85	21	4.71 \pm 0.39	3.89-5.53	
Hospital Stay (days)				<0.001
0-2 days	123	3.88 \pm 0.15	3.59-4.18	
3 or more	228	4.64 \pm 0.13	4.38-4.90	
Number of Medications				0.021
0-5	198	4.31 \pm 0.10	4.11-4.52	
6-8	23	4.11 \pm 0.20	3.70-4.52	
9-10	354	4.50 \pm 0.12	4.27-4.73	
11 or more	76	4.50 \pm 0.12	4.27-4.73	

There is significant differences in most of the characteristics that is number of medications

(P=0.021), hospital stay days (<0.001), gender (0.006) and socioeconomic status have p-value 0.002.

3.8 PIPs and Quality of Life

Table 3.4

Characteristics	N	Number of PIPs	CI	P
		Mean \pm SD		
Mobility				0.033
No Problem in walking	108	4.09 \pm 0.11	3.38-4.20	
Some Problem in walking	154	4.12 \pm 0.11	3.90-4.75	
Confined to Bed	89	4.47 \pm 0.20	4.05-4.88	
Self-care				0.116
No Problem in self-care	180	4.31 \pm 0.89	4.07-4.63	
Some Problem in self-care	127	4.35 \pm 0.19	4.04-4.56	
Unable to do self-care	44	4.43 \pm 0.78	4.14-5.26	
Usual Activities				0.043
No Problem	141	4.48 \pm 0.10	4.27-4.70	
Some Problem	145	4.57 \pm 0.11	4.16-4.93	
Unable to perform usual activities	65	4.87 \pm 0.17	3.95-6.55	
Pain/ Discomfort				0.113
No Problem	89	4.62 \pm 0.13	4.37-4.88	
Some Problem	176	4.76 \pm 0.11	4.03-5.25	
Extreme Pain	86	4.88 \pm 0.18	4.19-6.18	
Anxiety/ Depression				
No Problem	118	4.61 \pm 0.13	4.21-4.93	0.458
Some Problem	186	4.64 \pm 0.11	4.11-4.98	
Extremely depressed	47	4.71 \pm 0.89	4.20-5.63	

Patient quality of life and PIPs has association in mobility ($p=0.02$) and usual activities ($p=0.043$). there life quality domains are asspiciated with PIPs which means it effect QoL.

4. DISCUSSION

In this chapter discussion of the findings of the research are given which is further divided in three sections.

4.1 Prevalence of PIPs

Potentially inappropriate prescribing covers, medications use in a condition, in which the adverse drug events (ADE) outweighs the clinical benefit, especially when more effective and safe choices are available and omission of medications that are clinically indicated having no contraindication in patients with significant expectancy of life (Beers *et al.*, 1991). To detect and identify of the types of PIPs would help for the designing of intervention in order to reduce its impact and to improve quality of life.

4.1.1 Prevalence of PIM

In current study the prevalence of PIM and PPOs are determined in hospitalized elderly patients with CVD using START/STOPP tool. About 351 patients were assessed for PIPs and it was determined that about 157 (44.72%) PIM occurred and about 41% were reported in Israeli gastric patients (Dalleur *et al.*, 2014) and more than 50% were also reported in Belgium (Wright *et al.*, 2003). Abegaz *et al.* (2018) also reported 48% of PIM. All these findings of the studies are closer to each other.

The use of Spironolactone with K-sparing medications without checking the level of K⁺ was reported 29 (8.3%) while (Abegaz *et al.*, 2018) reported it as 20 (9%) which is comparable (Abegaz *et al.*, 2018). The use of Loop diuretic as first-line treatment for hypertension in elderly cardiac patients was more common 50 (14.2%), physician should avoid the use of loop diuretics in elder cardiac patients without clear evidence of indication, if there is any doubt about HF, the therapy should be followed for at least four weeks after discontinuation of the loop diuretics (McDermott *et al.*, 1995).

Our study also determined the use of duplicate medications 30 (8.6%), while (Abegaz *et al.*, 2018) reported it as 2 (0-9%) and the difference is much more because of the comorbidities, most of them were antibiotics (ceftriaxone with another antibiotic) and according to a study in Pakistan about

70.3% patients had at least one antibiotic inappropriately. Cephalosporin antibiotics were extensively prescribed and used (Saleem *et al.*, 2019). The use of loop diuretics (furosemide) for the management of HTN in patients having problem of urinary incontinence was determined to be 20 (5.7%), as it may aggravate the symptoms of urinary bladder syndrome as compared to non-loop diuretics (Ekundayo *et al.*, 2009).

4.1.2 Prevalence of PPOs

Elderly patients admitted in hospital with cardiovascular disorders usually needed medications for their better survival. Such type of drugs are considered very important to decrease the effects and complications of the disease. If such medications are missed in their prescriptions are said to be potentially prescribing omissions (PPOs). Total 154 (43.87%) PPOs were reported in current study using START tool kit. (Barry *et al.*, 2007) reported 57.9% PPOs (Barry *et al.*, 2007) while in Ethiopia it was reported to be 52% (Abegaz, Birru *et al.* 2018). The difference in earlier study is because of the use of guidelines and advancement with time and the healthcare system of the developing countries.

The omission of ACEIs in patients having systolic or coronary artery disease was common in current study 46 (13.1%) as it is used commonly in patients having such type of disorders to inhibit remodeling of heart tissues, maintain cardiac function and revert VT. In hospitalized elderly cardiac patients, underutilization has been reported (Ahmed *et al.*, 2002) and also by (Abegaz *et al.*, 2018). 32 (14.5%) (Abegaz, Birru *et al.* 2018). PPOs of appropriate beta blockers 39 (11.1%) in patients with ischemic heart diseases was determined in our study. β -Blockers are effective in IHD and failure by sympathetic nervous system inhibition and reduce the mortality and morbidity (Tannenbaum and Johnell, 2014).

Amongst the omitted ones another drug was statin. Statin therapy was not started appropriately in 33 (9.4%) elderly patients. According to a study patients with history of coronary, cerebral and peripheral vascular disease, statin should be indicated (Mills *et al.*, 2011). Another study reported it as 7 (3.16%) (Abegaz *et al.*, 2018).

The use of appropriate antihypertensive drug is challenging in patients having blood pressure greater than 160/90 mm of Hg. In current study 7 (2%) out of the total patients omitted appropriate drugs for

B.P management. In Spain more than one-half of the elderly patients fail to receive appropriate antihypertensives (Márquez *et al.*, 2017) and a study in Irish Population reported it as most frequent omitted drug in hypertensive patients (Rollason and Vogt, 2003).

4.2 Sample characteristics and PIPs

In recent study some characteristics of sample population were considered to effect the occurrence of PIPs amongst elderly cardiac patients.

In recent study it was determined that gender was associated with increase prevalence of PIPs ($P=0.006$) and male were more exposed as compared to female while (Barry *et al.*, 2007). reported in contrast to our findings (Barry *et al.*, 2007). The ratio of male CVPs is more than female which increase the likelihood of PIPs. Socioeconomic status of the patients was also associated to PIPs prevalence ($P=0.010$).

Hospitalization days were determined to more associated with occurrence of PIPs ($P=0.021$), as the days increases the prevalence of PIPs increased. Napolitano et al also determined that frequency of PIPs are affected by increased hospital stay days (Chang *et al.*, 2014). As there should be reason for longer stay at hospital that may be new diagnosis, poor outcome of prescribed medications, worsening of the disease etc.

Number of medications prescribed at ward increases with hospital stay days, comorbidities, new diagnosis and improper medication prescribing and utilization. Our study confirmed that PIPs and medications number are associated with each other by such a way, number of medications increased the chances of PIPs are also increased in current study. Ryan et al also had reported that prevalence of PIPs occurs with increased number of medications prescribed (Ryan *et al.*, 2009).

4.3 Quality of life

Findings of our study revealed that most of the elderly patients with CVDs have some problems in daily life domains i.e. mobility (43%), usual activities (41%), pain/discomfort (50.1%) and anxiety/depression (52.99%) while majority has no problem in self-care domain(51.2%).

Due to the fact of aging the patients with CVDs problems like pain and discomfort are common. As it is a chronic condition which leads to depression, severe pain, mobility problems and limitation in performing daily activities (Alfredsson and Alexander, 2016).

Conditions like comorbidities with heart problems decreases physical activities, feeling of loneliness in nursing homes and leads to anxiety and depression (Yen and Lin, 2018). Most of the patients with cardiac disease has poor quality of life (Norton *et al.*, 2011).

Anxiety and depression patients' number is more as compared to other domains. A study results similar to our study reported 55.99% of their participants had anxiety/depression (Warraich *et al.*, 2018).

4.4 PIPs and Quality of Life

Patients using appropriate medication will have a good quality of life as compared to patient with inappropriate use. It means that there is immense need for the assessment of the patient's prescription in order to improve his quality of life (Olsson *et al.*, 2011).

According to the results of our study it is revealed that cardiovascular patients exposed to PIPs had significantly low quality of life than other cardiac patients of same age group. The reported positive PIPs patients had some problem in mobility ($P=0.033$) and some problem in usual activities of daily life ($P=0.043$). A study performed using elderly patients who are using medication inappropriately, had a quality of life poorer than who taking appropriately. The risk associated to inappropriate medications use may range from minor pain to life threatening conditions, which reflects a poor quality of life (Fu *et al.*, 2004). These findings of the above study support my results.

Limitation of the study

The limitations of my study was that it was single center oriented, cross-sectional observational study, which does not reflect the whole picture of KPK population. The study did not include prescribers' perspective. The study results were not normal statistically that is my certain test were not applied. The study was also performed and limited to cardiovascular patients. Lack of follow-up and exclusion of out-patients.

CONCLUSION

The study concluded that the practice of PIPs in elderly cardiac patients was commonly utilized. The common PIM were the use of loop diuretics, duplication of medications, spironolactone with potassium sparing drugs and the most common PPOs were ACEIs, beta-blockers and statins. Higher prevalence rate of PIPs was because of following local and international guidelines. It was also concluded that patients' characteristics affect the occurrence of PIPs. Age, socioeconomic status, hospital stay days and medication number are the characteristics that affect PIPs occurrence. The findings of our study also agreed with the hypothesis that PIPs and QoL has a direct relationship with each other. Higher the occurrence of PIPs, poorer the quality of life. Hence for the better outcomes of the medication therapy there will be an immense need of appropriate prescribing by following such types of criteria, protocol and guidelines.

Pharmacists can play a vital role in achieving this goal by using their skills and knowledge for the betterment of elderly patients at primary, secondary and tertiary care settings. It will help in improving patients' quality of life and reducing the avoidable burden of unnecessary drugs on the patients. Parallel to this there is also a need of improving our health care system by making certain educational and research based interventions to educate and aware the prescribers and patients on the appropriate use of medications.

It is recommended that there should conduct long term follow-up cohort studies in order to determine and explore the hidden factors which are associated with the PIPs and quality of life.

REFERENCES

- Abegaz TM, Birru EM and Mekonnen GB (2018).Potentially inappropriate prescribing in Ethiopian geriatric patients hospitalized with cardiovascular disorders using START/STOPP criteria. PloS one, 13(5):0195949.
- Ahmed A, Allman RM, DeLong JF, Bodner EV and Howard G (2002) Age-related underutilization of angiotensin-converting enzyme inhibitors in older hospitalized heart failure patients Southern Med J, 95(7): 703-711.
- Alfredsson J and Alexander KP (2016) Multiple chronic conditions in older adults with acute coronary syndromes Clinics in geriatric medicine, 32(2): 291-303.
- Alhawassi TM, Krass I, Bajorek BV and Pont LG (2014) A systematic review of the prevalence and risk factors for adverse drug reactions in the elderly in the acute care setting Clinical interventions in aging, 9: 2079.
- Ashiq U and Asad AZ (2017) The rising old age problem in Pakistan. J of the Rea Society of Pak, Vol 54(2).
- Baernholdt M, Hinton I, Yan G, Rose K and Mattos M (2012) Factors associated with quality of life in older adults in the United States. Quality of Life Res, 21(3): 527-534.
- Beck CA, and Shah S (2012) Research on health-related quality of life and cardiac conditions Home Healthcare Now, 30(1): 54-60.
- Beers MH, Ouslander JG, Rollinger I, Reuben DB, Brooks J and Beck JC (1991) Explicit criteria for determining inappropriate medication use in nursing home residents Archives of internal medicine, 151(9): 1825-1832.
- Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, Floyd J, Fornage M, Gillespie C and Isasi C (2017) Heart disease and stroke statistics-2017 update: a report from the American Heart Association circulation, 135(10): e146-e603.
- Brahma DK, Wahlang JB, Marak MD and Sangma MC (2013) Adverse drug reactions in the elderly J of pharmacology & Pharm, 4(2): 91.
- Aziz VM, Hill N and Kumar S (2018). Completed audit cycle to explore the use of the STOPP/START toolkit to optimise medication in psychiatric in patients with dementia. BJPsych bulletin, 42(1): 37-41.

Barry P, Gallagher C, Ryan and O'mahony D (2007). START (screening tool to alert doctors to the right treatment) an evidence-based screening tool to detect prescribing omissions in elderly patients. *Age and ageing*, 36(6): 632-638.

Chang CB and Chan DC (2010) Comparison of published explicit criteria for potentially inappropriate medications in older adults *Drugs & aging*, 27(12): 947-957.

Chang CB, Lai HY, Yang SY, Wu, RS HC, Liu, Hsu HY, Hwang SJ and Chan DC (2014) Patient-and clinic visit-related factors associated with potentially inappropriate medication use among older home healthcare service recipients *Plos one*, 9(4).

Courtney R (2015). *The Health Consequences of Smoking 50 Years of Progress: A Report of the Surgeon General*, 2014 Us Department of Health and Human Services Atlanta, GA: Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, pp 2014-1081 Available at: <http://www.surgeongeneral.gov/library/reports/50-years-of-progress>. *Drug and Alcohol Review* 34(6): 694-695.

Castillo-Páramo A, Clavería A, Verdejo González A, Rey Gómez-Serranillos I, Fernández-Merino MC and Figueiras A (2014). Inappropriate prescribing according to the STOPP/START criteria in older people from a primary care setting. *The European J of general practice*, 20(4): 281-289.

Frankenthal D Lerman Y, Kalendarjev E and Lerman Y (2014). Intervention with the screening tool of older persons potentially inappropriate prescriptions/screening tool to alert doctors to right treatment criteria in elderly residents of a chronic geriatric facility: A randomized clinical trial. *J of the American Geriatrics Society*, 62(9): 1658-1665.

Dalleur O, Boland B, Losseau C, Henrard S, Wouters D, Speybroeck N, Degryse JM and Spinewine A (2014) Reduction of potentially inappropriate medications using the STOPP criteria in frail older inpatients: a randomised controlled study *Drugs & aging*, 31(4): 291-298.

Ekundayo OJ, Markland A, Lefante C, Sui X, Goode PS, Allman RM, Ali M, Wahle C, Thornton PL and Ahmed A (2009) Association of diuretic use and overactive bladder syndrome in older adults: a propensity score analysis *Archives of gerontology and geriatrics* 49(1): 64-68.

Elliott RA, and Stehlik P (2013) Identifying inappropriate prescribing for older people *J of Pharm Practice and Res*, 43(4): 312-319.

Erickson P and Patrick D (1993) Health status and health policy: quality of life in health care evaluation and resource allocation, Oxford University Press New York.

Fick D, Semla T, Beizer J, Brandt N, Dombrowski R, DuBeau C, Eisenberg W, Epplin J, Flanagan N and Giovannetti E (2015) American Geriatrics Society 2015 Beers Criteria Update Expert Panel American Geriatrics Society 2015 updated Beers criteria for potentially inappropriate medication use in older adults *J Am Geriatr Soc* 63(11): 2227-2246.

Fick DM, Mion LC, Beers MH, and Waller JL, (2008) Health outcomes associated with potentially inappropriate medication use in older adults *Res in nursing & health*, 31(1): 42-51.

Frankenthalss D, Lerman Y, Kalendaryev E and Lerman Y (2014) Intervention with the screening tool of older persons potentially inappropriate prescriptions/screening tool to alert doctors to right treatment criteria in elderly residents of a chronic geriatric facility: a randomized clinical trial *J of the Amer Geriatrics Soc*, 62(9): 1658-1665.

Gallagher P, PO Lang, Cherubini A, Topinková E, Cruz-Jentoft A, Errasquín BM, Mádlová P, Gasperini B, Baeyens H and Baeyens JP (2011) Prevalence of potentially inappropriate prescribing in an acutely ill population of older patients admitted to six European hospitals *European J of clinical pharmacology* 67(11): 1175.

Gallagher P, O'connor M and O'mahony D (2011). Prevention of potentially inappropriate prescribing for elderly patients: a randomized controlled trial using STOPP/START criteria. *Clinical Phar & Therapeutics* 89(6): 845-854.

Gallagher P, Ryan C, Byrne S, Kennedy J and O'Mahony D (2008). STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment) Consensus validation. *Int' l J of clinical Ph and Thera*, 46(2): 72-83.

Gjeilo KH, Stenseth R, Wahba A, Lydersen S and Klepstad P (2018). Long-term health-related quality of life and survival after cardiac surgery: a prospective study. *The J of Thoracic and cardiovascular Sur*, 156(6): 2183-2190 e2182.

Hamilton HP, Gallagher, Ryan C, Byrne S and O'Mahony D (2011). Potentially inappropriate medications defined by STOPP criteria and the risk of adverse drug events in older hospitalized patients. *Archives of internal medicine*, 171(11): 1013-1019.

Harrison SL, O'Donnell LK, Bradley , R Milte, Dyer SM, Gnanamanickam ES, Liu E, Hilmer SN and Crotty M (2018). Associations between the drug burden index, potentially inappropriate medications and quality of life in residential aged care. *Drugs & aging*, 35(1): 83-91.

Heider D, Matschinger H, Meid AD, Quinzler R, Adler JB, Günster C, Haefeli WE and König HH (2018). The impact of potentially inappropriate medication on the development of health care costs and its moderation by the number of prescribed substances. Results of a retrospective matched cohort study. *PloS one* 13(7): e0198004.

Hekster YA and Vree TB (1986). Drug utilization research in clinical practice. *Drug intelligence & clinical Phar*, 20(9): 679-682.

Horne R, Weinman J, Barber N, Elliott R, Morgan M, Cribb A and Kellar I (2005). Concordance, adherence and compliance in medicine taking. London: NCCSDO, 2005: 40-46

Howard R, Avery A, Howard P and Partridge M (2003). Investigation into the reasons for preventable drug related admissions to a medical admissions unit: observational study. *BMJ Quality & Safety*, 12(4): 280-285.

Lang PO, Hasso Y, M Dramé Vogt-Ferrier N, Prudent M, Gold G and Pierre Michel J (2010). Potentially inappropriate prescribing including under-use amongst older patients with cognitive or psychiatric co-morbidities. *Age and ageing*, 39(3): 373-381.

Miquel M, Cuervo CMS, Silveira ED, Machuca IS, González-Blazquez S, Errasquin BM and Cruz-Jentoft A (2010). Potentially inappropriate drug prescription in older subjects across health care settings. *European Geriatric Medicine*, 1(1): 9-14.

Pyszka L, Seys Ranola T and Milhans S (2010). Identification of inappropriate prescribing in geriatrics at a Veterans Affairs hospital using STOPP/START screening tools. *The Consultant Pharmacist*, 25(6): 365-373.

Ryan C, O'Mahony D, Kennedy J, Weedle P and Byrne S (2009). Potentially inappropriate prescribing in an Irish elderly population in primary care. *British J of clinical Phhar*, 68(6): 936-947.

Jastaniah NA, Almaqati AS, Alsuraihi AK, Abughanim SA and Aseeri M (2018). Inappropriate Prescribing in Elderly Inpatients at a University Hospital in Saudi Arabia. *Drugs-real world outcomes*, 5(4): 211-216.

Jokanovic N, Tan EC, Dooley MJ, Kirkpatrick CM and Bell JS (2015). Prevalence and factors associated with polypharmacy in long-term care facilities: a systematic review. *J of the Ameri Med Directors Assoc*, 16(6): 535 e531-535 e512.

Komagamine J (2018). Prevalence of potentially inappropriate medications at admission and discharge among hospitalised elderly patients with acute medical illness at a single centre in Japan: a retrospective cross-sectional study. *BMJ open*, 8(7): 021152.

Konrat C, Boutron I, Trinquart L, Auleley GR, Ricordeau P and Ravaud P (2012). Underrepresentation of elderly people in randomised controlled trials The example of trials of 4 widely prescribed drugs. *PloS one*, 7(3): e33559.

Lam MP and Cheung BM (2012). The use of STOPP/START criteria as a screening tool for assessing the appropriateness of medications in the elderly population. *Expert review of clinical Pharm*, 5(2): 187-197.

Lang PO, Hasso Y, Dramé M, Vogt-Ferrier N, Prudent M, Gold G and Pierre Michel J (2010). Potentially inappropriate prescribing including under-use amongst older patients with cognitive or psychiatric co-morbidities. *Age and ageing*, 39(3): 373-381.

Laporte G, Nobert Y and Desrochers M (1985) .Optimal routing under capacity and distance restrictions. *Operations R*, 33(5): 1050-1073.

Laroache M, Teng L, and Kalamas M (2001). Consumer evaluation of net utility: effect of competition on consumer brand selection. *Japan Psych res*, 43: 168.

Lunde P, Baksaas I, Halse M, Halvorsen I, Stromnes B and Oydvin K (1979) .The methodology of drug utilization studies. *Studies in drug utilization Copenhagen: WHO Regional Office for Europe*: 17-28.

Mangoni, A A and S H Jackson (2004) .Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. *British J of clinical pharmacology* 57(1): 6-14

Márquez, P H P, O H Torres, A San-José, X Vidal, A Agustí, F Formiga, A López-Soto, N Ramírez-Duque, A Fernández-Moyano and J Garcia-Moreno (2017) .Potentially inappropriate antihypertensive prescriptions to elderly patients: results of a prospective, observational study. *Drugs & aging* 34(6): 453-466

Mazhar F, Akram S, Malhi SM and Haider N (2018). A prevalence study of potentially inappropriate medications use in hospitalized Pakistani elderly. *Aging Clinical And Exp Res*, 30(1): 53-60.

McDermott M, Feinglass J, Sy J and Gheorghide M (1995). Hospitalized congestive heart failure patients with preserved versus abnormal left ventricular systolic function: clinical characteristics and drug therapy. *The Amer J of Med*, 99(6): 629-635.

Mills E, Wu P, Chong G, Ghement I, Singh S, Akl E, Eyawo O, Guyatt G, Berwanger O and Briel M (2011). Efficacy and safety of statin treatment for cardiovascular disease: a network meta-analysis of 170 255 patients from 76 randomized trials. *QJM: An Int'l J of Med*, 104(2): 109-124.

Milton JC, Hill-Smith I and Jackson SH (2008) .Prescribing for older people. *Bmj* 336(7644): 606-609.

Miquel MC, Cuervo MS, Silveira ED, Machuca IS, González-Blazquez S, Errasquin BM and Cruz-Jentoft A (2010) .Potentially inappropriate drug prescription in older subjects across health care settings. *European Geriatric Medicine*, 1(1): 9-14

Morin L, Laroche ML, Texier G and Johnell K (2016) .Prevalence of potentially inappropriate medication use in older adults living in nursing homes: a systematic review. *J of the Amer Med Directors Ass*, 17(9): 862 e861-862 e869

Norton C, Georgiopoulou VV, Kalogeropoulos AP and Butler J (2011). Epidemiology and cost of advanced heart failure. *Progress in cardiovascular diseases*, 54(2): 78-85

Olsson IN, Runnamo R and Engfeldt P (2011). Medication quality and quality of life in the elderly, a cohort study. *Health and Quality of life Outcomes* 9(1): 95.

Opondo D, Eslami S, Visscher S, De Rooij SE, Verheij R, Korevaar JC and Abu-Hanna A (2012). Inappropriateness of medication prescriptions to elderly patients in the primary care setting: a systematic review. *PloS one*, 7(8): 43617

Panel AGSBCUE, Fick DM, Semla TP, Beizer J, Brandt N, Dombrowski R, DuBeau CE, Eisenberg W, Epplin JJ and Flanagan N (2015). American Geriatrics Society 2015 updated beers criteria for potentially inappropriate medication use in older adults. *J of the Ameri Geriatrics Soc*, 63(11): 2227-2246.

Pyszka L, Seys T Ranola and Milhans S (2010) .Identification of inappropriate prescribing in geriatrics at a Veterans Affairs hospital using STOPP/START screening tools. *The Consultant Pharmacist*, 25(6): 365-373.

Reason B, M Turner, A Moses McKeag, B Tipper and G Webster (2012). The impact of polypharmacy on the health of Canadian seniors. *Family practice* 29(4): 427-432.

Revicki DA, Kleinman L and Cella D (2014). A history of health-related quality of life outcomes in psychiatry. *Dialogues in clinical neuroscience*, 16(2): 127.

Rich MW, Chyun DA, Skolnick AH, Alexander KP, Forman DE, Kitzman DW, Maurer MS, McClurken JB, Resnick BM and Shen WK (2016). Knowledge gaps in cardiovascular care of the older adult population: a scientific statement from the American Heart Association, American College of Cardiology, and American Geriatrics Society. *J of the Am College of Cardio*, 67(20): 2419-2440.

Rochon P A and J H Gurwitz (1999). Prescribing for seniors: neither too much nor too little. *Jama* 282(2): 113-115.

Rollason V and Vogt N (2003). Reduction of polypharmacy in the elderly. *Drugs & Aging*, 20(11): 817-832.

Roth GA, Huffman MD, Moran AE, Feigin V, Mensah GA, Naghavi M and Murray CJ (2015). Global and regional patterns in cardiovascular mortality from 1990 to 2013. *Circulation*, 132(17): 1667-1678.

Runciman WB, Roughead EE, Semple SJ and Adams RJ (2003). Adverse drug events and medication errors in Australia. *Int'l J for Quality in Health Care*, pp 49-59.

Ryan C, O'Mahony D, Kennedy J, Weedle P and Byrne S (2009). Potentially inappropriate prescribing in an Irish elderly population in primary care. *British J of Cli Pharm*, 68(6): 936-947.

Saleem Z, Saeed H, Hassali MA, Godman B, Asif U, Yousaf M, Ahmed Z, Riaz H and Raza SA (2019). Pattern of inappropriate antibiotic use among hospitalized patients in Pakistan: a longitudinal surveillance and implications. *Antimicrobial Resistance & Infection Control* 8(1): 188.

Sarwar MR, Atif M, Scahill S, Saqib A, Qamar-uz-Zaman M and Babar Z (2017). Drug utilization patterns among elderly hospitalized patients on poly-pharmacy in Punjab, Pakistan. *J of Pharm Policy and Prac*, 10(1): 23.

Schmiedl S, Rottenkolber M, Szymanski J, Drewelow B, Siegmund W, Hippus M, Farker K, Guenther I, Hasford J and Thuermann P (2018). Preventable ADRs leading to hospitalization results of a long-term prospective safety study with 6,427 ADR cases focusing on elderly patients. *Expert opinion on drug safety* 17(2): 125-137.

Spinewine A, Schmader KE, Barber N, Hughes C, Lapane KL, Swine C and Hanlon JT (2007). Appropriate prescribing in elderly people: how well can it be measured and optimised?. *The Lancet*, 370(9582): 173-184.

Storms H, K Marquet, B Aertgeerts and N Claes (2017). Prevalence of inappropriate medication use in residential long-term care facilities for the elderly: A systematic review. *European J of General Practice* 23(1): 69-77.

Tannenbaum C and Johnell K (2014). Managing therapeutic competition in patients with heart failure, lower urinary tract symptoms and incontinence. *Drugs & aging*, 31(2): 93-101.

Tommelein E, E Mehuys, M Petrovic, A Somers, P Colin and K Boussery (2015) .Potentially inappropriate prescribing in community-dwelling older people across Europe: a systematic literature review. *European J of clinical pharmacology* 71(12): 1415-1427.

Vaarama M (2009). Care-related quality of life in old age. *European J of Ageing*, 6(2): 113-125.

Wahab MSA, Nyfort-Hansen K and Kowalski SR (2012). Inappropriate prescribing in hospitalised Australian elderly as determined by the STOPP criteria. *Int'l J of Cli Phar*, 34(6): 855-862.

Warraich HJ, Kitzman DW, Whellan DJ, Duncan PW, Mentz RJ, Pastva AM, Nelson MB, Upadhy B and Reeves GR (2018) .Physical Function, Frailty, Cognition, Depression, and Quality of Life in Hospitalized Adults \geq 60 Years With Acute Decompensated Heart Failure With Preserved Versus Reduced Ejection Fraction: Insights From the REHAB-HF Trial. *Circulation: Heart Failure* 11(11): 005254.

Weeda ER, Pilch NA and Annemans L (2019). Outcomes Research Clinical Pharmacy Education, *Practice and Res*, 289-301.

Wenge NS, Solomon DH, Amin A, Besdine RK, Blazer DG, Cohen H, Fulmer T, Ganz PA and Grunwald M (2007). Application of Assessing Care of Vulnerable Elders-3 quality indicators to patients with advanced dementia and poor prognosis. *J of the Ameri Geriatrics Soc*, 55: S457-S463.

Wright S, Verouhis D, Gamble G, Swedberg K, Sharpe N and Doughty R (2003). .Factors influencing the length of hospital stay of patients with heart failure. *European J of heart failure* 5(2): 201-209.

Yen HY, and Lin LJ (2018). Quality of life in older adults: Benefits from the productive engagement in physical activity. *J of Exercise Sci & Fitness* 16(2): 49-54

Zubair F, Nawaz SK, Nawaz A, Nangyal H, Amjad N and Khan MS (2018) Prevalence of cardiovascular diseases in Punjab, Pakistan: a cross-sectional study. *J of Public Health* 26(5): 523-529.

WHO (2003). Introduction to drug utilization research, World Health Organization Available at: <http://appswhoint/medicinedocs/pdf/s4876e/s4876epdf> (Accessed: 31 January 2019).

WHO (2015). WHO | 10 facts on ageing and the life course, World Health Organization Available at: https://wwwwhoint/features/factfiles/ageing/ageing_facts/en/ (Accessed: 24 December, 2019).

World Population Prospects: The 2017 Revision | Multimedia Library - United Nations Department of Economic and Social Affairs (2017). Available at: <https://wwwunorg/development/desa/publications/world-population-prospects-the2017-revisionhtml> (Accessed: 25 December, 2019).

The World Factbook Central Intelligence Agency (2017) Available at: <https://wwwciagov/library/publications/the-world-factbook>.

World Health Organization Cardiovascular diseases [Aug; 2018]; [https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds))

WHO and WHOQOL: Measuring Quality of Life (2014). World Health Organization Available at: <https://www.who.int/healthinfo/survey/whoqol-qualityoflife/en/> (Accessed: 28 January 2019).

Potentially inappropriate prescribing prevalence_Abbas

by Abbas Ahmad

Submission date: 07-Feb-2020 10:31AM (UTC+0500)

Submission ID: 1253024253

File name: final_thesis_abbas.docx (1.76M)

Word count: 9784

Character count: 54341

Potentially inappropriate prescribing prevalence_Abbas

ORIGINALITY REPORT

14%

SIMILARITY INDEX

8%

INTERNET SOURCES

10%

PUBLICATIONS

9%

STUDENT PAPERS

PRIMARY SOURCES

1	www.mdpi.com Internet Source	2%
2	www.tandfonline.com Internet Source	2%
3	Handbook of Disease Burdens and Quality of Life Measures, 2010. Publication	2%
4	Submitted to University of Hong Kong Student Paper	1%
5	"Developing Drug Products in an Aging Society", Springer Science and Business Media LLC, 2016 Publication	1%
6	Submitted to 46632 Student Paper	<1%
7	www.besjournal.com Internet Source	<1%
8	mdpi.com Internet Source	<1%