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Evaluation of Drug Utilization Pattern in Cardiovascular Diseases Using WHO/ INRUD Prescribing Indicators at Cardiology OPD of Tertiary Care Hospitals in South India: A Multicenter Cross-Sectional Study

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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ABSTRACT

Objective: Aim of this study is to assess the drug utilization pattern of cardiovascular drugs in cardiology outpatient department (OPD).
Methodology: This prospective, multicenter, cross-sectional observational study was conducted at three selected tertiary care hospitals from different regions in South India. A total of 1026 prescriptions of the patients attending cardiology OPD of these selected hospitals 342 each over a period of 12 months was randomly identified and included in this study then critically analysed for WHO/INRUD core prescribing indicators.
Results: Medicines prescribed from NLEM were 89.27%, average drugs prescribed was 5, medicines prescribed by its generic name were 2.33% and encounters with an injection prescribed were 14.52%. Commonly prescribed different class of drugs for CVDs patients were Anti-platelets (67.73%) followed by Statins (62.57%), Beta blockers (49.51%), ACE-inhibitors (40.93%), Angiotensin receptor blockers (30.40%), Calcium channel blockers (30.11%), Nitrates (25.34%),

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Diuretics (20.56%), Anticoagulants (20.27%), Vasodilators (9.94%) rest of the cardiovascular drugs were prescribed within 0.5-5% only, other class of drugs also prescribed for patients with different comorbidities are Anti-ulcers (69.10%), Opioid analgesics (4.09%), Antacids (3.80%), Anti-emetics and Pro-kinetics (1.85%), a pattern of poly-pharmacy was clearly evident, majority of drugs were prescribed as single drug (86.78%) whereas 13.21% as FDCs. The most commonly prescribed single drug was Aspirin (59.93%) and FDCs were Aspirin + Clopidogrel (40.24%). Anti-thrombotic agents' particularly antiplatelet drugs expected to overtake anti-cholesterol drugs as the sales leader in the market. Maximum drugs were prescribed from the recent NLEM of India by most of practitioners its shows its acceptance and implementation by the prescribers.

Conclusion: Deprescribing PPIs for the non-required patients is suggested to lower the risk of adverse drug interactions and economic burden to patients, also pharmacists needs to encourage the prescriptions with drugs in generic name if it's deviated from the standards recommended by WHO/INRUD.

Keywords: Cardiovascular drugs; drug utilization pattern; NLEM of India; fixed dose combinations; antiplatelet drugs; proton pump inhibitors; adverse drug interactions.

1. INTRODUCTION

Cardiovascular diseases (CVDs) are the number one cause of death globally, more people die annually from CVDs than any other cause [1]. According to the reports of World Health Organization (WHO) an estimated 17.9 million people died from CVDs in 2016, representing 31% of all global deaths, of these deaths 85% are due to heart attack and stroke [2], by 2020 deaths from CVDs are predicted to rise to almost five million per year in India [3]. According to the WHO, world-wide more than 50% of all medicines are prescribed, dispensed or sold inappropriately and about one-third of the world's population lacks access to essential medicines [4] on the other side 50% of patients take them incorrectly. WHO defined drug utilization study as "a structured process which is used to assess the quality of drug therapy by engaging in the evaluation of data on drug prescribing, dispensing, and patient use in a society with special emphasis on the resulting medical, social, and economic consequences" [5]. Correct diagnosis, accurate prescribing, proper dispensing, appropriate packing and good patient counseling are the important criteria for rational use of drugs [6]. Prescription is a critical issue in the rational treatment [7]. A study of prescription patterns is an important to determine rationality of drug therapy and to maximize the utilization of resources [5]. The prescribing pattern reflects the physician's knowledge about the disease process and application of pharmacotherapeutics [8].

In the 1990′s, WHO in collaboration with the International Network of Rational Use of Drugs (INRUD) developed standard indicators to evaluate drug use practices at healthcare centres [9]. These indicators are called "core drug use indicators" are classified into prescribing, patient-care and facility-specific indicators. Studies on drug utilization pattern have become a potential tool to be used in the evaluation of healthcare system [10]. Drug utilization research encourages rational prescribing of drug, contributes to the knowledge of current use of drugs in the society and explore whether a particular intervention affects the drug use in the population by observing the drug use pattern [5]. The fundamental steps to limit the irrational use of medicines are to identify the types, extent and reasons of their irrational use [11]. Hence, this study was planned to assess the drug utilization patterns in cardiology OPD at different tertiary care hospitals in South India using WHO/INRUD prescribing indicators and also to measure the degree of implementation of national drug policy by the practitioners as indicated as prescribing drugs in National List of Essential Medicine (NLEM) in India. The findings of this study will further help future policymakers to take necessary measures to stimulate appropriate use of medicines.

2. METHODOLOGY

2.1 Study Design

The present prospective, multicenter, cross-sectional observational study was conducted in three selected tertiary care hospitals in South India for the period of 12 months. Prescriptions from the patients attending the cardiology OPD from January 2016 to 2017 were included in this study.

2.2 Study Protocol

2.2.1 Data collection

The standard prescribing indicator forms were used to collect the data. As per WHO recommendations, it has been suggested that at least 600 encounters should be included in a cross sectional survey with a greater number if possible. Therefore, a total of 1026 prescriptions of the patients attending cardiology OPD of these selected three hospitals 342 prescriptions from each over a period of 12 months was randomly identified and included in this study according to the following inclusion criteria. To minimize the sampling bias (i.e., seasonal alterations or supply cycle of medicines), the encounters per year were uniformly divided into four quarters and at least 256 prescriptions were randomly selected from each quarter, irrespective of acute or chronic illnesses, including a mixture of health conditions and different range of patient ages. The data collected from prescriptions were transferred to master chart then critically analysed using WHO/INRUD core prescribing indicators, particularly different types of drugs prescribed and their prescribing pattern was find out using pre-determined parameters.

2.2.2 Inclusion criteria

Prescriptions of patients aged between 30 to 80 years old (NPCDCS-National Program for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke) [13], both males and females with all kind of cardiovascular diseases, prescriptions of cardiology outpatient department only, prescriptions of cardiovascular disease patients with or without other complications and prescriptions of patients only those willing to participate were included in this study.

2.2.3 Exclusion criteria

Prescriptions of patients with age <30 and >80, pregnancy, lactation, critically ill patients, patients with life style modification alone, prescriptions of outpatients of other departments, prescriptions of patients diagnosed with non-cardiac diseases, prescriptions of patients who were advised to hospitalize, prescriptions of patients those not willing to participate were excluded from this study.

2.2.4 Prescribing indicators

WHO/INRUD prescribing Indicators include i) Average number of drugs per encounter, ii) Percentage of drugs prescribed by generic name, iii) Percentage of encounters with an antibiotic prescribed, iv) Percentage of encounters with an injection prescribed and v) Percentage of drugs prescribed from essential drugs list or formulary [14]. All assessed values were compared with the optimal level prescribed by WHO/INRUD and each prescription was also analysed for the completeness of prescription using other important components such as the presence of demographic data, diagnosis, doses of drugs, route of administration, frequency, treatment duration and amount of Fixed Dose combinations (FDCs) prescribed.

2.3 Statistical Analysis

The collected data was numerically coded and descriptive statistical analysis was performed using Microsoft Excel™ software version 2010 and results were expressed as Mean ± Standard Error of Mean (SEM) for numerical variables and as percentage (%) for categorical variables.

3. RESULTS

3.1 Age and Gender Wise Distribution of CVD Patients

Based on the results obtained it is found that male patients 64.61% had high frequency of cardiovascular incidences when compared to female patients 35.38%. Out of 1026 patients, 37.62% of patients (Male 25.14% & Female 12.47%) belong to the age group of 51-60 years which is considered to be highest percentage when compared to all other age groups and 8.10% of patients (Male 5.06% & Female 3.02%) present in the age group of 71-80 years which is considered to be lowest percentage among all age groups, these demographic data reveal the influence of gender and age in disease and prescribing pattern as mentioned in (Fig. 1).

3.2 Estimation of Prescribing Indicators

In this study the average number of drugs prescribed per encounter was 5, which was far more when compared with the WHO recommended standard value 1.6-1.8 [14]. The number of drugs in each encounter was ranging from one drug to maximum number of 7 drugs this suggesting a trend of Polypharmacy in the prescription pattern (Table 1).

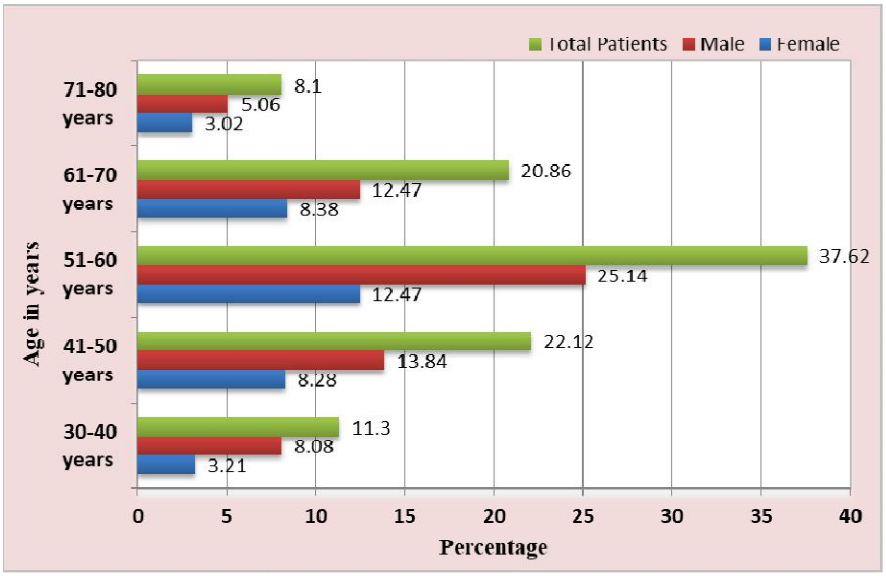

Fig. 1. Age and gender wise distribution of CVD patients

Table 1. WHO/INRUD core prescribing indicators

Prescribing indicators	Results	Optimal values
Average number of drugs prescribed per patient encounter	5	1.6 - 1.8
Percent medicines prescribed by generic name	2.33	100
Percent encounters with an antibiotic prescribed	3.11	20.0 - 26.8
Percent encounters with an injection prescribed	14.52	13.4 - 24.1
Percent medicines prescribed from NLEM	89.27	100

**NLEM: National List of Essential Medicines 2015*

3.3 Average Number of Drugs Prescribed

This finding was more than other studies conducted in India such as Hazra et al. (3.2), [15] Tripathy et al. (2.9), [16] Rehan et al. (2.4), [17] as well as studies conducted in some other countries Bimo et al. (3.8), [18] and Wang et al. (3.52), [19] Polypharmacy leads to many consequences such as adverse drug reactions; drug-drug interactions even though it is found to be unavoidable in certain diseases and cases particularly in hypertensive, type 2 diabetes mellitus and elderly patients characterized by comorbidities. The advantage of using Polypharmacy over monotherapy has been proven in many common disease entities. For example, in Angio-Scandinavian Cardiac Outcomes Trial (ASCOT) nearly 90% of patients with hypertension had to use at least two antihypertensive drugs to reach the target blood pressure values [20].

3.4 Medicines Prescribed by Generic Name

In this study medicines prescribed by its generic names were only 2.33%, which is very less when compared to the WHO standard optimal value (100%). It was more than findings from the study by Rehan et al. (1.5%) [17], Chandelkar and Rataboli (0.05%) [21], but it was very less when compared to findings from other studies by Tripathy et al. (68%) [16], Hazra et al. (46.2%) [15] and other international studies [22,23]. This indicates that prescribing practices are directly influenced by some medical representatives of drug companies, impressive and continuous communication with prescribers by some pharmaceutical companies made prescribers more likely to prescribe proprietary (branded) products than generic products. Generally generic prescribing reduces the chances of dispensing errors and also reduces the economic burden to the patient because generic drugs are available for lesser prices compared to various branded drugs.

3.5 Encounters with an Antibiotic Prescribed

This study is carried out in cardiology OPD and it is based on cardiovascular drugs hence measuring this objective is not applicable even

though it is measured in this study the percentage of encounters with antibiotics prescribed was 3.11%, this is not falls within the WHO prescribed optimal values (20-26.8%). Appropriate and less use of antibiotics will prevent the development of drug resistance and also reduces the cost of drug therapy.

3.6 Encounters with Injections Prescribed

Percentage of encounters with injections prescribed in this study was 14.52% which is within the WHO prescribed standard values (13.4-24.1%) This was clearly more comparable to the findings from Tripathy et al. (8%) [16]. But it was less when compared to findings from other countries like South Ethiopia (38.1%) [22], the lower rate of use of injections would reduce the cost of the treatment and economic burden to the patient and reduces the non-compliance of the patient to the treatment.

3.7 National List of Essential Medicines

Essential medicines are those that satisfy the priority health care needs of the population and intended to be available at all times, in adequate amount and at affordable price [24]. The percentage of drugs prescribed from the NLEM in this study was 89.27%, which was found to be fare when compared to the WHO prescribed ideal value (100%). This finding was more than other studies conducted in India such as Hazra *et al.* (45.71%) [15], this finding was almost similar to finding from study conducted by the other country Nepal (88%) [18], at the same time it is found to be less when compared to the other countries such as South Ethiopia (99.6%) [22]. The percentage of prescribing drugs from NLEM is higher in South India compared to North India but lower when compared to other countries.

3.8 Estimation of Cardiovascular Diseases Present in the Patients

Out of 1026 patients, 32.55% patients had an Ischemic Heart Disease, which is consider being highest among all other CVDs, next to that hypertension patients (31.87%) took the second place which is similar to the study conducted in Pakistan [25], then patients with both ST Elevation myocardial infarction (STEMI) & Non-ST Elevation myocardial infarction (NSTEMI) was found to be (12.08%), apart from all above other CVDs falls within (0.5% to 7.8%) and we found only few patients with Endocarditis (0.19%) as mentioned in (Table 2).

3.9 Estimation of Comorbidities in Cardiovascular Disease Patients

Various other associated medical conditions also diagnosed in CVD patients, out of 1026 patients 25.53% of patients were having Diabetes mellitus mostly Type-2 than Type-1, other studies also indicated that high levels of insulin frequently occurs in Type-2 diabetes mellitus, is one of the independent factor related with cardiovascular disease [26]. Next to that we found 14.71% of CVD patients with renal dysfunction, 13.06% patients were having disordered lipid profile and 11.20% patients with various Gastro intestinal tract (GIT) disorders, and all other comorbidities present within (1.46% to 5.45%), in total 80.25% of patients having comorbidities as shown in (Table 3).

Table 2. Percentage of different CVDs present in the patients

Observed cardiovascular diseases	Number of patients	Percentage
Ischemic Heart Disease	334	32.55
Hypertension	327	31.87
Myocardial Infarction	124	12.08
Stable Angina (Angina pectoris)	81	7.89
Cardio Vascular Atherosclerosis	58	5.65
Unstable Angina	56	5.45
Cardiac Arrhythmia	27	2.63
Cardiomyopathy and myocarditis	11	1.07
Congestive heart failure	06	0.58
Endocarditis	02	0.19

Table 3. Percentage of comorbidities in CVD patients

Comorbidities	Number of patients	Percentage
Diabetes mellitus	262	25.53
Renal dysfunction	151	14.71
Dyslipidaemia	134	13.06
GIT disorders	115	11.20
COPD	56	5.45
Other respiratory disorders	28	2.72
Rheumatoid Arthritis	24	2.33
CNS disorders	22	2.14
Blood disorders	17	1.65
Thyroid disorders	15	1.46
Total	824	80.25

4. DISCUSSION

4.1 Estimation of Associated Risk Factors in Cardiovascular Disease Patients

During this study different adjustable risk factors associated with CVDs were also observed in the patients, particularly inadequate diet (3.50%), physical inactivity (5.16%), tobacco consumption (18.90%), alcoholics (21.05%) and obesity (29.04%) as shown in (Fig. 2).

4.2 Prescribing Pattern of Different Cardiovascular Drugs in OPD Patients

The prescribing trend of various cardiovascular drugs for different types of CVDs in OPD patients were given in (Fig. 3).

The results indicate that most commonly prescribed class of drugs were found to be Anti-platelets (67.73%), Lipid-lowering (62.57%), Beta blockers (49.51%), ACE Inhibitors (40.93%), Angiotensin receptor blockers (30.40%), Calcium channel blockers (30.11%) and Diuretics (20.56%) then all other class of cardiovascular drugs were prescribed within (0.87%-25.34%), it is also found that apart from cardiovascular drugs most frequently prescribed non-cardiovascular class of drugs in CVDs patients was Anti-ulcers (69.10%) rest of the other drugs present less than 5.0% only.

4.2.1 Anti-platelets

In this study most frequently prescribed drugs were Antiplatelet agents (67.73%) such as Aspirin and Clopidogrel, which is comparable as in other studies [27], most commonly prescribed single drug was Aspirin (59.93%). The Association of Physicians of India recommends that all patients with myocardial infarction should receive dual antiplatelet therapy. It is found that Ticagrelor is mostly preferred only for the patients those Clopidogrel is not successive.

4.2.2 Lipid-lowering and beta blockers

Statins are known for their primary and secondary cardiovascular prevention [28]. Atorvastatin was the highly preferred Anti-hyperlipidemic drug in this study as similar to another study [29]. Simvastatin and Rosuvastatin also were prescribed in some patients. Beta blockers such as Atenolol and Metoprolol were highly prescribed than Carvedilol and Propranolol. Beta-blockers decreases the mortality rate when prescribed for the prevention of myocardial infarction [30], in few prescriptions we observed the drug Ivabradine which belongs to the class called hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blocker could potentially be an efficient and safe alternative to beta-blockers.

4.2.3 ACE inhibitors and angiotensin receptor blockers

According to the findings of this study, it is observed that angiotensin converting enzyme (ACE) inhibitors such as Ramipril and Lisinopril are frequently prescribed than Enalapril and Captopril. In angiotensin receptor blockers (ARBs) Telmisartan leads the lineup and preferred by most of prescribers due to its prolonged action about 24 hours. It has the longest elimination half-life than other ARBs [31], Candesartan is only prescribed for hypertension patients with congestive heart failure. Candesartan and its pro-drug have stronger blood pressure lowering effects than Losartan [32].

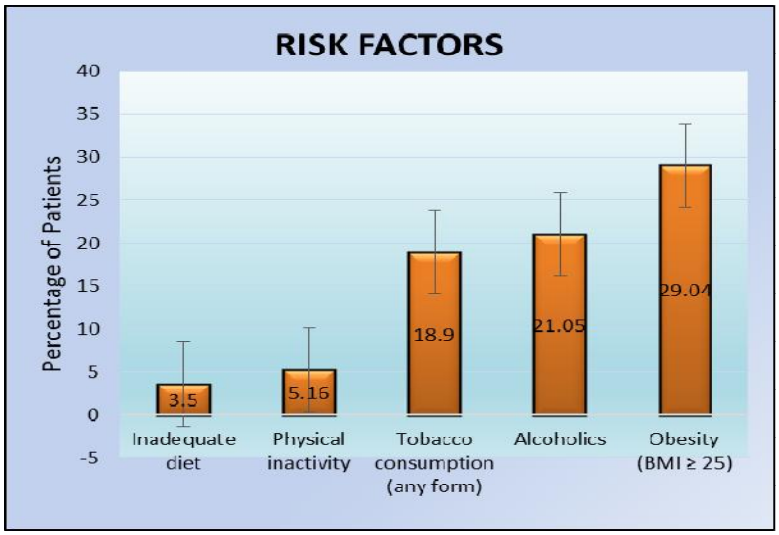

Fig. 2. Distribution of selected risk factors in CVD patients

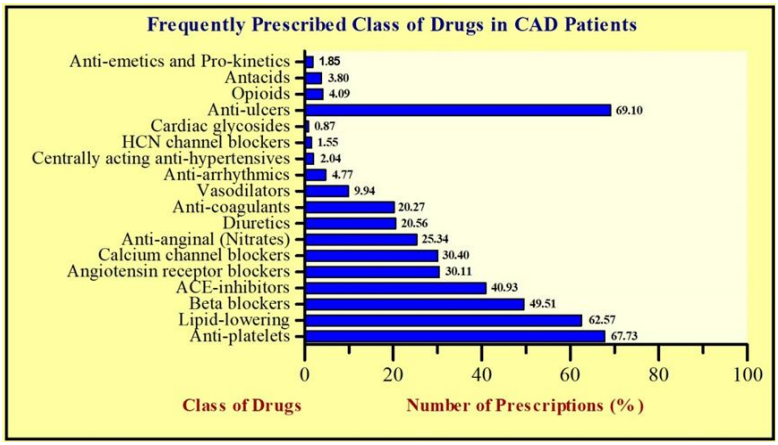

Fig. 3. Frequently prescribed class of drugs for patients with different CVDs

4.2.4 Calcium channel blockers

Amlodipine is found in many prescriptions of CVDs patients and consider as successive Calcium channel blocker (CCB). Significantly high use of CCBs was observed in male patients aged ≥60 years, this observation is in line with the 2011 National Institute for Health and Care Excellence (NICE) guidelines, which recommend the use of CCBs in patients aged ≥55 years, blood pressure is more effectively lowered with the use of CCBs in older than younger patients with hypertension, therefore CCBs are highly preferred in elderly patients [33]. Verapamil is prescribed in few patients those have migraines and cluster headaches, both the drugs is on the WHO List of Essential Medicines, the most effective and safe medicines needed in a health system [34].

4.2.5 Anti-anginals

Drugs both Isosorbide dinitrate and Nitroglycerin are vastly prescribed in patients with chest pain. Nitroglycerin available in many formulations and reported to protect from heart pain for about one hour, while Isosorbide dinitrate is an intermediate-acting nitrate approved for prevention of angina pectoris protect from pain for 2 to 3 hours. For emergency purposes nitroglycerin sublingual tablets are prescribed for many patients and advised to keep with them always. It is also suggested to use nitrates along with vasodilator (hydralazine) to treat congestive heart failure.

4.2.6 Diuretics

Hydrochlorothiazide diuretic represent one of the most commonly used agents in combination with other drugs to maintain the normal blood pressure and also to decrease the requirements for renal support particularly in elderly patients. Next to that furosemide was the major diuretic prescribed among the critically ill patients with acute renal failure and congestive heart failure [35].

4.2.7 Anti-coagulants

Enoxaparin were found to be highly prescribed anti-coagulant in this study, Dalteparin and Tazaparin also found in some prescription, all these drugs are mostly preferred for patients with medically managed ST-segment elevated myocardial infarction with subsequent percutaneous coronary intervention (PCI) and also for few patients who has Deep vein thrombosis (DVT) as comorbidity. However, compared with unfractionated heparin (UFH) a low molecular weight heparin (LMWH) has many advantages in terms of its pharmacodynamics profile and efficacy. Enoxaparin (LMWH) was significantly more effective than UFH in patients presenting with STEMI [36]. In this study it is also found that anti-coagulants are the only drugs always prescribed as parenteral dosage for the out patients during their regular follow-up after PCI.

4.2.8 Vasodilators and anti-arrhythmics

Hydralazine is mostly preferred vasodilators by most of prescribers but found only in 9.94% of prescriptions. For patients having an exacerbation of heart failure as symptoms Digoxin or Amiodarone are used as a first-line therapy for ventricular rate control. Amiodarone can also be used in patients who are refractory or have contraindications to beta-blockers, non-dihydropyridine (CCBs) and digoxin but depends on patient's health condition.

4.2.9 Other non-cardiovascular drugs

4.2.9.1 Antiulcers

It is observed in this study, the drug which is highly prescribed in CVDs patients surprisingly a non-cardiac drug that is Pantoprazole. It belongs to a class of proton pump inhibitors (PPIs). PPIs are widely used in modern medicine particularly for drug induced ulcers [37,38]. Pantoprazole is used to treat certain stomach and oesophagus problems, particularly damage from gastroesophageal reflux disease (GERD) this medication relieves symptoms such as heartburn, difficulty swallowing, and persistent cough. Omeprazole showed an inter-individual variability**,** only one compound proved superior to omeprazole and that was the (S)-(−) isomer esomeprazole, which was developed as the magnesium salt, it has more pronounced inhibition of acid secretion and less inter-patient variation compared to omeprazole [39,40]. Omeprazole may decrease the effectiveness of clopidogrel by inhibition of cytochrome P450 2C19 [41]. Pantoprazole provides earlier healing and superior pain relief in peptic ulcer and Gastroesophageal Reflux Disease (GERD) as compared to omeprazole and H2 receptor antagonists [42,43]. Ranitidine is more cost-effective and best alternate to a PPI [41]. That is why Pantoprazole is highly prescribed by most of physicians in order to manage the polypharmacy.

4.2.9.2 Antacids

Antacids which contains Aluminium hydroxide dried gel, Magnesium hydroxide and Simethicone are prescribed for some patients those have heartburn as one of the symptom. Simethicone is used to relieve the painful symptoms of too much gas in the stomach and intestines. Antacid is a substance which neutralizes stomach acidity and is used to relieve heartburn, indigestion or an upset stomach [44]. Opioids such as Tramadol and Fentanyl are prescribed in 4.09% of CVDs patients to treat their pains in different areas due to comorbidities. These opioid pain medications are used to treat moderate to moderately severe pain [45].

It is observed in this study that patient's aged ≥60 years had more number of prescriptions of both cardiovascular and non-cardiovascular drugs. Prescription containing cardiovascular drugs was significantly higher in male patients aged ≥60 years than in male patients aged between 30-59 years, on the other hand female patients aged ≥60 years were prescribed with more non-cardiovascular drugs than those aged between 30-59 years. This may be due to the greater number of comorbidities and associated conditions, such as renal dysfunctions and GIT disorders, respiratory disorders and etc., in the elderly patients.

4.3 Prescribing Pattern of Drugs as FDCs in Patients

FDCs are another significant form of drugs being prescribed nowadays as given in (Table 4).

In this study, a total of (13.21%) of prescribed drugs were found to be FDCs rest of drugs were prescribed as single dose (86.78%) also indicates that (70.50%) of patients were prescribed with two drugs combination while (27.58%) and (1.91%) of patients were found to be prescribed with three and four drugs combinations respectively as shown in (Fig. 4).

But FDCs prescribed here was less when compared to findings (22.55%) from Goel et al [8]. FDCs are found to have some advantages like increasing patient compliance by bring about synergistic action which can reduce the dose of the individual component and adverse effects. On the other hand, rationality of FDCs has become one of the most controversial and debatable issues in general practice. The use of irrational FDCs can lead to increased adverse reactions, unnecessary hospitalization and financial burden to the patients [46]. Aspirin + Clopidogrel combination is found to be highly prescribed FDC (40.24%) among all, next to that Telmisartan + Hydrochlorothiazide (14.22%) and Amlodipine + Atenolol (12.62%) were highly prescribed, rest of the FDCs are prescribed within (2-6%) only as shown in (Table 5).

Most of Cardiac FDCs are two drug combinations particularly anti-hypertensives. FDCs of different categories of drugs also found in some prescriptions with numerous drugs, particularly Metformin SR + Atorvastatin (750+20 mg) were prescribed in few Cardio-diabetic patients (2.08%), Aspirin + Atorvastatin (75+10 mg) like some other FDCs for comorbidities are prescribed less than 1% only. The extent of use of FDCs in cardiovascular diseases and their rationality are not much reported in India [47]. There are unfortunately no worldwide acceptable criteria to define irrational FDCs and no uniform principles or international standards for their development and regulatory assessment [48].

4.4 WHO/INRUD and Central Drugs Standard Control Organization

The WHO included 414 medicines in their 19th list of essential medicines in that 27 are FDCs. After due deliberations in national consultations with scientific justifications, the Government of India included 376 entities (in that 24 are FDCs) in their NLEM of India 2015. Some state drug authorities had issued manufacturing licenses for a very large number of FDCs without prior clearance from the Central Drugs Standard Control Organization (CDSCO) therefore in March 2016 the Ministry of health and family welfare of Government of India has banned a total of 344 FDCs for manufacturing and marketing [49].

Table 4. Other drug utilization parameters among CVD patients

Drug utilization parameters	No. of drugs (%)
Fixed dose combinations (FDCs)	678 (13.21)
Drugs prescribed as Single dose	4452 (86.78)
Drugs from National List of Essential Medicine-2015	4580 (89.27)
Drugs prescribed by proprietary names	5010 (97.66)

Table 5. Commonly prescribed FDCs in CVD patients

Class	FDCs	Strength (mg)	Percentage (%)
AP/ AP	Aspirin + Clopidogrel	75+75	40.24
ARB/ Diuretic	Telmisartan + Hydrochlorothiazide	40+12.5	14.22
CCB/ BB	Amlodipine + Atenolol	5+50	12.62
ACEI/ Diuretic	Ramipril + Hydrochlorothiazide	2.5+12.5	5.84
ARB/ BB	Telmisartan + Metoprolol	40+50	3.52
ARB/ Diuretic	Losartan + Hydrochlorothiazide	50+12.5	3.24
CCB/ ARB	Amlodipine + Losartan	40+5	2.48
ARB/ CCB/ Diuretic	Losartan + Amlodipine + Hydrochlorothiazide	50+5+12.5	2.24

AP: Antiplatelet; ARB: Angiotensin receptor blocker; CCB: Calcium channel blocker; BB: Beta blocker; ACEI: Angiotensin converting enzyme inhibitor

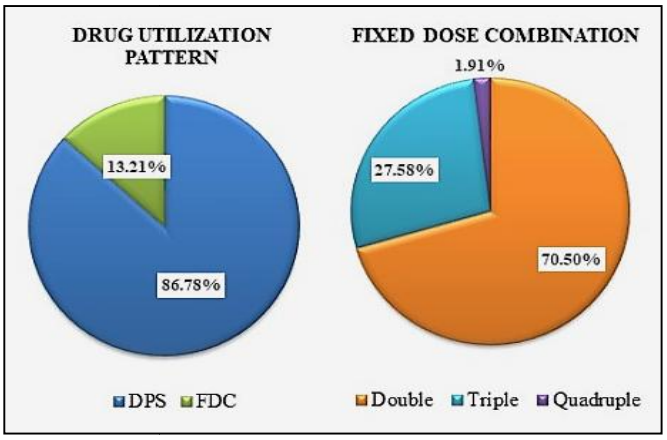

Fig. 4. Percentages of drug utilization pattern and different FDCs prescribed in CVD patients
DPS: Drug Prescribed as Single dose; FDC: Fixed dose combination

The recent NLEM-2015 does not include Losartan potassium in their list which is an Angiotensin-II receptor antagonist is removed from the Section 12-Cardiovascular medicines and Alprazolam which is a drug used to treat anxiety and panic disorder sometimes used as an antidepressant also deleted from Section 27-Psychotherapeutics of NLEM-2011 but we found few prescriptions (<4%) with FDCs of Losartan + Hydrochlorothiazide, Amlodipine + Losartan and Losartan + Amlodipine + Hydrochlorothiazide, some patients prescribed with Alprazolam in order to treat their insomnia. But as per the Rule 122E of Drugs and Cosmetics Act 1940, the FDCs are considered as new drugs and CDSCO after due examination of data on rationality, safety and efficacy issues approval, on the basis of the report State Licensing Authority (SLA) gives the manufacturing and marketing permission. This "disconnects" between the CDSCO and SLAs has precipitated a roadblock in the action against irrational FDCs [50]. It is observed in this study that maximum drugs were prescribed from the recent NLEM of India 2015 by most of practitioners which shows the acceptance and implementation of national drug policy by the prescribers as well as hospitals but adherence to generic prescription was found to be deviated from the standards recommended by WHO/INRUD.

4.5 Importance of Generic Prescription

Generally increase in prescriptions with generics from recent NLEM will increase the compliance of patient to the treatment due to reduced cost. In this study it is found that the anti-thrombotic agents' particularly antiplatelet drugs expected to overtake anti-cholesterol drugs as the sales leader in the market. It is also found that effect of FDCs of two different classes of anti-hypertensives like Telmisartan + Hydro-chlorothiazide is higher compared to doubling the dose of a single drug but FDCs are not always safe and usually prescribed by their proprietary name and this may be another important reason responsible for the low percentage of drugs prescribed by its generic name.

4.6 Limitation of the Study

There are few limitations in this study as it is a time bound study with a limited sample size it cannot detect seasonal variations in the pattern of drug use and other indicators such as health facility indicators are not assessed which would have been able to explain the unfortunate prescription of drugs from NLEM and availability of key drugs in the dispensing pharmacy. The differences between individual prescribers have also not been assessed.

5. CONCLUSION

Apart from drug utilization pattern in cardiovascular diseases, the important finding of this study is prescriptions containing non-cardiovascular drugs was significantly higher in patients aged ≥60 years, use of anti-ulcer drugs particularly PPIs (84.79%) for ulcer prophylaxis in low-risk patients is often perceived by practitioners as a harmless and relatively inexpensive remedy, this may be due to the greater number of comorbidities and associated conditions in elderly patients, for them Polypharmacy is usually unavoidable but

unnecessary co-administration of PPIs with cardiovascular drugs is not always safe it has potential for harm and leads economic implications. So deprescribing PPIs for the non-required patients is suggested to lower the risk of adverse drug interactions and economic burden to patients, also pharmacists needs to encourage the prescriptions with drugs in generic name. Updated knowledge about the banned drugs, deleted drugs, irrational FDCs and recent NLEM are highly essential for both prescribers and pharmacists.

CONSENT AND ETHICAL APPROVAL

This study was approved by the main centre's Institutional Ethics Committee for Human Research with the approval number SVCP/IEC/ JAN/2016/11 dated 27/01/2016. Hence it is a non-interventional, patients' prescription analysis based observational study it was exempt from obtaining separate informed consent from each participant. As per Helsinki Declaration of 1964 revised in 2000 [12], the objective of this present study was explained to all participants and consent was obtained using patient/ participant information sheet (PIS) and also by verbal communication.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

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