Analyzing Prescribing Pattern of Evidence-Based Medications for Coronary Artery Disease Management in a North Indian Tertiary Care Center

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ABSTRACT: Background: Appropriate use of evidence-based medications (EBM) has shown to decrease the risk and rate of cardiovascular mortality and morbidity. In public health interest regular Drug utilization studies are important to analyze prescription pattern of EBM therapies in varied healthcare settings. Purpose: To analyze the prescribing pattern of cardioprotective evidence-based medications (EBM) for the treatment of coronary artery disease (CAD) patients in a North Indian Tertiary Care Center. Methods: A cross sectional, observational, descriptive study was conducted in the cardiology outpatient department of a Tertiary Care Center in Gurgaon, Haryana, India. A total of 250 prescriptions of diagnosed cases of CAD were screened and analyzed. Results: We included 250 CAD patients (74% male) with a mean age of 58.5±10.4 years in this study. Unstable angina was the most common diagnosis (60.8%) and hypertension (54%), diabetes (38%), and dyslipidemia (36%) were the most common co-morbidities observed in this study population. On an average 7 drugs were prescribed per patient. Analysis of the prescription pattern revealed that majority of the patients received Single Antiplatelet therapy (93%) followed by Dual Antiplatelet therapy (74%). Statins were prescribed to 72% patients; Beta-blockers to 69% patients; Angiotensin Converting Enzyme inhibitor (ACEIs) to 40% and Angiotensin II receptor blockers (ARBs) to 37% of the patients. No statistically significant difference (p>0.05) based on either age or gender was observed in the prescribing pattern of various drug classes among this study population. Conclusion: Prescription of majority of EBMs for CAD management in this healthcare setting was found to be rational and appropriate. © 2020 iGlobal Research and Publishing Foundation. All rights reserved.


INTRODUCTION
Globally drug utilization studies play a significant role in examining the use of medicines in a society. Such regular assessments of prescribing, dispensing, and use of medicines in different healthcare settings are of great social, economic, and medical importance and critical in avoidance of inappropriate and sub-optimal drug use [1]. Accurate diagnosis coupled with evidence-based prescribing, proper dispensing, and effective patient counselling are important criteria for rational use of drug [2]. As part of drug utilization research, descriptive studies target to describe variations and
trends in the quality, reach, and costs, of the usage of medicines among individuals and populations [3]. Thus, Drug utilization research not only can highlight a particular discrepancy in patient care in a healthcare setting but also is a tool to rectify gaps by ensuring stakeholder accountability and implementation of corrective measures.

Currently cardiovascular diseases (CVD) present as the leading cause of non-communicable disease (NCD) related mortality in India. Among all, coronary artery disease (CAD) is the largest contributor to this CVD disease burden [4,5]. In an attempt to improve survival benefits in CAD patients, based on results of multiple controlled trials, American College of Cardiology Federation/American Heart Association (ACCF/AHA) and European Society of Cardiology recommended pharmacotherapy with a wide range of Evidence-Based Medications (EBM) [6-9]. This includes antiplatelets, Angiotensin Converting Enzyme (ACE) inhibitors, Beta-blockers, Angiotensin Receptor Blockers (ARBs) and Statins [10-12].

However, despite of standard guidelines several studies worldwide have shown a wide variation in the prescription pattern for the management of CAD across different clinical settings [13-15]. Bhatt et al analyzed a large, international patient database namely “The Reduction of Atherothrombosis for Continued Health” (REACH) Registry and reported sub optimal use of long term cardioprotective EBM therapies [16]. Another study conducted by Sharma et al in a tertiary care center in India, reported underuse of antiplatelet therapy, beta-blockers, statins, angiotensin receptor blockers (ARBs), angiotensin-converting enzyme inhibitors (ACE -inhibitors) in CAD patients [17]. Similar outcomes were reported by Yusuf et al, in ‘PURE’ study, an epidemiological survey of 17 countries. The authors reported significant underutilization of EBM therapies for the management of CAD in low-income countries in contrast to high income countries [18]. In a study conducted in Estonia, authors reported that only 40% of patients diagnosed with Acute coronary syndrome (ACS) had been prescribed with a combination therapy of beta-blockers, statins and ACE-inhibitors [19]. These studies highlight that lack of suitable long term follow up along with less focus on secondary prevention programs for CAD patients seem to be major contributing factors for increased CVD related mortality in the south Asian region including India.

Additionally, studies have reported underutilization of EBM therapies in women and among the elderly. Attributable reasons for these age- and gender-related differences in treatment may include social and economic issues like gender bias, clinical inertia, or cost-related financial issues [20-24].

The objectives of present study were to evaluate the demographics, disease characteristics and prescription patterns of EBM drug classes among diagnosed cases of CAD attending cardiology outpatient department in a North Indian Tertiary care center. We also evaluated if there was any age and gender related disparities in the prescription pattern of EBMs in the given healthcare setup.

**MATERIALS AND METHODS**

**Study Design**

This was a cross sectional, descriptive, observational study conducted in cardiology outpatient department (OPD) of a reputed tertiary care center located in the heart of Gurugram, Haryana. Permission to conduct the study was obtained from Hospital Independent Ethics Committee in accordance with the Declaration of Helsinki (E.C Registration no: ECR/249/Inst./HAR/2013). The study was conducted during the period between March 2018 to December 2018. Inclusion and Exclusion criteria were determined after careful review of literature and post detailed discussion with the clinical advisor (Director of Cardiology division at Paras Hospitals) for this study.

**Inclusion criteria**
- Patients of either gender above 18 years and below 75 years of age
- Patients with the established diagnosis of CAD attending cardiology OPD
- Patients who consented to participate in the study

**Exclusion criteria**
- Pregnant and lactating women
- Patients with malignancy
- Patients with any serious systemic illness

**Data collection**
A total of 250 prescriptions were obtained, screened and analyzed for final analysis. Patients were contacted during their hospital OPD visit. Informed consent was obtained from
those who fulfilled the inclusion criteria. The socio-

demographic and clinical data were recorded from the OPD
prescription sheet. The privacy and the confidentiality of the
data were maintained.

**Descriptive Data Analysis**

We used MS Excel™ to conduct a descriptive analysis of the
patient demographic and disease characteristics (age, gender,
diagnosis, comorbidities). Utilization patterns of EBM drug
classes was also done in this study population. For the purpose
of this project EBMs included Antiplatelet drugs, Dual
antiplatelet therapy, Beta-blockers, Statins, Angiotensin
Converting Enzyme Inhibitors (ACEIs), and Angiotensin
Receptor Blockers (ARBs). Additionally, prescription analysis
for other important classes of drugs was also done.

Proportions of drugs prescribed per patient was also
determined. Descriptive statistics expressed in terms of actual
numbers, and the percentage was used for data analysis.

**Statistical Analysis**

The statistical analysis was done using R Statistical Software,
version 3.6.1. Age and gender wise analysis of the prescription
pattern of EBM drug classes was conducted. Aim was to
determine if there was any statistically significant difference
in prescription pattern of these medications based on either
age or gender of the patient. Based on age, we divided the
patients into three groups, Group 1- 25-45 years, Group 2- 46–
65 years and Group 3 –65 -75 years. We used the Chi-square
test to examine the difference in prescription frequency for
various drug classes among the different age groups and
gender. A P-value <0.05 was considered significant.

**RESULTS AND DISCUSSION**

**Patient demographic and clinical characteristics**

Out of 250 patients, 74% were male and 26% females. The
mean age was 58.5 ±10.4 years. The majority (55%) of the
patients belonged to middle age group of 46-65 years. **Figure
1.** summarizes the age-wise distribution of the study
population.

As shown in **figure 2.** Unstable angina was the most common
diagnosis accounting for 60.8% cases followed by single-
vessel disease (32.4%) and double vessel disease (17.2%).

The common co- morbidities among the study population are
presented in **figure 3.** Hypertension (54%), diabetes (38%),
and dyslipidemia (36%) were the most common co-
morbidities followed by COPD (18%), renal dysfunction (6%)
and peripheral vascular disease (5%).

**Utilization Pattern of Cardiovascular Drugs Among CAD
Patients**

A total of 1803 drugs were prescribed to 250 patients. Thus,
on average 7 drugs were prescribed per patient. **Figure 4**
gives a snapshot of the proportion of drugs prescribed.

**Table 1** summarize the distribution of drugs for major EBM
therapies along with other drug classes. Antiplatelet therapy
was prescribed in 93% of the total patient population. 74%
patients received dual antiplatelet therapy comprising of
aspirin and clopidogrel. 72% patients received statins; 69%
received beta-blocker therapy and a combined 77% patients
were prescribed ACE inhibitor and ARB agents. Calcium
channel blockers were prescribed for 32% of the total study population.

**Figure 4: Proportion of drugs per prescription**

**Table 1: Utilization Pattern of Common Cardiovascular Drug Classes**

<table>
<thead>
<tr>
<th>Drug classes</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiplatelet</td>
<td>232</td>
<td>93%</td>
</tr>
<tr>
<td>Dual antiplatelet therapy</td>
<td>186</td>
<td>74%</td>
</tr>
<tr>
<td>Statins</td>
<td>179</td>
<td>72%</td>
</tr>
<tr>
<td>Beta-Blocker</td>
<td>173</td>
<td>69%</td>
</tr>
<tr>
<td>Diuretics</td>
<td>101</td>
<td>40%</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>99</td>
<td>40%</td>
</tr>
<tr>
<td>Angiotensin Receptor Blockers</td>
<td>93</td>
<td>37%</td>
</tr>
<tr>
<td>Calcium Channel Blocker</td>
<td>79</td>
<td>32%</td>
</tr>
<tr>
<td>Anticoagulant</td>
<td>25</td>
<td>10%</td>
</tr>
<tr>
<td>Antianginals</td>
<td>21</td>
<td>8%</td>
</tr>
<tr>
<td>Alpha Blocker</td>
<td>18</td>
<td>7%</td>
</tr>
</tbody>
</table>

**ACE inhibitors: Angiotensin Converting Enzyme Inhibitors**

Table 2 shows the number of patients in the different age groups with the recommended EBMs along with other cardiovascular medications. Utilization of these medications varied slightly among different age groups, but no statistically significant difference was detected among the three age groups in the prescription frequency of either of the drug classes (p>0.05).

**Table 2. Age Specific Prescription of Cardiovascular Medications**

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>25-45 yrs</th>
<th>46-65 yrs</th>
<th>65-75 yrs</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=28)</td>
<td>(N=137)</td>
<td>(N=85)</td>
<td></td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>26</td>
<td>93%</td>
<td>126</td>
<td>92%</td>
</tr>
<tr>
<td>Dual antiplatelet therapy</td>
<td>21</td>
<td>75%</td>
<td>101</td>
<td>74%</td>
</tr>
</tbody>
</table>

**Table 3 summarizes the prescription proportion of various cardiovascular drug classes in this study population by gender. The results as indicated show that there is no gender disparity in the use of evidence-based medications in this study population (p>0.05).**

**Table 3. Gender-specific Prescription of Cardiovascular Medications**

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Male (N=185)</th>
<th>Female (N=65)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>172</td>
<td>93%</td>
<td>60</td>
</tr>
<tr>
<td>Dual antiplatelet therapy</td>
<td>137</td>
<td>74%</td>
<td>49</td>
</tr>
<tr>
<td>Statins</td>
<td>130</td>
<td>70%</td>
<td>49</td>
</tr>
<tr>
<td>Beta-Blocker</td>
<td>131</td>
<td>71%</td>
<td>42</td>
</tr>
<tr>
<td>Diuretics</td>
<td>76</td>
<td>41%</td>
<td>25</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>71</td>
<td>38%</td>
<td>28</td>
</tr>
<tr>
<td>Angiotensin Receptor Blockers</td>
<td>72</td>
<td>39%</td>
<td>21</td>
</tr>
<tr>
<td>Calcium Channel Blocker</td>
<td>60</td>
<td>32%</td>
<td>19</td>
</tr>
<tr>
<td>Anticoagulant</td>
<td>18</td>
<td>10%</td>
<td>7</td>
</tr>
<tr>
<td>Antianginals</td>
<td>16</td>
<td>9%</td>
<td>5</td>
</tr>
<tr>
<td>Alpha Blocker</td>
<td>15</td>
<td>8%</td>
<td>3</td>
</tr>
</tbody>
</table>

ACE inhibitors: Angiotensin Converting Enzyme Inhibitors

p < 0.05 considered as statistically significant (Chi square test)
In this study, we analyzed prescriptions of 250 CAD patients visiting the OPD of cardiology department at a tertiary care hospital in North India. In our study a large percentage (55%) of patients were of middle age between 46-65 years as reported by Rajanandh et al [28]. Patients in our study were younger (58.5±10.4) than those in a few previous observational studies conducted in developed countries [29,30]. This generates more evidence to the already established fact of early onset of CVD in Indian population as compared to global average.

Optimal pharmacotherapy plays a critical role in secondary prevention and management of cardiovascular complications. Moreover, in the era of evidence-based medications (EBMs), the clinical diagnosis and treatment should be based on standard of care recommended in the guidelines [11,12,31]. EBMs have since long proven improvement in survival rates and secondary prevention of coronary artery disease related complications [32]. However, CAD being a chronic disease, long-term adherence to EBMs require clinical focus on secondary prevention along with complicated medication dose adjustment and maintenance [33]. Despite of standard guidelines, still variability and large gap exists in leveraging the optimal potential of EBM therapies in secondary prevention of cardiovascular complications [34,35]. For most patients with ACS, ACC/AHA and other guidelines recommend antiplatelet or dual antiplatelet therapy, a beta-blocker, an ACEI or ARB and a statin unless any of these is contraindicated.

The major finding of present drug utilization study was that prescription of EBMs was appropriate for most of the drug categories in this population. In our study, antiplatelet therapy is given to a large percentage (93%) of patients. Dual antiplatelet therapy (DAPT) comprising of a P2Y12 inhibitor and aspirin is a prescription choice in many patients for better clinical outcomes. In this study we found dual antiplatelet therapy prescribed to 74% patients indicating prescription choice aligned with the recommendation from international guidelines. Clopidogrel was the most commonly prescribed P2Y12 inhibitor.

Beta-blockers were prescribed to 69% patients in this study. Metoprolol was the most commonly prescribed agent. This was similar to the one reported in CREATE registry in which 61% patients received beta-blockers. Another drug utilization study done in Saudi Arabia on ACS patients also reported similar utilization of beta-blockers and ACE inhibitors [36]. In earlier studies use of these agents was found to be more in patients younger than 60 years and with a STEMI diagnoses. Mortality benefit of beta-blockers is well established among mild to moderate heart failure cases. However univariate analysis suggests that in clinical practice, heart failure, renal dysfunction and brady-arrhythmias decrease the prescribing of beta-blockers. Guidelines also suggest removing patients from the use of beta-blockers in an ICU environment and beginning treatment after they have been stabilized. Since present study recruited only stable patients during their OPD visits, we found the prescription of beta blockers to be reasonably moderate though not on a higher side. The utilization of beta blockers in patients was also less to some extent due to the comorbidities like renal dysfunction among our patient population. However, use of beta-blockers could be increased after careful consideration of individual patient risk profile for cardiogenic shock, heart blocks (greater than first degree) and other relative beta-blockade contraindications [37].

Statins were prescribed in 72% study population and ACEIs, and ARBs combined together were prescribed to 77% of patients respectively in this study. This prescription pattern is similar to other studies done in the past, although there is scope for increasing the prescription of these classes of medications after careful patient evaluation [20,38]. The primary reason for limited use of ACE inhibitors is the side effects observed with this category of medication in this population. The most common side effect of ACE inhibitors is cough. The frequency of this side effect is high in this population leading to medication non-compliance and change of medication required in a high number of such cases. Another factor that decrease ACE inhibitor prescription in clinical practice is renal dysfunction. ACE-inhibitors can interfere with the auto-regulation of GFR mediated by angiotensin-II and lead to deterioration of renal function. Patients with bilateral renal artery stenosis are at higher risk. Therefore, renal dysfunction was found to significantly decrease the utilization of ACE-inhibitors in many other studies as well [37].

Several studies in the past have reported that women and elderly patients receive less evidence-based treatments [20-24]. There are both patient-based and practitioner-based factors leading to this gap and disparity in age based EBM utilization specifically in elderly population. At patient end these factors include age related poor prognosis, comorbidities, disease related risks and complications, decreased capacity to survive CVD events, and decreased tolerance to medicine. Because of this elderly patient are more concerned about side effects of medicines and therefore doesn’t adhere to therapies. At the clinical practitioner end as well there are clinical reservations due to potential risk of cerebral hemorrhage and gastrointestinal bleeding in elderly patients especially with dual antiplatelet therapy. General
clinical practice therefore is to limit use of EBM therapies in elderly population. Earlier studies have also demonstrated that liver and kidney dysfunctions limit the use of statins and ACEI/ARB drugs in elderly population. Thus, the generalization of above risk factors to entire elderly population without careful evaluation of individual risk factors of renal and liver status can be attributed as a key reason for disparity in EBM utilization in elderly patients. Thence this compromises the potential value of EBM therapies in many people for whom these might have been of higher benefit [21].

Gender based differences in use of beta-blocker is observed, although guidelines advocate the use of these cardioprotective medicines equally in men and women [10,39]. Reasons for gender-based disparity may include clinical judgement related to safety concerns of EBMs in females, and comorbidities among these patient population apart from other multiple socio-economic factors.

However, the gender and age-based differences were not recorded in the present study. There was no significant age and gender related disparities in EBM prescription for CAD management in the analyzed study population. Although this is a positive indication of appropriate prescription practices focused on secondary prevention of CAD; considering that prescription practices may vary widely from one healthcare set up to another, one must be careful in extrapolating and generalizing the results. Systematic analysis of similar prescription studies done at multiple Indian healthcare centers would be useful to draw a conclusion in this regard.

The major notable prescription issue identified in this study was polypharmacy. In more than 45% prescriptions, 5-10 drugs were prescribed. The prescription of multiple drugs rationally tends to high risk of drug interactions, drug toxicities, reduced medication compliance and increased cost burden on the patients. However, the results from this study are comparable to similar numbers of drugs given for CVD patients in previous studies [40]. One reason to polypharmacy could be attributed to higher number of male patients in the study. As shown in previous studies the incidence of cardiovascular drug prescriptions for men was higher than that for women [41]. Another factor to consider is that elderly patients had higher number of drugs per prescription as compared to younger population. Besides, a large number of our study patients had undergone percutaneous coronary intervention; or were presented at an advanced level of disease, thus necessitating higher number of medications per prescription. Overall considering the complexity and comorbidities among majority of this patient population prescription of multiple therapies may be considered justifiable to cater to individual patient needs.

CONCLUSION
Appropriate utilization of proven evidence-based medications may help in secondary prevention and risk reduction in patients with coronary and other atherosclerotic vascular diseases. There is scope for increasing the prescription of certain drug classes like beta blockers after careful evaluation of individual risk profile of patients. Overall the prescribing practices for use of majority of evidence-based medications in CAD management were found to be rational in this North Indian Tertiary care center.

DATA AVAILABILITY
Not declared.

CONFLICTS OF INTEREST
The authors declare no conflict of interest in this research article.

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