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A prospective study of prescription pattern in patients with coronary artery disease at a tertiary care teaching hospital

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Abstract
Background: Cardiovascular diseases include several conditions like coronary artery disease (CAD), aortic aneurysm, rheumatic heart disease, congenital heart disease, valvular heart disease, cardiomyopathy, arrhythmias and heart failure. Recently, CAD is upcoming as one of the leading cause of death worldwide. Hypertension and diabetes are found to be the two most common co-morbidities associated with CAD. Different classes of drugs like anti-platelet drugs, anti-coagulant drugs, anti-hypertensive drugs, antihyperlipidemic drugs, anti-anginal drugs etc are prescribed to patients diagnosed with CAD to reduce both morbidity and mortality and to enhance the quality of life.
Objectives: The aim of the present study is to evaluate the drug utilization pattern in treating patients with coronary artery disease at a tertiary care teaching hospital.
Methods and Materials: The present study is a prospective, observational prescription based study conducted from July 2017 to December 2018 for a duration of 18 months in the Department of Cardiology, Gauhati Medical College and Hospital, Guwahati after getting approval from Institutional Human Ethics committee. All patients diagnosed with CAD above 18 years of age irrespective of gender and giving proper written informed consent were included in this study.
Results: In the present study, a total of 887 patients were included. Among these, 69.22% were male and 30.78% were female. The most common age group diagnosed with CAD was 61-70 years (31.56%). Hypertension (68.09%) and diabetes (42.34%) were most commonly observed associated co-morbidities. The most common diagnosed category of CAD patients was anterior and inferior myocardial wall infarct (28%). The cardiovascular drugs prescribed for CAD were observed as anti-platelet drugs (98.53%), anti-hyperlipidemic drugs (97.40%), anti-anginal drugs (78.91%), anti-hypertensive drugs (68.09%), anti-coagulants (63.02%). Apart from these, other drugs prescribed were antibiotics (60.09%), diuretics (57.15%), bronchodilators (28.41%) and various miscellaneous drugs like proton pump inhibitors, multivitamins, NSAIDs etc (40.47%). The average number of drugs per prescription was found to be 6.78 and 23.38% of drugs were prescribed by generic name.
Conclusion: In the present study, it was observed that the risk for CAD increased with increasing age and co-morbid conditions like hypertension and diabetes. The optimal use of Fixed Drug Combinations of drugs, generic drugs and minimal polypharmacy should be promoted to increase the quality of life and to reduce economic burden on the patients.

Keywords: Coronary Artery Disease, cardiovascular drugs, prescription pattern, drug utilization pattern

Introduction
The term "Cardiovascular disease" in broad spectrum reflects upon several conditions like coronary artery disease (CAD), aortic aneurysm, rheumatic heart disease, congenital heart disease, valvular heart disease, cardiomyopathy, arrhythmias and heart failure. [1] In all of the above conditions, either heart or its associated blood vessels remain in diseased state. The most common risk factors for Cardiovascular disease (CVD) are high blood pressure, high blood cholesterol, diabetes mellitus, sedentary life style habits, obesity, family history of CVD, ethnic background, older age group, male gender, smoking and alcohol etc. Approximately 23.6 million people are estimated to die from Cardiovascular diseases by the year 2030. [2]

CAD is emerging as one of the leading cause of death worldwide. The National Commission and Macroeconomics and Health, Government of India has reported in a survey that 30 million patients have been diagnosed with CAD till the end of last century in India. [3]

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In Indian subcontinent, a trend has been found that CAD is diagnosed at younger age i.e. approximately 10 years earlier in comparison to their respective counterparts in other continents. Thereby in India, it has lead to tremendous loss of productive working years and eventually there has been an alarming rise in mortality rate amongst CAD patients. [4, 5] World Health Organization (WHO) has estimated that 47 million CAD patients are going to suffer from Disability Adjusted Life Years by the year 2020 worldwide. [6]

CAD is a heterogeneous group of clinical manifestations which encompasses acute ST segment elevated Myocardial Infarction (STEMI), non ST segment elevated Myocardial Infarction (NSTEMI), unstable angina, chronic stable angina and Congestive Heart Failure. [7] CAD mainly occurs due to the accumulation of atherosclerotic plaques in the inner lining of blood vessels, thereby occluding the lumen of blood vessels i.e. coronary arteries supplying the heart. Due to deprivation of blood and essential nutrients to myocardial cells in stressful conditions, ischemia of heart tissue occurs which presents clinically as chest pain or difficulty in breathing. Various randomized controlled trials have established the guidelines that patients diagnosed with CAD (i.e. chronic stable angina or post-acute Myocardial Infarction or following percutaneous coronary intervention or coronary bypass surgery) should be treated with the following secondary evidence based drugs – Aspirin, Clopidogrel, Beta-adrenergic blockers, ACE Inhibitors and hydroxyl methylglutarate coenzyme-A (HMG CoA) reductase inhibitors (statins).[8, 9, 10] Both the morbidity and mortality were greatly reduced by approx. 75% following the treatment with these drugs. [11]

Proper medical audit of prescription pattern of drugs used in CAD is of utmost importance, as in day to day clinical practice there is underuse of the appropriate antiplatelet drugs, anticoagulant drugs, Beta-adrenergic blockers, ACE Inhibitors, ARB's and anti-hyperlipidaemic drugs. Rational prescription pattern of these drugs can delay the risks associated with CAD and stabilize them for longer duration. Further CAD patients should be advocated to eat healthy foods like DASH diet, maintain a healthy weight, increase physical activity, stop smoking and alcohol consumption, control blood pressure, maintain adequate blood cholesterol and glucose level if present, routine health check-ups and proper intake of medications prescribed by physicians.

Therefore, the present study has been conducted in order to analyze the prescription pattern in vogue of CAD patients attending the tertiary care teaching hospital at present. This analysis will further highlight the fallacies of current drugs prescribed for CAD as well as modifications required in future drug usage in this category of patients.

Materials and Methods
Study Site: The study has been conducted in the Department of Cardiology, Gauhati Medical College and Hospital, Guwahati. It is a tertiary care teaching hospital providing both specialized and super specialized services.
Study Design: A prospective prescription- based observational study.

Study Criteria
Inclusion criteria: [1, 7]
▪ All the In-patients as well as Outdoor visit patients diagnosed with CAD in the Department of Cardiology, Gauhati Medical College and Hospital, Guwahati.

- Patients ≥ 18 years of age, of both gender.
- Patients giving proper written informed consent

Exclusion criteria [1, 7]
- Patients unwilling to participate in the study.
- Patients admitted in critical care units.
- Patients diagnosed with other cardiac diseases apart from CAD.

Study Duration
This study has been conducted from July 2017 to December 2018 for total duration of 18 months in the Department of Cardiology, Gauhati Medical College and Hospital, Guwahati after getting proper approval from Institutional Human Ethics Committee.
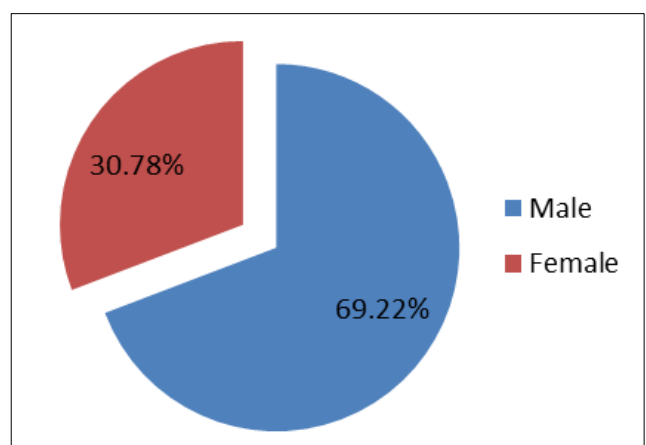
Method of Data Collection
A total of 887 CAD patients diagnosed by practicing cardiologists were included. The clinical, biochemical and all other related information were recorded in preformed format. Demographic profiles, personal habits, associated co-morbidities like hypertension, diabetes etc and the prescribed medications were also taken into account from all the patients. The detailed history of drugs about the group, dosage schedule, duration of treatment, concomitant medications if any, whether prescribed in generic name or brand name as well as number of total drugs prescribed per prescription was recorded.

Statistical Analysis
Results of the study were evaluated by using descriptive statistical analysis. Data was entered in MS Excel 2007 and statistical software Graph Pad Prism version 5 was used in the study.

Results
A total number of 887 patients diagnosed with CAD were enrolled in the study. Out of these 887 patients, 69.22% were male and 30.78% were female (figure 1). The male to female ratio was found to be 2.25:1 with a higher male preponderance to CAD.
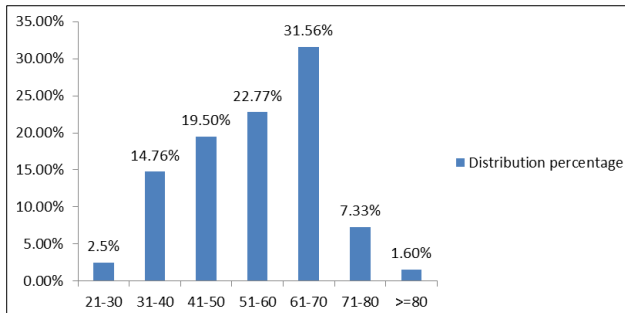

Fig 1: Gender wise distribution of CAD patients

In the present study, the most common age group diagnosed with CAD was found between the age range of 61-70 years i.e.31.56% (table 1 & figure 2).

Table 1: Age-wise distribution of CAD patients.

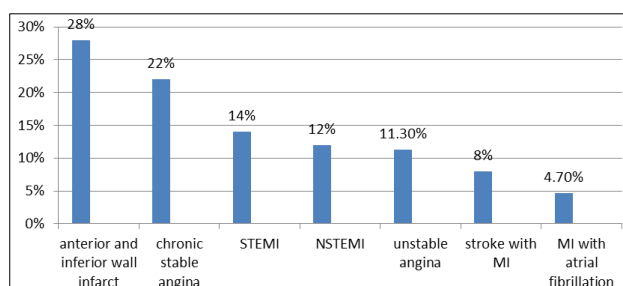| Age groups (in years)	Number of patients (n=887)	Percentage (%)
21-30	22	2.5
31-40	131	14.76
41-50	173	19.50
51-60	202	22.77
61-70	280	31.56
71-80	65	7.32
≥80	14	1.6

Fig 2: Age-wise Distribution of CAD patients

Various co-morbid conditions were found to be associated with CAD patients like hypertension, diabetes mellitus, chronic kidney disease, hypothyroidism, dyslipidemia, chronic obstructive pulmonary disease, bronchial asthma, peptic ulcer etc. Amongst them hypertension and diabetes mellitus were found to be the most commonly associated ones with coronary artery disease (table 2)

Table 2: Different associated co-morbidities of CAD patients

Associated co-morbidities	Percentage (%)
Hypertension	16.92
Hypertension + Diabetes	29.34
Hypertension + others(CKD, hypothyroidism, dyslipidemia, COPD)	12.13
Hypertension + Diabetes + others (hypothyroidism, dyslipidemia, bronchial asthma, COPD)	9.7
Others (bronchial asthma, COPD, APD)	3.2
Diabetes + others (dyslipidemia, hypothyroidism, COPD)	3.3

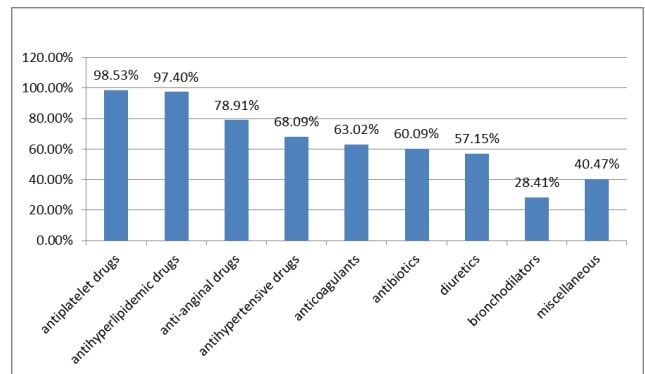(CKD- chronic kidney disease, COPD- chronic obstructive pulmonary disease, APD- acid peptic ulcer disease)

Anterior and inferior myocardial wall infarct appeared to be the commonest category of CAD patients (28%) followed by chronic stable angina (22%) (Figure 3)

Fig 3: Distribution of different categories of CAD patients

The CAD patients were treated with the following categories of drugs- antiplatelet drugs, antihyperlipidemic drugs, anti-anginal drugs, antihypertensive drugs,

anticoagulants, antibiotics, diuretics, bronchodilators and some miscellaneous drugs. Detailed records of the usage of these drugs were evaluated (figure 4, table 3)

Fig 4: Distribution of different classes of drugs prescribed to CAD patients

Table 3: Distribution of different classes of the drugs prescribed to CAD patients

Drug classes	Number of patients (n=887)	Percentage (%)
Antiplatelet drugs	874	98.53
Antihyperlipidemic drugs	864	97.40
Anti-anginal drugs	700	78.91
Antihypertensive drugs	604	68.09
Anticoagulants	559	63.02
Antibiotics	533	60.09
Diuretics	507	57.15
Bronchodilators	252	28.41
Miscellaneous	359	40.47

Different combinations of anti-thrombotic drugs were prescribed to CAD patients. Antiplatelet drugs and anticoagulant drugs combination was found to be most commonly prescribed (table 4)

Table 4: Distribution of different anti-thrombotic drug combinations prescribed to CAD patients.

Antithrombotic drugs	Number of patients (n=874)	Percentage (%)
Antiplatelet drugs	325	37.18
Antiplatelet drugs + anticoagulants	493	56.40
Antiplatelets + anticoagulants +fibrinolytics	56	6.41

Aspirin and Clopidogrel combination was found to be the highest prescribed one (64.98%) followed by Aspirin alone (28.03%) and Clopidogrel alone (6.97%) in the antiplatelet group of drugs. (Table 5).

Table 5: Distribution of antiplatelet drugs prescribed to CAD patients.

Antiplatelet drugs	Number of patients (n=874)	Percentage (%)
Aspirin	245	28.03
Aspirin + clopidogrel	568	64.98
Clopidogrel	61	6.97

Atorvastatin was the highest prescribed anti-hyperlipidemic drug (79.16%) followed by Atorvastatin and Fenofibrate combination (8.33%) and Rosuvastatin (6.01%). (Table 6)

Table 6: Distribution of anti-hyperlipidemic drugs prescribed to CAD patients.

Anti-hyperlipidemic drugs	Number of patients (n=864)	Percentage (%)
Atorvastatin	684	79.16
Rosuvastin	52	6.01
Fenofibrate	23	2.6
Atorvastatin + Fenofibrate	72	8.33
Atorvastatin + Rosuvastatin	21	2.43
Rosuvastatin + Fenofibrate	12	1.39

Enoxaparin sodium was found to be the highest prescribed anticoagulant drug (50.62%) followed by LMW Heparin (42.57%) and Dalteparin sodium (6.79%). (Table 7)

Table 7: Distribution of anticoagulant drugs prescribed to the patients.

Anticoagulant drugs	Number of patients (n= 559)	Percentage (%)
Heparin (LMW)	238	42.57
Enoxaparin sodium	283	50.62
Dalteparin sodium	38	6.79

Heparin (LMW)- Low molecular weight Heparin.

Amongst all the anti-anginal drugs prescribed, Nitrates were found to be the highest prescribed drugs (60.42%) (Table 8).

Table 8: Distribution of anti-anginal drugs prescribed to CAD patients.

Anti-anginal drugs	Number of patients (n=700)	Percentage (%)
Nitrates	423	60.42
Nicorandil	45	6.42
Ivabradine	28	4
Nitrates + Nicorandil	89	12.71
Nitrates + Ivabradine	71	10.14
Nicorandil + Ivabradine	7	1
Nitrates + Nicorandil+ Ivabradine	37	5.28

A Total number of 604 CAD patients received various categories of antihypertensive drugs out of which Beta blockers alone were the most commonly prescribed drugs (51%) (Table 9).

Table 9: Details of antihypertensive drugs prescribed to the CAD patients.

Antihypertensive drugs	Number of patients (n=604)	Percentage (%)
Beta blockers	308	51
Alpha & beta blockers	39	6.45
ACE inhibitors	98	16.22
ARB's	90	14.91
Calcium channel blockers(CCB's)	38	6.29
Beta blockers + ACE inhibitors	8	1.32
Beta blockers+ CCB's	6	1
ACE inhibitors + CCB's	9	1.5
Beta blockers + ACE inhibitors + CCB's	8	1.32

ACE inhibitors- Angiotensin Converting enzyme inhibitor, ARB's- Angiotensin Receptor Blocker

Furosemide was the highest prescribed diuretic (70.25%) to CAD patients followed by Torsemide (15.82%) and Hydrochlorthiazide (8.23%) (Table 10)

Table 10: Details of diuretics prescribed to CAD patients

Diuretics	Number of patients (n= 507)	Percentage (%)
Furosemide	356	70.21
Torsemide	80	15.77
Hydrochlorthiazide	42	8.28
Spironolactone	19	3.74
Amiloride	10	1.97

Some patients of CAD were even prescribed bronchodilators, out of which Formoterol + Budesonide combination was the most highly prescribed bronchodilator (61.11%) (Table 11)

Table 11: Details of bronchodilator drugs prescribed to the patients.

Bronchodilator drugs	Number of patients (n= 252)	Percentage (%)
Theophylline + Etophylline	132	52.38
Salbutamol + Ipratropium bromide	52	20.63
Formoterol + Budesonide	154	61.11
Salmeterol + Fluticasone	85	33.73
Tiotropium	147	58.33

533 number of CAD patients were prescribed antibiotics out of which Piperacillin and Tazobactam combination use was found to be the highest prescribed antibiotic (68.66%) (Table 12)

Table 12: Details of antibiotics prescribed to the patients.

Antibiotics	Number of patients (n= 533)	Percentage (%)
Piperacillin and Tazobactam combination	366	68.66
Penicillins	87	16.32
Cephalosporin	42	7.87
Quinolones	16	3.02
Aminoglycosides	9	1.7
Others	13	2.45

Various miscellaneous drugs were prescribed to the CAD patients details of which have been mentioned in table 13.

Table 13: Details of miscellaneous drugs prescribed to CAD patients.

Miscellaneous Drugs	Number of patients (n=359)	Percentage (%)
Proton pump inhibitors	252	70.2
Multivitamins	209	58.21
Lactulose	182	50.69
NSAID's	105	29.24
Benzodiazepines	112	31.19
Anti thyroid drugs	37	10.31
Anti arrhythmic drugs	24	6.68

A total number of 6016 drugs were prescribed to the patients, out of which an average number of 6.78 drugs were prescribed per prescription (table 14). Moreover, it was also observed that 23.39% of drugs were prescribed by generic name.

Table 14: Details of prescription prescribed to the CAD patients.

Details of prescriptions	Number of patients (n=887)
Total number of drugs prescribed	6016
Average number of drugs per prescription	6.78
Number of drugs prescribed by generic name	1415 (23.38%)

Discussion

A total of 887 patients were included in the present study, out of which 69.22 % were male and 30.78 % were female, indicating a higher preponderance of male towards occurrence of CAD. This finding was found to be quite comparable to other similar types of studies done by Kamath A *et al.*, Tasneem Sandozi *et al.* and Dawalji *et al.* wherein 81 %, 68.57 % and 72.94 % male preponderance towards occurrence of CAD was observed respectively. [1, 12, 13]

In the present study, the most common age group was found to be between 61-70 years. This finding is quite comparable with the finding of previous studies done by Kamath A *et al.*, Tasneem Sandozi *et al.*, Dawalji *et al.* where the most common age group was found to be between 61-70 years also. [1, 12, 13]

After evaluating the associated co-morbidities in the present study, hypertension (68.09%) and diabetes mellitus (42.34%) were found to be the most commonly associated co-morbidities in CAD patients. Similar type of finding was observed in another study done by Kiran P. Vakade *et al.* wherein the most commonly associated co-morbidities was hypertension (42.24%) followed by diabetes mellitus (19.51%). [14] In another similar type of studies done by Shruthi Dawalji *et al.* and Belhekar MN *et al.*, hypertension and diabetes were found to be the two most commonly associated co-morbidities with CAD. [1, 7]

As per the present study, anterior and inferior wall myocardial infarct (28%) was found to be the most commonly diagnosed category of CAD followed by Chronic stable angina (22%) and unstable angina (11.3%). In another study done by Kiran P. Vakade *et al.*, myocardial infarction (50%) was the most commonly diagnosed category of cardiovascular disease followed by unstable angina (36.58%). [14]

In the present study, on evaluating the data regarding the different classes of drugs prescribed to CAD patients, antiplatelet group of drugs was found to be the highly prescribed group (98.53%) followed by antihyperlipidemic group of drugs (97.40%), antianginal group of drugs (78.91%), antihypertensive group of drugs (68.09%) and anticoagulant group of drugs (63.02%). This finding was quite comparable with the findings observed in similar type of previous studies done by Sharma *et al.*, Alam *et al.*, Dawalji *et al.*, Patel *et al.*, Sandozi *et al.*, Mendis *et al.*, Belhekar MN *et al.*, Choudhury *et al.* and Thaker *et al.* [7, 15, 16, 17, 18, 19, 20, 21, 22]

In the present study, amongst the antiplatelet group of drugs prescribed, Aspirin and Clopidogrel combination was found to be the highest (64.98%) followed by Aspirin alone (28.03%) and Clopidogrel alone (6.97%) which is quite similar to a study conducted by Dawalji *et al.* wherein Aspirin and Clopidogrel combination was prescribed in 91.76 % of CAD patients, followed by Aspirin alone (5.92%) and Clopidogrel alone (1.78%). [1]

In the present study, the use of Enoxaparin sodium was higher (50.62%) followed by low molecular weight Heparin (42.57%) and Dalteparin sodium (6.79%) which is quite comparable to a similar type of finding found in a study conducted by Dawalji *et al.* wherein the use of Enoxaparin sodium (47.27%) and low molecular weight Heparin (40 %) were higher with very limited use of unfractionated Heparin. [1] In the present study, amongst the prescribed antianginal drugs, Nitrates (60.42%) were found to be highest

prescribed antianginal drugs which is quite similar to the observations of studies done by Banerjee S *et al.* and Dawalji *et al.* [1, 23]

In the present study, Atorvastatin (79.16%) was the most commonly prescribed anti-hyperlipidemic drug followed by Rosuvastatin (6.01%) and Fenofibrate (2.6%). In similar type of studies conducted by Banerjee S *et al.* and Dawalji *et al.*, Atorvastatin was the most highly prescribed anti-hyperlipidemic drugs. [1, 23]

In various studies conducted by Kiran P. Vakade *et al.*, Ian A. Scott *et al.*, Venus menon *et al.*, F venturini *et al.*; Aspirin and Clopidogrel combination was highest prescribed drug in the antiplatelet group of drugs, Atorvastatin was highest prescribed drug in anti-hyperlipidemic group of drugs and Nitrates were highest prescribed in antianginal group of drugs. All these findings were comparable to the respective findings of the present study. [14, 24, 25, 26]

In the present study the most commonly prescribed antihypertensive drugs was found to be Beta blockers (61.09%) followed by ACE inhibitors (20.36%), ARB's (14.91%) and Calcium channel blockers (10.11%). This finding is comparable to similar type of finding seen in a study conducted by Muntwyler *et al.* wherein the highest prescribed antihypertensive drug was found to be Beta blockers (58%) followed by ACE inhibitors / ARB's (50%). [27] In another study done by Dawalji *et al.*, it was also found that Beta blockers were the highest prescribed antihypertensive drugs (59.41%) followed by ACE inhibitors (27.06%) and CCB's (21.18%). [1] Beta blockers (65%) followed by ACE inhibitors (60 %) were also the highly prescribed antihypertensive drugs in a study conducted by Belhekar MN *et al.* [7]

Along with the various miscellaneous drugs, some fixed drug combinations were also found to be used in the present study in antihypertensive drugs, antiplatelet drugs, antianginal drugs, antihyperlipidemic drugs, bronchodilators etc.

In the present study, the average number of drugs prescribed per prescription was found to be 6.78 which is comparable to the finding of a previous study done by Sreedevi *et al.* where the average number of drugs prescribed per prescription was found to be 5.5. [28] Moreover, in this study 23.38 % of drugs were prescribed by generic name.

Limitations of this Study: The results of this study cannot be extrapolated to the entire population of that region as it was conducted only in one tertiary care teaching hospital and did not include the patients visiting other tertiary care teaching hospitals of that region.

Conclusion

In the present study conducted it has been observed that the incidence of CAD occurs more in case of male patients in comparison to their female counterparts. Moreover, the risk factor for CAD increases with age thereby showing higher incidence rate after 60 years of age. Hypertension and diabetes mellitus were the two most commonly found associated co-morbidities and they in turn have been found to increase the risk factors for CAD. The most commonly diagnosed category of CAD was found to be anterior and inferior wall myocardial infarct. The most commonly prescribed drugs for the treatment of CAD were found to be antiplatelete drugs (98.53%), antihyperlipidemic drugs (97.40%), antianginal drugs (78.91%), antihypertensive

drugs (68.09%) and anticoagulants (63.02%). Extensive polypharmacy was not seen as the average number of drugs per prescription was found to be 6.78 and 23.38 % of the drugs were prescribed by generic name.

After evaluating the findings of the present study, this conclusion could be drawn that drugs were prescribed to CAD patients in a rational manner as per the standard guidelines for CAD treatment. Since extensive polypharmacy was not there so it lead to less economic burden in medical treatment. Also 23.38% of prescribed drugs in generic name were available free of cost in the central pharmacy of the tertiary care teaching hospital.

Further such medical audits for prescription pattern analysis of CAD patients should be encouraged in near future. Such audits will help in highlighting the upcoming newer highly efficacious drugs, newer technologies like nanorobots for removing the atherosclerotic plaques etc to reduce the morbidity and mortality rates as well as to increase the life span of CAD patients in current scenario. Frequent awareness programs in form of seminars, continuing medical education i.e. CME's should be conducted amongst the practicing clinicians regarding the findings available after different prescription pattern analytical studies for CAD. This in turn will help the practicing clinician to assess the merits and demerits of current treatment procedure and will enable them to propose necessary changes in future if any required.

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