

## Study of drug utilization, morbidity pattern and cost of hypolipidemic agents in a tertiary care hospital

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### ABSTRACT

**Background:** Data on the extent of use and costs of lipid-lowering agents are not widely available. Our aim was to study the drug utilization and morbidity pattern, cost of different hypolipidemic drugs along with the risk assessment for coronary heart disease.

**Methods:** After approval of protocol by the Institutional Review Board, an observational, prospective study was carried out in 300 patients using NCEP and ATP III Guidelines-2002 for evaluation of presence or absence of risk factors for coronary heart diseases. Data were analysed using SPSS software version 16.0 and WHO Core Drug Prescribing Indicators.

**Results:** Patient's morbidity pattern revealed that 62%, 49.3%, 28% suffered from ischemic heart disease, hypertension and type 2 diabetes mellitus respectively. On risk assessment, 48%, 13.3% patients had borderline and high level of total cholesterol respectively; 42%, 22.7% had borderline and high triglyceride levels respectively; 71.1% men and 62% women had low HDL cholesterol levels while 17.3%, 6% and 2.7% patients had borderline high, high and very high level of LDL cholesterol levels respectively. Frequency of prescriptions was atorvastatin (82%), rosuvastatin (9.3%) and simvastatin (4.7%) among the most frequently prescribed statins drug group. The mean number of drugs per prescription was 7.34. Drugs prescribed by generic name and from essential drugs list was 24.96% and 71.81% respectively. Mean cost of hypolipidemic agents/prescription/day was 10.74 ( $\pm 1.96$ ) Indian Rupees with rosuvastatin being the costliest.

**Conclusion:** Rational use of hypolipidemic agents with an increasing trend of statins prescriptions will significantly reduce the morbidity and mortality from coronary heart diseases.

**Keywords:** Coronary heart disease, Dyslipidemia, Hypolipidemic agents, Statins

### INTRODUCTION

In India, Cardiovascular diseases (CVD) is projected to be the largest cause of death and disability by 2020 with 2.6 million. Indians are predicted to die due to coronary heart diseases, which constitutes 54.1% of all CVD deaths. It is estimated that, nearly half of these deaths are likely to occur among young and middle-aged individuals (30-79 years). This is because Indians experience CVD deaths at least a decade before their counterparts in the developed countries.<sup>1</sup>

Currently, lipid-lowering agents are widely used to reduce the risk of coronary events. However, there is wide variation in the selection and use of lipid-lowering agents.<sup>2,3</sup> Data on the extent of use and costs of lipid-

lowering agents are not widely available. Moreover, guidelines for management of dyslipidemia released by the U.S., National Cholesterol Education Program (NCEP)<sup>4</sup> have been questioned for their relevance in Indian populations because these populations are reported to have significantly different lipoprotein parameters and atherogenic risk factors than Western populations.<sup>5</sup>

Therefore, studies on the prescription pattern and costs of these drugs, particularly in our country are needed to better support decision making processes (from individual clinical setting to the wider national regulatory or public health settings). Hence, our objective was to study the utilization and morbidity pattern, and cost of different hypolipidemic drugs in hospitalized patients along with the risk assessment for coronary heart disease.

## METHODS

A prospective and observational study was carried out in 300 patients of either sex at a medicine outpatient department (OPD) at a tertiary care teaching hospital in Ahmedabad, India during 12 months period from June 2010 to May 2011. Patients who were prescribed any of the hypolipidemic medications irrespective of clinical condition either as monotherapy or in combination with other agents were included in the study. The study protocol, proforma, patient information sheet and informed consent form were approved by Institutional Review Board (IRB). All the patients were evaluated for presence or absence of risk factors for Coronary Heart Disease (CHD) based on the Third report of National Cholesterol Education Program (NCEP) – The Expert Panel; Adult Treatment Panel (ATP) III Guidelines-2002. The morbidity pattern and the risk assessment were studied by analysing the data of the patients collected in a pre-designed proforma which included patient's demographic details, presenting complaints, past and family history, co-morbidity, provisional diagnosis, laboratory investigations and complete prescription. The mean number of drugs per prescription, percentage of drugs prescribed by generic name and percentage of drugs prescribed from essential drugs list were analysed using WHO Core Drug Prescribing Indicators. Since, majority of the patients often required long-term or life-long therapy with hypolipidemic drugs, monthly cost of the drug was determined. Analysis of prescriptions containing hypolipidemic drugs was done using SPSS software version 16.0.

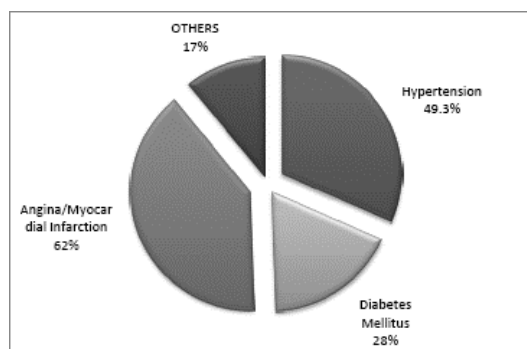
## RESULTS

Demographic pattern of the 300 patients enrolled in a one year study revealed that 166 (55.33%) were males and 134 (44.67%) were females. Majority of males and females were in the age group of 40-69 years and 50-79 years with mean age of 55.19 ( $\pm 11.11$ ) years and 57.18 ( $\pm 11.67$ ) years respectively. The demographic data demonstrated the influence of gender and age in disease and prescription pattern.

Morbidity patterns demonstrated that majority of the patients were diagnosed with ischemic heart disease which includes angina / myocardial infarction (62%) followed by hypertension (49.3%), type II diabetes mellitus (28%) and other diseases like stroke (5%), acute heart failure (9%), hypothyroidism (9%), complete heart block (6%), peripheral vascular disease (1%), osteoporosis (1%), acute renal failure (1%) and epistaxis (3%). This suggests that one patient may present with more than one diseases (Figure 1). Majority of the patients presented with complaints of chest pain (86%) followed by gabbhraman (36%), perspiration (26.7%), gastrointestinal (18.7%) and respiratory tract complaints (13.3%).

All the patients were evaluated for risk of Coronary Heart Diseases (CHD). based on the Third Report of the

National Cholesterol Education Program (NCEP) – The Expert Panel, Adult Treatment Panel (ATP) III Guidelines-2002. On identifying the level of risk factors, it was found that 77.2% males and 47.8% females were more than 45 years and 55 years of age respectively. 10.67% had history of CHD, 25.4% patients were smokers with or without tobacco chewing and 67.34% patients had low level of HDL cholesterol (Table 1).



**Figure 1: Morbidity pattern.**

Note: One Patient may have more than one diseases.

**Table 1: Risk factors for ischemic heart disease.**

| Sr. No. | Risk factors              | No. of patients (%) |
|---------|---------------------------|---------------------|
| Age     |                           |                     |
| 1       | Male > 45 yr              | 232 (77.20%)        |
|         | Female > 55 yr            | 143 (47.80%)        |
| 2       | History of CHD            | 32 (10.67%)         |
| 3       | Smoking                   | 76 (25.40%)         |
| Low HDL |                           |                     |
| 4       | Male <40 mg/dL            | 202 (67.34%)        |
|         | Female <50 mg/dL          |                     |
| 5       | Hypertension              | 148 (49.30%)        |
| 6       | Type II diabetes mellitus | 84 (28%)            |

The mean Baseline Plasma Lipid levels (mg/dL) were carried out in all patients. Lipid profile revealed mean ( $\pm$ SD) level of total cholesterol 207.13 ( $\pm 29.1$ ) mg/dL which was borderline high, triglycerides 161.62 ( $\pm 47.1$ ) mg/dL which was borderline high, HDL-C 41.5 ( $\pm 14.4$ ) mg/dL which was low for women, LDL-C 110.63 ( $\pm 31.4$ ) mg/dL which was near optimal and VLDL-C 40.97 ( $\pm 13.3$ ) mg/dL (Table 2). On risk assessment, it was found that 48% and 13.3% patients had borderline and high level of total cholesterol respectively; 42% and 22.7% had borderline and high triglyceride levels respectively; 71.1% men and 62% women had low HDL cholesterol levels while 17.3%, 6% and 2.7% patients had borderline high, high and very high level of LDL cholesterol levels respectively (Table 3).

**Table 2: Mean baseline plasma lipid level (mg/dL).**

| LIPID Parameters  | Mean (±SD)     |
|-------------------|----------------|
| Total Cholesterol | 207.13 (±29.1) |
| Triglycerides     | 161.62 (47.1)  |
| HDL – C           | 41.5 (±14.4)   |
| LDL – C           | 110.63 (±31.4) |
| VLDL – C          | 40.97 (±13.3)  |

**Table 3: Risk assessment based on plasma lipid level.**

| Plasma Lipid Level (mg/dL) | Comments                   | No. of Patients (%) |
|----------------------------|----------------------------|---------------------|
| <b>Total Cholesterol</b>   |                            |                     |
| < 200                      | Desirable                  | 116 (38.7%)         |
| 200-239                    | Borderline High            | 144 (48.0%)         |
| >240                       | High                       | 40 (13.3%)          |
| <b>Triglycerides</b>       |                            |                     |
| <150                       | Normal                     | 106 (35.3%)         |
| 150-199                    | Borderline High            | 126 (42.0%)         |
| 200-499                    | High                       | 68 (22.7%)          |
| >500                       | Very High                  | -----               |
| <b>HDL – C</b>             |                            |                     |
| < 40                       | Low (Men)                  | 118 (71.1%)         |
| < 50                       | Low (Women)                | 84 (62.7%)          |
| <b>LDL – C</b>             |                            |                     |
| < 70                       | Optimal for very high risk | 20 (6.70%)          |
| < 100                      | Optimal                    | 102 (34.0%)         |
| <100 – 129                 | Near optimal               | 120 (40.0%)         |
| 130 – 159                  | Borderline High            | 52 (17.3%)          |
| 160 - 189                  | High                       | 18 (6.0%)           |
| >190                       | Very High                  | 8 (2.7%)            |

Ref: Third Report of the National Cholesterol Education Program (NCEP) - The Expert Panel, Adult Treatment Panel (ATP) III Guidelines-2002.

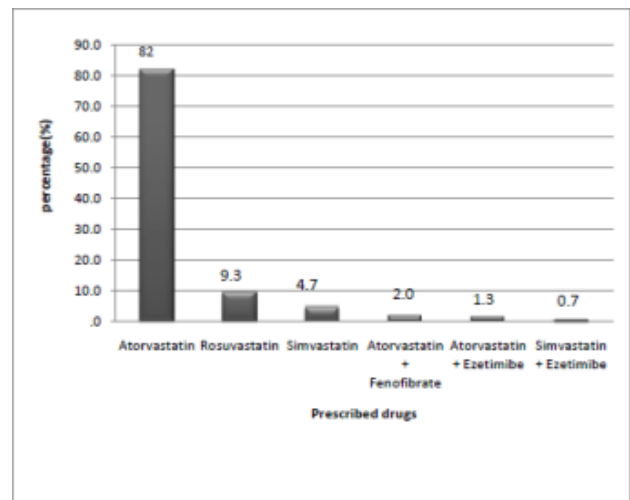
Total 2203 drug formulations were distributed among 300 prescriptions. Apart from hypolipidemic agents, patients were prescribed concomitant drugs based on morbidity patterns. On prescription analysis, it was revealed that 96% of the patients received statins. Fibrin acid derivatives (Fenofibrate) and Cholesterol absorption inhibitors (Ezetimibe) were used rarely (4%) and only in combination with statin in patients with severe dyslipidemia not controlled by statin monotherapy. Among statins, atorvastatin (82%) was most commonly prescribed, followed by rosuvastatin (9.3%) and simvastatin (4.7%) (Figure 2). Apart from hypolipidemic agents, concomitant drugs used were antiplatelets (96.7%), nitrates (88.3%), beta blockers (79.3%), ACE inhibitors/ARBs (75.6%), anticoagulants (62.3%), fibrinolytics (49.3%), diuretics (35.4%), calcium channel

blockers (15.0%), oral hypoglycemic agents (27.6%) and insulin (5.3%). This suggests that one patient may had taken more than one drug because majority of the study populations had one or more risk factors.

As majority of the patients often require long-term or life-long therapy with hypolipidemic agents, monthly cost were analysed. The mean cost of hypolipidemic agents / prescription / day was 10.74 (± 1.96) INR (Indian Rupees) with rosuvastatin being the costlier (Table 4).

**Table 4: Cost of various hypolipidemic agents.**

| Drug                                    | Total Cost/month (INR) Mean ± SD |
|---|----------------------------------|
| Atorvastatin -10 mg                     | 187 ± 11.3                       |
| 20 mg                                   | 362.89 ± 11.2                    |
| 40 mg                                   | 468 ± 12.2                       |
| Mean                                    | 327.3 ± 11.4                     |
| Rosuvastatin -5 mg                      | 186 ± 22.2                       |
| 10 mg                                   | 447.7 ± 20.5                     |
| 20 mg                                   | 795 ± 45.7                       |
| Mean                                    | 422.7 ± 43.5                     |
| Simvastatin -10 mg                      | 174 ± 33.5                       |
| 20mg                                    | 335 ± 11.5                       |
| Mean                                    | 312 ± 56.7                       |
| Atorvastatin+Ezetimibe (10mg+ 10mg)     | 304.8 ± 3.5                      |
| Atorvastatin + Fenofibrate (10mg+ 10mg) | 327                              |
| Simvastatin + Ezetimibe (10mg+ 10mg)    | 240                              |



**Figure 2: Prescription of hypolipidemic agents.**

The mean number of drugs per prescription according to WHO Core Drug Prescribing Indicators were found to be 7.34 ± 1.4 in our study. The percentage of drugs prescribed by generic name was 24.96%. Percentage of

drugs prescribed from essential drugs list was 71.81% (Table 5).

**Table 5: WHO core drug prescribing indicators.**

| Sr. No. | Indicator   | Value             |
|---------|---|-------------------|
| 1.      | Mean ( $\pm$ SD) number of drugs per prescription       | 7.34 ( $\pm$ 1.4) |
| 2.      | Percentage of drugs prescribed by generic name          | 24.96             |
| 3.      | Percentage of encounters with antibiotic prescribed     | 23.67             |
| 4.      | Percentage of encounters with an injection prescribed   | 91.67             |
| 5.      | Percentage of drugs prescribed from essential drug list | 71.81             |

## DISCUSSION

In the present study, the demographic data demonstrated that baseline study population was comparable to earlier studies done in India and abroad with an influence of gender and age in prescription patterns, as reported in other studies.<sup>6,7</sup> In our study males (55.33%) were more on hypolipidemic therapy compared to females (44.67%) which may be due to the contributing risk factors like smoking, alcohol intake, diet rich in saturated fat seen commonly in males in India. The findings are in accordance with the study carried out in Hyderabad.<sup>8</sup> Majority of males and females were in the age group of 40-69 years and 50-79 years respectively which is in accordance with the study carried out in Mumbai.<sup>9</sup> This was not surprising since the risk of Coronary Heart Disease (CHD) is high in this age group.

On identifying the level of risk factors it was found that majority of the study populations had one or more risk factors which are associated with increased risk of CHD event. Apart from risk factors for CHD, assessment of plasma lipids was essential to guide and monitor the treatment. Therefore, Mean Baseline Plasma Lipid levels (mg/dL) were carried out in all patients. Lipid profile revealed that mean ( $\pm$ SD) level of total cholesterol 207.13 ( $\pm$ 29.1) mg/dL which was borderline high, triglycerides 161.62 ( $\pm$ 47.1) mg/dL which was borderline high, HDL-C 41.5 ( $\pm$ 14.4) mg/dL which was low for women, LDL-C 110.63 ( $\pm$ 31.4) mg/dL which was near optimal and VLDL-C 40.97 ( $\pm$ 13.3) mg/dL. On risk assessment, it was found that 48% and 13.3% patients had borderline and high level of total cholesterol respectively, 42% and 22.7% had borderline and high triglyceride levels respectively, 71.1% men and 62.7% women had low HDL cholesterol levels while 17.3%, 6% and 2.7%

patients had borderline high, high and very high level of LDL cholesterol levels respectively. The findings are in accordance with the study carried out in North India. Thus, risk assessment revealed that majority of the patients were at risk of developing CHD, thereby requiring lipid-lowering treatment prior to development of clinical CHD.

The prescription analysis of hypolipidemic agents revealed that 96% of the patients received statins. Fenofibrate and Ezetimibe were used rarely (4%) and only in combination with statins in patients with severe dyslipidemia not controlled by statin monotherapy. Among statins, atorvastatin (82%) was most commonly used, followed by rosuvastatin (9.3%) and simvastatin (4.7%). Similar prescription patterns were found in studies carried out in European countries<sup>10</sup> and Indian cities such as Jaipur<sup>11</sup> and Hyderabad.<sup>8</sup> This suggests a more rational use of hypolipidemic agents with a higher prescription of first-line drugs for the treatment of dyslipidemia – statins. This is recommended as the most effective and better tolerated therapy for lowering LDL-C – together with the reduced use of older, less effective drugs.<sup>12</sup> Several trials have indicated that cholesterol lowering therapy with statins reduces the numbers of coronary deaths and nonfatal myocardial infarctions.<sup>13,14</sup> Thus active treatment of hypercholesterolemia significantly reduces the risk of morbidity and mortality from CHD.

Apart from hypolipidemic agents, patients were prescribed concomitant drugs such as antiplatelets (96.7%), nitrates (88.3%), beta-blockers (79.4%), ACE- inhibitors / Angiotensin Receptor Blockers (75.6%), anticoagulants (62.3%), fibrinolytics (49.3%), oral hypoglycaemic agents (27.6%) which can be justified, as the prevalence of ischemic heart disease (62%), hypertension (49.3%) and type II diabetes mellitus (28%) were high in the present study population. The findings are in accordance with the studies carried out in North America,<sup>15</sup> Indian CREATE registry,<sup>16</sup> Jaipur<sup>11</sup> and Mangalore.<sup>17</sup>

The cost analysis revealed that the mean cost of hypolipidemic agents / prescription / day was 10.74 ( $\pm$  1.96) INR (Indian Rupees) which was higher than the study carried out in Mangalore,<sup>17</sup> This could be because of promoting and prescribing drugs by brand names (75.04%). Rosuvastatin was costlier as compared to other statins prescribed alone or in combination. The practice of prescribing drugs with generic names or choosing less expensive brands should be encouraged which will be cost-effective.

Average number of drugs per prescription is an important index of clinical judgement of the prescribers and intervention in prescribing practices. According to WHO core drug prescribing indicators, the mean number of drugs per prescription were found to be 7.34  $\pm$  1.4 in our study, which are comparable to the studies conducted in Brazil (8.6) and Hyderabad (5.5) suggesting

polypharmacy. However, in certain conditions like cardiovascular problems, the patients may require more than one drug.<sup>8,18</sup>

Moreover, percentage of drugs prescribed by generic names were only 24.96% suggesting greater tendency to prescribe drugs by brand names which may be due to greater influence of the pharmaceutical companies on the prescribing habits thereby increasing the cost of therapy. Percentage of drugs prescribed from essential drugs list were 71.81%. This suggests that the compliance of the patient may be better due to availability of drugs at affordable price.

## CONCLUSION

The study depicts that over-all prescribing habit in this set-up is appropriate and rational to a large extent. Only step-back is the lesser number of drugs prescribed by generic name suggesting need for sincere efforts to improve situation. The use of statins was higher in the study which is recommended as the most effective and better tolerated first-line therapy for dyslipidemia. Such a rational use of hypolipidemic will significantly reduce the morbidity and mortality from coronary heart disease. This is the preliminary study and further studies are required to find out broader evaluation of the hypolipidemic agents. Hence, such periodic studies are further required in diverse environment, social, educational and cultural conditions, so that the therapeutic guidelines could be revised accordingly to give proper care to the community.

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*Ethical approval: The study was approved by the Institutional Review Board*

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