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## Are we Falling Short from protecting our Hypertensive Patients? A Drug Utilization Study of Aspirin and Lipid Lowering Agents in Diabetic and Non-Diabetic Hypertensive Patients.

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### ABSTRACT

The worldwide prevalence and the number of patients on antihypertensive treatment with CV complications is increasing. Present drug utilization study was aimed at finding the trends of use of aspirin and lipid lowering agents in hypertensive patients. Hypertensive patients of all age group consenting to contribute their data were enrolled. No personally identifiable information was collected about the patient / prescriber. Data about drugs prescribed for hypertension and aspirin and lipid lowering agents was copied. It was observed that in 58.13 % non - diabetic hypertensive patients and 57.63 % diabetic hypertensive patient's aspirin and/or lipid lowering agents were prescribed. Generic drugs' prescriptions were 0 %. This has increased the cost of prescription. The observations in the present study pointed a lesser incidence of use of aspirin and lipid lowering agents, to as advocated. Multiple studies have pointed usefulness of concomitant use of aspirin and lipid-lowering agents for reduction in future complications. The study data showed much less prescribing of aspirin and / or lipid-lowering agents. This may prove a factor in increased long term complications specially in diabetic patients. This study has pointed a shortfall in protection of prospective cardiovascular complications in hypertensive patients which needs an attention; may be through some educational intervention .

**Keywords:** aspirin, lipid-lowering agents, drug utilization, hypertensive patients

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## INTRODUCTION

India is on the borderlines of a cardiovascular diseases epidemic. Hypertension is the most common cardiovascular disease, posing a major public health challenge to socioeconomic and epidemiological transition. It is one of the major risk factors for cardiovascular mortality, which account for 20 – 50 % of all deaths.

Elevated arterial pressure causes pathological changes in the vasculature & hypertrophy of the left ventricle. As a consequence, hypertension is the principle cause of stroke, leads to disease of the coronary arteries with myocardial infarction & sudden death & is a major contributor to cardiac failure, renal insufficiency & dissecting aneurysm of the aorta.

A lot of studies have observed the effects of control of hypertension and its effect on reduction of future complications. Effective anti-hypertensive treatment will almost completely prevent hemorrhagic stroke, cardiac failure, and renal insufficiency particularly in diabetic patients [1,2,3].

Consistent drug treatment decreases both mortality and morbidity associated with hypertension. In clinical practice, however, poor compliance, intermittent or switched prescriptions, and termination of use of drugs disrupts the consistency of treatment. The resulting suboptimal treatment is associated with progression of coronary atherosclerosis, congestive heart failure, and renal disease as well as considerably higher rates of readmission to hospital for hypertensive crises [4].

A lot of guiding principles in the form of guidelines are available for treatment of hypertension e.g. JNC VII, National guidelines for India etc. Guidelines are also laid down for concomitant use of antiplatelet agents and lipid lowering agents. However whether they are followed or else is a question [5,6]. JNC VIII is published and under the cloud of counter statements and hence not considered for discussion.

The risk of cardiovascular disease, disability & death in hypertensive patients also is increased markedly by concomitant cigarette smoking & by elevated low-density lipoprotein. Hence by addition of lipid lowering agents and antiplatelet agents to the treatment reduction in risk is predicted and observed by researchers [7-11]. Appropriate addition of antiplatelet and lipid lowering agents in regular treatment of hypertension is thus advocated by some researchers [7-11].

The present study was aimed at finding the trends of use of Aspirin and Lipid lowering agents in hypertensive patients.

## MATERIALS AND METHODS

After appropriate ethical clearance this study was undertaken from Feb 2010. Data was collected till August 2013. Prescriptions were collected from randomly selected pharmacy stores in each area selected for data collection. Adult patients from both sex and all ages were considered for inclusion.

**Inclusion Criteria**

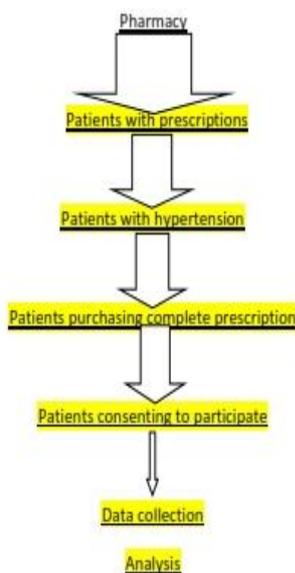
- Patients who are diagnosed hypertensive and receiving treatment for the same.
- Patients not suffering and receiving medication for any other major disease except diabetes as indicated by their information or prescription.

**Exclusion Criteria**

- Patients not willing and consenting to participate in the study.
- Patients who do not verbally confirm regular use of the drugs.
- Patients being treated by prescriptions from Ayurvedic or homeopathic or Unani physicians.
- Patients who do not have prescriptions at the time of purchase of drug from the pharmacy.
- Patients receiving drugs in the same prescription for any other ailment not influencing or not related with hypertension; for example any infection or contraceptive advice etc.

Patients fulfilling the inclusion criteria were eligible to be included in the study. Out of such patients, patients were selected randomly and with their consent included for collection of data. Randomisation was carried out to achieve sufficient representation of the population under scrutiny. Prescriptions of such patients were copied, without retrieving any personally identifying feature of the prescribing physician. The data was recorded from the copies of these prescriptions and analysed. Results were expressed in percentages of sample size. A total of 12,632 prescriptions were collected from Pune, Pimpri-Chinchwad, Kolhapur and Sangli in Western Maharashtra with a care to sample each area almost equally.

**Fig.1 Indicating the process of data collection**



*(The process of patient enrolment and data collection area of arrow approx. indicative of no. of patients)*

**RESULTS**

Totally more than 15,000 hypertensive patients were screened out of which 12,632 consented to contribute their data in the study. Out of the total 12,632 prescriptions recorded during the study. 1231 prescriptions had prescribing error like non-legible handwriting and hence only 11,401 prescriptions were subjected to detailed drug utilization analysis. Out of the total prescriptions analyzed in the present study (n = 11,401) the prescriptions issued to Non-DM patients was n = 5308 [46.55 %] and to DM patients was n = 6093 [53.45 %]

**Table 1 Aspirin and or Lipid lowering agents in hypertensive patients**

Drug	Non - Diabetic hypertensive Patients	Diabetic hypertensive Patients
Aspirin alone	33.06 % 1755	29.80 % 1816
Lipid lowering agents alone	45.21 % 2400	48.48 % 2954
Aspirin and lipid lowering agents	46.72 % 2480	49.71 % 3029

at p< 0.05, NS = Not Significant as compared to the Non- diabetic hypertensive patients

It was observed that in 58.13 % non - diabetic hypertensive patients and 57.63 % diabetic hypertensive patients the aspirin and/or lipid lowering agents were prescribed. By Chi-square test non-Significance at p<0.05 indicates that both groups are equally unprotected. Since no guideline has unequivocally produced an exact figure of patients who must have aspirin and / or lipid lowering agents , the figures cannot be further analyzed for statistical significance.

**Table2: Use of Aspirin and or lipid lowering agents in hypertensive patients**

	Non - Diabetic hypertensive Patients	Diabetic hypertensive Patients
Aspirin and /or lipid lowering agents	3086 i.e. 58.13 % of 5308	3512 i.e. 57.63 % of 6093

at p< 0.05 NS = Not Significant as compared to the Non- diabetic hypertensive patients

**Table 3: Cost of hypertension treatment (Rs.) per day observed in hypertensive patients**

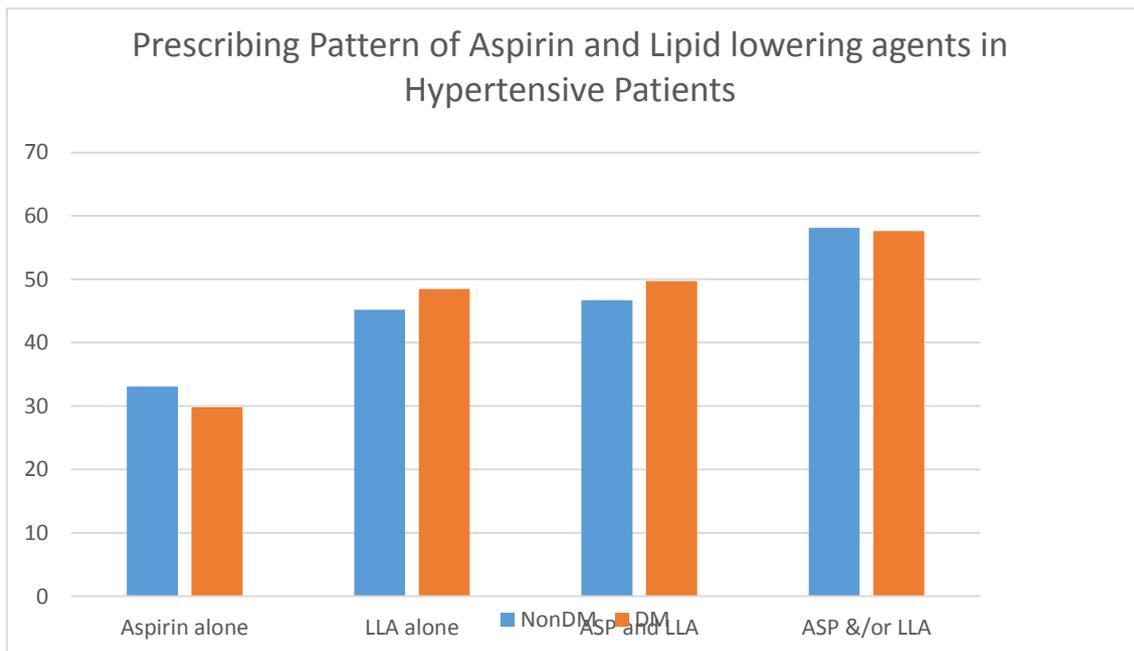
	Non - Diabetic hypertensive Patients	Diabetic hypertensive Patients
Average cost of treatment per day (Rs.)	4.11	4.55

**Table4: Increase in the cost per day observed in case of additional use of aspirin and or lipid lowering agents in hypertensive patients.**

Type of drug treatment	Increase in the cost per prescription (Rs.)
Aspirin alone	0.29
Lipid lowering agents alone	3.79*
Aspirin and Lipid lowering agents	4.18*

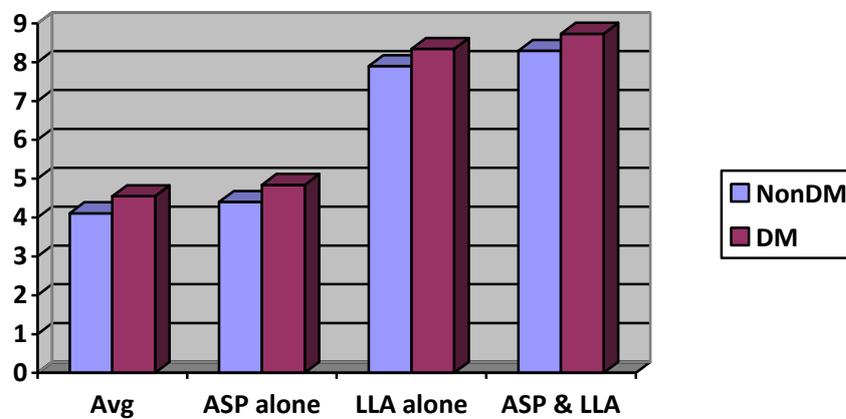
At p<0.05 results were statistically significant for cost elevation

**Fig. 2 Prescribing Pattern of Aspirin and Lipid lowering agents in Hypertensive Patients**



Legends: ASP – Aspirin, LLA – Lipid Lowering Agents, NonDM – Non- Diabetic , DM- Diabetic

**Fig.3 Increase in cost of prescription because of branded drugs’ prescription**



ASP – Aspirin, LLA – Lipid Lowering Agents, NonDM – Non- Diabetic , DM- Diabetic  
Avg – Average cost of prescription of hypertensive drugs alone

## DISCUSSION

Hypertension is known to be associated with an increased risk of thrombotic complications (strokes, myocardial infarction), as mentioned by Nadar et al 2003, Lip et al 2003, these are likely to result from the prothrombotic or hypercoagulable state associated with this condition [8,11]. The use of aspirin in high-risk hypertensive patients leads to a reduction in intra-platelet angiogenic growth factors and platelet activation. Aspirin is the most widely used antiplatelet agent for reducing the risk of cardiovascular and cerebrovascular events in both primary prevention and secondary prevention [7]. Its mode of action is inhibiting cyclooxygenases (COX) enzymes that catalyze the conversion of arachidonic acid to eicosanoids and thus may play an important role in platelet-vessel wall interactions. Thromboxane is the major COX product in platelets, and its biosynthesis is increased in conditions associated with platelet activation such as unstable angina and peripheral vascular disease. Therefore, its inhibition leads to a reduction in platelet activation [12-14].

Diabetes is now accepted as a multi system metabolic disorder and is associated with lipid abnormalities. Vijan et al in two different studies in diabetics express that, due to the epidemiology of diabetes complications, emphasize management of cardiovascular risk in diabetics. As expressed by Vijan et al- by treating hypertension and using lipid-lowering agents along with anti-hypertensive drugs modify the cardiovascular complication risks. This in diabetic patients is of importance and may prove to be more effective and cost-effective.- The present authors agree with this statement. The goal of therapy in type 2 diabetes should aim at preventing cardiovascular disease through optimization of risk factor modification. This includes aggressive treatment of hypertension [9,10]. Current medical evidence suggests that lipid-lowering medications lead to about a 22 % to 24 % reduction in major cardiovascular events in patients with diabetes. Hence most patients with diabetes should be taking at least moderate dosages of statins [10].

The ASCOT and ALLHAT-LLT studies contributed a lot to formulation of concepts about use of statins in hypertensive patients. The present recommendations made therefore indicate the utility of statins, especially in high risk patients like diabetics.

The area in which the present study was conducted is primarily urban area, well served by many doctors practicing modern medicine. Hence the findings indicate representative present prescribing trends. The present study finds, the state of present prescribing behaviors in the urban area and possible high risk (high risk as indicated by WHO) behavior. Thus the results of this study give some important information and pose some questions.

In the present study it was observed that in 57 % diabetic hypertensive and 58% non-diabetic hypertensive patients aspirin and/or lipid lowering agents were prescribed. Similarly aspirin alone and lipid lowering agents alone are also being prescribed. The use of lipid lowering agents alone is almost double the use of aspirin alone.

These results are consistent with present guidelines. However the use of these agents is still falling short of its expected values indicated in guidelines and various studies.

The present study has not evaluated use of other antiplatelet agents as their use was being studied in many studies and not completed when this study was planned as mentioned also by Cochrane review [17].

Since we can not find any study published from the same area. Closest was data from a previous study done at Pune area ,but it was before 2007, hence we did not compare the historical data with our study observations.

In comparison to present guidelines published, this study indicates still a significant shortfall in prescribing of lipid lowering agents as well as aspirin. Predictions mentioned in the published data indicate that this may reduce protection of these patients to increased risks of cardiovascular complications [7-17]. Similarly 0 % prescriptions contained generic drugs (aspirin and lipid-lowering agents) contributing to increase in cost of prescription. This increase in cost can prove detrimental for patient compliance in a subset of patients who are very old, poor, and dependents. This in turn can predispose these patients to a reduced protection from increased risk of cardiovascular complications.

### CONCLUSION

It is expressed that drug utilizations studies will contribute towards creating National Drug Policies. It is also observed that there is a guidelines incongruency in treatment of Hypertension by some studies in US and Bahrain. In India in general prescription analysis studies such errors are also observed. Such behavior contributes to sub optimal treatment of the disease as feared by some researchers [18-22]. Hence such studies are advocated. In the present study prescribing practices in urban areas was evaluated. It highlights prescribing errors. These include guideline incongruency, increased cost. These are preventable errors. And they are not done by junior doctors as some have projected in some studies [5]. This also underlines the fact that 'physicians must be committed to lifelong learning and responsible for maintaining their own medical knowledge' [23-25]. Contrary to expectations, use of statins was found low. None of the agents were given in generic form. This contributed to high cost of prescriptions.

The use of aspirin and statins are advocated with specific guidelines. Despite these guidelines use of these agents is guideline incongruent and with high cost brands.

Whether educational or other interventions are needed and in what format can be evaluated by a larger prospective study. Such a multi centric study will be helpful in giving guidelines for concomitant use of statins and / or aspirin in hypertensive patients.

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