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## ANTIHYPERTENSIVE MEDICATION PRESCRIBING PATTERNS IN A UNIVERSITY TEACHING HOSPITAL IN SOUTH DELHI

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### ABSTRACT

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**Study objective:** To investigate the use of antihypertensive drugs in hypertensive patients and to identify whether such pattern of prescription is appropriate in accordance with international guidelines for management of hypertension.

**Methods:** This was a prospective analysis. A prescription based survey among patients with established hypertension was conducted at the Medicine Out-Patient Department of University Teaching Hospital in South Delhi, India. Data were collected from patients' medical records as well as patients' interviews.

**Results:** A total of 192 hypertensive patients fulfilled the criteria for inclusion in the study analysis. Combination therapy was used more commonly than monotherapy (54.6% vs 45.4). Among the monotherapy category, the various classes of drugs used were as follows: beta- blockers (28.8%), diuretics (24.1%), calcium channel blockers (21.8%), ACE inhibitors (18.4%), angiotensin II receptor blockers (5.7%) and  $\alpha$  1- blocker (1.1%). With respect to overall utilization pattern, diuretics (42.2%) were the most frequently prescribed class, beta- blockers (41.2%) ranked second followed by calcium channel blockers (39.1%), ACE inhibitors (26.0%), angiotensin II receptor blockers (23.4%) and  $\alpha$  1- blocker (9.4%). As for individual medicines, amlodipine (35.4%) was the most commonly prescribed antihypertensive drug followed by atenolol (17.8%), ramipril (17.2 %) and furosemide (13.0 %). Among the combination therapies, 2- drug treatment was preferred for 75% of the hypertensive patients with CCB and  $\beta$ -blocker being the most frequent drug combination (22.4%).

**Conclusion:** The general pattern of antihypertensive utilization seems to be in accordance with the international guidelines for management of hypertension.

**INTRODUCTION:** Hypertension is associated with fibrillation, heart failure, peripheral vascular disease, increased risk of stroke, myocardial infarction, atrial and renal disease<sup>1</sup>.

The World Health Report 2002 of the World Health Organization (WHO) states that high blood pressure is the primary or secondary cause of 50% of all cardiovascular diseases worldwide <sup>2</sup>.

The worldwide burden of hypertension in 2000 was estimated to be 972 million or 26.4% of the adult world population, with 333 million in economically developed and 639 million in economically developing countries. It has been estimated that by 2025, 1.56 billion individuals will have hypertension; an increase of 60% from 2000. Most of this rise can be attributed to an expected increase in the number of people with hypertension in economically developing countries. On the basis of these estimates, almost three-quarter of the world's hypertensive population will be in developing countries <sup>3</sup>.

Hypertension is highly prevalent in India. Data on nationwide survey are unavailable, but there are abundance of region based and local population-based studies on prevalence of hypertension. The Hypertension Study Group, in their multi-centre study in India, found that the overall prevalence of hypertension among elderly individuals was 65% <sup>4</sup>. In India, the various studies estimated a prevalence rate of hypertension among urban population ranging from 1.24% in 1949 to 36.4% in 2003, and for rural people from 1.99% in 1958 to 21.2% in 1994 <sup>5</sup>.

Bharucha study showed a progressively increasing prevalence with age, with 56.3% of those  $\geq 60$  years and 64.2% of those  $\geq 70$  years having hypertension <sup>6</sup>. Few studies were also carried out comparing different socio economic groups. In the initial study from urban Chennai, Mohan *et al.*, <sup>7</sup> reported 8.4% prevalence of hypertension among men and women aged 20 years and above and belonging to the low socio economic group (based on household income, occupation and dietary pattern). Misra *et al.*, <sup>8</sup> reported 12% prevalence of hypertension in the slums of Delhi.

A number of national and international guidelines for the treatment of hypertension have been published. The JNC 7 guidelines recommend diuretics as the first line treatment in hypertension <sup>9</sup>. The European guidelines, on the other hand, suggest that unless a special indication exists, any of the five anti hypertensive classes can be used as first line treatment

<sup>10</sup>. A combination treatment has been recommended as first line intervention, particularly in patient with severe hypertension <sup>9</sup>. A number of drug in various combinations are generally used for effective long term management <sup>11</sup>.

Changes over time in terms of recommended guidelines and innovation in drug formulations have resulted in modification to the prescription patterns of antihypertensive drugs. Therefore, drug utilization studies, which evaluate, and analyze the medical, social, and economic outcomes of the drug therapy are more meaningful, and observe the prescribing attitude of physicians with the aim to provide drug rationally <sup>12</sup>. This kind of medical audit highlights the lacunae in the present prescribing practice of physicians and help in improving the patient health care further <sup>13</sup>.

The present prescription monitoring study for antihypertensive drugs was undertaken in the medicine outpatient department (OPD) of university teaching hospital. The purpose of this study was to investigate the use of antihypertensive drugs in hypertensive patients in order to establish the current trend of pattern of prescribing of antihypertensive drug; and to identify whether such pattern of prescription is appropriate and accordance with international guidelines for pharmacotherapy of hypertension.

**METHODS:** It was a prospective analysis of medicine utilization patterns in patients with established hypertension. The study protocol was assessed and approved by Jamia Hamdard Institutional Review Board (Approval letter No. JHIRB 07/07, February 15, 2007). The study was carried out in the medicine outpatient department (OPD) of Majeedia hospital, a 150 staffed bed teaching hospital in New Delhi that caters to the health needs of low socioeconomic group population of South Delhi and a campus community consisting of students, faculty, non-teaching and administrative staff and their family members.

The patients included were those who were registered in the medicine OPD during the period February 2007-June 2007. An informed consent was taken from patients participating in the study. All hypertensive patients irrespective of age and sex visiting medicine OPD and treated with at least one antihypertensive

agent were included in the study. Patients who were not treated with antihypertensive drug, mentally retarded and unconscious patients (patients depending on other people for medication administration), drug addicts and patients unable to comply were excluded from the study. The following data were collected: age, sex, registration number, height, weight, waist circumference, hip circumference, diagnosis, duration of illness. Each drug prescribed to the patient was noted as follows: brand/generic name, indication, route of administration, dose, frequency of administration and date of starting the drug.

**RESULTS:** During the study period, a total of 192 hypertensive patients fulfilled the criteria for inclusion in the study analysis. Demographic characteristics of these 192 patients are presented in **Table 1**. Of the 192 hypertensive patients 87 (45.4%) were males and 105 (54.6%) were females indicating that hypertension is slightly more prevalent in the female gender. The mean age of the patients included in the study was found to be  $48.5 \pm 14.5$  years. The age distribution of hypertensive patient was 15 (7.8%) below the age of 30 years, 135 (70.3%) were between 30 and 60 years and 42 (21.8%) were above 60 years.

**TABLE 1: DEMOGRAPHIC CHARACTERISTICS OF HYPERTENSIVE PATIENTS**

Demographic parameter	All (%)	Male (%)	Female (%)
Gender	192 (100)	87 (45.4)	105 (54.6)
<b>Age groups (years)</b>			
Under 30	15 (7.8)	12 (13.8)	03 (2.8)
31-40	48 (25.0)	20 (23.0)	28 (26.6)
41-50	49 (25.5)	11 (12.6)	38 (36.2)
51-60	38 (19.8)	23 (26.4)	15 (14.3)
61-70	25 (13.0)	12 (13.8)	13 (12.4)
71-80	15 (7.8)	07 (8.0)	08 (7.6)
Above 80	02 (1.0)	02 (2.3)	---
<b>Body mass index (kg/m<sup>2</sup>)</b>			
<18.5 (Under weight)	13 (6.8)	06 (6.9)	07 (6.7)
18.5-22.9 (Normal range)	60 (31.2)	38 (43.7)	22 (20.9)
23-24.9 (Over weight)	45 (23.4)	22 (25.3)	23 (21.9)
25-29.9 (Pre-obese)	47 (24.5)	18 (20.7)	29 (27.6)
>30 (Obese)	27 (14.1)	03 (3.4)	24 (22.8)
<b>Waist Circumference (Cm)</b>			
< 90	----	69 (79.3)	----
> 90	----	18 (20.7)	----
< 80	----	----	46 (43.8)
> 80	----	----	59 (56.2)
<b>Waist-Hip Ratio</b>			

**TABLE 2: PATTERNS OF USE OF VARIOUS CLASSES OF ANTIHYPERTENSIVE DRUGS AS MONOTHERAPY AND OVERALL UTILIZATION IN HYPERTENSIVE PATIENTS**

Antihypertensive class	Overall prescriptions frequency (%)	Monotherapy prescriptions frequency (%)
Diuretics	82 (42.2)	21 (24.1)
$\beta$ -Blockers	79 (41.2)	25 (28.8)

$\leq 0.95$	----	56 (64.4)	----
$> 0.95$	----	31 (35.6)	----
$\leq 0.85$	----	----	19 (18.1)
$> 0.85$	----	----	86 (81.9)

The maximum number of male hypertensive patients belonged to the age group of 51-60 years whereas female patients were the highest in the age group of 41-50 years. The mean body mass index (BMI) of the study population was  $24.10 \pm 4.62$  kg/m<sup>2</sup>.

Out of 192 hypertensive patients a total of 74 (38.5%) had a BMI  $> 25$  kg/m<sup>2</sup>, 18% of the male and 59% of the female patients had a waist circumference higher than the normal limits of  $> 90$  cm and  $> 80$  cm respectively whereas 86% of the female and 31% of the male patients had a waist-hip ratio higher than the acceptable limits (i.e.,  $> 0.85$  in females and  $> 0.95$  in males).

A total of 87 (45.3 %) patients received monotherapy. The majority (n= 105) of the subjects (54.7%) were on the multiple drug therapy. **Table 2** presents the prescription pattern and rate of antihypertensive drug prescribed for hypertensive patients both as monotherapy and overall utilization profile (mono and combined therapies).

Among the monotherapy category, the various classes of drugs used were as follows  $\beta$ -blockers (28.8%), diuretics (24.1%), calcium channel blockers (21.8%), ACE inhibitors (18.4%), angiotensin II receptor blockers (5.7%) and  $\alpha 1$ - blocker (1.1%).

Amlodipine (21.8 %) was the most commonly prescribed antihypertensive agent as monotherapy followed by propranolol (17.3 %). However incase of overall utilization pattern of antihypertensive agents, diuretics (42.2%) were the most frequently prescribed class,  $\beta$ -blockers (41.2%) ranked second followed by calcium channel blockers (39.1%), ACE inhibitors (26.0%), angiotensin II receptor blockers (23.4%) and  $\alpha 1$ - blocker (9.4%). Amlodipine (35.4%) was the most commonly prescribed antihypertensive drug followed by atenolol (17.8%), ramipril (17.2 %) and furosemide (13.0 %).

Calcium Channel Blockers	75 (39.1)	19 (21.8)
ACE Inhibitors	50 (26.0)	16 (18.4)
Angiotensin II Receptor Blockers	45 (23.4)	05 (5.7)
$\alpha$ 1- Blocker	18 (9.4)	01 (1.1)

A total of 105 (54.7%) patients received some combination of antihypertensive agents (**Table 3**). The most prevalent combination of drug was a 2-drug therapy of CCBs +  $\beta$ -blockers which was found to be 22.4% followed by ACEI + Diuretics (7.8%). Among the three drug combinations, ACEIs,  $\beta$ -blockers and calcium channel blockers comprised the most commonly prescribed combination (**Table 4**).

**TABLE 3: SINGLE ANTIHYPERTENSIVE THERAPY VS. MULTIPLE ANTIHYPERTENSIVE THERAPIES**

Drug therapy prescribed	No. of prescriptions	% of prescriptions
<b>Single drug therapy</b>	87	45.3
<b>Multidrug therapy</b>		
2 drug therapy	79	75.2
3 drug therapy	19	18.1
4 drug therapy	07	6.7
Total	105	54.7

**TABLE 4: PATTERNS OF USE OF ANTIHYPERTENSIVE COMBINATION THERAPY AMONG HYPERTENSIVE PATIENTS**

Combination therapy drug regimen	No. of prescriptions	Percentage (%) of total prescription	Percentage (%) receiving combination therapy
<b>Two drug combination</b>			
CCBs + $\beta$ -Blockers	43	22.4	40.9
ACEI+ Diuretics	15	7.8	14.3
ACEI + CCBs	11	5.7	10.5
ACEI + $\beta$ -Blockers	07	3.6	6.7
CCBs + Diuretics	03	1.6	2.8
<b>Three drug combination</b>			
ACEI + $\beta$ -Blockers + CCBs	10	5.2	9.5
ACEI + $\beta$ -Blockers + Diuretics	07	3.6	6.6
ACEI + CCBs+ Diuretics	02	1.1	1.9

CCBs: calcium channel blocker; ACEI: angiotensin converting enzyme inhibitor

Morisky scale was used to predict adherence to prescribed medication therapies. Of the study population, 45.3% showed a good adherence with the prescribed treatment. Adherence was found to be slightly better in males (24%) than in females (21.3%). The Morisky score 4, which indicate a high adherence to pharmacological treatment, was observed in 10.4% of the patients only.

**DISCUSSION:** The results of our study suggest that hypertension is more prevalent in female patients (54.6%) than their male counterparts (45.4%). The above trend is in conformity to previous Indian study<sup>13</sup> who reported about 61% female as against 39% male hypertensive patients. The number of men (51%) and women (49%) was found to be anomalous in another Indian study on hypertensive patients<sup>14</sup>.

In an overseas study conducted in Hong Kong<sup>15</sup>, the prevalence of hypertension was reported as 57% in females and 43% in males. A German study<sup>16</sup> mentions 57% female vs. 43% male hypertensive populations. In

a contradictory report<sup>17</sup> out of 1076 patients, 43.9% females and 56.1% males, suffered from hypertension in Chandigarh city.

In our study, patients under the age groups of 31-40 years and 41-50 years presented with more complaints of hypertension (25% each) than the other age groups. The above result gives an indication that advanced age is not the only risk factor for hypertension in India. Instead, the above trend can be attributed to the sedentary life style, unhealthy eating habits and increased stress at work. This is an agreement with previous study<sup>13</sup> reporting 26% hypertensive patients in 40-49 years age group.

The mean BMI of the patients in our study was approximately 24 kg/m<sup>2</sup> which implies that the patients are overweight (BMI  $\geq$  23 kg/m<sup>2</sup>) and are on the borderline of becoming obese (BMI  $\geq$  25 kg/m<sup>2</sup>), which in itself is a significant risk factor for hypertension. A very high percentage (38.5%) of the study patients had BMI  $\geq$  25 kg/m<sup>2</sup> when first reported

for the study, which is a very common observation in the hypertensive patients. As precedence, mean BMI of hypertensive patients in a study was 28.4 kg/m<sup>2</sup> indicating a tendency towards obesity<sup>16</sup>.

In a survey called "Sentinel Surveillance Systems for CVD in Indian Industrial Population" involving ten centers from different parts of the country, it was concluded that the overall prevalence of overweight/obesity in patients of cardiovascular disorders was 31%<sup>18</sup>. Another study<sup>19</sup> carried out among industrial population in Delhi illustrated a prevalence of 35% in males, with 5% increase in overweight /obese patients in five years time.

The average number of antihypertensive medicines prescribed per prescription is only 1.8 in our study which is in proximity to 1.9 as reported earlier<sup>17</sup>. There were no generics prescribed during the study period, as the hospital does not have its own formulary and the drugs are being purchased from an in-house retail pharmacy. The prescribing pattern of antihypertensive in our university hospital seems to be in compliance with JNC 7 guidelines.

Diuretics were most frequently prescribed antihypertensive medicines followed by  $\beta$ -blockers, calcium channel blockers, ACE inhibitors, ARBs and  $\alpha$ -blockers. The JNC 7 report recommends that in the absence of any specific indications, a diuretic or  $\beta$ -blocker should be selected as the initial therapy for hypertension<sup>9</sup>. Medicine utilization studies elsewhere have documented major deviations from the guidelines by the prescribers.

For the purpose of sampling, Malhotra *et al.*,<sup>17</sup> reported that  $\beta$ -blockers were prescribed in 51% of prescription followed by CCBs (47%) and ACE inhibitors (46%) which was very similar to Hong Kong study<sup>15</sup> which documents 51%  $\beta$ -blockers, 49% CCBs, 27% ACE inhibitors and 24% diuretics as prescribed antihypertensives. Another report mentions 47%  $\beta$ -blockers, 34% CCBs, 30% ACE inhibitors and 16% diuretics<sup>14</sup>.

$\beta$ -blockers and CCBs were equally prescribed (68%) in another study with 6% prescriptions for ACE inhibitors and only 4% for diuretics<sup>13</sup>. Two recent studies<sup>16, 20</sup> document ACE inhibitors as the most frequently utilized antihypertensive drug category whereas  $\alpha$ -

blockers were the least prescribed. CCBs were the most preferred antihypertensive followed by ACE inhibitors, Diuretics and  $\beta$ -blockers in a study conducted on inpatients in Bangalore, India<sup>21</sup>. A common observation in all the above studies is the under utilization of diuretics which needs intervention by the formulary committees and the health policy makers.

It was observed that 55% of the patients were prescribed combination therapy (i.e. more than one antihypertensive in the prescription) which is lower than the recommendations<sup>22</sup> and observations of several other studies which demonstrated that the combination therapy was necessary in at least 70% of the study population to attain optimal blood pressure control<sup>23, 24</sup>. Single drug therapy was recommended for 45% patients in our hospital. Higher probability of adverse drug reactions due to combination of antihypertensive medicines with concomitant drugs and pharmacoeconomic consideration might be the reasons which can be attributed to lesser inclination of physicians to go for combination therapy in general in our hospital.

For comparison, 73% of hypertensive patients were prescribed antihypertensive combination in a survey conducted in Nigeria<sup>25</sup>. In another African study conducted in Ghana, 67% of the hypertensive patients were put on combination therapy and only 33% received monotherapy<sup>26</sup>. In an Indian study 60% and 40% of patients received combination and monotherapy respectively<sup>21</sup>.

Elsewhere, 71% of hypertensive patients were administered multiple drugs which are consistent with the recommendations (20). More in synchronization with the results of our study, 54% of the hypertensive patients were prescribed drugs in combination<sup>17</sup>. On the contrary, monotherapy was preferred for 51% of the patients in a Hong Kong study<sup>15</sup>.

In a major Japanese study conducted on 12,437 hypertensive patients, approximately 62% of the patients were given monotherapy as against 35% who received combination treatment and non-pharmacological interventions were recommended for remaining 3% of the patients<sup>27</sup>. In agreement to above study 58% of the patients were administered with

single drug vis-à-vis 42% hypertensive patients who were put on combination therapy in an Indian study<sup>13</sup>.

The above pattern is further corroborated by another study conducted in India, wherein 59% of the patient population was prescribed with monotherapy<sup>(14)</sup>. Among the combination therapies 2- drug treatment was preferred for 75% of the hypertensive patients with CCB and  $\beta$ -blocker being the most frequent drug combination. In other studies too, CCB +  $\beta$ -blocker with 91%<sup>13</sup>, 36%<sup>17</sup>, 32%<sup>15</sup>, and 9%<sup>14</sup> prescriptions was the most preferred drug combination.

A good number of patients (45%) adhere to the treatment regimen and followed the instructions. Still, more number of patients (55%) failed to observe the physicians advice and thus were considered poor in compliance. Compliance parameter was much better in our study population than the one reported in an African study with as high as 93% patients found short on good compliance<sup>26</sup>.

Comprehensive patient counseling in easy language by the healthcare providers might improve the patient's performance on compliance scale.

**CONCLUSION:** Although this study lacks both breadth and depth, however it provides a reasonable indication of the prescription patterns of antihypertensive agents in a hypertensive population. Our findings suggest that diuretics and  $\beta$ -blockers were used in large proportion of hypertensive patients and the pattern of antihypertensive therapy was generally consistent with JNC 7 guidelines, those being the current guidelines at the time of our study.

However, there remains potential room for improvement in drug utilization and a critical need for better blood pressure control. Further research is needed to qualify rationale for choice of drug based on demographic data, economic status, concomitant conditions and complications to give additional insight into prescribing patterns of antihypertensive in India.

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