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PREVALENCE OF RESISTANT HYPERTENSION & ASSOCIATED FACTORS IN HYPERTENSIVE POPULATION

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ABSTRACT

BACKGROUND

Aim of the study was to investigate the prevalence of RH by ambulatory blood pressure monitoring (ABPM) and the factor associated in hypertensive populations.

METHODS:

We examined the control of blood pressure in a randomly selected sample of patients with hypertension

in a community based setup. All the patients with hypertension who provided informed written consent were recruited to the study (n = 341). The required data was collected from the subjects and recorded in a pre-designed patient profile form. Resistant hypertension is defined as failure to achieve target blood pressure of < 140/90 mmHg while on full doses of an appropriate three-drug regimen that includes a diuretic.

RESULTS:

A total of 341 patients with hypertension were entered into the study. Mean age of the patients was 66.8 ± 9.7 years More than half of the subjects (56.9%) had diabetes mellitus. Overall prevalence of resistant hypertension was ***6.15%*** (N= 21/341). In multivariate logistic regression analysis, presence of chronic kidney disease is more likely to be associated with resistant hypertension (odds ratio [OR] 2.89, 95% confidence interval [CI] 1.56-5.35).

CONCLUSION:

We concluded that the prevalence of RH was 6.15% which was significantly associated with the presence of smoking, alcohol consumption, obesity, diabetes mellitus and lack of physical

exercise and patients with RH. These patients can be treated more aggressively earlier in order to achieve blood pressure target and thus reduce cardiovascular events.

Keywords: Hypertension, Resistant Hypertension, Prevalence, Risk Factors, Ambulatory Blood Pressure Monitoring, CVS complications.

INTRODUCTION

Resistant hypertension is an important medical condition as uncontrolled blood pressure (BP) is associated with a four-fold risk of cardiovascular events compared with hypertensive patients achieving BP targets [1,2]. The definition of resistant hypertension varies. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High BP defines resistant hypertension as failure to achieve BP to target despite adherence to appropriate treatment with full doses of at least 3 drug regimens including a diuretic [3].

Studies also show that resistant hypertension is associated with increasing age, female gender, presence of diabetes, obesity and smoking [4-12]. Early recognition of resistant hypertension followed by aggressive treatment is important to reduce both cardiovascular morbidity and mortality. However the exact prevalence of resistant hypertension is not precisely known due to its varied definition and the setting of where the study was done [13]. As such, based on several studies resistant hypertension has been reported to range from 5% to 50%. Furthermore most studies on resistant hypertension were done in secondary care and very few have been conducted in primary care [14].

Patient factors such as compliance and knowledge, and health care system factors like limitation of resources and lack of reminders of appointments also plays a major role in poor blood pressure control [15-21].Managing resistant hypertension is difficult and involves expensive testing to look for underlying secondary causes. Furthermore, patients with uncontrolled blood pressure are more likely to have target organ damage and have higher cardiovascular risks than patients with well controlled blood pressure [22]. Uncontrolled blood pressure affects patient's mental, physical and social well-being, while also increasing the health care expenditure of a country.

RH has been linked with type 2-diabetes mellitus (DM). The presence of DM can be both causes and consequences of RH. On comparison with the general population or hypertensive individuals, a higher frequency of RH has been observed in subjects with type 2 DM. [23]

As per the studies conducted, the incident rate of total cardiovascular events as well as the total mortality rate related with the

cardiovascular events has increased in a higher rate in resistant hypertensive subjects. Cardiovascular (CVS) organ damage is represented by left ventricular hypertrophy, carotid wall thickening and arterial stiffness. Cardiovascular event rate are significantly higher in resistant hypertensive compared with non-resistant [24].

Recent experimental and clinical data support the hypothesis that cigarette smoke exposure increases oxidative stress as a potential mechanism for initiating increased BP and cardiovascular dysfunction [25].

In India majority of the population are hypertensive of which a vast number of people are resistant hypertensive. Due to very limited research conducted in this field, most of the resistant hypertensive patients are unaware of their condition and its severity. Resistant hypertension is associated with a significantly increased risk of adverse cardiovascular events, stroke, and renal disorders as compared with non-resistant hypertension and represents an important public health issue. It has also been suggested that the resistant hypertension population is at disproportionately higher risk for target organ damage and cardiovascular events compared to the general hypertension population.

Patient factors such as compliance and knowledge, and health care system factors like limitation of resources and lack of reminders of appointments also plays a major role in poor blood pressure control .Managing resistant hypertension is difficult and involves expensive testing to look for underlying secondary causes. Uncontrolled blood pressure affects patient's mental, physical and social well-being, while also increasing the health care expenditure of a country. Therefore there is a serious need to spread the awareness regarding RH.

Through our study, we wanted to estimate the prevalence of resistant hypertension through ABPM in hypertensive population. To identify and evaluate the contributing factors and secondary causes of hypertension and to spread awareness regarding RH, its associated factors and complications. We also aim at providing patient specific counselling regarding better management of the patient condition so as to improve quality of life.

Since the study was only for a period of 6 months, the study was limited to only a small group of population and as our study required the enrolled subjects to come for a follow up in a 24 hour period, subject compliance was less, not all subjects came back for follow up. Being a community based study, most of the data was obtained only through the patient and there was no way to check for its accuracy. This could

lead to lot of information bias (e.g. Smokers saying they don't smoke).

METHODS

Subjects

Among 586 who were enrolled into the study during the period from 1st October, 2016 to the end of March 2017, 341 subjects with relevant clinical information and who were treated with at least one Antihypertensive medication (AHM) and who turned up for the follow-up were selected for the study.

Clinical and laboratory variables

Information obtained from the subjects includes: age, gender, height, weight, presence of DM, hyperlipidemia, presence of clinical cardiovascular disease, time of diagnosis, mode of treatment, and prescribed medications.

And the questionnaire for each subjects included: smoking status, alcohol intake, extent of physical exercise, family history of HTN and premature cardiovascular death, past medical history; HTN, DM, hyperlipidemia, stroke, coronary artery disease (CAD), heart failure and renal disease. The collected information for the AHM was the commercial names of the drugs and dosing at the time of enrolment. The antihypertensive drugs currently used by the patients were recorded according to their classes and drugs used for other co-morbidities were also documented. Patients' compliance to treatment was also evaluated.

Study sampling

Health camps were conducted once a month for six months in which the subjects were randomly selected. Upon arrival, they were made to sign the informed consent form. All the demographics including the past medical and medication history were collected while the subject was on a five minute rest. The first BP reading was recorded followed by a second reading after a gap of one minute. The subjects were provided with specific counselling and asked to come for a follow up the next day. The same BP recording procedure was followed for the subjects the next day.

BP Measurements:

BP was measured with a calibrated device, after 5-minute rest in a sitting position. BP values were estimated as the mean of 2 readings. Thereafter, 24-hour ABPM was performed using the Hick's Xperia automated digital blood pressure monitoring device. The patients were instructed to maintain their usual activities, return the following morning for device removal, and keep the arm extended and immobile at the time of each cuff inflation. All the demographics including the past medical and medication history were collected while the subject was on a five minute rest. The first BP reading was recorded followed by a second reading after

a gap of one minute. The subjects were provided with specific counselling and asked to come for a follow up the next day. Thereafter, a 24-hour ABPM was performed during the follow-up wherein two consecutive BP readings were recorded.

Statistical Analysis:

The variables were reported using mean ± SD for the normally distributed variables. Categorical variables were reported using number and percentages. The variables, which were normally distributed, were compared between categories using *Dependant Student T-test* and *Linear Regression.* The association and strength of association between the variables were examined using *Odds Ratio* and *Pearson's Correlation Coefficient* respectively. All the analysis were done using SPSS version 24.All the analysis was considered statistically significant at 5% level (p-value< 0.05).

RESULTS

We found a significant proportion of resistant hypertension with a prevalence of 6.15%

among all hypertensive individuals.

During the study period of 6 months, a total of 341 patients were included in the study.They were 220 (64.51%) men and 121 (35.48%) women, with a mean age of 62.2±8.8years. Obesity (body mass index 30 kg/m2) was present in 23% of subjects, 29% were current smokers, 31.2% were consuming alcohol and 37.8% had type 2 diabetes mellitus. A history of previous cardiovascular disease was present in 5.0%, cerebrovascular disease 2.1% and Hyperlipidemia 10% *(fig 1)*. *Table 1* compares clinical characteristics between patients with controlled and uncontrolled BP. As seen, R-HTN was associated with a slightly older age (62.2±8.8years), and a higher proportion of women (8%). In comparison with these subjects, those with R-HTN (elevated ABPM) had a worse cardiovascular risk profile (19%), including higher proportions of smokers (23.8%), alcohol consumption (33.3%), diabetics (42.8%), family history of HTN (76.1% versus 70%); all comparisons $P<0.05$.

R-HTN received calcium channel blockers (76.1% versus 45.9%), loop diuretics (19% versus 0.90%) and thiazide diuretics (9.5% versus 6.2%) were used more frequently and β-blockers (0% versus 10.9%), Angiotensin converting enzyme inhibitor (ACEI) are not used *(table 1).*

The mean systolic BP of R-HTN group was 179.9±9.3mmHg and mean diastolic BP was 95.4±7.9 mmHg. *(table 1)*

We had carried out odds ratio and Pearson's correlation ratio to find out the association and strength between R-HTN, its associated factors and complications. And the results showed that, there was a positive association between them. Odd

ratios for smoking & alcohol (1.2), obesity (1.7), DM (1.2), hyperlipidemia (2.8), CVS complication (3.6), stroke (3.8) were positively associated *(table 2)*. Pearson's Correlation Ratio strength with R-HTN was maximum shown by Gender (r-value=1), Family history (r-value=1), and exercise (r-value=1) followed by social history (rvalue=0.98), BMI(r- value=0.92), signs and symptoms (r- value=0.91) and age (r-value=0.8) *(table 3).*

DISCUSSION

The most important finding of the present study is that the prevalence of RH is 6.15 %.

During the study period of 6 months, a total of 341 patients were included in the study. It may be attributed to age-related changes in blood vessels and an increase in frequency of all related conditions (e.g., obesity, diabetes mellitus, CKD).[26]

According to our study greater number of resistant hypertensive patients was found to be above the age of 50 years. The number of older patients (62.9±7.96yrs) was significantly higher in resistant hypertensive group compared to controlled hypertensive group (p-value-0.02). [27]

Out of 341 hypertensive patients enrolled, 220 (65%) were male patients and 121 (35%) were female patients. Among hypertensive patients the male patients were more than the female patients. In hypertensive male patients, 5% were found to be resistant hypertensive *(fig.2)* whereas in hypertensive female patients, 8.2% were found to be resistant hypertensive *(fig.3).* Our study result is similar to study carried on hypertensive patients reported that prevalence of R-HTN increased with age, particularly in females as compared to males; implying that gender and age may be used to predict development of R-HTN. [28]

Hypertension is the most common and preventable cardiovascular disease risk factor. Numerous professional organizations and committees recommend exercise as the initial lifestyle therapy to prevent, treat and control hypertension. The effect of physical exercise in controlling hypertension depends on its frequency, intensity and time that are being carried out by the patient. [29]

Out of 341 hypertensive patients enrolled, 240(70%) patients had a family history of BP. Family history is an important non-modifiable risk factor for HTN. [30] Among 21 R-HTN patients in our study, 16(76%) patients had a family history of BP and hypertension had an association in the study population, as the prevalence of hypertension was significantly higher in those with a family history of hypertension. We also observed an increase in the prevalence with the increasing number of generations affected. Family History (FH) of hypertension was also associated with

the prevalence of obesity and metabolic syndrome. Individuals with a FH of hypertension form an easily identifiable group who may benefit from targeted interventions. The number of patients with a family history of BP was significantly higher in both HTN and R-HTN groups (P-Value: 0.04).

Out of 341 hypertensive patients enrolled, 107(32%) patients were having a habit of drinking alcohol. Heavy alcohol intake increases the risk of HTN. Epidemiological evidence suggest that heavy alcohol consumption is strongly associated with increased risk of HTN which in-turn can lead to R-HTN thereby finally causing CVS and CKD complications. [31]

In our study, 32% of the total hypertensive population is having a habit of alcohol intake; of which 34% are resistant hypertensive. The above result from our study confirms a positive association with alcohol intake and R-HTN. Cigarette smoking (CS) continues to be a major health hazard, and it contributes significantly to cardiovascular morbidity and mortality. In our study, out of 341 hypertensive patients enrolled, 99(30%) of them were smokers. Among 21 R-HTN patients, 5 were smokers in our study. Epidemiologic studies strongly support the assertion that cigarette smoking (CS) in both men and women increases the incidence of uncontrolled BP, myocardial infarction (MI) and fatal coronary artery disease (CAD).[32]

Patients with social history of smoking and drinking alcohol were found to be significantly at higher risk of R-HTN (P-Value:0.001).

We have analyzed the co-morbidities and complications of the study population by considering the past medical history of the patients. It was found that out of 341 hypertensive patients, 130(38%) had DM, 12(4%) were hyperlipidemia patients, 20(6%) had a history of CVS disorders, 9(3%) had a history of stroke and 5(1%) had a renal disease history. Diabetes mellitus, Hyperlipidemia, Kidney disease are the major co-morbidities leading to resistant hypertension. [33]

And according to our study results majority of R-HTN patients were diabetic patients .i.e. out of 21, 9 (38%) had DM. The significance of co morbidities DM and Hyperlipidemia in R-HTN group was proved statistically significant (P-Value :< 0.05). Resistant hypertensive patients are at higher risk of cardiovascular complications, stroke and CKD compared to controlled hypertensive population. [34,35]. Out of 21 R-HTN patients in our study, 4(19%) had a history of CVS complication, 2(10%) had a history of stroke. But we couldn't find kidney failure patients in our resistant hypertensive population. The higher risk of CVS complication and stroke in R-HTN

patients in HTN population were significantly proved (P-Value:0.02).[36] In our study, majority of patients are prescribed with CCB (44%), followed by ARB (32%), beta blockers (9%), ACEI (6%) and others. The patients who were prescribed with CCB in our study were found to be under the age category of 50 years and above.[37]

An adequate counselling was carried out to these patients to improve their medication adherence and made them understand how it will reflect in their quality of life and in better management of the disease. We counselled HTN & R-HTN subjects about its condition and made awareness about how to control its complications through medication adherence and lifestyle modifications. Therefore, as a clinical pharmacist, an ideal person who can contribute to better patient outcome by being the member of healthcare team, we were able to give patient specific counselling and educate them about the disease condition and the lifestyle modification they needed to control the BP and to improve the condition, thereby preventing them by being resistant hypertensive.

CONCLUSIONS

A significant proportion of the hypertensive patients were identified as having resistant hypertension in our study and the prevalence rate of R-HTN was *6.15%*. A substantial portion of the hypertensive population was found uncontrolled in our study even after taking more than three drugs.

According to our study, R-HTN was significantly associated with the presence of smoking, alcohol consumption, obesity, diabetes mellitus, and lack of physical exercise, higher risks for cardiovascular events and stroke than those with non-RHTN. Most of the hypertensive patients in our study were unaware of R-HTN condition and its severity. Therefore, through our study; we spread awareness regarding R-HTN, its associated factors and complications. We also provided patient specific counselling regarding better management of the patient condition so as to improve quality of life. From the results obtained from our study, it was clearly observed that R-HTN patients are more likely to develop CVS complications, stroke when compared with HTN patients. Maintenance of weight, regular exercise, medication adherence can control the hypertensive condition thereby preventing the patients from undergoing complications and decreasing the mortality rate.

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