

## Prevalence and clinical profile of patients with resistant hypertension

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**Objective:** To find prevalence and clinical profile of patients with resistant hypertension. **Methods:** In a Prospective Observational Study, 100 Hypertensive patients were evaluated in Hypertension OPD, Medical OPD, and Medical Wards. Hypertensive Patient on more than 3 drugs with uncontrolled BP were included for this study. Patients were subjected to Clinical examination, Laboratory investigations and Ultrasound. BP is recorded in all 4 limbs with appropriate cuff size, Patients drug history (Both antihypertensive and other medications for concomitant illness will be enquired), Physical activity and Drug compliance were enquired. **Result:** Among the 100 patients studied, 18% patients were found to have Resistant hypertension. Of this, 5 patients were in incorrect drug combination, 7 patients were not drug compliant, 12 patients had Uncontrolled Diabetes, 15 patients had Dyslipidemia, 6 patients had Medical Renal disease, 2 patients had Fatty Liver, 1 patient had Contracted Kidney and 1 patient had Aortailiac Thrombosis. **Conclusion:** Incorrect Drug prescription, non-adherence to drugs and metabolic factors played a major role in resistant hypertension in the present study group.

**Keywords:** Diabetes, Dyslipidemia, Resistant Hypertension

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## Introduction

Hypertension is a non-communicable disease associated with long term morbidity and higher mortality. It causes a major global burden of disease. The incidence of hypertension is on increasing trend because of changing lifestyle, food pattern and increasing urbanization.

The prevalence of resistant hypertension as defined by criteria, when blood pressure is more than 140/90 despite of adequate full doses of 3 different drug classes of drugs, one of them should be a diuretic, is on increasing trend among the hypertensive individual [1]. The risk of cardiovascular morbidity and mortality is higher among patients with resistant hypertension than among those whose hypertension is well controlled [1,2].

Hence, all the effort has to be made to identify causes for secondary hypertension, which may be contributing, or any correctable cause has to be identified. This may be due to pseudo resistant hypertension such as white coat hypertension or due to thickening of vessels as seen in elderly individual or due to true hypertension. Resistant hypertension prevalence estimated to be 12.8% in a large cohort study with higher rates in black race and obesity and little higher rate found in males and older age [3,4,5].

## Materials and Methods

**Place of study:** Department of General Medicine, Hypertension OPD, Medical OPD, Medical Wards Govt. Kasturibai Gandhi Memorial Hospital, Chennai – 600005.

**Sample size:** 100

**Duration:** July 2018 To January 2019

**Study design:** Prospective Observational Study

**Inclusion criteria:** Hypertensive patients with Age group of 40 to 70 years

### Exclusion criteria

01. Age < 40 years and > 70 years
02. Patient with known secondary causes of hypertension

### Methodology

01. Patient who are known case of hypertensive on more than 3 drugs with uncontrolled BP are included for this study.

Patients will be subjected to Clinical examination, Laboratory investigations and Ultrasound. The final analysis will be made at the end of the study to achieve the aforementioned goals.

02. BP is recorded in all 4 limbs with appropriate cuff size.
03. Patients drug history (Both antihypertensive and other medications like usage of NSAIDS, Aspirin, and Acetaminophen for concomitant illness were enquired).
04. Patients physical activity was enquired.
05. Patients drug compliance was enquired. Morisky questionnaire was utilized to assess adherence to antihypertensive medications, following which all cases of RH were further classified into those with pseudo-resistance and those with true resistant hypertension.
06. Patients will be subjected to basic investigation.
07. ECG, Echo and USG abdomen (To assess renal size) were done.
08. Depending upon patient's profile, Patient were subjected to optional investigations like Thyroid profile test, Serum Cortisol, Urine metanephrine, Renal Doppler/ARR (Angiotensin Renin ratio)
  - Classification of blood pressure (JNC SEVEN)
    01. Normal: sys <120 mmHg and dias <80 mmHg
    02. Pre-hypertension: sys-120-139mmHg and dias-80-89mmHg
    03. Stage 1 hypertension: sys-140-159mmHg and dias-90-99mmHg
    01. Stage 2 hypertension: sys>160mmHg and dias > 100mmHg
    02. Isolated systolic hypertension: sys >140mmHg and dias <90mmHg

## Results

Among the 100 patients studied, 39 patients were found to be in the age group of 40-50. This constitutes 39% of the study group. 40 patients were found to be in the age group of 51-60.

This constitutes 40% of the study group. 21 patients were found to be in the age group of 61-70. This constitutes 21% of the study group. There were no patients above age group of 70 in this study (Table 1).

**Table-1: Age distribution.**

Age (years)	Number of patients	Percentage (%)
40-50	39	39
51-60	40	40
61-70	21	21
Total	100	100

Among the 100 patients studied, 52 patients were females. This constitutes 52% of the study group. 48 patients were males. This constitutes 48% of the study group (Table 2).

**Table-2: Gender distribution.**

Gender	Frequency	Percent	Valid Percent	Cumulative Percent
Female	52	52.0	52.0	52.0
Male	48	48.0	48.0	100.0
Total	100	100.0	100.0	

Among the 100 patients studied, 15 patients were found to be in Stage I hypertension. 67 patients were found to be in Stage 2 hypertension. 18 patients were found to have resistant hypertension (Table 3).

**Table-3: Patient distribution by stages of hypertension.**

Stages of hypertension	Frequency (%)		Valid Percent	Cumulative Percent
	No	Yes		
Stage 1	No	85.0	85.0	85.0
	Yes	15.0	15.0	100.0
Stage 2	No	33.0	33.0	33.0
	Yes	67.0	67.0	100.0
Resistant Hypertension	No	82.0	82.0	82.0
	Yes	18.0	18.0	100.0

Among the 100 patients studied, 18 patients were found to have Resistant Hypertension. In this, 13 patients were found have correct drug combination. This constitutes 72.22% of the Resistant Hypertensive patients. 5 patients were found not to be in correct drug combination. This constitutes 27.78% of Resistant Hypertensive patients (Table4).

**Table-4: Drug prescription in resistant hypertension.**

Number of patients	% of Patients
Correct	13
Incorrect	5
Total	18

Among the 100 patients studied, 18 patients were found to have Resistant Hypertension. In this 11 patients were found be drug compliant. This constitutes 61.10% of the Resistant Hypertensive patients.

7 patients were not found to be drug compliant. This constitutes 38.90% of the Resistant Hypertensive patients (Table 5).

**Table-5: Drug compliance in resistant hypertension.**

	Number of patients	% of patients
Compliant	11	61.10
Non-compliant	7	38.90
Total	18	100.00

Among the 100 patients studied, 18 patients were found to have resistant hypertension. In these 6 patients were found to have resistant hypertension due to other drugs. This constitutes 33.3% of the resistant hypertensive patients. 11 patients were found to be not on any other drugs. This constitutes 66.7% of resistant hypertensive patients (Table 6).

**Table-6: Other drugs contributing to resistant hypertension.**

	Number of patients	% of patients
Not Contributing	12	66.7
Contributing	6	33.3
Total	18	100.0

Among the 100 patients studied, 18 patients were found to have resistant hypertension. In these 12 patients were found to have resistant hypertension due to diabetes. This constitutes 66.7% of the resistant hypertensive patients. 15 patients were found to have dyslipidemia. This constitutes 83.33% of resistant hypertensive patients (Table 7).

**Table-7: Prevalence of modifiable risk factors in resistant hypertension.**

	Number of patients	% of total hypertensive patients
Diabetes	12	66.7
Dyslipidemia	15	83.33

Among the 100 patients studied, 18 patients were found to have resistant hypertension. In these 6 patients were found to have elevated renal parameters. This constitutes 33.33% of the resistant hypertensive patients. 12 patients were found to have normal renal parameters. This constitutes 66.67% of resistant hypertensive patients (Table 8).

**Table-8: Renal parameters in resistant hypertension.**

	Number of patients	% of total hypertensive patients
Elevated	6	33.33
Normal	12	66.67

Among the 100 patients studied, 18 patients were found to have resistant hypertension. In these 6 patients were found to have Medical Renal disease. This constitutes 33% of the resistant hypertensive patients. 2 patients were found to have Fatty Liver. This constitutes 11% of resistant hypertensive patients. 1 patient was found to have Contracted Kidney. This constitutes 6% of resistant hypertensive patients. 1 patient is found to have Aortailiac Thrombosis. This constitutes 6% of resistant hypertension patients. 8 patients were found to be normal. This constitutes 44% of resistant hypertension patients (Table 9).

**Table-9: Ultrasound in resistant hypertension.**

	Normal	MRD	Fatty Liver	Contracted Kidney	Aortailiac Thrombosis
Ultrasound	8	6	2	1	1

## Discussion

This was a prospective observational study among 100 hypertensive individuals. They were catagorised according to the age, gender, stages of hypertension. Their clinical profile, drug prescription, compliance and other drugs contributing to hypertension were evaluated.

The prevalence of RH among the present study population was 18% [6]. This finding is consistent with other observational studies conducted in Europe and North America. In the Controlled Onset Verapamil Investigation of Cardiovascular Endpoints trial, the prevalence of RH was 18%. Prior studies have often over-estimated tRH without ruling out pseudo-resistance.

Pseudo resistance can be caused by various factors, including inaccurate measurement of BP, poor adherence (61.1% in the present study) or suboptimal treatment regimens (27.78%), physician’s inertia or white-coat effect, produces a false impression of tRH if not taken into account [8]. The incapacity of ruling out pseudo-resistance is very important in order to avoid over treatment and avoid complications.

The limited data gathered from the studies conducted in the neighboring Southeast Asian countries show that the prevalence of Resistant Hypertension is on the rise [9,10,11]. According to Daugherty et al., approximately 1 in 6 patients on 3 or more antihypertensive drugs will continue to meet the criteria for RH after 1 year [12].

Physicians can expect to encounter RH one in every ten hypertensive patients on treatment. This situation is worrisome and highlights that treatment resistant BP will continue to be a clinically important hypertension phenotype. A study carried on hypertensive patients reported that prevalence of RH increased with age, particularly in females as compared to males; implying that gender and age may be used to predict development of RH [13].

Moreover, it was also observed that a significant association with the female gender. Several studies have reported sexual dimorphism in BP such that incidence of hypertension is much higher in males during early adulthood, but this level alters after the sixth decade of life.

The rise in the BP after the age of 55 is steeper in females as compared to males, which also shows features of treatment resistance [1]. Women are more likely to have difficulty adhering to optimum BP, have a higher prevalence of co-morbidities and obesity influenced by estrogen withdrawal and, therefore, are more likely to develop RH.

It was observed that an increased use of painkillers contributes to the poor control found in RH. Increased use of non-narcotic analgesics including the NSAIDs, aspirin and acetaminophen are contributing agents concerning BP control [14,15]. This is established in the literature [16,17]. The number of people consuming excessive painkillers were not aware of the side effects of these drugs and their role in reducing the efficacy of the BP control by antihypertensive drugs.

In addition, painkillers like acetaminophen, have been found to develop hypertension [15] but in comparison to NSAIDS (particularly ibuprofen), acetaminophen are less likely to worsen BP control in already treated patients [16] hence these medications should be avoided or withdrawn in resistant hypertensive patients. Since it is clinically very difficult, the lowest effective dose should be administered as and when needed.

In the present study, it was observed that a strong association between diabetes mellitus and resistant hypertension. This observation is concordant with other previous studies which have shown a positive relation [3,13,18]. “Blood pressure control in diabetes is extremely important,” says Dr. Fonseca. “It has a huge impact on complications, particularly nephropathy, and cardiovascular events.”

It has been shown that chronic kidney disease and advanced retinopathy are significantly higher in individuals with resistant hypertension than in those with nonresistant hypertension or uncontrolled hypertension. Patients with resistant hypertension were older, more frequently women, and had significantly higher waist circumference, albuminuria and serum creatinine, and lower glomerular filtration rate [19].

In the present study, dyslipidemia was seen in 15 patients that contributes to 83.33% of the study population. This corresponds to the Framingham Heart Study data on the hypertensive population reported that more than 80% had at least one additional cardiovascular disease risk factor and predominantly these risk factors were atherogenic in nature. Studies have consistently indicated that hypertension and hypercholesterolemia frequently coexist, causing what is known as dyslipidemic hypertension (DH) [20,21].

The risk of CVD associated with concomitant hypertension and dyslipidemia is more multiplicative than the sum of the individual risk factors [22,23] the coexistence of dyslipidemic hypertension has been termed as 'LIPITENSION'. There is some evidence to suggest that treating dyslipidemia has beneficial effects on blood pressure (BP).

Studies by Borghi et al., [24,25] have found that patients receiving concomitant antihypertensive and statin therapy experienced a reduction in BP that could not be explained solely by the lipid-lowering effect of the statin or the effect of the antihypertensive medication. These results suggest that the use of statins in combination with antihypertensive drugs may improve BP control in patients, with uncontrolled hypertension and high serum cholesterol levels.

This study has few limitations. First, the sampling data was collected from a single tertiary care hospital. Secondly, when compared to the prevalence of Hypertension in general population the sample size used in this study is small.

Thirdly, the data like adherence to the drug and other contributing drugs like painkillers were collected orally from the patients. However, the data correlates with the findings of previous studies discussed here. These points, which are important, can help better understand the key role players in the development, progression and prognosis of RH.

## Conclusion

Hypertension is a non-communicable disease with increasing trend having both modifiable and non-modifiable factors. The stage of hypertension increases with increase in age. In the present study 15% were in stage 1 hypertension, 67% were in stage 2 hypertension and 18% were in resistant hypertension. The major factors contributing to resistant hypertension in the present study were

- Incorrect / Suboptimal drug prescription, which contributes to about 27.78%
- Non-Compliance of drug, which contributes to about 61.10%
- Consumption of other drugs for co-existing illness, which contributes to about 33.3%
- The other metabolic factors such as
- Uncontrolled diabetes which contributes to about 66.7%
- Dyslipidemia which contributes to about 83.3% Should be addressed

01. Adequate knowledge of pharmacology is essential for dosing and in choosing a right combination of antihypertensive drugs in order to overcome the problem of resistant hypertension.

02. In patients with resistant hypertension, the patient should be personally interviewed to check whether he is consuming other commonly used over the counter drugs that could hamper adequate control of blood pressure.

## What the study adds to the existing knowledge?

As in other similar studies done in various places, the present study also supports the fact that pseudo resistant hypertension is more common than true resistant hypertension. In patients with resistant hypertension it is mandatory for the physician to personally verify whether right drug has been delivered to him and whether he is taking as prescribed.

## Author's contributions

**Dr. Umamaheswari B:** Concept, study design.

**Dr. P. Suganya:** Manuscript preparation, data analysis.

**Dr. A Revathi:** Data analysis

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