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## Observed factors responsible for resistant hypertension in a teaching hospital setting

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### Summary

Assessment of control of hypertension by some authors has revealed that optimal blood pressure control is not yet achieved in many of those that are on treatment. Resistant hypertension, plays a part as one of the factors responsible for this poor control state. Because of the peculiar problems posed by this group of hypertensives, we assessed the burden and factors responsible for resistant hypertension among hypertensive subjects attending the medical outpatient clinic of the University College Hospital, Ibadan, Nigeria. Resistant hypertension was defined as blood pressure  $\geq 140/90$  mmHg in the presence of use of a combination of three antihypertensive drugs, including a diuretic at near maximum doses for at least one month. Five hundred and sixty-six consecutive subjects (218 males and 348 females) with a mean age of  $56.0 \pm 14.3$  years were screened for resistant hypertension. One hundred and forty-four (mean age  $54.55 \pm 15.1$  years), were fully controlled with a blood pressure of  $120 \pm 9/77 \pm 2$  mmHg. 394 men age of  $56.7 \pm 11.7$  years had non-resistant hypertension with blood pressure of  $167.5 \pm 23/102.3 \pm 1.2$  mmHg. Only 28 (5%) of the whole study group (mean age  $51.8 \pm 9.7$  years) were found to have resistant hypertension with a blood pressure of  $176.4 \pm 43/109.6 \pm 14.8$  mmHg. The subjects with resistant hypertension were significantly younger than those with non-resistant hypertension  $P < 0.02$ . There was no significant difference between their systolic blood pressure ( $P > 0.3$ ) whereas; there was a significant difference between their diastolic blood pressure  $P < 0.002$ . Among those who had resistant hypertension, non-compliance was documented in 14 (50%) while it was in 73 (18.5%) of those without resistant hypertension  $P < 0.00053$ . Alcohol, tobacco, Obesity, use of non-steroidal anti-inflammatory drugs and excessive use of salt were not found as key factors responsible for resistant hypertension in this study.

**Keywords:** *Observed, factors, resistant hypertension, teaching hospital*

### Résumé

Une estimation de contrôle d'hypertension par quelques auteurs a révélé que ce contrôle de la tension optimal n'est pas toujours accompli dans beaucoup de ce qui sont sur traitement. L'hypertension résistante qui joue une partie comme un des facteurs responsable pour cet état du contrôle pauvre. À cause des problèmes particuliers posés par ce groupe d'hypertensives, nous avons réparti le fardeau et facteurs responsable pour l'hypertension résistante parmi les malades d'hypertensive à la clinique du malade en consultation externe de l'Hôpital du Collège de l'Université, Ibadan, Nigeria. L'hypertension résistante a été définie comme tension  $140/90$  mmHg dans la présence d'usage d'une combinaison de trois médicament anti-hypertensive, y compris un diurétique à doses du maximum proches pour au moins un mois. Les cinq cents et soixante-six sujets consécutifs (218 mâles et 348 femmes) avec un âge moyen de  $56.0 \pm 14.3$  years a été masqué pour l'hypertension résistante. Cent et quarante-quatre (âge moyen  $54.55 \pm 15.1$  années), était complètement contrôlé avec une tension de  $120/77 \pm 2$  mmHg. 394 hommes vieillissent de  $56.7 \pm 11.7$  années avait de l'hypertension non résistante avec tension de  $167.5 \pm 23/102.3 \pm 1.2$  mmHg. Seulement 28 (5%) du groupe de l'étude entier (âge  $51.8 \pm 9.7$  years moyen) a été trouvé pour avoir de l'hypertension résistante avec une tension de  $176.4 \pm 43/109.6 \pm 14.8$  mmHg. Les sujets avec l'hypertension résistante étaient considérablement plus jeune que ce avec l'hypertension non résistante  $P < 0.02$ . Il n'y avait aucune différence considérable entre leur tension du systolique ( $P > 0.3$ ) alors que; il y avait une différence considérable entre leur tension du diastolique  $P < 0.002$ . Parmi ce qui avaient de l'hypertension résistante, le non-respect a été documenté dans 14 (50%) pendant que c'était dans 73 (18.5%) ceci sans hypertension résistante  $P < 0.00053$ . L'alcool, le tabac, l'obésité, l'usage de médicament non-steroidal anti-inflammatoires et l'usage excessif de sel n'ont pas été trouvés comme facteurs responsable pour l'hypertension résistante dans cette étude.



## Introduction

Treatment of hypertension has been shown to be beneficial in all races[1], however, assessment of control in some quarters revealed that optimal blood pressure control is yet to be achieved in many of those that are on treatment[2,3,4]. Various factors have been put forward as reasons for this poor control, including resistant hypertension which, though constitutes a small fraction. Non-compliance, alcohol, tobacco, obesity, excessive salt intake and non-steroidal anti-inflammatory drugs were the other factors[1,5]. A lot of attention has been drawn to various aspects of hypertension in the past, but resistant hypertension has not enjoyed the same, especially in Nigeria, where hypertension is still responsible for significant cardiovascular disability and morbidity. Moreover, most patients with resistant hypertension later develop target organ damage in the form of cardiac hypertrophy, retinal haemorrhages and/or renal impairment, following difficulty in controlling blood pressure[6]. The prevalence of resistant hypertension ranges between 2.9% and 13% in various studies[3,7]. Because of the peculiar problem posed by this group of hypertensives, we assessed the burden and factors responsible for resistant hypertension among hypertensive subjects attending the medical outpatient clinic of the University College Hospital, Ibadan, Nigeria in order to plan appropriate intervention strategy for them.

## Methods

Five hundred and sixty-six hypertensive subjects (348 females and 218 males) presently being followed up at the University College Hospital, Ibadan, Nigeria were assessed for resistant hypertension. Resistant hypertension was defined as blood pressure of  $\geq 140/90$  mmHg in the presence of use of a combination of three antihypertensive drugs, including a diuretic at near maximum doses for at least one month[8,9]. Patient with history of cerebrovascular disease, heart failure, malignant hypertension and chronic renal diseases presently and or in the past were excluded from the study. Blood pressure was measured in the subjects using a standard mercury sphygmomanometer after 5 minutes of rest and an average of two measurements was taken. An appropriate cuff size was applied to the exposed right upper arm and was rapidly inflated to 30mmHg above the level at which the pulse disappeared and then deflated gradually. Systolic (SBP) and diastolic blood pressure (DBP) was taken as Korotkoff sound phases I and V respectively.

Data were collected from all the subjects using a structured questionnaire to obtain information on age, gender, duration of treatment, regularity of taking anti-

hypertensives and number of drugs and doses per patient. Information was sought relating to factors responsible for resistant hypertension like the use of coffee or tobacco, steroids, non-steroidal anti-inflammatory drugs (NSAIDs), tricyclic antidepressants, alcohol, sympathomimetics and salt. Weight and height were also measured to the nearest 0.5kg and 1centimeter and body mass index (BMI) was calculated in them using the formula:  $BMI = \text{Weight (kg)} / [\text{Height}]^2 (\text{m}^2)$ . A BMI of more than  $25\text{kg/m}^2$  was considered as indicative of obesity. [3] Secondary hypertension was assessed by urinalysis, urine microscopy, serum electrolytes, urea, creatinine and renal ultrasonography assessed the kidney and the adrenals while chest x-ray was used to assess Coarctation of the aorta and vanillyl/mandelic acid urinary excretion assessed Pheochromocytoma. Statistical analysis was by Students' t-test and chi square. Level of significance was put at  $P < 0.05$ .

## Results

Five hundred and sixty-six subjects with a mean age of  $56.0 \pm 14.3$  years were screened for resistant hypertension. They comprised of 218 males (mean age of  $56.6 \pm 11.5$  years) and 384 females (mean age of  $55.3 \pm 16.5$ ). The most commonly used combination of drugs for blood pressure control in patients with resistant hypertension included calcium channel blockers, thiazide diuretics and  $\alpha$ -methyl dopa.  $\beta$ -blockers occasionally replace  $\alpha$ -methyl dopa in this combination in 4 cases. Table 1 shows the comparison of the mean age and the blood pressure of the 3 categories

**Table 1:** Comparison of mean age and blood pressure of subjects in the 3 categories

Category	Age (years)	SBP (mmHg)	DBP (mmHg)
A. Controlled N=144	54.55 $\pm$ 15.1	120 $\pm$ 9	77 $\pm$ 2
B. Resistant hypertensives N=28	51.8 $\pm$ 9.7	176.4 $\pm$ 43	109.6 $\pm$ 14
C. Non-resistant hypertensives N=394	56.7 $\pm$ 11.7	167.5 $\pm$ 23	102.3 $\pm$ 12

### ANOVA

Age-F= 3.12,  $P < 0.04$

SBP-F= 261.01,  $P < 0.0001$

DBP-F= 328.0,  $P < 0.0001$

of subjects. One hundred and forty-four (25.4%) (48 males mean age  $54.47 \pm 14.5$  years) and 96 females (mean age  $53.64 \pm 15.7$  years) were fully controlled with a blood



**Table 2:** Frequency of likely factors responsible for resistant hypertension in hypertensive subjects

Factors	Resistant HBP (A) N=28	Non-Resistant HBP (B) 394	A vs B
Non-compliance	14(50%)	73(18.6%)	P<0.001
Obesity	10(36%)	162(41.1%)	P>0.799
Non-steroidal anti-inflammatory drugs	9(32%)	126(32%)	P>0.905
No cause found	3(1.07%)	0 (0%)	N/A
Renal insufficiency	2(0.07%)	13(3.2%)	P>0.2
Antidepressants	1(0.04%)	0(0%)	N/A
Coffee	1(0.04%)	39(9.9%)	P>0.15
Alcohol	0(0%)	17(4.5%)	N/A
Tobacco	0(0%)	4(1.1%)	N/A
Excessive salt intake	0(0%)	26(6.5%)	N/A

pressure of  $120 \pm 9/77 \pm 2$  mmHg. 394 (163 males and 231 females) had non-resistant hypertension. Only 28 (5%) of the whole study group (mean age  $51.8 \pm 9.7$  years) were found to have fulfilled the definition of resistant hypertension used in this study. There were significant differences between their ages ( $F=3.12$ ,  $P<0.04$ ), SBP ( $F=261.01$ ,  $P<0.001$ ) and DBP ( $F=328.0$ ,  $P<0.0001$ ).

Table 2 shows the frequency of the suspected factors responsible for resistant hypertension in the patients. Non-compliance was documented in 14(50%) of them, and was the most frequent likely factor responsible for resistant hypertension, as compared to 73(18.5%) of those without resistant hypertension ( $P<0.0001$ ). Thus non-compliance occurred more significantly among subjects with resistant hypertension. Ten of the subjects with resistant hypertension (36%) were classified as obese (BMI greater than  $25 \text{ kg/m}^2$ ), this proportion did not differ significantly from 162(41.1%) of the subjects without resistant hypertension ( $P>0.799$ ). Ingestion of non-steroidal anti-inflammatory drugs was documented in 9(32%) of the patients with resistant hypertension and 126(32%) of those without. There was no significant difference between these proportions  $P>0.985$ . Alcohol, tobacco, and excessive use of salt were not found as key factors among subjects with resistant hypertension whereas, 4.5%, 1.1%, and 6.5% of subjects without resistant hypertension ingested alcohol, tobacco and excess salt in that order.

## Discussion

This study found a frequency of resistant hypertension of 5% in our clinic. This figure is relatively low when compared with reports from other parts of Africa[6,9,10].

However, this group of patients especially, in a homogenous Black population in which hypertension ordinarily runs a more aggressive course constitutes a primary concern to the managing physicians who often refer them to tertiary centers. It is a problem to the patient and the committed physician to control this grade of blood pressure, more so in the African society where poverty is an impediment to management. This therefore, calls for a systematic approach to evaluate the factors responsible for resistance. The mean age of the subjects with resistant hypertension in this study was significantly lower than in those without, this perhaps being due to the fact that younger hypertensives are more likely to discontinue their medications. Although females outnumbered males, it is probably a reflection of the distribution of males and females in the whole group. Several factors responsible for resistant hypertension have been documented[1,8,12]. In the present study noncompliance to antihypertensive therapy or poor adherence was the most frequently encountered factor responsible for resistance in our patients. This has been known to lead to higher cardiovascular morbidity. True drug resistant hypertension where all the factors noted in this study were absent may therefore be said to contribute little to factors responsible for resistance in this study, judging from the magnitude of the role played by poor compliance to antihypertensive therapy. Moreover, it was in only 3 of the subjects that no obvious cause for resistance was found. They therefore, probably represent the true drug resistant hypertensives among them. Further invasive investigations like renal angiography may however, provide other clues in these 3 subjects.

The relationship between obesity and blood pressure is a very strong one, and reduction in weight is well known to lower blood pressure[10,12]. Although we did not evaluate weight reduction in relation to blood pressure, obesity did not seem to play a significant part as factors responsible for resistant hypertension in this study as there was no significant difference in its frequency between the two groups. But, because of its high frequency it may be partly responsible for poor control in the whole study population. Non-steroidal anti-inflammatory drugs, which, are well known to raise blood pressure, were also prominently used by some of the subjects.

Dietary indiscretion in the form of alcohol, tobacco and excessive use of salt did not appear to play any significant role here as factors responsible for resistance. Although, the relationship between these three factors and blood pressure is well established[1,11], this finding is perhaps, a result of health education on life style



modification techniques in our clinic, which centered mainly on these factors. Thus non-compliance was the most frequent likely factor responsible for resistant hypertension in our subjects.

Renal insufficiency, use of coffee and antidepressant played very little role as possible factors responsible for resistance. Ensuring medication compliance in hypertensives may therefore serve as the single most important strategy for intervention in this group of subjects. Use of less complicated drug regimen, cheap and effective drugs may also assist in providing appropriate intervention. The physician should therefore, inform the patients about the implications of uncontrolled hypertension. Education of patient should include emphasis on the importance of compliance, lifestyle modification techniques and reduction of indiscriminate ingestion of NSAIDS in this group of patients.

In conclusion, the low frequency of resistant hypertension in our clinic contrasts with some previous works and may be described as low compared to some previous works, non-compliance being the most important. Ensuring medication compliance thus, appeared to be the single most important strategy to prevent resistant hypertension in our subjects.

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