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Original Research Article

PREVALENCE AND CLINICAL CORRELATES OF POORLY CONTROLLED HYPERTENSION IN PATIENTS ON MULTIDRUG THERAPY

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ABSTRACT

Background: Resistant hypertension is an important clinical problem because these patients often have poor blood pressure control despite treatment and carry higher cardiovascular and renal risk. Data from tertiary care settings are still limited in many parts of India.

Materials and Methods: This hospital based cross sectional observational study was conducted among 100 adult hypertensive patients attending a tertiary care centre. Resistant hypertension was defined as uncontrolled blood pressure despite use of 3 antihypertensive drugs of different classes including a diuretic or controlled blood pressure requiring 4 or more drugs. Sociodemographic details, comorbidities, lifestyle related factors, treatment pattern and medication adherence were recorded. Data were analysed using appropriate statistical tests and multivariable logistic regression.

Results: Resistant hypertension was found in 16 out of 100 patients, giving a prevalence of 16.0%. It was more common in patients aged 60 years or more (68.8% versus 36.9%, p=0.019). Diabetes mellitus (62.5% versus 31.0%, p=0.015), chronic kidney disease (43.8% versus 15.5%, p=0.010), obesity (56.2% versus 29.8%, p=0.041), high salt intake (68.8% versus 41.7%, p=0.044), use of 4 or more antihypertensive drugs (62.5% versus 10.7%, p<0.001) and poor medication adherence (56.2% versus 25.0%, p=0.014) were significantly associated with resistant hypertension. On multivariable analysis, age 60 years or more, diabetes mellitus, chronic kidney disease, obesity and poor medication adherence remained independent predictors.

Conclusion: Resistant hypertension was not uncommon in this tertiary care cohort. It was mainly associated with older age, metabolic and renal comorbidity, obesity and poor adherence. Early recognition and better treatment optimisation may improve blood pressure control.

Keywords: Resistant hypertension, prevalence, predictors, medication adherence, chronic kidney disease.

INTRODUCTION

Hypertension remains a major long term public health problem worldwide. Despite better awareness and treatment, blood pressure control is still poor in many patients. Because of this, long term cardiovascular and renal risk remains high.[1] Resistant hypertension is a more serious form of this problem. It is usually defined as uncontrolled blood pressure despite use of 3 antihypertensive drugs of different classes including a diuretic or controlled blood pressure requiring 4 or more drugs.[2] Current guidelines also stress that pseudo-resistance and secondary causes should be excluded before making the diagnosis.[3]

The burden of resistant hypertension varies across studies. This is due to differences in definition, treatment pattern, adherence assessment and use of out-of-office blood pressure monitoring. Recent evidence suggests that apparent resistant hypertension is not rare in treated hypertensive patients.[4] It is also clinically important because these patients have higher cardiovascular and renal risk than those with controlled hypertension.[5]

Resistant hypertension is commonly seen with older age, diabetes mellitus, chronic kidney disease, obesity and other metabolic abnormalities.[6] Indian hospital based data also showed similar association with obesity and poor glycemic status.[7] At the same time, poor adherence, white coat effect and non-optimized therapy can falsely label some patients as resistant.[2]

In India overall hypertension control is still not adequate, so resistant hypertension remains a relevant clinical issue in tertiary care practice.[8] However, hospital based data on its frequency and associated factors are still limited. Therefore the present study was planned to assess the frequency of resistant hypertension among adult hypertensive patients attending a tertiary care centre and to identify the sociodemographic, clinical, lifestyle and treatment related factors associated with it.[7]

MATERIALS AND METHODS

This hospital based cross sectional analytical study was conducted in the Department of General Medicine at RIMS Medical College Hospital Raipur with prior Permission & Consent was taken from patients.

A total of 100 randomly selected adult patients with known hypertension and on antihypertensive treatment were included in the study. Patients with incomplete clinical details or uncertain treatment history were excluded. The study period was 6 months. The collected data were entered and analysed using RStudio software. Categorical variables were expressed as frequency and percentage. Appropriate statistical tests were applied to compare resistant and non-resistant hypertension groups. Multivariable logistic regression analysis was done to identify independent predictors of resistant hypertension. A p value of less than 0.05 was taken as statistically significant.

RESULTS

Table 1: Sociodemographic and clinical profile of the hypertensive patients included in the study

Variable	Frequency (n)	Percentage (%)
Age group (years)		
<40	12	12.0
40–59	46	46.0
≥60	42	42.0
Sex		
Male	58	58.0
Female	42	42.0
Residence		
Urban	61	61.0
Rural	39	39.0
Education		
Literate	68	68.0
Illiterate	32	32.0
Comorbidities / risk factors		
Diabetes mellitus	36	36.0
Chronic kidney disease	20	20.0
Obesity (BMI ≥30 kg/m²)	34	34.0
Dyslipidemia	40	40.0
Current smoking	24	24.0
High salt intake	46	46.0
Poor medication adherence	30	30.0

Table 1 shows the baseline profile of the study participants. A total of 100 known hypertensive patients were included in the study. Most patients were aged 40 years and above. The largest age group was 40–59 years with 46 patients, followed by 42 patients aged 60 years or more. Only 12 patients were below 40 years. Males were slightly more than females, 58% versus 42%. Urban patients were more common than rural patients, 61% and 39% respectively. Most participants were literate (68%), while 32% were illiterate. Among the clinical risk factors, diabetes mellitus was present in 36%, chronic kidney disease in 20%, obesity in 34%, dyslipidemia in 40%, current smoking in 24%, high salt intake in 46% and poor medication adherence in 30%.

Table 2: Frequency of resistant hypertension among the studied hypertensive patients

Blood pressure status	Frequency (n)	Percentage (%)
Non-resistant hypertension	84	84.0
Resistant hypertension	16	16.0
Total	100	100.0

Table 2 presents the prevalence of resistant hypertension in the study population. Out of 100 hypertensive patients, 16 patients had resistant hypertension, giving a prevalence of 16.0%. The

remaining 84 patients had non-resistant hypertension. So in our study nearly one out of every six hypertensive patients showed resistant hypertension.

Table 3: Comparison of sociodemographic factors between resistant and non-resistant hypertension groups

Variables	Resistant HTN n (%) (N=16)	Non-resistant HTN n (%) (N=84)	p-value
Age ≥60 years	11 (68.8)	31 (36.9)	0.019*
Male sex	10 (62.5)	48 (57.1)	0.689
Urban residence	11 (68.8)	50 (59.5)	0.481
Illiteracy	8 (50.0)	24 (28.6)	0.091

Table 3 compares the sociodemographic variables between resistant and non-resistant hypertension groups. Resistant hypertension was more frequent in older patients. Among resistant cases, 68.8% were aged 60 years or above, compared to 36.9% in the non-resistant group and this difference was statistically significant (p=0.019). Male sex was slightly higher in the resistant group (62.5%) than the non-resistant group (57.1%), but this was not statistically significant. Urban residence was also somewhat higher among resistant hypertensive patients, though the association was not significant. Illiteracy was seen more often in resistant hypertension (50.0%) compared to non-resistant hypertension (28.6%), but this did not reach statistical significance.

Table 4: Comparison of clinical and lifestyle related factors in resistant and non-resistant hypertension

Variable	Resistant HTN n (%) (N=16)	Non-resistant HTN n (%) (N=84)	p-value
Diabetes mellitus	10 (62.5)	26 (31.0)	0.015*
Chronic kidney disease	7 (43.8)	13 (15.5)	0.010*
Obesity (BMI ≥30 kg/m²)	9 (56.2)	25 (29.8)	0.041*
Dyslipidemia	9 (56.2)	31 (36.9)	0.145
Current smoking	5 (31.2)	19 (22.6)	0.454
High salt intake	11 (68.8)	35 (41.7)	0.044*

Table 4 shows the association of clinical and lifestyle factors with resistant hypertension. Diabetes mellitus was present in 62.5% of resistant hypertensive patients, while it was seen in 31.0% of non-resistant patients and this difference was significant (p=0.015). Chronic kidney disease was also more common in resistant hypertension, 43.8% versus 15.5%, with significant association (p=0.010). Obesity was found in 56.2% of resistant cases compared to 29.8% of non-resistant cases, which was also significant (p=0.041). High salt intake was reported by 68.8% of resistant hypertensive patients and 41.7% of non-resistant patients, showing a significant association (p=0.044). Dyslipidemia and current smoking were numerically higher in the resistant group, but these associations were not statistically significant.

Table 5: Treatment pattern and medication adherence in resistant and non-resistant hypertension

Variable	Resistant HTN n (%) (N=16)	Non-resistant HTN n (%) (N=84)	p-value
≥4 antihypertensive drugs	10 (62.5)	9 (10.7)	<0.001*
Diuretic use	14 (87.5)	60 (71.4)	0.170
ACEI/ARB use	13 (81.2)	66 (78.6)	0.812
Poor medication adherence	9 (56.2)	21 (25.0)	0.014*
Fixed-dose combination use	6 (37.5)	39 (46.4)	0.505

Table 5 describes the treatment profile and adherence pattern in both groups. Use of four or more antihypertensive drugs was markedly higher in the resistant hypertension group, 62.5% versus 10.7% and this was highly significant (p<0.001). Diuretic use was also higher in resistant hypertensive patients, though the difference was not statistically significant. ACE inhibitor or ARB use was almost similar in both groups. Poor medication adherence was observed in 56.2% of resistant hypertensive patients compared to 25.0% of non-resistant patients and this association was significant (p=0.014). Fixed-dose combination use was lower in resistant hypertension, but no significant difference was found.

Table 6: Independent predictors of resistant hypertension on multivariable logistic regression

Variable	Adjusted odds ratio (AOR)	95% CI	p-value
Age ≥60 years	2.74	1.08–6.98	0.034*
Diabetes mellitus	2.89	1.12–7.47	0.028*
Chronic kidney disease	3.56	1.24–10.18	0.018*
Obesity	2.31	1.01–5.28	0.047*
High salt intake	2.22	0.93–5.31	0.072
Poor medication adherence	3.18	1.23–8.20	0.017*

Table 6 shows the multivariable logistic regression analysis for predictors of resistant hypertension. Age 60 years or more remained an independent predictor with adjusted odds ratio of 2.74 (95% CI: 1.08–6.98, p=0.034). Diabetes mellitus was also independently associated with resistant hypertension (AOR 2.89, 95% CI: 1.12–7.47, p=0.028). Chronic kidney disease showed a strong independent association with resistant hypertension, with adjusted odds ratio of 3.56 (95% CI: 1.24–10.18, p=0.018). Obesity also remained significant in the final model (AOR 2.31, 95% CI: 1.01–5.28, p=0.047). Poor medication adherence was another significant independent predictor, increasing the odds of resistant hypertension by more than three times (AOR 3.18, 95% CI: 1.23–8.20, p=0.017). High salt intake showed increased odds, but it did not remain statistically significant after adjustment.

DISCUSSION

Among 100 treated hypertensive patients, resistant hypertension was found in 16% cases. It was seen more often in older patients, especially those aged 60 years or more. Diabetes mellitus, chronic kidney disease, obesity and high salt intake were significantly more common in the resistant group. Use of 4 or more antihypertensive drugs and poor medication adherence were also higher in these patients. On multivariable analysis, age 60 years or more, diabetes mellitus, chronic kidney disease, obesity and poor medication adherence remained independent predictors of resistant hypertension. The results show that resistant hypertension in this cohort was mainly linked with higher comorbidity burden and treatment related factors.

In the present study, the baseline profile in Table 1 shows that most patients were middle aged or elderly and males were slightly more common than females. This pattern is broadly in line with other resistant hypertension cohorts where the patients were usually older and carried substantial comorbidity burden. Kumara et al. reported a mean age of 61 years in a South Asian cohorts while Chan et al. also found a predominantly older treated hypertensive population in primary care.[9,10] Our baseline burden of diabetes, CKD and obesity in Table 1 also suggests that this was a clinically high risk group rather than a low risk community sample.

As shown in Table 2 resistant hypertension was present in 16.0% of our patients. This looks reasonable and is close to several published cohorts. Holmqvist et al. found a prevalence of 17% in Swedish primary care.[11] Jafari et al. reported 16.7% in OneFlorida and 11.3% in REACHnet using real world EHR data.[12] In the Sri Lankan study by Kumara et al. the prevalence was 19.1%, while Chan et al. from Hong Kong reported a lower figure of 7.43%.[9,10] So our value falls within the range reported in hospital and registry based studies and does not look unusually high or unusually low.

The findings in Table 3 suggest that older age had a clear association with resistant hypertension in our cohort, while male sex and urban residence did not show significant association. Older age has been repeatedly linked with resistant hypertension in prior work. In the Sri Lankan cohort, age above 55 years remained significantly associated with resistant hypertension on regression analysis.[9] In contrast Chan et al. found male sex to be an independent factor in their primary care population.[11] This difference is not surprising because sex effects are less consistent across studies but age usually remains more stable as a risk marker. Illiteracy was more common in our resistant group though it did not reach significance and this may still reflect differences in health awareness, follow up and treatment behaviour.

In Table 4, diabetes mellitus, chronic kidney disease, obesity and high salt intake were significantly more common in resistant hypertension. This pattern is very similar to published evidence. Jafari et al. found diabetes, CKD and higher BMI among the strongest predictors in two large real world populations.[12] Holmqvist et al. also showed higher frequencies of diabetes and chronic kidney disease among treatment resistant patients.[11] Kumara et al. reported that diabetes and obesity were significantly associated with resistant hypertension in a South Asian sample.[9] The association with high salt intake in our study is also clinically meaningful because sodium restriction has been shown to produce marked blood pressure reduction in resistant hypertension.[13] Dyslipidemia and smoking were numerically higher in our resistant group, but they did not become statistically significant, which can happen in smaller hospital based samples.

The treatment related findings in Table 5 also deserve attention. Use of four or more antihypertensive drugs was much higher in the resistant group, which is expected because this is built into the clinical phenotype itself. More important is the adherence signal. Poor medication adherence was present in 56.2% of resistant hypertensive patients in our study and remained significant on bivariate analysis. This agrees well with published work showing that nonadherence is a major contributor to apparent resistance. Hyman and Pavlik highlighted medication adherence as a core issue in resistant hypertension.[14] In the SYMPATHY substudy, de Jager et al. found objective nonadherence in 68% of patients with apparent resistant hypertension based on serum drug testing.[15] So our Table 5 finding is clinically important because it points to a modifiable factor and not only to disease severity. Diuretic and ACEI/ARB use were common in both groups, which suggests that mere prescription of drugs is not enough if adherence and regimen optimization are not properly addressed.

The final model in Table 6 is probably the most clinically useful part of the study. After adjustment,

age ≥60 years, diabetes mellitus, CKD, obesity and poor medication adherence remained independent predictors. Among these, CKD showed the strongest adjusted association in our dataset. This is again consistent with published literature. Jafari et al. showed CKD, diabetes and higher BMI as strong predictors in large EHR cohorts.[12] Holmqvist et al. also showed strong comorbidity clustering with diabetes and CKD.[11] In the CRIC analysis Thomas et al. further showed that apparent treatment resistant hypertension is common in CKD and identifies a clinically high risk subgroup.[16] High salt intake showed increased odds in our model but lost statistical significance after adjustment. This may mean that part of its effect overlaps with obesity, diabetes and adherence related factors already present in the model.

The present discussion supports that resistant hypertension should not be seen as only a blood pressure number problem. In our study, the signal comes mainly from age, metabolic disease, kidney disease, obesity and adherence failure as seen from Tables 3 to 6. This matters clinically because resistant hypertension is associated with poorer outcomes in longitudinal studies. Daugherty et al. showed higher cardiovascular event risk in patients who developed resistant hypertension.[17] Muntner et al. reported increased risk of coronary heart disease, stroke, heart failure, all cause mortality and end stage renal disease in apparent treatment resistant hypertension.[18] Bangalore et al. also showed higher cardiovascular morbidity and mortality in coronary disease patients with apparent treatment resistant hypertension.[19] Patients who are older, diabetic, obese, renally impaired or poorly adherent need earlier recognition, closer follow up and more systematic treatment review.

This study has some limitations. Firstly, it was a single centre hospital based study, so the findings may not fully represent the general hypertensive population. Second, the sample size was modest, which may have reduced the power for some variables like smoking, dyslipidemia and education status. Thirdly resistant hypertension was identified from clinic based blood pressure and treatment history, so some patients with white coat effect or apparent resistance may have been included. Fourth, medication adherence and salt intake were assessed mainly from patient history, so recall bias and reporting bias can be present. Lastly, because of the cross sectional design, association could be assessed but causal relation cannot be confirmed.

Resistant hypertension was not uncommon in our study. It was mainly related to older age, diabetes, CKD, obesity and poor adherence. These patients need closer follow up and more careful treatment review. Better adherence assessment and early risk factor control may improve overall outcome.

CONCLUSION

In the present study, resistant hypertension was seen in a clinically important proportion of treated hypertensive patients. Older age, diabetes mellitus, chronic kidney disease, obesity and poor medication adherence were the main factors associated with resistant hypertension. These findings suggest that resistant hypertension in tertiary care is strongly linked with comorbidity burden as well as treatment related issues. Early identification of high risk patients, proper evaluation of adherence and timely optimization of therapy may help improve blood pressure control and reduce future cardiovascular and renal risk

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