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Original Article

Prevalence and characteristics of resistant hypertensive patients in an Asian population

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ABSTRACT

Background: Resistant hypertension is a well-recognized clinical challenge yet there are no reported data on its prevalence in Pakistan. These patients are subjected to a higher risk of developing hypertensive complications. The objective of our study was to evaluate the prevalence and determinants of resistant hypertension in an Asian cohort of hypertensive patients.

Methods: This cross-sectional study was carried out among hypertensive patients visiting a tertiary care hospital in Karachi from September–December 2015. Patient data and characteristics were recorded using a pre-coded questionnaire. Morisky and Berlin questionnaires were used to assess compliance to medications and determine the risk of developing obstructive sleep apnea, respectively. Pearson's chi-square test was used to analyze statistical differences between hypertensive patients and related factors. **Results:** A total of 515 patients were included in the study. Overall, 12% of the total patients (n = 62) were resistant hypertensives and 25% (n = 129) had pseudo-resistant hypertension. Resistant patients were more often females, older and had a higher body mass index (all $P < 0.001$). Use of painkillers and noncompliance to dietary recommendations were found to be significant determinants of resistant hypertension. Prevalence of comorbid conditions, including diabetes ($p = 0.33$), hyperlipidemia ($p = 0.46$), and chronic kidney disease ($p = 0.23$), was not significantly higher in patients with resistant hypertension. **Conclusion:** Nearly one in ten hypertensive patients had true resistant hypertension, and twenty-five percent of patients had pseudo-resistance. Resistance hypertension is significantly associated with female gender, older age, obesity, dietary noncompliance and increased use of NSAIDs.

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1. Introduction

Hypertension is one of the most important risk factors for cardiovascular and renal diseases. Approximately 1 billion adults have hypertension and the prevalence is increasing.¹ Despite best efforts to control blood pressure, resistant hypertension (RH) may occur.² In spite of increased recognition and therapeutic interventions, studies show that the efficiency of blood pressure control in hypertensive patients continues to decline,^{1,3,4} with an increase in the incidence of RH worldwide.^{5–8} The failure to achieve target values of blood pressure has several causes such as poor treatment

adherence, scarcity of resources and failure to intensify treatment in a timely manner.⁹

Nearly 1/5th of the population of Pakistan suffers from hypertension with prevalence expected to rise in the coming years.¹⁰ However, RH prevalence values have yet to be reported. Despite an increase in the number of clinical studies on the prevalence of RH, the growing incidence of this condition among treated hypertensive patients is established to be between 5 and 30% in the developed part of the world.^{2,4,10–12} This disparity is primarily because of the difference in definition employed in the study or failure to rule out pseudo-hypertension. There is a dearth of published literature providing up-to-date estimates of the prevalence of RH across developing regions of the world.

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Existing researches have, hitherto, mainly focused on Western population while the prevalence of RH in South Asia has not been well explored. Therefore, these RH prevalence estimates may differ from what would be found in a middle-income metropolis like that of Karachi.

An interesting development is the proof offered by prevalence surveys and genome-wide association studies that the incidence of hypertension and its resistant category has a genetic component and predisposes population of South Asians and Central and Eastern.^{13–15} However, the disease remains idiopathic in its essence, with its proximal causes still not well defined.¹⁶

Defining optimal treatment for patients with RH is a clinical challenge. Hence, a greater understanding of this subgroup of hypertensive patients is crucial for establishing known determinants and facilitate the development of targeted strategies for prevention, treatment, and control. Thus, the objective of our study was to assess the prevalence and predictors of resistant hypertension in an Asian cohort of hypertensive patients.

2. Method

This cross-sectional study was conducted at a tertiary care hospital in Karachi, Pakistan for a duration of four months from September 1, 2015 to December 31, 2015. It consisted of a survey of all patients older than 18 years, previously diagnosed with essential hypertension, who had records of 3 or more blood pressure measurements within the past one year, presenting to the clinics. Essential hypertension was defined as a systolic blood pressure that is persistently ≥ 140 mmHg on 2 or more occasions, or a diastolic blood pressure persistently ≥ 90 mmHg on 2 or more occasions, when an average of each is measured at every visit using at least 2 values.¹⁷ Patients who were known cases of hypertension secondary to tumors or other diseases of the endocrine system, obesity, pregnancy, coarctation of aorta, and use of hormonal contraceptives were excluded from the study. The study was approved by the Institutional Review Board of Dow University of Health Sciences (DUHS)

Participants were selected via convenience sampling; all patients visiting the clinic on a given day were interviewed after written consent. Participant cooperation rate was 96%, which yielded a total of 515 complete cases for analyses. For the purpose of this study, we used a pilot-tested questionnaire that was administered to each patient with the help of an interviewer. Moreover, interviewer bias was eliminated by training interviewers who were kept unaware of the outcome of interest for the study. From each patient, we obtained information on socio-demographic details, duration of hypertension, current medications, co-morbid conditions, lifestyle and family history of hypertension. In addition to these, Berlin questionnaire was used to determine the risk of developing obstructive sleep apnea (OSA), dividing the patients into high and low-risk categories. Morisky questionnaire was utilized to assess adherence to antihypertensive medications, the results of which were classified into high, average and poor adherence, following which all cases of RH were further classified into those with pseudo-resistance and those with true resistant hypertension. True resistant hypertension (tRH) was defined as blood pressure that exceeds target values in spite of best possible regimen consisting of 3 antihypertensive drugs of different classes, where one should ideally be a diuretic.¹⁸ Pseudo-resistance was defined as uncontrolled hypertension as a result of inaccurate measurement, poor adherence to prescribed medications, incorrect drug choices/doses, or white-coat effect.¹⁹ Moreover, to measure blood pressure (BP) of each patient, the physician used a mercury sphygmomanometer. After an initial resting period of 5 minutes, two measurements were taken with an interval of 10 min in between, and mean values of both systolic and

diastolic blood pressure were recorded. In addition to these, 3 previous blood pressure values were extracted from the patients' files. WHO defines a BMI ≥ 25 kg/m² as overweight, whereas obesity is categorized as BMI ≥ 30 kg/m².²⁰

For the purpose of this study, all data entry and analyses were done using the IBM Statistical Package for Social Sciences (SPSS), version 23 for Windows. Frequencies with percentages were calculated for all categorical variables and the Chi-square test was used to check the significance of relationships between characteristics of patients with essential hypertension and those with true resistant hypertension. No imputation methods were used to replace missing values, and only completely filled questionnaires were considered for our use. A p-value of less than 0.05 was considered to be significant.

3. Results

The mean age of patients was 64.3 ± 12.3 years, with a mean BMI of 29.1 ± 4.5 kg/m². The mean systolic and diastolic blood pressures were 142 ± 15.2 mmHg and 88 ± 11.7 mmHg, respectively. More than half the patients had diabetes mellitus ($n=287$, 55.7%), while 78 patients (15.1%) had a positive family history for hypertension. Approximately a third of the total patients ($n=174$, 33.8%) were non-compliant to dietary recommendations. It was found that patients were ($n=317$, 61.6%) moderately adherent to prescribed antihypertensive medications. Among the sample cohort, 112 patients (21.7%) were at a high risk of developing OSA. Table 1 summarizes the baseline characteristics of the sample population.

Prevalence of true resistant hypertension was low ($n=62$, 12%), a quarter ($n=129$, 25%) of the population were pseudo-resistant hypertensive patients while most ($n=320$; 63%) had essential hypertension with no form of RH (Fig. 1). The study population was divided into two groups according to patients exhibiting essential

Table 1
Baseline characteristics of patients.

Characteristics	
Male, n (%)	309 (60.0)
Married, n (%)	463 (89.9)
Average systolic blood pressure, mmHg	142 ± 15.2
Average diastolic blood pressure, mmHg	88 ± 11.7
Mean BMI, (kg/m ²)	29.1 ± 4.5
Drugs, n (%)	
Steroids	33 (6.4)
Painkillers	171 (33.2)
Lifestyle risk factors, n (%)	
Dietary non-compliance	174 (33.8)
Smoking	194 (37.7)
Alcohol	26 (5.0)
Co-morbidities, n (%)	
Diabetes Mellitus	287 (55.7)
Hyperlipidemia	114 (22.1)
Chronic kidney disease	39 (7.6)
Family history, n (%) ^a	78 (15.1)
Adherence, n (%) ^b	
High	151 (29.3)
Average	317 (61.6)
Poor	47 (9.1)
Risk of OSA, n (%) ^c	
High	112 (21.7)
Low	403 (78.3)

^a Patients with positive family history for hypertension.

^b Adherence to prescribed antihypertensive agents.

^c Obstructive sleep apnea.

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