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Original Article

Prevalence of Essential Hypertension and Assessment of Cardiovascular Risk of Pakistani Adults in Outpatient Setting

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Abstract

Background :To assess the prevalence of essential hypertension and evaluate cardiovascular risk in patients in Pakistan.

Methods:This cross-sectional, non-interventional study was conducted at multiple centres throughout Pakistan. Data was collected from patients of either gender, ≥18 years of age, seeking routine medical consultation. Diagnosis and staging of hypertension was carried out using guidelines laid by Seventh Report of Joint National Committee (JNC 7). Gender-wise Framingham scores were calculated based on non-laboratory and laboratory parameters.

Results: Out of 2336 patients evaluated, prevalence of hypertension and prehypertension was 51.5% and 31.4% , respectively. A total of 501 patients had co-prevalent diabetes and hypertension. Ten-year Framingham scores calculated using non-laboratory parameters showed 56% (947/1693) patients aged ≥30 years were at medium-to-high risk for cardiovascular disease (CVD). While Framingham scores based on laboratory or non-laboratory parameters were not significantly different for men, in women the non-laboratory based score was higher. Angiotensin-converting enzyme inhibitors and calcium channel blockers were antihypertensive agents of choice.

Conclusions: Since prevalence of pre-hypertension and hypertension in Pakistani adults continues to be on rise and substantial proportion of study population is at medium-to-high risk of developing CVD within the next 10 years, regular BP monitoring and risk scoring is mandated for identification of at-risk population and optimal management of CVD.

Key Words:Hypertension, Physicians, Primary care.

Introduction

Hypertension is an independent risk factor for coronary heart disease, heart failure, cerebrovascular disease, and chronic renal failure and a leading cause of cardiovascular (CV) morbidity and mortality. [1,2] Over 2/3rd of patients with hypertension are from developing countries and this is attributed to modern lifestyles and increasing life spans. The global burden of hypertension is predicted to cross 1.5 billion by 2025.[3-5]

Hypertension is widely prevalent in Pakistan and the number of cases has doubled from 17% in 1980 to 35% in 2008. [6] Results from Pakistan National Health Survey in the late nineties showed that incidence of hypertension in adults >45 years of age (33%) was twice that in the general population (≥15 years and older; 18%). [7] In addition, approximately 1/4th of middle-aged adults in Pakistan have coronary artery disease and 17% population carries at least two associated risk factors. [8,9]

Since hypertension is a progressive disease, early detection and blood pressure control are the keys to reduction in CV risk. Clinical evidence demonstrates that screening for high blood pressure has benefits in reduction of CV events.[10] Guidelines laid down by the 7th report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) recommends screening individuals ≥18 years of age for hypertension, and evaluating those with hypertension for associated CV risk factors. [2] In recent years, rapid and significant changes in lifestyle practices in Pakistan have a direct bearing on CV risk. Consequently, there is an urgent need to determine the burden of hypertension as well as the associated CV risk in Pakistani adults.

Risk prediction models are a useful tool in clinical practice to identify, communicate with, and treat high-risk individuals before disease complications set in. Numerous risk factors interact and contribute to the pathology of CV disease. Epidemiological and clinical evidence suggest that translating risk factors into scores can predict an individual's CV risk with a certain amount of accuracy.Risk prediction algorithms such as Framingham Risk Score (FRS), Systematic Coronary Risk Evaluation (SCORE), and World Health

Organisation/International Society of Hypertension(WHO/ISH) score are widely used to identify and manage patients at high CV risk. [1,11,12] The Framingham model employs either laboratory parameters (such as serum lipid levels) or non-laboratory parameters (such as body mass index and anthropometrics) for calculation of risk score. A comparative study published in the Lancet in 2008 showed that scoring with non-laboratory parameters not only identifies patients at risk, but also offers the advantages of feasibility and cost-effectiveness.[13] Laboratory investigations in Pakistan are generally expensive to conduct and can be an economic strain to a majority of the population, especially those in the low-income strata. Hence, a risk scoring model that combines predictability with practicality and can be used in primary care physicians' (PCP) clinic would be quite useful in CV risk estimation in Pakistan.

Focusing on these issues, the primary goal of our study was to assess prevalence of hypertension in general population visiting PCPs for medical consultation. In addition, we also sought to compare non-laboratory based parameters over standard laboratory parameters in predicting CV risk in adults ≥30 years of age, to stratify our hypertensive patients as per JNC 7 guidelines and to assess the antihypertensive therapy prescribed to them.

Patients and Methods

This was a national, cross-sectional, multicenter hypertension registry conducted between November to October 2014 at 140 sites in 12 cities in Pakistan. Study investigators were community-based PCPs from these cities and were randomly selected from the physician database of Sanofi-Aventis Pakistan Ltd. The study was conducted in compliance with all international and applicable guidelines, national laws and regulations of Pakistan. The study was conducted in the ambulatory care setting, at individual outpatient clinics.Adults ≥18 years of age, who were seeking medical consultation with their PCP, irrespective of their hypertension status were included. Patients with a past history of myocardial infarction or objectively confirmed angina pectoris, suspected/known secondary hypertension, or were pregnant, were excluded. Each investigator recruited 20 consecutive patients.

Data collected by the investigator at the time of enrolment included patient demographics and anthropometrics, lifestyle choices, CV risk factors and medical history, and two consequent blood pressure recordings taken at the site at a 5-minute interval. Patients ≥30 years of age were directed to a predetermined laboratory for estimation of serum cholesterol and high-density lipoprotein (HDL). Laboratory tests were conducted by Aga Khan University Hospital Clinical Laboratory.Prevalence estimation and staging of hypertension were done using JNC 7 guidelines. Hypertension was characterized as systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg for patients without diabetes, and SBP ≥130 mmHg or DBP ≥80 mmHg for patients with diabetes. For each patient ≥30 years,Framingham risk scores were calculated (Models A and B, Suppl. Fig. 1 and 2) based on their laboratory and non-laboratory parameters. Scores for each patient were multiplied by a factor of 1.4 as recommended by the National Institute for Health and Care Excellence (NICE) in order to make them applicable to the South Asian phenotype. [14]

Based on an estimated prevalence of hypertension of 18% with a 1.5% margin of error, 95% confidence level and anticipating 10% data unworthiness (due to incomplete information, missing forms, etc.) a sample size of 2800 patients was required. This sample size also allowed us to meaningfully evaluate CV risk with both Framingham models with a 95% confidence limit and 1.5% margin of error. Differences between scores generated by Model A and B were probed for statistical validity by paired t-test. Patients' scores were also categorized for risk as low (<10%), medium (10%-20%), or high (>20%) and differences in proportion within each category were compared using Chi-square testThe statistical analyses were performed using SPSS version 18 (SPSS Inc., Chicago, USA)

Results

The study population comprised 56% males and had an average age of 40.8±13.1 years (Table 1). The proportion of patients ≥30 years in the cohort was 72.5% (1693/2336. BMI at 28.2±5.1 kg/m^2 was marginally higher in this subpopulation, as was the proportion of patients with BMI ≥25 kg/m^2. In patients ≥30 years, the proportion of women with BMI ≥25 kg/m^2 was greater than men (78.0% vs. 67.8%). This trend was replicated in the case of prevalence of diabetes i.e29.4% (497/1693) patients ≥30 years had diabetes and a larger proportion of women presented with diabetes (32.1% versus 26.9% in men). The proportion of smokers in patients ≥30 years was 21.3% (n=363). Average cholesterol and fasting HDL levels in these patients were 192.9±45.0mg/dL and 44.6±12.8 mg/dL, respectively.

As per JNC 7 guidelines, 51.5%(n=1202, 95% CI. 48.6% - 54.4%)of patients in our study had hypertension. Average SBP and DBP in the overall cohort was 137.5±21.1 mmHg and 87.6±11.3 mmHg respectively, and both were marginally higher in patients ≥30 years [SBP: 141.9±20.7 mmHg; DBP: 89.7±10.7mmHg]. The study population had 31.4%patients with prehypertension, 29.9% patients with Stage 1 hypertension, and 26.0% patients with Stage 2 hypertension. Staging of hypertension in diabetes versus non-diabetes showed that a substantially higher proportion of patients with diabetes were either in pre-hypertensive stage or had hypertension when compared to patients without diabetes (96.3% versus 84.7%; Table 2). The incidence of diabetes in hypertensive patients was 47.1% (501/1202) in comparison to 3.0% (34/1134) in normotensive patients. The prevalence of hypertension in non-diabetic patients was 30% (C.I. 28.2 – 31.9) while the prevalence of hypertension in patients with diabeteswas 21.4% (C.I. 19.8 – 23.2). (Table 2).Mean Framingham score in women calculated using non-laboratory parameters (Model A;18.1±9.1) was significantly higher than that estimated using laboratory parameters [Model B; mean score: 14.8±7.4; paired mean difference: 3.17±4.27; p<0.01; (Table 3). In men, mean scores were 16.3±8.3 with Model A and 16.9±85 with Model B with a paired mean difference of -0.68±3.4 (p<0.01). The use of individual Framingham scores for risk stratification showed disparate results in women (Table 3). Model B indicated 62.7% (n=502) and 8.9% (n=71) women in the low-risk and the high-risk category, respectively. In comparison, Model A calculated 45.6% (n=366) and 25.3% (n=203) women in low- and high-risk categories, respectively (p<0.01). In contrast, both Model A and B showed a similar proportion of men in either of the risk categories. At the time of enrolment, 84% (1014/1202) of patients with hypertension were prescribed antihypertensive medications (Table 4). The most widely prescribed class of agents was angiotensinogen-converting enzyme (ACE) inhibitors (in 41% [493/1202] patients). Of the 734 patients in the pre-hypertensive stage, 251 (34.2%) were prescribed antihypertensive agents. Of 139 patients with co-prevalent prehypertension and diabetes, 57% (n=80) were prescribed antihypertensive agents. The agents of choice in patients with co-prevalent diabetes and hypertension were ACE inhibitors and beta blockers.

Table 1. Patient Characteristics

Characteristics	Total study population (n=2336)		Patients ≥30 years of age (n=1693)	
	n (%)	Mean (±SD)	n (%)	Mean (±SD)
Age, in years		40.8 (±13.1)		46.6 (±10.4)
Gender				
Male	1307 (56.0)		892 (52.7)	
Female	1029 (44.0)		801 (47.3)	
Height, in cms		163.5 (±10.6)		162.7 (±10.5)
Weight, in kg		72.9 (±13.5)		74.1 (±13.0)
BMI, in kg/m²		27.4 (±5.3)		28.2 (±5.1)
Patient with BMI ≥25 kg/m²	1530 (65.5)		1231 (72.7)	
Blood pressure, in mmHg				
SBP		137.5 (±21.1)		141.9 (±20.7)
DBP		87.6 (±11.3)		89.7 (±10.7)
Hip circumference, in cms		101.0 (±14.6)		103.6 (±14.4)
Waist Hip Ratio (WHR), overall		0.93 (±0.10)		0.94 (±0.10)
WHR males		0.95 (±0.09)		0.95 (±0.09)
WHR females		0.91 (± 0.10)		0.92 (± 0.10)
Truncal Obesity				
Males with WHR ≥0.90	957 (41.0)		701 (41.4)	
Females with WHR ≥0.80	928 (39.7)		743 (43.9)	
Pre-existent diabetes	535 (22.9)		497 (29.4)	
Smoking	513 (22.0)		363 (21.4)	
Total cholesterol ;192.9 (±45.0)				
<160			329 (19.4)	
160-199			620 (36.6)	
200-239			422 (24.9)	
240-279			134 (7.9)	
≥280			62 (3.7)	
Fasting HDL;44.6 (±12.8)				
≥60			139 (8.2)	
50-59			255 (15.1)	
45-49			251 (14.8)	
35-44			670 (39.6)	
<35			252 (14.9)	

SD – standard deviation; BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure; HDL – high density lipoprotein; SD – standard deviation

Table 2. Prevalence and staging of hypertension as per JNC 7 guidelines

Prevalence		(N = 2336)	
	BP cut-off ranges	Prevalence	
		n	% (95% CI)
Non-diabetic patients	SBP≥140 or DBP≥90	701	30.0 (28.2 – 31.9)
Diabetic patients	SBP≥130 or DBP≥80	501	21.4 (19.8 – 23.2)
Staging		n (%)	
Total Study Population (N = 2336)			
Normal*		295 (12.6)	
Prehypertension†		734 (31.4)	
Stage 1 Hypertension‡		699 (29.9)	
Stage 2 Hypertension∫		608 (26.0)	
Non-diabetic patients ≥18 yrs (N = 1801)			
Normal*		275 (15.3)	
Prehypertension†		595 (33.0)	
Stage 1 Hypertension‡		505 (28.0)	
Stage 2 Hypertension∫		426 (23.7)	
Diabetic patients ≥18 yrs (N = 535)			
Normal*		20 (3.7)	
Prehypertension†		139 (26.0)	
Stage 1 Hypertension‡		194 (36.3)	
Stage 2 Hypertension∫		182 (34.0)	

*Normal:SBP <120 mmHg and DBP <80 mmHg;† Prehypertension:SBP 120–139 mmHg or DBP 80–89 mmHg;‡ Stage 1 Hypertension: SBP 140–159 mmHg or DBP 90–99 mmHg;∫ Stage 2 Hypertension: SBP ≥160 mmHg or ≥100 mmHg;JNC 7 – Seventh Report of the Joint National Committee in Prevention, Detection, Evaluation and Treatment of High Blood Pressure;BP – blood pressure;SBP – systolic blood pressure; DBP – diastolic blood pressure; CI – confidence interval

Table 3. Gender-based Framingham scores (A) and risk stratification (B) using non-laboratory & laboratory predictors in patients aged ≥30 years

(n=1693)

(A) Framingham scores				
	Non-laboratory predictors (Model A)	Laboratory predictors (Model B)	Paired Mean Difference (±SD)	p-value
Females, N = 801				
Mean total score (±SD)	18.1 (± 9.1)	14.8 (± 7.4)	3.17 (± 4.27)	<0.01
Range	-4 to 45	-6 to 39		
Males, N = 892				
Mean total score (±SD)	16.3 (± 8.3)	16.9 (± 8.5)	-0.68 (± 3.4)	<0.01
Range	-3 to 39	0 to 41		
(B) Risk stratification				
Risk category	Score	n(%)		
		Non-laboratory predictors (Model A)	Laboratory predictors (Model B)	p-value
Female, N = 801				
Low: < 10%	≤ -2 to 12	366 (45.6)	502 (62.7)	<0.01
Medium: 10%-20%	13 to 17	232 (28.9)	228 (28.4)	0.59
High: >20%	18 to ≥21	203 (25.3)	71 (8.9)	<0.01
Male, N = 892				
Low: < 10%	≤ -3 to 10	380 (42.6)	367 (41.1)	0.53
Medium: 10%-20%	11 to 14	213 (23.9)	222 (24.9)	0.62
High: >20%	15 to ≥18	299 (33.5)	303 (34.0)	0.84

SD – standard deviation

Table 4. Therapeutic management according to stage of hypertension

Treatment prescribed	Hypertensives without diabetes			Hypertensives with diabetes		
	n (%)			n (%)		
	Prehypertension n=734	Stage 1 n=699	Stage 2 n=608	Prehypertension n=139	Stage 1 n=194	Stage 2 n=182
Angiotensin Converting Enzyme Inhibitors	67 (9.1)	269 (38.5)	277 (45.6)	30 (21.6)	79 (40.7)	81 (44.5)
Calcium Channel Blockers	53 (7.2)	154 (22.0)	191 (31.4)	22 (15.8)	32 (16.5)	44 (24.2)
Angiotensin Receptor Blockers	45 (6.1)	140 (20.0)	141 (23.2)	21 (15.1)	44 (22.7)	48 (26.4)
Beta Blockers	36 (4.9)	113 (16.2)	139 (22.9)	16 (11.5)	54 (27.8)	61 (33.5)
Diuretics	12 (1.6)	68 (9.7)	108 (17.8)	4 (2.9)	29 (14.9)	40 (22.0)
Fixed Dose Combination	32 (4.4)	60 (8.6)	73 (12.0)	13 (9.4)	24 (12.4)	28 (15.4)
Others	6 (0.8)	21 (3.0)	36 (5.9)	2 (1.4)	7 (3.6)	12 (6.6)

Discussion

In this nationwide estimate of the burden of essential hypertension in Pakistani adults, we discovered that prevalence of hypertension in outpatient settings is substantially higher than in previous population-based surveys, and every second patient ≥18 years of age visiting a primary care physician (PCP) is likely to have high blood pressure. After staging patients' blood pressureas per JNC 7, we determined that only 12.6% of our study population was normotensive and this proportion further decreased to 3.7% in patients with diabetes. Furthermore, analysis of Framingham scores revealed that >50% of the study population was at a medium-to-high risk of developing CV events within the next 10 years. The rising prevalence of hypertension in Pakistan has been attributed to a plethora of factors like genetic predisposition, urbanization, dietary habits, concomitant rise in prevalence of obesity and diabetes, sedentary lifestyles, and lack of health awareness.[15,16] Our estimated prevalence of 51.4% is substantially higher than figures reported from previous studies in Pakistan, South Asia, the United States, and Europe. However, we must consider that since our study was conducted in clinical settings,the study cohort could have a higher proportion of hypertensive patients than the general population. [4,6,7,17]

Prehypertension is defined as SBP of 120-139 mmHg or DBP of 80-89 mmHg per the JNC 7 guidelines and is a precursor stage to hypertension. [2] Approximately 1/3rd of pre-hypertensive patients are estimated to progress to hypertensive stage within 4 years.[18]Prehypertension, by itself, is also associated with adverse CV outcomes and progression of

diabetes. [19,20] Hence, it becomes imperative to also monitor the prevalence of prehypertension and suggest appropriate intervention as per guidelines. Various elaborate global studies such as the NHANES or a meta-analysis by Guo, et al estimate the global burden of prehypertension to be 31%-36%. [21,22] Our study population had 31.4% patients in the pre-hypertensive stage, which corroborates with the global estimate. Additionally, the prevalence of prehypertension in our study is comparable to those estimated from other regional studies in Asia – India, Korea, Japan, China, and Iran.[23-26]

The United Kingdom Prospective Diabetes Study determined that hypertension is comorbid in approximately 70% of patients with diabetes, and is twice as prevalent in patients with diabetes. [28] A sizeable proportion of newly diagnosed diabetes patients have also been shown to have pre-existent hypertension. In our study, approximately 1/5th of the patients (n=501, 21.4%; CI: 19.8 – 23.2) had co-prevalent diabetes and hypertension, and 701 (30.0%, CI: 28.2 – 31.9) patients had hypertension exclusively. The prevalence of diabetes in hypertensive patients was 41.7% . These findings are consistent with the belief that hypertension can worsen diabetic complications and strongly corroborate the association of hypertension and diabetes in CV pathology.

Despite proven usefulness of aforementioned risk prediction models, issues that have most likely hindered their routine use in clinical practice at a PCP level in Pakistan are awareness of these models among the physicians' community and the need for expensive and time-consuming laboratory tests to implement these. There is limited data on the applicability of these models in a population that is as heterogeneous in terms of ethnicity, lifestyle, socioeconomic status, and genetics, as in Pakistan. A recent study that compared these models (FRS, SCORE, and WHO/ISH) in Malaysian population suggests use of FRS for identifying individuals at high risk. [29] In our study, non-laboratory Framingham scores indicated a higher risk profile in females in comparison with laboratory-based scores, with a paired difference of 3.17±4.27 between the average scores ($p<0.01$). In contrast, risk profiles were similar for males when either model was used. However, almost a quarter of Pakistani women and approximately one-third of Pakistani men over the age of 30 years are at a high risk of developing cardiovascular disease within the next 10 years. Thus, our results demonstrate utility of non-laboratory based Framingham risk scoring for identification of high CV risk individuals in Pakistan and validate similar findings from other studies. [13,30-32]

The Pakistan Hypertension League has drafted guidelines for therapeutic management of hypertension in Pakistan and these are largely based on those laid by the National Institute for Health and Care Excellence (United Kingdom). These recommend the use of ACE inhibitors, ARBs or CCBs as first line of treatment depending on the patients' age (ACE inhibitors or ARBs for patients < 55 years and CCBs for patients > 55 years) and ethnicity and are in stark contrast with the JNC 7 guidelines which advocate use of thiazide diuretics for lowering BP. In our study we observed an adherence to the Pakistani guidelines, since ACE inhibitors were the drugs of choice across the hypertensive fraction of the study cohort. Interestingly, despite 31.4% of the study cohort being pre-hypertensive, we discerned that only 1/3rd of them were prescribed antihypertensive medications. In pre-hypertensive patients with diabetes, only 57% were prescribed medical intervention. This is indeed alarming since JNC 7 guidelines specify pre-hypertension with diabetes to be a compelling indication that warrants the use of BP-lowering agents to ameliorate disease progression. [2]

Conclusion

1. Prevalence of hypertension in clinical settings in Pakistan is undesirably high and these patients are at a significant risk of developing cardiovascular disease.
2.This major health issue needs to be addressed by a concerted effort from the medical community and governmental authorities.
3 Current national guidelines need to be harmonized with latest evidence-based guidelines to increase disease awareness and optimize treatments.

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