Observational Assessment of Blood Pressure Goal Achievement in Patients on Antihypertensive Therapy in Urban Pakistan: Results of ACTION Registry

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Abstract

Background: To assess the proportion of Pakistani patients achieving blood pressure goal while on existing antihypertensive therapy and reasons for not achieving BP goal.

Methods: This descriptive study was conducted in 60 centers across 10 cities of Pakistan by simple random sampling. It was a national, multi-centre, non-interventional, cross-sectional, epidemiological disease registry. Patients, who were ≥15 years of age, on antihypertensive medications for ≥4 weeks and had taken a dose on the day of visit, were included. Investigators were randomly selected from a list of physicians within a given geographical territory (Urban) in major cities of Pakistan. Approximately 58% of the physicians were general practitioners and 42% were specialist such as medical internist and cardiologist. Reasons for not achieving BP goal was determined by assessing different variables. Changes made in BP management in patients not at BP goal and therapeutic regimens prescribed to patients at BP goal were also documented. Differences in the profile of patients according to the attainment of BP goal were analyzed using bi-variate analysis. A p <0.05 was considered significant.

Results: Mean age of patients (n=1130) was 52.6 ± 11.9 years. Of them 49% were females. Mean duration of HTN was 6.1 (±6.2) years. Of 1130 patients, 23.80% achieved BP goal. In patients not achieving BP goal, history of sedentary lifestyle (60.27%), diabetes (42.97%), and dyslipidemia (40.30%) were identified as risk factors. Coronary artery disease (21.25%) was the most common co-morbid condition. Lack of patient understanding on treatment importance (47.03%) was major reason for not achieving BP goal. Lifestyle modification (37.74%) and addition of another drug (37.74%) were recommended. Majority of patients at BP goal received angiotensin-converting enzyme inhibitors (36.05%).

Conclusion: In Pakistan, only one in four patients taking antihypertensive medications and presenting to physicians achieves BP goal as per JNC VII guidelines. This has significantly improved as compared with previous survey. Lack of understanding of importance of BP treatment remains the major impediment in achieving better BP control.

Key Words: Hypertension, Risk factors, Antihypertensive agents, Blood Pressure goal

Introduction

The National Health Survey of Pakistan reports that only 3% hypertensive patients in Pakistan are at blood pressure (BP) goal despite availability of antihypertensive drugs and treatment recommendations. During the last decade, new therapies have been introduced and international and local guidelines have been revised to set improved BP goals for patients. Hypertension is one of the major risk factors for cardiovascular and kidney diseases, and an important public health concern. Worldwide, there were 978 million adults (aged ≥25 years) who had uncontrolled hypertension in 2008 and this number is predicted to increase to 1.56 billion by 2025.[1,2] Within Asia the prevalence of hypertension is high, with rates of 19% in China (2002) and 46% in India (2009-10).[3,4] The National Health Survey of Pakistan (NHSP; 1990-1994) reports indicate that while hypertension affects 18% of adults >15 years of age and 33% of adults >45 years of age in Pakistan. Only 37% of people have ever had their blood pressure (BP) checked and only 3% of people with hypertension achieve BP goal (≤140/90 mm Hg).[5]

Hypertension causes high mortality, imposes huge economic burden, and negatively impacts the health related quality of life (HRQoL).[6-8] Hypertension has a considerable psychological impact. Patients who are aware of their hypertension status show reduced physical functioning and general health scores during HRQoL assessment compared to patients who are unaware of it. [9] Hypertension plays a crucial role in the development of cerebrovascular disease, ischemic heart disease, cardiac and renal failure, and some of its co-morbidities aggravate its cardiovascular risk.[10] Risk factors for hypertension include age, smoking, physical inactivity, overweight/obesity and a positive family history.[11,13] Inadequately addressing these risk factors in hypertensive patients results in higher morbidity and mortality, thus, making them appropriate targets for management. [10,12] Evidence

indicates that physical activity of 30 minutes a day significantly reduced mean BP levels.[14]

Current data suggests that most patients require more than one antihypertensive agent for achieving BP goals.[15] Feldman et al. proposed a simplified antihypertensive algorithm which sequentially progresses therapy in response to the control status of hypertension: a) an initial low-dose, fixed-dose combination therapy (angiotensin-converting enzyme;ACE) inhibitor+diuretic combination or angiotensin receptor blocker [ARB]+diuretic combination) b) increasing combination therapy to highest dose, c) addition of a calcium channel blocker and up-titration and d) addition of a non-first-line antihypertensive agent.[16]

Despite, the availability of clear treatment guidelines and efficient therapeutic modalities, large number of patients in many parts of the world including Asia , do not achieve BP goals. [12,17-20] As per the last available estimates, only 6.4% of patients in Pakistan showed controlled BP levels (≤140/90 mm of Hg) between 2003-05.[21]

It has been posited that lack of patient understanding of treatment importance, non-adherence to prescribed medication, economic barriers, clinical inertia, presence of co-morbid conditions and lack of access to healthcare impede the achievement of BP goals.[17,22,23] Currently, there is a lack of nation-wide data from Pakistan on the extent of BP control in patients taking antihypertensive therapy. To address this need, the disease registry, ACTION - ACchievement of Target BP In patients ON antihypertensive therapy, was aimed at documenting the proportion of patients achieving target BP goal (based on local and international (JNC VII) guidelines; <140/90 mm Hg for patients without diabetes and <130/80 mm Hg for patients with diabetes and/or chronic kidney disease (CKD) on existing antihypertensive therapy.[24] Secondary objectives of the study include describing the profile of patients not at BP goal, identifying reasons for not achieving BP goal, documenting the change in existing antihypertensive treatment for patients not at BP goal and antihypertensive therapeutic categories (including mono and combination therapy) prescribed to patients at BP goal.

Patients and Methods

The study was conducted from April 2011 to August 2011, in 60 centers across 10 cities of Pakistan by simple random sampling. The present study was a national, multi-centre, non-interventional, cross-sectional, epidemiological disease registry that recorded the demographic and clinical characteristics of patients with hypertension and treatment practices of physicians. Data was recorded from each patient during a single visit to randomly selected, primary care centres of various cities in Pakistan, in a span of five months. This study was conducted in accordance with the principle and laid by the 18th Medical Assembly and the guidelines for Good Epidemiology Practice. The study was conducted in private clinics in Urban/major cities of Pakistan. Since ERC does not exist for such clinics. Administrative approval was taken from all investigators. Patients, who were ≥15 years of age, on antihypertensive medications for ≥4 weeks and had taken a dose on the day of visit, were included in the study. Exclusion criteria included newly diagnosed hypertensive patients, hypertensive patients not on drug therapy and refusal of consent. Investigators were randomly selected from a list of qualified physicians within a given geographical territory (Urban) in major cities of Pakistan. Approximately 58% of the physicians were general practitioners and 42% were specialists such as medical internist and cardiologist.

Data was recorded on the case report form by the physician for 16 variables, which included demographic characteristics, BP control status, general profile, existing risk factors and co-morbid conditions of patients according to the attainment of BP goal. A history of physician-diagnosed diabetes mellitus (DM), coronary artery disease (CAD) congestive heart failure (CHF) and peripheral artery disease (PAD) was noted from the patient's history based interview at the time of visit. DM was defined as fasting plasma glucose $\geq$126 mg/dl.[45] CAD was defined as any measurable coronary atherosclerosis in a non-dilated or non-bypassed coronary artery. CHF was defined as a clinical syndrome due to heart disease and characterized by breathlessness and abnormal sodium and water retention resulting in edema. [46] PAD was diagnosed by history of positive intermittent claudication or an ABI index < 0.9. Reasons for not achieving BP goal was determined by providing the investigator with the following options in the protocol: 1)lack of access to health care, 2) non-adherence to treatment, 3) lack of understanding on importance of treatment, 4) real or perceived adverse effect, 5) presence of depression, 6) economic barriers to treatment, 7) comorbid medical condition, 8) inadequate therapies especially in presence of risk factors, 9) addition of another drugs and 10) an open option of 'others' to identify any other reason not listed amongst these ten. Changes made in BP

management in patients not at BP goal and therapeutic regimens prescribed to patients at BP goal were also documented.

Based on a previous study from Pakistan, 18% of population had hypertension and only <3% of them had controlled BP.[5] For an absolute precision of ±1% at 95% confidence level, a sample size of 1118 was required. Accounting for incomplete forms, ineligible patients etc., a sample size of 1200 patients was determined. Continuous variables were reported as means with standard deviations. Skewed data was presented as median. Differences in the profile of patients according to the attainment of BP goal were analyzed using bi-variate analysis. A p <0.05 was considered significant.

Results

A total of 2400 patients were screened to enrol 1197 patients who matched the eligibility criteria, of these only 1130 patients were evaluable. Data of 67 patients could not be analysed due to missing information on 2nd reading of systolic blood pressure (SBP) / diastolic blood pressure (DBP) in 26 patients, chronic kidney disease (CKD) status in 39, age in 1 and diabetes status in 1.

There was an almost equal distribution of males (51.00%) and females (49.00%) in the study population with a mean age of 52.68 (±11.86) years (Table 1). The mean SBP and DBP recorded in the study population were 145.9 (±21.90) and 91.25 (±12.60) mm Hg, respectively. Around 23.80% (n=269) patients achieved the BP goal and 76.19% (n=861) did not achieve the BP goal. Majority of patients at BP goal (90.33%, n=243) did not have either diabetes or CKD compared to 54.35% (n=468) of patients who were not at BP goal (Table 2).The mean age of the patients who were not at BP goal was 53.10 (±11.74) years with a mean duration of 6.25 (±6.28) years of hypertension. Obesity (BMI ≥30.0) was observed in 36.00% (n=310) of patients not at BP goal. In majority of patients not at BP goal, risk factors such as sedentary lifestyle (60.27%, n=519), history of (both type1 and type 2) diabetes (42.97%, n=370) and dyslipidaemia (40.30%, n=347) was assessed on patient's history based interview on the study visit. Patients not at BP goal had 21.25% (n=183) prevalence of coronary artery disease (CAD) and a significantly higher prevalence of congestive heart failure (CHF) (p<0.01), peripheral artery disease (p<0.01), history of transient ischemic attack (p=0.01), and CKD (p<0.01) (Table 3).Physicians identified lack of understanding of the importance of treatment (47.03%), and non-adherence to treatment (34.49%) as

important reasons for patients not achieving BP goal. Among these patients, 73.51% (n=633) were suggested changes in hypertension management. Lifestyle modifications (37.74%), addition of another drug (37.74%) and increase in dose of drug (21.37%) were the most common changes suggested (Table 4).

Table 1: Demographic and clinical characteristics of hypertensive patients (n=1130)

Parameters	Values
Age (years), mean ± S.D	52.68 ± 11.86
Age at diagnosis (years);mean ± S.D	45.79 ± 11.72
Duration of hypertension (years)	6.13 ± 6.21
Weight (kg), mean ± S.D	74.76 ± 14.67
Height (cm), mean ± S.D	160.23 ± 13.57
Gender	
Male	576 (51.00)
Female	554 (49.00)
BMI	
Overweight (25.0 – 29.9 (kg/m²)	396 (35.04)
Obesity (≥ 30.0 kg/m²)	394 (34.86)
Waist circumference	
Males ≥ 90 cm	382/576 (66.31)
Females ≥ 80 cm	434/554 (78.33)
Waist hip ratio	
Male >0.90	436/576 (75.69)
Female >0.80	484/554 (87.36)

BMI=Body mass index;Values are expressed as n (%) for gender, BMI, waist circumference and waist hip ratio.

Table 2: Distribution of patients by blood pressure control status (n=1130)

Groups	At BP goal (n=269) n (%)	Not at BP goal (n=861) n (%)
Non-diabetic, non CKD	SBP<140 and DBP<90 243 (90.33)	SBP≥140 & DBP≥90 468 (54.35)
Either diabetic or CKD or both	SBP≥130 and DBP≥80 26 (9.66)	SBP≥130 and DBP≥80 393 (45.64)

BP=Blood pressure, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, CKD=Chronic kidney disease

Antihypertensive therapeutic classes such as ACE inhibitors (36.05%), beta blockers (34.57%), calcium channel blockers (31.59%) and ARBs (27.88%) were the most common ones prescribed to patients at BP goal. Monotherapy was prescribed to 54.64% and polytherapy to 45.35% of patients at BP goal (Table 5). Combination therapy included, ACE inhibitors+beta blockers (7.43%), ACE inhibitors+calcium channel

blockers (4.46%) and beta blockers+calcium channel blockers (3.71%) (Table 5).

Table 3: Profile of patients by attainment of blood pressure goal (n=1130)

Parameters	At BP goal (n=269)	Not at BP goal (n=861)	p-value
Age (years), mean ± SD	51.34±12.16	53.10±11.74	0.03
Duration of hypertension (years), mean ± SD	5.72±5.99	6.25±6.28	0.22
BMI			
Overweight (25.0-29.9 (kg/m^2)	110 (40.89)	286 (33.21)	
Obese (≥ 30.0 kg/m^2)	81 (30.11)	310 (36.00)	0.10
Waist circumference			
Male ≥ 90 (cm)	100/148 (67.56)	282/428 (65.88)	0.71
Female ≥ 80 (cm)	97/121 (80.16)	337/433 (77.82)	0.58
Presence of truncal obesity			
≥ 0.90 – Males	104/148 (70.27)	332/428 (77.57)	0.07
≥ 0.80 – Females	112/121 (92.56)	372/433 (85.91)	0.05
Existing risk factors			
Sedentary life style	129 (47.95)	519 (60.27)	0.002
Diabetes	26 (9.66)	370 (42.97)	<0.01
Dyslipidemia	96 (35.68)	347 (40.30)	0.23
Family history of premature CVD in first degree relative			
<65 years in males	57 (21.18)	234 (27.17)	<0.01
<55 years in females	38 (14.12)	158 (18.35)	0.03
Smoking	56 (20.81)	181 (21.02)	0.86
History of co-morbid conditions			
Coronary artery disease	68 (25.27)	183 (21.25)	0.14
Myocardial infarction	30 (11.15)	70 (8.13)	0.007
Congestive heart failure	6 (2.23)	69 (8.01)	<0.01
Transient ischemic attack	15 (5.57)	50 (5.80)	0.01
Peripheral artery disease	2 (0.74)	44 (5.11)	<0.01
Chronic kidney disease	3 (1.11)	43 (4.99)	<0.01

BP=Blood pressure, BMI=Body mass index, CVD=Cardio vascular disease; Values are expressed as n (%) except for age and waist circumference.

Discussion

Most of the studies in the developing countries including Pakistan have shown very poor BP control.[44] Present study shows significant improvement in overall control of blood pressure as compared to previous studies (NHSP, 1990-94). There could be several factors resulting in better control of BP including, higher literacy rates in urban population, better awareness campaigns by the professional societies, better clinic follow ups, availability of cheaper generic antihypertensive drugs and exponential increase in print and electronic media

Table 4: Reasons for not achieving blood pressure goal and changes made in patient management (n=861)

	No (%)
Reasons for not achieving BP goal	
Lack of understanding on importance of treatment	405 (47.03)
Non-adherence to treatment	297 (34.49)
Presence of depression	197 (22.88)
Economic barriers to treatment	191 (22.18)
Lack of access to health care	190 (22.06)
Presence of co-morbid medical conditions	168 (19.51)
Inadequate therapy specially in presence of risk factors	149 (17.30)
Addition of another drug (NSAIDs, OCPs, TZDs) Interacting with antihypertensives	61 (7.08)
Real or perceived adverse effects	45 (5.22)
Changes of hypertension management	
Lifestyle modification	325 (37.74)
Add another drug	325 (37.74)
Increase dose	184 (21.37)
Switch medication to combo	146 (16.95)
Switch medication to another monotherapy	75 (8.71)
Others	17 (1.97)

BP=Blood pressure, NSAIDs=Non-steroid anti-inflammatory drugs, OCPs=Oral contraceptive pills, TZDs=Thiazolidinediones

Table 5: Anti-hypertensive therapeutic classes and medications prescribed to patients at blood pressure goal and not at goal (n=1130)

Drugs	AT BP GOAL N=269 (%)	Not AT BP GOAL N=861 (%)	p-value	AT BP GOAL MEAN (SD) DURATION (MONTHS)	NOT AT BP GOAL MEAN (SD) DURATION (MONTHS)	Mean difference	p-value
ACEI	97 (36.0)	277 (32.2)	0.237	20.8 (25.9)	17.12 (30.7)	3.6	0.559
BB	93 (34.6)	206 (23.9)	<0.01	22.8 (31.5)	24.0 (39.1)	-1.17	0.871
CCB	85 (31.6)	222 (25.8)	0.06	29.24 (46.5)	28.4 (48.4)	0.892	0.931
ARB	75 (27.8)	161 (18.7)	<0.01	21.8 (31.3)	17.7 (32.4)	4.161	0.583
DIURETIC	39 (14.5)	116 (18.1)	0.670	16.8 (19.3)	17.9 (35.5)	-1.03	0.923
FDC	22 (8.17)	105 (12.2)	0.069	28.1 (64.8)	3.0 (3.7)	25.1	0.025
AB	4 (1.5)	16 (1.9)	0.687	3.0 (0.0)	7.3 (11.3)	-4.1	0.742
Others	15 (5.57)	27 (3.1)	0.065	24.3 (42.5)	31.7(58.2)	-7.4	0.744

AB=Alpha Blockers, ACEI=Angiotensin Converting Enzyme Inhibitor, ARBs=Angiotensin Receptor Blockers, BB=Beta Blocker CCB=Calcium Channel Blockers, FDC=Fixed-Dose Combination

showing programs on consequences of hypertension over last few years. Although there still remains significant gap in control and appropriate treatment

options offered to patients especially in rural population where most of the factors mentioned above are lacking.

Patients not at BP goal had significantly higher rates of sedentary lifestyles, diabetes, and family history of premature cardiovascular disease. The most common co-morbid conditions in patients not at BP goal were CAD, previous incidence of myocardial infarction (MI) and CHF. Lack of patient understanding of the importance of treatment and non-adherence to prescribed medication were the important reasons cited by physicians for patients' inability to achieve BP goal. ACE inhibitors, beta blockers and calcium channel blockers, both as monotherapy and combination (2-drug) therapy, were prescribed more often by physicians to patients at BP goal.

There have been variable reports of hypertension management and control in Pakistan, with the estimates of patients who had their BP under control ranging from <3% (NHSP, 1990-1994) to 6.4% (2003-2005).[5,21] In our study, however, 23.8% of patients (n=1130) during a single visit to primary care center reported to have achieved a predefined BP goal. The difference in estimates could be due to the larger sample size used in the current study and improvement in BP control over time. It could also be due to a difference in study populations assessed, where NHSP was a population based household survey conducted over 4 years, while our study population included patients making a single visit to their general practitioners in urban Pakistan. Awareness campaigns by national and international societies on BP control may have contributed to some extent on better control .According to a data brief published by US center for Disease Control and Prevention's National center for Health Statistics , about 47% of Americans with hypertension did not have BP under control. [43] Risk factors such as dyslipidemia, smoking, age, ethnicity, obesity and family history of premature CVD are known to elevate BP levels an association confirmed by a previous study from Pakistan. [21,25,27]

Prevalence of diabetes was found to be significantly more in patients who did not achieve the BP goal than those who did (p<0.01). Diabetes and hypertension have common underlying risk factors and are, in turn, common risk factors for both micro and macro vascular complications that lead to target-organ failure.[28] It is established from previous studies conducted in Pakistan, that hypertension is a risk factor for cardiovascular morbidity and mortality.[21,29] . In long-standing hypertension and/or diabetes, co-

morbid conditions such as CAD, MI, stroke, CHF, peripheral vascular disease and CKD are well recognized in patients. [28] In the current study population where the mean duration of hypertension was 6.3 years (not at BP goal) and 5.7 years (at BP goal), patients not at BP goal had significantly higher prevalence of macrovascular complications such as CHF, transient ischemic attack, periphery artery disease. Hypertension is known to initiate end-stage renal disease and is associated with rapid progression of CKD in patients with both hypertension and diabetes. [30-32] The observed prevalence of CKD (a microvascular complication) in the present study is in agreement with previous reports.

Studies from Indian sub-continent and Western countries demonstrate simple treatment modalities for hypertension control.[14,16] Studies from Pakistan and Spain have highlighted issues related to patient's medication adherence , and social and financial barriers that are known to impede the achievement of BP goal, and lead to poor health outcomes in patients with hypertension. [22,33-35] Most physicians in the current study reported that patients' lack of understanding of the importance of treatment was the single biggest reason why BP goals were not being achieved. Hashmi et al. found that lack of understanding of the effectiveness of medication was responsible for reduced treatment adherence.[22] Consequently, the rate of non-adherence to treatment (34.5%), observed in current study, is higher (23%) than that reported by Hashmi et al.; Almas et al. reported a rate of 43% in a Pakistani sample population with hypertension.[36] Lack of access to healthcare reported in the study population might be a result of poor services at primary healthcare systems in rural areas, as indicated by some studies done in low-income countries.[34] Economic barriers to BP control are observed in urban men from developed countries too.[35] In addition, failure to achieve BP goals is also associated with clinical inertia in intensifying or initiating antihypertensive therapy.[17]

Among the therapeutic categories prescribed to patients achieving BP goal, majority (54.6%) of patients were on monotherapy. Recent studies from Pakistan and India reported low rate of prescription of monotherapy (41% each). [15,37] Overall ACE inhibitors, beta blockers, calcium channel blockers and ARBs are the most prescribed drugs for the management of hypertension in Pakistan both according to the current study and previous reports.[15] This is in line with the recommendations about the antihypertensive drug classes to be used in the management of co-morbid

conditions.[17] Both American Diabetes Association and Seventh Report of Joint National Committee on Hypertension recommend ACE inhibitors or ARBs as first line therapy in hypertension with diabetes. [17, 38] This current study reports only 27.9% patients on ARB therapy; a low rate of usage compared to other Asian studies , and recommendations . [17,25,37,38] The current study reports only 18.7% of uncontrolled patients who were prescribed ARBs.

A prudent strategy that incorporating combination of pharmacological and non-pharmacological interventions is necessary to control BP. Education and awareness of risks of poor BP control will significantly improve the compliance to antihypertensive medications and hence the BP control. Lifestyle modifications are the first line treatment for patients with hypertension and diabetes. Regular physical activity of moderate intensity is known to reduce BP levels in patients with hypertension.[14,39]Treatment intensification (medication change or dose increase) is found to be associated with BP improvement in patients with hypertension.[40] Therapeutic strategies like addition of another drug, increase in dose and change in medication recommended by physicians in the current study to patients not at BP goal, are in agreement with global practices.[41] In patients unable to achieve the BP goal, intensification of therapy must be complemented by measures to improve adherence. Even a small reduction in the mean BP of a population will produce a large reduction in the incidence of complications.[42]

Although the present study collected data on real life clinical practice and observations reported by physicians in urban Pakistan, accurate definition of study population and correlation to entire population of Pakistan may not possible. Since the study is a clinic based cross-sectional study carried out during a single visit, an indication of sequence of events and/or narrowing on causes of inability to control BP cannot be inferred accurately.

Conclusions

1. A low proportion of patients (23.8%), are achieving blood pressure goals in urban Pakistan according to JNC VII and local guidelines.
2. Control of blood pressure was much lower (6.2%) in patients with diabetes and/or CKD.
3.The major impediments in poor blood pressure goal achievement remains the lack of understanding of importance of blood pressure treatment and poor compliance which is in line with other national and international studies.

Acknowledgements

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