Hypertension: Detection and Management in South Africa

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Key Words

Hypertension • Black South Africans • Westernized eating habits • Lifestyle changes • Genetic factors

Abstract

High blood pressure in South Africa is estimated to have caused 46,888 deaths and 390,860 disability-adjusted life years in 2000. Detection and management of hypertension remains suboptimal due to inadequate public health care facilities. Mass migration of rural blacks to urban areas and rapid changes in lifestyle and risk factors account for the rising prevalence of hypertension, but genetic factors may also play an important contributory role. Black South Africans also appear to be more prone to complications of hypertension, particularly stroke, heart failure, and hypertensive nephrosclerosis, and respond poorly to ACE inhibitors as monotherapy. Proactive public health interventions at a population level need to be introduced to control this growing epidemic.

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Introduction

South Africa (SA) is in the midst of a complex health transition with the collision of an HIV/AIDS pandemic and a rising occurrence of noncommunicable diseases. Hypertension is one of the most important risks for car-

diovascular disease, and rapid urbanization and changing lifestyles are contributing to a rising epidemic of cardiovascular disease, especially amongst the majority black ethnic group. Although SA spends 8.7% of its gross domestic product on health care, the distribution of spending largely occurs in the private sector, leaving the majority of the population, who lack health insurance, to be cared for in an ailing and underfunded public health system resulting in suboptimal detection and management of hypertension. There is also competition of limited financial resources between hypertension and infectious diseases.

Prevalence and Risk Factors for Hypertension

The first Demographic and Health Survey in SA was conducted in 1998 on a random sample of 13,802 people aged 15 years and older, of whom 76% were black, 13% of mixed ancestry, 8% white and 3% Indian/Asiatic [1]. The age-adjusted prevalence of hypertension (blood pressure, BP $\geq$ 140/90 mm Hg) was 21%, with males and females having equal rates. The risk factors for hypertension were less than tertiary education, older age (50–60% were hypertensive), overweight and obesity, excess alcohol use, and a family history of hypertension and stroke. Hypertension risk was lowest in rural blacks and significantly higher in obese black women [2].

Similar findings were reported in a survey conducted in the adult population of Durban in 1983 using World Health Organization criteria $\geq 160/95$ mm Hg [3]. The prevalence of hypertension was highest in urban blacks (25%), intermediate in whites (17%), lower in ethnic Indians (14%) and lowest in rural blacks (9%).

Environmental Factors

The observation that the prevalence of hypertension is higher in urban black South Africans compared to their rural counterparts suggests a strong environmental influence on the pathogenesis of hypertension. Similar rural/urban trends have been described in the rest of Sub-Saharan Africa [4]. The rise in BP is often seen with weeks of rural-urban migration, and the reasons for the change are likely to be multi-factorial.

Tribal South Africans and the Khoi-San tribes traditionally lived a hunter-gatherer lifestyle with low levels of obesity, plenty of exercise and a low sodium and high potassium diet. In the transition between rural and urban, there is a dramatic change in lifestyle with the adoption of more westernized eating habits. There is a higher salt and calorie intake with reduced potassium. In a study by Charlton et al. [5] of 325 South African subjects, all population groups largely residing in an urban area had habitually excess sodium intake with suboptimal potassium. Additionally, as exercise levels decline and calories increase, the prevalence of obesity increases dramatically. Over the past 50 years, fat intake has risen by 59.7% in urban blacks [6]. In the 2003 South African Health and Demographic Survey, obesity (BMI ≥ 30) was present in 21% of rural blacks compared to 33.8% of urban dwellers [7]. Black females had the highest prevalence of obesity and the largest waist circumferences. Socioeconomic circumstances of black people in SA may also be important determinants of hypertension. Due to the policies of apartheid, blacks were condemned to live in overcrowded townships with extremely poor infrastructure and limited access to primary health care clinics, which has not substantially changed since the democratic transition. The stress of living in these conditions contributes to alcoholism, reduced physical activity and increased autonomic activity that may contribute to hypertension.

The Barker hypothesis suggests that birth weight and adult BP are inversely related. In SA, Levitt et al. [8] showed birth weight was inversely related to systolic BP (but not diastolic BP) in black children living in Soweto,

a sprawling township outside Johannesburg. There was a 3.4 mm Hg decline in systolic BP for every 1 kg increase in birth weight. This may account for the higher prevalence of hypertension between urban and rural dwellers, but there are no data regarding birth weight and adult BP from rural areas in SA to definitely support this hypothesis.

Genetic Factors

The heritability of hypertension is thought to range from 30 to 60%, with variable clinical presentation and drug response due to multiple contributory genes, genetic/ethnic heterogeneity and environmental effects. In SA, the first Demographic and Health Survey demonstrated that hypertension was associated with a family history of hypertension and stroke [2]. The search for the genetic contribution to hypertension in SA has largely followed a candidate gene approach particularly in regard to genes that regulate sodium excretion. This is based on the observation that African Americans are more likely to have salt-sensitive hypertension. In a study from SA, suppressed plasma renin activity (an index of salt sensitivity) was significantly lower in both normotensive and hypertensive indigenous African patients compared to whites despite comparable sodium intake [9]. The epithelial sodium channel (ENaC) is the final regulator of sodium balance in the kidney and is an attractive candidate gene. The T594M variant of the β -chain was found to be associated with hypertension in blacks living in London, but this was not confirmed in SA. We sequenced the entire β -chain and found a unique mutation, namely the R563Q, which is 3 amino acids from the original Liddle's syndrome mutation and in the active site for the degradation of the ENaC. This mutation has been associated with low renin, low aldosterone hypertension and early severe pre-eclampsia in black and mixed ancestry hypertensives [10, 11]. Further studies have shown that about 5–10% of hypertensives in SA (excluding whites) carry this mutation. Affected individuals often have resistant hypertension that responds dramatically to amiloride, the specific inhibitor of the ENaC. The frequency of the mutation and the response to amiloride makes routine screening viable in our specialist hypertension clinic.

Twenty percent of unselected Khoi-San people (the original indigenous people of southern Africa, who live mainly in the arid areas) carry this mutation, suggesting that the mutation originated from the Khoi-San. It is well established that there is significant genetic admixture

Table 1. Genetic associations with hypertension in black South Africans

Gene	Mutation	Importance
ENaC	T594M	associated with hypertension in London, but not SA
ENaC	R563Q	associated with low renin-low aldosterone hypertension and pre-eclampsia
Angiotensinogen promoter	M235T	hypertension associated with increased body mass
Aldosterone synthase (CYP11 β 2)	C344T	associated with systolic BP in untreated hypertensives
α -Adducin	460-Trp variant	associated with hypertension
ANP	T1766C	no association with hypertension
ANP	C1364A	association with normotension
NPRC	C55A	no association with hypertension

ANP = Atrial natriuretic peptide; NPRC = natriuretic peptide clearance receptor.

between the Khoi-San and black South Africans. The mutation is not found in other black populations in Africa or those living outside Africa. However, the R56Q mutation does not fully explain the suppressed plasma renin activity in black South Africans. Another far more common genetic mutation/s that affects sodium metabolism must be associated with this phenomenon. Recently, Bochud et al. [12] showed that segmental reabsorption of sodium was highly heritable between black South Africans and whites living in Belgium. Blacks had enhanced sodium absorption in the proximal tubule compared to whites, and genes influencing sodium metabolism in the proximal tubule may be a fruitful avenue of further research.

Other genes have been linked to hypertension in South Africans and are summarized in table 1.

Screening, Detection and Control of Hypertension

There is no clear policy for screening for hypertension in SA. In the 1998 Demographic Survey, it was estimated there were 6 million hypertensives in SA [1], and this number is likely to be even larger in 2010 because of population growth and growing urbanization. Currently,

Table 2. Treatment status of hypertension ($\geq 140/90$ mm Hg, and/or on treatment) and controlled hypertension ($< 140/90$ mm Hg) [1]

Group	Aware %	Treated %	Controlled %
Total men	26	21	10
Total women	51	36	18
Black men	20	14	7
Black women	47	29	15
White men	47	43	17
White women	63	64	19
Colored men	24	19	7
Colored women	57	48	14
Asian men	37	46	28
Asian women	75	71	5

there are not the staff, facilities and funds available to implement a population-based screening program, particularly in the face of the HIV/AIDS pandemic. Possible solutions would be to raise the threshold for the diagnosis of hypertension in low-risk individuals to $\geq 160/95$ mm Hg and concentrate on patients with more severe hypertension or those at high cardiovascular risk to maximize the benefits of treating hypertension.

In the first South African Health and Demographic Survey, awareness, treatment status and control varied substantially between men and women, and between different ethnic groups (table 2) [1]. In summary, women were substantially more likely to be aware of their hypertension than men (51 vs. 26%), treated (36 vs. 21%) and controlled (18 vs. 10%). There were substantial ethnic differences as well, with blacks having the lowest rates of awareness, treatment and control of hypertension. This was particularly evident in young black men, where $< 1\%$ were aware of their diagnosis. These differences probably largely represent the poorer socioeconomic status of black people in SA and their limited access to health care.

Clinical Features, Complications and Burden of Disease

Hypertension in black South Africans differs in its clinical presentation, frequency and type of target organ damage or complications from comparable hypertensives from developed countries or white South Africans. Malignant hypertension is still frequently seen in young

black hypertensives even in the absence of obesity or secondary causes and is commonly complicated by renal failure. In a survey from Bloemfontein, end-stage renal disease was attributed to hypertensive nephrosclerosis in 51.2% of black patients [13]. A similar high prevalence of ESRD due to hypertension has been reported in African Americans.

Cardiovascular complications of hypertension are different between blacks and whites. There is a higher prevalence of stroke and hypertensive heart disease, and a lower incidence of coronary disease. In the Heart of Soweto Study, cardiac heart failure was the most common primary diagnosis, and 68% of cases were attributable to dilated cardiomyopathy or hypertensive heart disease, or both [14]. Black Africans were more likely to have heart failure than were the rest of the cohort, but were less likely to have coronary artery disease (38 vs. 6%) despite the high prevalence of cardiovascular risk factors. In an analysis of deaths attributable to noncommunicable diseases, Mayosi et al. [15] found a sustained 20 and 23% increase in deaths due to hypertensive heart disease and ill-defined heart disease from 1999 to 2006, respectively. Stroke had the highest death rates per 100,000 population compared to other cardiovascular diseases, and the stroke mortality was twice as high in blacks. The lower prevalence of atherosclerotic complications of hypertension in blacks may be attributed to lower cholesterol and higher HDL cholesterol levels.

In a study examining determinants of target organ damage in 403 black hypertensives attending primary health clinics in Cape Town, renal impairment by any criteria was identified in 26% and ECG left ventricular hypertrophy in 35%. [16] Interestingly, ischemic ECG changes were seen in 49%, but this is unexplained given the low prevalence of coronary disease in blacks, and may be attributable to repolarization changes. The higher prevalence of target organ damage in black hypertensives has also been reported in African Americans and other studies in SA.

Norton et al. [17] showed that the relationship between BP and left ventricular mass index depended on excess adiposity in black South Africans, possibly explaining the excess risk of cardiac disease. Left ventricular mass index increased by 1.61 g/m compared to 5.24 g/m in patients with normal or increased waist circumference for every 1 standard deviation in BP, respectively.

Norman et al. [18] estimated the burden of disease related to high BP in SA based on the 1998 Health Survey, and calculated that it caused 48,888 deaths, 9% of all deaths and 2.4% of all disability-related life years.

Management

The South African Hypertension Guidelines recommend lifestyle changes in all hypertensive patients. Management of obesity, exercise, reduction in alcohol and increased dietary intake of potassium and reduced salt are the obvious targets but remain difficult to implement. Population-based strategy of reducing involuntary intake of sodium in processed food is a realistic option, and demonstrated to be effective in a recent randomized clinical trial [19]. As bread is an important component of the diet, government intervention to reduce sodium in bread is an attractive option but will require intensive lobbying at a national level.

Black South Africans appear also to respond to anti-hypertensive drugs in a similar manner to African Americans. The South African Hypertension Guidelines recommend low-dose diuretics for first line treatment of uncomplicated hypertension either as monotherapy or in combination with ACE inhibitors or calcium channel blockers. Of note, enalapril was effective in only 1% of subjects compared to 26% for hydrochlorothiazide and 67% for calcium channel blockers [20]. However, enalapril in combination with reserpine or hydrochlorothiazide increased control rates to 67%. Calcium channel blockers also appear to be more effective than enalapril in reducing left ventricular hypertrophy, but it must be noted that there have been no large-scale randomized hypertension studies in SA, and data are extremely limited.

Conclusions

Detection and management of hypertension in SA is inadequate. Rapid urbanization, change in diet and rising levels of obesity are causing a rising prevalence of hypertension in urban areas. Important genetic factors have been identified as contributory factors. Target organ damage, especially stroke, hypertensive heart failure and hypertensive nephrosclerosis, are major problems in black South Africans.

References

- 1 Steyn K, Gaziano TA, Bradshaw D, Laubscher R, Fourie J; South African Demographic and Health Coordinating Team: Hypertension in South African adults: results from the Demographic and Health Survey, 1998. *J Hypertens* 2001;19:1717–1725.
- 2 Steyn K, Bradshaw D, Norman R, Laubscher R: Determinants and treatment of hypertension in South Africans: the first Demographic Health Survey. *S Afr Med J* 2008;98:376–380.
- 3 Seedat YK, Seedat MA, Hackland DB: Prevalence of hypertension in the urban and rural Zulu. *J Epidemiol Community Health* 1982;36:256–261.
- 4 Seedat YK: Hypertension in developing nations in sub-Saharan Africa. *J Hum Hypertens* 2000;14:739–747.
- 5 Charlton KE, Steyn K, Levitt S, et al: Diet and blood pressure in South Africa: intake of foods containing sodium, potassium, calcium, and magnesium in three ethnic groups. *Nutrition* 2005;21:39–50.
- 6 Bourne LT, Lambert EV, Steyn K: Where does the black population of South Africa stand on the nutrition transition? *Public Health Nutr* 2002;5:157–162.
- 7 South African Demographic Health Survey. Adult Risk Profiles, Chapter 13: <http://www.doh.gov.za/docs/reports/>.
- 8 Levitt NS, Steyn K, de Wet T, Morrell C, Edwards R, Ellison GTH, Cameron N: An inverse relationship between blood pressure and birth weight from 5 year old children in Soweto, South Africa. *J Epidemiol Community Health* 1999;53:264–268.
- 9 Rayner BL, Myers JE, Opie LH, Trinder YA, Davidson JS: Screening for primary aldosteronism – normal ranges for aldosterone and renin in three South African population groups. *S Afr Med J* 2001;91:594–599.
- 10 Rayner BL, Owen EP, King JA, Soule S, Vreede H, Opie LH, Marais D, Davidson JS: A new mutation, r563q, of the beta subunit of the epithelial sodium channel associated with low-renin, low-aldosterone hypertension. *J Hypertens* 2003;21:855–858.
- 11 Dhanjal M, Owen EP, Davidson JE, Anthony JA, Baines D, Rayner BL: Association of pre-eclampsia with the R563Q mutation of the β -subunit of the epithelial sodium channel. *BJOG* 2006;113:595–598.
- 12 Bochud M, Staessen JA, Maillard M, Muzeko MJ, Kuznetsova T, Woodiwiss A, Richart T, Norton G, Thijs L, Elston R, Burnier M: Ethnic differences in proximal and distal tubular sodium reabsorption are heritable in black and white populations. *J Hypertens* 2009;27:606–612.
- 13 Van Rensburg BW, van Staden AM, Rossouw GJ, Joubert G: The profile of adult nephrology patients admitted to the Renal Unit of the Universitas Tertiary Hospital in Bloemfontein, South Africa from 1997 to 2006. *Nephrol Dial Transplant* 2010;25:820–824.
- 14 Stewart S, Libhale E, Carrington M, Damasceno A, Abbasi H, Hansen C, Wilkinson D, Sliwa K: The clinical consequences and challenges of hypertension in urban-dwelling black Africans: insights from the Heart of Soweto Study. *Int J Cardiol* 2009, Epub ahead of print.
- 15 Mayosi BM, Fisher AJ, Lalloo UG, Sitas F, Tollman SM, Bradshaw D: The burden of non-communicable diseases in South Africa. *Lancet* 2009;374:934–947.
- 16 Peer N, Steyn K, Dennison CR, Levitt NS, Nyo MT, Nel JH, Commerford PJ, Fourie JM, Hill MN: Determinants of target organ damage in black hypertensive patients attending primary health care services in Cape Town: the Hi-Hi study. *Am J Hypertens* 2008;21:896–902.
- 17 Norton GR, Majane OH, Libhaber E, Maseko MJ, Makaula S, Libhale C, Woodiwiss AJ: The relationship between blood pressure and left ventricular mass index depends on excess adiposity. *J Hypertens* 2009;27:1750–1752.
- 18 Norman R, Gaziano T, Laubscher R, Steyn K, Bradshaw D; South African Comparative Risk Assessment Collaborative Group: Estimating the burden of disease attributable to high blood pressure in South Africa in 2000. *S Afr Med J* 2007;97:692–698.
- 19 Charlton KE, Steyn K, Levitt NS, Peer N, Jonathan D, Gogela T, Rossouw K, Gwebushe N, Lombard CJ: A food-based dietary strategy lowers blood pressure in a low socio-economic setting: a randomized study in South Africa. *Public Health Nutr* 2008;11:1397–1406.
- 20 Sareli P, Radevski IV, Valtchanova ZP, Libhale E, Candy GP, Den Hond E, Libhale C, Skudicky D, Wang JG, Staessen JA: Efficacy of different drug classes used to initiate antihypertensive treatment in black subjects: results of a randomized trial in Johannesburg, South Africa. *Arch Intern Med* 2001;161:965–971.

Editorial Comment

M. El Nahas, Sheffield

In this review, Brian Rayner comprehensively discusses issues related to the detection and management of hypertension (HTN) in South Africa. He reminds readers of the ongoing collision between the HIV/AIDS pandemic and the rising occurrence of non-communicable disease. He also puts the economical context of healthcare in South Africa in sharp focus including the inequities of healthcare funding. It has been argued by others that in view of financial constraints in Africa, the best cure for HTN may be prevention. This may be all the more relevant as younger and more active individuals seem to be increasingly affected. Attempts should be made, at the community level, to detect hypertensive patients early before irreversible end organ damage has occurred [1]. Rayner singles out reduction in salt intake including possible government intervention to reduce sodium in bread. A recent publication on the burden of HTN in rural sub-Saharan Africa villages (in Malawi, Rwanda and Tanzania) showed that frequent meat and fat intake were associated with higher HTN

prevalence, whilst frequent fruit and vegetable intake was significantly associated with lower blood pressure. HTN and pre-HTN are common in rural sub-Saharan Africa [2]. Lifestyle changes are clearly essential for HTN prevention, but cheap and affordable anti-hypertensive drugs may be the answer for the many who present late with established HTN compounded by poverty. This was shown many years ago in India by Mani and his colleagues in Chennai.

References

- 1 Twagirumukiza M, Van Bortel LM: Management of hypertension at the community level in Sub-Saharan Africa (SSA): towards a rational use of available resources. *J Hum Hypertens* 2010, Epub ahead of print.
- 2 de Ramirez SS, Enquobahrie DA, Nyadzi G, Mjungu D, Magombo F, Ramirez M, Sachs SE, Willett W: Prevalence and correlates of hypertension: a cross-sectional study among rural populations in sub-Saharan Africa. *J Hum Hypertens* 2010, Epub ahead of print.