REVIEW

Hypertension and hypertensive heart disease in African women

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Abstract Hypertension and hypertensive heart disease is one of the main contributors to a growing burden of non-communicable forms of cardiovascular disease around the globe. The recently published global burden of disease series showed a 33 % increase of hypertensive disorders in pregnancy in the past two decades with long-term consequences. Africans, particularly younger African women, appear to be bearing the brunt of this increasing public health problem. Hypertensive heart disease is particularly problematic in pregnancy and is an important contributor to maternal case-fatality. European physicians increasingly need to attend to patients from African decent and need to know about unique aspects of disease presentation and pharmacological as well as non-pharmacological care. Reductions in salt consumption, as well as timely detection and treatment of hypertension and hypertensive heart disease remain a priority for effective primary and secondary prevention of CVD (particularly stroke and CHF) in African women. This article reviews the pattern, potential causes and consequences and treatment of hypertension and hypertensive heart disease in African women, identifying the key challenges for effective primary and secondary prevention in this regard.

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Hypertension: a global epidemic

The global impact of elevated blood pressure (BP)/hypertension is profound, being responsible for more deaths worldwide than any other cardiovascular risk factors including tobacco use, obesity and lipid disorders [1, 2]. The recently published Global Burden of Disease Study showed a marked increase in years lived with disabilities (YLDs) for all ages of 33 % from 1990 to 2010 due to hypertensive disorders of pregnancy. In the USA hypertension still contributes to the greatest population attributable risk for all-cause (30 %) and cardiovascular disease (CVD) related deaths (40 %) [3]. Moreover, longitudinal, population and cohort studies demonstrate a continuous relationship between elevated BP and increased risk of cardiovascular events that defy simple thresholds for applying treatment [4]. As such, hypertension is a key contributor to a global epidemic of CVD that is indirectly manifested via a range of conditions such as stroke, chronic heart failure (CHF), acute coronary syndromes and chronic kidney disease [5–8]. In

spite of the profound contribution of hypertension to the global burden of non-communicable forms of CVD, efforts to control the massive influence of uncontrolled hypertension are still limited. Beyond the developed world, 80 % of worldwide CVD-related deaths now occur in low- and middle-income countries (LMIC) [5]. Unlike in developed countries [5–8], in LMIC, morbid and fatal CVD-related events typically occur at a younger age and affect more women, commonly in pregnancy, thereby exerting a more profound impact on the family unit and the workforce [9, 10]. In the immediate future, this adverse impact is likely to rise with predictions that non-communicable forms of CVD will become the leading cause of death and disability globally by 2020 [5]. These trends reflect a growing need to truncate a disproportionate burden of CVD in vulnerable communities with hypertension as a key target.

Hypertension in Africa

The complex challenge preventing, or at least truncating, the next epidemic of CVD with hypertension representing a major target is particularly problematic for the diverse peoples of the African continent and, specifically, those living in sub-Saharan Africa. In contrast to established market economies with good clinical medical data surveillance systems (in particular northern Europe and North America), comprehensive data on the burden of hypertension in Africa are often lacking or conflicting (representing the heterogeneous nature of its people, lifestyles and economic development) [11]. Throughout Africa, a formal system of medical information is unavailable in most countries. Local community studies and single centre health records are often used to obtain information about population health. However, a systematic review of 25 studies (>400 subjects in each) from ten sub-Saharan countries during the period 1987–2004 showed a reported prevalence of hypertension in the region, ranging from 13 to 48 %, with lower prevalence in rural versus urban gradients linked to epidemiologic transition and a large burden among women of African descent [12]. Figure 1 summarizes the estimated rate of hypertension by the World Health Organisation in sub-Saharan Africa according to country [2]. Population prevalence estimates for the region ranging from 33.9 % in Eritrea to 52.5 % in Niger.

Fig. 1 World Health Organisation estimates of prevalence of hypertension in major populations across Africa. Estimated proportion (%) of adult men (*blue*) and women (*red*) [62]
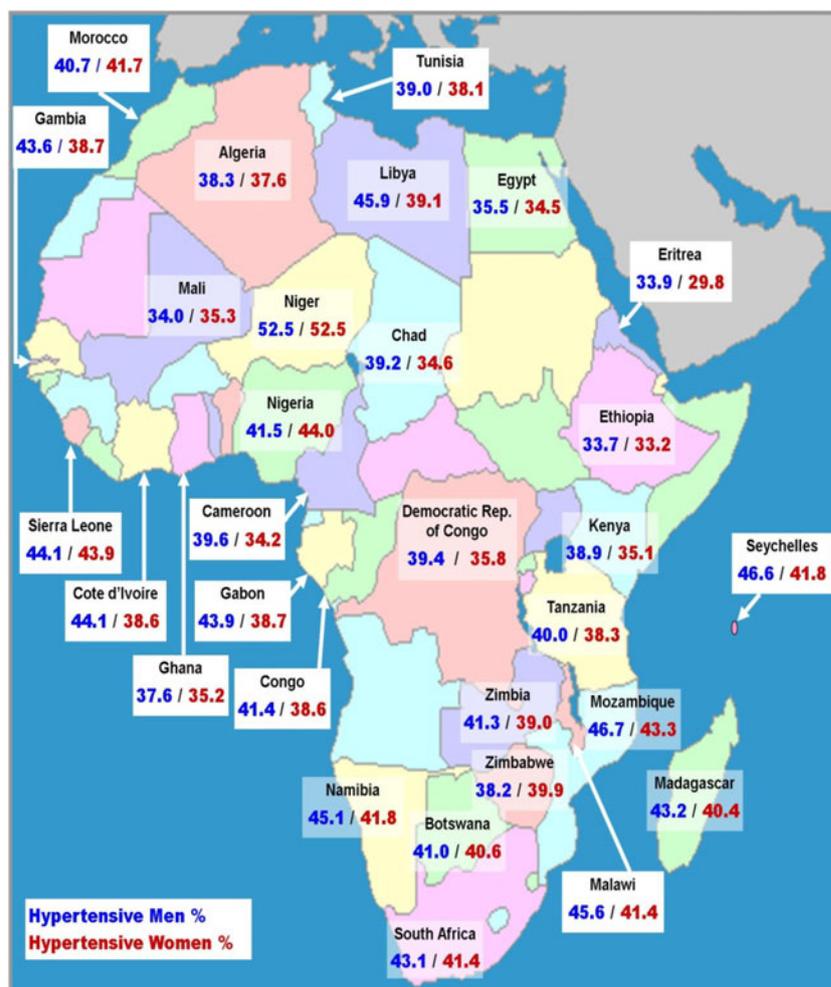
Hypertension in African women

Despite a wealth of data to describe the pattern of hypertension in those of Afro-American descent, supplemented by a number of single centre (hospital and primary care) registries in Africa focussing on presentations related to hypertension [13–16], there is a paucity of analyses and reporting based on gender in particular black African women. Given the size of the populations at risk, understanding the specific risk factors, progression of hypertension to hypertensive heart disease with end-organ damage and the consequences of largely undetected and untreated hypertension in African women are keys to minimise the emergence of non-communicable forms of CVD, both from a primary and secondary prevention perspective.

Hypertension in the black African population is considered a distinct biological entity. Not only do Africans develop more hypertension, but also compared to other ethnic groups hypertension in Blacks is often more severe [17] and more resistant to treatment [12]. Hypertensive target organ damage in Ghanaian civil servants with hypertension is more likely to be fatal on an age-adjusted basis.

Studies on possible pathophysiological mechanisms are not yet conclusive, particularly in respect to gender-based heterogeneity. However, observed gender-based differences in the underlying prevalence and characteristics of hypertension in black Africans are often marked. For example, a contemporary registry that captured data from 1311 consecutive primary care patients (99 % African), from two primary care clinics in the townships of Soweto, South Africa, included a predominance of women (862 cases) with 66 % of those women demonstrating higher overall BP levels com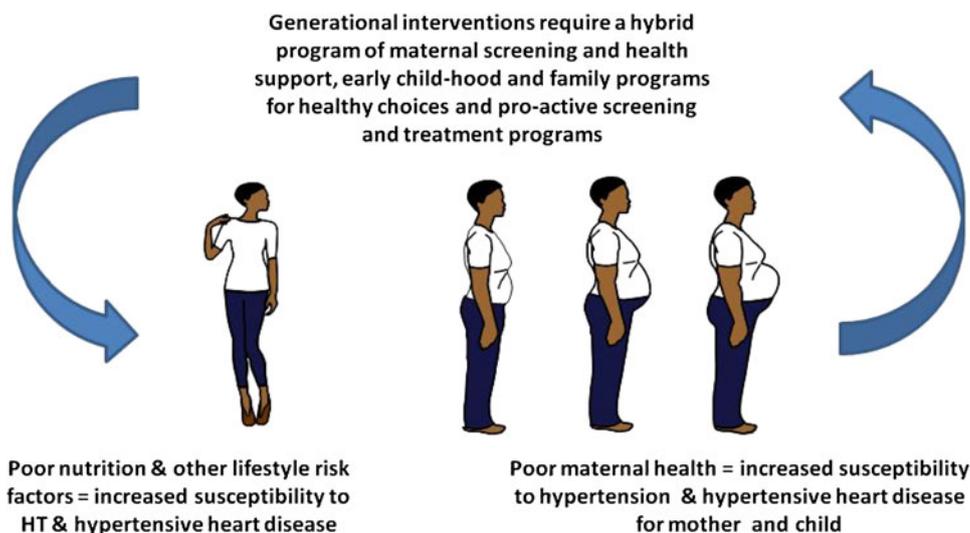pared to men [13]. Overall, compared to their male counterparts, women, who were 3 years older than men were more likely to report a family history of any form of heart disease, were more likely to have a personal past history of hypertension and were far more likely to be obese (42 versus 14 %; OR 4.54, 95 % CI 3.33–5.88).

Hypertensive heart disease in African women

In the Heart of Soweto hospital registry which captured detailed information on >6000 de novo presentations (5328 with confirmed heart disease) to the Cardiology Unit of the Baragwanath Hospital, which services a community in profound epidemiological transition [10, 12–15], African women were the single biggest contributor to case presentations (2863—54 %) with many relatively young cases on non-communicable heart disease (see Fig. 2). Of these, 575 (20 %) presented with a primary diagnosis of hypertension and a further 1196 (42 %) had a secondary diagnosis of hypertension. Among the latter, hypertensive heart failure (682/1196—57 %, mean age 60 ± 14 years) was the most common manifestation of hypertensive heart disease [10]. Interestingly, level of education and non-communicable risk factors such as family history of CVD, smoking, being obese and Type II diabetes correlated with advance disease.

Historically, these data contrast with that collected in Nigeria in the 1960s and 1970s showing a higher prevalence of hypertension in men than in women at least up to the age of 40 years when the prevalence equalized [18, 19]. However, a more contemporary report from rural Nigeria showed that amongst 858 cases of hypertension, more than two-thirds were female suggesting a possible shift in epidemiology [20].

Fig. 2 The cyclical challenge of preventing maternal and inter-generational susceptibility to hypertension and hypertensive heart disease in African women

Generational interventions require a hybrid program of maternal screening and health support, early child-hood and family programs for healthy choices and pro-active screening and treatment programs

Poor nutrition & other lifestyle risk factors = increased susceptibility to HT & hypertensive heart disease

Poor maternal health = increased susceptibility to hypertension & hypertensive heart disease for mother and child

Proposed mechanisms for increased susceptibility to hypertension

A number of studies have documented a change of life-style in sub-Saharan Africa [21, 22] contributing to an increasing prevalence of hypertension—particularly in women and those living in urban centres. As shown in the Heart of Soweto Primary Care Registry [23], obesity was the most common contributor to hypertensive heart disease, especially in young women moving from rural to urban areas.

Birth weight for gestational age, an indicator for foetal growth, has been identified as an independent predictor of elevated BP in adulthood in a number of studies but the strength in this relationship remains not entirely clear [24]. There is a paucity of data investigating this relationship that has been published in those of black African descent. Kruger and colleagues investigated the determinants of overweight and obesity among 10- to 15-year-old school children in the North West Province, South Africa in the THUSA BANA (Transition and Health during Urbanisation of South Africans; BANA, children) study [25]. They found a low prevalence of excess weight (7.8 %) amongst the 1257 children studied. However, the Bogalusa cohort studies followed up 158 children from a USA cohort of 48 black and 47 white boys, as well as 41 black and 49 white girls for a period of 15–17 years [26]. Birth weights were significantly lower ($p < 0.001$) in black boys and girls than in whites who developed higher BPs as adolescents. In regression analysis, birth weight accounted for ethnic differences in adolescent BP. Running the regression models for black boys and girls separately showed no difference. Post-natal or first year growth seems to have a possibly independent effect compared to intrauterine growth performance. This type of 'catch up growth' across centiles of growth trajectories has also been associated with the development of coronary artery disease in later life [27]. The Bogalusa cohort showed that the timing of the somatic growth on vascular development was important as it was only evident between birth and 4–5 years, with no significant additional impact in growth from 4–5 to 15 years.

These are all interesting and important findings. However, much larger and more comprehensive fully longitudinal data sets are needed with relevant standardized measures at several time points included. If these data can be reproduced in other studies and, in particular, in African adolescents and women it would be possible to reduce the excess prevalence of hypertension currently observed in black Americans and black Africans via the combination of promoting appropriate early growth and then restraining excess weight gain by adolescence.

Pregnancy and hypertension

Hypertension occurring in pregnancy can manifest as pre-existing chronic hypertension, gestational hypertension, pre-eclampsia and eclampsia (Fig. 2). Hypertensive disorders are responsible for 14 % of the more than 4687 cases of maternal death in South Africa reported for 2008–2010 (http://www.hst.org.za/saving-mothers-2008-2010) and, therefore, require special consideration and attention. Chronic hypertension prior to pregnancy is increasing due to the world-wide obesity epidemic and is prevalent in 3 % of all US pregnant women [28]. The prevalence in African women is unknown. However, the recently published systemic analysis for the Global Burden of Disease Study on YLDs for 1160 sequelae of 289 diseases and injuries: 1990–2010 documented a 33 % increase in hypertensive disorders of pregnancy worldwide [17].

In a tertiary hospital-based study in Nigeria, hypertension was seen in 9.8 % of 409 pregnant women studied at booking and this rose to 26.2 % at delivery [17]. In another hospital-based single centre study in Nigeria, chronic pre-existing hypertension was seen in 4.5 % of 442 hypertensive subjects studied [17]. Chronic hypertension leads to increased frequency of pre-eclampsia (17–25 % versus 3–5 % in the general population), as well as placental abruption, foetal growth restriction and preterm birth [28]—all common problems occurring in pregnant African women. Endothelial dysfunction associated with levels of circulating endothelial cells, circulating progenitor cells and plasma von Willebrand factor have been reported recently in hypertension in pregnancy [29].

A particularly important form of CVD in African women is peripartum cardiomyopathy (PPCM). This condition occurs in 1:1000 women in Africa and is a diagnosis of exclusion with a large differential diagnosis [30, 31]. However, there is no agreement on the exclusion of hypertension and pre-eclampsia. Unfortunately, the inclusion of patients with varying degrees of gestational hypertension, in index as well as prior pregnancies, has contributed greatly to the discrepancy in reported characteristics of PPCM. Studies comprising greater proportions of patients with pre-eclampsia and severe hypertension tend to have a far greater frequency of PPCM cases presenting in the last month of pregnancy [32]. In contrast, studies that have attempted to minimize the inclusion of patients with pre-eclampsia and only including milder forms of hypertension show a clear postpartum peak in the presentation of PPCM with reported onset of symptoms most commonly being 1–2 months postpartum [30, 33, 34]. The Study Group on PPCM has therefore not reached consensus on the inclusion/exclusion of patients with pre-eclampsia and severe hypertension as requisite to the diagnosis of PPCM [31].

Transition from hypertension to hypertensive heart disease

The presence of left ventricular hypertrophy (LVH) adversely affects the prognosis of patients with arterial hypertension. In the Framingham Study, cardiovascular mortality among patients with arterial hypertension and increased left ventricular mass measured by echocardiography was double in comparison with patients with normal mass [35]. LVH can be characterized by geometric subtypes, based on LV mass index (LVMI) for body size and relative wall thickness (RWT), which further refines cardiovascular risk assessment. Patients with concentric LVH, defined by increased RWT and LVMI, have been shown to have worse clinical outcomes compared to patients with other subtypes of LV geometric pattern [36]. A recent study on gender differences in LV size and geometric pattern of 676 newly presenting adults in Nigeria showed that more women (26.9 %) had concentric LVH compared to men (26.9 versus 20.1 %; $p = 0.04$) with posterior wall thickness, and weight being predictors of this LV geometric pattern [37]. These data are supported by earlier data published by Weinberg and colleagues who also observed that hypertensive women had a greater degree of increase in LV wall thickness and concentric LVH [38]. Gender-related differences in serum aldosterone correlating positively with LVH in women were also reported [38], but not separately investigated in African women. In the Heart of Soweto Study almost 40 % of patients presented with left ventricular hypertrophy (LVH) confirmed by echocardiography. Moreover, two-thirds of cases had previously undiagnosed heart disease (predominantly HF and renal failure) [39]. Significantly, these findings had been predicted because of worryingly low levels of detection, treatment and control of HT in urban sub-Saharan Africa [40].

Fortunately, hypertension is an easily detectable condition that can be readily controlled with treatments that are not only inexpensive, but relevant to salt-sensitive black Africans (e.g. thiazides and dihyrdopiridine calcium antagonists [41]) in whom regression of LVH is achievable—see below [42]. In this context, it is clear from our own and previous African and African-American studies [43] that hypertension is an extremely important antecedent for CHF. However, the progression from concentric LVH to CHF has not well been defined in African women and Africans altogether.

Early detection of hypertensive heart disease via 12-lead ECG

The 12-lead ECG remains an important diagnostic tool for detecting manifestations of hypertensive heart disease [44].

However, a recent publication [45] describing the electrocardiographic findings of African adults found to be both free from heart disease and any underlying cardiac dysfunction/pathology via echocardiography, requires comment. Of the 387 urban South Africans studied 199 (51 %) had an ECG 'abnormality' and 67 ECGs (17 %) had major and minor abnormalities by Minnesota coding. Sokolow-Lyon Index voltage exceeding 38 mm indicative of LVH was more prominent in males than in females (23.6 versus 6.4 %; OR 4.5, 95 % CI 2.3–8.5). These findings are important as 'false positive' ECGs can be a confounding factor indicative of underlying heart disease but representing normal ECG variants in the African population [45]. A cost-effective way to detect advanced heart disease in patients with hypertension (potentially using a combination of 12-lead ECG and N-terminal brain natriuretic peptide [46]) in the primary care setting is yet to be determined, but is of great importance given the apparent limitations of the ECG in this context.

Managing hypertension/hypertensive heart disease in African women

Detection of individuals

Although hypertension represents an important and preventable risk factor for more advanced forms of CVD, it cannot be considered in isolation. As described in a recent review of the global management of hypertension [6] and consistent with the approach adopted in high income countries, the World Health Organization's Choosing Interventions that are Cost-Effective program recommends an absolute risk approach to risk factor management in LMIC [47]. In practical terms, this means actively treating those with multiple risk factors and, therefore, intrinsically at higher risk unless presenting with an extreme individual value—e.g. a BP >180/100. Any profiling of African women with suspected hypertension should therefore incorporate, where possible, a basic assessment of the affected individual's age, family history, lipid profile, smoking status and anthropometrics. It should also include noting the caveats described above, a 12-lead ECG to determine the potential presence of LVH, in addition to screening for other signs of end-organ damage including proteinuria/micro-albuminuria, bearing in mind that Africans often present with more advanced forms of hypertensive disease [39, 48]. The challenge of adequately controlling BP and other risk factors in this setting has been highlighted by the recently reported HiHi study of hypertensive black Africans in Cape Town townships [22].

Although there are internet-based risk profiling algorithms, the use of chart-based calculations is still a

potentially popular and effective means to guide effective BP management [49]. From a life-style perspective, it is important to note that being overweight is culturally acceptable (and even desirable) in many African countries. Regardless, efforts to achieve weight reduction, coupled with a low-salt diet as well as lower saturated fat intake (particularly in urban areas where traditional diets have been replaced with salt, fat and sugar-enriched diets) are often mandatory [50]. Regardless of the setting and chosen pharmacological agents, a recent Cochrane review of BP management in primary care [51] highlighted the importance of a structured and intensive care approach to effectively lowering BPs in affected individuals and this applies equally to the African context. For example, while it is generally accepted that African Americans suffer more severely from the consequences of hypertension, in the hypertension detection and follow-up program (the largest and most influential study in the aforementioned Cochrane Review), African-American men benefited more than their white counterparts [52].

Role of salt

Salt is known to affect blood pressure via a linear association. Average salt intake in South African adults is 8.1 g/day and much higher than the 4–6 g/day recommended by the World Health Organisation [53]. Much of salt consumption arises from non-discretionary intake such as bread, margarine and soup mixes [54]. As highlighted in a recent publication by Bertram and colleagues, proposed reduction in selected foods, such as bread, would decrease the average salt intake by 0.85 g/person/day. This would result in 7400 fewer cardiovascular death and 4300 less fatal strokes per annum, with substantial cost-saving to the individual, family and society. As such, the broad evidence suggests that a reduced sodium diet has an effect on hypertension equivalent to that of first-line drug treatment with a diuretic [55].

Pharmacological and non-pharmacological management

With respect to medical therapy, while there is clear evidence to demonstrate that every anti-hypertensive agent is effective in lowering BPs to reduce primary and secondary events in a roughly linear fashion in all races [4]., there are clearly defined population groups which require special consideration [56]. For example, there is some evidence that African Americans achieve a lesser reduction in BP when beta-blockers, angiotensin receptor inhibitors and angiotensin receptor blockers are applied in mono-therapy form, compared to white Americans [56]. The introduction of an additional diuretic appears to attenuate this lack of

effect [57–59]. Conversely, the ALLHAT trial, including more than 15,000 subjects of African descent, showed that an ACE inhibitor was less effective in lowering BP, compared to a thiazide diuretic or calcium channel antagonist, resulting in 20–40 % more CVD events (including CHF and stroke) [57]. In a study of 125 hypertensive Africans (68 % female), Libhaber and colleagues demonstrated that initiating therapy with 1.5 mg of indapamide SR and then adding 4 mg of perindopril is equally as effective as amlodipine therapy alone at reducing BP and modifying target organ damage [41]. Although treating hypertensive female patients has become very easy with different choices of medications, this can pose a problem in pregnancy as few medications, especially the short-acting calcium channel blocker (Nifedipine) and Alpha methyldopa, have been found to be safe in pregnancy.

The recent development of the renal sympathetic denervation therapy might have important implications for a population group, often presenting with severe hypertension and requiring multiple drug therapy, without achieving sufficient control. The recent publication by Vogel B et al. [60] highlights experiences with renal denervation in the real world set up.

Practical aspects of BP measurement in Africa

The recent development of a low cost solar-powered blood-pressure device may be a step in the right direction in tackling the increasing burden of hypertension in sub-Saharan Africa [61]. The WHO commissioned the development of a manual and/or automated, non-mercury, solar-powered, accurate and robust device for low-resource settings, making it affordable for many and will, hopefully, equip resource-poor health-care systems to readily identify and treat at-risk women.

Perspectives

In conclusion, there is convincing evidence that hypertension is becoming increasingly prevalent in African women due to epidemiological transition with geographic and socio-economic gradients evident across the African continent. Moreover, hypertensive heart disease typically affects women at a far younger age in sub-Saharan Africa than that observed in high income countries. Hypertensive heart disease is particularly problematic in pregnancy and is an important contributor to maternal case-fatality. Population-wide reduction in salt consumption, as well as timely detection and treatment of hypertension and hypertensive heart disease, remains a priority for effective primary and secondary prevention of CVD (particularly stroke and CHF) in African women. Relatively cheap

treatment options are available to effectively treat affected women. The challenge is to establish cost-effective and sustainable screening and subsequent management programs in the community to ensure that as many affected African women are detected and treated in a timely manner. This will entail targeting women at a much younger age than would be expected in a high income setting.

Conflict of interest None of the authors has a conflict of interest related to this manuscript.

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