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The highly neglected burden of resistant hypertension in Africa: a systematic review and meta-analysis

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ABSTRACT

Objective: The hypertension epidemic in Africa collectively with very low rates of blood pressure control may predict an incremented prevalence of resistant hypertension (RH) across the continent. The aim of this study was to determine the prevalence of RH and associated risk factors in Africa.

Data sources: We conducted a comprehensive search of electronic databases (PubMed, EMBASE, Africa Wide Information and Africa Index Medicus) completed by manual search of articles, regardless of language or publication date.

Methods: We included studies which have reported the prevalence and/or risk factors for RH in Africa from inception to 19 May 2016. Forest plots were drawn to visualise the combined prevalence of RH and extent of statistical heterogeneity between studies.

Results: Out of 259 retrieved studies, only 5 from Cameroon, Nigeria, Burkina Faso, Lesotho and Algeria with a total population of 4 068 patients were finally included in this review. There was no study from the Eastern part of Africa. Though the definition of RH was not similar across studies, its prevalence was respectively 11.7%, 4.9%, 14.6%, 14.3% and 19.0%, with an overall pooled prevalence of 12.1% (95% CI 8.0% to 17.7%). Potential risk factors were: non-compliance to treatment, ageing, male sex, dyslipidaemia, metabolic syndrome, previous cardiovascular events, physical inactivity and stress, but not excessive salt intake, alcohol and coffee ingestions. Moreover, diabetes, smoking, obesity and renal insufficiency yielded discrepant results.

Conclusions: There is a huge dearth of research on the epidemiology of RH in Africa. Thereby, an extensive study of RH prevalence and risk factors is still largely warranted to curtail the high and continuously increasing burden of hypertension across Africa.

Strengths and limitations of this study

- To the best of our knowledge, this is the first and only systematic review and meta-analysis that has focused on resistant hypertension in Africa.
- Strong and reliable methodological and statistical procedures were used in this review.
- Only five studies were found eligible for inclusion in the qualitative and quantitative analyses.
- The definition of resistant hypertension was different from one study to another, with a consequential high clinical heterogeneity across studies.

deaths annually.[1 2] Africa carries the heaviest burden of hypertension across the WHO regions, with an estimated prevalence of 30% that contrasts with very low rates of awareness, treatment and control.[2–6] Unfortunately, if left uncontrolled, hypertension causes stroke, myocardial infarction, cardiac failure, dementia, renal failure and blindness.[2 3 7]

Treatment-resistant hypertension (RH) has been increasingly recognised as one of the major reasons for uncontrolled blood pressure (BP). It is defined by a systolic BP (SBP; and/or diastolic BP (DBP)) ≥140 (90) mm Hg while being on at least three antihypertensive drugs at optimal dosages including a diuretic.[8 9] The prevalence of RH varies between 8.4% and 17.4% across American and European countries.[9–11] Multiple non-modifiable and modifiable risk factors for RH including black ethnicity, ageing, stress, obesity, hyperaldosteronism, excessive salt intake and chronic kidney disease have been described in Western studies.[11–15] It is notable that RH substantially impacts on the hypertension epidemic worldwide.[11–16]

Given that the highest prevalence rates of hypertension are yielded within Africa, the burden of RH may also be most likely

INTRODUCTION

Globally, hypertension is the leading cause of cardiovascular disease and cardiovascular mortality, with more than 1 billion adults affected worldwide and 10.4 million related

increased across the continent.[1] [2] [4] [5] In this regard and in the absence of accurate epidemiology capturing the burden of RH in Africa, we conducted a systematic review aiming to investigate the prevalence and associated risk factors for RH in Africa. To the best of our knowledge, this is the first and only systematic review and meta-analysis that has focused on RH in Africa.

METHODS

We used the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines as the template for reporting the present review.[17]

Data sources and search strategy

In order to identify potentially eligible studies, we conducted a comprehensive search of the following electronic databases: PubMed/MEDLINE, Excerpta Medica Database Guide (EMBASE), Africa Wide Information and Africa Index Medicus. The strategy used for the PubMed search is shown in online supplementary appendix 1. For the other databases, we used a combination of the terms: 'resistant hypertension', 'epidemiology' and 'Africa'. We searched for all relevant studies regardless of language or publication date, and supplemented the search by screening bibliographies of identified articles and other pertinent review papers, conference proceedings and specialist journals. The last electronic search was run on 20 May 2016.

Although no complete study protocol was written before starting this review, we developed and piloted a screening guide to make sure that the inclusion criteria were adhered to and consistently applied by all review authors. Three authors (JRNN, LNA and JJNN) independently reviewed the titles and abstracts of all citations retrieved, and subsequently assessed the full-text articles to identify eligible studies. Agreement between review authors was measured using Cohen's κ statistic.[18] Disagreements were resolved by discussion and consensus.

Study selection criteria

We systematically identified and appraised reports of original peer-reviewed publications conducted among African populations living inside the continent, including hypertensive patients aged 18 years and above, and published from inception to 19 May 2016. They must have reported the incidence, prevalence and/or risk factors for RH. RH must have been clearly defined in the study, as a SBP (and/or DBP) ≥140 (90) mm Hg while being on at least three antihypertensive drugs at optimal dosages including a diuretic.[8] [9] Studies with higher cut-offs could be included as well, considering that the definition might have changed over time. Other subsets of uncontrolled hypertension were not considered in this review. The study design of interest included observational studies (cross-sectional, prospective/retrospective cohort studies or case–control studies). Experimental studies, letters, reviews, commentaries,

editorials, case reports or case series were not included. In case of duplicate reports, the most comprehensive and up-to-date version was taken into account.

Extraction and collection of data

Data extraction used a preconceived and standardised data collection form, and was performed by two independent authors (JRNN and JJNN). Any discrepancies between these authors were reconciled through discussion. Data extracted comprised information about year of publication, country, objective and design of the study, diagnostic criteria of RH, mean age, sex (male proportion), duration of hypertension, signs and symptoms, mean BP, antihypertensive medications, complications, prevalence and/or incidence, and risk factors for RH.

Quality assessment of included studies

The methodological quality of included studies was evaluated using the Newcastle-Ottawa Scale.[19] The Newcastle-Ottawa Scale was designed to assess the quality of non-randomised studies in meta-analyses. This scale is primarily formulated by a star allocation system, assigning a maximum of 10 stars for the risk of bias in three areas: selection of study groups (4 or 5 stars), comparability of groups (2 stars) and ascertainment of the outcome of interest or the exposure (3 stars). There is no validation study that provides a cut-off score for rating low-quality studies; a priori, we arbitrarily established that 0–3, 4–6 and 7–10 stars would be considered at high, moderate and low risk of bias, respectively.

Data analysis and presentation of results

Data were analysed using the Comprehensive Meta-Analysis software, V.2 (Biosta). Data were summarised using ranges, means±SDs and frequencies (percentages) where appropriate. Forest plots were drawn to visualise the combined prevalence of RH and extent of statistical heterogeneity between studies. Statistical heterogeneity was assessed using the χ^2 test on Cochrane's Q statistic,[20] and quantified by calculating the I^2 statistic (with values of 25%, 50% and 75% being representative of low, medium and high heterogeneity, respectively).[21] There was a clinical heterogeneity between studies included in this study. In fact, the definition of RH was different across studies. Consequently, we used a random-effects meta-analysis to estimate the overall pooled prevalence of RH.[22] In order to assess possible publication bias, Egger weighted regression methods were used.[23] A p value <0.05 was considered indicative of statistically significant publication bias. Moreover, other relevant findings were summarised in a narrative format.

RESULTS

Figure 1 is a flow diagram outlining the process of identification and selection of included studies. We identified 259 records through a comprehensive search among which 25 duplicates were identified and removed.

Subsequently, we screened 234 titles and abstracts, and excluded 224 irrelevant papers. Then, nine full-text articles and one conference abstract were reviewed for eligibility, among which five publications were excluded for the following reasons: no reporting of RH prevalence, incidence or risk factors;[24 25] studies conducted on Africans residing outside Africa.[13 26 27] At the end of the process, only five studies met the inclusion criteria and were thus retained for qualitative and quantitative analyses (figure 1).[15 28–31] Agreement between reviewers was high (κ=0.88, p<0.001).

Table 1 summarises the characteristics of studies included in the review. The first study was conducted in Yaoundé (Cameroon, Central Africa) from January to December 1991,[28] the second in Ibadan (Nigeria, West Africa),[29] the third in Ouagadougou (Burkina Faso, West Africa) from 1 May 2010 to 31 May 2012,[15] the fourth in Maseru (Lesotho, Southern Africa) in April to May 2013,[30] and the last one in Blida (Algeria, North Africa) between June 2012 and June 2014.[31] This was a conference abstract, the full paper of which remains unpublished until now. All the studies were cross-sectional, hospital-based and the diagnostic criteria of RH varied from one study to another (table 1).

The study population comprised 565 patients in Cameroon, 566 in Nigeria, 692 in Burkina Faso, 70 in Lesotho and 2175 in Algeria, making a total of 4068
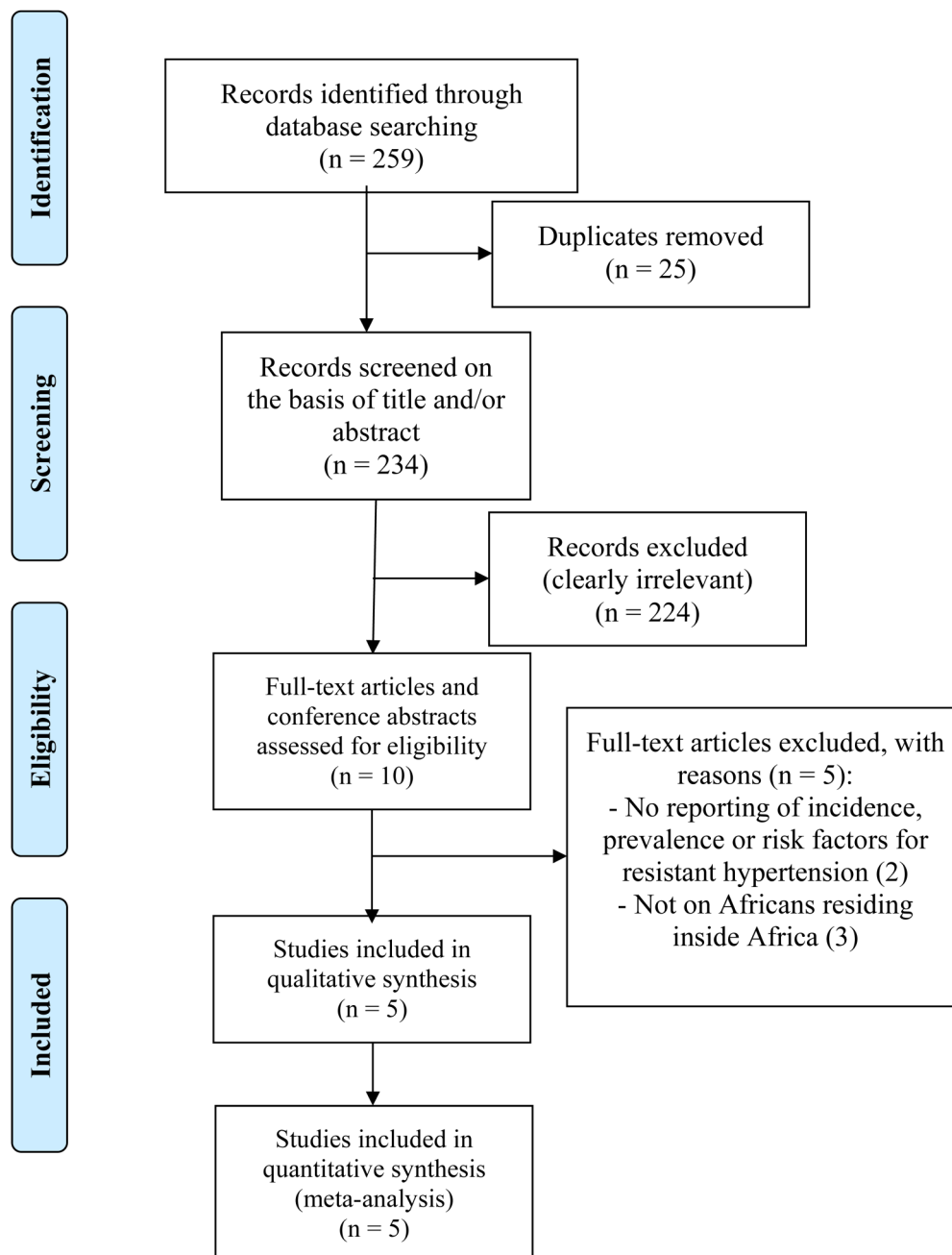
Figure 1 Process of identification and selection of studies for inclusion in the review (PRISMA flow diagram).
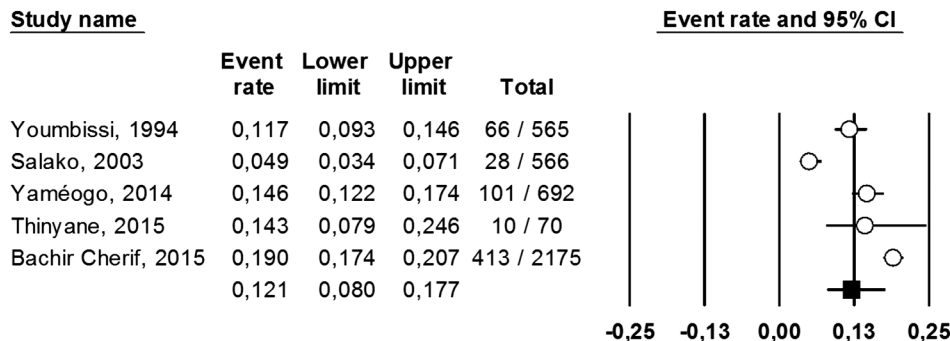
Table 1 Characteristics of studies included in the review

Author, year	Country	Study design	Diagnostic criteria of RH	Sample size	Mean age (years) RH/T	Male (%) RH/T	Mean SBP/DBP±SD (mm Hg)	Antihypertensive treatment	Prevalence of RH (%)	Associated factors*
Bachir Cherif et al, 2015[31]	Algeria	CS	Office blood pressure above the goal in spite of the concurrent use of 3 antihypertensive agents of different classes, including a diuretic, at full dose	2175	NM/49.71 ±13.56	NM/46.8	NM	NM	19% (95% CI 17.4% to 20.7%)	Older age (65.7±12.6 vs 57.7±13.4 years, p<0.001); sedentary status (87.1% vs 74.5% p<0.05); previous cardiovascular events (36.9% vs 17.7%, p<0.001); diabetes (41.8% vs 26.5%, p<0.001); hypercholesterolaemia (20.8% vs 11.4%, p<0.05); obesity (35.5% vs 16.3%, p<0.001); metabolic syndrome (48.2% vs 22.6%, p<0.03), chronic kidney disease (24.9% vs 14.1%, p<0.05)
Thinyane et al, 2015[30]	Lesotho	CS	BP>160/100 mmHg despite use of at least 3 different antihypertensive drugs with complementary mechanisms of action, 1 of which being a diuretic	70	NM/57.7 ±13.2	NM/10	NM	Hydrochlorothiazide, captopril, atenolol, nifedipine	14.3 (95% CI 7.9 to 24.6)	NM
Yaméogo et al, 2014[15]	Burkina Faso	CS	BP≥140/90 mm Hg despite at least 3 antihypertensive drugs including a diuretic; then after ambulatory BP monitoring:≥135/ 85 mm Hg in the morning and/or≥120/ 70 mm Hg in the night	692	64.2±5.4/54.8 ±11.1	48.5/39.7	166.4±10.7/ 98.8±5.5	Diuretics (100%), converting enzyme inhibitors (85.1%), calcium channel blockers (77.2%), β-blockers (66.3%), central antihypertensives (15.8%), angiotensin II receptor antagonists (12.9%), α-blockers (5%), antirenine (3%)	14.6 (95% CI 12.2 to 17.4)	Age ≥45 for men or ≥55 for females: 101 (100%) vs 300 (50.8%); p=0.0001 Male sex; 49 (48.5%) vs 226 (38.2%); p=0.003 Dyslipidaemia: 32 (31.7%) vs 164 (27.8%); p=0.01 Obesity/overweight: 34 (33.7%) vs 142 (24%); p=0.007 Physical inactivity: 45 (44.6%) vs 54 (9.1%); p=0.0001 Smoking: 12 (11.9%) vs 44 (7.4%)
Salako and Ayodele, 2003[29]	Nigeria	CS	BP≥140/90 mm Hg in the presence of use of 3 antihypertensive drugs including a diuretic at near maximum doses for at least 1 month	566	51.8±9.7/56 ±14.3	25/38.5	176.4±43/109.6 ±14	Calcium channel blockers, diuretics, central antihypertensives, β-blockers	4.9 (95% CI 3.4 to 7.1)	Mean age: 51.8 vs 54.6 years; p<0.04 Non-compliance with treatment: 14 (50%) vs 73 (18.6%); p<0.001
Youmbissi et al, 1994[28]	Cameroon	CS	BP≥160/95 mm Hg despite a well-conducted treatment with 3 medications or more taken by a compliant patient for at least 1 month	565	49.4±11.6 (men); 54.6 ±7 (women)/NM	62.1/51.9	190±27/116±20 (men) 200±29/124±22 (women)	NM	11.7 (95% CI 9.3 to 14.6)	Family history of hypertension 33 (50%) vs 274 (55%); regular alcohol intake 34 (52%) vs 274 (55%), heavy smoking 7 (10%) vs 65 (13%), associated diseases (gout and/ or diabetes mellitus: 21 (32%) vs 205 (41%), compliance with a low-salt diet 33 (50%) vs 250 (50%); poor compliance with treatment 30 (46%) vs 284 (57%)

*Comparison of the proportions of resistant versus non-resistant hypertensive patients (by the χ^2 test).
BP, blood pressure; CS, cross-sectional; DBP, diastolic blood pressure; NM, not mentioned; ref, reference number; RH, resistant hypertension; SBP, systolic blood pressure; T, total (study population).

Figure 2 Forest plot of random-effects meta-analysis showing pooled prevalence of resistant hypertension.

| Study name	Event rate	Lower limit	Upper limit	Total
Youmbissi, 1994	0,117	0,093	0,146	66 / 565
Salako, 2003	0,049	0,034	0,071	28 / 566
Yaméogo, 2014	0,146	0,122	0,174	101 / 692
Thinyane, 2015	0,143	0,079	0,246	10 / 70
Bachir Cherif, 2015	0,190	0,174	0,207	413 / 2175
	0,121	0,080	0,177	

patients.[15 28–31] The male proportion of patients with RH ranged between 48.5% and 62.1% (table 1).[15 28–30] The mean ages of participants across studies are presented in table 1.

The prevalence of RH was 11.7% (95% CI 9.3% to 14.6%) in Cameroon, 4.9% (95% CI 3.4% to 7.1%) in Nigeria, 14.6% (95% CI 12.2% to 17.4%) in Burkina Faso, 14.3% (95% CI 7.9% to 24.6%) in Lesotho and 19.0% (95% CI 17.4% to 20.7%) in Algeria.[15 28–31] The I^2 statistic was 94.1% (p<0.001) and the estimation of between-study variance (τ^2) was 0.234. Using a random-effects meta-analysis, the overall pooled prevalence was 12.1% (95% CI 8.0% to 17.7%; figure 2). There was no evidence of publication bias (figure 3), confirmed by the results of Egger's weighted regression test (t-value=2.6, p=0.07). Only one study (from Burkina Faso) reported signs and symptoms that presented patients with RH: 12 patients (11.9%) reported headaches, 10 (9.9%) dizziness, 9 (8.9%) precordial chest pains and 4 patients (4.1%) presented with hemiplegia (table 2).[15]

In Cameroon, the mean duration of hypertension since diagnosis was 7±5 years in men and 8±6 years in women;[28] in Burkina Faso, 11 (10.9%) patients with RH were followed for not more than 1 year and 15 (14.9%) for at least 10 years.[15] Three studies reported the antihypertensive drugs prescribed, namely: diuretics, ACE inhibitors, calcium channel blockers, β-blockers, α-blockers, α-methyl dopa, angiotensin-II receptor blockers and antirenine (table 1).[15 29 30] Fourteen patients with RH (50%) in Nigeria and 36 patients with RH (54%) in Cameroon were not compliant with treatment.[28 29] The mean SBP/DBP was 190±27/116±20 mm Hg among men and 200±29/124±22 mm Hg among women in Cameroon, 176.4±43/109.6±14 mmHg in Nigeria, and 166.4±10.7/98.8±5.5 mm Hg in Burkina Faso (table 1).[15 28 29] At all ages, Cameroonian women exhibited higher SBP and DBP than men (all p values <0.001).[28]

In Cameroon, the percentage of patients with RH with advanced fundal changes was significantly higher when compared with the non-resistant hypertensives. Likewise, ECG and radiology evidence of left ventricular hypertrophy was noticed in 36 patients with RH (54%) compared with 185 patients (37%) without RH. Serum creatinine and 24-hour urine albumin were significantly
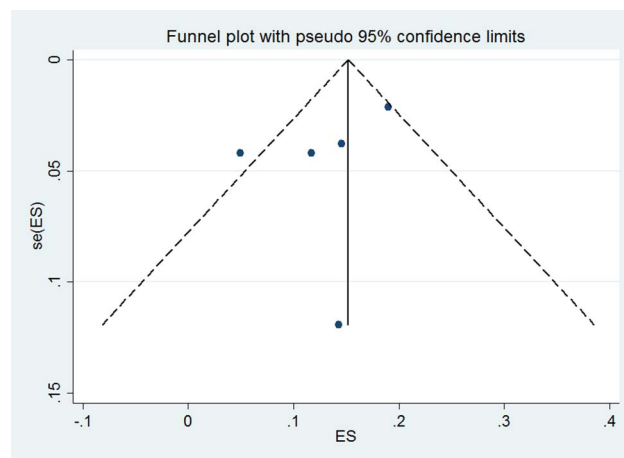
Figure 3 Funnel plot showing no evidence of publication bias across studies.

higher in patients with RH (p<0.01), whereas fasting blood sugar, plasma cholesterol and serum potassium were comparable between patients with and without RH.[28] The study from Burkina Faso revealed that left ventricular hypertrophy, renal insufficiency, hypertensive retinopathy, stroke and myocardial infarction were significantly more frequent in patients with RH than in patients without RH (p<0.001).[15]

Only one study (from Algeria) undertook logistic regression analyses to investigate the independent factors impacting RH, which pointed out metabolic syndrome and diabetes mellitus as the two factors associated with an increased probability to have RH.[31] In binary analyses, older age, sedentary status, previous cardiovascular events, diabetes, hypercholesterolaemia, obesity, metabolic syndrome and chronic kidney disease were significantly more represented in patients with RH (table 1).[31] In Nigeria, the authors observed that non-compliance with treatment might be the key factor responsible for RH in their setting. In contrast, obesity, ingestion of non-steroidal anti-inflammatory drugs, renal insufficiency, ingestion of antidepressants, coffee, alcohol, tobacco and excessive salt intake were not found to be associated with RH.[29] In Burkina Faso, the authors showed that RH men aged ≥45 years and women aged ≥55 years, males, those with dyslipidaemias,

Table 2 Quality assessment of included studies using the NOS

Author, year	Selection (maximum 5 stars)				Comparability (maximum 2 stars)		Outcome (maximum 3 stars)		Total (on 10 stars)
	Representativeness of the sample (1 star)	Sample size (1 star)	Non-respondents (1 star)	Ascertainment of the exposure (2 stars)	Controls for the most important factor	Controls for any additional factor	Assessment of the outcome (2 stars)	Statistical test (1 star)	
Thinyane et al, 2015[30]	*	*	0	**	0	0	**	0	6
Yaméogo et al, 2014[15]	*	*	0	**	0	0	**	*	7
Salako and Ayodele, 2003[29]	*	*	0	**	0	0	**	*	7
Youmbissi et al, 1994[28]	*	*	0	**	0	0	**	0	6

This table summarizes assessment of the methodological quality of studies included using the NOS score. This score allocates stars for each and every items.
*Equals one star or one point.
**Stands for two stars or two points.
NOS, Newcastle Ottawa Scale.

those obese or overweight, physically inactive ones, and smokers significantly outnumbered their counterparts with non-RH (all p values <0.05), but the proportion of individuals with diabetes was similar between patients with and without RH (p=0.09; table 1).[15] The study from Cameroon presented various proportions in patients with and without RH without any statistical comparison (table 1).[28]

Of note, the study from Burkina Faso identified stress (21 patients; 20.8%) and renal insufficiency (8 patients; 7.9%) as two aetiologies of RH. Moreover, addition of spironolactone to the antihypertensive regimen of patients with RH resulted in 22 (21.8%) of these patients shifting into the controlled hypertension group.[15]

The risk of bias assessment using the Newcastle-Ottawa Scale quality score is depicted by table 2. All studies failed to provide the response rate and characterise the non-respondents in comparison to the respondents; likewise, comparability between patients with and without RH was unsatisfactory. In studies from Cameroon and Lesotho, no statistical tests were used to compare patients with and without RH. On the whole, two studies (Cameroon and Lesotho) presented a moderate risk of bias (six stars each), while the two others (Nigeria and Burkina Faso) exhibited a low risk of bias (seven stars each; table 2). Owing to incomplete information, the methodological quality of the study from Algeria was not assessed.

DISCUSSION

This review points out a critical lack of data regarding the burden of RH in Africa, though the condition could substantially contribute to explaining the very high rate of uncontrolled BP in the region.[4 5] Indeed, we have recorded only five studies which have assessed the prevalence and/or risk factors for RH in the continent: one from Central Africa (Cameroon),[28] two from West Africa (Nigeria and Burkina Faso),[15 29] one from Southern Africa (Lesotho)[30] and one from Northern Africa (Algeria).[31] There was no study from the Eastern part of Africa. Besides, the study from Cameroon was conducted 25 years ago, that from Nigeria 13 years ago, the one from Burkina Faso 4 years ago and those from Lesotho and Algeria 3 and 2 years back, respectively. Therefore, the majority of data extracted from these studies are old and need to be updated, considering how the burden of hypertension has been continuously increasing in Africa over the recent decades.[1 2] This review highlights the crucial and urgent need to focus on the epidemiology of RH in Africa in order to better understand the condition and address specific action plans which will surely result in mitigating the morbidity and mortality due to hypertension and its related complications throughout the continent.

The definition of RH was different across included studies; it may be partly explained by the different

periods when these studies were conducted. Concurring with our results, Achelrod et al[10] observed from their review that the definition of RH was not identical across studies. Depending on the definition used, patients could be classified as true RH, controlled RH or pseudo-RH.[9] We learn from Judd and Calhoun's[9] review that the term 'apparent-RH' has been used in situations where ambulatory blood pressure measurement (ABPM) had not been performed to exclude pseudo-RH caused by the white-coat effect. In this review, only Yaméogo et al[15] (Burkina Faso) undertook the ABPM to exclude white-coat-related RH. Therefore, the four other studies may have reported the prevalence of apparent RH rather than true RH. Besides, Boswell et al[12] demonstrated that all potential definitions of RH do not describe the same patients. These observations call for a need to harmonise and standardise the definition of RH for a better reporting and pooling of its related patterns as proposed by Achelrod et al,[10] especially in Africa where national and/or regional guidelines and policies are lacking to guide healthcare practice across the continent.[2] Besides, clinicians and researchers must be bound to rely on international guidelines.

Moreover, studies from Nigeria[29] and Cameroon[28] exhibited, respectively, 50% and 46% of non-compliance to medication, this being even the key factor responsible for RH in Nigeria. These findings enabled Salako and Ayodele[29] to conclude that ensuring medication compliance may be the single most important strategy to prevent RH in their setting. Similarly, Hameed et al[32] bolstered that non-adherence to antihypertensive medication is very common among patients with RH. However, non-adherence or poor adherence to antihypertensive medication should be considered as a cause of pseudoresistance rather than a risk factor for RH, as well as suboptimal dosing.[9 10] RH is characterised by multiple side effects subsequent to intake of many drugs,[28] and the cost of its treatment may be prohibitive, especially in economically deprived environments.[33] Thereby, the patient may become less and less compliant over time. Consequently, a vicious circle of resistance is created. In this regard, specific measures need to be undertaken to reduce non-adherence and improve BP control.

The prevalence of RH was 11.7% in Cameroon, 4.9% in Nigeria, 14.6% in Burkina Faso, 14.3% in Lesotho and 19.0% in Algeria.[15 28–31] In Cameroon, the cut-off to define RH was high (BP≥160/95 mm Hg).[28] It is not surprising, therefore, that mean BP levels of patients with RH were higher in Cameroon than in the other countries (190/116 mm Hg in men and 200/124 mm Hg in women vs 176.4/109.6 mm Hg in Nigeria and 166.4/98.8 mm Hg in Burkina Faso).[15 28 29] Besides, it is possible that the real prevalence of RH in Cameroon and in Lesotho might have been higher than what was reported, given the high cut-offs used to define RH.

Our overall pooled RH prevalence of 12.1% approaches what has been obtained in other parts of the globe. For instance, Achelrod et al[10] compiled data from 20 observational studies and 4 randomised-controlled trials mainly from North America and Europe, and reported respectively 13.7% and 16.3% prevalence of RH. Likewise, Judd and Calhoun[9] reported an average rate of 14.8% (range 8.4–17.4) among treated hypertensives, and 12.6% (range 8.9–12.8%) of all hypertensives. In Brazil, Lotufo et al[11] reported an RH prevalence of 11% among 4116 patients taking treatment for hypertension. This review suggests that the prevalence of RH in Africa may mirror that of European and American countries, though there are very few data in Africa to confirm this trend. Studies are therefore warranted accordingly.

Without doubt, there is evidence that RH prevalence is higher among old patients, patients with diabetes and obese patients, those with renal insufficiency, Africans, West Indians and those in precarious conditions.[11–14] For instance, the old, blacks, less educated, obese and poorer were found to be at higher risk of RH than their counterparts in Brazil.[11] One of our studies carried out logistic regression analyses to seek independent factors driving RH, and pointed out metabolic syndrome and diabetes mellitus as these factors.[31] In addition to the Algerian study, two other studies reported bivariate analyses,[15 29] the results of which were somewhat in contradiction with the literature. In fact, obesity, smoking, excessive salt intake and renal insufficiency were not linked with RH in Nigeria,[29] whereas it was found in Burkina Faso that advanced age, male sex, stress, renal insufficiency, dyslipidaemia, obesity, physical inactivity and smoking, but not diabetes, were associated with RH.[15] In Algeria, older age, previous cardiovascular events, obesity, diabetes, hypercholesterolaemia, metabolic syndrome and chronic kidney disease were associated with RH in bivariate analyses.[31] Concerning age, we found that patients with RH were old (age nearing 50 years and above), in accordance with the 60.6 years average age reported by Achelrod et al[10] in their systematic review. Contrasting with what was observed in Burkina Faso, it is the female sex that has been found to be associated with RH elsewhere.[34] These discrepancies highlight the crucial need to conduct further studies in the continent to ascertain the real drivers of RH locally. It will then be possible to implement specific interventions addressing each of these identified factors to curb the burden of hypertension and related consequences in Africa.

Consistent with the literature,[11 16] studies from Cameroon and Burkina Faso showed that end-organ damage, notably left ventricular hypertrophy, renal insufficiency, hypertensive retinopathy, stroke and myocardial infarction, was significantly more frequent in patients with RH than in those with controlled hypertension.[15 28] In an attempt to control BP levels, it was observed in Burkina Faso that addition of spironolactone to the antihypertensive regimen of patients with RH resulted in 21.8% of these patients shifting into the controlled

hypertension group.[15] This is in line with findings from Williams *et al*[35] showing that spironolactone was the most effective add-on drug for the treatment of RH. Accordingly, this option needs to be encouraged among physicians taking care of Africans suffering from RH as other alternatives such as renal denervation and baroreceptor stimulation may be unavailable or largely unaffordable.

Unfortunately, we identified just a few studies to have a clear estimate of the prevalence of RH across Africa. No study was recorded from Eastern Africa. This could perhaps jeopardise generalisation of our results to the entire African continent. Furthermore, definition of RH was not homogeneous across studies, and regression analyses were not undertaken in all the studies to assess independent risk factors for RH. This lack of adequate statistical methods critically limited our ability to identify key factors against which intervention measures can be developed to curtail the burden of RH in Africa. Nonetheless, we conducted this review following the rigour and standards of the art. Besides, and to the best of our knowledge, this is the first systematic review and meta-analysis drawing a clear picture of the prevalence and risk factors for RH in Africa.

CONCLUSION

This review highlights the dearth of research on RH prevalence and risk factors in Africa. Data from the studies included revealed a prevalence ranging from 4.9% to 19.0%, not far from rates observed in other parts of the world. Contrariwise, the determinants, though not thoroughly investigated, may differ at some points from what has been observed elsewhere. There is therefore a crucial need to direct more attention to RH which may substantially contribute to increase the burden of hypertension in Africa. Large multicentre studies are urgently warranted to better assess the prevalence and drivers of RH all round the continent. For now, special efforts should be undertaken to reduce non-adherence to antihypertensive medication, and addition of spironolactone could be discussed while awaiting studies underpinning such a practice in the region.

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