

# Risk factors of heart failure among patients with hypertension attending a tertiary hospital in Ibadan, Nigeria: The RISK-HHF case-control study

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## Research article

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# Abstract

**Background:** Hypertension is the leading cause of heart failure in sub-Saharan Africa. Preventive public health approach to reduce the scourge of HF must seek to understand the risk factors of heart failure in at risk populations. The aim of this study was to characterize the modifiable risk factors of HF among patients with hypertension attending a cardiology clinic.

**Methods:** One hundred and one (101) case-control age- and sex-matched pairs were recruited. The study population were adults with a clinical diagnosis of hypertensive heart failure (cases) and hypertension. They were interviewed and evaluated for modifiable cardiovascular risk factors. Associations between variables were tested with McNemar's chi square test and paired sample t test as appropriate. Conditional logistic regression modelling was used to determine the risk factors of HF in the study population while 'punafcc' package in stata15 was used to calculate the population attributable fraction (PAF) of risk factors.

**Results:** Low education attainment ( aOR: 2.38, 95% CI: 0.91-6.20; PAF: 21.1%, 95% CI: 5.1-34.5 ) showed borderline association with HF while alcohol consumption (aOR: 10.40, 95% CI: 2.30-47.04; PAF: 33.5%, 95% CI: 21.6-43.6) and suboptimal medication adherence (aOR: 7.00, 95% CI: 2.31-21.26; PAF: 69.7%, 95% CI: 59.4-77.4) were strong risk factors for HF even after adjustment for other modifiable risk factors. These three dominant risk factors accounted for 89% of the PAF of HF. Dietary factors were not significantly associated with HF risk in adjusted analyses.

**Conclusions:** The risk factors for heart failure in hypertensive patients are largely modifiable. Public health interventions and preventive cardiovascular care to improve medication adherence and reduce alcohol consumption among patients with hypertension are recommended.

## Background

Hypertension is the leading risk factor for cardiovascular diseases and cardiovascular related morbidity and mortality globally and is responsible for about 7.6 million deaths every year worldwide.<sup>1</sup> It is the leading cause of heart failure (HF) globally and especially in sub-Sahara Africa. Hypertension is the most frequent cause of heart failure in Nigeria accounting for up to 61% in a cohort in Abuja and 75.7% in another cohort of heart failure group in Ibadan, Nigeria.<sup>2,3</sup> Despite improvement in care of patients with systemic hypertension and development of potent anti-hypertensives, heart failure incidence continues to rise even in Nigeria.<sup>2,4</sup> Hypertensive heart failure predominantly affect younger age group in African populations thus leading to loss of economic productivity and poor quality of life.<sup>5,6</sup>

The search for epidemiologic risk factors for heart failure in the general population has continued in recent times. Little is known till date about the unique and specific risk factors of hypertensive heart failure in Africans and Nigerians in particular. Most of the studies done in this area in Nigeria and other sub-Saharan countries have been largely descriptive. Even though, cardiovascular risk factors are largely

prevalent in the adult population in Nigeria, the specific ones responsible for hypertensive heart failure have yet to be characterised. Preventive public health approach to reducing the scourge of heart failure in patients with hypertension must seek to understand the risk factors and determinants of heart failure in at risk populations. This is important given that hypertensive heart failure is a unique entity from other heart failure aetiologies especially in Africans. Moreover, in clinical cardiology, early recognition and attention to preventing and treating these risk factors will lead to significant reductions in heart failure incidence and severity. There is therefore, a need to determine and characterise the modifiable risk factors of heart failure in this population.

The RISK-HHF study is a case-control study designed as an initial step in the determination and characterization of the risk factors of hypertensive heart failure in Nigerian-Africans. We included 102 patients with hypertensive heart failure and similar number of age and sex-matched hypertensive controls without heart failure. The specific objectives were to determine the strength of association between various modifiable cardiovascular risk factors and hypertensive heart failure and to ascertain the specific combination of risk factors and their population attributable fraction (PAF) responsible for the overall heart failure risk among hypertensive patients in Nigerian-Africans that are amenable to low-cost preventive cardiovascular health.

## Methods

### Participants

This study was approved by the joint University of Ibadan and University College Hospital Institutional Review Board (IRB) and complied with the principles outlined in the declaration of Helsinki.<sup>7</sup> The study also adhered to the STROBE guidelines on observational studies.<sup>8</sup> Written informed consent as approved by the IRB was obtained from all study participants. Participants were recruited from the cardiology clinic and medical wards of the Department of Medicine, University College Hospital, Ibadan. Participants recruitment started in June, 2018 and the whole study lasted about 8 months. Patients aged 18 years old or above with clinical diagnosis of heart failure secondary to hypertension who were attending the hospital for the first time were recruited into the study as cases while age (5-year age range) and sex matched hypertension with no heart failure served as controls. Exclusion criteria for both cases and controls were heart failure diagnoses of other aetiologies, previous myocardial infarction or history of ischaemic heart disease, chronic obstructive pulmonary disease, being pregnant and consumption of  $\geq 80$  g of alcohol per day for the past 5 years.

Clinical diagnosis of heart failure was based on the modified Framingham criteria.<sup>9</sup> A patient was considered to have heart failure secondary to hypertension on the basis of self-reported history of hypertension and/or the use of blood pressure-lowering medication or documented blood pressure  $\geq 140/90$  mmHg.<sup>10</sup>

Sample size (N) in each group was calculated using the formula for case control study:<sup>11</sup>

$$N = [Z_{1-\alpha/2}\sqrt{2\pi(1-\pi)} + Z_{1-\beta}\sqrt{\pi_1(1-\pi_1)+\pi_2(1-\pi_2)}]^2 / (\pi_1-\pi_2)^2$$

$Z_{1-\alpha/2}$ , standard normal deviate at  $\alpha$  of 0.05 = 1.96

$Z_{1-\beta}$  at 95% power = 1.64

$\pi_1$ , is the prevalence of electrocardiographic LVH (dominant marker) in hypertensives in heart failure in Agomuoh and Odia<sup>12</sup> = 49.3%

$\pi_2$ , is the prevalence of electrocardiographic LVH in hypertensives without heart failure in Agomuoh and Odia<sup>12</sup> = 22%

$$\pi = (\pi_1 + \pi_2) / 2;$$

Thus,  $N = 78.5$ , adding a non-response rate of 25%,  $N$  becomes 98. One hundred and one (101) participants were recruited consecutively into each group from the study sites.

## Procedures

A semi structured interviewer administered questionnaire was used for data collection. The questionnaire was developed and modified from a previous study and followed the STEPS format for epidemiologic surveys.<sup>13,14</sup> The questionnaire had three sections; sections A, B and C. Section A was divided into subsections on demographic data, medical history, lifestyle risk factors, symptoms and size, medications in use, examination and laboratory test results. Section B was the assessment of medication adherence using the Medication Adherence Questionnaire.<sup>15</sup> Section C contained the coding of electrocardiographic patterns according to the modified Minnesota coding system.<sup>16,17</sup> The questionnaire was pre-tested before the main study among 10 cases and 10 controls. The questionnaire was also translated into the Yoruba language which is the local language spoken by most patients attending the hospital.

Baseline clinical and demographic data was obtained from the subjects. Medication adherence was assessed using the Medication Adherence Questionnaire (MAQ).<sup>18</sup> Suboptimal medication adherence was defined as low or moderate medication adherence.

Blood pressure measurements were obtained with a mercury sphygmomanometer according to standard guidelines.<sup>19</sup> Systolic and diastolic blood pressure were measured at Korotkoff sounds phase I and V, respectively. Two readings were taken at intervals of at least 2 minutes, and the average of the readings was used to represent the patient's blood pressure.<sup>20</sup> If there is > 5 mm Hg difference between the first and second readings, additional (1 or 2) readings was obtained, and then the average of these multiple readings was used.<sup>21,22</sup>

Subjects were weighed without shoes and in light clothing on a standard beam balance. Height was measured to the nearest centimetre using anthropometrical plane with subjects not putting on shoes or headgear.<sup>23</sup>

Body mass index (BMI) was calculated using the formula:

$$\text{BMI} = \text{Weight (Kg)} / \text{Height}^2 (\text{m}^2).$$

Patients had full cardiovascular examination done. Patients with any of pedal oedema, abdominal distension, engorged neck veins, orthopnoea, paroxysmal nocturnal dyspnoea, basal lung crackles and rales were considered congested. Venous blood sample (20mls) was taken for serum electrolytes, serum urea, serum creatinine and fasting serum lipids from each subject along with 5mls of urine for dipstick urinalysis. Significant proteinuria was defined as more than trace proteinuria on dipstick.<sup>24</sup>

Electrocardiography was also done for each study participant. The New York Heart Association (NYHA) functional class was assigned at recruitment in those with heart failure.

## Statistical analysis

Data were analysed using STATA version 15 (StataCorp LLC, Lakeway Drive, College Station, Texas, USA). Normality of continuous variables were determined using Shapiro-Wilk test and histogram plots. Proportions were used to summarize variables that are categorical while categorical variables were summarized as means/medians and standard deviations/interquartile range as appropriate. Hypertension group and hypertensive heart failure group were compared using statistical tests for matched data. Association between categorical risk factors and heart failure risk were determined using McNemar chi square for matched data after recoding of these categorical variables into two categories while association between continuous variables and heart failure risk were determined using paired t-test for normally distributed variables and Wilcoxon signed rank sum test for non-normally distributed variables. Univariate and multivariable conditional logistic regression were used to explore the relationship between modifiable cardiovascular risk factors and heart failure risk. The multivariable conditional logistic regression analysis was based on a priori modelling of the modifiable risk factors to calculate the adjusted odds ratio of associations. The significant risk factors were also confirmed with iterative model building. The 'punafcc' package in stata was used to determine the population attributable fraction (PAF) of the risk factors of heart failure as post-estimation command after conditional logistic regression. Forest plot of the adjusted odd ratio of the modifiable risk factors was plotted using the 'ipdmetan' package in stata. A p value < 0.05 was considered statistically significant in all analyses.

## Results

A total of one hundred and one (101) age and sex matched case control pairs were recruited into this study. As shown in Table 1, the mean age of the subjects was 62.4 years (cases) and 60.7 years (controls) with similar proportion of males and females. Individuals with HF were more likely to have lower education attainment, more likely to have ever consumed alcohol and also more likely to have history of kidney disease. They were also less likely to have been on potent anti-hypertensives like angiotensin enzyme converting enzyme inhibitors/angiotensin receptor blockers (ACE-I/ARB) and

calcium channel blockers (CCBs) for hypertension control. Suboptimal medication adherence was significantly associated with HF.

Table 1

Association of participants' profile with heart failure risk (data are summarized as % for categorical variables, mean  $\pm$  SD for normally distributed continuous variables and median (IQR) for non-normally distributed continuous variables)§

Variables	Cases: HHF (101)	Controls Hypertension without HF (102)	P value
Age	62.4 $\pm$ 14.3	60.7 $\pm$ 13.0	0.53
Female	50 (49.5)	50 (49.5)	1.00
Low education (below tertiary education)	47 (46.5)	32 (31.7)	0.04*
Unemployed	39 (38.6)	37 (36.6)	0.76
Diabetes	12 (11.9)	16 (15.8)	0.35
Kidney disease	11 (10.9)	3 (3.0)	0.03*
Obesity	16 (15.8)	20 (19.8)	0.48
Exercise	42 (41.6)	54 (53.5)	0.08
Ever smoked	86 (85.1)	91 (90.1)	0.23
Ever consumed alcohol	47 (46.5)	29 (28.7)	0.002**
Frequent Fruits	14 (13.9)	40 (39.6)	< 0.001
Frequent Vegetables	19 (18.8)	36 (35.6)	0.01*
Adding salt to food on the table	14 (13.9)	11 (10.9)	0.49
Low/moderate medication adherence	81 (80.2)	41 (40.6)	< 0.001**
<b>BP Medications</b>	21 (20.8)	30 (29.7)	0.19
$\beta$ Blockers	54 (53.5)	74 (73.3)	< 0.01*
ARB/ACE-I	22 (21.8)	61 (60.4)	< 0.001**
Calcium channel blocker	39 (38.6)	53 (52.5)	0.07
Diuretics			

Variables	Cases: HHF (101)	Controls Hypertension without HF (102)	P value
<b>Clinical profile</b>	27.6 ± 9.4	27.8 ± 6.7	0.51
BMI (Kg/m <sup>2</sup> )	0.96 ± 0.10	0.95 ± 0.11	0.58
Waist hip ratio	87.9 ± 1.5	89.3 ± 6.4	0.01*
Pulse (/min)	20 (16, 24)	18 (14, 20)	0.001**
Respiratory rate (/min)	126.8 ± 23.6	145.7 ± 20.1	< 0.001**
SBP (mmHg)	79.4 ± 18.3	86.0 ± 19.0	0.01*
DBP (mmHg)			
ARB: angiotensin receptor blocker; ACE-I: angiotensin converting enzyme inhibitor; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure			
§paired analysis; *p < 0.05; **p < 0.01			

Subjects with hypertensive heart failure had higher respiratory rate, but lower systolic (SBP) and diastolic (DBP) blood pressure than hypertensive individuals without heart failure.

The crude odds ratios of the associations between modifiable risk factors and heart failure risk are shown in Table 2. Individuals with low education attainment had a 80% increased risk of HF with a PAF of 21%; alcohol consumption was associated with about 4-fold increased HF risk (PAF 33%); smoking was not significantly associated with HF risk; suboptimal medication adherence was associated with almost 8-fold increased HF risk, accounting for the highest PAF (70%); fruits and vegetables consumption were protective and associated with 80% and 55% reduced risk of HF respectively, though with negligible PAF while at least weekly exercise was associated with a trend towards reduced HF risk. Obesity and adding salt on the table were not significantly associated with HF risk. The composite of low education attainment, alcohol consumption and suboptimal medication adherence accounted for 89% of the PAF of HF in individuals with hypertension. Inclusion of all the nine investigated modifiable risk factors only increased the PAF to 91%, thus showing that these three aforementioned factors were the dominant risk factors of HF in individuals with hypertension in this study.

Table 2  
Univariate Conditional Logistic Regression of Potential predictors of HF

Variables	Unadjusted OR (95%CI)	P value	PAF % (95% CI)
Low education (below tertiary education)	1.83 (1.03, 3.26)	0.04*	21.1 (5.1, 34.5)
Ever consumed Alcohol	3.57 (1.54, 8.26)	< 0.01**	33.5 (21.6, 43.6)
Ever smoked	1.57 (0.6, 4.05)	0.35	39.8 (-70.7, 78.8)
Obesity	0.78 (0.39, 1.56)	0.48	-4.5 (-19.8, 8.8)
Low/moderate medication adherence	7.67 (3.27, 17.95)	< 0.001**	69.7 (59.4, 77.4)
Fruits consumption	0.19 (0.08, 0.45)	< 0.001**	-60.1 (-139.4, -7.0)
Vegetables consumption	0.45 (0.24, 0.85)	0.01	-22.8 (-52.2, 0.8)
Adding salt on the table	1.37 (0.55, 3.42)	0.49	3.8 (-5.8, 12.5)
Exercise	0.59 (0.32, 1.07)	0.08	-29.3 (-79.6, 6.8)
Composite of all nine risk factors	-	-	91.3 (52.6, 98.4)
Composite of low education, alcohol consumption and low/moderate medication adherence	-	-	89.2 (79.3, 94.3)

In adjusted analyses (Fig. 1), alcohol consumption and suboptimal medication adherence remained significant risk factors of HF while low education attainment was associated with a trend towards increased HF risk. In the presence of all nine modifiable risk factors, the effects of low education attainment (aOR 2.38; p = 0.08) and alcohol consumption (aOR 10.40; p < 0.01) were magnified while suboptimal medication adherence showed only minimal attenuation with 7-fold increased risk of HF. The other lifestyle risk factors were not significantly associated with HF in adjusted analyses (see Fig. 1).

## Discussion

In this study, patients with HHF (cases) were matched with patients with hypertension who were not in HF (controls) by sex and 5-year age range. Comprehensive evaluation for various lifestyle modifiable risk factors was done. This is a unique study considering that few studies have used this method in Nigeria in characterising the risk factors of heart failure. The mean age of the cases and controls in this study is  $62.5 \pm 14.3$  years and  $60.7 \pm 13.0$  respectively. This is in tandem with the findings by Akintunde *et al.*<sup>25</sup> and Mene-Afejuku *et al.*<sup>26</sup> who have reported a higher mean age of  $62.1 \pm 14.2$  years and  $64.56 \pm 11.85$  years respectively among patients with hypertensive heart failure. However, Ogah *et al.*<sup>5</sup> in the Abeokuta HF registry and Ojji *et al.*<sup>2</sup> in Abuja have reported a mean age of  $56.6 \pm 15.3$  years and  $54.8 \pm 13.2$  years respectively. The age of the hypertension group here is higher than that reported by most investigators in Nigeria.<sup>27,28</sup> However, this is because they were matched with the cases who had a higher age. There were about equal number of both sexes in this study. The patients were selected to reduce confounding from age and sex.

The high rate of smoking and alcohol consumption is in keeping with other epidemiologic studies in the general population and also in heart failure and hypertensive patients.<sup>29,29</sup> This has enormous implication for preventive cardiovascular health to stem this tide. Drug adherence was suboptimal in this population with only 19.8% and 60.4% of the cases and controls achieving high medication adherence since they were diagnosed with hypertension. This was significant in bivariate and regression analysis. In univariate models, low education attainment was associated with increased HF risk even though this was only marginally significant in the multivariable model. This may be because those with lower education may not fully understand the need for adherence, coupled with their low social and family support, these population of patients are at increased of adverse outcomes like HF when they develop hypertension. It is well known that low education leads to low income, poor social class, poor family support and reduced affordability of medications and vulnerability to alcohol abuse, which act in concert to put this group of individuals at higher risk of disease progression.

Also, HF patients had lower blood pressure though with higher respiratory rate which is in keeping with the chronic sympathetic drive in heart failure that results in reduced cardiovascular conditioning in the long-term. The reduced blood pressure in the later stage of heart failure is due to the loss of myocardial function and ejection fraction with failure of forward circulation. In this study, obesity was not associated with heart failure even though it was present appreciably in both the cases and controls. This is contrary to reports from the MESA<sup>30</sup>, Framingham<sup>31</sup> studies and other published studies by Lam *et al.*<sup>32</sup> and Saguner *et al.*<sup>33</sup>. Thinness in heart failure has been regarded as the 'obesity paradox'.<sup>34</sup> However, it seems more likely that thinness in HF is a marker of chronic inflammation in longstanding disease such that these patients often present at the late stage of adipose tissue burn-out. Also, in the setting of HF, especially in HF with reduced ejection fraction (HFrEF), the heart cannot sustain adequate forward output and the pump failure in this condition is responsible for the low blood pressure and compensatory tachycardia and tachypnoea.

The significant risk factors of heart failure among hypertensives in this study were low educational attainment (a surrogate for low social class), alcohol consumption and suboptimal drug adherence. Low education attainment was associated with a 2-fold increased risk of HF and a PAF 21% in crude analysis and a borderline significant 2-fold increased risk of HF in adjusted analysis. Low education attainment is a surrogate for low social class in Nigeria and may lead to economic inequality and disparities in access to and provision of medical care. It also limits access to information and education about healthy lifestyle and preventive healthcare. This is similar to findings from the Heart of Soweto study<sup>6</sup>. The high alcohol consumption in both the cases and controls echoes the findings of Laabes *et al.*<sup>35</sup> in an earlier report in Nigeria among individuals with hypertension and represent an opportunity for cardiovascular preventive care given the myocardial depressive effect of alcohol and associated increased susceptibility to arrhythmias.

The role of alcohol is particularly intriguing. Earlier studies like the INTERHEART study had suggested that moderate alcohol ingestion is cardioprotective and prevents ischaemic heart disease and consequent heart failure.<sup>36</sup> Also, though the relationship between alcohol and heart failure is controversial, it is known that heavy alcohol intake more than 90 g per day causes the alcohol associated cardiomyopathy with myocardial burnout.<sup>37</sup> Evidence for lower quantities of alcohol predisposing to heart failure is controversial.<sup>38</sup> However, in this study, patients with significant amount of alcohol used for the classification of alcohol heart muscle disease were excluded. Thus, it seems that any amount of alcohol is associated with increased risk of heart failure even in non-ischaemic patients with hypertension who frequently have other clustered cardiovascular risk factors. Alcohol in adjusted analysis is associated with a 10-fold increased risk of heart failure and a 33% population attributable fraction of the risk of HF, or better put; 33% of the proportion of HF in the hypertensives would be prevented if patients stopped alcohol consumption. A recent study systematic review has also shown that no amount of alcohol is safe for health.<sup>39,40</sup>

Cigarette smoke is atherogenic, vasculotoxic and pro-inflammatory causing the release of cytokines that activate the renin-angiotensin-aldosterone pathway with resultant adverse haemodynamics and myocardial toxicity and depression.<sup>41</sup> Interestingly, in our study, smoking was not a strong risk factor for HF. This may reflect the low smoking prevalence among Nigerians compared to other populations. It may also be that atherogenesis play little role in the pathogenesis of hypertensive HF unlike ischaemic HF.

Among patients with hypertension, only about a third are aware of their status. Among those who are aware of their hypertensive status, only about a third are on treatment with up to 40% being on inadequate treatment and remaining uncontrolled in different populations and studies.<sup>42-46</sup> Drug poor or non-adherence is perhaps the most common and important risk factor of heart failure among patients with hypertension. In the systematic analysis by Abegaz *et al.*<sup>47</sup>, 43 to 65.5% of patients who fail to adhere to prescribed medications are hypertensives. In this study, 45.2% of hypertensive patients were non-adherent to medications, 31.2% of those hypertensives with co-morbidities were non-adherent with 83.7% of non-adherence noticed in those with uncontrolled blood pressure. Though higher percentage of

women were non-adherent to medications, the risk of non-adherence was higher in men and overall Africans and Asians were the ones who are more likely to be poorly adherent to medications with 62.5% of non-adherence noted in these racial groups.<sup>47</sup> Similarly, in the study by Lee *et al.*<sup>48</sup>, 22.1% of patients with at risk of HF were non-adherent to medications. These patients were more likely to be men, African-American and have shorter time to readmission for HF. Corrao *et al.*<sup>49</sup> also reported that those with increasing grade of adherence have reduced risk of HF. It has also been found that those who used their medications 80% of the time tend to have reduced cardiovascular events.<sup>50</sup> These high rates of medication poor adherence in patients with hypertension and other high-risk individuals have stimulated interest in the reasons and factors promoting poor adherence to anti-hypertensives and other cardiovascular protective medications. Aggarwal *et al.*<sup>51</sup> in New York, reported that among patients with poor adherence to medications use, forgetfulness, polypharmacy, being symptom free were reasons why many patients fail to adhere to their medication regimen. In the longitudinal study of hypertensives by Saguner *et al.*, female sex, obesity, increased number of medications and medication non-adherence were the risk factors for hypertensive crises.<sup>33</sup> In this study, medication non-adherence was the most important risk factor. In our present study, suboptimal medication adherence was associated with a 7-fold increased risk of HF in adjusted analyses. This is similar to the report by Saguner *et al.*<sup>33</sup> Furthermore, Adeoye *et al.*<sup>52</sup> have reported similar suboptimal medication adherence among Nigerians with uncontrolled hypertension. This is particularly worrisome given that these were patients attending specialist clinics. Furthermore, suboptimal medication adherence was the single most important factor that accounted for much of the attributable fraction of HF (70%). This an important public health concern and an avenue for intensive patient education for preventive care.

The role of dietary practices is intriguing. In univariate models, fruits and vegetables consumption were both associated with about 80% and 55% reduced risk of HF. However, in adjusted analysis, they were not significantly associated with HF risk. Exercise was also associated with a marginally significant 40% reduction in risk of HF even though this became insignificant in adjusted analysis. Sedentary lifestyle and inadequate exercise have been reported as adverse cardiovascular risk factors in the general population. Having less than 150 minutes of moderate intensity aerobic exercise per week has been shown to predispose to obesity, dyslipidemia, with resultant insulin resistance and cardiovascular deconditioning.<sup>53,54</sup> Sedentary lifestyle acting in concert with other adverse lifestyle risk factors thus contribute to clinical deterioration and onset of heart failure.<sup>55</sup> Moreover, poor effort tolerance and exercise deconditioning reduces quality of life, worsens obesity, aggravates neurohumoral activation, myocardial remodeling and adversely affect cardiopulmonary oxygen consumption. It has been shown to be an independent risk factor of heart failure in the NHANES 1 epidemiologic follow up survey published by He *et al.*<sup>56</sup> Pena Sanchez et al and Rahman et al. have also reported similar findings.<sup>57,58</sup>

Addition of salt to food on the table was not associated with HF risk and had negligible PAF for HF. Excessive salt intake in the general population leads to expanded blood volume, increased glomerular filtration and may potentiate or accelerate hypertension in predisposed individuals. It is difficult to conclude on the role of dietary practices in HF given the often ascertainment bias in estimating dietary

intake of fruits, vegetables and salt. The composite of the nine modifiable risk factors identified in this study accounted for 91% of the PAF of HF and represent an attractive opportunity for cardiovascular prevention of 91% of the attributable fraction of HF among hypertensives.

The strength of this study includes the matching of cases with control which reduces the confounding effects of age and sex in heart failure risk. Furthermore, the use of a validated medication adherence questionnaire is another strength of this study thus reducing subjectivity in the classification of the patients. Moreover, the risk factors identified in this study can be easily addressed by public health preventive interventions.

This study is not without limitations. First, this is a highly selected group of patients, though efforts have been made to reduce confounding. Thus, the finding is only generalisable to patients with hypertension who are at risk of heart failure. Also, recall bias may have affected the estimation of consumption of salt, vegetables and fruits and characterisation of the lifestyle habits. However, the questionnaire used has been used in previous works and any misclassification would have been non-differential and randomly distributed between the two groups. Coronary angiography was not done to completely rule out co-existing ischaemic heart disease, however, the definitions used to exclude ischaemic heart disease have been used in other studies in this population and the probability of misclassification of patients is low. Moreover, the prevalence of ischaemic heart disease in Nigeria is still low and hypertension still accounts for most of the heart failure in our population.

## Conclusion

This study has characterised and determined the risk factors of heart failure among patients with hypertension. These risk factors include lifestyle habits and low education attainment which are largely modifiable representing 91% of the PAF of HF. In this case-control study, the authors have shown that suboptimal medication adherence, alcohol consumption and low education attainment are the dominant modifiable risk factors of HF in individuals with hypertension. This provides an opportunity for cardiovascular preventive care. Health education should be intensified in primary and specialist care settings. Setting up a medication adherence clinic may help to identify early those patients with poor adherence who may be at high risk of heart failure. A comprehensive heart failure registry should be established in all tertiary health institutions. This will help in further large-scale studies and validation of these results. Finally, a larger case-control study or even a cohort study is needed to confirm the findings of this research.

## Abbreviations

aOR

Adjusted odds ratio

ACEIs/ARBs

Angiotensin Converting Enzyme Inhibitors/Angiotensin Receptor Blockers

BMI  
Body mass index  
CCBs  
Calcium channel blockers  
DBP  
Diastolic blood pressure  
HF  
Heart failure  
HFrEF  
Heart failure with reduced ejection fraction  
MAQ  
Medication Adherence Questionnaire  
OR  
Odds ratio  
PAF  
Population attributable fraction  
SBP  
Systolic blood pressure

## **Declarations**

### **Ethics approval and consent to participate**

This study was approved by the joint University of Ibadan and University College Hospital Institutional Review Board (IRB) with reference number UI/EC/18/0218. Written informed consent as approved by the IRB was obtained from all study participants.

### **Consent for publication**

Not applicable

### **Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

### **Competing interests**

The authors declare that they have no competing interests

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This work was self-funded by the authors.

## Authors' contribution

AO conceived and carried out the study. He also analysed the data and wrote the study report. IA conceived the study, directed the analysis and supervised the conduct of the study and its report writing. Both authors contributed to the writing of the manuscript.

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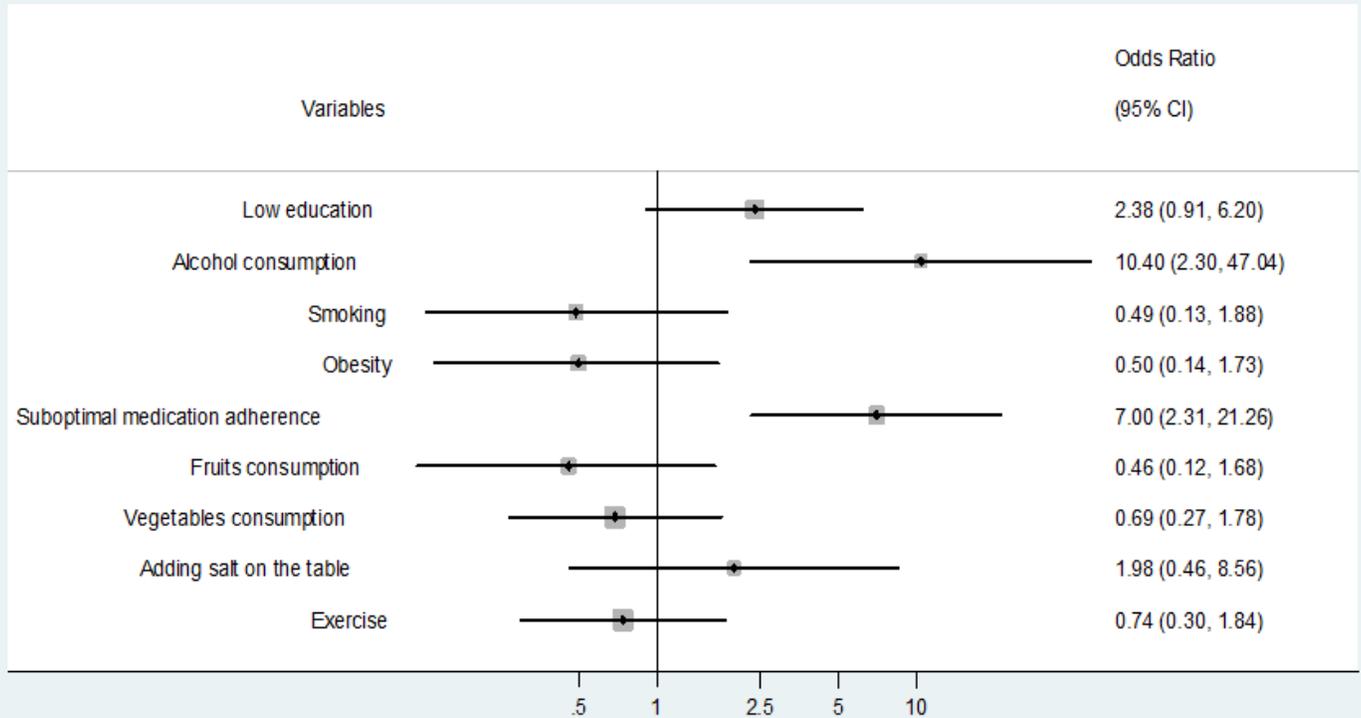
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## Figures

## Risk factors of heart failure in hypertension



**Figure 1**

Forest plot showing adjusted ORs of the modifiable cardiovascular risk factors of heart failure among individuals with hypertension