Short Report

Hemoglobin Levels and Blood Pressure are Associated in Rural Black Africans

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Objectives: The association between blood levels of hemoglobin (B-hgb) and blood pressure (BP) has been widely investigated in Caucasians and Asians but there is a paucity of data in rural black Africans. The objective was to investigate the association between B-hgb and BP in a rural black African population.

Methods: A cross-sectional study was conducted in three districts in Kenya (Bondo, Kitui, and Transmara) with the inclusion of participants aged ≥17 years. Background information, anthropometry, BP, B-hgb, hepatic insulin resistance (HOMA2-IR), standard lipid profile, and oral glucose tolerance test were obtained in each participant.

Results: Background characteristics among 1,167 participants showed that anemic and non-anemic participants differed significantly from each other as there were more women, lower body mass index and waist circumference (WC), lower degree of hepatic insulin resistance and plasma cholesterols among the anemic participants. Furthermore, anemic participants had significantly lower systolic and diastolic BP ($P < 0.01$) but not a significantly different prevalence of hypertension ($P = 0.08$). Multivariate linear regression models adjusted for—age, sex, plasma total-cholesterol, WC, Log2(HOMA2-IR), ethnicity, and smoking status—revealed that B-hgb (per mmol/l increment) was significantly associated with systolic BP (estimate: 1.18 (0.37–1.98)) and diastolic BP (estimate: 1.06 (0.54–1.57)) ($P < 0.01$).

Conclusions: B-hgb is associated with BP in rural black Africans. Am. J. Hum. Biol. 00:000–000, 2015.

INTRODUCTION

The association between blood levels of hemoglobin (B-hgb) and blood pressure (BP) has been widely investigated in Caucasians and Asians but has shown diverging results (Atsma et al., 2012; Chen et al., 2011; Irace et al., 2012; Jae et al., 2014; Kawamoto et al., 2012; Vázquez, 2012). Hematocrit and B-hgb can vary considerably among inhabitants of rural sub-Saharan Africa (SSA) due to nutritional deficiencies, hemoglobinpathies, variation in altitude level, and infections (Makani et al., 2011; Mugisha et al., 2013). A recent study in Uganda on risk factors for anemia (Mugisha et al., 2013) demonstrated that rural elderly with anemia had lower risk of hypertension, but otherwise the link between B-hgb and BP has not been investigated in SSA. Hence, it is possible that the living conditions of rural SSA often leading to lower levels of B-hgb may have a preventive role in terms of hypertension. The objective of this study was to investigate the association between B-hgb and BP in a rural black African population.

METHODS AND MATERIALS

Design, setting, and ethics

A cross-sectional study was conducted in three districts in Kenya (Bondo, Kitui, and Transmara) and included participants aged ≥ 17 years from three ethnic groups, that is, Luo, Kamba, and Maasai residing in those districts. Exclusion criteria were pregnancy, severe mental disease, or positive malaria smear. The majority (92%) of the Luo and Kamba participants were randomly invited to participate in the study by lot at local "barazas" (village meetings), while all Maasai living within a 20 km range of the study site were invited to participate. Data were collected during August through November 2005. The Luo, Kamba, and Maasai participants were examined at 1,200, 1,700, and 1,800 m above sea level, respectively. All participants gave written or oral informed consent. Ethical approval was given by the National Ethical Review Committee in Kenya, and consultative approval was given by the Danish National Committee on Biomedical Research Ethics in Denmark.

Procedures

Information including age, educational level, and smoking habits was obtained in interviews by a team investigator or trained local assistant. Each participant was weighed on an electronic scale, wearing light clothing only, and height was measured with a portable stadiometer. Body mass index (BMI, kg/m^2) was calculated. Waist circumference (WC) was measured with a body tape midway between the iliac crest and the costal margin following a quiet expiration. Systolic BP and diastolic BP were

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TABLE 1. Background characteristics of rural Kenyans (n = 1,167) by anemic status

Variable	Non-anemia $n = 857$	Anemia $n = 310$	*P*-Value
B-hemoglobin (mmol/l)	8.9 (0.9)	6.5 (1.0)	<0.01
Age (years)	38.9 (10.6)	38.0 (10.2)	0.24
Men [*n* (%)]	390 (45.5)	67 (21.6)	<0.01
Smoking [*n* (%)][a]	107 (12.9)	21 (7.2)	<0.01
Ethnicity [*n* (%)]			<0.01
Luo	264 (30.8)	140 (45.2)	
Kamba	299 (34.9)	102 (32.0)	
Maasai	294 (34.3)	68 (21.9)	
BMI (kg/m^2)[b]	21.9 (4.2)	21.2 (3.8)	<0.01
Waist circumference (cm)[b]	78.8 (10.7)	76.6 (8.6)	<0.01
HOMA2 IR[c]•	0.40 (0.26–0.61)	0.37 (0.22–0.54)	0.045
P-Total cholesterol (mmol/l)[d]	3.9 (0.9)	3.3 (0.8)	<0.01
P-LDL cholesterol (mmol/l)[e]	2.3 (0.8)	2.0 (0.7)	<0.01
P-HDL cholesterol (mmol/l)[e]	1.12 (0.30)	0.95 (0.36)	<0.01
B-ZNPP (mmol/heme)•	43.5 (30.5–60.0)	120.8 (59.0–231.0)	<0.01
Systolic BP (mmHg)	120 (15)	115 (17)	<0.01
Diastolic BP (mmHg)	74 (10)	72 (11)	<0.01
Hypertension [*n* (%)]	109 (12.7)	28 (9.0)	0.08

Values are means (SD) unless otherwise specified.
• Medians (interquartile ranges).
[a]Missing data: Nonanemic: 27 individuals; Anemia: 19 individuals.
[b]Missing data: Nonanemic: 2 individuals; Anemia: 1 individual.
[c]Missing data: Nonanemic: 14 individuals; Anemia: 22 individuals.
[d]Missing data: Nonanemic: 46 individuals; Anemia: 41 individuals.
[e]Missing data: Nonanemic: 17 individuals; Anemia: 42 individuals.
BP, blood pressure; B-ZNPP, blood zinc protoporphyrin.

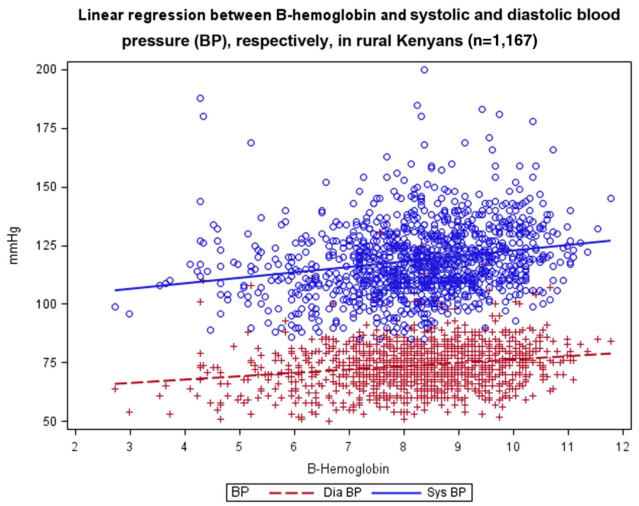

Fig. 1. Systolic BP = 98.4 + *x**2.37 (95%CI: 1.70–3.04) ($P < 0.01$). Diastolic BP = 61.8 + *x**1.44 (95%CI: 1.02–1.86) ($P < 0.01$). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

measured twice on the right upper arm with a full-automatic device (Omron M6, HEM-7001-E, Kyoto, Japan), while the participant was seated after a 15-min rest in a quiet room that had an approximate temperature of 25°C. There was a pause of at least 2 min between each BP measurement. If either the systolic BP or diastolic BP differed by > 5 mm Hg between the measurements then a third BP measurement was performed. The mean of the two latest measurements served as the actual systolic BP and diastolic BP. Hypertension was defined as BP ≥ 140 and/or ≥ 90 mm Hg or ongoing treatment with antihypertensive medication (Chalmers et al., 1999). A 75-g oral glucose tolerance test was performed in all participants who had not prediagnosed with diabetes mellitus (DM) and who had not been diagnosed (glucose > 6.1 mmol/l venous blood) with DM on a fasting blood sample. A glucose dehydrogenase method was used to determine blood glucose levels (HemoCue, Ängelholm, Sweden). Fasting serum insulin was measured by 1235 AutoDELFIA automatic immunoassay system (sensitivity 0.5 μU/ml) using time-resolved fluoro-immunoassay technique (kit no. BO80-101, PerkinElmer Life and Analytical Sciences, Wallace Oy, Turku, Finland). Level of hepatic insulin resistance was calculated by the homeostasis model assessment of insulin resistance (HOMA2-IR) (Levy et al., 1998). Standard lipid profile analyses were carried out based on fasting blood samples. B-hgb was determined using a standard Coulter counter technique (model KX-21N, Sysmex Corporation, Kobe, Japan). Anemia was defined according to WHO definitions (WHO, 2011) (B-hgb < 7.44 mmol/l for women and < 8.06 mmol/l for men).

Statistical analyses

Categorical variables were compared by the chi-square test or Fisher's exact test as appropriate. Normal distribution of each continuous variable was visually assessed in normal and q-q plots of the variable's residuals. The *t*-test was used to compare continuous variables if they were considered normally distributed and had equal variances. Otherwise the Kruskal–Wallis test was used. Mean values are presented with standard deviations and medians with interquartile ranges. Multivariate linear regression models for systolic BP and diastolic BP were constructed. Variables were included into the models if they were considered relevant for the estimation of BP. Assumptions of linearity, multicollinearity, normal distribution, and equal variances of the variables' residuals were assessed. Selected variables in the multivariate models were tested

TABLE 2. Multivariate linear regression models for systolic blood pressure (BP) and diastolic BP in rural Kenyans

Variable	Systolic BP $R^2 = 0.21$ $n = 1{,}032$ Estimate (95%CI)	*P*-Value	Diastolic BP $R^2 = 0.18$ $n = 1{,}032$ Estimate (95%CI)	*P*-Value
B-hgb (per mmol/l increment)	1.18 (0.37; 1.98)	<0.01	1.06 (0.54; 1.57)	0.01
Age (per year increment)	0.05 (−0.04; 0.15)	0.29	0.02 (−0.04; 0.08)	0.49
Women	−4.47 (−6.65; −2.29)	<0.01	−0.47 (−1.86; 0.92)	0.51
Waist circumference (per cm increment)	0.36 (0.26; 0.46)	0.01	0.23 (0.16; 0.29)	0.01
P-Total cholesterol (per mmol/l increment)	1.47 (0.41; 2.52)	0.01	0.96 (0.29; 1.64)	0.01
Log2 (HOMA2-IR)	1.75 (0.73; 2.76)	0.01	1.05 (0.40; 1.69)	0.01
Ethnicity				
Luo	−2.54 (−4.72; −0.36)	0.02	−1.20 (−2.59; 0.19)	0.09
Kamba	4.27 (2.12; 6.41)	0.01	1.51 (0.14; 2.88)	0.03
Maasai	1.0		1.0	
Smoking	−0.97 (−3.81; 1.88)	0.51	−0.08 (−1.90; 1.74)	0.93

95%CI, 95% confidence interval; hgb, hemoglobin.

for interaction. $P < 0.05$ was considered statistically significant. Data were analyzed using SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

Identification and characteristics of included participants

A total of 1,178 rural Kenyan participants were identified, of which 11 individuals did not have B-hgb measured. Thus, 1,167 participants (60.8% women) were included in the study. All background characteristics are presented in Table 1. The majority of the participants, 857 (73.4%) were non-anemic. These participants differed significantly from those who were anemic as there were more men, higher BMI and WC, higher degree of hepatic insulin resistance and plasma cholesterol levels (Table 1). The educational level did not differ significantly between the two groups ($P = 0.23$; data not shown). The participants who were anemic had significantly lower systolic BP [estimated difference 5.1 mm Hg, 95%CI (3.1–7.2)] and diastolic BP [estimated difference 2.7 mm Hg, 95%CI (1.4–4.0)] than the nonanemic participants. There was a tendency toward a higher frequency of hypertension in the non-anemic group but the difference was not significant [estimated difference: 3.7%, 95% CI (−0.2−7.6%)].

Linear regression models

B-hgb was linear associated with both systolic and diastolic BP (Fig. 1; $P < 0.01$). Moreover, B-hgb (per mmol/l increment) was linearly associated with systolic BP [estimate: 1.18 (0.37; 1.98)] and diastolic BP (estimate: 1.06, 95%CI: 0.54–1.57) in multivariate linear regression models that were adjusted for age, sex, plasma total-cholesterol, WC, Log2(HOMA2-IR), ethnicity, and smoking status (Table 2).

DISCUSSION

The key finding of this study, was a significant linear association between B-hgb and BP. The Study was conducted in a rural SSA population of which the majority had a traditional life style and living conditions. Moreover, anemic participants had lower BP compared with those who were non-anemic. In addition, the participants with anemia had a lower prevalence of hypertension but the difference did not reach statistical significance. The results were based on a large sample size and withstood adjustment for several relevant confounders. Hence, it is possible that the living conditions in rural SSA, often leading to lower levels of B-hgb and high frequency of anemia, may have a preventive effect in terms of BP increase and hypertension. Furthermore, that difference in B-hgb might contribute to the rural versus urban pattern of cardiovascular diseases (CVD) observed in SSA (Minicuci et al., 2014). Even though the BP difference between anemic and non-anemic participants was not dramatic; studies from the Western world have shown that BP variations or reductions as low as 5 mm Hg on population scale may cause significant decreases in CVD events and mortality (Atsma et al., 2012; Lewington et al., 2002). The mechanism that explains the link between B-hgb and BP is unclear. Differentiation in blood viscosity, activation of renin-angiotensin-aldosterone axis, and variation in erythropoietin secretion have all previously been proposed as explanatory suggestions (Atsma et al., 2012). However, in this field we did not have access to lab facilities to pursue any of these possible explanations. A potential reason that needs to be considered in this study is that higher values of B-hgb may simply reflect a more "Westernized" lifestyle as the risk markers of CVD was in general higher among the non-anemic participants. The study had other limitations. We were not able to provide information on underlying causes to the variations in B-hgb meaning that it could reflect conditions with a worse prognosis than hypertension. In conclusion, we found that B-hgb and BP was associated in rural black Africans.

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LITERATURE CITED

Atsma F, Veldhuizen I, de Kort W, van Kraaij M, Pasker-de Jong P, Deinum J. 2012. Hemoglobin level is possibly associated with blood pressure in a large cohort of healthy individuals. Hypertension 60:936–941.

Chalmers J, MacMahon S, Mancia G, Whitworth J, Beilin L, Hansson L, Neal B, Rodgers A, Ni Mhurchu C, Clark T. 1999. 1999 World Health Organization-International Society of Hypertension Guidelines for the management of hypertension. Guidelines sub-committee of the World Health Organization. Clin Exp Hypertens 21:1009–1060.

Chen H, Hua Q, Hou H. 2011. Association of hemoglobin with ambulatory arterial stiffness index in untreated essential hypertensive patients without anemia. Intern Med 50:2759–2765.

Irace C, Carallo C, Scavelli F, Loprete A, Merante V, Gnasso A. 2012. Lack of association between systolic blood pressure and blood viscosity in normotensive healthy subjects. Clin Hemorheol Microcirc 51:35–41.

Jae SY, Kurl S, Laukkanen JA, Heffernan KS, Choo J, Choi YH, Park JB. 2014. Higher blood hematocrit predicts hypertension in men. J Hypertens 32:245–250.

Kawamoto R, Tabara Y, Kohara K, Miki T, Kusunoki T, Katoh T, Ohtsuka N, Takayama S, Abe M. 2012. A slightly low hemoglobin level is beneficially associated with arterial stiffness in Japanese community-dwelling women. Clin Exp Hypertens 34:92–98.

Levy JC, Matthews DR, Hermans MP. 1998. Correct homeostasis model assessment (HOMA) evaluation uses the computer program. Diabetes Care 21:2191–2192.

Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. 2002. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 360:1903–1913.

Makani J, Cox SE, Soka D, Komba AN, Oruo J, Mwamtemi H, Magesa P, Rwezaula S, Meda E, Mgaya J, Lowe B, Muturi D, Roberts DJ, Williams TN, Pallangyo K, Kitundu J, Fegan G, Kirkham FJ, Marsh K, Newton CR. 2011. Mortality in sickle cell anemia in Africa: a prospective cohort study in Tanzania. PLoS One 6:e14699.

Minicuci N, Biritwum RB, Mensah G, Yawson AE, Naidoo N, Chatterji S, Kowal P. 2014. Sociodemographic and socioeconomic patterns of chronic non-communicable disease among the older adult population in Ghana. Glob Health Action 7:21292.

Mugisha JO, Baisley K, Asiki G, Seeley J, Kuper H. 2013. Prevalence, types, risk factors and clinical correlates of anaemia in older people in a rural Ugandan population. PLoS One 8:e78394.

Vázquez BY. 2012. Blood pressure and blood viscosity are not correlated in normal healthy subjects. Vasc Health Risk Manag 8:1–6.

WHO. 2011. Haemoglobin Concentrations for the Diagnosis of Anaemia and Assessment of Severity. Geneva: Vitamin and Mineral Nutrition Information System, World Health Organization, 2011, WHO/NMH/NHD/MNM/11.1. Available at http://www.who.int/vmnis/indicators/haemoglobin.pdf. Accessed March 1, 2015.