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ORIGINAL RESEARCH

Association Between Hemoglobin Level, Anemia, and Hypertension Among Adults in Northern Sudan: A Community-Based Cross-Sectional Study

Zainab Taha[1], Hiba Elhag[2], Ahmed Ali Hassan[2], Ishag Adam[3]

[1]Department of Health Sciences, College of Natural and Health Sciences, Zayed University, Abu Dhabi, United Arab Emirates; [2]Department of Public Health, Faculty of Medicine, University of Khartoum, Khartoum, Sudan; [3]Department of Obstetrics and Gynecology, College of Medicine, Qassim University, Buraidah, Saudi Arabia

Correspondence: Hiba Elhag, Department of Public Health, Faculty of Medicine, University of Khartoum, Khartoum, Sudan, Email hebaseedalhag28@gmail.com

Background: Hypertension and anemia are major health problems globally. However, data regarding the association between hypertension and hemoglobin/anemia among adults are few and controversial. Therefore, the current study aimed to investigate the associations between hemoglobin/anemia and hypertension among Sudanese adults.

Methods: A community-based cross-sectional study was conducted in Northern Sudan from September to December 2022. The participants' sociodemographic characteristics were assessed using a questionnaire. Standardized procedures measured participants' weight, height, body mass index (BMI), hemoglobin, and hypertension. Multivariate regression analysis was performed to determine the association between anemia and hypertension.

Results: Three hundred eighty-four adults were enrolled; 195 (50.8%) and 189 (49.2%) were males and females, respectively. The median interquartile age of the enrolled adults of age, BMI, and hemoglobin level was 45.0 (33.0–55.8) years, 26.6 (22.6–30.6) kg/m^2, and 13.4 (12.4–14.4) g/dl, respectively. Of 384 adults, 216 (56.3%) had hypertension, and 148 (38.5%) were newly diagnosed hypertensive. Eighty-six adults (22.4%) had anemia. In univariate analysis, while increasing age, being female, being unmarried, having a positive family history of hypertension, and increasing BMI were positively associated with hypertension, anemia was inversely associated with hypertension. Education, occupation, cigarette smoking, and alcohol consumption were not associated with hypertension. In multivariate analysis, age (adjusted odd ratio [AOR] = 1.05, 95% confidence interval [CI] = 1.03–1.07), BMI (AOR= 1.07, 95% CI = 1.03–1.12) were inversely associated with hypertension, being female (AOR = 2.92, 95% CI = 1.43–5.94), positive family history of hypertension (AOR= 1.73, 95% CI = 1.09–2.75), and hemoglobin level (AOR= 1.34, 95% CI = 1.12–1.61) were associated with hypertension. Anemia (AOR = 0.58, 95% CI = 0.34–0.99) was inversely associated with hypertension.

Conclusion: Both anemia and hypertension are major public health problems in Northern Sudan. Anemia is associated with hypertension. Further research is needed to explore the complex association between hemoglobin/anemia and hypertension.

Keywords: hypertension, hemoglobin, age, female, anemia, body mass index, Sudan

Introduction

Globally, both hypertension[1] and anemia[2] represent major health problems among adults, especially in Sub-Saharan Africa, including Sudan. Hypertension is recognized as a leading cause of global morbidity and mortality among adults, and 31.1% of adults aged ≥20 years were hypertensive.[3] The burden of hypertension is much higher in resource-limited settings such as Sub-Saharan Africa, where approximately one-third of the population has hypertension.[4] Several factors, such as increasing age, gender, and obesity, have been reported as risk factors for hypertension.[5,6] On the other hand, anemia is a known risk factor for mortality and morbidity, including hypertension and tuberculosis.[7,8] Recently, evidence has emerged regarding the association between hemoglobin/anemia and hypertension among adults. However, the exact relation is a controversial issue and needs to be explored further. For instance, most studies from different countries reported a positive association (hemoglobin level is

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positively associated with hypertension) among adults.[9–14] In contrast, others reported no association between anemia and hypertension.[15,16] Kim et al, in their cross-sectional and longitudinal study, reported that higher hemoglobin per se may not contribute to the development of hypertension in the longitudinal view; however, elevated hemoglobin levels are associated with high blood pressure in the cross-sectional view.[16] Conversely, our previous study revealed a negative association, ie, severe anemia is associated with a higher risk for preeclampsia in Eastern Sudan.[17] Moreover, in Ethiopia, Gela et al reported that patients with uncontrolled blood pressure were almost two times at risk of anemia.[18] So, the relationship between anemia and hypertension is controversial, and the direction of the association (ie, anemia influences hypertension or vice versa) remains a complex relationship.[12] Conducting further studies is paramount to substantiate the potential use of hematological parameters such as hemoglobin level as a predictor in diagnosing, controlling, and prognosing hypertension. Hemoglobin, a routine component of complete blood count tests, particularly warrants investigation.[11,14] For example, in our neighboring country, Ethiopia, Gela et al reported that nearly one-fifth of hypertensive patients had anemia; consequently, they recommended regular screening of hemoglobin levels to facilitate appropriate intervention.[18] Besides hypertension, literature from different countries showed that anemia is a risk factor for various other health problems, such as diabetes mellitus.[19,20]

The global high prevalence rates of both hypertension and anemia put heavy burdens on the health systems, incredibly fragile ones such as those in Sub-Saharan Africa,[3,21–24] including Sudan, where both hypertension[25] and anemia[23,24,26,27] and the associated complications among adults are more prevalent. These high burdens of both health problems can be attributed to their high contribution to multimorbidity.[28] High prevalence rates of hypertension are observed among various Sudanese groups in different regions of Sudan.[5,29] For instance, our previous data showed that two-fifths of the 600 studied adults were hypertensive in eastern Sudan [7], and one in ten adolescents was hypertensive in Northern Sudan.[29] Regarding anemia, there is a high prevalence of anemia among adults in different regions of Sudan, which hurts health.[23,24,26,27] For instance, anemia prevalence was 35.6% in Sudanese women of reproductive age,[23] (36.2%) in adults in Eastern Sudan,[24] and (27.6%) in adults in Central Sudan.[6] However, the association between anemia and hypertension has not been investigated in Sudan, representing a significant gap in current knowledge. Exploring such an association is crucial to addressing public health problems (anemia and hypertension). Therefore, the present study aimed to investigate the associations between hemoglobin/anemia and hypertension among adults in Almatamah, River Nile State, and Northern Sudan and provide novel insights into the intersection of these two prevalent public health problems.

Materials and Methods

Study Area

River Nile State is one of the total 18 states in Sudan. The total population of River Nile State was 1,120,441, based on the 2008 census.[30] There are seven localities in River Nile State.

Study Population and Design

This community-based cross-sectional study was conducted from September to December 2022 at four villages in the Wad Hamid district (the lowest administrative unit in Sudan), Almatamah Locality, River Nile State, northern Sudan. The Wad Hamid district borders Khartoum State and is approximately 100 kilometers from Khartoum city, the capital of Sudan.

Almatamah Locality was selected among the seven localities as it is an understudied area, and high blood pressure was reported even among adolescents.[29] Among the three districts of Almatamah Locality, one was chosen randomly (Wad Hamid). Four villages were chosen from the randomly selected district using systematic sampling. Then, 80 to 100 households from each village were selected based on population density to obtain the desired sample size. The first member in each household who agreed to participate and met the study inclusion criteria was selected. If the house chosen was uninhabited or its inhabitants refused to participate, the next house was selected to meet the target number for the study. The investigators trained five medical officers in data collection methods to standardize the data collection procedure and to have high-quality data.

After signing an informed consent form, all adults (male and female) aged ≥18 were enrolled from the households using a lottery method. Participants whose age was less than 18 years, pregnant women, patients with poor cognitive functions, and severely ill patients were excluded from this study.

Data Collection

The authors followed Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines to conduct this study.[31] The questionnaire was developed to collect relevant data based on previous similar studies.[9–13,15,18,32] The questionnaire included data on sociodemographic characteristics, such as age in years, sex (male or female), marital status (married or unmarried), educational level (<secondary or ≥secondary), occupational status (employed or unemployed), cigarette smoking (never or former/current), alcohol consumption (never and former/contemporary), and family history of hypertension. In addition, anthropometric measurements included weight, height (latter expressed as BMI), hematological investigation, including hemoglobin levels (categorized into anemia and nonanemic), and hypertension measurements (categorized into hypertensive and non-hypertensive).

Anthropometric Measurements

Each participant's weight was measured in kilograms (kg) using well-calibrated scales and adjusted to zero before each measurement as the standard procedure. The participant stood with minimal movement, with hands by their sides and shoes and excess clothing removed. The participant's height was measured centimeters after standing straight with their back against a wall and feet together. BMI was computed as the weight in kg divided by the square of the height in meters (kg/m^2).[33]

Blood Pressure Measurement

Blood pressure was measured using an appropriate cuff size with a standard mercury sphygmomanometer after resting for at least 10 minutes in a sitting position with the arm maintained at heart level. With an appropriately-sized cuff, the mean of two (at an interval of 1–2 min) blood pressure readings was calculated. If the difference between the two readings was >5mmHg, measurements were retaken until the reading stabilized. Participants were considered hypertensive if the systolic blood pressure reading was ≥140 mmHg, the diastolic blood pressure reading was ≥90 mmHg, or if both criteria were met in the repeated measurements. Participants who reported using anti-hypertensive medications for high blood pressure, regardless of their blood pressure values, were also considered hypertensive.[34]

Blood Analysis

Each participant was requested to provide 3 mL of blood drawn in an Ethylene diamine tetra acetic acid tube under aseptic conditions. These samples were used to measure hemoglobin per the manufacturer's instructions (Sysmex KX-21, Japan). As described in our previous work, an automated hematology analyzer was used to measure hemoglobin levels.[35] Based on the World Health Organization (WHO's) definition, anemia was diagnosed, ie, hemoglobin concentration of < 12 g/dl in non-pregnant women and < 13 g/dl in men.[21] Also, this definition was used in a similar previous study.[15]

Sample Size Calculation

OpenEpi Menu was used to compute the desired sample size. A total of 384 adults were included in the study. This sample size (384) of adults was estimated to have an assumed prevalence of hypertension of 50% to have enough sample size; a high prevalence of hypertension (40.8%) among adults has previously been reported in Eastern Sudan.[5] Then, we assumed that 40.0% of the hypertensive adults would have anemia and 25.0% of the adults without hypertension would have anemia. This assumption was based on the previous prevalence of anemia among adults in eastern Sudan.[24] This sample size was calculated to detect a difference of 5% at $\alpha = 0.05$, with a power of 80%.

Ethical Statement

The current work was conducted according to the Declaration of Helsinki. Almatamah Health Authority, Sudan, approved this study. The reference is #9, 2021. All participants signed written informed consent. The authors followed all measures to ensure participants' privacy, confidentiality, and safety, such as excluding personal identifiers during data collection.

Statistical Analysis

The IBM Statistical Package analyzed the data for the Social Sciences® (SPSS®) for Windows, version 22.0 (SPSS Inc., New York, United States). The proportions were expressed as percentages (%). The Kolmogorov–Smirnov test for determining the normality of continuous data such as age, BMI, and hemoglobin level revealed a non-normal distribution. The non-normally distributed data were expressed as the median (interquartile range; IQR). Univariate analysis was performed for hypertension (for binary regression) as dependent variables and sociodemographic variables (age, sex, educational level, occupational status, cigarette smoking, alcohol consumption, family history of hypertension, BMI, hemoglobin level, and anemia) as independent variables. A multivariate analysis was also performed, including all variables with a p-value < 0.2 to control for confounding variables. Adjusted odds ratios (AORs) and 95% confidence intervals (CIs) were calculated as they were applied. A two-sided P-value of <0.05 was considered statistically significant.

Results

Three hundred eighty-four adults were enrolled; 195 (50.8%) and 189 (49.2%) were males and females, respectively. The median (IQR) of the enrolled adults of the age, BMI, and hemoglobin level was 45.0 (33.0–55.8) years, 26.6 (22.6–30.6) kg/m^2, and 13.4 (12.4–14.4) g/dl, respectively. Of the 384 adults, 259 (67.4%) and 125 (32.6%) had education ≥ secondary and < secondary level. One hundred and seventy-four (45.3%) of the adults and 210 (54.7%) were unemployed. Of 384 adults, 216 (56.3%) had hypertension; of them, 148 (38.5%) were newly diagnosed hypertensive, and the rest, 68 (31.5%), were known hypertensive. Eighty-six adults (22.4%) had anemia, Table 1.

In univariate analysis, while increasing age, being female, being unmarried, having a positive family history of hypertension, and increasing BMI were positively associated with hypertension, anemia was inversely associated with hypertension. Education, occupation, cigarette smoking, and alcohol consumption were not associated with hypertension, Table 1.

In multivariate analysis, age (AOR = 1.05, 95% CI = 1.03–1.07), BMI (AOR= 1.07, 95% CI = 1.03–1.12), and hemoglobin level (AOR = 1.34, 95% CI = 1.12–1.61) were positively associated with hypertension, being female (AOR = 2.92, 95% CI = 1.43–5.94), and positive family history of hypertension (AOR = 1.73, 95% CI = 1.09–2.75), were associated with hypertension, anemia (AOR = 0.58, 95% CI = 0.34–0.99) was inversely associated with hypertension, Table 2.

Discussion

The main findings of this study were that hemoglobin was positively associated with hypertension, and anemia was inversely associated with adults' hypertension. This association between anemia and hypertension is supported by previous studies.[9–14,32] In Ethiopia, a comparative cross-sectional study (102 hypertensive vs 102 healthy controls) revealed among hematological parameters, hemoglobin and hematocrit were significantly higher in hypertensive patients compared to apparently healthy controls.[14] A cross-sectional study of 9398 Iranian adults aged 35–70 years revealed a positive trend of association between increasing hemoglobin level and blood pressure, ie, for each unit increase in hemoglobin level (1 g/dl), there was a 1.09 odds ratio of increasing blood pressure.[11] In India, a comparative cross-sectional study included 187 adults revealed that among participants without comorbidities, hemoglobin level had a positive correlation with systolic blood pressure and mean arterial pressure, ie, the magnitude of increases in systolic blood pressure and mean arterial pressure with one g/dl change in hemoglobin level were 3.24 mmHg, and 1.87 mmHg, respectively.[10] A large cohort study included a 9181 Chinese community-dwelling population with normal glucose metabolism and reported that hemoglobin level was positively associated with systolic and diastolic blood pressure.[9] Another large cohort of healthy individuals, including 101,377 Dutch donors, reported that hemoglobin level was positively associated with systolic and diastolic blood pressures in healthy individuals.[12] A cross-sectional study included

Table 1 Univariate Analysis of the Factors Associated with Hypertension Among Adults in Northern Sudan, 2022

Variables		Total (Number = 384)	Adults With Hypertension (Number = 216)	Adults Without Hypertension (number = 168)	Odd Ratio (95% Confidence interval)	*P* Value
Median (interquartile range)						
Age, years		45.0(33.0–55.8)	50.0(38.0–60.0)	38.5(28.0–50.0)	1.05(1.03–1.06)	<0.001
Body mass index, kg/m^2		26.6(22.6–30.6)	27.6(24.0–31.3)	24.5(19.9–28.5)	1.10(1.06–1.14)	<0.001
Hemoglobin level g/dl		13.4(12.4–14.4)	13.4(12.5–14.5)	13.3(12.3–14.2)	1.14(0.99–1.30)	0.060
Frequency (percentage)						
Sex	Male	195(50.8)	97(44.9)	98(58.3)	Reference	0.009
	Female	189(49.2)	119(55.1)	70(41.7)	1.72(1.14–2.58)	
Education level	≥ secondary	259(67.4)	146(67.6)	113(67.3)	Reference	0.945
	< secondary	125(32.6)	70(32.4)	55(32.7)	0.99(0.64–1.52)	
Occupation status	Employed	174(45.3)	91(42.1)	83(49.4)	Reference	0.156
	Unemployed	210(54.7)	125(57.9)	85(50.6)	1.34(0.89–2.01)	
Marital status	Married	95(24.7)	44(20.4)	51(30.4)	Reference	0.025
	Unmarried	289(75.3)	172(79.6)	117(69.6)	1.7(1.07–2.72)	
Family history of hypertension	No	198(51.6)	95(44.0)	103(61.3)	Reference	0.001
	Yes	186(48.4)	121(56.0)	65(38.7)	2.02(1.34–3.04)	
Cigarette smoking	Never	305(79.4)	177(81.9)	128(76.2)	Reference	0.168
	Current/former	79(20.6)	39(18.1)	40(23.8)	0.71(0.43–1.16)	
Alcohol consumption	Never	344(89.6)	197(91.8)	147(87.5)	Reference	0.300
	Current/former	40(10.4)	19(8.8)	21(12.5)	0.72(0.38–1.35)	
Body mass index, kg/m^2	Normal	125(32.6)	66(30.6)	59(35.1)	Reference	
	Underweight	35(9.1)	5(2.3)	30(17.9)	0.15(0.05–0.41)	<0.001
	Overweight	115(29.9)	73(33.8)	42(25.0)	1.55(0.93–2.61)	0.095
	Obese	109(28.4)	72(33.3)	37(22.0)	1.74(1.02–2.95)	0.040
Anemia	No	298(77.6)	177(81.9)	121(72.0)	Reference	0.022
	Yes	86(22.4)	39(18.1)	47(28.0)	0.57(0.35–0.92)	

1547 native Tibetans at high altitudes reported a positive association between hemoglobin level and hypertension, ie, an increase in hemoglobin level of 1 g/L was associated with a 1.02 odds ratio of hypertension, and the odds increased by increasing polycythemia.[13] It is worth mentioning that this association between hemoglobin level and blood pressure is not only confined to adults, as it was observed among adolescents as well. For example, a study population of 7950 adolescents aged 10–18 from the Korea National Health and Nutrition Examination Surveys (2007–2017) concluded hemoglobin level was positively associated with adolescents' systolic and diastolic blood pressure.[32]

In contrast to our result and the previous similar above-mentioned studies, other studies that reported no association between hemoglobin/anemia and hypertension attributed the lack of association to the studies' design (cross-sectional vs longitudinal) or analyses styles (adjusted vs not adjusted for variables).[15,16] For instance, a population-based cohort study

Table 2 Adjusted Multivariate Analysis for Factors Associated with Hypertension Among Adults in Northern Sudan, 2022

Variables		Odds Ratio	95% Confidence Interval	*P* Value
Age, years		1.05	1.03–1.07	<0.001
Body mass index, kg/m^2		1.07	1.03–1.12	0.001
Hemoglobin level g/dl*		1.34	1.12–1.61	0.001
Sex	Male	Reference		0.003
	Female	2.92	1.43–5.94	
Occupation status	Employed	Reference		0.903
	Unemployed	1.04	0.56–1.93	
Marital status	Married	Reference		0.436
	Unmarried	0.79	0.44–1.42	
Family history of hypertension	No	Reference		0.020
	Yes	1.73	1.09–2.75	
Cigarette smoking	Never	Reference		0.530
	Current/former	1.23	0.65–2.35	
Anemia*	No	Reference		0.048
	Yes	0.58	0.34–0.99	

Notes: *Hemoglobin level and anemia were entered one by one in the model.

investigated the cross-sectional and longitudinal associations between hemoglobin level and hypertension in a Korean population (2006–2013), which included 4899 adults aged 35–88 years from a rural community, revealed a positive association between hemoglobin level and hypertension in cross-sectional analysis, and no association in the longitudinal study; they concluded that hemoglobin per se does not cause of developing hypertension.[16] Yoon et al analyzed data from 16,060 adults aged ≥20 years from the fifth Korean National Health and Nutrition Examination Survey (2010–2012) reported after adjusting for related variables (except BMI and waist measurement), anemia was inversely associated with hypertension (OR = 0.83; 95% CI, 0.71–0.98) similar to this study, however, when further adjusted for BMI and waist measurement, anemia was not associated with hypertension (OR = 0.88, 95% CI, 0.75–1.04).[15]

Although the mechanisms by which hemoglobin/anemia influence hypertension or vice versa are not well understood, researchers suggested various explanations for such association; of them, the high hemoglobin can cause blood vessel contraction,[11] increased viscosity, and reduced availability of nitric oxide,[36] and the strong association between polycythemia and hypertension,[37] and raised in endothelial cell damage (vascular remodeling) and as a result, increased in the concentrations of growth factors[38] and as a consequence, increases blood pressure and hypertension. In addition, in this study, the association could be due to the lack of using antihypertensive medications as adults with newly diagnosed hypertension are common in Sudan [7], and even in this study, more than two-thirds of hypertensive adults (68.5%) were newly diagnosed hypertensive. Researchers observed that the usage of certain antihypertensive medications can be associated with a reduction in hemoglobin levels at follow-up [37], especially angiotensin-converting enzyme inhibitors (ACEIs).[39]

The current results about the prevalence of both anemia and hypertension confirm the global trend of increasing prevalence rates of both hypertension and anemia [1–5], including Sudan, where both hypertension [23] and anemia[23,24,26,27] are prevalent. This study mainly investigated the association between hemoglobin/anemia and hypertension. Besides hemoglobin/anemia, other factors were associated with hypertension, including increasing age, being

female, positive family history of hypertension, and increasing BMI. The authors discussed these factors in their previous work in Eastern Sudan.[5] In addition, discussion of such aspects might extend beyond the scope of the present article.

These study findings have implications for improving adults' health since both anemia and hypertension are preventable and treatable health conditions via introducing several preventive modalities, including a healthy diet, early screening programs, and lifestyle modification, including physical activity. The findings of the current study and its proposed recommendations will be shared with healthcare professionals and healthcare authorities to take further actions regarding the high prevalence of both anemia and hypertension among adults, especially newly diagnosed hypertensive adults. Not to mention, the ongoing war in Sudan remains a primary challenge in implementing such recommendations. In Vietnam, Korinek et al reported exposure to war during childhood was significantly associated with late adulthood cardiovascular disorders, including hypertension, especially among women who were exposed to violence during wartime.[40]

Strengths and Limitations of the Study

To the best of the authors' knowledge, the present study is the first to address the association between hemoglobin/anemia and hypertension among the Sudanese population. These data can add value to the few existing data regarding the association between hemoglobin/anemia and hypertension.[9–13,15,16] Healthcare professionals and decision-makers can use these study findings to improve adults' health, as both anemia and hypertension showed high prevalent rates in the studied area that necessitate interventions, especially for those newly diagnosed hypertensives. However, this study had some limitations that need to be noted to improve the design of future studies. Due to the nature of the current study (a cross-sectional study), it could not establish a causality association, ie, between different variables, especially the direction of association between hemoglobin/anemia and hypertension not yet clear. Therefore, conducting further prospective longitudinal studies will clarify the association between hemoglobin/anemia and hypertension compared to cross-sectional studies. This study was conducted on adults in one region of Sudan (Northern Sudan), thus limiting the generalization of its findings to the population in the entire Sudan. In addition, no information was collected about physical activity [17, 18] or lipid profiles[11] in the current study. Such information could influence the vulnerability of adults to anemia and hypertension.

Conclusion

Both anemia and hypertension are significant public health problems in Northern Sudan. Unlike anemia, increasing hemoglobin level is positively associated with hypertension. Further research is needed to explore the complex association between hemoglobin/anemia and hypertension.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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