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ORIGINAL ARTICLE

The association between red cell distribution width and newly diagnosed hypertension among adults in Northern Sudan: a case-control study

Ahmed A. Hassan [a], Shaza M. Musa[b], Husam-Eldin O. Omer[c] and Ishag Adam[d]

[a]Faculty of Medicine, University of Khartoum, Khartoum, Sudan; [b]Adjunct instructor- Biology, Tarrant County College Northwest Campus, Fort Worth, TX, USA; [c]Department of Pathology, Faculty of Medicine, Jazan University, Jazan, Kingdom of Saudi Arabia; [d]Department of Obstetrics and Gynecology, Unaizah College of Medicine and Medical Sciences, Qassim University, Unaizah, Kingdom of Saudi Arabia

ABSTRACT

The existing data have shown inconsistency about the association between red cell distribution width (RDW) and hypertension. Thus, the aim of the present study was to investigate the association between RDW and newly diagnosed hypertension among adults in Sudan. This was a case-control study conducted in Northern Sudan from July to September 2022. The cases were patients with newly diagnosed hypertension ($n = 78$), and the controls were healthy participants ($n = 78$). A questionnaire was used to collect the participants' sociodemographic, and clinical data. RDW was measured using an automated hematology analyzer. A logistic regression analysis was performed. The univariate analysis revealed no association between sex, educational level, occupational level, RDW, and newly diagnosed hypertension. In the multivariate analysis, increasing age (adjusted odds ratio [AOR], 1.05; 95% confidence interval [CI], 1.02–1.08) and body mass index (AOR, 1.12; 95% CI, 1.05–1.19) were associated with newly diagnosed hypertension. No association was found between RDW and newly diagnosed hypertension. No correlation was found between RDW and systolic ($r = 0.045$, $P = 0.577$) or diastolic blood pressure ($r = 0.023$, $P = 0.772$). In conclusion, no association in RDW was found between the patients with newly diagnosed hypertension and the healthy controls.

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1. Introduction

Hypertension represents a major public health problem worldwide [1]. Uncontrolled hypertension (blood pressure of ≥ 140/90 mmHg) is associated with co-morbidities such as stroke, cardiovascular diseases, and renal diseases [2,3]. Among non-communicable diseases, hypertension is considered the leading risk factor of death globally [1]. Various predictors of hypertension have been reported, including complete blood count (CBC) parameters such as red cell distribution width (RDW) [4,5].

CBC is a common investigation requested by health-care professionals, and RDW is one of its parameters. RDW measures the quantitative variation in the size of circulating red blood cells (RBCs). It is a marker of anisocytosis (red cell size variation) and calculated automatically using a hematology analyzer by simply dividing the standard deviation (SD) of the mean corpuscular volume (MCV) by the MCV and multiplying the quotient by 100 to yield a percentage value (i.e. [RDW-SD]/[MCV] ×100). RDW-SD is an actual measurement of the width of the red cell distribution curve in femtoliters (fl). RDW is usually expressed as RDW-coefficient of variation (RDW-CV), with normal values ranging from 11% to 15% in adults [6,7]. RDW-CV is usually written as RDW. Recent literature has shown that among the CBC parameters, elevated RDW is a novel biomarker used to predict the incidences and prognoses of many diseases, including hypertension [8], diabetes [9], acute ischemic stroke [10], and cardiovascular diseases [11].

A recent study in Ethiopia revealed a higher median RDW in hypertensive patients than in apparently healthy individuals [8]. Early diagnosis and prompt intervention are highly important to reduce the risks of hypertension and its complications (morbidity and mortality). Thus, identifying a cost-effective screening tool such as RDW that can detect hypertension at its early stages is crucial in avoiding such complications [5]. However, as a newly emerging screening tool, RDW needs more research to be approved and introduced into routine health-care services.

Existing data have shown inconsistency about the association between RDW and hypertension. While some studies have shown a significant positive association between RDW and hypertension (i.e. increased RDW in hypertensive patients) [5,8,12–14], other studies have shown no association [6,15,16] or a negative association [17].

CONTACT Ahmed A. Hassan aa801181@gmail.com Faculty of Medicine, University of Khartoum, P.O BOX: 102, Khartoum 11111, Sudan

Besides the inconsistent data, no data have been published regarding the association of RDW and hypertension in Sudan. In addition, our previous data indicated a high incidence rate of uncontrolled blood pressure in Sudan [18]. Thus, further study is needed to confirm this finding. Therefore, the present study aimed to investigate the association between RDW and newly diagnosed hypertension among adults in the River Nile State, Northern Sudan.

2. Methods

2.1. Study area

A case-control study was conducted in the River Nile State, Northern Sudan. The River Nile State is one of the 18 states of Sudan. Based on the 2008 census, the total population of this state was 1,120,441 [19]. The state has seven localities (the lowest administrative units in Sudan), of which one (Almatamah) was initially selected by simple random sampling. Two villages were selected randomly from the Almatamah locality. All Sudanese adults (>18 years of age) from the selected households who agreed to participate in the study were chosen. Two trained medical officers interviewed the participants during the study period (July to September 2022). After signing an informed consent form, the participants answered a questionnaire containing items on sociodemographics, clinical and physical measurements, blood pressure, weight, and height. The cases were adults with newly diagnosed hypertension (who were not previously known to be hypertensive), that is, having a systolic blood pressure of ≥140 mmHg or a diastolic blood pressure of ≥90 mmHg or both readings, on repeated examinations [20]. The controls were adults with normal blood pressures. Those with known hypertension, ages of <18 years, thyroid problems, diabetes, renal disease, and pregnancy were excluded from the study. The questionnaire was used to collect information such as age, sex, educational level, occupation, cigarette smoking, and alcohol consumption.

The participants' weights and heights were measured using standard procedures, and body mass index (BMI) was calculated using the equation: weight (kg)/height (m^2) [21]. Blood pressure was measured, and a venous blood sample of 3–5 ml was taken for CBC analysis.

2.2. Blood pressure measurement

Blood pressure was measured with a standard mercury sphygmomanometer using the appropriate cuff size after resting for at least 10 min in a sitting position, with the arm maintained at heart level. The mean of two blood pressure readings (with an interval of 1–2 min) was calculated. If the difference between the two readings was >5 mmHg, the measurements were retaken until the reading became stable.

2.3. Anthropometric measurements

The participants' weights were measured in kilograms using standard procedures (with well-calibrated scales adjusted to zero before each measurement). The participant stood with minimal movement and with arms at the side. Moreover, shoes and excess clothing were removed. Height was measured in centimeters while standing straight with the back of the participant against the wall and with the feet together.

2.4. Blood analysis

A 3–5 ml blood sample was collected under aseptic conditions from all participants. An automated hematology analyzer was used to measure RDW as described in our previous work [22].

2.5. Sample size calculation

The sample size was calculated by OpenEpi Menu [23]. The sample size of (n) was initially calculated with assumption of the prevalence (40.0%) of hypertension among adults as previously reported in eastern Sudan [24]: '$n = Z^2pq/d^2$, in which $q = (1 - p)$, $Z1 - \alpha$ = confidence interval (CI) of 95% = 1.96, and d = margin of error of 5% = 0.05)'. Our assumption (78 participants in each arm) was further extended depend on the mean (SD) RDW among hypertensive and non-hypertensive participants in Ethiopia in a previous study [8].

2.6. Statistical analysis

Data were entered into a computer using the IBM Statistical Package for the Social Sciences (SPSS) for Windows, version 22.0 (SPSS Inc., New York, NY). The proportions were expressed as frequencies (%). Continuous data were evaluated for normality using the Shapiro-Wilk test and were found to be non-normally distributed. The non-normally distributed data were expressed as median (interquartile range [IQR]) and compared between the two groups using the Mann-Whitney U test. Proportions were compared between the groups using the chi-square test. A univariate analysis was performed with hypertension as the dependent variable and other variables such as age, sex, cigarette smoking, alcohol consumption, BMI, and RDW as independent variables. Thereafter, variables with a P value of < 0.20 in the univariate analysis were entered into the multivariable logistic regression to adjust for covariates. Spearman correlation analyses were performed to examine the correlation between RDW and systolic and diastolic

blood pressures. Adjusted odds ratios (AORs) and 95% confidence intervals (CIs) were calculated when applicable. A two-sided P value of < 0.05 was considered statistically significant.

2.7. Ethical considerations

The present work was conducted in accordance with the Declaration of Helsinki. The study was approved by the Almatamah Health Authority under reference No. 2021, 04. All participants provided informed consent for participation in the study. The authors followed all measures to ensure the privacy and confidentiality of the participants, such as excluding personal identifiers during the data collection.

3. Results

No associations were found between sex, educational level, occupational level, cigarette smoking, alcohol consumption, and RDW between the two groups (Table 1). No significant difference in median (IQR) RDW was found between the patients with newly diagnosed hypertension and the healthy controls (14.1%[13.6–15.1%] vs. 14.5% (13.7–15.2%), $P = 0.102$) (Figure 1).

In the multivariate analysis, age (AOR, 1.05; 95% CI, 1.02–1.08) and BMI (AOR, 1.12; 95% CI, 1.05–1.19) were associated with newly diagnosed hypertension (Table 2). No correlations were found between RDW and systolic ($r = 0.045$, $P = 0.577$) and diastolic blood pressures($r = 0.023$, $P = 0.772$).

Table 1. Comparing characteristics of the participants with newly diagnosed hypertension and controls in northern Sudan.

Variable		Participants with newly diagnosed hypertension ($n = 78$)	Controls ($n = 78$)	Unadjusted odd ratio (95% confidence interval)	P-value
Range (Interquartile range)					
Age in years		45.0(34.0–55.0)	35.0(25.6–42.0)	1.05(1.03–1.08)	<0.001
Body mass index kg/m^2		28.4(24.9–31.7)	23.5(19.1–27.4)	1.13(1.06–1.19)	<0.001
Red blood cell distribution width %		14.1(13.6–15.1)	14.5(13.7–15.2)	0.91(0.73–1.14)	0.422
Frequency (Proportion)					
Gender	Male	43(55.1)	46(59.0)	Reference	0.629
	Female	35(44.9)	32(41.0)	1.17(0.62–2.21)	
Education status	<secondary	31(39.7)	24(30.8)	Reference	0.242
	≥secondary	47(60.3)	54(69.2)	1.49(0.77–2.87)	
Occupational status	Employed	42(53.8)	43(55.1)	Reference	0.872
	Unemployed	36(46.2)	35(44.9)	1.05(0.56–1.98)	
Marital status	Married	16(20.5)	28(35.9)	Reference	0.035
	Unmarried	62(79.5)	50(64.1)	2.17(1.06–4.45)	
Cigarettes smoking	Never	56(71.8)	60(76.9)	Reference	0.464
	Current/former	22(28.2)	18(23.1)	1.31(0.64–2.70)	
Alcohol consumption	Never	69(88.5)	72(92.3)	Reference	0.418
	Current/former	9(11.5)	6(7.7)	1.57(0.53–4.63)	

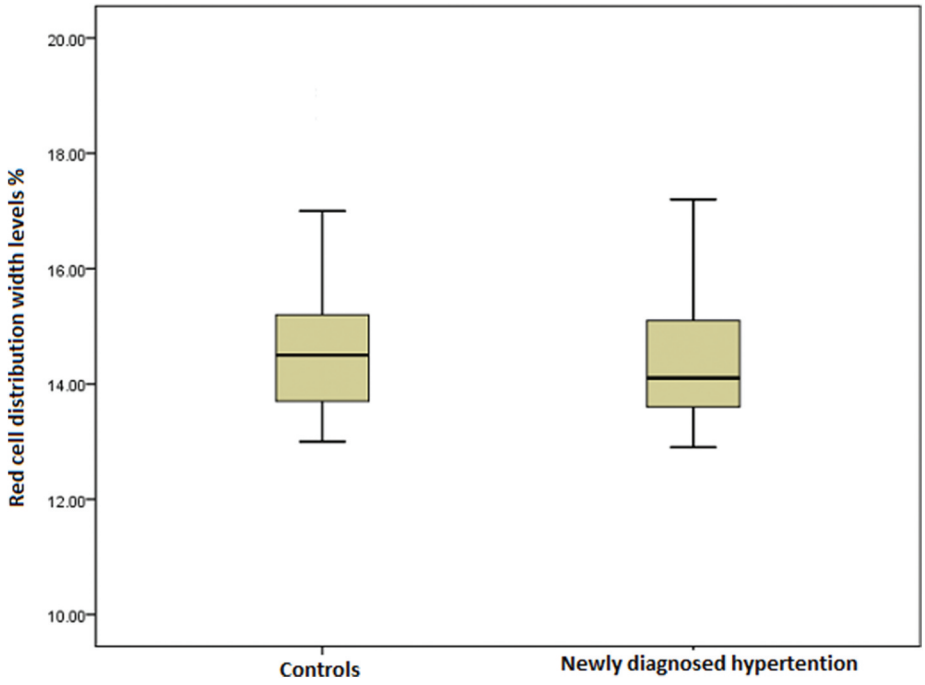

Figure 1. Comparison of red cell distribution width levels in the newly diagnosed hypertension and control groups.

Table 2. Multivariable logistic regression analysis of factors associated with newly diagnosed hypertension among adults in northern Sudan.

Variable	Adjusted odd ratio (95% confidence interval)	P-value
Age in years	1.05(1.02–1.08)	0.002
Body mass index kg/m^2	1.12(1.05–1.19)	<0.001
Marital status (married vs. Unmarried)	1.08(0.45–2.59)	0.859

4. Discussion

In the present study, RDW was not associated with hypertension. This is consistent with the results of several previous studies [6,15]. Our previous case-control study (65 women in each arm) conducted in Sudan showed no association between RDW and the presence or severity of preeclampsia [6]. In Iran, a recent case-control study (2227 in each group) revealed no significant association between RDW and hypertension [15]. In Nigeria, a case-control study (60 hypertensives and 30 controls) showed no significant difference in mean (SD) RDW [16].

On the other hand, several studies have shown a significant association between RDW and hypertension [8,12–14]. In Western Ethiopia, a cross-sectional study (hypertensive group, $n = 126$; healthy control group, $n = 126$) showed that RDW was higher in the hypertensive group than in the health control group [13]. Another comparative cross-sectional study (hypertensive group, $n = 102$; healthy control group, $n = 102$) conducted in Eastern Ethiopia showed similar results (higher RDW in hypertensive patients) [8]. In Pakistan, a cross-sectional study among 100 known hypertensive patients reported a significant association between RDW and hypertension [14]. In their recent longitudinal study (124,261 participants), Seo et al. reported that RDW was associated with hypertension in Korean adults [12].

The present study showed no correlations between RDW and systolic and diastolic blood pressures. Previous studies, including one of our studies, showed similar results [6,13]. However, other studies have reported contradicting results [25,26]. For example, Tanindi et al. reported that both systolic and diastolic blood pressures correlated with RDW [25].

The differences between the present result and the studies of other authors' results could be explained by the variation of factors that influencing RBCs heterogeneity among studied areas. Hence, the RDW is a parameter reflecting the heterogeneity of circulating RBCs, indicating the size and shape deformity, several causes have been reported for RBC heterogeneity such as cell age, environmental stress, and metabolic stress [27]. For instance, RBC survival can be affected by smoking [28], regional, and ethnicity [29]. A case-control study conducted by Aldosari et al. reported an increase in the percentage of macrocytic RBCs and a decrease in the RDW in smokers compared to nonsmokers [28].

Our results should be cautiously compared with the contradicting findings of studies for many reasons. First, our results were from a community-based study, whereas some contradicting results were from facility-based studies. Second, our study cases only included patients with newly diagnosed hypertension, whereas some studies included both patients with newly diagnosed hypertension and known hypertension. Finally, the difference in the adopted exclusion criteria among the studies influenced their discrepant results.

Different mechanisms could explain the association between RDW and hypertension. Researchers attributed the mechanism of this association to the specific markers of oxidative stress and inflammation [14,30,31]. It has been reported that heterogeneity of RBC properties is promoted by pathological conditions including inflammatory state, and metabolic-related disorders [27]. Rondanelli et al. speculated that oxidative stress increases RDW and, as a result, increases metabolic-related disorders, as assessed by the lipid profile (i.e. total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, and triglycerides), insulin, homeostatic model assessment (HOMA), and blood pressure in obese participants [30]. Moreover, RDW is an inflammatory marker [14,31]. RDW can affect the intravascular hemodynamic interactions between circulating blood cells and vessel walls by inducing local changes that lead to atherothrombosis [31]. Therefore, as mentioned earlier, increased RDW is a novel biomarker that can be used to predict the incidences and prognoses of many disease, including hypertension [7–11,32–34].

The present study was conducted mainly to assess the association of RDW and hypertension. In our previous work in Eastern Sudan, we discussed factors associated with hypertension, including age and BMI [24].

5. Limitations

The present study has limitations that must be addressed in future research. It assessed the association of RDW and hypertension at only one time point. A longitudinal study will provide more clarification regarding such an association between RDW and blood pressure. Moreover, in this study, we did not assess C-reactive protein (CRP) levels, although the combined effect of CRP level and RDW on health prediction has been reported [35].

6. Conclusion

No significant difference in RDW was found between the patients with newly diagnosed hypertension and the healthy controls.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

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Authors' contributions

AAH and IA conceived the study; SMM, and HOO supervised the work, guided the analysis and critically reviewed the manuscript; AAH, HOO and IA prepared the analysis plan, performed the data analysis and wrote the first draft of the paper; SMM, and HOO supervised data collection All authors reviewed and approved the final manuscript.

Data availability statement

The data supporting the findings of the present study are available upon reasonable request.

ORCID

Ahmed A. Hassan http://orcid.org/0000-0001-5510-6177

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