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Original Article

Hemoglobin, white blood cell, mean platelet volume, C reactive protein, and their association with overweight/obesity among adolescents: a multicenter cross-sectional study

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Abstract: Objectives: Recently, hematological parameters such as hemoglobin, white blood cell (WBC), mean platelet volume (MPV), and C-reactive protein (CRP) have received more attention as predictors of overweight/obesity among adolescents. We aimed to investigate the association between hemoglobin, WBC, MPV, and CRP and overweight/obesity among adolescents in two regions of Sudan: River Nile State in the north and Gadarif in the east. Methods: A multicenter community - based cross-sectional study was conducted from September 2022 to October 2023. A questionnaire was used to collect sociodemographic data. Weight, height, hematological parameters, and CRP were measured using standard procedures. Multivariate multinomial analysis was performed. Results: A total of 738 adolescents (male: 325 [44.0%], female: 413 [56.0%]) were recruited. The median (interquartile, [IQR]) age was 14.8 (13.1-16.3) years. Of the total, 492 (66.7%), 151 (20.5%), and 95 (12.9%) were normal, underweight, and overweight/obese, respectively. In multivariate multinomial analysis, increasing WBC and increasing hemoglobin have shown a progressive increase in the overweight/obese group (adjusted odds ratio [AOR] = 1.08, 95% confidence interval [CI] 1.01-1.16) and (AOR = 1.27, 95% CI 1.06-1.53), respectively. Compared with females, males were at higher risk of being underweight (AOR = 2.77, 95% 1.86-4.12). Conclusion: This study indicates that the identified hematological predictors, specifically WBC and hemoglobin levels, can be helpful indicators for predicting overweight and obesity in adolescents in Sudan.

Keywords: Adolescents, overweight, obese, hemoglobin, white blood cell, age

Introduction

Globally, there is an increasing trend of overweight and obesity in children and adolescents, and Sub-Saharan Africa is not an exception [1, 2]. According to recent global statistics, the pooled estimates of overweight and obesity in children and adolescents were 14.8% and 22.2% (95% CI 21.6-22.8), respectively [1]. Several factors, such as age, being female [3], cigarette smoking [4], are associated with overweight and obesity among adolescents.

Recently, hematological parameters such as hemoglobin, white blood cell (WBC) and mean platelet volume (MPV), and inflammatory biomarkers such as C-reactive protein (CRP) [5] have received more attention as predictive factors of overweight/obesity among adolescents [5-12]. For example, some studies showed elevated hemoglobin [6], WBC [6-8], platelets [6], and CRP [5, 7, 9-12] are associated with overweight/obesity among adolescents. This attention could be attributed to several reasons. Of them, the global increase in obesity among adolescents, including in Sub-Saharan Africa [1, 2], and its association with increasing risk of cardiovascular diseases, diabetes mellitus, and mental health disorders [1, 2]; the ease of performing hematological parameters, apart from the complete blood count (CBC), as a routine laboratory investigation. In Sudan, the adverse

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effects of obesity were observed in different population groups, including adolescents [13], adults [14] and pregnant women [15].

Researchers attributed adolescent obesity to some inflammatory biomarkers, including CRP, leptin, and chemerin, in the early stages of obesity development in children [16]. For example, CRP was found to be associated with abdominal obesity, overweight, and obesity, and all these are important risk factors for obesity-related diseases, including cardiovascular diseases [17]. In addition, the evaluation of CRP could identify overweight and obese children and adolescents with high-risk metabolic syndrome [14]; however, it is less reliable in distinguishing between children and adolescent patients who had metabolic syndrome and those who were obese [18]. Therefore, researchers recommend evaluating these hematological parameters and inflammatory biomarkers in obese children and adolescents [6].

Knowing the possible hematological and inflammatory predictors of overweight and obesity among children and adolescents is very important to preventing overweight and obesity and their complications (morbidity and mortality) [2, 3, 19]. This preventive approach should be followed, particularly in limited-resource settings, to prevent overweight and obesity and its related complications. In Sudan, overweight and obesity are a national health issue, especially among urban Sudanese adolescents (10.7%) [13]. In addition, our previous study included 594 adults in eastern Sudan and revealed that 26.8% and 32.2% were overweight and obese, respectively [20]. In Sub-Saharan Africa, the primary identified complications associated with adolescents overweight/obese are metabolic syndrome, hypertension, dyslipidemia, diabetes mellitus, and glucose intolerance [2]. Such complications put heavy burdens on the fragile health systems in Sub-Saharan Africa, including Sudan [2, 3, 19]. In addition, the healthcare system in Sudan is ill-equipped to meet the adolescents' health demands [21]. According to the World Health Organization (WHO) statistics, more than 20% of the population in Sudan are adolescents [22]. The present escalating war in Sudan and its negative impact on children and adolescents' health, especially those with obesity-related diseases such as diabetes mellitus that necessitate continuous medicines supplies and optimum storage conditions, e.g., insulin [23-25].

Although adolescents' nutritional status has been studied in different regions of Sudan, including the two areas [13, 26-28], the hematological parameters and inflammatory markers such as CRP and their association with overweight/obesity have not been studied among adolescents. It is worth mentioning that our previous studies among adults in central Sudan reported that obese women had higher WBC and hemoglobin levels [29]. Such predictive factors need to be investigated among adolescents, especially at the community level. Therefore, the current study aimed to investigate the association between hemoglobin, WBC, MPV, and CRP and overweight/obesity among adolescents in two regions of Sudan: River Nile State in the north and Gadarif State in the east.

Methods

Study area

This study was conducted in two regions of Sudan, namely, Almatamah Locality, River Nile State, northern Sudan, and Gadarif City, Gadarif State, Eastern Sudan, from September 2022 to October 2023. More information about the study areas was given in our previously published data [30, 31].

Study design and population

This multicenter community-based cross-sectional study adhered to strengthening the reporting of observational studies in epidemiology (STROBE) guidelines ("Checklists - STROBE" n.d.). The investigators trained five medical officers in data collection methods to standardize the procedure and ensure high-quality data.

Inclusion and exclusion criteria

Inclusion criteria: The adolescents and their guardians must sign an informed consent form. Sudanese adolescents (male and female) aged 10 to 19 were enrolled in the households using a lottery method. Participants whose age was less than 10 or more than 19, pregnant women, patients with poor cognitive functions, and severely ill patients were excluded from this study.

Sample size calculation

As previously noted [32] and using OpenEpi software for a sample calculation [33], a sample of 738 adolescents was calculated. Guided by the previous study in Sudan, we assumed that (10.7%) of the adolescents would be overweight/obese (3), giving a ratio between adolescents with normal weight and overweight/obesity of 9:1. Thereafter, we assumed a difference of 0.5 (standard devotion of 1.2) in the mean of the assessed parameters (hemoglobin, WBC, MPV, and CRP) in the adolescents with normal weight and adolescents with overweight/obesity. This sample size was calculated to detect a 5% difference at $\alpha = 0.05$ with a power of 80%.

Study variables and measures

The questionnaire was developed from previous similar studies [5-12, 34, 35]. The questionnaire (conducted through face-to-face interviews) included data on sociodemographic characteristics, such as adolescent age in years, sex (male or female), and cigarette smoking/tobacco use (yes or no); anthropometric measurements such as weight and height, which were later expressed as BMI z-score; and blood samples from each adolescent for hematological analysis.

The medical officers approached the selected adolescents after the participants and their guardians agreed to participate and signed an informed consent form. The selected adolescents were informed about the aims and all necessary information, including the voluntary participation in the study and their right to withdraw from the study at any time without giving any reason/s, and the preventive measures taken to ensure the privacy, confidentiality, and safety of the participants, such as excluding personal identifiers during data collection. The standard procedures below measured weight, height, and hematological parameters. The sociodemographic, hematological parameters and CRP were considered secondary outcomes, and underweight and overweight/obesity were considered the primary outcomes.

Weight and height measurements

The adolescents' weights were measured in kilograms (kg) using standard procedures, which were well-calibrated scales adjusted to zero before each measurement. Weight was measured to the nearest 100 grams (g). The adolescents stood with minimal movement, with their hands by their sides. In addition, shoes and excess clothing were removed. Height was measured to the nearest 0.1 centimeter (cm), with the adolescent standing straight with the back against the wall and the feet together. Furthermore, the BMI for the age z-score was determined based on the WHO's standards. BMI z-scores of < +1 SD to < -2 SD, < -2 SD, > +1 SD were classified as normal weight, underweight, and overweight/obese, respectively [36].

Blood samples processing

Each participant was requested to provide 5 mL of blood drawn in a plain tube under aseptic conditions. First, 1 ml was taken from each sample to perform the CBC per the manufacturer's instructions (Sysmex KX-21, Kobe, Japan). As described in our previous work, an automated hematology analyzer was used to perform CBC [37]. Second, the remaining blood sample (4 ml) was centrifuged and kept at -20°C until processed in the laboratory for CRP, as described in our previous published work [38] using Tina-quant immunoturbidimetric assay (Boehringer Mannheim GmbH, Mannheim, Germany).

Statistical analysis

The collected data were entered into IBM Statistical Product and Service Solutions (SPSS) for Windows (version 22.0; SPSS Inc., New York, NY) for analysis. Continuous data such as age, blood parameters (hemoglobin, WBC, MPV), and CRP were evaluated for normality by using the Kolmogorov-Smirnov test, and they were found to be not normally distributed. Consequently, they were expressed as median (interquartile range [IQR]). The level of hematological parameters (WBC, hemoglobin, MPV) and CRP were compared between the different BMI groups using non-parametric tests, Kruskal-Wallis H. Furthermore, significant variables (*p*-value < 0.05) in Kruskal-Wallis H were

Table 1. Sociodemographic characteristics of the studied adolescents in northern and eastern Sudan, 2022-2023 (n = 738)

Variable		Total (n = 738)	
		Median	Inter quartile range
Age, years		14.8	13.1-16.3
C reactive protein mg/L		2.50	2.50-3.07
White blood cell $\times 10^3$/mm^3		6.0	4.9-7.5
Haemoglobin g/dl		12.9	12.1-13.7
Mean platelet volume fL		9.0	8.4-9.8
		Frequency	Percentage
Sex	Male	325	44.0
	Female	413	56.0
Cigarette smoking/tobacco use	No	721	97.7
	Yes	17	2.3
Body mass index groups	Normal weight	492	66.7
	Underweight	151	20.5
	Overweight/obese	95	12.9

analyzed by post-hoc test to find the difference between the different BMI groups (the adjusted *p*-value). Normal weight, underweight, and overweight/obese were dependent variables for univariate multinomial analysis. The sociodemographic data, namely the adolescents' age, sex, and hematological parameters, were used as the independent variables for all analyses. Thereafter, variables with P < 0.05 in the Kruskal-Wallis H and/or univariate analysis were shifted to perform multivariate regression to control for the potential confounding factors. The results of adjusted odds ratios (AORs) and a 95% CI were calculated, and a *p*-value < 0.05 was considered significant.

Results

General characteristics

In this study, a total of 738 adolescents (male: 325 [44.0%], female: 413 [56.0%]) were recruited. The median (IQR) age was 14.8 (13.1-16.3) years. Of the total recruited adolescents (n = 738), 492 (66.7%), 151 (20.5%), and 95 (12.9%) were normal, underweight, and overweight/obese, respectively. The median (IQR) of CRP, WBC, hemoglobin, and MPV were 2.50 (2.50-3.07) mg/L, 6.0 (4.9-7.5) $\times 10^3$/mm^3, 12.9 (12.1-13.7) g/dl, and 9.0 (8.4-9.8) Fl, respectively (**Table 1**).

Factors associated with overweight/obesity

Kruskal-Wallis H test showed BMI z-score groups were associated with WBC, hemoglobin, and sex; age, cigarette smoking/tobacco use, CRP, and MPV were not associated with BMI z-score groups. Post-hoc test showed between BMI z-score groups, normal vs. overweight/obese were significantly different in WBC and hemoglobin with (5.9 [4.9-7.3] vs. 6.7 [5.0-8.1], adjusted *p*-value = 0.021 and 12.8 [12.0-13.7] vs. 13.2 [12.4-14.2]) adjusted *p*-value = 0.007, respectively (**Table 2**).

In univariate multinomial logistic regression analysis, while there was no significant difference in age, WBC, CRP, and MPV in underweight group and overweight/obese group compared to normal weight group, males were at risk of both being underweight (AOR = 2.71, 95% CI 1.86-3.94) and overweight/obese (AOR = 1.80, 95% CI 1.16-3.80); and hemoglobin levels have shown a progressive increase with overweight/obese (AOR = 1.32, 95% CI 1.11-1.56) (**Table 3**).

In multivariate multinomial logistic regression, there was no significant association between WBC and hemoglobin in an underweight group compared to the normal-weight group. Increasing WBC and increasing hemoglobin have shown a progressive increase overweight/obese group (AOR = 1.08, 95% CI 1.01-1.16) and (AOR = 1.27, 95% CI 1.06-1.53), respectively, compared with females, males were almost three times at risk of being underweight (AOR = 2.77, 95% 1.86-4.12), but there was no significant difference in overweight/obese group (**Table 4**).

Table 2. Hematological parameters and C reactive protein and their association with body mass index z-score groups among adolescents in northern and eastern Sudan, 2022-2023 (n = 738)

Variable	Normal (n = 492)	Underweight (n = 151)	Overweight/obese (n = 95)	*P* value	Adjusted *P* value
		Median (interquartile range)			
Age, years	14.9 (13.1-16.4)	14.2 (12.7-15.8)	14.9 (13.8-16.4)	0.167	
C reactive protein mg/L	2.50 (2.50-3.06)	2.50 (2.50-3.06)	2.50 (2.50-3.07)	0.154	
White blood cell $\times10^3$/mm^3	5.9 (4.9-7.3)	6.0 (5.0-7.4)	6.7 (5.0-8.1)	0.018	Normal vs. underweight = 0.999
					Normal vs. overweight/obese = 0.021
					Underweight vs. overweight/obese = 0.154
Haemoglobin g/dl	12.8 (12.0-13.7)	13.1 (12.4-13.7)	13.2 (12.4-14.2)	0.001	Normal vs. underweight = 0.033
					Normal vs. overweight/obese = 0.007
					Underweight vs. overweight/obese = 0.736
Mean platelet volume fL	9.0 (8.4-9.8)	9.0 (8.5-9.8)	9.1 (8.2-10.0)	0.830	
		Frequency (percentage)			
Sex	183 (37.2)	93 (61.6)	49 (51.6)		
	309 (62.8)	58 (38.4)	46 (48.4)	< 0.001	
Cigarette smoking/tobacco use	482 (98.0)	146 (96.7)	93 (97.9)		
	10 (2.0)	5 (3.3)	2 (2.1)	0.655	

Table 3. Univariate multinomial logistic regression analysis of factors associated with underweight and overweight/obesity among adolescents in northern and eastern Sudan, 2022-2023 (n = 738)

Variable	Underweight (n = 151)		Overweight/obese (n = 94)	
	Odds Ratios (95.0% Confidence Interval)	*P* value	Odds Ratios (95.0% Confidence Interval)	*P* value
Age, years	0.93 (0.85-1.01)	0.086	1.04 (0.94-1.16)	0.414
C reactive protein mg/L	0.99 (0.93-1.07)	0.964	1.04 (0.99-1.09)	0.107
White blood cell ×10^3/mm^3	0.99 (0.91-1.07)	0.811	1.06 (0.98-1.13)	0.112
Hemoglobin g/dl	1.10 (0.96-1.26)	0.170	1.32 (1.11-1.56)	0.002
Mean platelet volume fL	0.97 (0.87-1.07)	0.502	0.99 (0.91-1.07)	0.747
Sex (male vs. female)	2.71 (1.86-3.94)	< 0.001	1.80 (1.16-2.80)	0.009

Table 4. Multivariate multinomial logistic regression analysis for factors associated with underweight and overweight/obesity among adolescents in northern and eastern Sudan, 2022-2023 (n = 738*)

Variable	Underweight			Overweight/obese		
	Odds ratio	95% confidence interval	*P* value	Odds ratio	95% confidence interval	*P* value
White blood cell ×10^3/mm^3	1.01	0.94-1.10	0.729	1.08	1.01-1.16	0.049
Hemoglobin g/dl	0.98	0.85-1.13	0.801	1.27	1.06-1.53	0.009
Sex (male vs. female)	2.77	1.86-4.12	< 0.001	1.49	0.93-2.39	0.101

*The reference category is the normal weight.

Discussion

The primary findings of the present study were that 12.9% of the studied adolescents were overweight/obese in Sudan; both hemoglobin level and WBC levels have shown a progressive increase with overweight/obesity in adolescents; male adolescents were more likely to be underweight. This high prevalence of overweight/obese (12.9%) in adolescents was previously reported in central Sudan (10.7%) [13], and northern Sudan (20.9%) [28]. This high prevalence was aligned with the estimations of global and African countries that necessitate urgent intervention [1, 2]. For example, in our neighboring country, Ethiopia, a cross-sectional study included 522 adolescents aged 10-19 years revealed an overall prevalence of overweight/obesity of 12.5% [39]. This prevalence of overweight/obesity among adolescents might explain the rising of NCDs such as hypertension, dyslipidemia, diabetes mellitus, and glucose intolerance among children and adolescents in Sub-Saharan Africa, including Sudan [2].

In this study, adolescents with high WBC were 1.08 times at risk of being overweight/obese. Our previous study in central Sudan revealed that obese women had higher WBC and hemoglobin level [29]. This result was in line with other studies from different countries [6-9]. This association between high WBC and overweight/obesity could be explained by the inflammatory processes of adipose tissue [7, 8, 11]. Rumińska et al. revealed that adipose tissue promotes systemic inflammation, and its intensity depends on the degree of obesity and insulin resistance [7]. Furthermore, Rumińska et al. reported the reversible association between overweight/obese status and WBC, i.e., changes in homeostasis model assessment - insulin resistance (HOMA-IR) were independent predictors of changes in WBC counts after reduction of body weight [7]. In addition, researchers considered obesity as an inflammatory disease [11].

On the other hand, high hemoglobin level was positively associated with overweight/obesity in adolescents in Sudan. Likewise, other studies found an association between hemoglobin and high BMI in children and adolescents [6, 40]. For example, a study in Korea conducted by Jeong et al. included 7,997 children and adolescents aged 10 to 18 years reported a higher BMI was associated with specific hematological parameters, including elevated WBC and hemoglobin; they suggested considering higher levels of hematological parameters as potential risk factors for obesity-related diseases and recommended early evaluation of such hematological parameters in obese children and adolescents [6]. Previous studies, including in Sudan, reported high hemoglobin levels and a lower prevalence of anemia was observed among obese pregnant women [41, 42]. In contrast, Klisic et al. found no association between hemoglobin and overweight/obesity in adolescents [34]. Such contradictions indicate the relationship between high hemoglobin levels and obesity in adolescents is a complex and emerging topic of research. Various studies suggest high hemoglobin levels may be associated with multiple metabolic processes that contribute to obesity. One proposed mechanism is the role of high hemoglobin in increasing blood viscosity, which can lead to impaired blood flow and reduced insulin sensitivity. As reported by Shen et al., elevated hemoglobin A1c levels, often associated with obesity, can exacerbate inflammation and contribute to metabolic dysregulation, further promoting obesity-related complications [43]. As a result, this increased viscosity may hinder the delivery of nutrients to tissues, impacting metabolic processes and potentially leading to weight gain. Another mechanism involves the interaction between high hemoglobin levels and oxidative stress. A study indicates that high hemoglobin levels can lead to increased oxidative stress in the body, associated with insulin resistance and subsequent weight gain. High levels of oxidative stress can disrupt normal metabolic functions, leading to an accumulation of fat, particularly in adolescents who are already at risk for obesity due to lifestyle factors [44]. Furthermore, the association between hemoglobin levels and appetite regulation has been explored. Higher hemoglobin levels may influence hormones involved in hunger and satiety, such as leptin. Dysregulation of these hormones can increase appetite and caloric intake, contributing to obesity. This is supported by the findings of Mank et al., who observed a correlation between obesity and various metabolic markers, including hemoglobin levels, among adolescents in Burkina Faso [45]. Overall, the mechanisms by which high hemoglobin levels may contribute to obesity in adolescents appear to involve a combination of increased blood viscosity, oxidative stress, and hormonal dysregulation. Further studies are required to clarify these relationships and to explore potential interventions that may mitigate the impact of high hemoglobin on obesity in this vulnerable population (adolescents).

In this study, male adolescents were almost three times more likely to be underweight than female adolescents. This is similar to our previous data from northern Sudan, which showed that being male and smoking/tobacco use were associated with adolescents' thinness [26]. In this study, smoking/tobacco use was not associated with adolescents' BMI status, which is in line with a previous study that observed no significant association in many low-income and middle-income countries [4].

As this article aimed to focus on hematological parameters and CRP and their association with overweight/obesity, our previous published work provided more details of the prevalence and sociodemographic factors such as age [26, 27].

This study did not find an association between other investigated factors, such as MPV and CRP. In contrast, other studies showed high MPV and CRP were associated with overweight/obesity in adolescents as compared to normal-weight adolescents [5, 7, 10, 12, 34]. Klisi et al., in their cohort study of 156 adolescents, reported a positive association between BMI and MPV [34]. Also, the level of MPV was reported to be associated with low-grade inflammation, and it was a good inflammatory marker in type 2 diabetes mellitus and obesity [46].

Our results should be cautiously compared with the results of other studies. First, while the present study used the WHO's definition (cutoff age of 10-19 years), similar to previous studies [39, 47], other studies used different ages for their studied participants (early adolescent, late adolescent, or both children and adolescents) [34, 40, 48]. Using the WHO's cutoff age of 10-19 years is preferable to tailor programs that target adolescents in a precise approach. Second, this study was community-based among apparently healthy adolescents; other studies used different approaches, such as school-based ones [9, 49]. Third, different statistical methods used by various studies might hinder the association between BMI and hematological parameters and inflammatory biomarkers [5, 7, 9-12].

Such contradictory data in the association between different hematological parameters, including hemoglobin, WBC MPV, and CRP, might indicate the presence of other interaction factors. This interaction might depend on the study settings. Also, other anthropometric measurements such as waist circumference and skin fold thickness are recommended [9, 40, 50], since BMI does not differentiate between muscular and fat mass. Therefore, such contradictory data should be received positively by researchers as a stimulus factor to explore such complex associations in their countries/regions, aiming to develop precise preventive approaches to maintaining a healthy BMI during adolescence.

These study findings have implications for improving adolescents' health since overweight/obesity is a preventable, treatable, and reversible health condition via introducing several preventive modalities, including lifestyle modification such as promoting physical activity and following a healthy diet [39, 49-52]. Also, knowing such predictive factors as WBC and hemoglobin might help healthcare providers predict high BMI, including overweight/obesity, and, as a result, avoid its complications. Not to mention, the current escalating war in Sudan remains a significant challenge to maintain adolescents' health. Also, the long-run impacts of the ongoing conflict on health in adulthood, including obesity, stroke, hypertension, diabetes mellitus, and cardiovascular diseases, necessitate urgent action by all involved parties [53].

Strengths and limitations of the study

To the best of the authors' knowledge, this is the first study to investigate the association between BMI groups, different hematological parameters, and inflammatory biomarkers among adolescents in Sudan. These data can add value to the limited data regarding the hematological predictor of high BMI in Sudan [29]. However, this study had some limitations that need to be mentioned to enhance future study design. Due to the nature of this study (a cross-sectional study), a causal association between different variables could not be established. Therefore, further longitudinal study will give more clarification regarding the association between high BMI and the studied hematological parameters and inflammatory biomarker variables among adolescents, and most importantly, to know the direction of association between high BMI groups and these studied variables as up to the direction is not clear [6, 40, 54]. Exploring such a direction of association might give a better understanding of the mechanism/s of association. This study was conducted in two regions of Sudan (northern and eastern), thus limiting the generalization of its results to adolescents in the whole of Sudan, as the presence of some mediating factors cannot be ruled out. Moreover, in the present study, no information was collected about the adolescents' dietary patterns [38, 45, 51] and physical activity [45, 49, 50]. Those data could influence the studied variables BMI, hemoglobin, WBC, MPV, and CRP. For instance, in Burkina Faso, Mank et al. reported dietary diversity scores were significantly associated with both thinness and anemia in adolescents; in Portugal, Cabral et al. reported a higher frequency of vegetable/legume intake was inversely related to CRP among adolescents [51].

Conclusion

This study indicates that the identified hematological predictors, specifically WBC and hemoglobin levels, can serve as valuable indicators for predicting overweight and obesity in adolescents in Sudan. Future research should focus on investigating the mechanisms underlying the association between these predictors and overweight/obesity and exploring their interactions.

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Disclosure of conflict of interest

None.

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