

Cardiovascular Risk Factors for Hypertension and Diabetes among Overweight and Obese Adolescents in the City of Kerbala, Iraq

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ABSTRACT

Hypertension and diabetes share the highest contribution to global burden of cardiovascular (CVD) and metabolic diseases. Factors such as obesity, poor diet choices and sedentary lifestyle predisposes to dyslipidemia and hyperglycemia which leads to elevations in blood pressure and diabetes respectively. In this study, we show that the progression of these diseases can be identified in adolescence by identifying the prevalence of pre-hypertension and pre-diabetes as well as CVD risk factors for hypertension and diabetes among adolescents in Kerbala city, Iraq.

This is a cross-sectional study of 207 adolescents between the ages of 11-18 years that are resident in Kerbala city, Iraq. The subjects were selected by multi-stage sampling method and data were collected through questionnaire. Anthropometric and blood pressure measurements were carried out on eligible participants and biochemical parameters of lipid profile and blood glucose level were analysed from blood samples. Out of the 207 participants, 59 were identified as overweight while 48 were obese. 22.2% prevalence for pre-hypertension and 12.6% for pre-diabetes were recorded. Significant differences ($p < 0.05$) in lipid profile and blood glucose levels between the obese and control group was observed. Lipid ratios of VLDL-C indicated significant differences ($p < 0.001$) between the unhealthy weights (overweight 24.56 ± 2.23 mg/dl; Obese 26.10 ± 1.76 mg/dl) and the control (19.80 ± 1.02 mg/dl), AIP (i.e. overweight 0.35 ± 0.03 vs control 0.26 ± 0.03 and obese 0.51 ± 0.02 vs control 0.26 ± 0.03), as well as the LDL-C/HDL-C ratio (i.e. overweight 1.69 ± 0.10 vs control 1.52 ± 0.13 and obese 2.69 ± 0.24 vs control 1.52 ± 0.13). Obesity through BMI significantly correlated with dyslipidemia, elevated blood pressure and hyperglycemia.

There is a high prevalence of pre-hypertension and pre-diabetes among adolescents in Kerbala city, and this is associated with risk of developing hypertension and diabetes in adulthood. Early detection and healthful lifestyle modifications will prevent the development of these complications.

Keyword: Adolescents; Overweight; Obese; Hypertension; Diabetes; Cardiovascular diseases

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INTRODUCTION

Cardiovascular diseases (CVD) have reached epidemic levels globally with elevation in blood pressure (BP) and genetic factors leading the major causes of the disease burden as well as mortality from hemorrhagic stroke and ischemic heart disease (1, 2). Over the past years, guidelines interpreting elevation in BP suggested that BP $\geq 140/90$ mmHg be defined as Hypertension and as such BP should be maintained at $<140/90$ mmHg (3). However, in 2017, the American College of Cardiology/ American Heart Association (ACC/AHA) Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults defined hypertension as having BP $\geq 130/80$ mmHg (4). It is important to note however, that these guideline values do not take into account criteria such as gender, age and anthropometric measurements. Obesity and unhealthy weight in general, have been recognized as a major risk factor for hypertension. Also, studies have shown that overweight and obese hypertensive have a higher potential for CVDs than those with healthy weight (5, 6).

Global prevalence of hypertension as estimated by the World Health Organization in 2016, is an alarming 40% and

elevated systolic BP has been shown to be responsible for 10.5 million deaths globally (7, 8). This has prompted the need for a paradigm shift in the management of hypertension from a diagnostic approach to preventive approach thus advocating for the consideration of early signals and risk factors associated with hypertension at early stages of life (9, 10).

Hypertension is no longer considered an “Adult” disease, rather it is a significant public health challenge affecting both adults and children. The cognizance of childhood/ adolescence elevation in BP as a predictor of hypertension in adulthood, has triggered the curiosity of researchers on whether there is correlation between anthropometric factors vis-à-vis overweight and obesity, in adolescence with the tendency to develop hypertension in adult life. These studies have provided evidences implicating adolescent obesity as a major comorbidity of hypertension as well as dyslipidemia, Type 2 diabetes mellitus (DM) and non-alcoholic steatohepatitis (11-13). Moreover, an approximately 3-fold higher risk of developing hypertension have been identified in obese children when compared with their non-obese counterparts (11, 14).

With an estimated 32% of adolescents either overweight or obese globally (15), the preventive approach in management of hypertension prompted the Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) to defined the term pre-hypertension in adolescents as having BP (both systolic and diastolic) \geq 90th percentile but $<$ 95th percentile for age, sex, and height according to normative tables published in the Working Group report, or as BP \geq 120 / 80 mmHg but $<$ 95th percentile in cases where the 90th percentile exceed 120 / 80 mmHg, to aid early detection, treatment and/ or provision preventive strategies through recommendation of health-promoting lifestyle modifications (16)

Studies have also shown that prolong elevation in fasting plasma glucose even at levels lower than the diagnostic threshold of diabetes is associated with the risk of CVD and hence hypertension, thus implicating DM as a potent effectuator of hypertension (17, 18). Type-2 DM accounts for 91% of the approximately 415 million individuals diagnosed with DM globally as the International Diabetes Federation (IDF) estimates an increase in number of cases to 642 million by 2040 (19). Although, there is few available data associating risk of CVD with adolescents having elevated Fasting Blood Glucose (FBG) levels close to but below the diagnostic threshold of diabetes i.e. \geq 100mg/dL but $<$ 126 mg/dL - termed pre-diabetes, they have indicated a higher risk of developing Type 2 DM relative to those with normal FBG levels (20). Moreover, in adolescents with Type 2 DM, a high tendency of developing CVD has been established (17). Therefore, the consideration of adolescent pre-diabetes as a predictor of the tendency to develop CVD

in adulthood is not unrealistic.

In this study, we characterized adolescents' resident in Kerbala City, Iraq between the ages of 11–18 years, by Body Mass Index (BMI) as Overweight or Obese, and investigated CVD risk factors of hypertension, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, as well as FBG in comparison with those of adolescents with normal BMI (Control). From the results of this study, we aim to provide useful information for the formulation of health-care policy and prevention strategies peculiar to the local community as obtainable in developing countries where data are scarce.

METHODS

Study population

The target population of this study are the adolescent ethnic Iraqis, between the ages of 11 years and 18 years, resident in the city of Kerbala.

Therefore, a random sampling of total Iraqi population within the aforementioned age bracket was conducted as previously described (21). A total of 207 prospective subjects were recruited from Al-Hassan specialized center for endocrine and diabetes, Imam Al-Hussein medical city, Karbala City, Iraq, upon receipt of ethical approval from the College and the Hospital Research Committees. The prospective subjects underwent a questionnaire based interview after which the participating subjects were selected from all the respondents based on the selection criteria (Table 1). Informed consent was obtained from all subjects in accordance with individual preferences and the implementation of the selection criteria.

Table 1: Inclusion/ exclusion criteria for the participating subjects

Factors	Inclusion criteria	Exclusion criteria
Ancestry	3- Generational Iraqis	Other ethnicities within the last 3 generation.
Age	11 to 18 years old	$<$ 11 years and $>$ 18 years
Evidence of congenital or acquired disease condition	None	At least one
Medication	No ongoing conventional or herbal medication	With any form of ongoing conventional or herbal medication
Consent to participate	Consented	Not consented

The selection criteria employed in the study to minimise the possibility of bias.

Data collection

Questionnaire-based interview was conducted on the subjects and information on physical activity, diet, smoking, family history and socioeconomic status were extracted. Blood pressure (BP) was measured using a Mercury Sphygmomanometer (Riester Nova, Germany) by trained examiners at three intervals, with each interval separated by 5 minutes' rest period, after which the mean BP was calculated. Hypertensive and prehypertensive children were considered and checked half an hour apart and two readings were averaged. The age-adjusted and height-adjusted

expected systolic and diastolic blood pressures were identified for each subject based on the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents guidelines (22) Anthropometric parameters such as height, weight and waist circumference (WC) were measured in light clothing with no shoes and the values obtained were categorized based on age and sex. The values obtained were rounded up to the nearest 0.1 cm (for height) and 0.1 kg (for weight). All measurements were conducted in triplicates and mean values were computed. BMI and BMI z-score were

calculated and based on the Centers for Disease Control and Prevention (CDC) BMI-for-age growth chart, the subjects were grouped in line with BMI categories, normal weight (Group A), overweight (Group B) and Obese (Group C). The waist to height ratio (WHtR) of the subjects was also computed by dividing the WC (in centimeters) by the height (in centimeters). The height for age, weight for age, BMI for age and WHtR for age were also computed and recorded.

Biochemical analysis

The biochemical parameters, total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL), low density lipoprotein cholesterol (LDL) and FBG were measured using an automatic chemistry analyzer (Dimension RxL Max Integrated Chemistry System from Siemens Healthcare Diagnostics). Non-high density lipoprotein cholesterol (non-HDL-C), were calculated from the difference between the TC and the HDL-C (23). VLDL-C was calculated using the formula $VLDL-C = TG/2.2$ (24), while the atherogenic index of plasma (AIP) was calculated as $\log_{10}(TG/HDL-C)$ (25).

Statistical analysis

Data analysis was conducted using SPSS (version 24.0). All quantitative variables or numbers were expressed as mean

+/- standard deviation while percentages were used for categorical variables. Data was compared using student t-test for 2 groups and ANOVA for more than 2 groups. Multivariate regression analysis was done to estimate effect of each variable on obesity. For all the tests, p value < 0.05 was considered statistically significant. Correlation coefficient was used to describe strength of association between variables with significant probability value at p < 0.05.

RESULTS

Anthropometric and blood pressure measurements of the participants as shown in Table 2, enabled their categorization into normal weight “control” (56 males, 48 females), overweight (32 males, 27 females) and obese (27 males, 21 females), out of which 12 of the overweight and 34 of the obese participants were found to have pre-hypertension as presented in Figure 1A; thus representing 22.2% prevalence of pre-hypertension in the study population. Statistical significant difference (p < 0.001) between the overweight and obese compared to the control was recorded for values of weight, BMI, WC, WHtR as well as SBP, DPB and HR (Table 2).

Table 2: Anthropometric and blood pressure parameters of the participants

		Control (mean±SD)	Overweight (mean±SD)	Obese (mean±SD)	p-value	
					Control vs Overweight	Control vs Obese
Age (year)	All	14.16±1.26	14.26±1.38	14.04±1.34		
	Male	14.16±1.29	14.13±1.39	14.03±1.35		
	Female	14.17±1.24	14.37±1.39	14.05±1.35		
Height (cm)	All	161.47±7.55	159.82±5.51	161.41±7.56		
	Male	162.34±9.05	159.26±6.48	161.49±6.48		
	Female	160.46±5.22	160.30±4.60	161.29±9.15		
Weight (kg)	All	45.22±4.43	61.49±5.18	82.28±7.51	<0.001	<0.001
	Male	47.25±4.14	62.96±8.53	84.53±6.56		
	Female	42.85±3.53	61.26±4.36	78.85±7.70		
BMI (Kg/m ²)	All	17.39±1.73	24.25±1.71	31.59±2.14	<0.001	<0.001
	Male	17.99±1.63	24.75±2.32	32.43±1.94		
	Female	16.68±1.59	23.81±0.76	30.32±1.79		
WC (cm)	All	74.30±5.90	85.40±4.92	97.81±6.01	<0.001	<0.001
	Male	74.07±6.45	84.91±4.99	99.19±5.34		
	Female	74.56±5.24	85.81±4.92	95.71±6.49		
WHtR	All	0.46±0.04	0.53±0.03	0.61±0.04	<0.001	<0.001
	Male	0.46±0.05	0.53±0.03	0.61±0.03		
	Female	0.47±0.03	0.54±0.03	0.60±0.05		
SBP (mmHg)	All	101.80±3.42	110.70±7.00	124.15±7.32	<0.001	<0.001
	Male	102.78±3.42	111.38±5.38	125.47±6.57		
	Female	100.66±3.08	110.12±5.48	122.14±8.08		
DPB (mmHg)	All	61.99±2.65	66.47± 3.25	80.55±4.81	<0.001	<0.001

	Male	61.16±3.61	66.96±3.12	80.97±4.80		
	Female	61.15±2.57	66.05±3.37	79.92±4.87		
HR (bpm)	All	73.23±4.30	84.60±4.19	101.21±8.52	<0.001	<0.001
	Male	72.05±4.84	72.05±4.84	98.94±6.25		
	Female	74.60±3.09	83.30±3.62	104.67±10.36		

*p-value was calculated as p<0.05 level.

Evaluation of risk factors associated with atherogenicity is summarized in Figure 1B. High frequency of physical inactivity was observed in unhealthy weight males compared to their healthy weight counterparts. Low fruits intake was high in unhealthy weight females relative to the other categories while consumption of mainly fried meals as well as high intake of sweets impacted highly among unhealthy weight males and females. Participants with family history of obesity showed equal frequency in males but family history had a strong influence among overweight females.

The lipid profile provides an instrument for asserting whether the identified overweight and obesity is associated

with the risk of cardiovascular diseases. Figure 2 compares the concentration of biochemical parameters between the control and unhealthy weight groups. Although there was no significant difference in levels of TC between the groups i.e. p = 0.2 (Control vs overweight) and p =0.09 (control vs obese), statistical significant difference (p < 0.001) in mean values of TG, LDL-C, HDL-C as well as FBG between the obese and control groups. Twenty-six (26) obese participants had FBG levels > 100 mg/dl and were classified as pre-diabetics; thus representing 12.6% prevalence in the study population (Figure 1A).

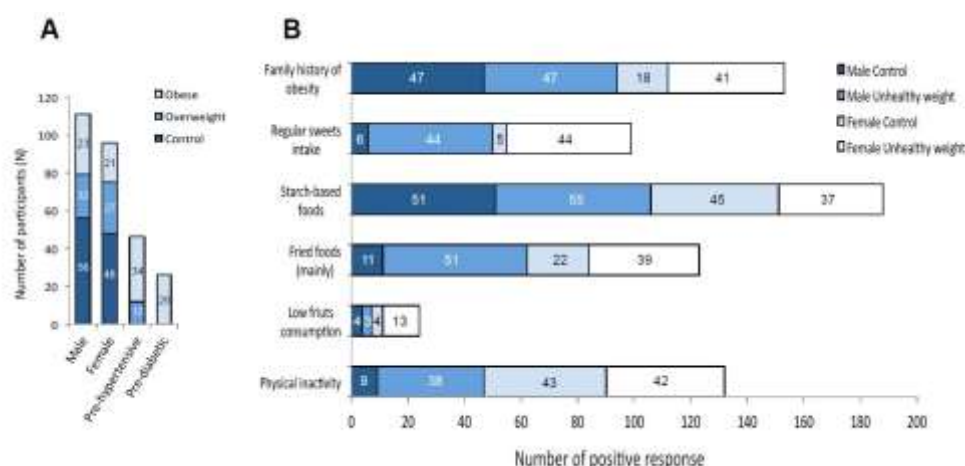


Figure 1: Frequency of overweight and obesity as well as pre-hypertension and pre-diabetes among the participants (A). Frequency of positive responses for some CVD risk factors (B).

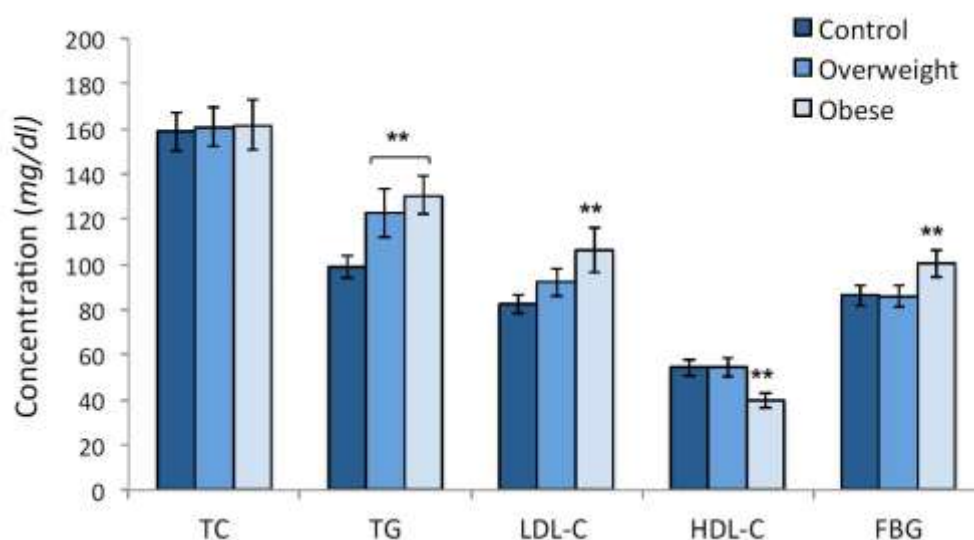


Figure 2: Biochemical parameters of participants based on BMI categories

Mean concentration of lipid profile (TC, TG, LDL-C and HDL-C) as well as FBG in the overweight and obese groups in relation to the control.

** signifies statistical significant difference compared to the control at $p < 0.05$.

From Table 3, mean values of the analysed biochemical parameters of the overweight and control groups, differed significantly ($p < 0.001$) only in mean levels of TG i.e. overweight 122.78 ± 10.99 mg/dl vs control 98.99 ± 5.07 mg/dl. However, the computation of VLDL-C indicated significant differences ($p < 0.001$) between the unhealthy weights (overweight 24.56 ± 2.23 mg/dl; Obese 26.10 ± 1.76 mg/dl) and the control (19.80 ± 1.02 mg/dl) with the same outcome observed for the AIP (i.e. overweight 0.35 ± 0.03 vs

control 0.26 ± 0.03 and obese 0.51 ± 0.02 vs control 0.26 ± 0.03), as well as the LDL-C/HDL-C ratio (i.e. overweight 1.69 ± 0.10 vs control 1.52 ± 0.13 and obese 2.69 ± 0.24 vs control 1.52 ± 0.13). For the TC/HDL-C ratio and the Non-HDL cholesterol, statistical significant difference at $p < 0.001$, from the control was achieved only when compared to the obese group i.e. obese, 4.10 ± 0.37 vs control 2.94 ± 0.27 for TC/HDL ratio and obese 121.96 ± 10.89 vs control 104.56 ± 9.94 for non-HDL cholesterol.

Table 3: Biochemical parameters of the participants

	Control	Overweight	Obese	p-value Control vs. Overweight	Control vs. Obese
TG (mg/dl)	158.79±8.56	160.66±8.67	161.45±11.11	0.2	0.09
TG (mg/dl)	98.99±5.07	122.78±10.99	130.48±8.29	<0.001	<0.001
LDL-C (mg/dl)	82.16±4.21	91.89±5.89	105.98±9.93	0.07	<0.001
HDL-C (mg/dl)	54.23±3.61	54.41±4.40	39.48±3.01	0.77	<0.001
FBG (mg/dl)	86.11±4.46	85.96±4.86	100.18±5.95	0.85	<0.001
VLDL-C	19.80±1.02	24.56±2.23	26.10±1.76	<0.001	<0.001
AIP	0.26±0.03	0.35±0.03	0.51±0.02	<0.001	<0.001
TC/HDL-C ratio	2.94±0.27	2.96±0.23	4.10±0.37	0.6	<0.001
LDL-C/HDL-C ratio	1.52±0.13	1.69±0.10	2.69±0.24	<0.001	<0.001
Non-HDL cholesterol	104.56±9.94	106.25±7.65	121.96±10.89	0.29	<0.001

*p-value was calculated as $p < 0.05$ level

Table 4 shows Pearson's correlation matrix indicating the relationship between the BMI of the participants and their biochemical as well as blood pressure parameters. Strong uphill correlation was observed between BMI and FBG ($r = 0.69$; $p = 0.001$), LDL ($r = 0.66$; $p = 0.001$), heart rate ($r = 0.76$; $p = 0.001$) with the strongest being DBP ($r = 0.91$; $p = 0.001$) and SBP ($r = 0.81$; $p = 0.001$). BMI and HDL showed strong downhill correlation ($r = -0.67$; $p = 0.001$) while BMI and TG indicated a moderate uphill correlation ($r = 0.57$; $p = 0.001$). Lipid profile indices showed strong correlation with blood pressure parameters – the strongest uphill

correlation being LDL vs SBP ($r = 0.74$; $p = 0.001$), and LDL vs heart rate ($r = 0.73$; $p = 0.001$) while the moderate uphill correlation between TG and heart rate ($r = 0.43$; $p = 0.001$) was the smallest. HDL indicated moderate downhill correlation with SBP ($r = -0.49$; $p = 0.001$), DBP ($r = -0.64$; $p = 0.001$) and heart rate ($r = -0.58$; $p = 0.001$). The FBG showed a moderate downhill correlation with HDL ($r = 0.57$; $p = 0.001$), a strong uphill correlation with LDL ($r = 0.60$; $p = 0.001$), DBP ($r = 0.68$; $p = 0.001$) and heart rate ($r = 0.76$; $p = 0.001$) with the weakest correlation being FBG vs TG ($r = 0.31$; $p = 0.001$).

Table 4: Pearson's correlation matrix showing relationship between BMI and clinical characteristics

Variables	BMI	FBG	LDL	HDL	TG	SBP	DBP	Heart rate
BMI								
FBG	0.69							
LDL	0.66	0.60						
HDL	-0.67	-0.57	-0.41					
TG	0.57	0.31	0.53	-0.45				
SBP	0.81	0.59	0.74	-0.49	0.56			
DBP	0.91	0.68	0.69	-0.64	0.55	0.80		
Heart rate	0.76	0.66	0.73	-0.58	0.43	0.69	0.78	

DISCUSSION

The study evaluated cardiovascular risk factors associated with hypertension and diabetes among adolescents in the

city of Kerbala, Iraq. Through application of the JNC-7 guidelines (16) on our anthropometric and blood pressure measurements, a prevalence of 51.7% for unhealthy weight,

22.2% for pre-hypertension and 12.6% for pre-diabetes were observed. These outcomes are indicative of a potential cardiovascular health challenge within the study population as previous studies have established association between adolescent cardiovascular risks with onset of CVDs in adulthood (26, 27). The design of this study enabled us to explore the social factors vis-à-vis, the clinical indices that predisposes the subjects to CVD risks, with the aim of identifying key targets that would aid the development of strategies applicable to the local community.

Lethargy or physical inactivity and family history have been identified as major contributors to unhealthy weight (28). Similarly, consumption of mainly fried meals, starchy foods and sweets results to dyslipidemia and hyperglycemia which are known antecedents of hypertension and diabetes respectively (29, 30). Thus emphasizing the need to reduce risk of CVD through lifestyle changes.

Assessment of lipid profile can be used as a diagnostic tool for CVDs in clinical practice and as a prognostic tool for dyslipidemia as well as other CVD risks in population based studies. Here, we explored the plasma levels of marker lipid biomolecules in relation to the categorised weight groups and identified significant elevations of “unhealthy” blood lipid components i.e. LDL-C, and TG, coupled with a decrease in the “healthy” blood lipid component – HDL-C, in the obese group compared to the control. The overweight group significantly differed from the control only in TG. Interestingly however, computation of specific lipid ratios revealed the atherogenic risks associated with the obese group and the overweight group as well. The LDL-C/HDL-C ratio have been used to predict progression of atherosclerosis (31), coronary heart disease (32) as well as carotid intima-media thickness where the investigators suggested that analysing this ratio provides superior prognostic insights than LDL-C or HDL-C alone (33). In this study, the LDL-C/HDL-C ratio was significantly elevated in the overweight and obese groups, an outcome that connotes serious risk of CVDs. Moreover, values for this ratio proximate to those obtained in this study have been reported previously where associations with intima media thickness was established (33). Another important index is the VLDL-C, which have been linked with risk of coronary artery disease from childhood to young adulthood (34). The significant elevation in VLDL-C as observed in this study also indicates strong relationship between adolescent unhealthy weights and risks of developing CVDs. However, to reliably associate unhealthy weights with CVDs, we assessed the atherogenic index of plasma (AIP) – an established marker of CVDs (35) and a prognostic index for reduction of BMI in obese and overweight individuals (36). The AIP which is linked with the size of pre- and anti-atherogenic lipoprotein particle (37), serves as the true reflection of the relationship between atherogenic and protective lipoprotein (38). We recorded significantly high AIP (> 0.30) values in the overweight and obese groups; these values are cognate to high risk of CVD (39). This provides evidence that the identified unhealthy weight among the study population is strongly connected to high risks of developing CVDs in adulthood hence, it is

recommended that the AIP be routinely monitored especially in high risk individuals.

The relationship between dyslipidemia and hyperglycemia have been widely reported and established in many studies. Similarly, studies have identified different pre-diabetic phenotypes in obese adolescents (17, 40). Interestingly, the present study identified pre-diabetes in the obese group and this reiterates that adolescent obesity does not only predispose and individual to hypertension, but also to diabetes in adulthood.

Our correlation analysis strongly suggests that obesity (through BMI) may be independently associated with elevations in SBP, DBP and dyslipidemia (i.e. elevations in LDL, and TG coupled with decrease in HDL) as well as hyperglycemia through elevation of blood glucose levels.

It is important to note some limitations of the present study. There could be an overestimation of pre-hypertension as they are solely based of BP measures. Also, as a cross-sectional study, interpretation of the postulated relationships cannot be spontaneously done.

In conclusion, this study illuminates the challenge of adolescent obesity as it relates to CVDs and risk of developing hypertension, diabetes in adulthood. The study also identified key biochemical targets that can be used to routinely monitor the prognosis of these risks. Since adolescence provides a critical period in human development, it should be used as a period for arresting the predicted risk of developing CVDs through engaging the population in new healthful lifestyle modifications as the grow into adulthood. We recommend that prospective follow-up large-scale longitudinal studies be carried out to assess the impression obesity, dyslipidemia and hyperglycemia may have on these individuals.

CONFLICT OF INTEREST

None

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