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A CROSS - SECTIONAL STUDY ON ADOLESCENT OBESITY AND ITS ASSOCIATION WITH CARDIOMETABOLIC RISK FACTORS

Mohammed Nazrul Islam*[1], Mohd Rasheeduddin Imran[1], Sayeeda Anjum[2], Shaik Karimulla[3] and Ram Lochan Yadav[4]

[1]Department of Physiology, College of Pharmacy, University of Hafr Al Batin, Kingdom of Saudi Arabia
[2]Department of Anatomy, College of Pharmacy, University of Hafr Al Batin, Kingdom of Saudi Arabia
[3]Department of Pharmacology, College of Pharmacy, University of Hafr Al Batin, Kingdom of Saudi Arabia
[4]Department of Physiology, Chitwan Medical College, Bharatpur, Nepal

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***Corresponding author:**
Mohammed Nazrul Islam

ABSTRACT

Objective: To determine the prevalence of obesity indices and investigate their association with cardiometabolic risk factors in overweight and obese adolescents. **Materials and Methods:** A total of 90 adolescents with matched sex and age -14(2) years were selected for the study and divided into three groups: Normal weight (NW), Overweight (OW) and Obese (OB) based on the BMI (body mass index) percentile for age and sex. Weight, BMI, BMI percentile and waist circumference (WC) were measured to evaluate their association with cardiometabolic parameters. Fasting blood sugar (FBS), glycated haemoglobin (HbA1c), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C), c-reactive protein (CRP), serum uric acid (SUA), T_3, T_4 and thyroid stimulating hormone (TSH) are considered as cardiometabolic risk factors. The obesity and cardiometabolic parameters were compared between groups using Mann Whitney U test and the association between these parameters were evaluated by Spearman correlation test using SPSS V.20. **Results:** The obesity parameters - BMI, BMI percentile and WC for age and sex were statistically significant ($p<0.001$) between NW Vs OW, NW Vs OB and OW Vs OB groups. Cardiometabolic parameters - TC (NW Vs OB, $p<0.05$) and its fractions HDL-C (NW Vs OW, $p<0.001$ and NW Vs OB, $p<0.001$), LDL-C (NW Vs OW, $p=0.03$ and NW Vs OB, $p=0.009$) were statistically significant. Nevertheless, other cardiometabolic parameters like VLDL-C, TG, FBS, HbA1c, CRP, T_3, T_4, and TSH are statistically insignificant between the three groups. The obesity measures were positively correlated to TC and LDL-C levels and inversely related to HDL- C levels (Wt: rho = -0.325, $p=0.002$; BMI: -0.343, $p<0.001$; BMI percentile: rho= -0.361, $p<0.001$; WC: rho= -0.402, $p<0.001$) with statistical significance. The obesity indices are negatively correlated insignificantly to TSH levels. **Conclusion:** Findings revealed that poor lipid profile measures with elevated TC and LDL-C levels and lowered HDL-C and TSH levels were able to identify adolescents that are at risk for early onset of cardiometabolic diseases. FBS, HbA1c, TG, CRP, SUA, T_3 and T_4 measures are not correlated with obesity indices. Hence, our study concluded that in adolescents, obesity/overweight parameters are partially associated with cardiometabolic parameters to the fulfillment of criteria for metabolic syndrome.

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INTRODUCTION

Obesity is a growing global health issue, with increasing prevalence in developed and developing countries (1). Obesity is characterized by excessive lipid build-up in fat tissue and ectopic fat accumulation, contributing to adiposopathy. This process results in systemic inflammation, oxidative stress, altered blood adipokine concentrations, endocrine abnormalities and insulin resistance (2).

Childhood obesity is regarded as one of the major public health issues of the 21st century. Globally, about one in ten young people aged 5 to 17 are overweight or obese, and levels have increased rapidly in many countries over the past few years (3). Saudi Arabia faces a challenge while managing obesity levels in young children between the ages of 5 and 19 affecting both genders and it is crucial to design effective policies and strategies to control this health problem (4).

Obese children are at higher risk for type 2 diabetes, asthma, certain types of cancer, sleep difficulties, musculoskeletal problems and future cardiovascular diseases, as well as school absence, psychological problems and social isolation (1,5,6). Data from the American National Survey indicated that about 10% of adolescents had cardiometabolic abnormalities that are usually stable until adult age, thereby, increasing the risk of premature mortality (7,8). Many obese adolescents already have cardiometabolic comorbidities that often begin around early puberty. There is now a lot higher incidence of arterial hypertension, dyslipidemia, non-alcoholic fatty liver disease NASH, hyperuricemia, hyperinsulinemia and insulin resistance among obese adolescents and young adults compared to normal weight peers (9,10). Therefore, early detection of cardiometabolic abnormalities is important since control of these abnormalities is most effective in the early stages of the disease and/or at an early age (1). For children and adolescents, overweight and obesity are defined through age- and gender-specific normograms for the body mass index (BMI). Children with a BMI equal to or higher than the 95th percentile specific to age and gender are defined as obese. Those with BMI equal to or exceeding the 85th but are below 95th percentiles are defined as overweight and are at risk for obesity related co-morbidities (11). Furthermore, abdominal obesity, evaluated by waist circumference (WC) has been shown to predict the health risks associated with obesity (12), and the weighted evidence indicates that WC -coupled BMI more accurately predicts health risks than BMI alone (13). Indeed, recent discoveries indicate that WC is a stronger marker of a health risk than BMI (14). The utility of BMI and WC in anticipating the health risks associated with obesity has been acknowledged by the National Heart, Lung, and Blood Institutes of Health (NIH) (15). Moreover, understanding the relationships between the different parameters used to assess overweight/obesity and cardiovascular risk factors is critical and how each parameter may reflect the early evolution of risk factors among children (16).The literature on the trajectory of obesity and cardiometabolic outcomes in adolescents is still sparse. Therefore, this study is aimed at assessing the association between patterns of overweight/obesity and cardiometabolic risk factors in overweight and obese adolescents.

MATERIALS AND METHODS

Subjects: This cross-sectional study was conducted on adolescents aged between 11 and 15 years of both sexes recruited from elementary and middle schools. The study was conducted according to the guidelines of the Declaration of Helsinki and approval was taken by the institutional ethics review committee.

Inclusion criteria:

- Both the parent or guardian and children give their written informed consent.
- Having ≥5th percentile of body mass index (BMI), according to the age- and gender-specific reference values of the 2007 CDC, WHO.

Exclusion criteria

- The subjects having below the 5th percentile of BMI according to age and sex.
- The subjects having any diagnosed systemic disease and under medication.

Variables studied

Obesity parameters: The subjects were classified into 3 groups: (1) normal weight (NW, 5th- 85th percentile); (2) overweight (OW, 85th- 94th percentile) and (3) obesity (OB, ≥95th percentile) according to the age- and gender-specific reference values of 2007 WHO, CDC National Growth Charts (17,18). According to International Diabetes Federation (IDF) criteria, adolescents with abdominal obesity (WC≥90th percentile for age and sex), Waist-height ratio >0.4 and 2 or more of the following criteria: TG≥150 mg/dL; HDL≤40 mg/dL; fasting glucose≥100 mg/dL; and systolic BP≥130 mmHg or diastolic BP≥85 mmHg were diagnosed as Metabolic Syndrome related to obesity (19). Weight was measured to the nearest 0.1 kg with a METTLER TOLEDO weighing machine, and height was measured to the nearest 0.1 cm using a wooden stadiometer. Weight and height were measured with the respondents wearing light school uniforms, without head or footwear, and without accessories such as purses, keys and mobile phones, to avoid overestimation (20). BMI was calculated using the formula: weight (kg)/height squared (m^2).The calculated BMI was used to classify respondents as normal weight, overweight or obese, using the IOTF age- and sex-specificcut-off points (17,21).The waist circumference (WC) in centimeters was measured midway between the tenth rib and the top of the iliac crest to the nearest 0.1 cm, using a non-stretchable tape measure (20).

Cardiometabolic parameters: The cardiometabolic parameters such as fasting (12hrs) blood glucose (FBS), glycated haemoglobin (HbA1c), lipid profile and its fractions-total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and triglycerides (TG)), c-reactive protein (CRP), serum uric acid, triiodothyronine (T_3), thyroxine (T_4), and thyroid stimulating hormone (TSH) were assessed using venous blood sampling, which was automatically analyzedusing Roche Cobas 6000 Chemistry and Immuno Analyser (Roche Diagnostic International Ltd, Rotkreuz, Switzerland). Very low density lipoprotein cholesterol (VLDL) was calculated by the Friedewald equation, in mg/dL: VLDL-C = TG/5 (22,23).

Statistical analysis: The data obtained were analyzed with SPSS (version 20; IBM Corporation, Armonk, NY, USA). All the study variables were tested for normalcy with the Shapiro-Wilk test. The comparison of obesity and cardiometabolic parameters between the groups were done by Mann Whitney U test for the non-parametric data and student 't' test for the parametric data. Most of the data were non-parametric and hence the Spearman's correlation test was applied to observe the relation between obesity and cardio metabolic parameters. Statistical significance was considered to be p≤0.05.

RESULTS

The total 90 participants with median age -14(2) years, height -158(8) cm and weight 60.44±7.71 kg were divided into three groups Normal weight (NW), overweight (OW), and Obese (OB) of 30 participants in each, based on the BMI percentile for age and sex. The age and sex of the participants were matched between the above groups having 15 male and 15 female participants in each group.

Table 1. Participants (N=90) overall descriptive parameters with Shapiro-Wilk normality test

Parameters	Mean±SD/ Median (Interquartile Range)	Confidence interval CI (95%)	Shapiro-Wilk test P value
Age (Yrs)	14(2)	13.13-13.67*	<0.001
Ht (cm)	158(8)	157.73-159.74*	<0.001
Wt (Kg)	60.44±7.71	58.83-62.06	0.07
BMI	24.1(5.1)	23.4-24.55*	0.002
BMI percentile	91(15)	84.71-89.11*	<0.001
WC	78(21)	75.02-80.11*	<0.001
FBS	82(21)	81.49-86.97*	0.001
HbA1c	5(0.51)	5.28-5.48*	<0.001
TC	150(20)	149.04-157.43*	<0.001
HDL	42(8)	41-43.51*	0.012
LDL	87(22)	84.46-92.01*	0.006
VLDL	17(9)	16.81-19.46*	<0.001
TG	86(37)	83.72-95.40*	0.001
CRP	1(1)	0.86-1.16*	<0.001
SUA	5(3)	4.08-4.72*	<0.001
T_3	148(29)	147.43-154.74*	<0.001
T_4	8(2)	8.27-9.13*	<0.001
TSH	3.5(2)	2.98-3.49*	<0.001

*p≤0.05 considered as statistically significant.

Table 2. Comparison of obesity and cardiometabolic parameters between normal weight (n=30) and overweight (n=30) adolescents

Parameters	Normal weight Median (Interquartile Range)/ Mean ± SD	Overweight Median (Interquartile Range)/Mean ± SD	Mann-Whitney U test/ Student t test P value
Age (Yrs)	13.5(3)	14(4)	0.45
Ht (cm)	158(8)	157(7)	0.69
Wt (Kg)	52.67±4.27	61±4.29*	<0.001
BMI	20.8(1.45)	24.2(2.15)*	<0.001
BMI percentile	77.5(14)	91(5)*	<0.001
WC	64(4)	78(6)*	<0.001
FBS	83(16)	81.5(24)	0.6
HbA1c	5(0)	5(1)	0.06
TC	147(29)	153(11)	0.113
HDL	45.5(8)	40(6)*	<0.001
LDL	79(16)	92.5(25)*	0.03
VLDL	15(8)	19(15)	0.34
TG	81(18)	91(71)	0.22
CRP	1(1)	1(1)	0.36
SUA	4(2)	5(3)	0.56
T_3	149.5(24)	152(38)	0.72
T_4	8(2)	8.5(2)	0.19
TSH	4(2)	3(2)	0.68

Table 3. Comparison of obesity and cardiometabolic parameters between normal weight (n=30) and obese (n=30) adolescents

Parameters	Normal weight Median (Interquartile Range)/ Mean ± SD	Obese Median (Interquartile Range)/Mean ± SD	Mann-Whitney U test/ Student t test P value
Age (Yrs)	13.5(3)	13.5(2)	0.85
Ht (cm)	158(8)	157.5(10)	0.98
Wt (Kg)	52.67±4.27	67.67±5.4*	<0.001
BMI	20.8(1.45)	26.8(2.05)*	<0.001
BMI percentile	77.5(14)	96(2)*	<0.001
WC	64(4)	90(12)*	<0.001
FBS	83(16)	82(19)	0.225
HbA1c	5(0)	5(1)	0.1
TC	147(29)	154(27)*	0.04
HDL	45.5(8)	38(6)*	<0.001
LDL	79(16)	91(23)*	0.009
VLDL	15(8)	17(8)	0.43
TG	81(18)	91(39)	0.07
CRP	1(1)	1(1)	0.36
SUA	4(2)	4.5(3)	0.84
T_3	149.5(24)	145(38)	0.93
T_4	8(2)	9(3)	0.1
TSH	4(2)	3(2)	0.61

The age (Normal weight Vs Overweight: 13.5(3)- 14(4) years, p=0.45; Normal weight Vs Obese:13.5(3) - 13.5(2) years, p=0.85; and Overweight Vs Obese:14(4) - 13.5(2) years, p=0.46) was comparable between the groups (Table 2, 3 and 4).

Obesity parameters: Normality distribution of all the variables with Shapiro-Wilk test was illustrated in the Table 1. All the obesity related parameters are normally distributed ($p<0.01$) except the weight ($p = 0.07$).

Table 4. Comparison of obesity and cardiometabolic parameters between overweight (n=30) and obese (n=30) adolescents

Parameters	Overweight Median (Interquartile Range)/ Mean ± SD	Obese Median (Interquartile Range)/ Mean ± SD	Mann-Whitney U test/ Student t test P value
Age (Yrs)	14(4)	13.5(2)	0.46
Ht (cm)	157(7)	157.5(10)	0.78
Wt (Kg)	61±4.29	67.67±5.4*	<0.001
BMI	24.2(2.15)	26.8(2.05)*	<0.001
BMI percentile	91(5)	96(2)*	<0.001
WC	78(6)	90(12)*	<0.001
FBS	81.5(24)	82(19)	0.46
$HbA1_C$	5(1)	5(1)	0.79
TC	153(11)	154(27)	0.49
HDL-C	40(6)	38(6)	0.57
LDL-C	92.5(25)	91(23)	0.85
VLDL-C	19(15)	17(8)	0.64
TG	91(71)	91(39)	0.7
CRP	1(1)	1(1)	1
SUA	5(3)	4.5(3)	0.67
T_3	152(38)	145(38)	0.76
T_4	8.5(2)	9(3)	0.68
TSH	3(2)	3(2)	0.91

Table 5. Spearman's Correlation of obesity parameters with cardiometabolic variables (N=90)

Obesity parameter	Cardiometabolic variables - rho (p value)											
	FBS	$HbA1_C$	TC	HDL-C	LDL-C	VLDL-C	TG	CRP	SUA	T_3	T_4	TSH
Wt.	0.172 (0.106)	0.180 (0.089)	0.233* (0.027)	-0.325* (0.002)	0.233* (0.027)	0.063 (0.554)	0.025 (0.815)	0.111 (0.299)	0.203 (0.055)	0.063 (0.557)	0.154 (0.147)	-0.022 (0.839)
BMI	0.144 (0.175)	0.195 (0.066)	0.303* (0.004)	-0.343* (0.001)	0.234* (0.027)	0.032 (0.763)	0.155 (0.145)	0.078 (0.464)	0.097 (0.365)	0.098 (0.359)	0.172 (0.106)	-0.012 (0.910)
BMI percentile	0.127 (0.232)	0.134 (0.208)	0.248* (0.018)	-0.361* (<0.001)	0.244* (0.021)	0.027 (0.797)	0.154 (0.148)	0.083 (0.436)	0.029 (0.783)	0.047 (0.661)	0.148 (0.165)	0.001 (0.989)
WC	0.178 (0.093)	0.170 (0.109)	0.148 (0.164)	-0.402* (<0.001)	0.230* (0.029)	0.075 (0.480)	0.188 (0.075)	0.084 (0.430)	0.082 (0.441)	-0.05 (0.637)	0.181 (0.088)	-0.015 (0.888)

The obesity measures- BMI (NW (20.8(1.45)) Vs OW (24.2(2.15)), p<0.001 and NW (20.8(1.45)) Vs OB (26.8(2.05)), p<0.001), BMI percentile (NW (77.5(14)) Vs OW (91(5)), p<0.001 and NW (77.5(14)) Vs OB (96(2)), p<0.001) and WC (NW (64(4)) Vs OW 78(6)), p<0.001 and NW (64(4)) Vs OB (90(12)), p<0.001) for age and sex were statistically significant between NW Vs OW and NW Vs OB groups (Table 2 and 3).These parameters are also compared between OW and OB groups (Table 4) - BMI (OW (24.2(2.15)) Vs OB (26.8(2.05)), p<0.001), BMI percentile (OW (91(5)) Vs OB (96(2)), p<0.001) and WC (OW (78(6)) Vs OB (90(12)), p<0.001).

Cardiometabolic parameters: The normalcy of all the cardiometabolic parameters are statistically significant (p<0.01). The total cholesterol (NW(147(29)) Vs OB (154(27)), p<0.05) and its fractions HDL-C (NW (45.5(8)) Vs OW (40(6)), p<0.001 and NW (45.5(8)) Vs OB (38(6)), p<0.001), LDL-C (NW (79(16)) Vs OW (92.5(25)), p =0.03 and NW 79(16)) Vs OB (91(23)) p=0.009) were statistically significant. Other lipid parameters like VLDL-C and triglycerides are nonsignificant between the three groups. The glycemic variables (FBS and HbA1c), CRP, SUA and endocrine parameters (T_3,T_4 and TSH) are insignificant between the groups (Table 2 and 3). Comparative study of obesity and cardiometabolic parameters between overweight and obese adolescents elicited insignificant difference.

Relation between obesity parameters and cardiometabolic parameters: The obesity parameters revealed a positive correlation with TC and LDL-C levels and a strong negative correlation with HDL- C levels (Wt.: rho = -0.325, p=0.002; BMI: rho = -0.343, p<0.001; BMI percentile: rho= -0.361, p<0.001; WC: rho -0.402, p<0.001) and their correlations are statistically significant (Table 5). TG levels, glycemic variables (FBS and HbA1c), CRP, SUA and endocrine parameters (T_3 and T_4) are correlated positively with insignificance. TSH variable is also negatively correlated insignificantly.

DISCUSSION

The results of our study elicited relevant considerations about the early development of cardiometabolic risk factors in a representative sample of the adolescent. Firstly, there is an evidence that in the cross-sectional comparative study among normal weight (NW), overweight (OW) and obese (OB) adolescent's obesity parameters such as weight, BMI, BMI percentile for age and sex and WC are significantly elevated in adolescents with OW and OB compared to NW. There is a significant rise in obesity variables in OB during our comparative analysis with OW. The cardiometabolic parameters including TC and LDL cholesterol were increased and HDL cholesterol decreased significantly in overweight and obese groups when compared with normal weight adolescents. These results are consistent with studies of Reinehr et al., reporting higher lower density lipoprotein (LDL) and lower high density lipoprotein (HDL) in obese children compared to normal weight children (24) and are in line with the described lipid's pathophysiology as secondary to obesity (25). But, there were no significant changes in triglyceride levels between the three groups. The IDF consensus definition of metabolic syndrome (MS) in children and adolescents state that the syndrome criteria for age group between 10-<16 are WC: >90th percentile, TG: ≥ 150mg/dL, HDL-C: < 40mg/dL and FBS: >100mg/dL. (19).

Contrary to this, our findings depicted that there were no significant changes in the fasting blood glucose and glycated haemoglobin levels among three groups. Our findings are in consistent with other studies (26). Other cardiometabolic parameters such as c-reactive protein, serum uric acid are also insignificant among the three groups. We evaluated the levels of T_3, T_4 and TSH in normal, overweight and obese children. There were no significant changes elicited among the three groups. Although various studies evaluate thyroid hormone and TSH levels in obese children and possible related complications but the results are not consistent (27,28). On correlation, this study revealed a significant positive association of individual obesity parameters with the cardiometabolic variables. As the BMI/BMI percentile for age and sex of adolescent's progress across the NW, OW and OB groups, the total cholesterol, and LDL cholesterol are significantly elevated. Such positive correlations were also true for WC to LDL cholesterol (Table 5). Our findings are incoherent with the previous reports stating the adolescents classified with high body mass index, waist circumference, and waist to height ratio demonstrated a high association of presenting high triglycerides and fasting blood glucose levels (29).

Moreover, the individual obesity parameters were inversely related to the HDL - cholesterol and TSH levels on increasing BMI/BMI percentiles for age and sex. This shows the importance of establishing the relationship between body fat or obesity measures to cardiometabolic risk factors. By combining these findings with the poorer HDL-C and TSH levels in OW and OB adolescents, we can conclude the poor cardiometabolic profile among OW/OB adolescents. These findings are in consistent with other studies of 5- and 16-year-old children, in whom, fat indicators such as weight-for-height, BMI and skin fold thicknesses have been associated with higher total and LDL cholesterol, lower HDL cholesterol, and higher triglyceride concentrations (30, 31).

CONCLUSION

In our study, we observed that there is a high prevalence of cardiometabolic risk factors such as TC, HDL-C, LDL-C and TSH in overweight and obese adolescents evidenced by their correlation with obesity indices. FBS, HbA1c, CRP, SUA, T_3 and T_4 measures are not adequate for early detection of metabolic risk in adolescents. Our study showed that in adolescents the association between the patterns of overweight/obesity and cardiometabolic risk factors is in partial fulfillment to the criteria of metabolic syndrome.

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