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Interaction between Central Obesity, Lipid Profile and Adiponectin in Children.

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ABSTRACT

Waist circumference (WC) is the simplest way to assess central obesity, which is the precursor for many cardiovascular diseases. To study the relation between central obesity; indicated by waist circumference, adiponectin and cardiovascular disease risk factors (blood pressure, lipid profile) among obese children. This study was a cross sectional case-control one. Anthropometric measurements (weight, height, BMI, waist and hip circumferences), blood pressure, serum adiponectin and lipid profile (cholesterol, TG, HDL, LDL) were obtained on 40 obese children and 40 healthy non-obese control, aged 6- 11 years. Waist circumference (WC) was significantly wider among obese males than among obese females, but it had insignificant sex difference among control. Obese males had statistical significant higher values in all the anthropometric measurements under study, some markers of lipid profile (triglyceride, total cholesterol), and diastolic blood pressure (DBP), and lower values in high density lipoprotein (HDL) and adiponectin. The same results were observed on comparing obese and control females, except for blood pressure (either systolic or diastolic). Central obesity (WC > 90th percentile for age and sex -72 cm) was detected among obese not controls. WC had positive significant correlation with diastolic blood pressure, triglyceride and total cholesterol for obese males, and triglycerides only for obese females, and negative significant correlation with high density lipoprotein (HDL), total cholesterol/ HDL ratio and adiponectin for both obese males and females. When the effect of age was excluded in the partial correlations, these significant correlations disappeared. Central obesity; indicated by WC, is significantly correlated with adiponectin and lipid profile; except LDL; for both sexes, and with diastolic blood pressure among obese males only. The age has an important effect on these correlations.

Keywords: Waist circumference, Central obesity, Blood pressure, lipid profile-Adiponectin.

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INTRODUCTION

Prevalence of obesity in children has increased so significantly in recent years that many consider it a major health concern of the developed world. The National Health and Nutrition Examination Survey (NHANES) indicated that the prevalence of obesity is increasing in all pediatric age groups, in both sexes, and in various ethnic and racial groups [1]. The rapid increase in the prevalence and severity of obesity in children is likely to lower the age of onset and increase the incidence of cardiovascular disease (CVD) (hypertension and atherosclerosis) worldwide [2].

Central obesity is an excess accumulation of fat in the abdominal area, particularly due to excess visceral fat. As visceral fat is supplied by the portal blood system, excess fat in this area can lead to the release of fatty deposits into the blood stream. Fatty buildup in the blood is responsible for the majority of negative health consequences associated with obesity [3].

Measuring a person's waist circumference (WC) is the simplest way to assess central obesity**.** WC has been shown to be one of the most accurate anthropometrical indicators of abdominal fat. It is closely correlated to the waist to hip ratio (WHR), but is thought to be a more reliable measure of abdominal fat; the WHR can mask the status of abdominal obesity with a disproportionately large hip circumference [3].

One role of adipose tissue is as a secretory organ, producing a range of bioactive proteins collectively called adipokines such as (leptin, adiponectin, retinol binding protein 4(RBP4), resistin, interleukin-6(IL-6) and tumor necrosis factor-α (TNF-α) [2].

Also, Adiponectin release from adipocytes undergoes extensive regulation at the post-translational level. The current working hypothesis is that increases in central adiposity results in a down-regulation of adiponectin production by visceral adipose tissue [4].

So, the purpose of this research is to assess the relation between central obesity; indicated by waist circumference; adiponectin and cardiovascular disease risk factors (blood pressure and lipid profile) among Egyptian obese children.

EXPERIMENTAL

Patients and Methods

Subjects

The present study was a cross-sectional case control one, carried out at Al-Zahraa University Hospital and National Research Centre; Egypt; during the period from March 2013 to March 2014. It included 80 children aged 6-11 years, of both sexes. They were divided into 2 groups. The first group included 40 obese children; their body mass index (BMI) above 95^{th}percentile according to the Egyptian Standard Growth Curves [5] for corresponding age and sex. While the second group included 40 healthy non -obese children with body mass index (BMI) ranged from 15^{th} percentile to 85^{th} percentile of the same age and sex as a control group. Children with history of type 1 and type 2 diabetes mellitus, congenital heart disease, rheumatic heart disease, genetic causes of obesity and endocrinal causes of obesity were excluded from the study. An informed written consent was obtained from all mothers of the children before getting them involved in the study, and oral acceptance from the children after taking an approval from Ethical Committees of "Al-Zahraa University Hospital" and "National Research Centre".

Methods

All studied children were subjected to full history taking and physical examination including measurement of blood pressure, anthropometric assessment and laboratory investigation.

Blood pressure (BP): Three resting BP measurements were obtained from the right upper arm using sphygmomanometer and appropriate size cuff, the first measurement was discarded and the average of the other two measurements was recorded.

Anthropometric assessment: Body weight, height, waist circumference (WC) and hip circumference (HC)] were measured according to the recommendation of the International Biological Program [6] . Anthropometric measurements were performed in the morning, before breakfast, with the subject wearing light clothing, without footwear. Body weight *was* measured *using the original weight scale present at the pediatric outpatient* clinic to the nearest 0.5 Kg. Height was measured using Holtain Stadiometer to the nearest 0.1 cm. Waist Circumference was measured at the level of umbilicus with child standing and breathing normally by using a non-stretchable plastic tape. Hip Circumference was measured at the level of iliac crest with child standing by using a non-stretchable plastic tape. Body mass index [BMI= Weight (kg)/Ht (m^2)] and waist to hip ratio [WC (cm)/ HC (cm)] were calculated.

Laboratory investigations

Venous blood samples were obtained to measure serum lipid profile [triglycerides (TG), total cholesterol and high density lipoprotein (HDL)] and adiponectin in the morning by venipuncture after 12-hours overnight fasting by ELIZA technique. Professional staff performed venipuncture. The blood samples were left to clot; sera were separated by centrifugation for 10 minutes at 5000 rpm then stored at –80ºC until assays. Plasma concentrations of total cholesterol [7], triglycerides [8], and high-density lipoprotein-cholesterol (HDL-C) [9] were measured using commercially available kits provided by STANBIO Laboratory Inc.(1261 North Main Street Boerne Texas 78006 USA). Then total cholesterol/ HDL-C ratio was calculated. LDL-C was calculated according to an equation developed by Friedewald et al., [10] as follows:

LDL-C= Total cholesterol –Triglycerides/5+ HDL-C.

Adiponectin ELISA test is a solid-phase ELISA assay designed to measure the quantitative amount of total (low, middle, and high molecular weight) human adiponectin in cell culture supernates, serum and plasma. [11].

Statistical Analysis

Data was analyzed using Statistical package for Social Science (SPSS) computer programs version 16. The standard deviation score (Z score); to exclude the effect of age; was calculated for weight (WAZ), height (HAZ) and BMI (BMI-Z) according to the Egyptian Growth Curve [5] *by the following equation*:

$$Z\ score = \frac{\text{individual's variable - mean value of reference population}}{\text{SD of reference population}}$$

WC data was ranked in ascending order, and its percentile was calculated. The estimated 90^{th} percentile was 72 cm. Children with WC values ≤90^{th} percentile were considered to have normal WC (no central obesity), and those with WC values ≥ 90^{th} percentile were considered to have high WC (central obesity) [12, 13] . Fortunately, the entire obese group (according to their BMI) was having central obesity, while none of the control group have central obesity.

Data are reported as the mean ± SD. Student’s t-test was used to examine sex differences in addition to differences between obese and control group. Pearson´s correlation coefficients were used to measure the strength of association between adiponectin with anthropometric measurements, blood pressure and lipid profile. Then partial correlation was done to exclude the effect of age. The correlation coefficient denoted symbolically “r” defines the strength and direction of the linear relationship between two variables. The level of significance was set at a probability of less than 5% ($p<0.05$).

RESULTS

For obese children, there were statistical significant sex differences in waist circumference (WC), weight (Wt) and weight-for-age Z score, where obese males had higher values than obese females (table 1).While insignificant sex differences were recorded for control children in all the parameters under study (table 2). As WC is a parameter of central obesity, the analysis was completed with sex differentiation.

Comparison between obese and control males (table 3) revealed that obese males had statistical significant higher values in all the anthropometric measurements under study (weight, weight for age Z-score (WAZ), height, height for age Z-score (HAZ), body mass index (BMI), BMI Z-score, waist and hip circumferences), some markers of lipid profile (triglyceride, total cholesterol ($p<0.001$), and diastolic blood pressure (DBP) ($p<0.01$).While they had statistical significant lower values in high density lipoprotein (HDL) and adiponectin ($p<0.001$) . The same results were observed on comparing obese and control females (table 4), except that females had statistical insignificant differences in blood pressure (either systolic or diastolic), and obese females had statistical significant lower values in total cholesterol/ HDL-C ratio ($p<0.01$).

Correlation analysis recorded positive significant correlation between waist circumference (as indicator for central obesity) on one side and diastolic blood pressure, triglyceride and total cholesterol for obese males, and triglycerides only for obese females. Moreover, waist circumference had negative significant correlation with high density lipoprotein (HDL), total cholesterol/ HDL-C ratio and adiponectin for both obese males and females (table 5).When the effect of age was excluded in the partial correlations, there were insignificant correlation between waist circumference, blood pressure, lipid profile and adiponectin (table 6). This means that age has an important effect on the correlation between waist circumference and these parameters.

DISCUSSION

Adipose tissue is increasingly recognized as an endocrine Organ with many secretory products called adipokines. Dysregulated production of adipokines participates in the pathogenesis of obesity-associated co-morbidities, including abnormal lipid and glucose metabolism, altered satiety, increased inflammation, disordered hemostasis and angiogenesis, elevated blood pressure, and cardiovascular function. These adipokines communicate both within adipose tissue and between adipose and other organ systems, and may serve as the common intercellular denominator mediating the development of CVD in the obese state [2] . Many of these substances have been implicated in blood pressure control. Circulating adiponectin is one of this peptide .Activation of the renin-angiotensin system may be induced in adipose tissue by hypoadiponectinemia, resulting in an increase in fat mass and blood pressure [14].

The purpose of this research is to assess the relation between central obesity; indicated by waist circumference; adiponectin and cardiovascular disease risk factors (blood pressure and lipid profile) among obese children.

Adult studies have revealed that waist circumference is a good anthropometric surrogate for visceral adipose tissue (VAT) area. Men are characterized by a preferential accumulation of abdominal adipose tissue as revealed by an increased waist circumference and a greater VAT accumulation compared with women with the same amount of total body fat mass [15] . Current research revealed highly significant sex difference in waist circumference (mean in obese male >mean in obese female) ($P<0.01$). Asayama et al [16] reported waist circumference of 83 Japanese children, 53 obese (33 boys and 20 girls) and 30 non-obese (16 boy and 14 girls) aged from 6 to14-year-old, they found that the waist circumference in the boys were greater than in the girls as in the present study.

Comparing obese with control males, current results showed that obese males had statistical significant higher values than control males in all the anthropometric measurements under study, some markers of lipid profile (triglyceride, total cholesterol and diastolic blood pressure (DBP)) and statistically significant lower values in high density lipoprotein (HDL) and adiponectin. The same results were observed on comparing obese and control females, except that females had statistical insignificant differences in blood pressure (either systolic or diastolic), and obese females had statistical significant lower values in total cholesterol/ HDL-C ratio. The same results were observed by Reinehr et al [17], who observed that cardiac risk factors including higher triglyceride (TG) and low-density lipoprotein (LDL) and lower high-density lipoprotein (HDL) in obese children compared to children with normal weight. In addition, Asayama et al [16], found that the triglyceride, total cholesterol, low-density lipoprotein-cholesterol and total cholesterol/high-density lipoprotein-cholesterol in obese children were higher than the reference values.

The current study also revealed that serum adiponectin level in obese children decreased compared with non-obese children. In agree with these results, Abaza et al [18], and Hassan et al [19, 20], reported serum adiponectin in Egyptian school children and they found reduction in serum adiponectin levels in obese children compared with non-obese one. Asayama et al [16], also assess plasma adiponectin concentration in Japanese children, and found decreased serum adiponectin level in obese children, which was restored toward normal level by slimming. This is explained by that the adiponectin gene expression in adipose tissue paradoxically decreases despite the increase in tissue mass in obesity. The paradox is at least partly explained by the antagonism of tumor necrosis factor-α (TNF-α) to adiponectin and vice versa. TNF-α, which is over expressed in adipose tissue of obese subjects, reduces the expression of adiponectin in adiposities by suppressing its promoter activity [21].

Regarding correlation between waist circumference with blood pressure, lipid profile and adiponectin in this research, it showed that: positive significant correlation between waist circumference (as indicator for central obesity) on one side and diastolic blood pressure, triglyceride and total cholesterol for obese males, and triglycerides only for obese females. Moreover, waist circumference had negative significant correlation with high density lipoprotein (HDL), total cholesterol/ HDL-C ratio and adiponectin for both obese males and females. Significance disappeared between waist circumference, blood pressure, lipid profile and adiponectin when the effect of age was excluded in the partial correlations. This means that age has an important effect on the correlation between waist circumference and these parameters.

In agree with these results, Hassan, et al [13], studied 983 Egyptian school children (502 males, 481 females) aged 7 to12 years old, and found high significant positive correlations between WC on one side and blood pressure (both systolic and diastolic) on the other side. For males, they reported high significant positive correlations between WC on one side and TG, TC and LDL, while for females, insignificant correlations were detected between WC and any parameters of lipid profile. Moreover they found that WC is more sensitive than BMI in predicting hypertension in children. The study of Mahassni et al [22], on 100 Saudi females, found significant positive correlation between waist circumference, triglycerides and LDL, significant negative correlation with HDL and adiponectin, and insignificant correlation with total cholesterol. Kettaneh et al [23], studied 398french children of both sex aged 8to18years old, and found that there was significant negative correlation between WC and adiponectin only in males.

Table (1): Sex differences in anthropometric measurement and blood pressure for obese

sex / variable	Male (no=20)		Female (no=20)			
	mean	**±SD**	**mean**	**±SD**	**t**	**P**
Age (years)	**9.80**	**1.25**	**9.33**	**1.48**	**1.09**	**0.281**
Weight(Kg)	**59.98**	**12.64**	**52.49**	**10.17**	**2.07**	**0.046**
WAZ	**3.06**	**0.78**	**2.48**	**0.71**	**2.43**	**0.020**
Height(Cm)	**144.92**	**10.32**	**139.24**	**9.89**	**1.77**	**0.084**
HAZ	**1.23**	**0.89**	**0.83**	**0.94**	**1.38**	**0.175**
BMI(Kg/m2)	**28.18**	**2.45**	**26.81**	**2.28**	**1.83**	**0.076**
BMI-Z	**2.46**	**.56**	**2.59**	**0.52**	**-0.75**	**0.459**
WC(Cm)	**83.10**	**5.59**	**77.19**	**4.06**	**2.778**	**0.010**
hipC(Cm)	**95.83**	**8.72**	**91.50**	**7.73**	**1.66**	**0.105**
SBP(mmHg)	**110.25**	**16.82**	**106.00**	**14.19**	**0.86**	**0.393**
DBP(mmHg)	**72.25**	**13.23**	**70.25**	**10.82**	**0.52**	**0.604**
Triglyceride (mg/dl)	**132.74**	**30.18**	**134.41**	**43.12**	**-0.14**	**0.890**
Total cholesterol (mg/dl)	**195.78**	**48.94**	**171.82**	**50.43**	**1.51**	**0.141**
HDL (mg/dl)	**21.00**	**5.02**	**21.20**	**4.96**	**-0.13**	**0.900**
Total cholesterol/HDL-C (mg/dl)	**5.57**	**3.07**	**4.81**	**2.13**	**0.89**	**0.378**
LDL cholesterol (mg/dl)	**128.19**	**47.12**	**102.69**	**56.22**	**1.54**	**0.132**
Adiponectin (ng/ml)	**1.72**	**0.45**	**1.69**	**0.37**	**0.18**	**0.860**

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Table (2): Sex differences in anthropometric measurement and blood pressure for controls

sex / variable	Male (no=20)		Female (no=20)			
	mean	±SD	mean	±SD	t	P
Age (years)	8.68	1.67	8.800	1.76	-0.23	0.821
Weight(Kg)	27.93	4.85	26.47	4.87	0.94	0.351
WAZ	-0.35	0.29	-0.57	-0.57	1.98	0.056
Height(Cm)	130.50	7.83	127.55	6.94	1.26	0.215
HAZ	-0.01	0.58	-0.504	0.91	2.03	0.051
BMI(Kg/m2)	16.26	1.12	16.19	2.07	0.13	0.899
BMI-Z	-0.45	0.29	-0.46	0.59	0.07	0.947
WC(Cm)	59.85	5.19	57.75	3.77	1.47	0.152
hipC(Cm)	67.80	6.88	65.55	4.85	1.19	0.239
SBP(mmHg)	104.25	4.06	106.25	5.35	-1.33	0.191
DBP(mmHg)	64.00	4.17	65.50	4.56	-1.09	0.248
Triglyceride(mg/dl)	85.15	20.12	96.78	50.67	-0.96	0.346
Total cholesterol (mg/dl)	139.30	26.79	140.65	27.15	-0.16	0.875
HDL (mg/dl)	41.13	15.63	41.35	17.59	-0.04	0.968
Total cholesterol/HDL-C (mg/dl)	7.07	2.29	6.91	1.89	0.23	0.817
LDL cholesterol (mg/dl)	144.65	41.65	120.71	35.59	1.95	0.058
Adiponectin (ng/ml)	3.93	0.74	4.11	1.01	-0.65	0.520

Table (3): Comparison between obese and control males according to anthropometric measurements and blood pressure

group / variable	Control (no=20)		Obese (n=20)			
	mean	±SD	mean	±SD	t	P
Age (years)	8.68	1.76	9.80	1.25	-2.33	0.026
Weight(Kg)	27.93	4.85	59.98	12.64	-10.59	0.000
WAZ	-0.35	.29	3.05	0.78	-18.27	0.000
Height(Cm)	130.50	7.83	144.92	10.32	-4.98	0.000
HAZ	-0.01	0.58	1.23	0.89	-5.20	0.000
BMI(Kg/m2)	16.26	1.12	28.18	2.45	-19.76	0.000
BMI-Z	-0.45	0.29	2.46	0.56	-20.44	0.000
WC(Cm)	59.85	5.19	83.10	8.59	-10.35	0.000
hipC(Cm)	65.84	6.88	67.80	8.72	-11.29	0.000
SBP(mmHg)	104.25	4.06	110.25	16.82	-1.55	0.136
DBP(mmHg)	64.00	4.17	72.25	13.23	-2.66	0.014
Triglyceride (mg/dl)	85.15	20.12	132.74	30.18	-5.82	0.000
Total cholesterol (mg/dl)	139.30	26.79	195.78	48.94	-4.44	0.000
HDL (mg/dl)	41.13	15.62	21.00	5.03	5.36	0.000
Total cholesterol/HDL-C (mg/dl)	7.07	2.29	5.57	3.07	1.73	0.096
LDL cholesterol (mg/dl)	144.65	41.65	128.19	47.13	1.17	0.249
Adiponectin (ng/ml)	3.93	0.74	1.72	0.45	11.43	0.000

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Table (4): Comparison between obese and control female according to anthropometric measurement and blood pressure

group / variable	Control (no=20)		Obese (n=20)			
	mean	±SD	mean	±SD	t	P
Age (years)	8.80	1.69	9.33	1.48	-1.05	0.000
Weight(Kg)	26.48	4.87	52.49	10.17	-10.32	0.000
WAZ	-0.57	0.43	2.48	0.71	-16.59	0.000
Height(Cm)	127.55	6.94	139.24	9.89	-4.33	0.000
HAZ	-0.50	0.91	0.83	0.93	-4.56	0.000
BMI(Kg/m2)	16.19	2.07	26.81	2.28	-15.39	0.000
BMI-Z	-0.46	0.59	2.59	0.52	-17.39	0.000
WC(Cm)	57.75	3.77	77.19	4.06	-15.70	0.000
hipC(Cm)	65.55	4.85	91.50	7.73	-12.72	0.000
SBP(mmHg)	106.25	5.35	106.00	14.19	0.07	0.942
DBP(mmHg)	65.50	4.56	70.25	10.82	-1.81	0.078
Triglyceride (mg/dl)	69.78	50.67	134.41	43.12	-2.53	0.016
Total cholesterol (mg/dl)	140.65	27.15	171.82	50.43	-2.43	0.021
HDL (mg/dl)	41.35	17.58	21.20	4.96	4.81	0.000
Total cholesterol/HDL-C (mg/dl)	6.91	1.89	4.81	2.13	3.27	0.002
LDL cholesterol (mg/dl)	120.71	35.58	102.69	56.22	1.20	0.237
Adiponectin (ng/ml)	4.11	1.02	1.69	0.38	10.01	0.000

Table (5): Correlation between waist circumference with blood pressure, lipid profile and adiponectin of obese males and females

	Waist circumference			
	Obese males		Obese Females	
	r	p		
SBP(mmHg)	0.248	0.123	0.009	0.954
DBP(mmHg)	0.318	0.045	0.280	0.080
Triglyceride(mg/dl)	0.754	0.000	0.450	0.004
Total cholesterol(mg/dl)	0.475	0.002	0.290	0.070
HDL(mg/dl)	- 0.615	0.000	- 0.517	0.001
Total cholesterol/HDL-C	-0.360	0.024	-0.399	0.012
LDL cholesterol(mg/dl)	-0.194	0.230	-0.148	0.370
Adiponectin (ng/ml)	-0.758	0.000	-0.724	0.000

Table (6): Partial correlation between waist circumference with blood pressure, lipid profile and adiponectin of obese males and females

	Waist circumference			
	obese males		obese Females	
	r	p	r	p
SBP(mmHg)	-0.121	0.632	-0.079	0.754
DBP(mmHg)	-0.218	0.385	-0.413	0.089
Triglyceride(mg/dl)	0.394	0.106	0.310	0.211
Total cholesterol(mg/dl)	0.272	0.275	-0.119	0.638
HDL(mg/dl)	- 0.019	0.942	-0.185	0.464
Total cholesterol/HDL-C	-0.047	0.852	0.148	0.559
LDL cholesterol(mg/dl)	0.239	0.340	-0.097	0.703
Adiponectin (ng/ml)ELIZA	0.260	0.298	-0.069	0.787

SUMMARY

In spite of the finding that WC ;as an indicator for central obesity diagnosis; has a significant association with adiponectin and lipid profile parameters changes for both sexes, and with diastolic blood pressure among obese males , yet these associations disappeared when age was taken into *consideration .*

CONCLUSION

Great consideration of age must be taken on studying the relation between central obesity and cardio vascular risk factors among obese Egyptian school children.

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