Adiponectin in African Egyptian Obese Adolescents

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Abstract: Background: Adiponectin is the most abundant adipokine shown to have insulin-sensitizing, antiatherogenic, and anti-inflammatory properties. Adiponectin level, unlike that of other adipocytokines, is decreased in obesity and type 2 diabetes and increased after weight reduction. Recent studies suggest that adiponectin plays an important role in linking obesity with different cardiometabolic risk factors. Neverseless, a few studies have investigated this relationship in obese children. Racial differences in adiponectin level were observed, but little work has been done to determine if plasma adiponectin concentrations differ as a result of ethnicity. In few studies in African American, lack of a relationship between plasma adiponectin, obesity, and insulin sensitivity were reported despite the prevalence of obesity, diabetes, and insulin resistance in this population. However todate, there are no reports examining similar relationship of adiponectin and different cardiometabolic variables in African Egyptian. Aim of the study: To investigate the relationship between adiponectin, and different cardiometabolic and anthropometric variables in African Egyptian adolescence, in a trial to further explore, whether this relation in the African race differ from other ethnic population. Subjects and methods: A cross-sectional survey was conducted by the National Research Centre, Egypt. The survey comprised 3708 adolescents (48% boys and 52% girls), aged from 12 to 18 years (+ 6 months). Of the total sample, only 340 students (9.2%) were obese (8.1% boys and 10.2% girls); with mean age 14.36±1.66 years. The included 180 obese students; who accepted to share in the laboratory tests; underwent complete physical examination, including different anthropometric measures (Height, weight, body mass index, waist circumference, hip circumference and waist/hip ratio). Blood pressure was also measured. Fasting venous blood samples were collected to detect fasting blood glucose, fasting serum insulin and adiponectin levels. Meanwhile insulin resistance was calculated. Results: Serum adiponectin level was low compared to the kit reference range. It did not show any significant correlations with the studied anthropometric parameters; both the systolic and diastolic blood pressure, the fasting plasma glucose, insulin level and insulin resistance (HOMA-IR). Conclusion: Although the present study, proved that serum adiponectin level was low in the studied African Egyptian obese adolescence, but it could not prove a direct link between adiponectin and the studied anthropometric measures, and cardiometabolic variables. This may provide additional support for the notion that what applies to other ethnic populations might not apply to the African population.

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1. Introduction:

Over the past decade, childhood obesity has increased in a dramatic fashion. With increasing number of young obese populations diagnosed with the metabolic syndrome (MS), which is characterized by such complications as hypertension, glucose intolerance, dyslipidemia and hyper-insulinemia^[1,2]. The molecular basis of the pathogenesis of obesitylinked disorders has not been fully elucidated. Adipose tissue serves not only as an energy storage organ, but also as an endocrine organ. It releases many factors with autocrine, paracrine and endocrine functions. Adipokines such as leptin, resistin, tumor necrosis factor-, interleukin-6, adipsin, visfatin, and adiponectin are biologically active molecules produced by adipose tissue. They play a role in energy homeostasis, and in glucose and lipid metabolism^[3].

Adiponectin is one of the most abundant adipose tissue–specific cytokines that is closely linked to obesity in both children and adults ^[4,5]. Adiponectin level, unlike that of other adipocytokines, is decreased in obesity and increased after weight reduction ^[6,7].

The clinical relevance of adiponectin remained obscure for a number of years ^[8]. However, starting in 2001, several studies highlighted the potential antidiabetic, antiatherosclerotic and antiinflammatory properties of this protein complex. Recently a growing body of evidence suggests that, low level of adiponectin may constitute an early biomarker, identifying obese youth at high risk for the future development of diabetes and atherosclerosis^{[5,9].}

Adiponectin levels have been shown to decrease with age in both normoweight ^[10] and overweight youth ^[11], and thus, aging and maturation may be important regulators of adiponectin metabolism and disease risk in youth ^[5]. Moreover the association between variants in the adiponectin gene and metabolic profiles may differ between ethnic groups ^[12].

Several studies involving different age groups ^[13,14,15] proved that adiponectin level is lower in normal-weight African-Americans compared with Caucasian peers, furthermore the prevalence of obesity, ^[16] diabetes, ^[17] and insulin resistance ^[18] were noticed in African-American population compared to Caucasians of similar age and total adiposity. Whether this difference is because of the racial differences in adiponectin level is currently unknown. However recent studies suggest that differences in adiponectin gene polymorphism could underlie the observed racial differences in adiponectin and its association with physical and metabolic parameters. . In fact, little is understood about the determinants influencing adiponectin levels, particularly at critical stages of development such as adolescence ^[19].

So this study was done on African Egyptian adolescence in a trial to investigate more about the influence of African race on the relation between adiponectin and different variables including adiposity anthropometric measures, and cardiometabolic variables (insulin level, insulin resistance, blood sugar and blood pressure).

2. Subjects and methods:

A cross-sectional survey, comprised 3708 adolescents (1779 boys (48%) and 1929 girls (52%)), aged from 12 to 18 years (±6 months) was conducted by the National Research Centre, Egypt. The studied adolescence was recruited from two Preparatory and two Secondary public Schools situated in Giza governorate, during the period of October, 2007 to April 2009. Permission to perform the study was granted by the Ministry of Education, and the directors of the school included in the research. Parents were informed about the purpose of the study and their permission in the form of written consent was obtained. Another assent was taken from the students to be involved in this research. The protocol was approved by the "Ethical Committee" of the "National Research Centre".

Of the total sample, three hundred and forty students (9.2%); who were diagnosed as having obesity, as they fulfilled the inclusion criteria which

are BMI greater than the 95th percentile for age and gender based on the Egyptian Growth Reference Charts 2002 ^[20], were included. They were 144 boys (8.1%) and 196 girls (10.2%); with mean age of 14.36+1.66 years. Subjects were excluded if they had a prior major illness, including type 1 or 2 diabetes, received medications or had a condition known to influence body composition, insulin action or insulin secretion (e.g. glucocorticoid therapy, hypothyroidism and Cushing's disease). Informed consent and assent were obtained from 180 students and their parents who accepted to share in the laboratory data.

Each student underwent a complete physical examination, including anthropometric measures. The height and weight were measured. The height was measured to the nearest 0.5 cm using a Holtain portable anthropometer, and the weight was determined to the nearest 0.01 kg using a Seca scale Balance with the subject dressed minimum clothes and no shoes. Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in meters) squared. Waist circumference (WC) was measured at the level of the umbilicus with the subject standing and breathing normally, hip circumference (Hip C) at the level of the iliac crest, using non-stretchable plastic tape to the nearest 0.1 cm. Waist/hip ratio (WHR) was calculated (cm/cm). Each measurement was taken as the mean of three consecutive measurements, using standardized equipments and following the recommendations of International Biological programmes ^[21]. Blood pressure was measured with standard mercury а sphygmomanometer after the subjects had rested at least 10 min. Systolic blood pressure was recorded at the appearance of sounds, and the diastolic blood pressure was recorded at the disappearance of sounds. Fasting venous blood samples were collected into plain tubes using standard venipuncture aseptic technique. The samples were allowed to clot and sera were separated by centrifugation and stored in aliquots at - 80° until assays. Fasting blood glucose was measured using quantitative enzymatic colorimetric commercial kit provided by Stanbio according to glucose oxidase method ^[22]. Fasting serum insulin and adiponectin levels where measured using commercially available enzyme linked immunosorbent (ELISA) assay kits, provided by DRG Instruments GmbH, Germany and AviBion Orgenium Laboratories, Finland respectively. HOMA-IR (The homeostatic model assessment for insulin resistance) was calculated:

HOMA-IR= fasting insulin concentration (μ U/mL) x fasting glucose concentration (mmol/L)/22.5.

Statistical analysis

Data were expressed as mean \pm S.D. BMI was expressed in terms of standard deviation score (Z-score), using the standard growth curves for Egyptian children and adolescents 2002 as reference population ^[20]. Student's unpaired t test was used to examine the sex differences. Pearson's correlation coefficients were used to assess the relationships between independent variables. The level of significance was set at a probability of less than 5% (p<0.05).All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS/Windows Version 9.05, SPSS Inc., Chicago, IL, USA).

3. Results:

The prevalence of obesity among 3708 adolescents' students (1779 boys and 1929 girls), aged from 12 to 18 years was 9.2% (8.1% in boys and 10.2% in girls); their mean age was 14.36 ± 1.66 years. However, the prevalence of overweight (those with BMI between 85th and 95th percentile for age and gender based on the Egyptian Growth Reference Charts 2002 ^[20]), was 11.4%; 9.9% in boys and 12.6% in girls (table 1).

The clinical characteristics of the obese adolescents are provided in Table 2. A highly significant sex difference was observed in BMI-Z score, and significant differences in systolic and diastolic blood pressure, where the girls had higher values more than the boys. In contrast, boys were highly significant taller and had significant wider WC and higher values of fasting plasma glucose than the girls. Serum adiponectin level was low for both sexes compared to the kit reference range. However, there are insignificant sex differences in the age, weight, hip C, WHR, and the other laboratory data: fasting adiponectin, insulin level and HOMA-IR.

Correlations between adiponectin and the anthropometric data, blood pressure and laboratory data for the total sample are presented in table 3. Inspite of the finding that serum adiponectin level was low compared to the kit reference range, it showed insignificant correlations with the anthropometric parameters under study; both the systolic and diastolic blood pressure, and the other laboratory data; fasting plasma glucose, insulin level and HOMA-IR. The same findings were observed when the correlations were repeated for each sex separately.

 Table 1: Prevalence of obesity and overweight in the studied adolescents

Sex	Ν	Obese	Obese		Overweight	
		N	%	Ν	%	
Boys	1779	144	8.1	177	9.9	
Girls	1929	196	10.2	244	12.6	
Total	3708	340	9.2	421	11.4	

Table (2): Com	parisons between anth	opometric and laborator	y data of the obese	e adolescents by sex
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	Boys $(N = 82)$		Girls (N= 98)		
	Mean	SD	Mean	SD	Р
Age	14.19	1.23	14.27	1.87	NS
WEIGHT(Kg)	84.33	13.12	85.19	11.39	NS
Height(cm)	162.71	9.90	159.28	6.58	0.008
BMI-Z Score	2.51	0.62	3.21	0.96	0.000
WC (cm)	100.12	14.35	95.16	18.11	0.048
Hip C (cm)	110.93	9.86	110.88	18.10	NS
WHR (cm/cm)	0.90	0.12	0.88	0.27	NS
SBP(mm Hg)	114.76	12.76	119.06	13.74	0.034
DBP (mm Hg)	75.85	8.88	82.09	14.01	0.013
Lab.:					
Adiponectin	1.45	0.26	1.48	0.29	NS
(µg/L)					
Fasting glucose	98.42	14.72	91.85	15.65	0.004
(mg/dl)					
Fasting insulin(µU/ml)	10.52	8.18	10.58	9.04	NS
HOMA-IR	2.46	1.90	2.71	1.96	NS
$(\mu U/mL)/(mmol/L)$					

	U	Adiponectin
Age	r	- 0.007
	р	0.921
Weight	r	0.004
	р	0.959
Height	r	-0.015
	р	0.842
BMI-Z Score	r	0.004
	р	0.957
WC	r	-0.033
	р	0.661
Hip C	r	-0.069
	р	0.367
WHR	r	0.018
	р	0.808
SBP	r	0.046
	р	0.549
DBP	r	0.029
	р	0.707
Fasting glucose	r	-0.141
	р	0.058
Fasting insulin	r	0.043
-	р	0.567
HOMA-IR	r	0.008
	р	0.922

Table	(3):	Correlations	between	adipon	ectin and
	the	anthropomet	ric data,	blood	pressure
	and	laboratory da	ata for the	e total s	ample

4. Discussion:

The prevalence of obesity, and metabolic syndrome (MS) and its associated risk factors in children and adolescents have increased dramatically over decades ^[4]. Adipokines leptin and adiponectin are proposed as biomarkers in children for predicting MS, Type 2 diabetes, or cardiovascular disease ^[23].

In Youth, investigators could emphasize the role played by adiponectin in the development of insulin resistance, hypersinsulinemia, dyslipidemia, and metabolic syndrome, which make adiponectin an attractive therapeutic target for obesity-related conditions ^[24, 6]. In general serum adiponectin levels were found to be lower in obese children than in non-obese children,_however, still little is known about change in adiponectin plasma levels during puberty ^[25].

In the light of evidence showing the important role of adiponectin and the possible ethnic difference in its level, the present cross sectional study done on 180 obese African Egyptian school adolescence, showed that adiponectin level were found to be low compared to the reference range. Other studies involving different age groups prepubertal ^[13], adolescents ^[15], and adults ^[14] proved that adiponectin level is lower in normal-weight African-Americans compared with Caucasian peers.

The mechanism(s) responsible for the lower adiponectin levels in African population remain to be undetermined ^[12].

Furthermore this study gave results that could not declare correlation between adiponectin and adiposity anthropometric measures (BMI, waist circumference, hip circumference and waist/hip ratio), or the metabolic variables (fasting insulin concentrations, insulin resistance and fasting blood glucose level). This goes in concordance with that of, Lee et al. ^[12] who did not demonstrate any correlations between plasma adiponectin, BMI, insulin concentrations, and insulin resistance in African Americans when compared with the Caucasians peers who showed statistically significant negative correlations between adiponectin and any of the above parameters. An equally intriguing finding was that, in Indian teenagers or adults' adiponectin did not correlate directly with measures of insulin sensitivity, overweight, and other cardiometabolic variables ^[26]. Also in pubertal Spanish children, adiponectin was weakly related to anthropometric variables (weight, BMI, WC and HC) and was not correlated with body fat. Whether these different findings can be attributable to the ethenic differences, is unknown and warrants further investigation ^[27].

However the present results were at variance publications with several showing inverse relationship between plasma adiponectin concentrations and both adiposity markers and fasting insulin levels in both adults and children [7, 25] Studies in other populations including Pima Indian, Hispanic, and Asian-American children showed positive correlation of adiponectin with glucose metabolism and negative correlation of adiponectin with fasting insulin level, insulin resistance, proinsulin, and BMI^[9,28]. Also a significant inverse relationship between plasma adiponectin concentrations and BMI was noted in Taiwanese school children >10 years old ^[7]. Kettaneh et al., ^[29] noted that adiponectin in Indian teenagers correlated with waist circumference and BMI, and insulin resistance in boys but not in girls and they concluded that these correlations with adiponectin display a sexspecific picture throughout puberty.

It is interesting to note that although it is generally accepted that hypoadiponectinemia is a novel predictor of hypertension ^[30], the present study, could not prove that serum adiponectin levels correlate with systolic or diastolic blood pressure (SBP or DBP) in obese adolescence which is consistent with previous reports done on obese boys showing also lack of correlation between adiponectin and either SBP or DBP ^[31]. Lambert et al., ^[32] stated that although animal studies support the role of leptin and adiponectin in controlling BP, they are not independently associated with BP in youth.

In contrary other cross-sectional studies, reported independent association between hypoadiponectinemia and hypertension ^[33, 34]. This was confirmed by Chow et al. ^[35] who demonstrated, that hypoadiponectinemia predict the development of hypertension on long-term follow-up of the normotensive subjects, independent of the effects of known risk factors of hypertension, including sex, age, and BMI. Other clinical studies showed that the association between adiponectin and hypertension is evident, and that hypoadiponectinemia is a risk factor for hypertension independent of insulin resistance and diabetes ^[36].

Ohashi and his colleagues ^[37] suggested that hypoadiponectinemia obesity-related hypertension, may be due to its direct effect, in addition to its effect via insulin resistance, and that adiponectin therapy can be potentially useful for hypertension in patients with the metabolic syndrome.

Nevertheless, very few studies address the relationship between adiponectin and hypertension at a mechanistic level. So, further studies on the relationship between adiponectin and childhood hypertension will be needed ^[37].

5. Conclusion:

In the studied African Egyptian obese adolescence, although serum adiponectin level was low, but there were no direct link between adiponectin and the selected anthropometric measures, fasting insulin level, insulin resistance, blood glucose concentration and blood pressure. Which may provide additional support for the notion that what applies to other ethnic populations might not apply to the African population. This finding may spark future research to establish the relationship among adiponectin and different variables in African population.

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