High-Sensitivity C-reactive protein and Plasminogen Activator Inhibitor 1 as markers of cardiovascular risk in Egyptian obese adolescents

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Abstract: Obese aldolescent are suffering of adverse health consequences of obesity that include insulin resistance, glucose intolerance, dyslipidemia, elevated blood pressure which are components of metabolic syndrome. The inflammotry protein hs CRP and PAI-1are reported to be increased in obese subject and these are reflected on cardiovascular atherosclerotic changes. High-sensitivity C-reactive protein (hs CRP) and plasminogen activator inhibitor-1 (PAI-1) are useful predictive markers of cardiovascular events in obese adolescents. The study was performed to evaluate high sensitivity C-reactive protein and plasminogen activator inhibitor-1 as markers of cardiovascular risk in obese adolescents. The study was carried out on eighty eight (88) Egyptian adolescents. All of them were collected from Al Hussein hospital, Al Azhar University, between December 2012 and June 2013. These were classified into two groups: Group A- Normal non obese adolescents (28) (16 females-12 males). Group B- (60) obese adolescents (32 females- 28 males). All of the adolescents aged 16-18 years old (17±1). In normal adolescent group ; (BMI) was less than 25kg/ m2 (22.1±0.7). But In obese adolescents, (BMI) exceed 30 kg/ m2 (32±0.6) with exclusion of secondary obesity. All subjects were submitted to Clinical assessment for exclusion Congenital or acquired illness, and secondary obesity. Anthropometric measures :(height, weight, BMI, W/C and waist/hip ratio were done). Blood pressure in the studied subjects was measured. Family history of diabetes and or hypertension was considered. Measurements of FBS, PPBS, HbA1C., lipid profile (HDL dl, triglyceride)., fasting serum insulin levels to assess insulin resistance by HOMA test, high sensitivity c reactive protein (hs CRP) and plasminogen activator inhibitor 1 levels (PAI-1) were done. Obese groups had significantly higher hs CRP and PAI-1 levels than non obese group (p<0.01). 40% of 60 obese adolescents showed 3 or more criteria of metabolic syndrome and considered to be obese with metabolic syndrome according to IDF definition of metabolic syndrome. Hs CRP and PAI-1 among adolescents were more significant in group 4 (obese adolescents with metabolic syndrome with glucose intolerance) than group 3 (obese adolescents with metabolic syndrome without glucose intolerance) than group 2 (obese adolescents without metabolic syndrome or glucose intolerance) (P<0.001). Significant high BMI, WC, FBS,HbA1c, F.insulin, HomatestIR,blood pressure, LDL, triglyceride and lower HDL in obese groups than the non obese group (P<0.001). Hs CRP and PAI-1 showed a significant positive correlation with BMI (p< 0.001), WC (P<0.001), blood pressure (p<0.001), and TG (p<0.001), FBS (P<0.001), HbA1c(<0.001), Homatest: Ir(p 0.001). We conclude that hs CRP and PAI-1 are significantly higher in obese adolescents especially those with metabolic syndrome and glucose intolerance and these markers can be used as predictive factors for future cardiovascular events.

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1. Introduction

The prevalence of obesity in adolescence has more than doubled in the last 15 years in many regions of the world **(Monzavi *et al.*, 2008)**. This phenomenon is associated with rapidly increasing cases of type 2 diabetes in childhood. Obesity in adolescents also seems to harbor a number of risk factors for cardiovascular disease (CVD) in adult life, but is not yet clear whether these are determined by glycemia, degree of obesity, or other demographic, clinical, or biochemical features of the obese adolescent **(Brown *et al.*, 1999).**

Adolescents obesity seems to contribute to the development of vascular inflammation and the progression of arterial wall changes. High sensitivity C - reactive protein (hs CRP) has recently emerged as a useful biomarker for vascular inflammation associated with atherosclerosis (**Ridker, 2008)**. Risk factors for cardiovascular disease currently under investigation, high-sensitivity C-reactive protein (hs CRP) is the most promising. Many prospective

epidemiologic studies have demonstrated that (hs CRP) independently predicts vascular risk (**Schlager *et al.*, 2007**).

Obesity is an independent risk factor for the development of cardiovascular thrombotic disease **(Alessi *et al.*, 2006)**. The increased incidence of cardiovascular disease may be associated with elevated levels of coagulation factors (e.g. factor VII, fibrinogen) and plasminogen activator inhibitor-1 (PAI-1) in plasma, which have been observed in obese adolescents **(Samad *et al.*, 2008).** Plasminogen activator inhibitor-1 is the primary inhibitor of plasminogen activation in vivo, and increased PAI-1 in plasma compromises the normal fibrin clearance mechanisms promoting thrombosis **(Rega *et al.*, 2004)** which can be taken the form of coronary artery disease**.**

In obese adolescents, increased plasma PAI-1 levels have been correlated with the amount of visceral fat, suggesting that adipose tissue is the primary source of PAI-1 in this condition **(Alessi *et al.*, 2006).**

The present study was performed to evaluate high sensitivity C-reactive protein and plasminogen activator inhibitor-1 as markers of cardiovascular risk and determine factors associated with it in obese adolescents.

2. Material& Methods

This study was carried out on 88 Egyptian adolescents, their ages ranged from 16-18 years. Sixty of them are obese (32 were females and 28 were males, the mean age 17 ±1 years) and 28 were non obese (16 were females and 12 were males All of them are collected from El- Hussein Hospital, Al-Azhar University; between December 2012 and June 2013. Obese group was divided into: **Group 2**: Obese adolescents with one or two criteria of metabolic syndrome (Obese adolescents without metabolic syndrome), **Group 3**: Obese adolescents with metabolic syndrome (three or more criteria) without glucose intolerance and **Group 4**: Obese adolescents with metabolic syndrome with impaired glucose intolerance.

All subjects were submitted to Clinical assessment for Exclusion Congenital or acquired illness, and secondary obesity. Assessment of Body Composition**:** All Anthropometric measures were performed twice: Body mass index (BMI) was calculated as the ratio of weight (kg) to height (m) squared (kg/m2). if exceeds 30 considered obese, if between 25-30 considered overweight, if between 20-25 considered normal weight. Waist circumference (WC) of (94+) cm in males, or (80+) cm in females used as cut-off values to identify adolescents with abdominal obesity if above age of 16 according to IDF definition of metabolic syndrome. Waist hip ratio (WHR) was calculated by dividing waist by hip circumference, and abdominal obesity was diagnosed when the WHR was >0.80 in girls and 0.95 in boys. **(Zimmet *et al.*, 2007).**

Biochemical and hematological profiles of the participants including:

Venous blood was sampled for the measurement of fasting plasma concentrations of glucose , 2 hrs post prandial blood glucose measured after 2 hours of 75 gm of glucose, [oral glucose tolerance test (OGTT)] and HbA1c was measured for each case before centrifugation of sample. And serum concentrations of HDL-cholesterol, triglycerides were measured by colorimetric method.

Serum insulin was measured by microparticle enzyme immunoassay kit to assess insulin resistance by HOMA IR: fasting Glucose (mg/dl) x fasting Insulin (μU/mL) / 405. Lower HOMA index values (<4) indicated higher insulin sensitivity, whereas higher values (>4) indicated lower insulin sensitivity **(Nagi *et al.*, 1996).** High-sensitivity serum CRP was measured by an automated analyzer (Olympus AU400) using a turbidimetric immunoassay kit (CRP-UL- assay, Wako Chemicals, Neuss, Germany). Plasminogen Activator Inhibitor-1(PAI-1) measurements were performed using chromogenic assay (Spectrolyse; American Diagnostic Inc., Greenwich, CT).

Metabolic Syndrome was defined according to IDF definition: Central obesity (defined as waist circumference ≥ 94cm for Eurpean men and ≥ 80cm for European women). Plus any two of the following four factors: (1) Raised triglycerides: ≥ 1.7mmol/L (≥150 mg/dl). (2) Reduced HDL-cholesterol: <1.03mmol/L (<40 mg/dL) in males and <1.29mmol/L (<50 mg/dL) in females, or specific treatment for these lipid abnormalities. (3) Raised blood pressure: systolic BP ≥130 or diastolic BP ≥85mm Hg, or treatment of previously diagnosed hypertension and (4) Impaired fasting glycemia (IFG): fasting plasma glucose (FPG) ≥5.6 mmol/L (≥100 mg/dL), or previously diagnosed type 2 diabetes (**Zimmet *et al.*, 2007).**

Statistical analysis:

Statistical analysis of the results was performed using an X2 test. Data were expressed as Mean ± SD. Differences between groups were tested with tailed-student's t-test for unpaired data. A value of $P \leq 0.01$ and a value of $r \geq 0.05$ were considered significant.

3. Results

Only 24 (40%) of 60 obese adolescents showed 3 or more criteria of metabolic syndrome and considered to be obese with metabolic syndrome according to IDF definition of metabolic syndrome.

Of the single components of the metabolic syndrome, **dyslipidemia** was the most frequent, decreased serum HDL was reported in 31 of 60 obese adolescents (51.6%), also increased serum TG was reported in 31 of 60 obese adolescents (51.6%). The prevalence of **hypertension** was 15 of 60 obese adolescents (25%). Total **impaired glucose tolerance** prevalence rate was 9 of 60 obese adolescents (15%). No cases of type 2 diabetes were seen. And total prevalence of **insulin resistance** was (75%).

According to this data we divided the adolescents into four groups: Non obese (28) adolescents with normal BMI, **(GROUP 1)**, obese adolescents without metabolic syndrome (36) **(GROUP 2)**, obese adolescents with metabolic syndrome without impaired glucose intolerance (15) **(GROUP 3)** and obese adolescents with metabolic syndrome with impaired glucose intolerance (9) **(GROUP 4).**

Table (1) showed that all studied parameters were significantly higher in obese patients than non-obese except HDL that significantly lower in obese versus non-obese (p<0.001). Cardiovascular risk factors (lipid profile, blood pressure, obesity, insulin resistance, Hs CRP and PAI-1 were significantly higher in G 4 than G 3 and in G 3 than G 2 (p<0.001) for all (Table 2).

In the present study component of metabolic syndrome in groups 3 and 4 correlated with obesity, blood pressure, lipid profile, insulin resistance hs CRP and PAI-1 (r > 0.5, p<0.001), table (3). Also both hs-CRP and PAI-1 were correlated with the same above parameters in all subjects in obese groups (r<0.05, p<0.001), (Table 4).

4. Discussion

Adolescent obesity has become a worldwide public health concern **(Morrison *et al.*, 2008).** Obese adolescents are at high risk for developing impaired glucose tolerance and type 2 diabetes mellitus later in life **(Weiss *et al.*, 2005).** Adverse health consequences of adolescent obesity are observed in many populations. This includes elevated blood pressure, insulin resistance and dyslipidemia which are components of metabolic syndrome (Met.S). Studies show that metabolic syndrome is strongly associated with increased risk of cardiovascular diseases in adults (**Schubert *et al.*, 2009).**

In our study the prevalence of metabolic Syndrome was (40%) of the studied obese adolescents (16-18 years). **Meshkani *et al.*, 2013** have reported that prevalence of metabolic syndrome was (29.2%) among obese children and adolescents (8-16 years). Also **Rodriguez-Moran, (2012)** have reported that the overall prevalence of metabolic syndrome was (28.4%) of 352 adolescents (11-17 years). In our study the constituent factors for Metabolic Syndrome were as follows, one factor was present in 19 adolescents with a prevalence of 31.7%, two factors in 17 adolescents with a prevalence of 28.3%, while 24 adolescents 40% of the sample of the study were having three or more criteria of metabolic syndrome. Our findings are in agreement with that of **Rodriguez-Moran, (2012)** who found the constituent factors for Metabolic Syndrome were as follows, one factor is 26.3% of obese adolescents, two factors in 35.6%, while 98 adolescents (27.8%) of the sample of the study i.e 352 obese adolescents were having three or more criteria of Metabolic Syndrome.

Table (1): shows comparison between all parameters of obese and non obese adolescents.

	Non-Obese	Obese	t-test	*P*-value
Age	**16.893 ±0.7**	**16.917±2.1**	**-0.135**	**0.893**
Weight	**56.321±5.2**	**82.233±3.2**	**-15.699**	**0.000**
Height	**159.571±6.5**	**159.917±9.5**	**-0.222**	**0.825**
BMI	**22.078±0.7**	**32.164±6.2**	**-27.192**	**0.000**
W/C	**73.643±5.2**	**99.500±6.2**	**-20.241**	**0.000**
H/C	**87.071±8.2**	**104.300±5.5**	**-32.603**	**0.000**
W/H ratio	**0.843±0.24**	**0.951±0.1**	**-10.255**	**0.000**
SBP	**105.35±8.8**	**125.75±0.5**	**-11.310**	**0.000**
FBS	**72.893±5.8**	**93.600±8.4**	**-15.578**	**0.000**
PPBG	**88.571±4.5**	**116.333±9.8**	**-12.204**	**0.000**
HBA1c	**4.429±1.2**	**5.400±1.2**	**-14.571**	**0.000**
HDL	**50.500±6.1**	**44.583±2.4**	**4.971**	**0.000**
TG	**77.179±5.4**	**149.667±9.2**	**-35.264**	**0.000**
F Insulin	**5.214±0.2**	**20.200±3.2**	**-24.729**	**0.000**
HOMA IR	**0.936±0.1**	**4.702±0.5**	**-17.283**	**0.000**
DPB	**64.643±5.2**	**80.500±5.2**	**-15.669**	**0.000**
Hs CRP	**0.827±0.12**	**2.417±0.1**	**-9.995**	**0.000**
PAI-1	**13.354±2.1**	**23.977±2.3**	**-18.593**	**0.000**

Table (2): shows comparison between all parameters of obese Adolescents with G 2, G 3 and G 4

	G 2 Vs. G 3	G 2 Vs. G 4	G 3 Vs. G4
Mean±S D Age	**16.9 ± 7.0 V S 17.2 ± 9.0 0.142(NS)**	**16.9 ± 7.0 VS 16.6 ± 0.86 0.124(NS)**	**17.2 ± 0.9 VS 16.6 ± 0.86 0.157(NS)**
Weight	**80.9 ± 6.8 VS 80.3 ± 6.6 0.05***	**80.9 ± 6.8 VS 91.0± 7.9 0.0001*****	**80.3 ± 6.6 V S 91.0±7.9 0.001****
Height	**161.1 ± 7.1 VS 157.7± 5.8 0.125(NS)**	**161.1 ± 7.1 VS 159.1 ± 7.2 0.25(NS)**	**157.7± 5.8 VS 159.1 ± 7.2 0.514 (NS)**
BMI	**31.2 ± 0.7 VS 32.3 ± 0.6 0.05**	**31.2 ± 0.7VS 35.9 ± 1.9 0.0001*****	**32.3 ± 0.6 VS 35.9 ± 1.9 0.001****
W/C	**97.5 ± 3.6 VS 98.5 ± 3.2 0.05***	**97.5 ±3.6 VS 109.2 ±6.7 0.0001*****	**98.5 ±3.2 VS 109.2 ± 6.7 0.001****
H/C	**103.2 ± 1.9VS 105.1 ± 1.4 0.05***	**103.2 ± 1.9 VS 107.2 ± 2.9 0.001****	**105.1 ± 1.4 VS 107.2 ± 2.9 0.01***
W/H ratio	**0.9 ± 0.1 VS 0.9 ± 0.1 0.427**	**0.9 ± 0.1 VS 1.0 ± 0.01 0.0001*****	**0.9 ± 0.1 VS 1.0 ± 0.01 0.001****
SBP	**120.8 ± 3.1 VS** 127.0 **± 5.3 0.05***	**120.8 ± 3.1 VS 143.3 ± 6.6 0.001*****	**127.0 ± 5.3 VS 143.3 ± 6.6 0.001****
FBS	**90.1 ± 2.8 VS 94.2 ± 2.2 0.05***	**90.1 ± 2.8 VS 106.6 ± 6.2 0.0001*****	**94.2 ± 2.2 VS 106.6 ± 6.2 0.001****
PPBG	**111 ± 3.4 VS 116.4 ± 4.0 0.05***	**111 ± 3.4 VS 137.4 ± 17.1 0.0001*****	**116.4 ± 4.0 VS 137.4 ± 17.1 0.001****
HBA1c	**5.2 ± 0.2 VS 5.4 ± 0.1 0.05***	**5.2 ± 0.2 VS 6 ± 0.2 0.0001*****	**5.4 ± 0.1 VS 6 ± 0.2 0.001****
HDL	**46.8 ± 4.5 VS 43.8 ± 3.4 0.05***	**46.8 ± 4.5 VS 36.6 ± 5 0.001****	**43.8 ± 3.4 VS 36.6 ± 5 0.01***
TG	**144.5 ± 6.3 VS 152.6 ± 4.2 0.05***	**144.5± 6.3 VS 165.4 ± 9.4 0.0001*****	**152.6 ± 4.2 VS 165.4 ± 9.4 0.001****
F Insulin	**18.5 ± 1.5 VS 20.8 ± 1.6 0.05***	**18.5 ± 1.5 VS 25.7 ±3.1 0.0001*****	**20.8 ± 1.6 VS 25.7 ± 3.1 0.001****
HOMA IR	**4.1± 0.5 VS 4.8± 0.5 0.05***	**4.1 ± 0.5 VS 6.8 ± 1.2 0.0001*****	**4.8 ± 0.5 VS 6.8 ± 1.2 0.001****
DPB	**78.4 ± 2.8 VS 81.0 ± 3.4 0.05***	**78.4 ± 2.8 VS 87.7 ± 3.6 0.0001*****	**81.0 ± 3.4 VS 87.7 ± 3.6 0.001****
Hs CRP	**1.8 ± 0.3 VS 2.8 ± 0.2 0.05***	**1.8 ± 0.3 VS 3.9± 0.7 0.0001*****	**2.8 ± 0.2 3.9 ± 0.7 0.001****
PAI-1	**21.9 ±1.5 VS 25.9 ± 0.5 0.05***	**21.9 ± 1.5 VS 28.6 ±1.1 0.0001*****	**25.9 ± 0.5 VS 28.6 ± 1.1 0.001****

*=significant, **=highly significant, ***=very highly significant

Table (3): Correlations between Metabolic Syndrome (g 3 & G 4) and all other parameters of the study

	Correlation coefficient (r)	*P*-value
Weight	0.88	<0.001*
Height	0.245(NS)	0.254(NS)
BMI	0.92	<0.001*
W/C	0.84	<0.001*
H/C	0.75	<0.001*
W/H ratio	0.68	<0.001*
SBP	0.89	<0.001*
FBS	0.92	<0.001*
PPBG	0.89	<0.001*
HBA1c	0.91	<0.001*
HDL	-0.61	<0.001*
TG	0.9	<0.001*
F Insulin	0.91	<0.001*
HOMA IR	0.91	<0.001*
DPB	0.88	<0.001*
Hs CRP	0.97	<0.001*
PAI-1	0.96	<0.001*

Table (4): Correlations between Hs-CRP, PLA-1 and all other parameters of the study

	Hs-CRP		PAI-1	
	r	*P*-value	r	*P*-value
PAI-1	0.932	<0.001*		
BMI	0.889	<0.001*	0.972	<0.001*
W C	0.834	<0.001*	0.923	<0.001*
W/H ratio	0.705	<0.001*	0.775	<0.001*
SBP	0.909	<0.001*	0.906	<0.001*
FBS	0.930	<0.001*	0.955	<0.001*
PPBG	0.925	<0.001*	0.908	<0.001*
HBA1c	0.921	<0.001*	0.947	<0.001*
HDL	-0.705	<0.001*	-0.663	<0.001*
TG	0.836	<0.001*	0.945	<0.001*
F Insulin	0.895	<0.001*	0.967	<0.001*
HOMA IR	0.936	<0.001*	0.963	<0.001*
DPB	0.843	<0.001*	0.906	<0.001*

Table (5): Shows study of Hs CRP, PAI-1, F. Insulin and HOMA-IR among the 4 groups

	M±SD				ANOVA	
	Hs-CRP	PAI-1	F. Insulin	HOMA-IR	F	*p*-value
Group I	5.2±0.9	13.5±1.2	0.83±0.07	0.9±0.2	277.3	<0.001*
Group II	18.5±1.6	21.9±1.6	1.87±0.32	4.1±0.5	517.7	<0.001*
Group III	2.9±1.7	25.9±0.5	3.83±0.23	4.9±0.5	580.1	<0.001*
Group IV	25.7±3.1	28.7±1.1	3.9±0.68	6.8±1.2	370.1	<0.001*
Tukey's test						
	I&II	I&III	I&IV	II&III	II&IV	III&IV
	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*

Weiss *et al.*, (2005) revealed that the prevalence of Metabolic Syndrome reaches as high as (50%) in severely obese youngsters. Each half-unit increase in BMI stepwise increases the risk of Metabolic Syndrome in overweight persons. The mechanisms underlying the development of the metabolic derangements that occur in Metabolic Syndrome are not fully understood. The most widely accepted hypothesis involves a complex interaction between insulin resistance and obesity that is modified by social, environmental, and genetic factors.

In our study the prevalence of insulin resistance was high 75 %(6.8±1.2) *P*-value <0.001. This is in agreement with **Weiss *et al.*, (2005)** who reported that Obesity has been associated with increased plasma levels of insulin and this denotes insulin resistance that resulting in diminished ability of insulin to stimulate glucose uptake by the skeletal muscles and adipose tissue, in addition to reducing insulin's ability to suppress hepatic glucose Production.

In our study, we found higher concentrations of Hs CRP in obese adolescents than in non obese adolescents and higher in concentrations in obese with metabolic syndrome than obese without metabolic syndrome and highest concentrations were in those with metabolic syndrome and impaired glucose tolerance. **Mullenix *et al.* (2011)** found higher concentrations of this inflammatory protein in abdominally obese healthy children compared with their normal-WC counterparts even before the onset of puberty. Also **Oliveira *et al.*, 2008** had shown high values of hs-CRP among obese children and adolescents, indicating that in early stages there already exists a certain level of inflammation.

Published evidence associates Hs CRP with the development of cardiovascular events considering it as an important determinant of atherosclerotic vascular changes even in young obese adolescents **(Van *et al.*, 2007)**.A number of studies demonstrated a strong predictive association between elevated hs CRP levels and future atherothrombotic events (coronary events, stroke and peripheral arterial disease) **(Nakou *et al.* 2008).**

So, Hs CRP proved to be increased in obese aldolescent especially with metabolic syndrome and glucose intolerance; and this inflammatory protein hs CRP can be used as predictor marker for cardiovascular events in obese adolescents.

In our study PAI-1 concentrations was about 2 times higher in obese adolescents than non obese adolescents and higher in concentrations in obese with metabolic syndrome than obese without metabolic syndrome and highest concentrations were in those with metabolic syndrome and impaired glucose tolerance. **Rega *et al.* (2008)** found PAI-1 levels to be approximately 50% higher in obese versus non-obese adolescents. Also **Merte et al, (2011)** found that levels of PAI-1 were 4 to 8 times higher in overweight adolescents compared with normal weight adolescents.

Increased PAI-1 levels may predispose patients to the formation of atherosclerotic plaques prone to rupture with a high lipid-to-vascular smooth muscle cells ratio as a result of decreased cell migration **(Sobel *et al.*, 2000).** Impaired fibrinolysis in obesity is probably also due to an increased expression of PAI-1 in adipose tissue **(Bastelica *et al.*, 2009).**A reduced fibrinolytic capacity, caused by elevated PAI-1 activity, independently predicts cardiovascular events in young men after myocardial infarction **(Hamste et al 2000).**

The parallelism between circulating increased PAI-1levels and the features of metabolic syndrome may be the reflection of an active TNF/TGF-beta (cytokines produced by visceral fat in obese person) pathway that modulates both insulin resistance and PAI-1 synthesis.

In our study hypertension is recognized as an important component of metabolic syndrome where 25% of obese adolescents have had high systolic blood pressure and 18.3%have had high diastolic blood pressure with a total of 25% of obese adolescents are hypertensive according to the IDF definition of metabolic syndrome. This comes in agreement with **Cruz *et al.* (2008)** who have found that (21%) 321 obese adolescents have high Pressure ≥130/85 mm/Hg, and also with that of **Cruz *et al.*(2008)** who have found that prevalence of hypertension was (24.1%) of 1080 obese Italian adolescents.

In our research impaired glucose tolerance or high fasting blood glucose was reported only among (15%) of the studied obese adolescents, although insulin resistance was observed in (75%) of them. This comes also in agreement with **Cruz *et al.*(2008)** whohave found that (2%) only of 321 obese adolescents have impaired glucose tolerance Fasting blood glucose ≥100 mg/dl, without any case of type2 DM, although insulin resistance was observed in (65%) of the same sample of adolescents.

This can be explained that impaired glucose tolerance and hyperinsulinemia precede type 2 diabetes in case of metabolic syndrome. **Cruz *et al.*, 2004** reported that hyperinsulinemia can precede the development of type 2 diabetes mellitus by more than 10 years**. Abbasi *et al.*(2002)** reported that many of macro vascular changes associated with diabetes mellitus and cardiovascular complications begin before diagnosis of diabetes.

In our study we found that decrease HDL <40mg/dl in males and <50 mg/dl in females in obese

adolescents above age of 16 years was (51.6%) of 60 obese adolescents and hypertriglyceridemia was present also in (51.6 %). This can be compared with that of **Nicola *et al.*, 2013** who found that (43.6%) of 1080 obese adolescents have decrease HDL and increase triglycerides (TG). Also in agreement with **Rodriguez-Moran, (2012)** who reported that (65.3%) of 352 obese adolescents have decrease HDL and (33.5%) have hypertriglyceridemia. Also **Maria *et al.*, 2013** who reported that HDL was decreased in (60%) of 110 obese adolescents and (85%) have had increase TG. Besides acting as the central regulator of glucose, insulin also plays an important role on lipid homeostasis. It has long been known that there is a highly significant correlation among insulin resistance, compensatory hyperinsulinemia, and hypertriglyceridemia **(Reaven, 2006).**

We conclude that Hs CRP (inflammatory protein) and PAI-1 are significantly higher in obese adolescents especially those with metabolic syndrome and glucose intolerance and these markers can be used as predictive risk factor for future cardiovascular events. So adolescent obesity seems to contribute to development of vascular inflammation and progression of arterial wall changes (vascular inflammation, atherosclerosis and thrombotic tendency) and cardiovascular events later in life.

References

1. Abbasi FB, Brown WB and Lamendol C. (2002). Relationship between obesity, insulin resistance, and coronary heart disease risk. J. Am. Coll. Cardiol. 40: 937–943.
2. Alessi MC, Bastelica D, Mavri A, Morange P, Berthet B, Grino M, Juhan-Vague I.(2006). Plasma PAI-1 levels are more strongly related to liver steatosis than to adipose tissue accumulation. Arterioscler Thromb Vasc Biol.;23:1262–1268.
3. Bastelica D, Morange P, Berthet B, Borghi H, Lacroix O, Grino M, Juhan-Vague I, Alessi MC.(2009). Stromal cells are the main plasminogen activator inhibitor-1 producing cells in human fat: evidence of differences between visceral and subcutaneous deposits. ArteriosclerThrombVascBiol; 22:173–178.
4. Brown NJ, Agirbasli M, Vaughan DE. (1999). Comparative effect of angiotensin- converting enzyme inhibition and angiotensin II type 1 receptor antagonism on plasma fibrinolytic balance in humans. Hypertension; 34: 285-90.
5. Cruz ML and Goran MI. (2004). The metabolic syndrome in children and adolescents. CurrDiab Rep.; 4:53-62.
6. Cruz ML, Huang TT, Johnson MS, Gower BA and Goran MI. (2008). Obesity, Insulin sensitivity and blood pressure in black and white children. Hypertesion 40: 18-22.
7. Hamsten A, Wiman B, de Faire U, Blombäck M. (2000). Increased plasma levels of a rapid inhibitor of tissue plasminogen activator in young survivors of myocardial infarction. N Engl J Med; 313:1557-1563.
8. Maria L, Evia V, Edel R, Rodea M, Evelia A and Silvia Q. (2013). Metabolic syndrome and its components among obese (BMI ≥ 95th) Mexican adolescents Published online before print 2013, doi: 10.1530/EC-13-0057 Endocr ConnectEC-13-0057
9. Mertens I, Verrijken A, Michiels JJ, Van der Planken M, Ruige JB, Van Gaal LF.(2011). Among inflammation and coagulation markers, PAI-1 is a true component of the metabolic syndrome. Int J Obes. 7:48–54
10. Meshkani R and Adeli K. (2013). Hepatic insulin resistance ,metabolic syndrome and cardiovascular disease, Department of Biochemistry, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran, 2009 Sep;42(13-14):1331-1346.
11. Monzavi R, Dremaine D and Geffner ME. (2008).Improvement in risk factors for metabolic syndrome and insulin resistance in overweight youth who are treated with lifestyle intervention. Pediatrics. 117:e1111-e1118.
12. Morrison JA, Ford ES and Steinberger J.(2008). The pediatric metabolic syndrome. Minerva Med 99: 269–287.
13. Mullenix, PS, Steele SR, Martin MJ, Starnes B.W, Andersen CA. (2011). C-reactive protein level and traditional vascular risk factors in the prediction of carotid stenosis. Arch. Surg., 142, 1066-1071.
14. Nagi DK, Tracy R, Pratley R. (1996). Relationship of hepatic and peripheral insulin resistance with plasminogen activator inhibitor-1 in Pima Indians. Metabolism. 45:1243–1247.
15. Nakou, E.S.; Liberopoulos, E.N.; Milionis, H.J.; Elisaf, M.S. (2008). The role of C-reactive protein in atherosclerotic cardiovascular disease an overview. Curr. Vasc. Pharmacol, 6, 258-70.
16. Oliveira AC, Oliveira AM, Almeida MS, Silva AM, Adan L &Ladeia AM. (2008).Alanine aminotransferase and high sensitivity C - reactive protein: correlates of cardiovascular risk factors in youth. Journal of Pediatrics, 152 337–342.
17. Reaven GM. (2006).The metabolic syndrome: is this diagnosis necessary? Am J ClinNutr.;83:1237-47.
18. Rega G, Kaun C, Weiss TW, Demyanets S, Zorn G, Kastl SP, Steiner S, Seidinger D, Kopp CW,

Frey M, Roehle R, Maurer G, Huber K and Wojta J.(2004). Inflammatory cytokines interleukin-6 and oncostatin m induce plasminogen activator inhibitor-1 in human adipose tissue. Circulation. 111:1938 –1945.
19. Ridker PM, Danielson E, Fonseca FA and Glynn RJ. (2008). JUPITER Study Group. Rosuvastatin to preventvascular events in men and women with elevated C-reactive protein. N. Engl. J. Med., 359, 2195-2207.
20. Rega G, Kaun C, Weiss TW, Demyanets S, Zorn G, Kastl SP, Steiner S, Seidinger D, Kopp CW, Frey M, Roehle R, Maurer G, Huber K, Wojta J.(2008). Inflammatory cytokines interleukin-6 and oncostatin m induce plasminogen activator inhibitor-1 in human adipose tissue. Circulation. 111:1938 –1945.
21. Rodriguez-Moran M, Salazar-Vazquez B, Violante R and Guerrero- Romero F.(2012). Metabolic syndrome among children and adolescents aged 10–18 years. Diabetes Care; 27:2516 –7.
22. Samad F, Yamamoto K, Loskutoff DJ. (2008). Distribution and regulation of plasminogen activator inhibitor-1 in murine adipose tissue in vivo. Induction by tumor necrosis factor-alpha and lipopolysaccharide. J Clin Invest; 97:37– 46.
23. Schlager O, Exner M, Mlekusch W, Sabeti and Schillinger M. (2007). C-reactive protein predicts future cardiovascular events in patients with carotid stenosis. Stroke, 38, 1263-1268
24. Schubert CM, Sun SS, Burns TL, Morrison JA and Huang TT.(2009).Predictive ability of childhood metabolic components for adult metabolic syndrome and type 2 diabetes. J Pediatr155 ((3)) S6.e1–e7.
25. Sobel BE, Woodcock-Mitchell J, Schneider DJ, Holt RE, Marutsuka K, Gold H. (2001). Increased plasminogen activator inhibitor type 1 in coronary artery atherectomy specimens from type 2 diabetic compared with non diabetic patients: a potential factor predisposing to thrombosis and its persistence. Circulation. 97:2213–2221.
26. Van P, Voors AA, Volbeda M and Gilst WH. (2007). Usefulness of preoperative C reactive protein and soluble intercellular adhesion molecule-1 level for predicting future cardiovascular events after coronary artery bypass grafting. Am. J. Cardiol., 97, 1697-1701.
27. Weiss R, Dziura J, Burgert TS, Tamborlane WV and Taksali SE.(2004). Obesity and the metabolic syndrome in children and adolescents. N Engl JMed350:2362-23742:951–957.
28. Weiss R, Taksali SE, Tamborlane WV, Burgert TS, Savoye M, Caprio S.(2005). Predictors of changes in glucose tolerance status in obese youth. Diabetes Care; 28:902–909.
29. Zimmet P, Alberti G, Kaufman F, Tajima N, Arslanian S, Wong G, Bennett P, Shaw J and Caprio S. (2007). International Diabetes Federation Task Force on Epidemiology and Prevention of Diabetes: The metabolic syndrome in children and adolescents. Lancet, 369:2059-2061.

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