

## Apelin and Some Biomarkers in Females with Metabolic Syndrome

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### ABSTRACT

The metabolic syndrome (MS) is one of the main public fitness issues around the world. The superiority of MS was increasing in parallel with weight problems and diabetes worldwide. Many of the various standards for the identification of MS, its most important additives are atherogenic dyslipidemia, insulin resistance, high blood pressure and abdominal weight problems. Apelin is newly bioactive adipokine that plays a vital role in the control of glucose homeostasis, dyslipidemia, cardiovascular diseases and obesity. The aims of this study is to study the relation between apelin and metabolic syndrome in women. The materials and methods start by taken 75 females were involved in this study (15 of them control and 60 had metabolic syndrome divided into four groups according to the criteria of International Diabetes Federation 2005. All subjects have reported contain anthropometric and biochemical investigation. Blood samples collected from all subjects at Baghdad teaching hospital during September 2015 to April 2016. Serum apelin was estimated using ELISA technique. While serum TG, HDL, HbA1C and FBG measured used colorimetric methods. The conclusion of current study reported high significant elevated in apelin concentration in women with MS make suggested that apelin has potential role in metabolic syndrome.

**Keywords:** Apelin, Metabolic syndrome, BMI, WC, triglyceride, HDL, HbA1C.

### INTRODUCTION

The metabolic syndrome is a gathering of many risk factor metabolic, along with increased plasma triglyceride (TG), decreased high density lipoprotein cholesterol (HDL-C), extended blood pressure, and elevated blood glucose<sup>1</sup>. This aggregation is identified as a several risk issue for atherosclerotic cardiovascular disorders and T2DM.<sup>2</sup> Metabolic risk factors are extra commonplace in obese individuals. For this reason, weight problems are usually covered inside the clinical definition of metabolic syndrome<sup>3,4</sup>.

In recent years, interest has targeted at the visceral adipose tissue resulting from the presence of adipocytokines synthesis and secretion from adipocytes<sup>5,6</sup>. Apelin is a novel adipokine secreted by mature adipocytes, is thirty-six amino acid prepeptide and endogenous ligand of APJ receptor the G-protein-coupled receptor, which discovered in different types tissues included the central nervous system, rise releasing in the hypothalamus, stomach, heart, skeletal muscle, and white adipose tissue<sup>7-9</sup>. Apelin has paracrine function by combined and activated the apelin receptor (Aplnr or APJ).<sup>10</sup> Several types of potential apelin found involving



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apelin-36, apelin-17, apelin-13, and apelin-13 with the pyroglutamated form<sup>11</sup>. Recent the system of apelinergic that exist to interact in the multiple conditions pathogenesis as obesity, disturbances in carbohydrate metabolism and type 2 diabetes mellitus, hypertension, cardiac failure<sup>12,13</sup>.

This adipokine has been reported that involved in physiological balance of storage and

developed, metabolism, and eat behavior and also has important function in obesity-associated disorders involved type II diabetes and hypertension. Although apelin has been revealed to be expressed in white adipose tissue of rats<sup>14,15</sup>, the cells directly responsible for its secretion were not identified. Numerous cell types present in this tissue, other than the adipocyte itself, could be responsible of the detection of apelin transcripts<sup>16,17</sup>.

**Table 1: Descriptive clinical data and anthropometric parameters of control and metabolic syndrome groups**

Features	Control	Group I	Group II	Group III	Group V
Age (years)	39.7±1.64	39.7±2.42	39.9±1.21	39.2±1.93	39.5±1.12
BMI (kg/m <sup>2</sup> )	24.6±0.45	27.5±0.47	34.3±0.93 a***, b***	34.3±0.93 a***, b***	34.8±0.79 a***, b***
SBP (mmHg)	121.1±0.64	121.2± 0.64	121.3±0.54	121±0.62	136.9±0.64 a***, b***, c***, d***
DBP (mmHg)	80.7±0.69	80.1±0.6	80.9±0.67	82.4±0.78	90.4±0.35 a***, b***, c***, d***
WC (cm)	70.5±1.26	116.7±1.6 <sup>a***</sup>	117.2±1.73 <sup>a***</sup>	119±1.8 <sup>a***</sup>	121±1.79 <sup>a***</sup>

<sup>a</sup>ANOVA test: Group I,II,III, and IV vs Control group: \*\*\*p<0.001.

<sup>b</sup>ANOVA test: Group II,III and IV vs Group I: \*\*\*p<0.001

<sup>c</sup>ANOVA test: Group III and IV vs Group II: \*\*\*p<0.001.

<sup>d</sup>ANOVA test: Group III vs Group IV: \*\*\*p<0.001.

**Table 2: Biomarkers feature of studies groups**

Features	Control	Group I	Group II	Group III	Group V
HbA1C %	4.6±0.22	4.4±0.18	5.2±0.18 a*, b**, d*	5.04±0.24 b*	5.7±0.13 a***, b***, d*
FBS(mg/dl)	83.5±2.39	78.3±2.89	86.07±3.03 b***	88.5±2.54 b***	89.6±2.03 b***
HDL-cholesterol(mg/dl)	50±1.56	47.73±1.64	43.3±1.86 a**, b*	34.7±0.83 a***, b***, c***	34.7±0.83 a***, b***, c***
Triglycerides (mg/dl)	107.5±6.46	119.8±5.24	180.2±10.6 a***, b***	198.4±10.3 a***, b***	196.9±12.4 a***, b***
Apelin ng/ml	1.27±0.08	1.94±0.15 a**	2.7±0.06 a***, b***	2.72±0.19 a***, b***	3.14±0.12 a***, b***, c*

d\*

<sup>a</sup>ANOVA test: Group I,II,III, and IV vs Control group: \*\*\*p<0.001, \*\*p<0.01, \*p<0.05

<sup>b</sup>ANOVA test: Group II,III and IV vs Group I: \*\*\*p<0.001, \*\*p<0.01, \*p<0.05

<sup>c</sup>ANOVA test: Group III and IV vs Group II: \*\*\*p<0.001, \*\*p<0.01, \*p<0.05

<sup>d</sup>ANOVA test: Group III vs Group IV: \*\*\*p<0.001, \*\*p<0.01, \*p<0.05.

The metabolic syndrome is a risk factors for several conditions such diabetes and prediabetes, abdominal obesity, dyslipidemia and high blood pressure<sup>18</sup>. Increasing clues revealed that apelin regulates several physiological roles such fluid balance, intake food, proliferation of cell, regulation pressure of blood, angiogenesis and utilization of glucose<sup>19,20</sup> and therefore was able to interfere with many conditions like obesity, type I and II diabetic, hypertension or cardiac diseases<sup>21</sup>. The system of cardiovascular reveals that a vital role of apelin since each of apelin and apelin receptor were present in heart, both large and small conduit vessels, and endothelial cells<sup>22</sup>.

**MATERIALS AND METHODS**

This study included 75 women collected from Baghdad teaching hospital from September 2015 to April 2016. Subjects were divided into control group (fifteen healthy individual) and four group with metabolic syndrome: Group I (n =15; obese), Group II (n =15; obese + '! TG), group III (n=15; obese + '! TG+ '! HDL), (n=15; obese + '! TG + '! HDL + hypertension). These groups classified according to the criteria of International Diabetes Federation 2005 [23]. This study was approved by the Institute Review Board at the College of dentistry, baghdad University. Each participant gave a written consent showing her agreement for the participation in this

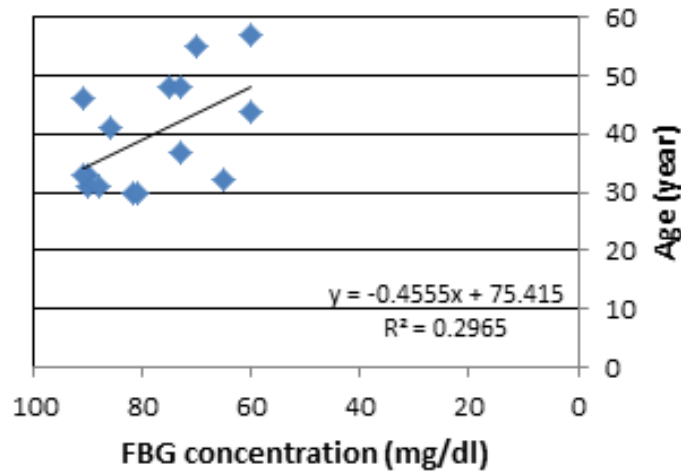


Fig. 1: Correlation between serum FBG levels and Age in group I

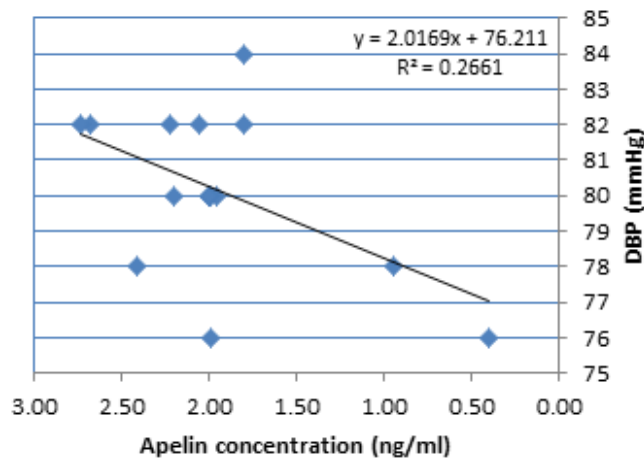


Fig. 2: Correlation between serum Apelin levels and DBP in group I

study. Abdominal obesity plus two of the other criteria are needed for the diagnosis of the metabolic syndrome. We analyzed:

- Abdominal obesity (BMI > 30 kg/m<sup>2</sup>).
- Fasting plasma glucose e" 110 mg/dl .
- Systolic (SBP) e" 130 or diastolic (DBP) e" 85 mmHg.
- Level of high density lipoproteins (HDL) < 40 mg/dl.
- Level of triglycerides (TG) e" 150 mg/dl.

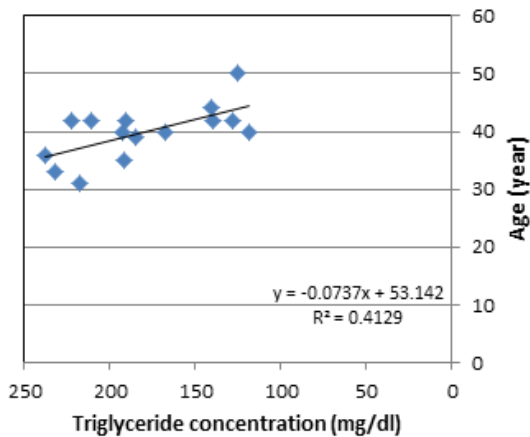
Five milliliters of the blood sample was collected morning into plane tube after fasting for 12 hours. Centrifugation at 3200 rpm for 10 min used for separating the blood into small parts for measurements of serum fasting blood glucose and

triglyceride and HDL-Cholesterol by colorimetric methods and apelin (mybiosource, USA) by using ELISA technique.

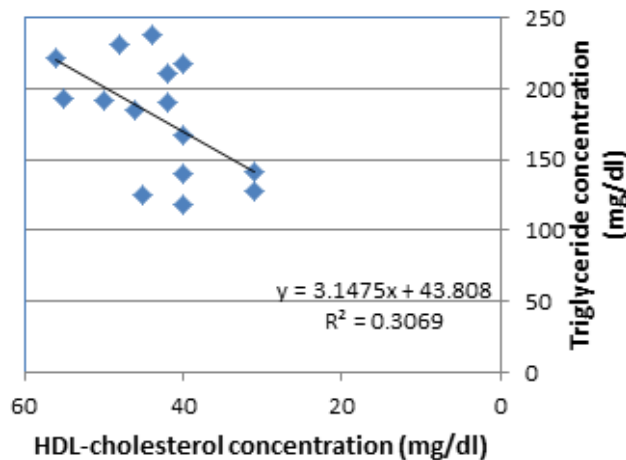
Statistical analysis for all data was done using convenient methods for each analysis in the program of computer SPSS v.16.0. The data were expressed as mean± standard error of mean (mean ± SEM). Results were compared by one way analysis of variance (ANOVA) and the least significant differences (LSD) were calculated. Correlations between variables were evaluated using Pearson's correlation coefficient and simple regression analysis. The association or difference was considered statistically significant when P-value d" 0.05<sup>24</sup>.

**RESULTS**

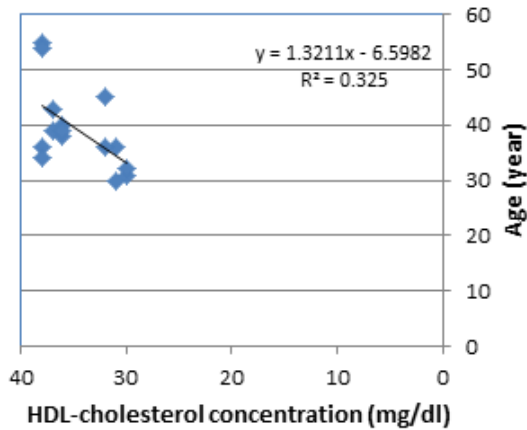
75 subjects included in current study. Control group has 15 subjects, while the four metabolic syndrome were 60 participants. All metabolic syndrome and control groups were match by age. BMI differ significantly between MS and control group. Table I reveals the mean value of waist circumference was significantly in all metabolic syndrome group than control group. While the systolic and diastolic blood pressure shows highly significant differences in group (IV) MS compared with control and other MS groups. As shown in table (2) the mean value of apelin significantly increase as MS components number increase (p<0.001).



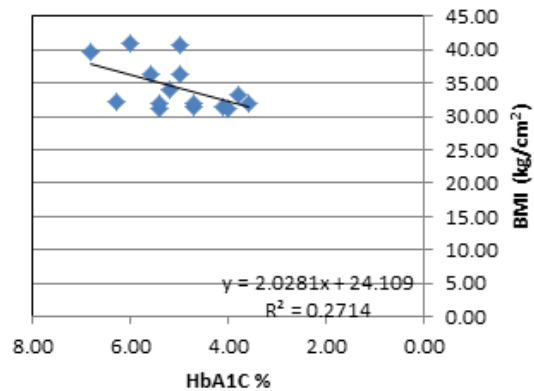
**Fig. 3: Correlation between serum Triglyceride levels and Age in group II**



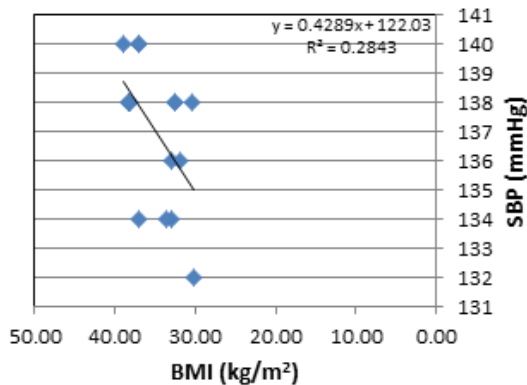
**Fig. 4: Correlation between serum HDL-cholesterol and Triglyceride levels in group II**



**Fig. 5: Correlation between serum HDL-cholesterol and age in group III**



**Fig. 6: Correlation between serum HbA1C % and BMI in group III**



**Fig. 7: Correlation between serum BMI and SBP in group IV**

## DISCUSSION

Metabolic syndrome like insulin resistance, diabetes, hypertension, fatty liver disease (FLD), polycystic ovarian syndrome, and many types of cancer were caused by severe adiposity<sup>21</sup>. Adipose tissue secreted several adipokine such as apelin has an important role in complications of obesity<sup>9,19</sup>. High plasma apelin has been reported by different authors in severe obesity and correlated with adiposity<sup>22,25</sup>. Obesity propagation was increasing industriously mean while the lastest 30 years<sup>26</sup>. Results of present study reveals that the level of apelin was significantly increased in all MS group than control group. This finding agree with the results of Yu *et al.*<sup>27</sup>. In that study, they investigate patients with diabetes and

obesity and reported significantly higher apelin levels in the patients compared to the control group.

Data of current study was not found significant correlation with BMI, as illustrated in other studies also<sup>25,28</sup>. perhaps the causes for that state was the tissue of fat was not the only source of apelin synthesis and secretion, and other places such as the vascular endothelium can visor less release from there<sup>28-30</sup>. Furthermore, expression low level of apelin was elucidating after weight decreased<sup>31</sup>.

Our data shows that obese women had significantly increased in triglycerides concentration and HDL-C levels, when comparison to control individuals. The same findings are reported by many other authors<sup>32-34</sup>. Many studiess describe acute effects of apelin on metabolism of lipid. In both extraction adipocytes and differentiated 3T3-L1adipocytes, adipokine like apelin is shown to inhibit isoproterenol (b-adrenergicagonist)-induced lipolysis through a pathway involving Gq,Gi, and AMPK<sup>35</sup>. This data was confirmed by Than *et al.*<sup>36</sup>, who revealed that apelin decreasing the release of FFA by 3T3-L1 adipocytes through AMPK activation and by increasing the amount of perilipin surrounding the lipid vacuoles, giving them a greater stability and a lipase resistance<sup>36</sup>. Indeed, Higuchi *et al.* showed that daily apelin injections during 2 weeks decrease the triglycerides content in adipose tissue and the weight of different fat depots in standard mice and in HFD fed mice<sup>15</sup>.

### CONCLUSION

A significant remarkable increase in serum apelin level in the all metabolic syndrome classes made additional evidence that apelin play a potential role in women with metabolic syndrome.

In this study we focused on the effect of metabolic syndrome on the level of apelin in women. Further studies should be larger to clarify the effect of

MS on apelin levels and the mechanisms involved in this interaction. This data was also other limitations because small number of participants.

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