Are obese women potential for inflammatory process? A pilot study

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Abstract:

This study was designed to look for certain biochemical markers(serum uric acid and serum peroxynitrite) in women presented with obesity and to compare the level of these markers with non-obese women. A total number of 63 women were recruited from outpatients and private clinics to admit in this study. The patients were grouped into non obese women (Group I) and obese women (Group II). The anthropometric and blood pressure were determined and venous blood was obtained from each patient for determination of C-reactive protein, uric acid and peroxynitrite. The results showed that there were no significant differences in age or in concomitant or associated diseases in both groups except rheumatoid arthritis which account 80% of group I and 25% of group II. The body mass index of Group I patients was 25.27 ± 4.19 kg/h^2 compared with 40.03 ± 16.64 kg/h^2 of Group II ($p < 0.001$). There were no significant differences in waist to hip ratio between two groups. The means systolic and diastolic blood pressures were higher in Group II compare with Group I. Positive C-reactive protein was observed in 53.3% and 52.1% of patients in Groups I and II respectively. Serum uric acid and peroxynitrite were non-significantly higher in Group II compared with Group I. It was concluded that obesity in women is associated with increased level of metabolic and nitrosative markers as well as alteration in inflammatory marker.

Key words: Women, Obese, Peroxynitrite, C-reactive protein

Introduction:

There is no doubt that obesity is considered as one of several risk factors of cardiovascular and metabolic diseases. Obesity is also associated with inflammatory diseases by evidence of significant increase serum levels of proinflammatory markers and inflammation is involved in etiopathology of obesity. Obesity is a common condition on every continent. National surveys in the United States have shown a prevalence of obesity of 20% in men and 25% in women [1]. The striking increase in prevalence in the last 2 decades of the past century also indicates that a population-wide increase in obesity may occur over a short period of time. In obesity, the visceral fat is a key regulator of inflammation, as it secretes proinflammatory cytokines like tumor necrosis factor-α and interleukin-6 which can influence endothelial function, and induce endothelial expression of chemokines and adhesion molecules, which are central event in the early stage of the atherogenetic process. It is believed that CRP plays an important role as an early defense system against infections in the body; in situations of acute inflammation CRP levels increase as much as 50,000 times above normal, typically within 6 hours and peaks at 48 hours. Markedly increased uric acid levels (>370 μM) are known to cause

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gout and nephrolithiasis, but more importantly have been associated with increased risk for the development of cardiovascular disease, particularly hypertension, obesity/metabolic syndrome, and kidney disease [2, 3]. Moreover, uric acid is an important scavenger of one of the nitrosative stress radicals known as peroxynitrite. Peroxynitrite, a byproduct of the reaction of nitric oxide with superoxide, is a potent and versatile oxidant that can attack a wide range of biological molecules. The peroxynitrite anion is relatively stable under basic conditions but is protonated at physiological pH; under physiological condition. The half-life of the protonated species, peroxynitrous acid, is about 1 second. The peroxynitrite anion can react with DNA, proteins, and lipids at physiological conditions, leading to cellular damage and cytotoxity.

The aim of this study is designed to look for certain biochemical markers in women presented with obesity and to compare the level of these markers with non-obese women.

Materials and methods:

The patients were recruited from Al-Yarmouk Teaching Hospital, and Al-Kindy Teaching Hospital. Each woman was examined by consultant physician, and the anthropometric and blood pressure measurements were recorded. The anthropometric measurements included: weight (kg), height (m) and waist circumference (cm). The body mass index (kg/m^2) was calculated using Quettlet's equation:

$$Body\ mass\ index\ (BMI) = \frac{weight}{squared\ height}$$

Waist circumference $\geq$ 102 cm is an indicator of central obesity.

Systolic and diastolic blood pressures were measured in sitting position and the mean of three readings was obtained.

A total number of sixty three women who fulfill the above criteria were admitted in the study. The women were grouped into:

Group I (n=15): nom obese women

Group II (n=48): obese women

Venous blood sample was obtained from each patient and the serum was separated for the determination of C-reactive protein, serum uric acid and peroxynirite. C-reactive protein was qualitatively determined using C-reactive protein (Spectrum, Germany) taking the cut-off level of $\geq$ 6 mg/L as an indicator of inflammation.

Serum uric acid was determined using uric acid (Biomaghreb, France) taking the cut-off level of $\geq$ 420 µmol as a significant high level.

Serum peroxynitrite was measured using the procedure

• The procedure was done at dark room.

• Add to test sample (50 µl), a final volume of 3 ml of 50 mM sodium phosphate buffer.

• Incubate at 37°C (dark place for 2 hours).

• Read the absorbance at λ412 nm.

• The yield of nitrophenol was calculated from the equation:

Extinction coefficient (ε) = 4400 M^{-1} cm^{-1}

The serum ONOO$^-$ level (µmol/L) =

$$\frac{O.D\ Sample}{4400}$$

Statistical analysis

The results are presented as number, percent and mean $\pm$ SD. The data were analyzed using student "t" test (unpaired, two tailed) and the differences between percentages test taking the $p < 0.05$ as the lowest limit of significance.

Results:

There was no significant difference in the mean age between Group I and

Group II (Table 1). Significant differences were observed between Group I and II regarding the concomitant illnesses. Rheumatoid arthritis was significantly presented in higher percent in Group I compared with Group II (Table 1). Non-significant higher percent of diabetes mellitus was observed in Group II (Table 1). There were no significant differences between Group I and Group II in respect to the previous medical history (Table 1). Table 2 shows the anthropometric measurements in which the significant high BMI in Group II is related to the significant increase in the body weight rather than to the changes in the height. Central obesity was significantly existed in Group II compared with Group I b the evidence of the mean value of waist circumference exceeded the cut-off point of 102 cm. Table 3 shows that there were no significant differences between Groups I and II in the mean values of blood pressures. Women in Group I responded positively to the C-reactive protein in 53.3 % (eight out of fifteen patients) which is comparable to the obese women who responded positively to C-reactive protein by 52.1% (25 out of 48 patients); such differences did not reach significance (Figure 1). The serum uric acid level was non significantly higher in obese compare with non-obese women and it attended the levels 258.5 ± 107.3 μmol vs238.4 ± 149.3 μmol (Figure 2). The serum perxynitrite was non significantly higher in Group II compared with Group I; $21.39\pm17.7\mu mol$ vs18.136 ± 6.7 μmol (Figure 3).

Table1. Characteristics of the study

	Group I (n=15)	Group II (n=48)
Age (year)	47.1±15	48.7±12
Concomitant illness		
Rheumatoid arthritis	12 (80)	12 (25)*
Type 2 diabetes	3 (20)	18 (37.5)
Hypertension	4 (26.7)	13 (27.1)
Osteoarthritis	2 (13.3)	7 (14.6)
Psoriasis	2 (13.3)	4 (8.3)
Vitiligo	0	1 (2.1)
Autoimmune diseases e.g. systemic lupus erythematosus	0	1 (2.1)

The results are expressed as number (%) and mean ±SD. *$p< 0.001$

Table 2. This table shows the anthropometric measurements

	Group I (n=15)	Group II (n=48)
Anthropometric measurements		
Weight (kg)	60.4 ± 9.3	92.6±15.8*
Height (m)	1.547±0.049	1.551±0.123
Body mass index	25.27±4.19	40.03±16.64*
Waist circumference (cm)	86.25±10.28	106.5±11.8*

The results are expressed as number (%) and mean ±SD. *$p< 0.001$

Table 3. This table shows the blood pressure measurement

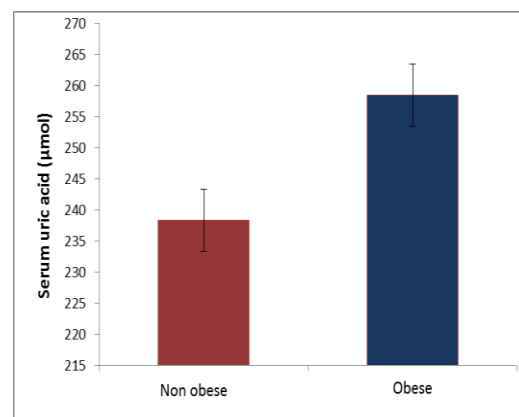|	Group I (n=15)	Group II (n=48)
Blood pressure (mmHg)		
Systolic	129.7±17.2	133.1±17.26
Diastolic	83.0±11.9	86.66±16.7

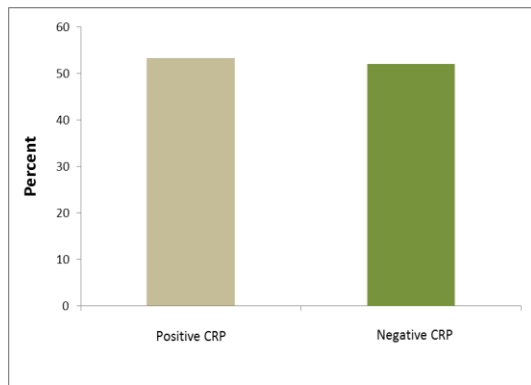**Fig. 1 Serum uric acid level in women.**

Fig.2 Distribution of obese women according to their response to C-reactive protein (CRP)
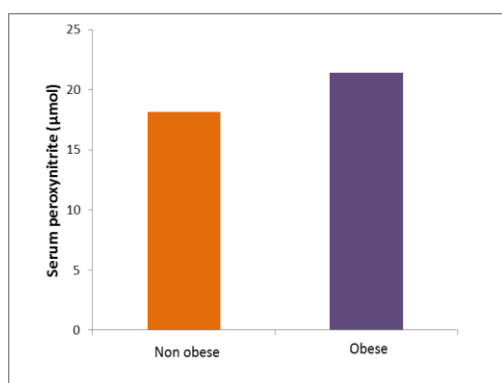

Fig. 3 Serum peroxynitrite level in women

Discussion:

The results indicate that low grade inflammation, metabolic derangement and evidence of nitrosative syndrome are associated with obesity. The non-significant differences are attributed to the small size number of participants. Previous studies mentioned that several inflammatory biomarkers are increased in obesity and many authors believed that these proinflammatory markers played a role in the etiology of obesity [4, 5,6]. C-reactive protein was strongly related to total and central abdominal obesity, blood pressure, and lipid levels, independent of genetic influences[7]. The increase level of C-reactive protein does not only serve as a biomarker of cardiovascular events but indicates the occurrence of co-morbidities. The data reported by [8] suggested that chronic inflammation

may be a key determinant of depressive symptoms in obesity. The high level of serum uric acid that reported in this study may due to activation of nitrosative stress syndrome because uric acid acts as scavenger of peroxynitrite. Recent study found that serum uric acid is a significant predictor of unhealthy obesity in juveniles and adults i.e. obese people with high serum uric acid are at risk of cardiovascular diseases [9]. The increase serum peroxynitrite level indicates that there is a link between obesity and nitrative free radicals. Recent study found that inflammation induces an increase in free radicals and subsequently promotes oxidative stress, which may create a microenvironment favorable to tumor development in obese persons [10]. It could be concluded that there is a link between obesity and inflammatory marker as well as with metabolic (uric acid) and nitrosative marker (peroxynitrite) which also linked with inflammation.

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هل النساء البدينات تتأثر بالعمليات الالتهابية ؟ دراسة تجريبية

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الخلاصة:

صـممت هـذه الدراسـة للكشـف عـن العلامـات البيوكيميائيـة فـي مصـل الـدم والتـي تتضـمن حـامض اليوريـك والبيروكسي نايتريت في النساء البدينات ومقارنـة مستوى هذه العلامـات مع مستواها في النساء غير البدينات. كان العدد الكلي للنساء 63 امرأة أخذت لغرض الدراسة من العيادات الخارجية والعيادات الخاصة وتم تقسيمهن إلى مجموعتين المجموعة الأولى تشمل النساء الغير البدينات والمجموعة الثانية تشمل النساء البدينات أو اللواتي يعانين من السمنة ، تم تحديد ضغط الدم واخذ القياسات البشرية التي تشمل (الطول والوزن ومحيط الخصر ومحيط الورك) بعدها تم الحصول على الدم الوريدي من كل مريضة لتحديد البروتين الفعال سي وحامض اليوريك والبيروكسي نايتريت. أظهرت النتـائج انـه لا توجـد أي فـروق معنويـة فـي العمـر أو فـي الأمـراض المصـاحبة أو مـا يـرتبط بهـا فـي كـلا المجموعتين باستثناء التهـاب المفاصـل الرثـوي والـذي يمثل 80% مـن المجموعة الأولى و25% من المجموعة الثانية وكان مؤشر كتلـة الجسم لمرضى المجموعة الأولى (25.27 ± 4.19) كغم/م^2 مقارنة مع (40.03±16.64) كغم/م^2 للمجموعة الثانية (0.001>ρ) . لم تكن هناك فروق معنوية في نسبة الخصر إلى الورك بين المجموعتين وكان ضغط الدم الانقباضي والانبساطي أعلى في المجموعة الثانية مقارنة مع المجموعة الأولى ، وقد لوحظ ايجابية البروتين الفعال سي في 53.3% و 52.1% من المرضى في المجموعتين الأولى والثانية على التوالي. حامض اليوريك والبيروكسي نايتريت في المصل كان غير معنوي في المجموعة الثانية مقارنة مع المجموعة الأولى.استنتج أن السمنة في النساء مرتبطة مع زيادة مستوى التمثيل الغذائي والعلامات النيتروسيتف فضلا عن التغير عن العلامة الالتهابية.

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