

Risk of Obesity on Oxidative Stress Indicators in Sera Ofiraqi Women with and without Polycystic Ovarian Syndrome

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Abstract:

Obesity is a disorder of body weight caused by a collection of excess body fat, it can be classified according to body mass index (BMI). It has spread widely in the world related with many diseases as well as women's health. Polycystic ovary syndrome (PCOS) is a common endocrinologic and reproductive disorder found in about 10% of the female. This study aimed to investigate the risk of obesity on women health by determining levels of some parameters related to oxidative stress for women with and without PCOS. In addition, total oxidant capacity (TOC), total antioxidant capacity (TAC) and malondialdehyde (MDA) levels were evaluated in sera of Iraqi women with and without PCOS; oxidative stress index (OSI) value was also calculated. The participant was grouped according to the BMI into six groups (Each group contains 20 women): Normal weight women with PCOS (PNwt), Overweight women with PCOS (POwt), Obese women with PCOS their BMI ≥ 30 (Pobese). The three patient groups were matched with three apparently healthy women (Normal weight; HNwt, Over weight; HOWt, Obese; Hobese, respectively). TOC, MDA and OSI levels were elevated gradually ($p < 0.001$) from normal weight to obese in sera of in apparently healthy women as well as PCOS women; while The results of TAC were vice versa. However, the differences for the PCOS women were higher than apparently healthy women, based on the above results. Obesity considered as a serious problem and it's effect is clear on increasing oxidative stress in women, knowing that it's risk is greater for PCOS women.

Keywords: Obesity, Iraqi women, Polycystic ovary syndrome, Oxidative stress.

1. Introduction

Obesity is a complex disorder of body weight regulatory systems involving a collection of excess body fat. It becomes a global problem (the spread of obesity is around tripled ever after 1975), affects nearly all physiological functions of the body and comprises a significant public health threat [1,2]. There are many anthropometric indices such as body mass index (BMI), waist circumference (WC), waist to hip ratio (WHR), waist to height ratio (WHtR). For example, Tutunchi et al. demonstrated that the WHR and WHtR indicators are stronger indicators [3], while suggested that WHtR is the best predictor of diabetes risk compared to other indices [4]. However, BMI considered as a simplest indicator for measuring obesity. Nowadays obesity increases the risk for many disease conditions, such as cardiovascular disease, diabetes mellitus [1,2], gallstone [5], several types of cancers and infertility conditions like polycystic ovary syndrome (PCOS) [6]. The PCOS considers as a prevalent endocrinologic and reproductive disorder found in 6-10% of the female population [7]. The major phenotype characteristics of PCOS are hyperandrogenism (including hirsutism, acne, alopecia as well as biochemical hyperandrogenism), polycystic ovaries and ovulatory dysfunction [8,9]. Recently, the workers in the field of nutrition science have been found that adiposity has a powerful effect in distinct

PCOS phenotypes and influence the direction of symptoms and fertility consequence, the main mechanisms that underlie the relation between PCOS and obesity, from manifold perspectives of weight-gain contributing to evolution of PCOS and vice versa [10]. In addition, the androgenization of female fetus, genetics, host, dietary and other environmental, lifestyle factors, oxidative stress (OS; an imbalance between pro-oxidants and antioxidants) is likewise related in the occurrence of PCOS. Worth to mention that oxidative status is evaluated by circulating markers, such as malondialdehyde (MDA; the monitoring of lipid peroxidation), superoxide dismutase, glutathione peroxidase and DNA oxidation [11,12,13]. Depending on the above, in this study it has been investigated the levels of oxidative status on sera of Iraqi women with and without PCOS by estimating total antioxidant capacity (TOC), total oxidant capacity (TAC) and Malondialdehyde (MDA) concentrations and calculating oxidative stress index (OSI) to confirm the hidden risk on health.

2. Materials and Methods

This study has been performed in the period from November 2019 to February 2020 involving 120 participants including PCOS patients attending Kamal AL-Samaree Hospital for Infertility and *In Vitro* Fertilization at Baghdad. The participants (120 women in reproductive age) were grouped to two main groups apparently healthy women (control) and PCOS women and sub-grouped (according to BMI) into six groups as follows: 20 women with PCOS their BMI = 18.5-24.9 (Normal weight; PNwt), 20 women patients with PCOS their BMI = 25-29.9 (Over weight; POwt), 20 women patients with PCOS their BMI ≥ 30 (Obese; PObe). The three patient groups were matched with three apparently healthy women (Normal weight; HNwt, Over weight; HOwt, Obese; HObe, respectively). The exclusion criteria involved smoking, pregnancy, liver diseases, colon cancer and autoimmune diseases. Protocol was approved by the Ethics Committee of the College of Science/ University of Baghdad. Blood samples were collected from each woman and left at the laboratory temperature for 10 minutes, and centrifuged at 3000xg for 15 minutes. Subsequently Malondialdehyde (MDA) [14], total antioxidant capacity (TOC) and total oxidant capacity (TAC) [15,16] concentrations in sera of the designed groups were estimated, thereafter OSI (oxidative stress index) value was calculated according to the formula:

$$\text{OSI (arbitrary unit)} = \text{TOS } (\mu\text{mol H}_2\text{O}_2 \text{ Eq/L}) / \text{TAS } (\mu\text{mol Ascorbic acid Eq/L}).$$

The data were fully characterized using SPSS by licensed materials version 24 computer software. The data in this study were presented as a Mean $\pm$ Standard deviation (Mean $\pm$ SD) using independent-samples T-test.

3. Results

The study involved one hundred twenty Iraqi women (60 apparently healthy and 60 with PCOS) divided into 6 sub-groups were included in this study; three groups of patients and the others were healthy. The mean $\pm$ SD for ages, BMI, WHR and WHtR shown in (Table 1).

Table 1. Mean $\pm$ SD of Age, Body mass index, WHR and WHtR for all studied groups.

Groups	Age	BMI	WHR	WHtR
PNwt (patients with normal weight)	25.4 $\pm$ 5.5 6	22.98 $\pm$ 1.43	0.829 $\pm$ 0.048	0.523 $\pm$ 0.02
POwt (patients with overweight)	26.9 $\pm$ 4.8 4	27.07 $\pm$ 1.57	0.827 $\pm$ 0.030	0.576 $\pm$ 0.03

Pobese (patients with obesity)	26.6±6.5 4	33.34±4.24	0.912±0.060	0.685±0.09
HNwt (healthy control with normal weight)	27.3±6.0 0	22.68±1.19	0.799±0.031	0.476±0.01
HOwt (healthy control with overweight)	27.9±5.5 8	26.84±1.29	0.821±0.030	0.495±0.01
Hobese (healthy control with obesity)	27.5±6.3 5	32.23±1.77	0.804±0.020	0.560±0.01

According to the data on the above table, the women were grouped according to BMI value characterized as normal weight, overweight and obese in which the PCOS and apparently healthy women were in normal weight, overweight and obese (PNwt, POwt, Pobese, HNwt, HOwt, and Hobese, respectively).

Oxidative stress (OS) concept is a dropping in antioxidants defense mechanisms as a result of an imbalance between pro-oxidants and antioxidants, and is produced by increased levels of reactive nitrogen species (RNS) and/or reactive oxygen species (ROS) ^(12,13). Many studies have been revealed that OS level associated with many diseases in Iraq [17,18], it is significantly increased in PCOS women when compared with the normal ⁽¹²⁾. Oxidative stress indicators (TOC, TAC, OSI, and MDA) were estimated for healthy women (HNwt, HOwt, and Hobese) groups (Table 2).

Table 2. Mean ± SD of total oxidant capacity, total antioxidant capacity, oxidative stress index and malondialdehyde in sera of healthy control group (Hobese) comparison to healthy control groups (HNwt, HOwt).

Parameters	Group	Mean ± SD	Group	Mean ± SD	P-Value
TOC (μmol/L)	Hobese	23.28±1.14	HNwt	18.95±0.86	0.000**
			HOwt	19.83±1.33	0.000**
TAC (μmol/L)	Hobese	556.65±8.70	HNwt	642.60±9.09	0.000**
			HOwt	584.88±8.23	0.000**
OSI	Hobese	0.041±0.002	HNwt	0.0297±0.001	0.000**
			HOwt	0.033±0.002	0.000**
MDA (nmol/L)	Hobese	17.08±0.64	HNwt	13.50±0.63	0.000**
			HOwt	14.66±0.42	0.000**

Oxidative stress indicators (TOC, OSI and MDA) were in a highly significant increase ($p < 0.001$) for Hobese group when compared with both HNwt and HOwt groups.

In order to establish the relationship of obesity with PCOS, the studied parameters were evaluated and compared for apparently healthy women (control) and (PCOS women) between the two main groups (Table 3) and also between the six sub-groups (PNwt, POwt, Pobese, HNwt, HOwt, and Hobese) (Table 4).

Table3. Mean $\pm$ SD of total oxidant capacity, total antioxidant capacity, oxidative stress index and malondialdehyde in sera of PCOS patients groups comparison to that of healthy control groups.

Parameters	Groups	Mean $\pm$ SD	P-Value
TOC ($\mu\text{mol/L}$)	PCOS (n=60)	34.63 $\pm$ 5.12	0.000**
	Control(n=60)	20.68 $\pm$ 2.18	
TAC ($\mu\text{mol/L}$)	PCOS (n=60)	485.02 $\pm$ 28.32	0.000**
	Control(n=60)	596.33 $\pm$ 32.69	
OSI	PCOS (n=60)	0.071 $\pm$ 0.013	0.000**
	Control(n=60)	0.034 $\pm$ 0.005	
MDA (nmol/L)	PCOS (n=60)	37.88 $\pm$ 1.59	0.000**
	Control(n=60)	15.08 $\pm$ 1.60	

Table 4. mean $\pm$ SD of total oxidant capacity, total antioxidant capacity, oxidative stress index and malondialdehyde in sera of patients groups (PNwt, POwt, Pobese) comparison to that of healthy control groups (HNwt, HOwt, Hobese).

Parameters	Group	Mean $\pm$ SD	Groups	Mean $\pm$ SD	P-Value
TOC ($\mu\text{mol/L}$)	PNwt	31.06 $\pm$ 2.31	HNwt	18.95 $\pm$ 0.86	0.000**
	POwt	31.83 $\pm$ 2.53	HOwt	19.83 $\pm$ 1.33	0.000**
	Pobese	40.99 $\pm$ 2.34	Hobese	23.28 $\pm$ 1.14	0.000**
TAC ($\mu\text{mol/L}$)	PNwt	525.07 $\pm$ 13.59	HNwt	642.60 $\pm$ 9.09	0.000**
	POwt	484.81 $\pm$ 7.27	HOwt	584.88 $\pm$ 8.23	0.000**
	Pobese	447.25 $\pm$ 10.81	Hobese	556.65 $\pm$ 8.70	0.000**
OSI	PNwt	0.0606 $\pm$ 0.002	HNwt	0.0297 $\pm$ 0.001	0.000**
	POwt	0.066 $\pm$ 0.0066	HOwt	0.033 $\pm$ 0.002	0.000**
	Pobese	0.089 $\pm$ 0.004	Hobese	0.041 $\pm$ 0.002	0.000**
MDA (nmol/L)	PNwt	36.33 $\pm$ 0.86	HNwt	13.50 $\pm$ 0.63	0.000**
	POwt	37.69 $\pm$ 0.90	HOwt	14.66 $\pm$ 0.42	0.000**
	Pobese	39.63 $\pm$ 0.72	Hobese	17.08 $\pm$ 0.64	0.000**

TOC in the sera of patients groups (PNwt, POwt and Pobese) was a highly significant increase ($p < 0.001$) when compared to the healthy groups (HNwt, HOwt&Hobese), Likewise when patients groups were compared to each other was found that TOC in (Pobese) group a highly significant increase ($p < 0.001$) on (PNwt, POwt), this is also noted when compared healthy groups between each other TOC in (Hobese) group was a highly significant increase ($p < 0.001$) when compared to the (HNwt, HOwt) groups, while a highly significant decrease ($p < 0.001$) in

TAC in patients groups (PNwt, POwt&Pobese) was observed in comparison with their levels in corresponding healthy groups (HNwt, HOwt&Hobese), as well as highly significant decrease ($p<0.001$) in TAC of (Pobese group) was observed in comparison with their levels in corresponding (PNwt&POwt groups) that even noted when compared healthy groups between each other. A highly significant increase ($p<0.001$) in serum OSI of patient groups (PNwt, POwt&Pobese) in comparison to that of the healthy groups (HNwt, HOwt&Hobese). We measured total oxidant capacity, total antioxidant capacity and malondialdehyde concentrations in PCOS patients group (Pobese) in comparison with (PNwt, and POwt); a significant increase in TOC, OSI and MDA while a significant decrease in TAC were found (Table 5).

Table 5. mean $\pm$ SD of total oxidant capacity, total antioxidant capacity, oxidative stress index and malondialdehyde in sera of patients group (Pobese) comparison to other patient groups (PNwt, POwt).

Parameters	Group	Mean $\pm$ SD	Group	Mean $\pm$ SD	P-Value
TOC ($\mu\text{mol/L}$)	Pobese	40.99 $\pm$ 2.34	PNwt	31.06 $\pm$ 2.31	0.000**
			POwt	31.83 $\pm$ 2.53	0.000**
TAC ($\mu\text{mol/L}$)	Pobese	447.25 $\pm$ 10.81	PNwt	525.07 $\pm$ 13.59	0.000**
			POwt	484.81 $\pm$ 7.27	0.000**
OSI	Pobese	0.089 $\pm$ 0.004	PNwt	0.060 $\pm$ 0.002	0.000**
			POwt	0.066 $\pm$ 0.006	0.000**
MDA (nmol/L)	Pobese	39.63 $\pm$ 0.728	PNwt	36.33 $\pm$ 0.862	0.000**
			POwt	37.69 $\pm$ 0.906	0.000**

4. Conclusion

Obesity is common and complex disease. The worldwide prevalence of overweight and obesity has increased in all ages and both sexes. Overweight and obesity are characterized by excess amounts of body fat, their BMI are ≥ 25 and ≥ 30 kg/m², respectively; WHR and WHtR are also used for determination of obesity. Most persons are usual with the common health risks connected with obesity, including coronary artery disease, high blood pressure, type 2 diabetes, sleep apnea and cancer; however, fewer know that women affected by obesity are also more likely to face reproductive problems like polycystic ovarian syndrome (PCOS). Antioxidants that prohibit or reduce the damaging effects of oxygen radicals have been reported to have important roles in the female reproductive system and in the pathogenesis of its infertility[1,6]. The results of (Tables 2,3,4,5) show a highly significant increase ($p<0.001$) in oxidative stress indicators (TOC, OSI, and MDA) with a highly significant decrease ($p<0.001$) in TAC in sera of Hobese than in comparison with their levels in corresponding (HNwt&HOwt groups) that even noted when compared patient groups between each other. Likewise, women with PCOS had the same results according to the comparison between the two main groups (PCOS women verse apparently healthy women) as well as (HNwt, HOwt, Hobese) groups when compared with (PNwt, POwt, Pobese) groups. Therefore, PCOS subjected to an increased in OS situation, this can result from an imbalance between oxidants and antioxidants as clear from the results of the present study. Despite of this syndrome associated with many metabolic issues including obesity but many women with PCOS are likewise overweight or obese[10]. The observed increase in serum concentration of TOC may be due to increased oxidant molecules at the same

time in TAC (the accumulative of all antioxidants within body fluids including blood) which lead to the inability of antioxidants to control the oxidizing molecules and this caused a large increase in the free radicals which have the ability attack of phospholipids in the cell membrane and thus cause lipid peroxidation causing increasing MDA (a 3 carbon, low M.wt aldehyde) concentration. With this the changes in obese apparently healthy women was less than the obese PCOS women. The current study was in agreement with several authors for the TOC and TAC systems in PCOS. They found that patients with PCOS had significantly higher TOC and OSI and lower TAC than controls group [19,20]. Factors like obesity and hyperglycemia ordinarily detected in PCOS women are likely to contribute to an increase OS in PCOS individuals [21,22]. Physiological hyperglycemia generates increased ROS levels from mononuclear cells in these women. The increased OS makes an inflammatory environment that further elevates insulin resistance and participates to hyperandrogenism in these women[22,23]. Though OS is believed to be a potential inducement of PCOS pathogenesis, however it is still unknown whether the abnormal levels of OS markers in sera of PCOS patients derive from PCOS itself or they are related to the possible complications associated with PCOS[24]. Moreover, obesity mainly related to impairment in HPO axis (the hypothalamic-pituitary-ovarian); poor oocyte quality and altered endometrial receptivity. Obese women show poorer reproductive outcomes in any case of the mode of conception, and higher BMI is related to poorer fertility prognosis [25,26,27]. Our study was in agreement with several authors for the MDA in PCOS. They found that patients with PCOS had significantly higher MDA levels than the control group when using either serum or erythrocyte and tissue models[28,29]. it was proposed that increasing MDA could be due to increased generation of ROS which lead to increase the oxidation of many important biomolecules including membrane lipids[30]. The results of serum MDA disagree with some studies, such as the study by Karadeniz et al. (2008) that found MDA levels in PCOS patients were similar to those of controls[31]. The above data confirmed that obesity may be hard more common and needs more serious warning than we think. Lifestyle management of obesity for healthy individuals as well as the PCOS women is very important, it may be the main treatment of metabolic complications.

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