

# Protein Oxidation is Related to Body Mass Index in Obese Women

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## Abstract

Oxidative stress could be an early event in many pathological conditions, such as obesity. Additionally, advanced oxidation protein products (AOPPs) have been reported as the most appropriate parameter for determination of oxidative stress in chronic diseases. The aim of this study was to evaluate which oxidative stress biomarker is more related to obesity. This cross-sectional study evaluated 52 obese women aged (50, 5±1.06 years), and the participants were divided into three groups according to BMI: G1 (BMI 30-34.9 kg/m<sup>2</sup>), G2 (BMI 35-39.9 kg/m<sup>2</sup>) and G3 (BMI ≥40 kg/m<sup>2</sup>). Biochemical and oxidative stress biomarkers (FOX, AOPP and TRAP) were evaluated. The G3 group presented high levels of C reactive protein (CRP) when compared to G1 group (p<0.05), while serum AOPP levels were significantly increased in G3 group when compared to G1 and G2 and when G2 was compared to G1 (p<0.05). This study provided that serum levels of AOPP were elevated with increasing BMI and could be regarded as an early biomarker of protein oxidation in obese women.

**Keywords:** Obesity; Advanced Protein Oxidation; Oxidative Stress

## Introduction

Obesity, characterized by an increase in body weight that results in excessive fat accumulation, represents a social problem worldwide [1] and has been recognized as a major underlying factor in the pathogenesis of several diseases [2]. Several chronic diseases are the result of obesity (e.g. metabolic syndrome, diabetes mellitus, liver

and cardiovascular diseases, and cancer) and associated with oxidative stress (OS) [2]. Therefore, it has been hypothesized that inflammation of adipose tissue in obese patients plays a critical role in the pathogenesis of obesity-related complications [3]. OS, which is also referred to as a reactive oxygen species (ROS)-antioxidant imbalance, occurs when the net amount of ROS exceeds the antioxidant capacity. It has been suggested that oxidative stress could be an early event in

the pathology of the chronic diseases, rather than merely a consequence of this disorder [4].

Advanced oxidation protein products (AOPPs) have been reported as the most appropriate parameter for determination of oxidative stress in chronic diseases and are formed during oxidative stress by the action of chloraminated oxidants, mainly hypochlorous acid and chloramines, produced by myeloperoxidase in activated neutrophils [5]. An accumulation of AOPPs has also been considered the marker inflammation in diabetic and non-diabetic kidney and worsen inflammation and oxidative stress in artery in a hyperlipidemic model [6-8]. The aim of this study was to evaluate whether oxidative stress, represents mainly by protein oxidation, increases with increasing body mass index (BMI) in obese women.

## Patients and Methods

This cross sectional evaluated 52 obese women aged (50,5±1,06 years) selected among Internal Medicine ambulatory patients of the University Hospital of Londrina, Paraná, Brazil. Obesity criteria was defined following the World Health Organization (WHO) and the participants were divided into three groups according to (BMI), G1 (BMI 30-34.9 kg/m<sup>2</sup>), G2 (BMI 35-39.9 kg/m<sup>2</sup>) and G3 (BMI≥40 kg/m<sup>2</sup>). After fasting for 12 hours, the participants underwent the following laboratory blood analysis: triacylglycerol TG, total cholesterol, HDL-C, LDL-C, fasting glucose, uric acid which were evaluated by a biochemical auto-analyzer (Dimension Dade AR, Dade Behring, Deerfield, IL, USA), using Dade Behring kits. Plasma insulin levels were determined by MEIA (AXSYM, ABBOTT® Laboratory) and serum highly sensitive C-reactive protein (CRP) was measured using a nephelometric assay (Behring Nephelometer II, Dade Behring, Marburg, Germany). The Homeostasis Model Assessment insulin resistance (HOMA-IR) was calculated as follows: fasting insulin (μU/mL) x fasting glucose (mmol/L) / 22.5.

Analysis of plasma hydroperoxide concentrations by tertbutyl hydroperoxide-initiated chemiluminescence was evaluated [9] and results were expressed in counts per minute (cpm). Plasma lipid hydroperoxides levels were also determined by FOX assay [10] and results were expressed in mmol/L. Advanced oxidation protein products were determined in the plasma using the semiautomated method described by Witko-Sarsat et al [11]. Concentrations of AOPPs were expressed as micromoles per liter of chloramines-T equivalents. The total radical-trapping antioxidant parameter (TRAP) was determined as reported by Repetto et al [12]. This method detects hydrosoluble and/or liposoluble plasma antioxidants by measuring the chemiluminescence inhibition time induced by 2,2-azobis (2-amidinopropane). The system was calibrated with the vitamin E analog TROLOX, and the values of TRAP are expressed in equivalent of μM Trolox. As described in previous studies, TRAP was expressed after correction by uric acid levels [13].

Data are expressed as medians and inter quartile range (25%-75%). Wilcoxon test with post hoc Dunn was performed. The results were considered significant when  $p < 0.05$ . A statistical analysis program (Graph Pad Instant; Graph Pad Software, Inc, California, CA, USA) was used for evaluations.

## Results

The anthropometrical, biochemical and oxidative biomarkers are presented in (Table 1). As expect, with regard to anthropometrical parameters, there was a significantly increase in BMI and waist circumference (WC) according to obese grade ( $p < 0.05$ ). The G3 group presented high levels of C reactive protein (CRP) when compared to G1 group ( $p < 0.05$ ), while serum AOPP levels were significantly increase in G3 group when was compared to G2 and G1 groups and when G2 was compared to G1 group ( $p < 0.05$ ).

Parameters	G1 (BMI 30-34.9) (n: 16)	G2 (BMI 35-39.9) (n: 12)	G3 (BMI <sup>3</sup> 40) (n: 24)
Age (years)	50.5 (28-62)	50.5 (38-67)	50.0 (29-61)
BMI (kg/m <sup>2</sup> )	32.8 (30.0-34.6)	36.6 (35.2-38.7)	43.9 (40.0-52.1) a,b,c
WC (cm)	105 (93-114)	118 (105-126)	122 (108-140) a,b
SBP (mmHg)	123 (76-147)	126 (100-148)	139 (104-171)
DBP (mmHg)	79 (38-93)	75 (56-110)	80 (50-146)
TC (mg/dL)	176 (147-308)	196 (133-313)	209 (128-274)
HDL-C (mg/dL)	47 (29-59)	47.5 (33-64)	43 (32-67)
LDL-C (mg/dL)	116 (66-235)	116 (47-229)	127.5 (50-179)

TG (mg/dL)	143 (67-549)	122.5 (67-274)	215 (48-587)
Fasting glucose (mg/dL)	100 (84-110)	113.5 (85-155)	107 (88-372)
Fasting insulin (mg/dL)	11.3 (4.0-21.6)	12.4 (4.5-17.8)	15.35 (6.7-64.1)
HOMA-IR	2.9 (2.2-5.4)	3.5 (0.9-6.6)	4.3 (1.5-16.1)
Uric acid (mg/dL)	5.2 (1.7-8.2)	4.9 (2.7-7.2)	4.9 (3.4-7.1)
CRP (mg/dL)	2.9 (0.4-17.2)	8.2 (1.8-21.5)	11.2 (4.2-33.4)* b
Hydroperoxides (cpm)	14119 (7542-29085)	17887 (13291-26399)	16138 (10498-23451)
FOX (mM)	1.34 (0.43-2.35)	1.37 (0.54-2.82)	1.45 (0.36-3.23)
AOPP (mmol/L)	125.6 (79.4-225.7)	216.0 (103.9-387.3)	276.0 (141.1-545.6)* a,b,c
TRAP/uric acid index	173.7 (97.3-216.1)	166.3 (103.9-202.8)	160.4 (107.8-245.1)

Table 1: Anthropometric, biochemical and oxidative stress measurements according to the body mass indexes.

Wilcoxon test with post hoc Dunn was performed. Data are median and inter quartiles (25%-75%). BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC: total cholesterol; HDL-C: high density lipoprotein; LDL-C: low density lipoprotein; TG: triacylglycerol; HOMA-IR: Homeostasis Model Assessment-Insulin resistance; CRP: C reactive protein; FOX: Ferrous oxidation xilenol-orange assay; AOPP: Advanced oxidation protein products; TRAP: Total radical trapping antioxidant parameter; \*p<0.05; a: G1xG2; b: G1xG3; c: G2xG3.

## Discussion and Conclusion

The main finding of this study was that levels of advanced oxidation protein products (AOPPs) are closely linked to obesity. AOPPs have been studied in several metabolic conditions, such as in overweight subjects [13,14], and in patients with obesity [14,15], type 1 diabetes mellitus [15,16], type 2 diabetes mellitus [17] and Mets [18-20]. We have also revealed that AOPP raised progressively with the increase of fat mass assessed by body mass Index in obese women with BMI higher as 30. Piwo war et al (2007) demonstrated in type 2 diabetes patients significantly higher concentration of AOPP, especially in subgroups with macroangiopathy and obesity [17].

In this study was no statistical difference between the groups in relation to the parameters of lipid per oxidation and antioxidant capacity, possibly because the three groups studied were obese and the degree of obesity did not influence these parameters. Susceptibility to oxidative damage is even greater in obese subjects because of depleted antioxidant sources, including superoxide dismutase (SOD), glutathione peroxides (GPx), and catalase (CAT), vitamin A, vitamin E, vitamin C, and  $\beta$ -carotene [21]. Compared to normal weight a patient, the activity of SOD in obese individuals is significantly lowers [22].

On the other hand, serum hsCRP levels, a marker of chronic low-grade inflammation, is known to be a sensitive predictor of cardiovascular disease and is

related to obesity. In the present study, hsCRP levels were significantly higher in obese with BMI>40, demonstrating that obesity presents a low grade inflammation [23].

The current study has some limitations to be considered. First is the small number of participants; second, this cross sectional study is unable to determine causality between obesity and protein oxidation, third, we evaluated only women, which limits generalizability to men. In conclusion, this study demonstrated that serum levels of AOPP were elevated with increasing BMI and could be regarded as an early biomarker of protein oxidation in obese women.

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