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# Study on oxidant and antioxidant status in obese individuals

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**Abstract:**

Obesity is pertinent to a proinflammatory state, which contributes to chronic inflammation and oxidative stress, both of which lead to the onset of obesity-related problems. An imbalance in the oxidant-antioxidant systems favoring prooxidants results in oxidative stress, which may be detected by monitoring several indicators. The purpose of this study is to assess oxidant and antioxidant levels in obese subjects. This Case-Control research included 45 apparently healthy people and 41 non-obese apparently healthy adults over the age of 18 who were attending the Endocrinology and Metabolism department. Overnight fasting plasma samples were taken in order to test Serum oxidant and antioxidant levels. Serum malondialdehyde and protein carbonyl content levels in the obese group were significantly greater than in the non-obese group ($p<0.001$). Furthermore, the obese group's mean levels of the antioxidant indicators FRAP and protein thiols were considerably lower than the non-obese group (p0.001). The connection of BMI indicated a significant positive correlation with MDA and PCC and a negative correlation with antioxidant variables FRAP and protein thiols. The occurrence of greater MDA and protein carbonyl levels in obese patients in the current study indicates increased oxidative stress, according to our findings. Furthermore, obese persons have a poor antioxidant state, as seen by low antioxidant indicators FRAP and thiols.

**Keywords-** malondialdehyde; protein carbonyl content; ferric reducing ability of plasma; protein thiols

## Introduction

Obesity is a disorder characterized by an excess of adipose tissue mass that results from an imbalance between calorie intake and calorie utilization by the body. It is classified as a kind of malnutrition characterized by excessive fat accumulation, which can have a negative impact on health.

Body mass index (BMI) is a popular measure of a person's weight status. BMI is a basic weight-for-height index that is defined as a person's weight in kilograms (kg) divided by his height in meters squared ($kg/m^2$).[1] Overweight and obesity, formerly thought to be developed-country health issues, are increasingly emerging as important public health issues in developing nations.

Overweight and obesity have nearly increased globally over the last three decades, with around one-third of the entire population classified as overweight or obese.[2] According to Kelly et al., if the current trend continues, this might reach an alarming level of 57.8% by 2030.[3]

The mechanism underlying the course of development of obesity-related complications is not fully understood; recent studies show that obesity coincides with a pro-inflammatory state, which results in prolonged inflammation and oxidative damage, both of the factors associated with the occurrence of obesity-related hazards.[4]

Lipid peroxidation (LPO) is the oxidative breakdown of polyunsaturated lipids, which has been linked to chronic diseases such as obesity. Malondialdehyde (MDA) is a prominent byproduct of lipid peroxidation and is commonly used as a marker of lipid oxidative damage.[5] Lipid peroxidation products may potentially contribute to endothelial damage and produce oxidative changes in low-density lipoproteins. Various markers of free radical-mediated damage are utilized as indications of oxidant status.

CRP (C- reactive protein) sensitivity and other oxidative stress indicators are greater in obese people and correlate directly with BMI and body fat percentage, LDL (Low-density lipoproteins) oxidation, and TG (Triglyceride) levels.[6] In contrast, antioxidant defense indicators are decreased when body fat and central obesity increase.[7,8] Studies have shown that a high-fat, high-carbohydrate diet dramatically increases OS and inflammation in obese people.[9]

The innate immune system in adipose tissue is activated, which promotes pro-inflammatory state and oxidative stress, resulting in a systemic acute-phase response. As a result, it has been proposed that adipose tissue inflammation in obese people is important in the aetiology of obesity-related problems. [10] Adipokines also stimulate the generation of ROS under physiological and pathological situations, resulting in OS. [11] Several processes contribute to obesity-related OS. Furthermore, obese people have lower antioxidant levels, which makes them more susceptible to oxidative stress.

Additionally, oxidative stress can damage cellular structures, leading to the development of obesity-related problems. As a result of a rise in OS, the risk of problems develops in overweight and obese patients, and investigations were undertaken to determine the existence of oxidative stress in obese persons using several markers.[12]

When compared to normal weight patients, Ahmed et al. found considerably greater MDA and lower reduced glutathione (GSH) levels in overweight and obese subjects. Increased amounts of free radicals and/or reduced antioxidants cause oxidative stress, which has been linked to a variety of disorders in both human and animal obesity models.[13]

Agrawal et al., similarly, confirmed the presence of oxidative stress in obese participants by identifying elevated MDA levels as well as decreased superoxide dismutase (SOD) activity. They also discovered a positive link between MDA and BMI and an inverse relationship between SOD and BMI, indicating that in obesity, the oxidant-antioxidant balance is disturbed, which results in elevated oxidative damage in the body. [14]

The aldehydes generated as a result of free radical lipid peroxidation covalently alter proteins at histidine, lysine, and cysteine residues in a process known as protein carbonylation. The side chains of these amino acids are important in enzymatic protein activities or protein-protein interactions. As a result, protein carbonylation may result in protein function reduction or even protein loss.

Protein carbonylation occurs at a faster rate in the adipose tissue of obese persons than in lean patients, according to Frohnert et al. As a result, higher protein carbonyl content in obese persons has been documented and is used as a biomarker of oxidative stress. [15]

Uzun et al. revealed that morbidly obese patients had considerably higher plasma protein carbonyl concentrations and lower plasma and erythrocyte thiol concentrations than controls. Furthermore, when these obese people had laparoscopic adjustable gastric banding, their PCO was reduced and their thiol concentration increased after losing weight post-surgery.[16]

Furthermore, studies have indicated that weight loss in obese people by basic methods such as dietary changes and exercise helps to reduce oxidative vulnerability. In light of this, the current investigation was undertaken to assess the oxidant-antioxidant status of obese people.

## Materials and Methods

This observational Case-Control study included 45 apparently healthy subjects and 41 non-obese apparently healthy individuals over the age of 18 who attended the Endocrinology and Metabolism outpatient department, met the selection criteria, and were willing to participate after receiving informed consent.

**Inclusion Criteria:**

Obese subjects: Apparently healthy subjects over 18 years of age and with BMI $\geq$25 Kg/m$^2$ (obese) were included.

Non-obese subjects: Age and gender-matched apparently healthy subjects over 18 years of age and with BMI < 23 Kg/m$^2$ were included.

**Exclusion Criteria:**

Diabetes mellitus, Hypertension, Smoking and alcoholism, Cardiovascular disease, Liver and kidney diseases, Thyroid disorders, Acute or chronic inflammation, Polycystic ovary syndrome in women, Pregnant and lactating women, Medication such as steroids, antipsychotic drugs, and antioxidants.

## Measurement of laboratory parameters

Samples were collected after obtaining regulatory clearance from Institutional Ethics Committee [IEC No. 987]. Six mL of venous blood was collected into additive-free tubes from all the subjects after overnight fasting. Samples were allowed to stand for 30 minutes and centrifuged at 2000 revolutions per minute for 15 minutes. The separated plasma and serum were stored at -80ºC for biochemical analysis.

**Statistical Analysis:**

Continuous values were reported as mean SD, and categorical variables as percentages. To determine if the distribution of continuous variables was normal, the Kolmogorov-Smirnov test was utilized. To examine the significance of the difference in means between the control and obese groups, the unpaired two-tailed t-test was utilized. Depending on the data distribution, Pearson correlation analysis will be used to investigate the relationship between variables. A p-value of <0.05 was deemed statistically significant. Microsoft Excel spreadsheets and SPSS for Windows version 16.0 were used for statistical analysis.

**RESULT**

The current case-control research compared oxidant-antioxidant status in apparently healthy non-obese and obese people. The study also intended to determine the relationship between body mass index and oxidative stress indicators in the participants. The study comprised 41 obese people who were defined as obese according to WHO standards using Asian population cut-offs and compared them to 45 non-obese people. Oxidative stress indicators were assessed in both groups. Table-1 demonstrates the demographic information as well as the markers analyzed.

**Table-1. Demographic data and the markers studied in non-obese and obese subjects**

| Parameter | Non-obese | Obese | p-value |
|---|---|---|---|
| N | 45 | 41 | - |
| M/F | 08/37 | 15/26 | - |
| Age (years) | 25.33±7.75 | 28.8±9.13 | 0.062 |
| WC (cm) | 73.55±6.54 | 95.56±10.70 | <0.001 |
| HC (cm) | 91.73±5.15 | 109.46±7.19 | <0.001 |
| BMI ($Kg/m^2$) | 20.89±1.64 | 29.06±3.20 | <0.001 |
| MDA (µM/L) | 1.11±0.31 | 1.42±0.45 | <0.001 |
| PCC (nmol/mg protein) | 0.84±0.12 | 0.96±0.18 | <0.001 |
| FRAP (µMl/L) | 1063.20±154.20 | 965.30±131.20 | 0.002 |
| PT (nM/mL) | 331.60±53.10 | 301.20±44.31 | 0.005 |
| TP (g/dL) | 6.50±0.64 | 6.70±0.66 | 0.058 |

**Data presented as mean±SD, p<0.05 is considered statistically significant**
**N=sample size; M/F=male/female; WC=waist circumference; HC=hip circumference; BMI=body mass index; MDA=malondialdehyde; PCC=protein carbonyl content; FRAP=ferric reducing ability of plasma; PT=protein thiols; TP=total proteins**

As shown in Table-1 the study groups were matched with respect to age (p=0.062). The anthropometric parameters measured and calculated including waist circumference, hip circumference, and BMI were significantly higher in obese subjects compared to non-obese subjects (p<0.001).

The markers of oxidant status MDA and PCC were significantly higher (p<0.001) while the antioxidant

markers FRAP and PT were significantly lower (p=0.002 for FRAP and p=0.005 for PT) in obese individuals when compared to non-obese individuals.

***Table-3. Correlation of body mass index with the study parameters***

| Parameter | Correlation coefficient | p-value |
|---|---|---|
| AGE | 0.243 | 0.024 |
| WC | 0.816 | <0.001 |
| HC | 0.910 | <0.001 |
| MDA | 0.321 | 0.003 |
| PCC | 0.357 | 0.001 |
| FRAP | -0.226 | 0.037 |
| PT | -0.234 | 0.030 |

**p<0.05 is considered statistically significant**
**WC=waist circumference; HC=hip circumference; MDA=malondialdehyde;**
**PCC=protein carbonyl content; FRAP=ferric reducing ability of plasma; PT=protein thiols**

The correlation of BMI with the study parameters analyzed using Pearson's correlation analysis is shown in Table-2. BMI showed a significant positive correlation with WC, HC, MDA, and PCC (r=0.321; p=0.003 for MDA and r=0.357; p=0.001 for PCC) (Table-2) (Fig 1).and negative correlation with markers of antioxidant status FRAP and protein thiols (r=-0.226; p=0.037 for FRAP and r=-0.234; p=0.030 for PT) (Fig 2).

**Figure-1. Correlation of body mass index with Malondialdehyde and protein carbonyl content**

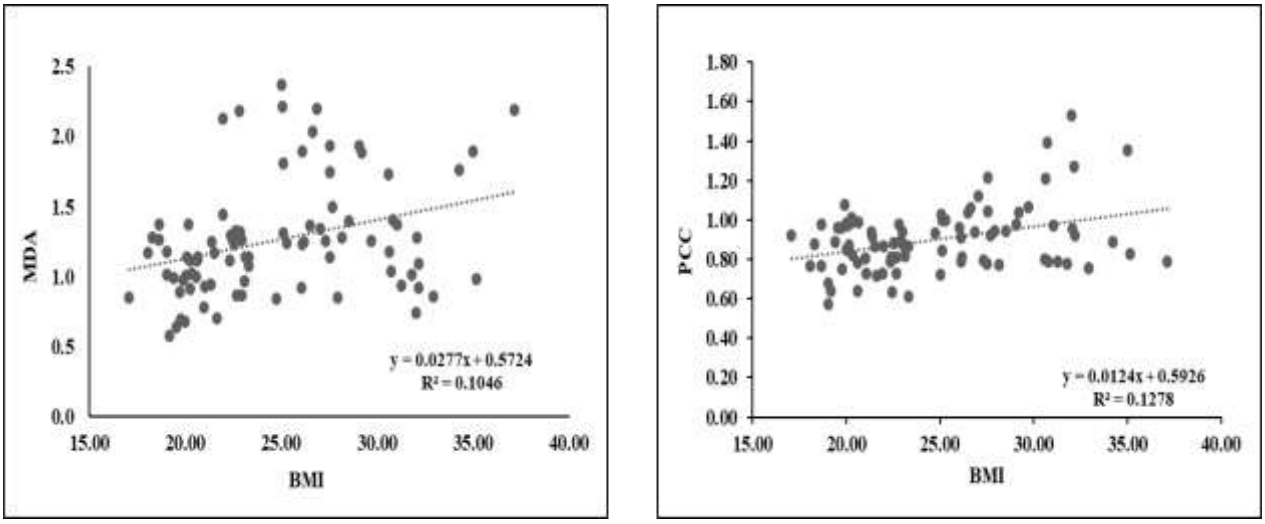
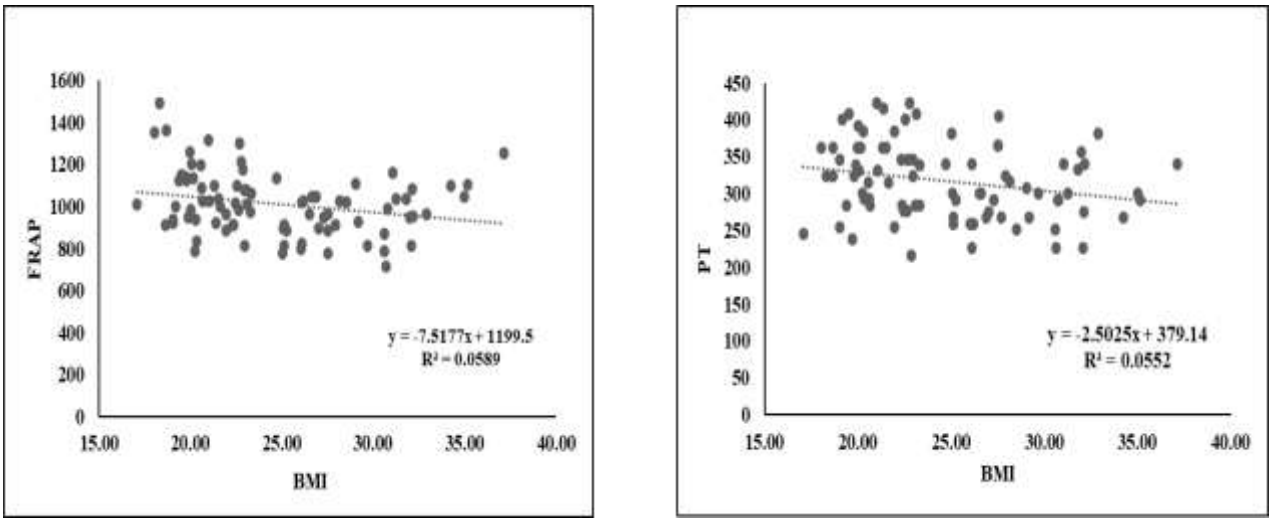


**Figure-2. Correlation of body mass index with ferric reducing ability of plasma and protein thiols**




## DISCUSSION

Obesity raises morbidity by increasing the risk of many chronic illnesses. Although the mechanism underlying the development of obesity-related complications is not fully understood, recent research indicates that obesity is associated with a proinflammatory state, which leads to chronic inflammation and oxidative stress, both of which are implicated in the development of obesity-related complications.[17]

The current study included 41 Asian Indians who were classed as obese according to WHO standards and were compared with 45 non-obese individuals. The two groups were matched for age (25.33±7.75 and 28.8±9.13 years for non-obese and obese subjects, respectively; p=0.062). The BMI ($Kg/m^2$), WC (cm), and HC (cm) of the obese subjects were significantly higher than non-obese subjects ($p<0.001$). It was found that the serum levels of MDA of obese subjects were significantly higher ($p<0.001$) when compared to non-obese individuals (1.11±0.31 and 1.42±0.45 µM/L for non-obese and obese subjects, respectively). Similarly, the PCC of obese subjects was significantly higher ($p<0.001$) than non-obese subjects (0.84±0.12 and 0.96±0.18 nmol/mg of protein for non-obese and obese subjects, respectively).

The existence of oxidative stress in obesity has therapeutic implications since it raises the risk of problems in obese people and is reversible. Yesilbursa et al. investigated the effect of weight reduction on lipid peroxide levels in obese participants using Orlistat, a medicine used to treat obesity. They discovered that MDA levels, which were considerably higher in obese participants at baseline, decreased significantly after 6 months of therapy, as did anthropometric indicators such as mean weight, BMI, waist and hip circumference, and lipid profile levels. Variations in BMI correlated with a decrease in MDA levels.

When morbidly obese individuals were compared to controls, their plasma protein carbonyl content was considerably higher. Furthermore, PCO levels were reduced after weight loss laparoscopic surgery. Thus, these studies show that losing weight has a positive effect on oxidative stress in obese

people. [18]

In opposition to the current study's findings, Yigitbasi et al. reported no significant difference in the total oxidant status, total antioxidant status, and oxidative stress index levels of obese and non-obese subjects, implying that there is no impairment of oxidant-antioxidant control in obesity. [19]

The progression of oxidative stress in obesity is caused in a number of ways. Obesity is defined as an excess of adiposity. Adipose tissue, which was formerly thought to be only a fat storage tissue, is now recognized as an active organ consisting of adipocytes and other cells that emit a variety of hormones and cytokines (adipocytokines) with a variety of critical activities.[20]

As a result of the increased oxidative stress, the rate of lipid peroxidation rises, as indicated by higher MDA levels in the current research. The aldehydes generated as a result of free radical lipid peroxidation further covalently alter proteins at particular amino acid residues by carbonylation, resulting in elevated quantities of protein carbonyls as shown in obese participants in the current research.

The ensuing OS might increase the risk of metabolic syndrome in fat people, and it has been observed that the chance of developing metabolic syndrome is higher in those who are overweight or obese.

Bitla et al., who studied oxidative stress in patients with metabolic syndrome, revealed that obese metabolic syndrome patients had considerably higher MDA levels than age and gender-matched healthy controls.

Similarly, Singh et al. discovered that the erythrocyte MDA and protein carbonyl content was highest in obese subjects with metabolic syndrome when compared to obese subjects without metabolic syndrome and normal BMI subjects when they studied various oxidant antioxidant markers in obese subjects with and without metabolic syndrome.[21,22]

The Pearson correlation analysis was used to examine the relationship between oxidative stress biomarkers and BMI. It was shown that BMI was strongly positively linked with MDA and PCC ($r=0.321$; $p=0.003$ for MDA and $r=0.357$; $p=0.001$ for PCC) (Table-2 and Figure-2). These data suggest that oxidative damage indicators are greater in obese people and correspond directly with body mass index.

In the present study, FRAP and protein thiols were measured in all the subjects as indicators of antioxidant status. It was observed that the levels of FRAP (1063.20±154.20 and 965.30±131.20 µM/L for non-obese and obese subjects, respectively) and thiols (331.60±53.10 and 301.20±44.31 nM/mL for non-obese and obese subjects, respectively) were significantly lower ($p=0.002$ and $p=0.005$ for MDA and PCC, respectively) in obese individuals when compared to non-obese subjects.

Earlier research integrating several enzymatic and non-enzymatic indicators found that obese people had a decreased antioxidant level. Chielle et al. discovered that blood and salivary levels of FRAP were considerably higher in obese people than in normal-weight people. When compared to the normal-weight group, blood levels of thiol groups were considerably lower in the obese group. [23]

While lipid hydroperoxides were found to be considerably higher in obese patients, total antioxidant status, superoxide dismutase, and reduced glutathione did not indicate a significant difference between obese, overweight, and normal-weight subjects, according to Brown et al. [24]

When the relationship between BMI and the antioxidant indicators was examined using correlation analysis, it was shown that BMI had a significant negative connection with FRAP and thiols ($r=-0.226$;

p=0.037 for FRAP and r=-0.234; p=0.030 for PT).

Kilic et al. discovered that total thiol groups were substantially adversely linked with BMI in obese children, which is similar to the current study. They did, however, notice an increase in total antioxidant status in these children that was positively connected with BMI, suggesting that the enhanced total antioxidant status might be a counter-balancing impact. [25]

Thus, blood levels of MDA and PCC, which are markers of oxidant status, were higher in obese people compared to non-obese persons in the current investigation. The antioxidant indicators FRAP and protein thiols, on the other hand, were shown to be considerably lower in obese persons than in non-obese participants. Furthermore, MDA and PCC were shown to have a substantial positive connection with BMI, whilst FRAP and thiols were found to have a significant negative association with BMI. As a result, these data point to the occurrence of oxidative stress in obese people.

Obesity-related adipose tissue deposition predisposes to a state of subclinical inflammation, which leads to the development of oxidant-antioxidant imbalance and, eventually, oxidative stress. Inflammation and oxidative stress are major contributors to atherosclerosis and CVD etiology. As a result, suitable actions to reduce obesity may not only enhance the quality of life but also assist to lower the risk of obesity-related problems.

## CONCLUSION

Excess adipose tissue causes a continuous low-grade inflammatory state, which leads to the production of free radicals and consequent oxidative stress. The oxidative damage generated by free radicals to biomolecules such as lipids and proteins leads to increased lipid peroxidation and protein oxidation, as shown by higher levels of MDA and protein carbonyls.

Thus, greater MDA and protein carbonyl levels in obese people in the current research imply increased oxidative stress. Furthermore, obese persons have a poor antioxidant state, as seen by low antioxidant indicators FRAP and thiols.

The results of the correlation analysis indicated that when BMI increases, so does oxidative stress. Obesity reduction has been proven to improve oxidant-antioxidant status. As a result, suitable weight-loss methods may aid in increasing quality of life and reducing obesity-related diseases.

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