

## Original Research Article

# Obesity: an independent risk factor for oxidative stress

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**Received:** 28 February 2017

**Accepted:** 28 March 2017

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### ABSTRACT

**Background:** Obesity is increasing in prevalence and presents a serious risk for the development of various disorders like diabetes mellitus, hypertension, heart disease, gall bladder disease and certain forms of cancer. Animal studies have shown that obesity is associated with increased myocardial oxidative stress and increased lipid peroxidation. The objective of this study was to test the hypothesis that obesity per se causes increased plasma lipid peroxidation and decreased erythrocyte cytoprotection.

**Methods:** A prospective randomized study including 300 obese subjects, was conducted in the Department of Medicine and Department of Biochemistry, G. R. Medical College, Gwalior. Age and sex matched 100 subjects having BMI between 19 to 25 kg/m<sup>2</sup> were also enrolled. Patients were grouped as Case (n=300) and Control (n=100). Detailed physical examination and laboratory investigations including lipid profile were performed. Venous blood was obtained and used for the estimation of Superoxide dismutase (SOD) and plasma malondialdehyde (MDA). Unpaired t test and analysis of variance (ANOVA) with post-hoc Bonferroni and Tukey test along with Pearson correlation was used to analyze the data using IBM SPSS ver. 20 software. Significance is assessed at 5 % level.

**Results:** Mean age of subjects among Case and Control group was 46.2±2.4 years and 44.5±2.2 years respectively with male predominance in each group. Mean weight, height, BMI, waist, hip, waist to hip ratio, mean blood glucose, total cholesterol, triglyceride, LDL-C, HDL-C and VLDL-C among Cases were 91.57±9.8 kg, 161.6±9.3 cm, 36.17±3.4 kg/m<sup>2</sup>, 114.7±6.2 cm, 114.23±17.12 cm, 0.98±0.22, 87.3±2.6 mg/dl, 196.0±12.6 mg/dl, 253.6±27.3 mg/dl, 135±47.03 mg/dl, 47.1±1.2 mg/dl and 45.8±14.03 mg/dl and among Control group were 61±5.2 kg, 163.1±8.7 cm, 21.24±1.88 cm, 21.24±1.88 kg m<sup>2</sup>, 85.2±1.4 cm, 97.32±9.12 cm, 0.86±0.14, 94.4 ± 3.2 mg/dl, 186.6 ± 6.9 mg/dl, 143.4±15.4 mg/dl, 95.73±27.48 mg/dl, 51.6±1.7 mg/dl and 22.4±10.45mg/dl respectively. Mean MDA level in Case and Control group was 4.68 ± 1.72 and 2.06±0.76 µmol/ml respectively (p< 0.001). Mean SOD level among Case and Control groups was 7.65±1.13 and 12.42±2.18 units/ml respectively (p<0.001). Female obese patients had lower level of SOD. A significant negative correlation of SOD was observed with BMI (n=300, r= -0.045, P<0.001), whereas, MDA was positively correlated with BMI (n=300, r= 0.342, P<0.001).

**Conclusions:** Obesity in humans is an independent risk factor for lipid peroxidation and depletion of cytoprotective enzymes even in the absence of other confounding factors such as diabetes and hyperlipidaemia.

**Keywords:** Lipid peroxidation, Obesity, Plasma malondialdehyde, Superoxide dismutase

### INTRODUCTION

Obesity is a chronic disease that is increasing in prevalence and poses a serious risk for the development

of various disorders like diabetes mellitus, hypertension, heart disease, gall bladder disease and certain forms of cancer. The degree of overweight can be expressed in several ways, but the most useful is the body mass index

(BMI).<sup>1</sup> Healthy weights is defined as a BMI between 19 to 25 kg/m<sup>2</sup>. Overweight is a BMI of 25 - 30 kg/m<sup>2</sup>. A BMI greater than 30 kg/m<sup>2</sup> is almost always associated with an increase in body fat and is synonymous with obesity, except in body builders and other athletes.<sup>1</sup>

Obesity has many negative effects on health. Various lipid/lipoprotein abnormalities have been observed in obese individuals, including elevated cholesterol, triglycerides, and apolipoprotein B (apoB); lower high-density lipoprotein cholesterol (HDL-C) levels.<sup>2,3</sup>

Lipid peroxidation is a free radical-generating process which occurs in every membranous structure of the cell. Obesity promotes increased plasma lipid peroxidation which has been confirmed by the findings in experimental rat models.<sup>4</sup> Lipid peroxidation in obese human subjects has been reported by previous workers.<sup>5,6</sup>

The objective of this study was to study that obesity per se causes increased plasma lipid peroxidation and decreased erythrocyte cytoprotection.

## METHODS

The present prospective randomized study including subjects with obesity was conducted in the Department of Medicine and Department of Biochemistry, G. R. Medical College, Gwalior. A total 300 patients were enrolled and compared with randomly chosen age and sex matched 100 subjects having BMI between 19 to 25 kg/m<sup>2</sup>. Patients were grouped as Case (n=300) and Control (n=100).

Male or female obese subjects defined as BMI > 25 kg/m<sup>2</sup>, age > 18 years and patients willing to give written consent were included. Patients with any severe or critical illness, pregnant and lactating women and patients with history of smoking, diabetes, hypertension and liver or renal disease were excluded from the present study.

The written consent was taken from all the subjects. The approval from Institutional Ethics committee was taken. All patients had undergone the detailed physical examination and laboratory investigations including lipid profile. BMI for each individual was calculated as weight divided by height squared and was used to grade the obesity.

5 ml of venous blood samples were obtained from median cubital vein and collected in standard tubes containing ethylenediamine tetra acetic acid (EDTA). Superoxide dismutase (SOD) and plasma malondialdehyde (MDA) were determined by the method of Mishra et al (1972) and Jean et al (1983) respectively.

All the analysis was done with IMB SPSS ver. 20 software. Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on mean± standard deviation

(SD). Unpaired t test and analysis of variance (ANOVA) with post-hoc Bonferroni and Tukey test was used to find out the significance between two and more than two groups respectively. Pearson correlation test was used to find correlation between study parameters. Significance is assessed at 5 % level.

## RESULTS

Mean age of subjects among Case and Control group was 46.2±2.4 years and 44.5±2.2 years (p>0.05) respectively. Male predominance was observed in both Case (61.33%) and Control group (54%) (p> 0.05).

MDA level in Control group ranged from 0.96 µmol/ml to 4.76 µmol/ml with a mean value of 2.06±0.76 µmol/ml whereas in Case group value ranged from 1.27 µmol/ml to 7.94 µmol/ml with mean of 4.68±1.72 µmol/ml (p< 0.001). Mean MDA level among male and female of Case and Control groups was 4.66±1.43 versus 5.03±1.26 µmol/ml (p<0.001) and 1.34±0.23 versus 1.49±0.14 µmol/ml (p<0.001) respectively (p<0.001 between groups).

SOD Level in control group ranged from 5.52 units/ml to 19.87 units/ml with mean value of 12.42±2.18 units/ml whereas in Case group it ranged from 2.68 units/ml to 13.7 units/ml with mean value of 7.65±1.13 units/ml (p<0.001). Mean SOD level among male and female of Case and Control groups was 7.16±1.01 versus 7.87±0.05 units/ml (p<0.05) and 11.38±0.21 versus 12.31±1.12 units/ml (p<0.05) respectively (p<0.05 between groups).

**Table 1: Baseline parameters among both the groups.**

| Parameters               | Case         | Control     | P value |
|--------------------------|--------------|-------------|---------|
| Weight (Kgs)             | 91.57±9.8    | 61±5.2      | <0.001  |
| Height (cm)              | 161.6±9.3    | 163.1±8.7   | NS      |
| BMI (kg/m <sup>2</sup> ) | 36.17±3.4    | 21.24±1.88  | <0.001  |
| Waist (cm)               | 114.7±6.2    | 85.2±1.4    | <0.001  |
| Hip (cm)                 | 114.23±17.12 | 97.32±9.12  | <0.001  |
| W/H ratio                | 0.98±0.22    | 0.86±0.14   | <0.001  |
| FBG (mg/dL)              | 87.3±2.6     | 94.4±3.2    | NS      |
| TC (mg/dL)               | 196.0±12.6   | 186.6±6.9   | <0.05   |
| TG (mg/dL)               | 253.6±27.3   | 143.4±15.4  | <0.001  |
| LDL-C (mg/dL)            | 135±47.03    | 95.73±27.48 | NS      |
| HDL-C (mg/dL)            | 47.1±1.2     | 51.6±1.7    | NS      |
| VLDL-C (mg/dL)           | 45.8±14.03   | 22.4±10.45  | <0.001  |

Data is expressed as mean± SD, P <0.001 is considered to be highly significant, NS; non-significant. FBG; fasting blood glucose, TC; total cholesterol, TG; triglyceride, LDL-C; low density lipoprotein cholesterol, HDL-C; high density lipoprotein cholesterol, VLDL-C; very low density lipoprotein cholesterol.

## DISCUSSION

Lipid peroxidation is a free radical-generating process which occurs on every membranous structure of the cell.

Free radicals are known to be involved in a number of human pathologies including atherosclerosis, cancer and hypertension.<sup>1</sup> The study was done to find association between obesity and lipid peroxidation. The mean age was similar in both the groups, eliminating the confounding effect of age on lipid peroxidation and enzyme activity. Gopal et al did a similar study on 80 patients and reported no significant difference in the mean age and gender of participants between the groups.<sup>7</sup> Bitla et al has also reported a mean age of 47.3±2.6 years and 42.1±1.8 years among Case and Control groups which is almost similar to present study.<sup>8</sup>

Anthropometric measurements of case and control groups showed that except for height of patients, all other characteristic had statistically significant difference ( $p < 0.05$ ). In present study, weight, BMI, waist, hip and waist to hip ratio were higher in case group compared to control group. Results reported by Selvakumar, Olusiand Gopaletal were consistency with the present study data.<sup>1,7,9</sup>

There was no significant difference in both the groups in blood glucose, LDL-C, HDL-C. Nirmitha et al reported that HDL, LDL and VLDL were comparable between both the groups.<sup>10</sup> Other lipid parameters like total cholesterol, triglycerides and VLDL-C were statistically different in both the groups ( $p < 0.05$ ) which shows that obese individuals with higher BMI tend to have altered lipid profiles. Patel et al has also reported non-comparable LDL levels between obese and control group but levels of TC, TAG and HDL levels were significantly higher ( $p < 0.001$ ) in obese compared to non-obese.<sup>11</sup> There was a propensity for hypercholesterolemia in the case group compared to control group, especially in male patients. Hormonal changes in female at puberty may act as a protective factor against changes in lipid profile. Before and after menarche, changes in lipid profile are sensitive to the influence of sex hormones, especially estrogen, which has a favorable effect on lipoproteins by increasing HDL-C and reducing LDL-C levels. In this context, females are at an advantage during adolescence and adulthood.<sup>6</sup> MDA is a three carbon, low molecular weight aldehyde that can be produced from free radical attack on polyunsaturated fatty acids of biological membranes.<sup>10</sup> The determination of MDA is used for monitoring lipid peroxidation in biological samples.

The MDA level in Case group was higher as compared to Control ( $p < 0.001$ ). This is in agreement with previous reports of increased MDA levels in patients with metabolic syndrome compared to controls. Gopal et al in their study on obese patients has reported mean MDA of 2.19±2.2 µmol/ml in case group and 1.58±1.6 µmol/ml in control group.<sup>7</sup> Sankhla and Patel et al had also reported higher levels of MDA in obese subjects as compared to normal-weight subjects ( $p < 0.001$ ).<sup>11,12</sup>

In present study, MDA level was higher in females compared to males in both the groups ( $p < 0.05$ ). But Lima

et al had reported higher MDA levels in the male obesity group compared to females.<sup>6</sup>

In normal healthy condition there is always redox homeostasis occurring in cell, any imbalance to this redox homeostasis leads to oxidative stress (OS). In obesity increased metabolic and mechanical load on myocardium, large body mass, nutritious diet leads to formation of lipid peroxidation, free radical and reactive oxygen species generation. All these mechanisms also stimulate antioxidant enzymes but over a period of time the stores of antioxidant enzymes are depleted and cannot cope with increasing OS.<sup>13</sup>

In present study, patients with obesity had lower level of SOD compared to normal non-obese patients. Sabitha et al reported an increased MDA levels ( $p < 0.001$ ) in obese individuals due to lipid peroxidation and decrease in SOD levels ( $p < 0.001$ ), which indicates decline of antioxidant defense capacity among obese individuals.<sup>13</sup> Bikkad et al has also found statistically significant ( $P < 0.001$ ) decrease in mean erythrocyte SOD level in obese cases (733.46±98.21 U/gmHb) as compared to healthy controls (952.58±92.25 U/gmHb).<sup>14</sup> The consequence of the low activity of cytoprotective enzymes in human obesity is progressive tissue damage, which may eventually lead to atherosclerosis. In present study, males were having lower level of SOD compared to females in both the groups ( $p < 0.05$ ).

There was an inverse linear relationship between MDA and SOD level. This means as level of MDA increases, SOD decreases and vice versa ( $r = -0.045$ ,  $p = 0.001$ ). In present study BMI of patients was inversely related to SOD and directly related to MDA which means as BMI of patients increases SOD decreases and MDA increases and vice versa. Amirkhiziet al have also observed an inverse relationship between BMI and erythrocyte CuZn-SOD ( $r = -0.52$ ,  $P < 0.0001$ ) and highly positive relationship between plasma MDA concentration and BMI ( $r = 0.75$ ;  $P < 0.0001$ ).<sup>5</sup>

## CONCLUSION

This study demonstrated that obesity in humans, even in the absence of other confounding factors such as diabetes and hyperlipidaemia, is an independent risk factor for lipid peroxidation and depletion of cytoprotective enzymes.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the institutional ethics committee*

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**Cite this article as:** Agrawal N, Singh SK. Obesity: an independent risk factor for oxidative stress. *Int J Adv Med* 2017;4:718-21.