International Journal of Medical and Health Research
ISSN: 2454-9142, Impact Factor: RJIF 5.54
www.medicalsciencejournal.com
Volume 3; Issue 3; March 2017; Page No. 69-71

Correlation of oxidative stress parameters with various grades of obesity

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Abstract
Background: Almost 30-65% of adult urban Indians are either overweight or obese or have abdominal obesity. The rising prevalence in India has a direct correlation with the increasing prevalence of obesity-related co-morbidities like hypertension, metabolic syndrome, dyslipidemia, type 2 diabetes mellitus and cardiovascular disease.
Aims and Objective: To compare oxidative stress parameters (superoxide dismutase (SOD) and plasma malondialdehyde (MDA)) in various grades of obesity.
Materials and methods: This was a prospective randomized studydone in the Department of Medicine and Department of Biochemistry, G. R. Medical College, Gwalior. Patients were groped as Case (n=300, obese patients, BMI > 25 kg/m^2) and Control (n=100, age and sex matched healthy subjects having body mass index between 19-25 kg/m^2). Complete physical examination along with lipid profile and fasting blood glucose was done for all the patients. Body mass index (BMI) was calculated as weight divided by height squared and was used to grade the obesity as Grade 1 obesity (25-29.9 Kg/m^2), Grade 2 obesity (30 - 39.9 Kg/m^2) and Grade 3 obesity (> 40 Kg/m^2). Venous blood samples were obtained and were used for superoxide dismutase (SOD) and plasma malondialdehyde (MDA) determination. All the analysis was done with IMB SPSS ver. 20 software. Significance was assessed at 5 % level.
Results: Mean age of patients among Case and Control groups was comparable (46.2 ± 2.4 vs. 44.5±2.2 years respectively), there was male predominance (61.33% and 54% respectively) (p> 0.05). Most of the patients had Grade 2 obesity (63.34%) followed by Grade 1 (27.66%) (p>0.001). Mean MDA level in Grade 1 and Grade 2 and Grade 3 obesity was 3.34±1.13 µmol/ml, 4.81±1.04 µmol/ml and 6.63±1.21µmol/ml respectively whereas mean SOD activity was 9.54±1.45 units/ml, 8.54±1.11 units/ml and 7.73±1.02 units/ml respectively. Males had low MDA and SOD levels compared to female. There was an inverse linear relationship between BMI and SOD level (n=300, r= -0.045, P<0.001) and linear relationship between BMI and MDA (n=300, r= 0.342, P<0.001).
Conclusion: Obesity at any grade was associated with increase in MDA levels and reduction in SOD levels, indicating the presence of oxidative stress due to the obesity itself in absence of any other disease.

Keywords: lipid peroxidation, obesity grading, SOD, MDA

1. Introduction
According to World Health Organization obesity has been doubled since 1980 globally. As per the 2014 data, > 1.9 billion adults of ≥18 years of age were overweight and out of these more than 600 million were obese [1]. In 21st century, obesity has become epidemic in India which has affected around 5% of Indian population [2].
Elevated level of reactive oxygen species (ROS) and decrease antioxidant defense mechanism (lower antioxidant enzymes) are the markersof oxidative stress in obese patient [3, 4].
Oxidative stress may occur because of endothelial cell proliferation and apoptosis, systemic inflammation and increased vasoconstriction which individually or all together leads to endothelial dysfunction [5]. 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.[4]Tinahones *et al.* reported a significant decrease in antioxidant capacityin severely obese patients (decrease in SOD activity) [6].
Lipid peroxidation and erythrocyte cytoprotection were assessed by measuring the concentrations of plasma malondialdehyde (P-MDA) and the activities of erythrocyte copper zinc-superoxide dismutase (CuZn-SOD) in subjects with various grades of obesity but with no confounding factors, and comparing the values with those obtained for age and sex matched subjects with healthy BMI. The present study was done to compare the oxidative stress parameters in various grades of obesity.

2. Materials and methods
A prospective randomized study including obese patients was conducted in the Department of Medicine and Department of Biochemistry, G. R. Medical College, Gwalior. Total 300 obese patients were grouped as Case and compared with 100 age and sex matched normal subjects having BMI between 19 to 25 kg/m^2 grouped as Control.
Obese subjects defined as BMI > 25 kg/m2 of either sex having age > 18 yrs and willing to give written informed consent were included in the study. 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.
Institutional Ethics Committee approval and written informed consent was obtained from each patient before starting study. A through physical examination along with lipid profile and

fasting blood glucose was done for all the patients. BMI for each individual was calculated as weight divided by height squared and was used to grade the obesity.

BMI was calculated as weight divided by height squared and was used to grade the obesity as Grade 1 obesity (25 - 29.9 Kg/m^2), Grade 2 obesity (30 - 39.9 Kg/m^2) and Grade 3 obesity (> 40 Kg/m^2)

Venous blood samples (5 ml) were obtained and collected in standard tubes containing ethylenediamine tetra acetic acid. 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. Pearson correlation test was used to find correlation between study parameters. Significance is assessed at 5 % level.

3. Results

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

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 was 91.57±9.8 kg, 161.6± 9.3 cm, 36.17± 3.4 kgm2, 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 was 61±5.2 kg, 163.1± 8.7 cm, 21.24 ± 1.88 cm, 21.24 ± 1.88 kg m2, 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.

Maximum patients [190 (63.34%)] had grade 2 obesity, 83 (27.66%) had Grade 1 and 27 (9%) had Grade 3 obesity. All three grades were statistically different from each other (p<0.001). There was a significant difference between different grades of obesity of cases compared to control group (p<0.001).

Among Grade 1, Grade 2 and Grade 3 obesity patients there were 51 (61.44%), 119 (64.74) and 14 (51.85%) males (p<0.001, between each Grades) and 32 (38.55%), 71 (37.37%) and 13 (48.15%) females respectively (p<0.001, between each Grades).

Table 1: Comparing Oxidative stress parameters with different Grades of obesity

Grade	MDA level Case	MDA level Control	SOD case	SOD Control
1 (n=83)	3.34±1.13	2.06±0.76	9.54±1.45	12.42±2.18
2 (n=190)	4.81±1.04		8.54±1.11	
3 (n=27)	6.63±1.21		7.73±1.02	

Data is expressed as Mean±SD, P <0.001is considered to be highly significant,for MDA; between grade 1 and 2 of cases (p<0.001), between grade 2 and 3of cases (p<0.001), between grade 1 and 3of cases (p<0.001), for SOD; between grade 1 and 2 of case (<0.001), between grade 2 and 3 of case (p<0.001), between grade 1 and 3 of case (p<0.001)

Table 2: Comparinglevel of MDA and SOD between male and female

Grade	Male		Grade	Female		P Value
	MDA	SOD		MDA	SOD	
1 (n=51)	3.14±1.23*	9.54±1.45#	1 (n=32)	3.83±1.34*	10.34±1.35#	*<0.001, #<0.0001
2 (n=119)	4.61±1.14*	8.54±1.11#	2 (n=31)	5.48±0.94*	8.82±1.21#	*<0.001, #<0.001
3 (n=14)	6.23±1.22*	7.73±1.02#	3 (n=13)	7.13±1.28*	8.12±1.13#	*<0.001, #<0.0001

Data is expressed as mean± SD, *between males, #between female, MDA; malondialdehyde, SOD; superoxide dismutase

There was an inverse linear relationship between BMI and SOD level (n=300, r= -0.045, P<0.001) and linear relationship between BMI and MDA (n=300, r= 0.342, P<0.001). This means as level of MDA increases, SOD decreases as the BMI of subject increased.

4. Discussion

Systemic oxidative stress results from an imbalance between oxidants derivatives production and antioxidants defenses. In present study we compared the oxidative stress parameters in different grades of obesity [7].

Mean age were comparable between the groups eliminating the confounding effect of age on lipid peroxidation and enzyme activity. Study done by Gopal *et al.* and Bitla *et al.* on 80 and 75 patients respectively also reported comparable age and sex between the groups [8, 9]. Bitla *et al.* reported a mean age of 47.3 ± 2.6 and 42.1 ± 1.8 years among Case and Control groups respectively [9].

Except for the height (P>0.05), all other anthropometric parameters like weight, BMI, waist, hip, and W/H ratio had statistically significant difference in both the groups. Most of the patients were having Grade 2 obesity followed by Grade 1. Grade 2 obesity predominantly observed among males and female of Cases.

Fasting blood glucose, LDL-C and HDL-C were comparable between both the groups. But total cholesterol, triglycerides and VLDL-C between both the groups were significantly different which shows that obese individuals with higher BMI tend to have altered lipid profiles. Nirmitha *et al.* and Sabitha *et al.* have also reported similar findings on lipid profile [10, 11].

In present study, MDA level was increased as the grade of obesity increased [12] performed a similar study and reported that the concentration of MDA increased with increasing BMI, which was found to be statistically in overweight subjects while obese subjects exhibited a statistically significant higher level of MDA as compared to normal-weight subjects [12].

Imbalance in the redox homeostasis in a cell leads to oxidative stress. In obese patients lipid peroxidation occurs as a result of

increase in metabolic and mechanical load on myocardium and large body mass. In turn antioxidant enzymes such as superoxide dismutaseare stimulated but over a period of time the stores of antioxidant enzymes are depleted and cannot cope with increasing oxidative stress.[11]The consequence of the low activity of cytoprotective enzymes in human obesity is progressive tissue damage, which may eventually lead to atherosclerosis.

In obese patients, level of SOD decreased as the obesity grades increased. Higher level of MDA and among females showed increased lipid peroxidation, SOD activity was diminished among male population. Findings are similar to Olusi, who found reduction in SOD levels with increasing BMI [4].

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). Amirkhizi *et 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 ($r = 0.75$; $P<0.0001$) [12].

5. Conclusion

It was found that obesity at any grade was associated with increase in MDA levels and reduction in SOD levels. It was found that MDA and SOD were inversely related to each other which indicate that obesity itself destroy the protective mechanism of body and increase the oxidative stress in body. Study also showed that obesity is independent risk factor in producing oxidative stress and can lead to serious damage to cells.

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