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EVALUATION OF LIPID PEROXIDATION AND TOTAL ANTIOXIDANT STATUS IN HUMAN OBESITY

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ABSTRACT

Obesity is one of today's most blatantly visible – yet most neglected – public health problem. An escalating global epidemic of overweight and obesity – "globesity" – is taking over many parts of the world. If immediate action is not taken, millions will suffer from an array of serious health disorders. Evidence of obesity-induced oxidative stress in humans has been accumulating over the past few years.Lipid peroxidation is an indicator of oxidative stress which is assessed by measuring malondialdehyde (MDA). The aim of this study is to investigate the relationship between BMI and lipid peroxidation and total antioxidant status (TAS). Hundred (n = 100) healthy males and females (n = 35/65) (31 normal weight (BMI: 20.42 ±1.24 kg/m^2), 37overweight (BMI: 27.04 ±0.95 kg/m^2),and 32 obese (31.60 ±0.97 kg/m^2)) participated in the study.The results of the study showed that over-weight and obese individuals had significantly increased MDA levels compared to normal-weight individuals (over-weight and obese vs. normal weight (1.18 ±0.25 and 1.39 ± 0.21 vs. 0.862 ±0.204 nmol/l, P < 0.001)) The levels were also significantly increased in obese compared to the overweight group (obese vs. overweight (1.39 ± 0.21 vs. 1.18 ±0.25 nmol/l, P < 0.001). Significantly decreased TAS levels were observed between groups. (over-weight and obese vs. normal weight (123.69 ±14.49 and 116.27 ± 13.99 vs. 167.91 ±13.04 µg/dl, P < 0.001). The levels were also significantly decreased in obese compared to the overweight group (obese vs. overweight (116.27 ± 13.99 vs.123.69 ±14.49 µg/dl, P < 0.05).This study concluded that over-weight and obesity elevates MDA levels and decreases the levels of TAS and should therefore receive importance to avoid related complications.

INTRODUCTION

Overweight and obesity are the fifth leading risk for global deaths. At least 2.8 million adults die each year as a result of being overweight or obese. In addition, 44% of the diabetes burden, 23% of the ischaemic heart disease burden and between 7% and 41% of certain cancer burdens are attributable to overweight and obesity. Once considered a high-income country problem, overweight and obesity are now on the rise in low- and middle-income countries, particularly in urban settings.(1) Obesity has reached epidemic proportions in India in the 21st century.(2) India is following a trend of other developing countries that are steadily becoming more obese.

Evidence of obesity-induced oxidative stress in humans has been accumulating over the past few years**.** Several research studies have suggested that obesity is associated with increased oxidant stress (3,4,5,6,7,8,9) i.e., increased free-radical production and/or depleted cellular antioxidant defence systems (10). Possible mechanisms contributing to the obesity-associated oxidant stress include increased oxygen consumption and subsequent radical production via mitochondrial respiration, diminished antioxidant capacity, increased fat deposition, and cell injury causing increased rates of radical formation such as O_2^- and OH^- (11). In addition, hyperglycemia, hypertension, and hyperleptinemia are also possible sources of increased oxidant stress in the obese state (12). It is not known whether obesity-associated oxidant stress is related to excess adipose tissue accumulation or is a consequence of obesity-related diseases i.e., hypertension, hyperlipidemia, hyperleptinemia, hyperglycemia (13).

Lipid peroxidation is a well-established mechanism of cellular injury in both plants and animals, and is used as an indicator of oxidative stress in cells and tissues. Malondialdehyde is a highly reactive three carbon dialdehyde produced as a byproduct of polyunsaturated fatty acid peroxidation and arachidonic acid metabolism. MDA readily combines with several functional groups on molecules including proteins, lipoproteins, and DNA. MDA-modified proteins may show altered physico-chemical behavior and antigenicity (14). MDA is formed at the end of long oxidative processes.(15) Therefore, measurement of malondialdehyde is widely used as an indicator of lipid peroxidation. The synergistic effect of antioxidants in human serum is known to provide

greater protection against free radical aggression than any single antioxidant alone(16).The current study measured the total antioxidant status (TAS) of serum because of its established ability to withstand oxidative stress (17). In this study, lipid peroxidation which is an indicator of oxidative stress levels were assessed by measuring the concentrations of serum malondialdehyde (MDA). We also evaluated total antioxidant capacity (TAC) of serum in subjects.

MATERIALS AND METHODS

The present study was carried out in the central research laboratory of Nitte University, Deralakatte, Mangalore.The study group consisted of 100 (*n* = 100) healthy male and female subjects (closely sex-matched by ratio in each subject group) who were divided into three categories of BMI: 18.5–24.99, 25–29.99, and ≥30 kg/m^2 according to the World Health Organization classifications of normal weight, overweight, and obese, respectively (18). 31 normal weight (BMI: 20.42 ±1.24 kg/m^2), 37 overweight (BMI: 27.04 ±0.95 kg/m^2), and 32 obese (BMI: 31.60 ±0.97 kg/m^2) healthy male and females (*n* = 35/65)) . An inclusion criterion was age between 20 and 60 years old and BMI between 18.5 and 35 kg/m^2 were selected randomly. Subjects with diabetes, cardiovascular or cerebrovascular disease, hepatic or renal disease, tobacco abuse, hypertension, taking treatment for dyslipidemia, taking any antioxidant supplementations, or a smoker or those on hormone replacement therapy were excluded. Informed consent was obtained from all the subjects. The research was given ethical approval by Concerned Institutional Ethics Committee. Body weight was measured to the nearest 0.05 kg and height without shoes to 0.1 cm, and used to calculate BMI (kg/m^2).

Venous blood was collected from the subjects under aseptic conditions by venipuncture using 2 ml sterile disposable syringe and needle. About 2 ml of blood was collected which was allowed to clot for one hour. Serum was separated by centrifugation at 3000 rpm for 10 min. at room temperature. The samples were stored at 4ºC before analysis and all the samples were analyzed within two days of blood collection. All the methods were standardized first and standard graphs were obtained. Serum Lipid peroxide was measured by precipitating lipoporoteins with trichloroacetic acid and boiled with thiobarbituric acid which reacts with Malondialdehyde to get pink colour the absorbance

of which is read at 535 nm as per Buege and Aust Method (19). The Molybdate reducing ability of serum assay was used to assess TAS in serum by the method of Prieto, Manuel, and Miguel (20). In brief, this quantitative assay measures the total "antioxidant" capacity of biological fluids. Molybdate to Molybdenum reduction at acidic pH which further reacts with phosphate to form a green-colored phospho–molybdenum complex. The absorbance of which is read at 695 nm. The antioxidant activity is expressed as the number of equivalents of ascorbic acid. All data were expressed as mean + SD.Two-tailed P values were used and statistical significance was considered at $P < 0.05$.

RESULTS AND DISCUSSION

This study examined the relationship between BMI, MDA and TAS. Although the relationship between obesity and oxidant stress parameters has been extensively studied it is unknown whether this relationship exists in overweight individuals.

BMI AND MDA

The results of the study showed (Table 2) that over-weight and obese individuals had significantly increased MDA levels compared to normal-weight individuals (over-weight and obese vs. normal weight (1.18 ±0.25 and 1.39 ± 0.21 vs. 0.862 ±0.204 nmol/l, $P < 0.001$)) The levels were also significantly increased in obese compared to the overweight group (obese vs. overweight (1.39 ± 0.21 vs. 1.18 ±0.25 nmol/l, $P < 0.001$).

BMI AND TAS

Significantly decreased TAS (Table 2) levels were observed between groups (over-weight, obese vs. normal weight (123.69 ±14.49 and 116.27 ± 13.99 vs. 167.91 ±13.04 µg/dl, $P < 0.001$). The levels were also significantly decreased in obese compared to the overweight group (obese vs. overweight (116.27 ± 13.99 vs.123.69 ±14.49 µg/dl,$P<0.05$).

Table 1 Subject Characteristics:

	Normal-Weight	**Over-Weight**	**Obese**
Age	28.77 ± 7.86	32.56 ± 9.22	32.28 ± 8.32
M:F	9:22	12:25	14:18
BMI	20.42 ± 1.24	27.04 ± 0.95	31.60 ± 0.97

Table 2 Serum MDA and TAC levels in normal, over-weight and obese

	Normal-Weight	**Over-Weight**	**Obese**
MDA	0.862 ± 0.204	1.180 ± 0.252	1.393 ± 0.214
TAC	167.91 ± 13.04	123.69 ± 14.49	116.27 ± 13.99

This study is supported by findings,in other human studies that increased lipid peroxidation in obesity has been frequently observed(3,5,6,7,8,9),it recorded significantly higher levels of malondialdehyde in obese adults compared to normal-weight controls. Farshad *et al*.(23) found significantly increased concentration of MDA in over weight and obese adults compared to normal weight and significantly decreased concentration of TAC in obese adults compared to normal weight. Chrysohoou *et al.*(24) found lower TAC concentrations in overweight and obese compared to normal weight. TAS were shown to be lower in obese compared to nonobese individuals (25). This study confirmed previous findings that obesity is associated with increased oxidant stress. Which may be explained by several mechanisms: increased O_2 consumption, cell injury/inflammation, increased fat deposition, and compromised antioxidant defense (11). However, whether obesity-associated oxidant stress is a cause and effect relationship or due to obesity-related diseases i.e., hypertension, hyperlipidemia, hyperleptinemia, and hyperglycemia (13) remains unclear. Because all the subjects in this study were healthy (free of obesity-related diseases) and sex and age was similar across the groups (factors also known to influence oxidant stress levels), it is possible that obesity or other factors caused the observed increased oxidant stress. The mechanisms responsible for altered antioxidant levels in obesity, are unclear from previous findings. In this study, we can only speculate following Wortsman *et al.*'s (26) study that the observed lower antioxidant levels in individuals with increased BMI levels may be due to the redistribution of antioxidant/antioxidant enzymes into fatty tissues, leaving fewer available in plasma and other essential sites. Similarly, the degree of obesity may influence antioxidant levels, for example the greater the obesity, the greater demand on antioxidant enzymes to combat free-radical damage, hence antioxidant enzymes become depleted.

CONCLUSION

It is concluded from this study that obesity in the absence of other confounding factors is an important risk factor for lipid peroxidation and decreased total antioxidant status, and should therefore receive huge importance to avoid future development of obesity related complications. Other potential research studies may identify suitable strategies to reverse the obesity-associated oxidant stress, for e.g. weight loss (27), calorie restriction (28), and exercise training (29) have been shown to positively reduce oxidant stress levels.

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