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Oxidative Stress in Non-Obese & Obese Young Healthy Adults

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ABSTRACT

Introduction: Obesity causes various diseases due to systemic oxidative stress. Young healthy obese are unaware of oxidative burden in their body. Total oxidant status (TOS) is a marker of oxidative stress in obesity.

Aims & Objectives: This study was planned to determine and compare levels of TOS in young healthy non obese and obese, males and females and individuals with active versus sedentary lifestyle.

Place and duration of study: This study was conducted over one month duration at six women and co-ed colleges of Lahore.

Material & Methods: This cross-sectional comparative study was conducted on samples collected within one month from 160 healthy males and females, aged 20 to 40 years at APWA College, Lahore College Womens University, Government College University, Gulberg College, PAC Lahore, Ameeruddin Medical College Lahore (n=30 each college). The participants were divided into two groups based on the respondents BMI. TOS was measured colorimetrically. Data was analyzed using IBM-SPSS version 25. Mann Whitney U test compared TOS levels between non obese and obese subjects.

Results: Fifty percent of the subjects had a normal BMI while 50% were obese according to the Asian Pacific criteria for BMI.Fifty-two percent of the population were males while forty-eight percent of the population was females. Group I (non obese) consisted of 55% males and 45% females with a significant difference in the levels of TOS. The population in Group II (obese) comprised of 50% males and females each also showing significant difference. Thirty-six percent (n=58) of the total population had active lifestyle while sixty-four percent (n=102) of the population had a sedentary lifestyle. While in Group 1(non obese) (64%) had an active lifestyle whereas the rest were sedentary. In comparison only 9% of group II subjects (obese) had an active lifestyle while the remainder were sedentary. A significant difference in level of TOS were seen when compared between subjects with active versus sedentary lifestyle in respective groups. A significant difference (p=0.03) was seen when TOS was compared between subjects with Active lifestyle 4.15(3.17-5.42) µmol/lversus subjects with sedentary lifestyle 4.9(3.70-7.22) µmol/l.

Conclusion: Increased levels of TOS were seen in young healthy obese as compared to non-obese. Both non obese and obese females had higher levels of TOS in comparison to males due to greater levels of body fat percentage. Subjects with a sedentary lifestyle have raised levels of TOS in comparison to subjects with active lifestyle.

Keywords: Obesity, Oxidative stress, Sedentary lifestyle

INTRODUCTION

Excess or abnormal accumulation of fat which may pose a danger to health is characterized as obesity.[1] Being overweight and obese is the root cause of oxidative stress which leads to multiple diseases like hypertension, diabetes, cerebrovascular diseases and cardiovascular diseases.[2] Reactive oxygen species (ROS) are the most common cause of damage to biological systems and are produced as a byproduct of cellular metabolism.Either increased production of ROS at abnormal sites or their decreased removal by the antioxidant systems leads to oxidative stress.[3] The several possible mechanisms in obesity that lead to generation of ROS and oxidative stress are hyperglycemia, increased level of lipids, chronic inflammation, decreased levels of antioxidants and production of ROS by the endothelium. These contributors act independently and also in an interlinked manner to produce oxidative stress.[4,5] It is difficult to measure ROS directly because of their short half-life. So oxidative stress is often measured by in vitro experiments based on evaluation of products formed during oxidative damage to different components of the cell. These products form markers. Until recently there was no gold standard parameter to define the redox status of clinical samples. Furthermore, the measurement of individual markers is only a partial reflection of the oxidative status.[6] So the use of TOS is a more practical approach which not only reveals the final oxidative status but also takes into account the interaction of various oxidants with each other.[7,8] Studies have shown increased levels of total oxidant status in obesity.[9, 10] This study was aimed to determine and compare serum levels of total oxidant status in young healthy non obese and obese subjects.

MATERIAL AND METHODS

The study was conducted in APWA College, Lahore College Womens University, Government College University. Gulberg College, PAC Lahore It was a cross sectional comparative study. After obtaining approval from the Ethical Committee of Postgraduate Medical Institute, Lahore vide 00-14-S-2013 signed informed consent was taken from each participant in current study. A total of 160 healthy males and females (n=30 each college), 20 to 40 years of age were selected and divided into two groups. The Non-Obese Group1 included 80 subjects with BMI<24.9kg/m^{2}and the Obese group 2 had 80 subjects with BMI ≥25kg/m^2.[11] The sample size was calculated by using reference article Mehmetoglu et al. 2012. The level of confidence was 95% and power of test was taken as 90%. The BMI was calculated by dividing weight in kg by height in meter squared (kg/m2). Both non obese and the obese group had normal physical examination and no medical history of any ailments. Smokers, pregnant females, and those with history of systemic diseases were excluded from the study.

Blood sample:

After an overnight fast, five ml of blood samples were obtained under aseptic measures. Blood was collected in plain tubes (for serum) without anticoagulant. It was allowed to clot at room temperature for 30 minutes before centrifugation at 3,000 revolutions per minute for 15 mins. Aliquots of serum sample were stored at -20˚C for measurement of total oxidant status.

Estimation of Total oxidant status:

Total oxidant status of the serum was measured colorimetrically using an assay kit manufactured by Rel Assay Diagnostics, Turkey (583-RL0024). The oxidants of sample oxidize Fe^{2+} chelator complex to Fe^{3+} which is coloured with xylenol orange in an acidic medium to be measured spectrophotometrically to calculate TOS.[13]

Statistical Analysis

Data was analyzed using IBM-SPSS version 25. It was tested for normality by using Shapiro-Wilk test. Median and interquartiles were calculated for quantitative non-normally distributed variables. Mann-Whitney U-test was applied to compare quantitative variables between the two groups. A *p*-value ≤0.05 was considered statistically significant.

RESULTS

There was no significant difference in age of subjects (*p*=0.26) Subjects of group I (non obese) had a median BMI of 19.36 (18.72-21) kg/m^2. While subjects in group II (obese) had median BMI of 34.9 (33.2-35) kg/m^2.TOS was significantly raised in group II (obese) subjects with a median of 5.3 (3.72-7.90) µmol/l (*p*-value<0.001).

Females of the non-obese and obese groups had higher values of TOS in comparison to males as shown in Table-1.

Levels of TOS were higher in subjects with sedentary lifestyle in comparison to subjects with active lifestyle as seen in Table-2.

Table-3 shows higher levels of TOS in subjects with sedentary lifestyle as compared to those with active lifestyle in group I (non obese). However higher levels of TOS were seen in subjects with active lifestyle as compared to subjects with sedentary lifestyle in group II (obese).

Parameter		Control n=80	*p*-value	Obese n=80	*p*-value
TOS (µmol/l)	Male	3.75 (3.00-4.20)	<0.001 ***	4.15 (3.20-7.97)	<0.001 ***
	Female	5.25 (3.70-6.60)		5.90 (4.17-7.87)	

Table-1: Comparison of total oxidative markers between males and females of control and obese groups.

****p*-value considered highly significantComparison done by Mann-Whitney U-test

TOS: Total oxidant status.

Parameters	Active n=58	Sedentary n=102	*p*-value
TOS (µmol/l)	4.15 (3.17-5.42)	4.9 (3.70-7.22)	0.03*

Table-2: Comparison of total oxidant status in subjects with active lifestyle versus subjects with sedentary lifestyle.

**p*-value considered significant Comparison done by Mann-Whitney U-test

TOS: Total oxidant status

Group		TOS (µmol/l)	*p*-value
Control	Active n= 51	3.90 (3.10-5.00)	0.02*
	Sedentary n=29	4.30 (3.60-6.90)	
Obese	Active n=7	9.40 (5.70-17.20)	0.03*
	Sedentary n=73	5.00 (3.70-7.80)	

Table-3: Comparison of total oxidant status in subjects with active lifestyle versus subjects with sedentary lifestyle of control and obese groups.

**p*-value considered significantComparison done by Mann-Whitney U-test

TOS: Total oxidant status

DISCUSSION

The results of this study indicate that serum levels of TOS are higher in obese subjects when compared with non- obese showing a significant difference ($p<0.001$). Aslan et al (2017) have reported similar results in Turkey with higher levels of TOS, lower levels of total antioxidant capacity (TAC) and an increase in oxidative stress index (OSI) in obese subjects suggestive of higher level of oxidative stress. The effect of total antioxidant/oxidant status in patients with perodontitis was studied by Dursun and his colleagues (2016) found an increase in both local and systemic levels of TOS in obese females. Altoum et al (2019) found a positive correlation between an oxidative stress marker malon-dialdehyde (MDA) and BMI. Maslov (2019) concluded that obesity itself can lead to increase in oxidative stress. Markers of oxidative stress like MDA, F2 isoprostanes and Thiobarbituric reactive acid substances (TBARS) are increased while levels of antioxidants like superoxide dismutase (SOD) are decreased in obesity.[17]

In obesity the mechanisms leading towards oxidative stress are multiple. With an increase in adipose tissue, the production of inflammatory cytokines and reactive oxygen species (ROS) increases. Angiotensin II levels also increase in obesity which increases the activity of NADPH oxidase enzyme and leads to production of ROS from the adipocytes. Mitochondrial and peroxisomal oxidation of fatty acids, protein kinase C (PKC) activation, polyol and hexosamine pathway and a lipid rich diet are all factors causing increased ROS generation in obesity.[18] As a result of this increased oxidative stress, its markers are also raised in obesity.[19]

Our findings reveal that levels of TOS are higher in females when compared with males in both the groups with significant difference of $p<0.001$ for control group and $p=0.04$ for obese group. Results similar to this study have been observed by Agarwal and Singh (2017) where levels of MDA were higher in females as compared to males in both obese and non-obese groups. In another study obese females have raised MDA levels in comparison to healthy controls.[21] Higher percentage of body fat in women maybe a factor leading to this difference. There are conflicting results in studies regarding gender difference in oxidative stress. Pinchuck et al (2019) have reported higher MDA values in males. The different methods used to determine the oxidative stress markers may be a reason for this difference.[23]

Another finding of current study is raised levels of TOS seen in subjects with sedentary lifestyle as compared to active subjects ($p=0.03$). Accattato et al (2017) in their study on effect of exercise on young sedentary obese subjects have found increased levels of antioxidants after increase in physical activity. Long duration of inactivity is also associated with increased production of muscle ROS in both rodents and humans.[25] Inactivity also reduces the antioxidant capacity, and this redox imbalance leads to oxidative stress.[26]Regular physical activity has many health benefits especially in overweight and obese individuals. The myriad of effects ranges from decrease in the degree of adiposity to improved functioning of almost all body systems including cardiorespiratory, metabolic, muscle and bone health.[27]

The current study shows that levels of TOS are raised in non-obese sedentary subjects as compared to non-obese active subjects ($p=0.02$). Klarod et al (2017) have also shown MDA levels to decrease significantly after exercise in twenty young, healthy non-obese subjects.[28] Regular physical activity has been shown to cause adaptive changes in the body which protect against oxidative damage via elevation of antioxidant enzymes. Consequently, substances producing free radicals decrease.[29]

This study also shows that levels of TOS are significantly raised in morbidly obese subjects with active lifestyle as compared to obese subjects with sedentary lifestyle ($p=0.03$). This is analogous to a study done by Accattato et al (2017) who suggested the greater the degree of obesity the higher the oxidative challenges faced by the body.[24] Hatami et al (2016) in their work on thirty subjects with metabolic syndrome also found significantly raised levels of serum total oxidant status in comparison to thirty-seven healthy controls.[10] Oxidative stress is markedly elevated in obesity which increases its markers.

Limitations:

Oxidative stress index (OSI) is an element of balance which cannot be commented upon as TAS was not measured due to budgetary constraints.

CONCLUSION

The present study concludes that obesity even in healthy individuals is a source of oxidative stress as is evident by raised levels of TOS. Also, obese females have more oxidative stress as compared to males, an aspect which needs to be further elucidated. Persistent inactivity increases oxidative stress in the body.

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