ORIGINAL RESEARCH PAPER
Volume-9 | Issue-2 | February-2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

MISSING LINKS BETWEEN CENTRAL OBESITY, OXIDATIVE STRESS & GLYCEMIC LEVELS IN DIABETES.

Biochemistry

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ABSTRACT

Obesity have been to be in epidemic proportion in the past few years. The doubling of the incidence of diabetes has also been observed. Hence this study was carried out to establish a link between obesity and diabetes. It can be concluded that increased abdominal fat leads to insulin resistance and metabolic abnormalities. The levels of MDA and antioxidants like GSH, SOD during early phase of the disease (recently diagnosed) in diabetic individuals and compare with normal subjects. A very significant increase ($p<0.0001$) was observed in the antioxidants levels, MDA ,HbA 1C and BMI, WHR in the study group as compared to the ones in the control. Decreased expression of antioxidant enzymes was found to be associated with the free radical levels at the same time a negative correlation between BMI and antioxidant levels have been observed. Hence we conclude that abdominal obesity is responsible for the development of diabetes and Oxidative stress, depleted antioxidant levels help in the progression of the disease.

KEYWORDS

Central Obesity, BMI, WHR, Oxidative stress, Antioxidants and Diabetes

INTRODUCTION:

In the past few years India has been undergoing through a rapid economic transition and also there is a wide spread epidemiological transition of increased burden of communicable and non-communicable diseases. "Diabetes" and also "Obesity" is emerging as an important health problem both in urban and rural India.[1,2,3] Obesity has been described as a global pandemic with approximately 50% of adults worldwide expected to be obese by 2030. [4]

A desirable BMI according to WHO recommended cut-off for Asians is considered to be between 18.5 and 22.9 kg/m2. A BMI of 23-24.9 kg/m^2 is defined as 'overweight' and > 25kg/m2 as 'obese.[5] While Generalized obesity (GO) was defined as a BMI≥25 kg/m2 for both genders (based on the World Health Organization Asia Pacific guidelines) with or without abdominal obesity (AO).

Abdominal obesity (AO) was defined as a waist circumference (WC) ≥90 cm for men and ≥80 cm for women with or without GO. Isolated generalized obesity (IGO) was defined as a BMI ≥25 kg/m2 with waist circumference of <90 cm in men and <80 cm in women. Isolated abdominal obesity (IAO) was defined as a waist circumference of ≥90 cm in men or ≥80 cm in women with a BMI <25 kg/m2. Combined obesity (CO): Individuals with both GO and AO. Non obese subjects: Individuals without either GO or AO. [1]

Oxidative stress occurs when there is an overproduction of the reactive oxygen species coupled with the deficiency of cellular antioxidant defense mechanisms. [6] An antioxidant is a molecule capable of slowing or preventing the oxidation of other molecules. Antioxidants such as superoxide dismutase and glutathione act as potent electron donors, they donate hydrogen atoms to pair up with unpaired electrons on free radicals. These antioxidants are produced either endogenously or received from exogenous sources and include superoxide dismuatase (SOD), Glutathione (GSH), Catalase(CAT), glutathione peroxidase(GPx) and glutathione reductase, minerals like Se, Mn, Cu and Zn, and vitamins like A,C,E. Other compounds with antioxidant activity include glutathione, flavonoids, bilirubin and uric acid[7] Thus Antioxidants are supposed to protect, prevent or reduce the extent of oxidative destruction of biomolecule. An imbalance in the levels of Oxidative stress and antioxidant in Diabetic individuals. Hence the present study was designed to evaluate the correlation between antioxidant and oxidative stress at the same time try to establish a link between obesity, oxidative stress, Antioxidant levels in Diabetic individuals.

AIMS AND OBJECTIVES:

1. To evaluate and assess the role of Obesity as an independent risk factor for development of Diabetes
2. To assess if the Oxidative stress related markers were altered Diabetic individuals.
3. To study relationship between Obesity, glycemic level and Oxidative stress in the Diabetic individuals.

METHODOLOGY:

120 subjects were included in the study. Dividing into two group i.e group I included type II DM (n=60), group II was age matched control (n=60). They were diagnosed as diabetic based on the WHO Criteria i.e. symptoms of diabetes plus random blood glucose concentration ≥11.1mmol/l (200mg/dl) or fasting plasma glucose ≥ 7mmol/l (126 mg/dl) at more than one occasion. Newly diagnosed patients (not more than one year duration) of DM type II were included in the study. Patients with complications like history of stroke, myocardial infarction or any other cardiovascular disease were excluded. These individuals of group I (test group) were treated only by oral antidiabetic drugs (sulfonylurea and metformin). The study protocol was approved by the Ethics Committee of the Institution (Sumandeep Vidyapeeth) .The participants were recruited in the study only after they willingly signed inform consent form. All ethical norms were followed during the entire course of the study.

Inclusion criteria **-**Purpose of the study was explained and those who showed interest to participate after giving consent were included in the study.

Exclusion criteria **-**Exclusion criteria were those who are not willing to participate in the study.

Collection of specimen: In all the participants of the study, both the control and test groups, venous blood sample was collected under aseptic conditions after 12 hrs of fast, in EDTA bulb for HbA_{1C} which was estimation by resin binding method [8] ,in plain bulb for estimation of serum SOD [9], MDA [10]. Acid citrate bulb was used for estimation of erythrocyte GSH [11].

Anthropometry:

A digital scale with an accuracy of ±100 g, was used to measure body weight (BW). Standing body height (BH) was measured to the nearest 0.5 cm with a commercial stadiometer without shoes with the shoulders in relaxed position and the arms in the hanging position. The BW and BH values were used to calculate the BMI (weight over squared height, Kg/m^2) Waist circumference (WC) was measured, at the level midway between the lower rib margin and the iliac crest. Hip circumference (HC) was measured at the fullest point around the buttocks. WHR was determined by dividing WC (cm) by the HC (cm). Normal reference value for WRH is <0.85 in females and <0.95 in males.

Statistical analysis

All results are expressed as mean ±S.D. Students "t" test was used to compare the continuous variables between groups. Pearson's correlation was employed to calculate the 'r' value. Statistical significance was defined as $p<0.05$. The statistical analysis was done

using SPSS version 14.0

RESULT:

The study group was divided into two - group I (diabetic individuals) while the group II (control). Table I summarizes the demographic data of participants in both the groups. There was no significant difference between the participants of both the groups with regards to age, sex, educational status, occupation, history of smoking and drug abuse etc.

Table1. Demographic data of the diabetic individuals (group I) and healthy controls (group II)

Parameter	DM (group I)	Healthy controls (group II)
Age(years)	42.4±5.2	44.4±6.8
Gender (M:F)	36:24	32:28
Smoking status : Never smoked Ex- smoker	27 15	36 12
Current smoker	18	12
Alcoholism: Never consumed	32	36
Ex- consumer	9	12
Currently alcoholic	19	12

Table 2. Levels of BMI, WHR, MDA, SOD, GSH, HbA 1C group I &group II

Sr. No.	Variables	Group I	Group II	P value
1	HbA 1C (%)	9.6±1.3	5.5±0.8	p<0.0001*
2	BMI (kg/m2)	25.2±4.4	22.9±2.3	p<0.0001*
3	WHR	0.96±0.11	0.81±0.33	p<0.0001*
4	MDA (nmol/ml)	6.2±1.8	3.1±1.6	p<0.0001*
5	SOD (units/ml)	3±1.09	3.8±0.59	p<0.005#
6	G red (µmol/l/min)	2.9±1.4	6.3±2	p<0.0001*

All values are mean ±SD. Total number of patients was 60 in each group. While p<0.0001* was considered to be highly significant. p<0.05# was considered to be significant.

Table 3. Correlation Analysis of Serum MDA with other parameters in Group I and group II

Sr. No.	Parameters	Correlation Coefficient(r)	
		Group I	Group II
1	G red (µmol/l/min)	-0.24*	+0.02
2	SOD(units/ml)	-0.67*	-0.51*
3	HbA 1C (%)	+0.33*	+0.21*

*Where * indicates p<0.0001 and is highly significant*

Table 4. Correlation Analysis of BMI with antioxidants in Group I and group II

Sr. No.	Parameters	Correlation Coefficient(r)	
		Group I	Group II
1	G red (µmol/l/min)	-0.28*	0.02
2	SOD(units/ml)	-0.36*	0.03

*Where * indicates p<0.0001 and is highly significant*

Laboratory findings of all the patients are summarized in table2,3. Serum MDA levels – the marker of lipid peroxidation was found to be significantly elevated (p<0.0001) and levels of antioxidants such as Superoxide dismutase and Reduced glutathione was significantly (p<0.001) in the group I than group II (Table -1) The antropometric measurements was significantly high (p<0.001) i.e BMI was 25.2 ±4.4 Kg/m^2 when compared to 22.9±2.3 Kg/m^2 indicating Obesity among Diabetic individuals & WHR which were used to be an indicator of abdominal obesity has been significantly high (p<0.001) in the Diabetic individuals (0.96 ±0.11) as compared to the 0.81±0.33.when correlated between the two groups.

Regression analysis, of oxidative stress and antioxidant status in both the groups is indicated in table 3 there is a negative correlation which is very significant (p<0.0001) between MDA and other parameters like GSH, SOD while a positive correlation exist between MDA and glycosylated hemoglobin in group I. Thus indicating the role of hyperglycemia in the oxidative stress development.The regression analysis between BMI and antioxidants indicate a very significant negative correlation in group I.

DISCUSSION:

The World Health Organization has revised the BMI cut-off for Asian Indians and suggested a BMI of 25 kg/m^2. While few studies have suggested cutoffs for BMI ranging from 19-22 kg/m2 while that of waist circumference ranges from 72-85 cm in men and 65.5 - 80 cm in women[12,13,14] hence if these cut offs are followed then it indicates Obesity in the diabetic individuals. The study also indicated abdominal obesity as the waist: hip ratio were significantly high p<0.001 (0.96±0.11 in group I and 0.81±0.33 group II). This location of fat deposits in the abdomen (viscera) is a better indicator of metabolic risk than total body fat and it is considered to be the link between insulin resistance and metabolic abnormalities inclusive of diabetes.[15,16] While lean body mass on the other hand is critical in avoiding the hyperinsulinaemia which predisposes individuals to type II diabetes as a greater insulin secretion is required for any given glucose load where levels of body fat are disproportionate.[17] Thus explaining the presence of obesity and more over the abdominal obesity among the diabetic individuals. The abdominal adiposity has in turn been associated with the enlargement and dysfunction of the adipose tissues which in turn secretes the pro-inflammatory biomarkers like prostaglandins, C-reactive protein (CRP), and cytokines such as interleukins (e.g. interleukin-6), tumor necrosis factor alpha (TNF-α), and leptin.[18] All these Inflammatory mediators released by adipose tissue contribute to the development of type II diabetes

Thus the following hyperglycemia due to diabetes triggers of Oxidative stress.The positive correlation between glycosylated hemoglobin and MDA indicates the role of hyperglycemia in the development of Oxidative stress which is very similar to the finding of other studies.[6,7] There is a significant increase (p<0.001) in the marker of Oxidative stress marker i.e MDA (6.2±1.8, 3.1±1.6) indicating lipid peroxidation with decreased activity of antioxidants in the obese subjects as observed in previous other studies.[19,20,21,22]. When the correlation was analyzed between MDA and antioxidants it was observed that SOD showed a negative correlation in both the groups and was significant but reduced glutathione showed a significant negative correlation in the group I only which has been the observation of other studies done on obese diabetic subjects.[22,23] The correlation between BMI and antioxidant levels indicated a significantly inverse relationship which was also observed other studies.[24,25]

CONCLUSION:

Most of the studies have shown the presence of a positive relationship between obesity and diabetes. At the same time the relationship between oxidative stress and antioxidants have been well established fact. Hence we conclude that the presence of obesity results in Insulin resistance and the oxidative stress which develops is related to the development of type 2 diabetes. Hence dietary restrictions and increased physical exercise could play a great role in preventing the development of the disease.

Disclosure:

The authors declared no conflict of interest.

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