To study the body fat composition and fasting blood glucose level in relation to Tumor Necrosis Factor-Alpha (TNF-α) level in obese subjects

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Abstract

Background: Obesity causes phenotypic alterations in adipose tissue, which leads to chronic low- grade inflammation. Obese people are more likely to acquire several health-related problems most prevalent is Type 2 DM. Obesity is considered as a crucial pathogenic factor for Insulin Resistance (IR).

TNF-α is a cytokine released as a result of phenotypic changes in adipose tissues. TNF-α involved in the pathogenesis of some inflammatory and autoimmune disease and proposed as a link between obesity and IR.

Aim: To study the body fat composition and Fasting Blood Glucose (FBG) Level in relation to TNF-α Level in obese subjects.

Material and Methods: A cross sectional study, 100 obese subjects aged between 18 to 24 years were included. Body fat composition measured by Bioelectric Impedance Analysis (BIA). FBG & TNF- α level were measured by semiauto analyser & ELISA respectively.

Result: TNF- α has a significant correlation with FBG level (r = 0.3884) with p-value (< 0.001), Waist Circumference (WC) (r = 0.491) with p-value (< 0.001) and

Percentage Body Fat (PBF) (r = 0.5247) with p-value (< 0.001) whereas blood glucose concentration is not significantly affected with WC and PBF.

Conclusion: In obese individuals, the measurements of TNF-α, Body Fat Composition (WC and PBF) and FBG levels all have a positive correlation**.** TNF- α may thereby contribute to the development of insulin resistance, which may result in Type 2 DM.

Keywords: Obesity, TNF-α, Insulin resistance (IR), Diabetes Mellitus (DM), BMI

1. Introduction

Obesity is a state which is characterized by the build-up of extra body fat, usually as a consequence of a discrepancy between calorie intake and calorie expenditure (1). Obesity in India has climbed among men from 21% to 24% and women from 19% to 23% (2). An individual is considered to be obese based on many parameters like Body Mass Index (BMI), Waist Circumference (WC), and Waist to Hip Ratio (WHR), out of which the most applicable parameter for measurement of generalized obesity is BMI whereas WC and WHR are better parameters for abdominal or truncal obesity (1,3). The study done by A. misra *et al*., the height and weight can be used to calculate BMI, which can be classified using the provided BMI chart as kg/m^2. BMI is calculated as weight in kg divided by height in m^2 (kg/m^2) (4). BMI less than 18 is underweight, BMI 18.0 to 22.9 is normal weight, BMI 23.0 to 24.9 is overweight, BMI 25.0 or higher is obese. It is well known fact that obese people are more likely to acquire Type II DM, Hypertension (HTN), dyslipidemia, CVD, stroke, and many other problems. Obese individuals with diabetes make up 58.68% of the population (5). The most prevalent metabolic illness like DM is marked by elevated blood sugar levels, affects 15.6% of men and 13.5% of women in India (6). As per the recent data there has been a rise in the occurrence of obesity among college-going students, which could be contributing to the increased trend of diabetes mellitus in this population as obesity has been shown to be an important pathogenic factor for IR (7). The foremost cause for Type II Diabetes Mellitus (T2DM) is resistance to the physiologic actions of insulin (8). Insulin Resistance is linked to T2DM and obesity (9). TNF-α, also known as cachectin, is a cytokine that was first discovered by Carswell *et al*. in 1975 (10). TNF-α is a cytokine with a pleiotropic character that is essential for controlling the immune system and the inflammatory response. It has been acknowledged as a crucial modulator of inflammatory response and is recognized as a contributor for the etiology of several inflammatory and autoimmune diseases (11). Monocytes and macrophages are the main cell types that synthesize TNF-α however another type of cells like T lymphocytes, B cells, Natural Killer Cells and endothelial cells, etc. can also produce it. The gene for TNF-α is located on chromosome 6p21.3 (12). Several studies have been conducted in the age range of 20 to 60 years but a limited information is available regarding blood glucose and TNF-α level in young obese individuals of 18 to 24 years of age group who are more prone to develop IR leading to severe complications at an early stage of their life. Hence, the present study will help to educate the young individuals on lifestyle measures to be undertaken to avoid complications and an early therapeutic intervention, if required.

2. Materials and Methods

A cross sectional study conducted by including subjects in the age group of 18 to 24 years from western U.P. visiting Sharda University, Greater Noida, Uttar Pradesh, India, were included as volunteers for the study, after obtaining ethical clearance from the Institutional Ethical Committee.

Inclusion Criteria: Obese subjects in the age group of 18 to 24 years and willing to participate in the study.

Exclusion Criteria: Non obese, under or above the age criteria, pregnancy, diabetes mellitus, under any medication and suffering from any chronic disease.

Out of 320 Volunteers, 100 obese subjects were selected for the study.

Anthropometry Measurements

Height (m) and weight (kg) were taken using standard techniques, and BMI was calculated as weight in kg divided by height in m^2, PBF is the total body weight measured by using a fully automated body composition analyser, Welcare Accuniq BC 310 using BIA method. WC & WHR were also measured by using a non-elastic measuring tape as per WHO guidelines. The WC protocol described by the WHO guideline is: A stretch-resistant tape is used to measure WC in centimeters at the horizontal plane halfway between the superior iliac crest and the bottom edge of the lowest rib. Divide the waist circumference by the hip circumference to get the WHR, which was measured around the area over the greater trochanters with a stretch-resistant tape (13).

Biochemical Measurements

After at least eight-hour overnight fast, participant's blood was drawn. The plasma and serum samples were separated and stored at -20 °C for analysis. Samples for Fasting Plasma Glucose (FPG) measurements were tested on the same day. Estimation of fasting blood glucose was done by GOD-POD method using semi-auto analyser. Estimation of Tumor Necrosis Factor-Alpha (TNF- α) was done by ELISA method. The standard curve was created by plotting the standard absorbances (vertical axis) against the standard concentrations (horizontal axis) on a linear graph. The curve was created by connecting the points in order to determine the value of TNF-α.

Statistical Analysis

Statistical software in version 22 of SPSS was used to conduct the analysis. One sample t-test was taken into consideration for the calculation of result. A p-value of ≤ 0.05 is significant and p-value of ≤ 0.001 is highly significant.

Result

One sample t-test was used to determine the statistical difference (statistically significance) between study group and population as shown in table 1.

Table 1: One-sample student t-value statistical analysis of various parameters

Parameters	n	Mean	S.D.	t-value	p-value
FBG	100	88.6	9.02	1.6	0.123
Serum TNF-α	100	12.81	1.76	49.8	< 0.001**
WC	100	82.24	6.58	20.79	< 0.001**
PBF	100	34.56	4.71	30.91	< 0.001**
BMI	100	28.12	2.36	27.20	< 0.001**

**Highly Significant

Table 2: Pearson Correlation between FBG, TNF- α & Body Composition

		Serum TNF-α	PBF	WC
FBG	Correlation Coefficient	0.388**	0.103	0.090
	Sig. (2-tailed)	< 0.001	0.304	0.372
	n	100	100	100

The blood glucose level is significantly correlating with TNF-α (r = 0.388) with p-value (< 0.001) shown in table 2.

Table 3: Pearson Correlation between TNF- α, FBG & Body Composition

		FBG	PBF	WC
Serum TNF-α	Correlation Coefficient	0.388**	0.524**	0.49**
	Sig. (2-tailed)	< 0.001	< 0.001	< 0.001
	n	100	100	100

TNF- α has significant correlation with Fasting blood glucose level (r = 0.388) with p-value (< 0.001), shown in table 2. Waist Circumference (r = 0.49) with p-value (< 0.001) and Percentage Body Fat (r = 0.524) with p-value (< 0.001) as shown in table 3.

Discussion

Type II DM, HTN, dyslipidemia and other chronic illnesses are all correlated with obesity. Obesity poses a serious threat to India's health care system in young people. It has been observed over the past ten years that young Indian population tend to develop diabetes at lower obesity levels and experience its effects early (14). TNF- α is suggested as a cross-link between obesity and IR (15).

This study conducted on obese subjects within the age group of 18 to 24 years as there is dramatic physiological, sexual, psychological and social developmental changes occurring concurrently as a person matures from childhood to adulthood. This change presents potential threat to their health and well-being (16).

The present study correlates body fat composition with FBG and TNF- α level. It has been observed that FBG level has a significant correlation with TNF- α in obese

individuals and vice versa. Also, TNF- α has a statistically significant correlation with Body fat composition (WC and PBF) in obese subjects in the study. Olszanecka-Glinianowicz M., *et al*. in 2011 also mentioned in their study that TNF-α levels were significantly correlated with both WC and PBF in a group of overweight and obese women. A study also revealed that drop in TNF-α levels were related to decreases in percentage of body fat and waist circumference. These findings emphasize the value of maintaining a healthy weight and WC in order to lower the risk of chronic inflammation and associated health issues (17). Nieto-Vazquez I., *et al*. in 2008 mentioned in their study that exposure to TNF-α can induce a state of insulin resistance by interfering with insulin signaling pathways in adipose tissue, hepatic tissues, and skeletal muscle. Inhibitory Kappa B Kinases (IKK) and Jun N-terminal Kinase (JNK) inhibitors prevent insulin receptor substrate-1 (IRS-1) from being phosphorylated and from activating signaling pathways downstream that are important in glucose uptake and metabolism. These are two downstream signaling molecules can be activated by TNF-α. They also boost the levels of some of other proinflammatory cytokines, including interleukin-6 (IL-6) and interleukin-1 beta (IL-1β), which can further contribute to insulin resistance by promoting inflammation and inhibiting insulin signaling. Therefore, TNF-α is considered as a crosslink between obesity and insulin resistance (15). Pausova Z., *et al*. mentioned in their study that a genetic variation in the TNF-α gene locus was significantly related with assessments of adiposity, including WC and WHR, in both Pima Indians and European whites. This shows that the development of obesity and its related metabolic issues may be influenced by genetic variation in the TNF-α gene locus (18). Yan WJ., *et al*. in 2009 found in their study that plasma adiponectin levels are lower in obese individuals, including children, compared to non-obese individuals. On the other hand, Obesity is associated with greater plasma TNF-α concentrations, which have been linked to metabolic problems such as insulin resistance and persistent low-grade inflammation. The interaction between Adiponectin and TNF-α in the development of childhood obesity suggests that both factors get indulged in the regulation of body fat and that the balance between them is important for maintaining metabolic health (19).

The present study showed that TNF-α has a significant correlation with fasting blood glucose level and also with the Body fat composition (WC and PBF) in obese subjects.

Wei J., *et al*., conducted a study on Chinese population in 2019 found that Chinese Visceral Adipocyte Index (CVAI) is a better indicator of metabolic disorders, including diabetes, than BMI, WC, and BSI, based on the Youden index. This is because CVAI takes into account both BMI and WC, which are important indicators of central obesity and metabolic health. However, considering their increased sensitivity and accessibility, BMI and WC may be better indications for diabetes screening than CVAI (7). Tuba Yalçın., *et al*. in 2022 found in their study that Central obesity, as indicated by a larger waist circumference, is a prime risk element for the onset of T2DM. It is also corresponded with increased levels of inflammatory markers, including TNF-α. The abdominal region consists of more adipose tissue metabolically active and produces more inflammatory cytokines, including TNF-α,

compared to adipose tissue in other regions of the body (20). In this study a FBG has non-significant correlation with body fat composition (WC, PBF). Despite insulin resistance, hyperglycemia does not manifest in the majority of obese people. Alpha-cells of the islet of Langerhans of the pancreas secrete adequate quantities of insulin that are sufficient to compensate for insulin level decreases under normal conditions, thereby preserving normal glucose tolerance (21).

Hence lifestyle modifications, including healthy nutrition and regular physical exercises, can be effective in reducing the onset of obesity and improving the underlying mechanisms of metabolic diseases such as redox imbalance (oxidative damage), inflammation, and impaired insulin sensitivity. Particularly in people with T2DM, weight loss has been demonstrated to lower TNF-α levels and enhance insulin sensitivity.

Conclusion

This study shows that in obese individual, measurements of cachectin (TNF-α), Body Fat Composition (WC and PBF) and FBG levels all have a positive correlation. TNF-α may thereby contribute to a development of insulin resistance, which may result in Type 2 DM (15). Lifestyle changes like as weight reduction through feeding substitution, regular exercise, and avoiding high- caloric diet may help to decrease the TNF-α levels in obese individuals. The decrease in TNF-α levels may improve the insulin sensitivity and potentially prevent the development of serious health complications as CVD, DM, HTN and dyslipidemia.

Limitation

This was a cross-sectional study with 100 subjects and area-specific. A longitudinal study needs to be conducted across a wider geographic area covering larger population.

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