Body mass index and total testosterone level in obese male pre-diabetic patients: correlation with homeostasis model assessment of insulin resistance

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ABSTRACT

Introduction: Men with comorbidities are typically more likely to have testosterone insufficiency. In this study, total testosterone levels in obese male pre-diabetic patients will be correlated with body mass index and a homeostasis model assessment of insulin resistance (HOMA-IR).

Methods: This investigation is a cross-sectional analytical observational study. Insulin resistance was measured by HOMA-IR. Enzyme link immunosorbent assay (ELISA) was used to measure the total testosterone levels. 35 obese male patients who were also pre-diabetic had these signs evaluated.

Results: In this study, 35 obese male individuals with a family history of type 2 diabetes mellitus and an average age of 31.91 were included (3.79). The total testosterone level was 328.72 (49.41) ng/mL, the HOMA-IR was 3.64 (1.00), and testosterone levels were lowered (300 ng/dl) in 48% of the individuals. In male pre-diabetic individuals, there was a strong negative connection between BMI and Total Testosterone levels (r = -0.567, p=0.001). In male pre-diabetic patients, there was a significant negative connection between HOMA-IR and total testosterone levels (r = -0.671, p=0.001). In pre-diabetic obese male patients, there was a strong inverse relationship between total testosterone level and BMI. In obese male pre-diabetic individuals, there is a substantial negative association between HOMA-IR and total testosterone level.

Conclusion: In pre-diabetic obese male patients, there was a strong inverse relationship between total testosterone level and BMI. In obese male pre-diabetic individuals, there is a substantial negative association between HOMA-IR and total testosterone level.

Keywords: diabetes, testosterone, male, obesity.


INTRODUCTION

Human physiology depends on testosterone in a significant way. Testosterone and its metabolites control male sexual and reproductive processes, as well as energy metabolism, muscle growth, and adipogenesis. The hypothalamic-pituitary-testis (HHT) axis controls the body's testosterone levels. Men who lack enough testosterone experience negative impacts on their general health and quality of life.

Around 10 to 40 percent of people worldwide lack enough testosterone. Men with comorbidities are typically more likely to have testosterone insufficiency. An estimated 17–33% of males in Asia and South America have low testosterone levels. Different illnesses, including metabolic problems, can lead to anomalies in the hypothalamus and pituitary, which can result in secondary testosterone insufficiency. The main contributors to low testosterone levels in males include metabolic diseases like type 2 diabetes mellitus (T2DM) and obesity. Impaired glucose tolerance, lower HDL (high-density lipoprotein) levels, and higher fat mass and triglycerides are all consequences of testosterone deprivation. Regardless of the existence or absence of clinical symptoms of testosterone shortage, the Food and Drug Administration (FDA) defines testosterone deficiency as a testosterone level of 300 ng/dL or less. Investigating how total testosterone levels relate to body mass index (BMI) and HOMA IR is crucial.

The Rancho Bernardo study found that men with impaired glucose tolerance or fasting glucose had lower serum total testosterone levels than the average population. Hyperinsulinemia, which is brought on by increased insulin resistance, can decrease kisspeptin neurons in the hypothalamus. Because kisspeptins activity is inhibited, the hypothalamus secretes less gonadotropin-releasing hormone (GnRH), which lowers luteinizing hormone (LH) levels. In a study of male T2DM patients in Nigeria, Agbecha et al. discovered a strong inverse relationship between testosterone and HOMA-IR values (r = -0.396, p 0.05). The deficiency of testosterone levels in men with pre-diabetics can worsen glycemlc control, thereby accelerating the progression to T2DM. In addition, a decrease in quality of life can occur due to testosterone deficiency in men. Low levels of sex hormone binding globulin (SHBG) due to the inhibitory influence on SHBG production in the liver caused by higher insulin concentrations are one
mechanism that is considered to produce total testosterone serum insufficiency in obese men. The decrease in SHBG levels is caused by an increase in the concentration of lipids in the liver, an increase in proinflammatory cytokines, an increase in the conversion of testosterone to estradiol in the periphery, and a negative feedback mechanism on the HHT axis, as well as direct or indirect effects of leptin on the HHT axis.\textsuperscript{5,6} This study aims to correlate BMI and HOMA-IR with total testosterone levels in obese male pre-diabetic patients.

**MATERIAL AND METHODS**

The M Djamil General Hospital and the Universitas Andalas Faculty of Medicine in Padang, Indonesia, served as the site of this study. An analytical observational model was used in this study. Pre-diabetic obese male individuals with a family history of T2DM are the inclusion criteria. Patients who meet the following criteria are excluded: T2DM, hyper or hypogonadotropic hypogonadism, hyperprolactinemia, hepatic cirrhosis, autoimmune disease, cancer, glucocorticoid therapy, chronic kidney disease, and testosterone therapy.

The HOMA-IR test is used to measure insulin resistance. Testosterone level was assessed by total testosterone level. The value of body mass index (BMI) was obtained from formula (body weight in kilograms divided by height in meters square). Evaluation of HOMA-IR value derived from formula (fasting blood glucose in mg/dl multiplied by fasting serum insulin in mIU/L divided by 22.5). Testosterone total level will be measured in those who have pre-diabetes, a BMI greater than 25 kg/m\(^2\), and a HOMA-IR greater than 2. SPSS 26 was used to analyze the data collected for this investigation, all values considered significant if \(p<0.05\)

**RESULTS**

Table 1 shows that all pre-diabetic patients are obese. The average BMI was 33.12 (4.11) kg/m\(^2\). With a mean waist circumference of 112.14 (13.31) cm, 94% of the patients in this study were centrally obese.

In table 2, On obese male pre-diabetic patients, the HOMA-IR mean was 3.64.
levels. It can be seen that the higher the BMI, the lower total testosterone levels.

According to Graph 2, in obese male pre-diabetic individuals, there was a negative, strong, and significant association between HOMA-IR levels and total testosterone levels (r = -0.671, r² = 0.469, p<0.001). It can be seen that the higher of HOMA-IR, the lower the testosterone levels.

DISCUSSION

The screening of the male population with a first-degree family history (biological parents, siblings, or biological children) suffering from T2DM, as many as 57 people, 35 obese men with pre-diabetes, were found. This number is 61.40% of men in the general population with a first-degree family history of having T2DM who were screened. This fits with the report from Wagner et al. which declared that a family history of diabetes was connected to 40% increase in the risk of developing pre-diabetes. Other factors, such as obesity and age, can lead to a 26% higher risk. Research by Hilding et al. (2006) in Sweden found that the risk of pre-diabetes increased to 50% in individuals with a family history of T2DM.9,10

In this study, based on BMI measurements, 100% of the samples were obese with an average BMI of 33.91 (3.79) kg/m², while based on waist circumference measurements, 94% (33) of the sample had central obesity with an average waist circumference of 112.14 (13.31) cm. Rajput et al. reported that more than 80% of pre-diabetics had central obesity, namely 80.2% in men and 82.2% in women with pre-diabetes.11

Differences in the percentage of obesity based on measurements of BMI and waist circumference in this study may occur due to genetic and environmental factors such as diet and physical activity that can affect waist circumference in obese patients.12,13

In this investigation, the average HOMA-IR score was 3.64. (1.00). This is almost the same as that obtained by Gupta’s research. In the study by Gupta et al. (2018), pre-diabetic patients had a HOMA-IR of 3.7 (0.1).14 Ho et al. (2013) found the average total testosterone levels in men with pre-diabetics was 397.2±133.6 ng/dl. This study’s total testosterone level was 328.72 (94.94) ng/dl. From the results of the study, it was also found that 48% of the study samples had testosterone deficiency. It may be said that in this study, the average testosterone levels were lower because all samples were obese with high levels of HOMA-IR.15

In this investigation, there was a negative correlation direction and moderate correlation strength (r = -0.567) between BMI and total serum testosterone levels in males with pre-diabetics (p<0.05). Boeri et al. it was observed that infertile males with pre-diabetics had a higher BMI, and the percentage of obese categories was more elevated than men who experience infertility without pre-diabetics.16 Osuna et al.16 study total testosterone levels and BMI have a moderately positive connection (r = -0.447; p < 0.01). According to Chen et al. (2018), BMI is a risk factor irrespective of low testosterone. In this study, it was found that the sample with testosterone deficiency had a higher average BMI of 35.37 kg/m² than the sample without testosterone deficiency, which was 30.98 kg/m².17,18

In this study, BMI has a 32% impact on total testosterone hormone levels, while other variables affect other variables. Total testosterone levels are influenced by genetic factors, primary abnormalities in the testes, the hypothalamic-pituitary axis, gonadotropin hormones (LH and follicle-stimulating hormone), SHBG, proinflammatory cytokines, and environmental factors.19 In a multicenter prospective cohort study by Lee et al. in Europe, The European Male Aging Study (EMAS) reported that 73% of adult men with total testosterone deficiency are overweight or obese.20,21

In men with pre-diabetes, there was a link between total testosterone levels and HOMA-IR (p<0.05), and the correlation was negative and strong (r = -0.671). Sedlak et al. reported a correlation between HOMA-IR and serum total testosterone (r= -0.63, p<0.01).22 According to Valsaraj et al. adult men’s serum total testosterone levels and HOMA-IR correlate, who are overweight and obese (p<0.0001). The increase in HOMA-IR in obese pre-diabetic patients causes a decrease in total testosterone levels.23-29

CONCLUSION

In obese male pre-diabetic individuals, there was a strong inverse relationship between BMI and total testosterone level. HOMA-IR significantly correlates significantly with total testosterone levels in obese male pre-diabetic patients.

CONFLICT OF INTEREST

All author reports no conflicts of interest in this work.

ETHICAL CONSIDERATION

This study has been approved by the health research ethics committee RSUP Dr. M. Djamil Padang with ethical clearance reference number No.: 410/KEPK/2021.
REFERENCES


