BERKALA KEDOKTERAN
doi: 10.20527/jbk.v21i2.24498
RESEARCH ARTICLE
OPEN ACCES

Relationship between Interleukin 6 and Estradiol Levels in Obese and Adult Men

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Abstract:

Obesity is a chronic disease characterized by a pathophysiological process that causes an increase in adipose tissue mass, leading to an increased risk of morbidity and mortality. Currently, there are many conditions that allow the interaction between environmental factors and genes that lead to various metabolic disease complications, such as diabetes mellitus and heart attack. Health workers are at the forefront of managing obesity and its associated complications. The study was conducted at Ngoerah Hospital from March to October 2024. The target population in this study were adult male medical personnel with and without obesity, working at Ngurah Hospital. The inclusion criteria in this study: male health workers in the environment at Ngoerah Hospital aged 18-45 years and willing to participate in the study by signing *informed consent*. Exclusion criteria in this study were all male health workers with infectious or inflammatory diseases, and or suffering from malignancies or a history of chemotherapy, and or with the use of hormonal therapy. The sample size of the study was 64 subjects. Data analysis included descriptive statistics, a normality test using the Kolmogorov-Smirnov test, a comparison test using the Mann-Whitney U test, and a correlation test using the Spearman rank correlation. This study was approved by the Research Ethics Commission, approval number 1697/UN14.2.2.VII.14/LT/2024. The results of this study found that IL-6 and estradiol levels in the obese group were higher than the non-obese group, however, the differences were not statistically significant. This may be attributed to the relatively young age of the subjects and the absence of significant inflammation in the early stages of obesity. There was no significant correlation between IL-6 and estradiol in all subjects, obese and non-obese groups.

Keywords: Estradiol; interleukin-6 (IL-6), obesity

Introduction

Obesity is a chronic disease characterized by a pathophysiological process that causes an increase in adipose tissue mass, leading to an increased risk of morbidity and mortality. There are many conditions that allow the interaction between environmental factors and genes that regulate weight gain, so that many people have a body mass index ≥ 25 kg/m^2 which is associated with various metabolic disease complications, such as diabetes mellitus, heart attack.[1]

Obesity is a major cause of hypogonadism which is associated with impaired gonadal function in men. Obese men have a higher risk of infertility than those who are at an ideal weight. Male fertility depends on good sperm count and quality. Spermatogenesis and maturation is a very complex process involving the regulation of sex hormones, testes, Sertoli cells and epididymal fluid. Too much fat can cause changes in hormone levels and trigger chronic inflammation in the genital tract. High fat content in the scrotal region can also lead to increased scrotal temperature. All these consequences of obesity damage the microenvironment of the testes and epididymis, which are essential for sperm production and maturation.[2]

Obesity is a chronic low-grade inflammatory condition caused by many factors. In the obesity, lipid deposition causes an increase in adipocyte volume, when adipocyte hypertrophy exceeds its limit, apoptosis will occur. Necrotic adipocytes secrete various inflammatory factors and chemokines, such as Intercellular Adhesion Molecule-1 (ICAM-1) and Vascular Cell Adhesion Molecule (VCAM-1). This process will induce macrophage, and monocytes proliferate and migrate into adipose tissue. Adipocytes release more fatty acids and endotoxins, which activate macrophages to transform into inflammation-inducing M1 macrophages, and then activate the NF-κB pathway, which significantly increases the release of proinflammatory factors such as Interleukin 6 (IL-6), while anti-inflammatory factors are reduced. In addition, hypertrophic adipocytes can also alter intracellular signal transduction, increase the expression of proinflammatory cytokines, and ultimately lead to chronic inflammation.[3]

During inflammation, the secretion of proinflammatory factors such as IL-6 increases the expression of aromatase in adipose tissue. The high expression of aromatase causes androgens be permanently converted into estradiol, thus disrupting the hormonal balance in men. This means that the body's androgen levels fall and estradiol levels rise. This causes spermatogenesis to be unable to proceed normally.[3]

Higher estrogen levels in obese men have been repeatedly shown in various studies, yet some other studies have found no increase in estrogen or no correlation with BMI. This is one of the reasons why the concept of decreased testosterone due to increased conversion to estrogen has been criticized, although it has not been fully refuted and is still being debated.[4]

Health workers are at the forefront of managing obesity and its associated complications. They play a crucial role as role models for the community in promoting awareness about the dangers of obesity and the importance of maintaining an ideal body weight. Research on the relationship between IL-6 and estradiol levels in adult populations with obesity, especially in health workers in Indonesia has never been done.[5,6]

One of the leading fields according to the Udayana University Research Master Plan is research in the field of medicine / health, which is derived into a research *roadmap* in the field of non-communicable diseases and a research *roadmap for the* Internal Medicine Study Program, so researchers want to examine metabolic disorders, especially obesity which is part of metabolic disease in relation to the male reproductive system. This research is included in the Technology Readiness Level 3, which is to prove a concept.

Based on the background of the above problems, the problem can be formulated how is the relationship between interleukin 6 and estradiol levels in adult men with obesity

and not obese. The purpose of this study was to determine the relationship between interleukin 6 and estradiol levels in adult men with obesity and not obese. The results of this study are expected to provide additional knowledge in the field of obesity, especially regarding the relationship between interleukin 6 and estradiol levels in the adult male population with obesity, and can be the basis for the development of future research. The results of this study are expected to provide guidance on the importance of obesity management to prevent or overcome hormonal disorders and improve fertility in men with obesity.

Research Method

This study used an analytic cross-sectional study design to find the relationship between IL-6 and estradiol in adult men with obese with a comparison group of non-obese. This study took place in March-October 2024. The subjects of this study were male health workers in the environment at Ngoerah Hospital aged 18-45 years, and willing to participate in the study by signing *informed consent*. Exclusion criteria in this study were all male health workers with infectious or inflammatory diseases, or suffering from malignancy or a history of chemotherapy or with the use of hormonal therapy. The number of subjects totaled 64 samples. The data analysis carried out is: descriptive analysis: to find the frequency distribution of each variable where the data will be displayed in the form of a table of basic data of the research subjects. Normality test using Kolmogorov-Smirnov test. Comparative test to determine the comparison of IL-6 and estradiol levels in obese and non-obese groups. Mann-Whitney test was used because the data was not nornally distributed.

Results

A total of 64 subjects participated, consisting of 40 obese (62.5%) and 20 people (37.5%) who were not obese. The median age of the subjects was 30 years with a minimum age of 22 years and a maximum age of 40 years.

The mean levels of IL-6 and estradiol in the obese group were higher than the non-obese group, but not statistically significant as shown in Table 1.

Table 1. Comparison of IL-6 and estradiol levels in obese and non-obese groups

Parameters	Obese Mean ± SD	Non-Obese Mean ± SD	p
IL-6 levels (ng/dL)	237.66 ± 221.14	163.05± 94.73	0.305 *
Estradiol Level (ng/L)	2116.88 ± 637.19	2111.42 ± 621.92	0,901 *

*Mann-Whitney test

There was no significant correlation between IL-6 and estradiol levels in all groups, obese and non-obese groups, as shown in Table 2.

Table 2. Correlation of IL-6 and estradiol levels in all, obese and non-obese groups

Group	r	p
All Groups	-0.002	0.987*
Obese Group	-0.013	0.938*
Non-Obese Group	-0.053	0.806*

*Spearman Correlation Test

Discussion

Obesity increases the expression of pro-inflammatory cytokines, ultimately leading to chronic inflammation. IL-6 is one of the main pro-inflammatory cytokines in obesity. The results showed that IL-6 levels in obesity were higher than in the non-obese group, but not statistically significant. This may be because the subjects were young and there was no

significant inflammation in the early phase of obesity.[7-9]

In obesity, during chronic inflammation, secretion of proinflammatory factors such as IL-6 increases aromatase expression in adipose tissue.[12,13] The high expression of aromatase causes androgens be converted into estrogen/ estradiol permanently, thus disrupting the hormonal balance in men.[2,12] This means that the body's androgen levels fall and estradiol levels rise The higher estradiol levels can then impact the hypothalamic-pituitary-gonadal axis and in men lead to an overall decrease in testosterone production.[14]

In this study estradiol levels in the obese group were slightly higher than the non-obese group, but not statistically significant. This may also be due to the fact that most of the subjects were young, where the chronic inflammatory process due to obesity has not fully occurred and lasted for a long time.

Conclusions

IL-6 and estradiol levels in the obese group were higher than the non-obese group, but not statistically significant. This may be because the subjects were young and there was no significant inflammation in the early phase of obesity. There was no significant correlation between IL-6 and estradiol in all subjects, obese and non-obese groups.

Acknowledgements

We express our gratitude to the research team at Ngoerah Hospital in Denpasar, Bali, for their diligent work in collecting, documenting, and analyzing the data.

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