Correlation Analysis of Galectin-3 Serum Level in Obesity with and without Obesity

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ABSTRACT

There are more than 3.4 million deaths every year in the world due to overweight and obesity. Obesity is a chronic proinflammatory condition marked by increased lipid and adipose tissues, leading to ectopic fat accumulation with increased levels of proinflammatory cytokines. Obesity causes a progressive increase in galectin-3 expression, especially in visceral and subcutaneous adipose tissue in experimental animals. Galectin-3 is upregulated in obesity and is defined as a proinflammatory molecule that can cause insulin resistance. This study aims to analyze differences in galectin-3 levels between obese and non-obese subjects. This was a cross-sectional study, using a total of 80 subjects. The study was conducted throughout August 2022. The samples were grouped into obese and non-obese based on Body Mass Index (BMI). The galectin-3 measurement used the Enzyme-Linked Immunosorbent Assay (ELISA) method. Statistical tests used the Mann-Whitney test and Spearman rho; the test results were significant if the p-value <0.05. The samples were divided into obese and non-obese groups, each group had 40 people. Galectin-3 levels in the obese group were 0.9±0.36 ng/mL significantly higher than the non-obese group's 0.43±0.11 ng/mL, (p<0.001). There was a strong positive correlation between levels of galectin-3 and BMI, (r=0.866, p<0.001). There is a positive correlation between serum galectin-3 levels and BMI. The greater value of the BMI, the higher levels of galectin-3.

Keywords: Galectin-3, obesity, BMI

INTRODUCTION

Obesity is a chronic proinflammatory condition that is marked by an increase in lipid and adipose tissue, causing an accumulation of ectopic lipids in various tissues and an increase of proinflammatory cytokines. The increasing prevalence of overweight and obesity prevalence in most countries has become a global concern. This is estimated to be the cause of more than 3.4 million deaths annually. The number of obesity in Indonesia in 2016, according to the National Health Indicator Survey (Survei Indikator Kesehatan Nasional/SIRKENAS), the obesity rate based on Body Mass Index (BMI), (BMI > 27) increased to 20.7% while obesity (BMI > 25) became 33.5%. This increase in body mass is a challenge for the medical world.¹³

Galectin-3 is a member of the soluble beta-galactoside binding lectin family and affects cell adhesion, proliferation, differentiation, inflammation, and angiogenesis. Galectin-3 activity is determined by cellular localization. Extracellular galectin-3 triggers apoptosis while intracellular galectin-3 is the inhibitor. Galectin-3 is expressed in various cells, especially in macrophages and adipocytes. Recombinant galectin-3 is proven to induce the proliferation of in-vitro pro-adipocytes.³

Galectin-3 can be secreted on the surface of damaged or inflamed cells, and galectin-3 can be used as a sensitive diagnostic or prognostic marker for various pathological conditions. In animals with heart failure, galectin-3 levels have been proven to be a diagnostic marker for early detection of heart degeneration in acute myocarditis and acute myocardial infarction.⁴

White Adipose Tissue (WAT) is the main location for energy storage, insulin controls the uptake and storage of glucose and fatty acid, and fatty acids inhibit lipolysis. Through secretion of adipokine, cytokine, and mature adipocyte hormone contribute to maintaining energy balance comprehensively. In obese conditions, dysfunction occurs and adipose tissue is infiltrated by proinflammatory CD11c+ macrophages and other leukocytes that produce proinflammatory cytokines and will interfere with insulin signaling, while the expression of the protective adipokine adiponectin is reduced. In overweight/obese subjects there is an increase in the
release of fatty acids and inflammatory cytokines that results in low-grade systemic inflammation called metaflammation.\(^3\)

In obese subjects, galectin-3 has positive correlations with leptin serum, resistin, IL-6, and age; while the general population has a positive correlation with blood pressure, lipid serum, kidney function, and age. Obesity causes a progressive increase in galectin-3 expression, especially in visceral and subcutaneous adipose tissues in research animals. Higher galectin-3 expression in visceral tissue compared to subcutaneous tissue can also be observed in human beings. Regulation of galectin-3 during obesity in experimental animals is independent of leptin, with proinflammatory CD11c+ macrophages being the main producers of this galectin. Adiponectin can directly suppress galectin-3 expression in monocytes and adipocytes.\(^3,5,6\)

Li et al. reported that galectin-3-knockout mice, in which circulating galectin-3 levels were reduced, required more insulin when exposed to a high-fat diet or aging.\(^4\) Galectin-3 is upregulated in obesity and is defined as a proinflammatory molecule that can contribute to insulin resistance. Ohkura et al. reported that galectin-3 was associated with reduced plasma insulin levels and insulin sensitivity in type 2 diabetics, but not with BMI.\(^4\) Yulmaz et al., reported high levels of galectin-3 in patients with diabetes and prediabetes leading to diabetes and complications. Karlson et al. reported that the overproduction of galectin-3 inhibited beta-cell damage caused by the cytotoxic effect of interleukin-1 beta.\(^4,6\)

Other further studies revealed that galectin-3 expression is detected in many disease conditions, such as heart disease, kidney disease, diabetes mellitus, viral infections, autoimmune diseases, neurodegenerative disorders, and tumor formation.

Based on this, the researchers were interested in examining the relationship between serum galectin-3 levels in obese and non-obese subjects.

**METHODS**

This research is an analytic descriptive study using a cross-sectional design. The research was carried out at the Clinical Pathology Laboratory Installation of Hasanuddin University Hospital for sampling and samples were examined at the Research Unit of the Hasanuddin University Faculty of Medicine. This study was held from August 2022 to September 2022 and 80 samples were obtained.

The study population was all students of the Specialist Medical Education Program, Faculty of Medicine, University of Hasanuddin, Makassar. The research sample was an affordable population that meets the inclusion and exclusion criteria. The inclusion criteria and exclusion criteria referred to were all volunteers who were classified as obese or non-obese and had no history of diabetes mellitus, hypertension, and malignancy. The anthropometric parameters used in this study were body weight and height to determine BMI. The way to determine BMI is by dividing your weight in kilograms by the square of your height in meters squared (kg/m\(^2\)).

Classification of obesity if BMI ≥ 25.0 and non-obese if BMI < 25.0. Serum galectin-3 levels were measured using the Enzyme-Linked Immunosorbent Assay (ELISA) method and using the Human galectin-3 kit, Assay Genie, which was measured in ng/mL units.

Data analysis was performed using SPSS 25.0. The data normality test used was the Kolmogorov-Smirnov. The statistical analysis tests used were the Chi-Square, Mann-Whitney, and Spearman rho correlation tests. The test results are significant if the p-value <0.05.

This research was carried out after obtaining ethical clearance by considering respect for the subject, beneficence, non-maleficence, and justice from the Health Research Ethics Commission (KEPK) Faculty of Medicine, Hasanuddin University/UH Hospital/Dr. Wahidin Sudirohusodo Makassar with number 437/UN4.6.4.5.31/PP36/2022.

**RESULTS AND DISCUSSIONS**

In this study, there were 80 samples divided into 40 obese subjects and 40 non-obese subjects. There were 41 (51.3%) male patients and 39 (48.8%) female patients with an age range of 22-0-40 years old. Mean BMI and galectin-3 levels were 26.3 kg/m\(^2\) and 0.66 ng/mL respectively (Table 1).

Based on Table 2 the comparison of mean age and BMI according to obesity, tested with Mann-Whitney tests, show a significant difference in age and BMI with p-value of 0.037 and < 0.001 (p < 0.05), respectively. The difference between the gender that was tested using Chi-Square showed no significant difference with a p-value of 0.823 (p > 0.05).

Mean galectin-3 levels in obese patients were 0.9 ng/mL while non-obese patients were 0.43 ng/mL. The comparison of mean galectin-3 according to obesity through Mann-Whitney tests shows a significant difference with a p-value < 0.001 (p < 0.05).

According to Table 3, the Spearman Rho test showed a strong positive correlation between galectin-3 levels with BMI with p < 0.001 (p < 0.05) with a strength of correlation as much as 0.866 (very strong correlation).
The study was conducted on 80 samples with 41 males and 39 females. Subjects were divided into 2 groups, 40 obese subjects, and 40 non-obese subjects. The age of subjects was between 32.33±3.8 years in obese subjects and 30.45±3.8 years in non-obese subjects. Globally, the prevalence of obesity increased by 13% in adults ≥18 years in 2016. This is in accordance with the 2018 Riskesdas, in Indonesia there was an increase in the prevalence of central obesity in adults aged > 15 increasing to 73.1% in 2017.

There was a difference in the average galectin-3 level in the obese group compared to the non-obese group. The mean galectin-3 level in the obese group (0.9±0.36) ng/mL was significantly higher than the mean galectin-3 level in the non-obese group (0.43±0.11) ng/mL (p<0.001). In addition, there is also a strong positive correlation with a p-value of <0.001 (p <0.05) and a correlation strength of 0.866 on galectin-3 levels with BMI. These results are in line with research conducted by Aksit et al. who say that galectin-3 levels were found to be higher in obese subjects. The study by Weigert et al. who said that galectin-3 levels were higher in obese subjects and positively correlated with BMI, which was associated with increased Visceral Adipose Tissue (VAT) in obesity.

In obesity, there is an increase in VAT, which will release adipokines together with galectin-3 released into the portal vein, and increased production in VAT compared to Subcutaneous Adipose Tissue (SAT) can be associated with higher galectin-3 in portal vein blood. An analysis of animal adipose tissue revealed a greater distribution of galectin-3 expression in VAT, supporting the finding that visceral fat is the preferred site of galectin-3 production. High expression of galectin-3 is known to occur in monocytes, tissue macrophages, and dendritic cells. Nevertheless, VAT macrophages are the main source of circulating galectin-3.
The results of this study are hoped that galectin-3 can be used as a biomarker to assess inflammation that occurs in people with obesity.

CONCLUSIONS AND SUGGESTIONS

Galectin-3 serum levels in obese people are higher than in non-obese; The greater the BMI, the higher the galectin-3 level; There is a positive correlation between galectin-3 levels and BMI. Further studies with more varied subject characteristics and populations are still needed.

REFERENCES