The Relationship Of Insulin-Like Growth Factor 1 With Bone Mass In Obese Female

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ABSTRACT

Obesity causes peripheral insulin resistance and hyperinsulinaemia, which causes a decrease in the secretion of Growth Hormone (GH) and Insulin-like Growth Factors 1 (IGF-1). Decreased GH and IGF-1 secretion decreases bone mineral density (BMD) and increases the risk of fractures. This study aimed to analyze the relationship of insulin-like growth factor 1 with bone mass in obese female. This study used a cross sectional study method using 30 obese female aged 19-23 years, body mass index (BMI) 25-35 kg/m^2, normal blood pressure, normal resting heart rate (RHR), normal hemoglobin (Hb) and fasting blood glucose (FBG) < 100 mg/dL. Measurement of IGF-1 levels used the Enzym Link Immunosorbent Assay (ELISA) method. Measurement of bone mass using TANITA (Body Composition Analyzer DC3607601 (2) -1604 FA, TANITA Corporation of America, Inc., USA). The data analysis technique used the Pearson product-moment test with Statistical Package for Social Science (SPSS). The results showed that mean levels of IGF-1 (1.17±0.10) ng/mL and bone mass (2.49±0.06) kg ($r = 0.712$, $p \leq 0.001$). Our findings suggest that there was a positive correlation between IGF-1 levels and bone mass in obese female.

Keywords : IGF-1 levels, Bone Mass, Obesity

BACKGROUND

Obesity is a condition that exceeds a person's relative body weight as a result of accumulation of nutrients, especially carbohydrates, fats and proteins. Obesity is currently a worldwide problem (Ayu and Handayani, 2016). Therefore, obesity is a dangerous condition. This is supported by the prevalence of obesity of ~ 20% (Pasquali *et al*., 2020). According to the World Health Organization (WHO) in 2014, the prevalence of overweight at over 18 years of age reached 39%, where 15% were female. This prevalence increased 2 times greater than the prevalence of obesity in 1980. According to WHO (2016), more than 1.9 billion people aged over 18 years are overweight and 600 million of them are obese. The high prevalence makes obesity a problem in the world.

Obesity is a risk factor for various health problems that are usually experienced by adults such as diabetes mellitus, hypertension and high cholesterol. The causes of obesity are very complex in the sense that there are many factors that cause obesity, such as

environmental, genetic, psychological, health, drugs, development and physical activity. The cause of obesity is multi-factorial, thus the food intake factor is one of many factors. Influential food intake is one that contains fat and is high in calories. Some of the factors that cause obesity include a history of obesity in the elderly, lack of consumption of vegetables and fruit and smoking habits (Dewi, 2015).

Obesity experiences hyperinsulinemia condition due to peripheral insulin resistance which causes reduced growth hormone (GH) secretion. The resulting decrease in GH can inhibit the liver from secreting IGF-1 (Lewitt *et al*., 2014). Growth hormone (GH) and its physiological mediator, insulin-like growth factor-1 (IGF-1), have a major role in bone growth. In general, the effect of GH promoting linear growth appears to depend on the production of IGF-1 and possibly other IGF peptides. IGF-1 acts on cartilage, stimulates cell proliferation and synthesis of Deoxyribo Nucleic Acid (DNA), Ribonucleic Acid (RNA), proteins and proteoglycans. IGF-1 is a major component of the organic skeleton matrix and is the most important differentiating factor for osteoblasts. If there is a decrease in the secretion of GH and IGF-1, it can reduce bone mineral density (BMD) and increase the risk of fracture (Ekbote *et al*., 2015). According to research conducted by Chalista *et al*. (2017) that there is a relationship between IGF-1 and low bone mineral density in the elderly. However, the relationship between IGF-1 and bone mineral density in obesity is unclear. On the basis of the above background, the researchers wanted to find out whether there was a relationship between IGF-1 and bone mass in obese female.

METHODS

This study used a cross sectional study method using 30 obese female aged 19-23 years, body mass index (BMI) 25-35 kg/m^2, normal blood pressure, normal resting heart rate (RHR), normal hemoglobin (Hb) and fasting blood glucose (FBG) < 100 mg/dL. All of these research procedures have been approved by the Health Research Ethics Commission of the Faculty of Medicine, Airlangga University, Surabaya number 81/EC/KEPK/FKUA/2020.

Measurement of height using a stadiometer (SECA, Chino, CA). Measurement of body weight, BMI, percentage body fat (PBF), fat mass (FM), free fat mass (FFM) and bone mas (BM) using TANITA (Body Composition Analyzer DC3607601 (2) -1604 FA, TANITA Corporation of America, Inc., USA). Blood pressure was measured twice at a 5 min interval on the right arm using a standard mercury sphygmomanometer (Baumanometer; Baum, Copiague, NY, USA) and recorded as an average of the two readings. Measurement of FBG using ACCU-CHEK (ACCU-CHEK® Performance, Mannheim, Germany) with mg/dL concentration units. Measurement of Hb using Mission Hemoglobin (Mission® Hb Test Strips (Whole Blood), ACON Laboratories, Inc. 10125 Mesa Rim Road, San Diego, CA 92121, USA) with a unit of concentration of g/dL.

Collecting blood was from cubital veins with 4ml after a 12-hour overnight fasting. Blood was centrifuged for 15 minutes at 3000 rpm. Serum was separated and stored at -80 ° C for analysis of IGF-1 levels the following day. Blood draws are conducted at 07.00 a.m. Measurement of serum IGF-1 levels using an Enzyme-Linked Immunosorbent Assay (ELISA) kit (Catalog No: E-EL-H0086; Lot No: 5KH3L8GCSC; Elabscience, China) with a standard curve range of 1.56-100 ng/mL and IGF-1 sensitivity level of 0.94 ng/mL.

Statistical analysis used packet statistical software for social science (SPSS) (Chicago, IL, USA). The normality test uses the Kolmogorov – Smirnov test. Correlation test using Pearson product-moment with a significant level ($p \leq 0.05$). All data are presented as mean±SE.

RESULTS

The basic profiles of the samples, including age, weight, height, body mass index, percentage body fat, fat mass, free fat mass, systolic blood pressure, diastolic blood pressure, resting heart rate, fasting blood glucose, hemoglobin, insuline-like growth factor-1, bone mass are displayed in Table 1 and Table 2.

Table 1. Characteristics of Research Subjects

Parameters	n	Mean	Std. Error
Age (years)	30	21.56	0.13
Weight (kg)	30	72.31	1.25
Height (m)	30	1.58	0.01
Body mass index (kg/m^2)	30	28.98	0.29
Percentage body fat (%)	30	44.54	0.57
Fat mass (kg)	30	33.00	0.90
Free fat mass (kg)	30	40.77	0.61
Systolic blood pressure (mmHg)	30	112.67	0.82
Diastolic blood pressure (mmHg)	30	75.00	0.93
Resting heart rate (bpm)	30	79.37	1.81
Fasting Blood Glucose (mg/dL)	30	90.16	1.20
Hemoglobin (g/dL)	30	15.23	0.25

Table 2. Association between IGF-1 serum levels with bone

Parameter	n	Mean±SE	r	p-values
IGF-1 (ng/mL)	30	1.17±0.10	0.712**	0.000
Bone Mass (kg)		2.49±0.06		

** Significant with $p \leq 0.01$ by Pearson's product-moment
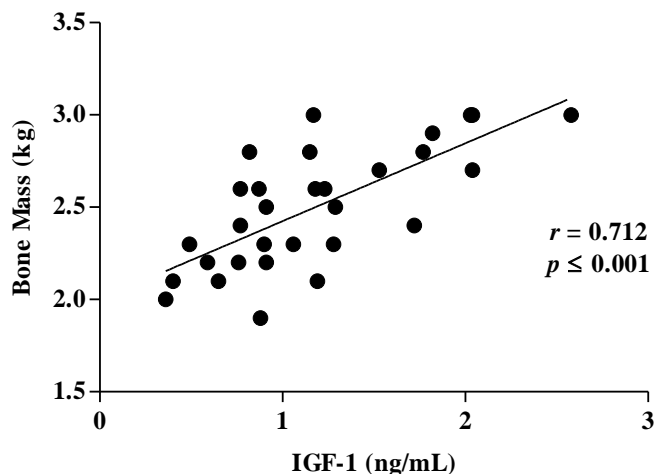
Figure 1. Correlations between IGF-1 levels and bone mass

Based on Table 2 and Figure 1, the results of the Pearson product-moment test show that there was a positive correlation between IGF-1 levels and bone mass ($r = 0.712$, $p \leq 0.001$).

DISCUSSION

Obesity is a world health problem that must be considered because obesity increases the risk of various chronic diseases such as type 2 diabetes (T2D), hypertension, and cardiovascular disease (CVD) (Gadde *et al*., 2018). In addition, the condition of obesity also occurs peripheral insulin resistance and hyperinsulinaemia, leading to decreased secretion of Growth Hormone (GH) (Lewitt *et al*., 2014) and Insulin-like Growth Factors 1

(Rasmussen *et al*., 1995). Decreased secretion of growth hormone (GH) and insulin-like growth factor-1 (IGF-1) reduces bone mineral density and increases the risk of fractures, such as fractures of the ankle, leg, humerus and vertebral column (Yakar *et al*., 2018; Premaor *et al*., 2014). The relationship of IGF-1 with bone mass or bone density has been studied in adults as well as elderly population. Some researchers have found a positive association of IGF-1 concentrations with bone density (Zhao *et al*., 2008; Rucker *et al*., 2004; Langlois *et al*., 1998; Szulc *et al*., 2004). The results showed that there was a positive correlation between IGF-1 levels and bone mass (Table 2). These results are in line with the results of research conducted by Chalista et al. (2017) that there is a relationship between IGF-1 levels and low bone mineral density (BMD). Likewise, the results of research conducted by Fornari *et al*. (2017) concluded that there was a correlation between IGF-1 levels and lumbar and femoral BMD in obese subjects.

Obesity is often associated with abnormalities in GH and IGF-1 secretion (Fornari *et al*., 2017). GH secretion abnormalities can inhibit the liver from secreting IGF-1 (Lewitt *et al*., 2014). GH and IGF-1 have a major role in bone growth and maintaining bone health (Fornari *et al*., 2017). In general, the effects of GH promoting bone growth appear to be dependent on IGF-1 production. The results of research by Fornari *et al*. (2017) showed that increased IGF-1 levels were associated with increased BMD in obesity. IGF-1 acts on cartilage, stimulates cell proliferation and synthesis of Deoxyribo Nucleic Acid (DNA), Ribonucleic Acid (RNA), proteins and proteoglycans. IGF-1 is a major component of the organic skeleton matrix and is the most important differentiating factor for osteoblasts. If there is a decrease in the secretion of GH and IGF-1, it can reduce bone mineral density (BMD) and increase the risk of fracture (Ekbote *et al*., 2015).

IGF-1 is also referred to as somatomedin C, mostly synthesized in the liver and regulated by GH which has a major role in cell growth and development (Guo *et al*., 2020), energy metabolism (TaeHo Kim *et al*., 2015). In addition, IGF-1 also plays a role in maintaining tissue homeostasis, anti-apoptosis, mitogenic, anti-inflammatory, antioxidant and metabolic properties, contributing to skeletal muscle plasticity, maintenance of muscle strength and muscle mass and increased bone mass (Guo *et al*., 2020; Vitale *et al*., 2019; Maggio *et al*., 2013). IGF-1 can be synthesized by endocrine, paracrine and autocrine mechanisms (Stein *et al*., 2018). IGF-1 synthesis is stimulated by nutrients and GH in the liver and other tissues (Lewitt *et al*., 2014). GH, through IGF-1 stimulates the proliferation of epiphyseal cartilage so that more space is formed for bone formation and stimulates osteoblast activity (Sherwood, 2014). Osteoblast is a type of bone cell that produces organic matrix in bone. According to Sihombing *et al*. (2012) osteoblasts make, secrete and precipitate new bone matrix organic elements called osteoid. Osteoblasts contain alkaline phosphatase enzymes which indicate that these cells are not only associated with matrix creation, but also mineralization. When osteoblast activity deposits new bone on the external surface, other cells in the bone, osteoclasts (bone destroyers), dissolve bone tissue on the inner surface beside the marrow cavity (Sherwood, 2014). Osteoclasts are large multinuclear cells located along the surface of the bone where bone resorption, remodeling and repair occur (Sihombing *et al*., 2012).

CONCLUSIONS
Based on the results of the study, it can be concluded that there is a positive correlation between IGF-1 levels and bone mass in obese female. Based on the results of the study, it is recommended that further research be carried out by adding other variables such as growth hormone (GH), insulin, glucose, Insulin-Like Growth Factor Binding Protein 3 (IGFBP3), serum glutamic pyruvic transaminase (SGPT) and serum glutamic oxaloacetic transaminase (SGOT).

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