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Relationship Between Anthropometric Parameters with Serum Follistatin-Like1 Level in Healthy Adults

Relación entre los parámetros antropométricos y el nivel sérico de folistatina similar a 1 en adultos sanos

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SUMMARY

Follistatin-like 1 (FSTL1) is a secreted glycoprotein, primarily produced in adipose tissue, that plays a role in various physiological and pathological processes, particularly in relation to cardiovascular, autoimmune, neoplastic, osteoarticular conditions, and obesity. Obesity is associated with chronic inflammation, characterized by the increased production of proinflammatory cytokines and the accumulation of macrophages in adipose tissue. Some indicators for determining obesity include anthropometric parameters, which are individual measurements, including height, weight, body mass index (BMI), waist circumference, and hip circumference ratio. In the present study, anthropometric measurements such as height, weight, body mass index (BMI), waist circumference, and hip circumference ratio were performed. In addition, blood pressure, fasting blood sugar examinations, and glucose tolerance tests were determined, and FSTL1 levels in serum were determined using the Enzyme-Linked Immunosorbent Assay (ELISA) method. Seventy healthy adult subjects participated to determine the relationship between anthropometric parameters and serum FSTL1 levels. Using the Pearson correlation test, it was shown that there was no relationship between BMI, Waist Circumference, Hip Circumference, Waist, and Hip Ratio with FSTL-1 (p-value > 0.05).

Keywords: *Healthy Adults, Anthropometry, FSTL-1*

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RESUMEN

La folistatina similar-1 (FSTL1) es una glicoproteína secretada, producida principalmente en el tejido adiposo, que interviene en diversos procesos fisiológicos y patológicos, en particular en enfermedades cardiovasculares, autoinmunes, neoplásicas, osteoarticulares y la obesidad. La obesidad se asocia con inflamación crónica, caracterizada por un aumento en la producción de citocinas proinflamatorias y la acumulación de macrófagos en el tejido adiposo. Algunos indicadores para determinar la obesidad incluyen parámetros antropométricos, que son mediciones individuales, como la altura, el peso, el índice de masa corporal (IMC), la circunferencia de la cintura y el índice de la circunferencia de la cadera. En el presente estudio, se realizaron mediciones antropométricas, como la altura, el peso, el índice de masa corporal (IMC), la circunferencia de la cintura y el índice de la circunferencia de la cadera. Además, se determinó la presión arterial, la glucemia en ayunas y la prueba de tolerancia a la glucosa, y se determinaron los niveles séricos de FSTL1 mediante el método de ensayo inmunoabsorbente ligado a enzimas (ELISA). Setenta sujetos adultos sanos participaron para determinar la relación entre los parámetros antropométricos y los niveles séricos de FSTL1. Utilizando la prueba de correlación de Pearson, se demostró que no hubo relación entre el IMC, la circunferencia de la cintura, la circunferencia de la cadera, la relación cintura-cadera con el FSTL-1 (valor p > 0,05).

Palabras clave: *Adultos sanos, antropometría, FSTL-1.*

INTRODUCTION

Health is a state of complete physical, mental, and social well-being, not merely the absence of disease or infirmity (WHO, 1948). Adulthood is a period of growth and development to reach a productive age; adulthood is seen as the healthiest age of the entire human population (the healthiest people in the population). Although many experience illness, it is rarely severe (1).

Obesity has become a problem in the world of health and nutrition; both developed and developing countries have the same issues related to obesity. World Health Organization (WHO) data in 2016 showed that out of 1.9 billion adults in the world, 600 million adults are obese (2). The incidence of obesity in Indonesia, according to the 2013 Basic Health Research (Riskesdas), was 15.4 %, increasing to 21.8 % in 2018 (3).

Some indicators to determine obesity include anthropometric parameters; these measurements are individual and include height, weight, body mass index (BMI), waist circumference, and hip circumference ratio. Anthropometry relates to various body dimensions and composition measurements from various ages and nutritional levels (4).

Anthropometry is commonly used to measure nutritional status from various imbalances between protein and energy intake. This disorder is usually seen in the pattern of physical growth and the proportion of body tissues such as fat, muscle, and water (5). One of the weaknesses of anthropometric measurements with BMI is that it cannot assess the distribution of fat in the body, so it is less sensitive to determining abdominal obesity (6).

Obesity is associated with chronic inflammation characterized by increased production of proinflammatory cytokines and accumulation of macrophages in adipose tissue (7). There are two types of adipose tissue in the body: white adipose tissue and brown adipose tissue (8). Excessive accumulation of visceral adipose tissue in obesity is associated with altered profiles of molecules secreted by this tissue, including adipokines (leptin, adiponectin), cytokines (IL-6, TNF-α, IL1β), and other macromolecules and metabolites. Altered secretory profiles of adipose tissue largely contribute to chronic inflammation and hormonal imbalance, which cause insulin resistance and collectively increase the risk of chronic diseases such as diabetes, dyslipidemia, fatty liver, and cardiovascular disease (9).

Follistatin-like 1 (FSTL1) is a glycoprotein produced in adipose tissue involved in various pathological conditions, including cardiovascular, autoimmune, neoplastic, osteoarticular, and obesity. Several studies have identified it as a biomarker to predict/monitor disease presentation and outcome, including FSTL1. FSTL1 is a secreted protein that circulates in plasma and, therefore, can function as an adipokine that regulates fat metabolism and inflammatory responses associated with obesity and metabolic syndrome and as a myokine that plays a role in tissue repair and recovery processes. FSTL1 plays

a significant role in adipogenesis based on its role in preadipocytes and significant downregulation in mature adipocytes (9).

In pathological and severe obesity, Follistatin-Like 1 (FSTL1) levels decrease due to a combination of factors related to increased adipocyte size and number, as well as other cellular changes. Specifically, the persistent increase in mature adipocytes, potentially leading to a decrease in adipogenesis, and increased cell senescence, can contribute to this downregulation. The elevated demand for FSTL1 to maintain anti-apoptotic activity may also play a role (11). Follistatin-like protein 1 (FSTL1) secretion is regulated by hyperinsulinemia and free fatty acids (FFAs). Studies have shown that high levels of insulin and FFAs can influence the release of FSTL1, suggesting a link between FSTL1 and glucose and lipid metabolism (11).

Thus, in the present study, anthropometric measurements were performed such as height, weight, body mass index (BMI), waist circumference, and hip circumference ratio, and assessed their possible correlation with Follistatin-like protein 1 serum levels.

MATERIALS AND METHODS

Design and Population

This cross-sectional study was conducted in November - December 2024; the research subjects were 70 healthy young adults aged 18-40 years who did not have diseases such as diabetes mellitus and did not have hypertension. Afterwads it was carried out anthropometric measurements including height, weight, body mass index (BMI), waist circumference and hip circumference ratio, blood pressure measurements, fasting blood sugar examinations, and glucose tolerance tests at the Clinical Pathology Laboratory of the Hasanuddin University State College Hospital. FSTL1 levels were determined in serum using the Enzyme-Linked Immunosorbent Assay (ELISA) method, ELISA Kits by MyBioSource (USA) at the Hasanuddin University Medical Research Center (HUM-RC) Laboratory of the Hasanuddin University State College Hospital. The kit has a Detection Range of 0.313- 20 ng/mL and a Sensitivity of Min: 0.188 ng/mL; Max: 20 ng/mL

Ethical approval was obtained from the Health Research Ethics Commission (KEPK) of the Hasanuddin University State College Hospital (RSPTN UH) number: 1067 / UN4.6.4.5.31. / PP36 / 2024.

Data analysis

Data was analyzed using the Statistical Package for the Social Sciences (SPSS), version 22. The statistical methods used were descriptive statistical calculations (range, median, mean, standard deviation, and data distribution) and statistical tests. The distribution of FSTL1 data and anthropometric parameter measurements was assessed using the Kolmogorov-Smirnov normality test. The relationship between anthropometric parameters and serum FSTL1 levels was examined using the Pearson correlation test, if the data were normally distributed and the Spearman correlation test, if the data were not normally distributed. The statistical test results were significant if the p-value <0.05.

RESULTS

Demographic characteristics of the research sample

A total of 70 subjects were based on age, of which 37 people were 21-30 years old (52.9 %), 17 people (24.3 %) were aged>30 years old, and 16 people (22.9 %) were aged <20 years old. As for gender, 35 people (50 %) were male and 35 people (50 %) were female. Based on the history of diabetes, based on interview results from 70 samples, 14 people (20 %) had a history of diabetes, and 56 people (80 %) did not have a history of diabetes. According to the smoking history, 8 people (11.4 %) had a history of smoking, and 62 people (88.6 %) did not (Table 1).

Table 1. Demographic characteristics of the research sample.

Variables	Frequency	Percentage (%)
Age		
< 20	16	22.9
21-30	37	52.9
> 30	17	24.3
Gender		
Man	35	50
Woman	35	50
History of Diabetes		
Yes	14	20
No	56	80
Smoking History		
Yes	8	11.4
No	62	88.6

Distribution of anthropometric examination results and serum FSTL-1 levels in healthy adult subjects

The anthropometric examination of the sample included assessment of height, weight, waist circumference, and hip circumference. As shown in Table 2, the average height of the sample was 160.61 cm, and the man-max value was 143.5-177.0 with a standard deviation (SD) of 8.52. The average weight was 65.06 kg, with a minimum weight of 42.1 kg, a maximum of 100.5 kg, and a standard deviation (SD) of 12.55 kg.

The average body mass index was 25.34 kg/m^2, with a minimum BMI of 16.8 kg/m^2, a maximum of 35.8 kg/m^2, and an SD of 4.55. The BMI variable was then classified into five groups: very thin, thin, normal, overweight, and obese. The analysis showed that most of the samples were in the normal category, although there was still a low number in the very thin, thin, overweight, and obese categories.

The average waist circumference of the sample was 80.94 cm, with a minimum value of 63 cm and a maximum of 105 cm, and SD 9.95. The hip circumference examination showed that the average circumference was 93.64 cm, with a minimum value of 67, a maximum of 122 cm, and a SD of 10.24. The waist-to-hip circumference ratio showed an average of 0.86, with a minimum value of 0.74, a maximum of 1.07, and a SD of 0.70. FSTL-1 serum levels were, on average, 1.51 ng/mL, with a minimum value of 0.16 ng/mL, a maximum of 3.04 ng/mL, and an SD of 0.69.

Table 2. Distribution of anthropometric examination results and serum FSTL-1 levels in healthy adult subjects.

Variables	Frequency	Percentage (%)	Mean	SD	Min-Max
Height (cm)	-	-	160.61	8.52	143.5-177.0
Weight (kg)	-	-	65.06	12.55	42.1-100.5
BMI (kg/m^2)	-	-	25.34	4.55	16.8-35.8
Very Thin	1	1.4			
Thin	4	5.7			
Normal	32	45.7			
Overweight	7	10			
Obesity	26	37.1			
Waist size (cm)	-	-	80.94	9.95	63-105
Hip circumference (cm)	-	-	93.64	10.24	67-122
Waist-to-Hip Ratio	-	-	0.86	0.70	0.74-1.07
FSTL-1 (ng/mL)	-	-	1.51	0.69	0.16-3.04

Results of the normality test with the Kolmogorov-Smirnov test

The results of the normality analysis indicate that the variables BMI, waist circumference, hip circumference, waist-to-hip ratio, and FSTL-1 are normally distributed, with a p-value greater than 0.05 (Table 3). Therefore, the analysis can proceed with a parametric test, specifically the Pearson correlation test.

Table 3. Results of the normality test with the Kolmogorov-Smirnov test

Variables	N	P-Value	Description
BMI	70	0.090	Normally
Waist size	70	0.062	Normally
Hip circumference	70	0.100	Normally
Waist-to-Hip Ratio	70	0.108	Normally
FSTL-1	70	0.094	Normally

Pearson correlation test results revealed no significant correlation between anthropometric parameters (BMI, waist circumference, hip circumference, and waist-to-hip ratio) and serum FSTL1 levels in healthy adult subjects (p-value > 0.05) (Table 4).

Table 4. Correlation test results: Pearson, examining the relationship between anthropometric examination results (BMI, waist circumference, hip circumference, and waist-to-hip ratio) and serum FSTL1 levels in healthy adult subjects.

Variables	n	r	P-value	Description
BMI	70	-0.019	0.873	Not correlated
Waist size	70	-0.026	0.830	Not correlated
Hip circumference	70	0.004	0.975	Not correlated
Waist-to-Hip Ratio	70	-0.042	0.733	Not correlated

DISCUSSION

The demographic characteristics of the study sample provide essential context for interpreting the results within the framework of obesity and FSTL1 research. The most significant proportion of the sample was in the 21–30-year age range (52.9 %). This young adult age group is relevant because it represents a period of lifestyle transition that often coincides with an increased risk of weight problems and changes in body composition. Epidemiological studies consistently show an increasing prevalence of obesity with advancing adult age, particularly in young and middle adulthood (12,13). A survey by Flegal et al. (12) analyzing adult BMI trends in the USA found a continued increase in the young adult age group. Similarly, a report from the National Center for Health Statistics (2015)

showed the highest prevalence of obesity in the 40-59-year-old age group, encompassing the middle age range adjacent to the dominant age group in this study (13). Therefore, the focus of this study on the young and middle-adult age groups has strong epidemiological relevance in the context of global obesity.

A balanced gender distribution of the sample (50 % male and 50 % female) is a crucial methodological aspect. This gender balance is essential to avoid potential biases arising from physiological differences between the sexes regarding body composition, metabolism, and hormonal responses that may affect anthropometric parameters and adipokine levels such as FSTL1. Pérez-López et al. highlighted gender differences in adipokines and their role in cardiovascular disease (14). Mauvais-Jarvis et al. (15) discussed gender differences in metabolic homeostasis, diabetes, and obesity. With a balanced gender representation, this study was able to provide a more general perspective and reduce potential gender bias in the analysis of the relationship between anthropometry and FSTL1.

The presence of a history of diabetes in 20 % of the interview sample and continued with fasting blood sugar and glucose tolerance tests with expected results indicate that the study subjects did not have a diagnosis of diabetes mellitus and were eligible to be sampled for further examination, namely FSTL1 level examination using the ELISA method, although categorized as "healthy," indicating heterogeneity of metabolic status in the sample group. In this context, the term "healthy" likely refers to the absence of a clinical diabetes diagnosis at the time of recruitment. However, the prevalence of a history of diabetes is relatively high (20 %), indicating the existence of a subgroup with a higher potential metabolic risk. Abdul-Ghani et al. (16) showed that metabolic syndrome and insulin resistance are associated with an increased risk of diabetes in high-risk individuals. At the same time, Tabák et al. (17) highlighted prediabetes as a high-risk condition for the development of diabetes. The presence of subjects with a history of diabetes in the "healthy" sample needs to be considered in interpreting the results because a history of diabetes can affect the profile of adipokines and inflammatory biomarkers. Smoking history, although with a low prevalence (11.4 %), is also a lifestyle variable that needs to be considered because of its impact on systemic inflammation and metabolic status, as shown in a study by Wannamethee et al. (18).

FSTL1 is a glycoprotein that plays a role in regulating inflammation, energy metabolism, and adipocyte differentiation. The results of this study found that there was no significant relationship between anthropometric parameters, such as Body Mass Index (BMI), Waist Circumference (WC), Hip Circumference (HC), and Waist-to-Hip Ratio (WHR), with serum FSTL1 levels in healthy adults. This is different from several previous studies that showed that FSTL1 has higher expression in individuals with obesity or other metabolic disorders. Santos et al. (9) stated that FSTL1 plays a role in the inflammatory and metabolic processes, especially in individuals with obesity or other metabolic diseases; in this study, although there were variations in BMI values and other anthropometric parameters, no significant correlation was found with serum FSTL1 levels.

FSTL1 is a protein expressed in various tissues, especially adipose and muscle tissues, and plays a role in inflammation and metabolic regulation. Fan et al. (7) showed that FSTL1 significantly increased in obese individuals and was associated with systemic inflammation. Another study by Santos et al. (9) stated that high FSTL1 levels can be related to insulin resistance and chronic inflammation in obese individuals, and levels of this protein tend to decrease after bariatric surgery. This suggests that FSTL1 may be an increased inflammatory biomarker in certain metabolic conditions. However, this study found no significant relationship between FSTL1 and anthropometric parameters because the subjects were healthy adults without metabolic disorders.

This lack of significant association is interesting to discuss further, especially compared to previous studies investigating the role of FSTL1 in obesity and metabolic conditions. Several studies mentioned in the background have shown that FSTL1 is produced in adipose tissue and affects various pathological conditions, including obesity, cardiovascular disease, and inflammation. Santos et al. (9) stated that FSTL1 can function as an adipokine that regulates fat

metabolism and obesity-related inflammatory responses. Parfenova et al.'s study in 2021 also stated that pathological and severe obesity decreases FSTL1 levels (11).

However, the results of this study did not find a positive correlation between anthropometric parameters reflecting the level of obesity (BMI, waist circumference, hip circumference) and serum FSTL1 levels. Several possible explanations for this result need to be considered:

1. Characteristics of Research Subjects: "Healthy Adults"

This study's definition of "healthy adults" may be too broad and heterogeneous. Although the study's inclusion criteria mentioned healthy adult subjects, variations in health status, lifestyle, and genetic factors among subjects may affect the results. Some of the study samples were classified as overweight and obese based on BMI, and 20 % had a history of diabetes. The "healthy" condition in this group may refer more to the absence of apparent clinical disease at the time of the study. Still, it does not rule out the possibility of subclinical metabolic dysfunction or mild inflammation that has not been detected clinically. These differences in "healthy" conditions between individuals may cause variability in FSTL1 levels that are not directly correlated with the measured anthropometric parameters.

The difference between the results of this study and those of previous studies may be due to differences in the conditions of the research subjects. Several previous studies involved individuals with obesity or metabolic diseases, while this study only involved healthy individuals with a relatively normal to overweight BMI range. Mattiotti et al. (19) found that FSTL1 showed high expression during the early phase of adipocyte differentiation but then experienced downregulation after mature adipocytes were formed. This means that in healthy individuals with stable body composition, serum FSTL1 levels may not show significant variations and have no direct relationship with anthropometric parameters.

Anthropometric parameters have limitations in describing the complexity of body composition and fat distribution in detail, especially visceral fat, which is metabolically more active and relevant in adipokine production, such as FSTL1. BMI does not distinguish between fat and fat-free mass or provide information about body fat distribution. Waist circumference and waist-to-hip ratio provide more specific details on central obesity but remain linear measurements that do not directly reflect visceral fat volume and metabolic activity.

In the context of FSTL1, previous studies using magnetic resonance imaging (MRI) to measure visceral fat found that serum FSTL1 levels were significantly correlated with visceral fat volume. Still, the correlation with BMI was weaker or non-significant. These studies suggest that serum FSTL1 may be more sensitive to visceral fat accumulation, the most metabolically and inflammatory active fat depot, compared to total body fat or subcutaneous fat, which are more reflected in standard anthropometric parameters. In the study by Gómez-Ambrosi et al. (20), the limited use of anthropometric parameters may be one reason why a significant association with FSTL1 levels was not detected.

2. Complexity of FSTL1 Regulation and Functions

Another factor that may explain these differences in results is the role of FSTL1 in the inflammatory process. FSTL1 is a multifunctional protein involved in various biological processes in addition to adipose metabolism and inflammation. Recent studies have shown the role of FSTL1 in cardiovascular, autoimmune, neoplastic, and osteoarticular processes (9). Regulation of FSTL1 production and secretion is likely influenced by various factors, including hormones (e.g., insulin), cytokines, and other metabolites. FSTL1 secretion can be regulated by hyperinsulinemia and free fatty acids, and FSTL1 can be modulated by inflammatory signals (11).

The complexity of FSTL1 regulation and function suggests that the relationship between obesity (as reflected by anthropometric parameters) and serum FSTL1 levels may not be linear and straightforward. Other factors not measured in this study, such as insulin levels, free fatty acids, other inflammatory cytokines, or genetic factors, may play an essential role in modulating FSTL1 levels and their interaction with obesity status. The absence of measurement of these other factors may be one of the reasons

why the relationship between anthropometric parameters and serum FSTL1 was not detected in this study.

Several studies have shown that FSTL1 has a dualistic nature; that is, it can be pro-inflammatory in chronic conditions and anti-inflammatory in acute situations. Wang et al. showed that FSTL1 plays a role in the activation of inflammatory pathways through NLRP3/IL-1β, which can increase inflammation in adipose tissue. However, because the subjects were healthy individuals in the present study, no inflammatory condition was sufficient to induce significant changes in FSTL1 levels (21).

These results also suggest that although obesity is often associated with low-grade chronic inflammation, not all individuals with high BMI have elevated FSTL1 levels. Other factors such as body fat composition, physical activity level, and diet may influence FSTL1 expression. Ouchi et al. (22) suggested that FSTL1 may be regulated by other adipokines, such as leptin and adiponectin, which also play a role in inflammation and energy metabolism. Therefore, the absence of a relationship between anthropometric parameters and FSTL1 in this study may be due to a complex regulatory mechanism involving body size and other metabolic factors.

3. Potential Influence of Other Factors

In addition to the factors mentioned, it is possible that other factors not controlled in this study could have influenced the results. Lifestyle, including diet, physical activity, and sleep quality, may influence metabolic and inflammatory status and FSTL1 levels. Variations in lifestyle among study subjects, even though they were categorized as healthy adults, may be a source of variability that makes it challenging to detect simple correlations between anthropometry and FSTL1.

Genetic factors also play a role in obesity and adipokine regulation. Genetic variation in the FSTL1 gene or other genes involved in adipose metabolism and inflammation may influence an individual's response to obesity and FSTL1 levels. Further studies considering genetic factors may be needed to better understand the variability in FSTL1 levels and their relationship to obesity.

It is difficult to compare this study's results directly with previous studies because studies on the relationship between anthropometric parameters and serum FSTL1 in healthy adult populations are still limited. Most studies on FSTL1 in the context of obesity have focused more on the role of FSTL1 in the pathogenesis of obesity, chronic inflammation, and obesity-related metabolic diseases such as diabetes and cardiovascular disease. However, referring to studies that mention the role of FSTL1 as an adipokine produced by adipose tissue and involved in the regulation of fat metabolism and inflammation, a positive correlation is expected between anthropometric parameters reflecting the amount of adipose tissue (such as BMI and waist circumference) and serum FSTL1 levels. This study's absence of a significant correlation may indicate that the relationship between obesity and FSTL1 is more complex than a simple linear correlation.

Some studies may have found correlations between FSTL1 and other obesity-related parameters, such as visceral fat content measured by imaging methods (e.g., CT scan or MRI) or specific inflammatory markers more sensitive to adipose tissue dysfunction. If such studies exist, comparing them with this study's results may provide further insight into the role of FSTL1 in obesity and the limitations of standard anthropometric measurements in reflecting this relationship.

Although the study hypothesis was not proven, the results still provide an essential contribution to understanding the role of FSTL1 in the context of obesity in healthy adult populations. The lack of correlation between standard anthropometric parameters and serum FSTL1 levels suggests that the relationship between obesity and FSTL1 is more complex and may be influenced by factors other than total adipose tissue or fat distribution as measured by anthropometry.

The results of this study underscore the importance of considering other factors that may influence FSTL1 levels and their role in obesity, such as systemic inflammation, genetic factors, and specific aspects of adipose tissue dysfunction that are not reflected in standard anthropometric measurements. Further research is needed to identify these other factors and to

more comprehensively explain the complexity of the relationship between obesity and FSTL1.

Overall, this study provides important insights that FSTL1 does not always correlate with anthropometric parameters in healthy individuals, although previous studies have shown stronger associations in pathological conditions. These results suggest that FSTL1 may act more as an inflammatory biomarker that is elevated in abnormal metabolic conditions than as an indicator of anthropometric status. Therefore, interpreting FSTL1 levels in human health must consider factors other than body size, including inflammation, insulin resistance, and interactions with other adipokines.

CONCLUSION

This study did not find a statistically significant relationship between anthropometric parameters (BMI, Waist Circumference, Hip Circumference, and Waist-to-Hip Ratio) and serum FSTL1 levels in healthy adult subjects.

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Conflict of Interest

All authors affirm that there are no conflicts of interest in this study.

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