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Analysis of Ferritin Levels, TIBC and Fe Serum In Central Obesity And Non Central Obesity

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ABSTRACT
Inflammation due to central obesity results in decreased iron levels and an increase in free fatty acids increases ferritin. Ferritin is an inflammatory marker in obesity, TIBC, Fe, and transferrin saturation by examining iron status. Anthropometric parameters of waist circumference are related to visceral fat. This study analyzed the levels of ferritin, TIBC, Fe, and transfer saturation in central and non-central obesity. The observational study (cross-sectional) used 75 subjects for 4 months. Ferritin using ECLIA, TIBC and Fe using immunoturbidimetric and colorimetric methods, transferrin saturation using the comparison method of Fe and TIBC values in percent units. This study showed significant results on TIBC levels, while levels of ferritin, Fe, and transferrin saturation were not significant. The Spearman correlation test showed significant results between ferritin and waist circumference levels while TIBC, Fe, and transferrin saturation were not significant. In conclusion, there are significant differences in TIBC while ferritin, Fe, and transferrin saturation do not have significant differences between central and non-central obesity.

Keywords: Central Obesity, Ferritin, TIBC, Fe Transferrin Saturation

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BACKGROUND

Central obesity is obesity that resembles apples, which is fat stored in the waist and the abdominal cavity. This fat accumulation is caused by excess fat content in the subcutaneous fat tissue and visceral abdominal fat. The accumulation of fat in the visceral fat tissue is a manifestation of the malfunctioning of the subcutaneous fat tissue to overcome the impact of excess energy due to excess fat consumption (Puspitasari, 2018). Central obesity arises due to lifestyle changes, such as high alcohol consumption, smoking habits, consumption of high-fat foods, high consumption of fast food, and low physical activity (Tumaluntung & Ticoalu, 2015). In the body of obesity, there is subclinical inflammation. The inflammatory process that occurs in fat tissue in obese individuals produces pro-inflammatory cytokines which then modulate acute phase protein production. inflammation due to increased fat tissue is thought to be a bridge between iron status and obesity. Individuals who are overweight or obese experience inflammation which can lead to iron deficiency (Alam, Memon, & Fatima, 2015)

Previous research has been conducted (Wowor, 2020) Concerning ferritin levels in male subjects with central obesity and non-central obesity, these findings indicate that there is an increase in ferritin levels in central obesity. Then research was also carried out by (Hendarto, Febriyanto, & Kaban, 2018) regarding iron deficiency in obese adolescents who checked serum iron, TIBC, and transferrin saturation. The results showed that the proportion of iron deficiency in obese adolescents was lower than in non-obese adolescents. What is new in this study is to use central and non-central obese subjects by checking ferritin levels as an acute-phase protein involved in the inflammatory process in central obesity while examining levels of ITBC, serum fe, and transferrin saturation values as tests that support iron status in central obesity.

The accumulation of free fatty acids in obese individuals increases proinflammatory cytokines such as IL-1, IL-6, and TNF-α which then increases the acute phase protein ferritin and results in an increase in the macrophage sequence which further reduces iron absorption. Chronic inflammation that occurs in individuals with central obesity will increase the acute phase protein, namely ferritin, which is modulated by pro-inflammatory cytokines and causes low iron levels in the body. Anthropometric measurements that are most associated with central obesity, namely waist circumference to predict the amount of visceral fat in centrally obese individuals, increased secretion of inflammatory mediators seen in obese individuals illustrates ongoing chronic inflammation (Syari, Hendrianingtyas, & Retnoningrum, 2019)

The increasing incidence of central obesity is a reference for researchers who conducted this study to see levels of inflammation and iron status in someone who is centrally obese. The role of ferritin as an acute-phase protein and iron storage protein makes the use of ferritin as a parameter of iron status as well as a marker of inflammation in obesity to be accompanied by examining other iron parameters such as Fe, *Total Iron Bond Capacity* (TIBC) and transferrin saturation in inferring iron status in central obesity

METHODS

The study design was observational (*cross-sectional*), the population of this study was all adult subjects who were centrally obese with the criteria of a male with waist circumference ≥ 90 cm and women with a waist circumference ≥ 80 cm. The research was carried out at the Installation of the Clinical Pathology Laboratory of the Hasanuddin University Hospital starting from sampling to examining TIBC, serum Fe, and ferritin levels. This study was conducted in August-December 2020 using serum samples from people with central obesity

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and non-central obesity. This study has received approval from the Health Research Ethics Committee, Hasanuddin University, Makassar. Faculty of Medical with registration number UH20090498.
Measuring tools for height, measuring waist circumference, measuring tools for body weight, body fat and visceral fat are Bioelectrical Impedance Analysis (BIA) tanita brand BC-541, Cobas e 411, and ABX pentra 400. ready-to-use ferritin reagent, ready to use iron reagent usable serum, ready-to-use TIBC reagent, and subject serum from central obesity and non-obesity.

Experimental protocol
Identification of subjects included in the research requirements is carried out first. Then given a detailed description of the actions to be performed on the subject during the study. Anthropometric measurements were carried out, namely waist circumference, height, weight, body mass, visceral fat, percent fat, and body of the research subject. Venous blood collection uses a vacuum tube with a red cover (no anticoagulant and contains a blood *clot activator*). The ferritin examination was carried out by the *electro-chemiluminescence immunoassay* (ECLIA) method using the e 411 test. The serum Fe and TIBC tests were carried out using the ABX Pentra 400 *Clinical Chemical Analysis* Tool. Then the transferrin saturation value was calculated using the ratio of serum iron yield and *Total Iron Capacity Ratio* (TIBC) in percent.

Data Analysis
Data analysis was performed using statistical software. Data distribution was assessed using the Kolmogorov-Smirnov normality test, then the waist circumference test was carried out with ferritin, TIBC, serum Fe and transferrin saturation using the Spearman correlation test. The results were considered statistically significant at $p < 0.05$.

RESULTS
Table 1. Characteristics of Research Subjects

Variable	N=75 (%)	Mean ±SD	Median	Min- Max
Age (years)	-	30.18±4.75	30,00	20–39
Gender:				
Male	40 (53,3 %)	-	-	-
Women	35 (46,7 %)	-	-	-
Group:				
Central obesity	40 (53,3 %)	-	-	-
Non obesity Central	35 (46,7 %)	-	-	-
Anthropometry:				
BW (kg)		71,09±17,27	71,00	48,70–137,60
BH (m)		1,61±0,80	1,67	1,49-1,84
BMI (kg/m^2)		27,00±5,65	25,58	19,73-47,61
WC (cm)	-	87.53±12.77	85,00	68–136
Ferritin (ng/mL)	-	156.82±114.51	122,70	9,17–569
Fe (µg/dL)	-	67.54±28.48	63,69	15,28-141,75
TIBC (µg/dL)	-	354.68±49.60	350,10	262–493
St (%)	-	19.44±8.56	18,60	4,00–42,40

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Description: BW=Body Weight, BH= Body Height, BMI=Body Mass Index, WC=Waist Circumference, Fe=Iron, TIBC=*total iron bindingcapacity,* St=Saturation transferrin, Mean=Average, Min=Minimum, Max=Maximum, SD=Standard Deviation

Table 1 shows the primary data obtained by the direct data collection method. General characteristics of research subjects are age, gender and anthropometric examination, namely body weight, height, body mass index, waist circumference. laboratory examinations, namely ferritin, Fe, TIBC and transferrin saturation.

Table 2. Differences in Ferritin Levels, TIBC, Serum Fe and Transferrin Saturation In Subjects of Central And Non-Central Obesity.

Variable	Central Obesity (n=40)		Non Central Obesity (n=35)		*Q*
	Median (Min-Max)	Mean±SD	Median (Min-Max)	Mean±SD	
Ferritin (ng/mL)	128,50 (19,11 – 569,00)	166.51±127.14	122,70 (18,28 – 395,30)	145.74±98.79	0,633*
Fe (µg/dL)	57,98 (15,28 – 141,75)	66.46±28.86	65,68 (18,8 – 131,76)	68.78±28.41	0,728**
TIBC (µg/dL)	357,80 (263,70 – 493,80)	366.14±51.35	337,60 (262,30– 449,20)	341.58±44.71	0,031**
St (%)	17,75 (4.00 – 40.80)	18.36±7.67	21,10 (5.10 – 42,40)	20.69±9.44	0,243**

Description: Min=Minimum, Max=Max, Mean=Average, SD=Standard Deviation, *P*=Probability, n=Amount, Fe=iron, TIBC=*Total Iron Binding Capacity,* St=Saturation transferrin
* Test Mann Whitney
** Test t Independent

The results of differences in ferritin levels, TIBC, serum Fe and transferrin saturation in central obese and non-centrally obese subjects are in Table 2. Where the mean ferritin levels in central obese subjects are 166,51 ng/mL higher than those in non-centrally obese subjects of 145,74 ng/mL. The average Fe level in central obesity was 66,46 µg/dL lower than non-central obesity which was 68,78 µg/dL. The average TIBC level in subjects with central obesity was 366,14 µg/dL, while the non-central obesity was 341,58 µg/dL. The average value of transferrin saturation in subjects with central obesity was 18.36%, for non-central obesity was 20.69%. Based on the results of different tests using the Mann Whitney and T-test which proved that there were significant differences in TIBC levels in the central and non-central obesity groups (p=0.031) while ferritin levels (p=0.633), serum Fe (p=0.726) and saturation transferrin (p=0.243) there was no significant difference from.

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Table 3. Correlation of Ferritin, TIBC, Fe Serum and Transferrin Saturation levels with Waist Circumference

Variable		Ferritin (ng/mL)	Fe (µg/dL)	TIBC (µg/dL)	Transferin saturation (%)
	n	75	75	75	75
WC (cm)	r	0,405	0,105	0,079	0,073
	q	0,000	0,370	0,502	0,531

Description: *p*=Probability, r=correlation coefficient, n=number of subjects, WC=Waist Circumference, Fe=iron, TIBC=*Total Iron Binding capacity*

The results of the *Spearman correlation test* stated that there was a significant relationship between ferritin levels and waist circumference, while serum Fe, TIBC and transferrin saturation did not have a significant relationship with waist circumference.

DISCUSSION

The results of this study indicated that ferritin levels were higher in central obese subjects than in non-centrally obese subjects but it was not statistically significant, This study is similar to research (Purnamawati, Faculty, & Selatan, 2018) which shows that the results of their research do not have a significant difference between ferritin levels in the overweight group and normal weights. The elevated ferritin levels in obese cases suggest that inflammation can play a role in inhibiting the iron profile in the central obese population and increasing ferritin in response to inflammation even in iron deficiency states. The research was also carried out by (Hendarto et al., 2018) which showed an increase in serum ferritin levels in obese subjects than non-obese subjects but no meaningful differences were found (p=0.069). Ferritin protein acute phase is increased in an inflammatory state, increased serum ferritin levels are modulated by pro-inflammatory cytokines, ferritin levels tend to be higher in overweight people as well as obesity caused by chronic inflammatory subclinical (Khan, Khan, Ayub, Humayun, & Haroon, 2016).

In this study, the central obesity group had lower serum iron levels in the blood than the non-central obesity subjects but statistically, none of it was significant (sal et al., 2018) conducted a study that aimed to determine the relationship between iron parameters. , leptin and hepcidin levels in obesity showed lower iron levels in obesity but there was no significant difference. Low iron levels in overweight or obese subjects are most likely due to inflammatory mechanisms, which retain iron in the reticuloendothelial system by releasing different inflammatory mediators such as cytokines and so on. A decrease in serum iron levels accompanied by an increase in ferritin levels due to adipocyte tissue has occurred with low-grade chronic inflammation because adipocytes are a major part of inflammation caused by obesity with increased secretion of various proinflammatory chemokines and cytokines (Wowor, 2020).

In this study, the TIBC level in the obese group was higher than in the non-central obesity group and had a significant difference with a value of p = 0.031. The results of this study are similar to the research conducted (sal et al., 2018) explaining that there is a significant difference between TIBC levels in the obese and non-obese groups. In that study, the obese group (375.8±54.2 µg/dL) had higher tibc levels than the group with normal nutritional status (288.3±59.8 µg/dL) with a significance of p=0.001. Increased levels of TIBC in obese subjects due to a continuous decrease in iron, iron administration for erythropoiesis decreases as a result of causing disorders in the form of erythrocytes and resulting in increased total iron tie capacity (TIBC).

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Based on the results of the calculation of transferrin saturation, the mean central obesity subject was slightly lower than the non-central obesity, but statistical tests did not find a significant difference. This study is in line with research conducted by (Hendarto et al., 2018) on deficiency in obese and non-obese adolescents, the results of the study showed that there was no significant difference in serum iron levels and transferrin saturation in the obese and non-obese groups. The explanation that we can explain is that Fe levels and transferrin saturation values are slightly lower in central obese subjects compared to non-central obesity but still within normal limits, this is probably because the subject has not yet experienced low-grade chronic inflammation as a result it is suspected that hepcidin secretion does not occur inhibits the absorption of iron in the gastrointestinal tract.

This study found a significant positive relationship ($p < 0.001$) between waist circumference and ferritin levels with a sufficient correlation coefficient ($r = 0.405$) in subjects with central obesity and non-central obesity. The positive relationship between waist circumference and serum ferritin in this study was strengthened by previous studies conducted by (Hämäläinen, Saltevo, Kautiainen, Mäntyselkä, & Vanhala, 2014) showed a significant relationship between increased serum ferritin and waist circumference ($p < 0.001$). Research in Indonesia was also conducted (Syari et al., 2019) regarding the relationship between waist circumference and ferritin levels in obesity, the results showed that there was a positive relationship between waist circumference and serum ferritin levels in obesity. Measurement of waist circumference is the total amount of accumulation of abdominal fat and has a close relationship with the homeostatic disorders found in abdominal obesity (central obesity) and waist circumference is closely related to visceral adiposity. (Arifin, Antari, & Albayani, 2019)

In this study, it was found that serum levels, TIBC, and transferrin saturation did not have a significant relationship with waist circumference. The correlation coefficient and significance of Fe, TIBC and transferrin saturation level were $p=0.370$; $r=0.105$, $p=0.079$; $r=0.502$, $p=0.531$; $r=0.073$. The research conducted (Davoudi-Kiakalayeh, Mohammadi, Pourfathollah, Siery, & Davoudi-Kiakalayeh, 2017) also proved that there was no significant relationship between Fe levels and waist circumference ($p = 0.754$; $r = 0.240$) but at the TIBC level which means a significant relationship with waist circumference and shows a positive direction of correlation with very weak correlation strength (Choma, Alberts, & Modjadji, 2015). conducted a study on the correlation between waist circumference and iron status which showed that waist circumference was positively related to transferrin saturation but not significant. The difference in the results of this study could most likely be based on the larger differences in the number of study subjects carried out by other researchers by reviewing food intake using quantitative, food frequency questionnaires, and a larger age range.

This study has several drawbacks. First, the cross-sectional design used cannot explain the causality of our results. Second, the iron intake in the diet of the subjects was not studied.

CONCLUSION

Central obesity subjects had TIBC levels that were significantly higher than non-central obesity and there was a significant difference ($p=<0.05$). There were no significant differences in ferritin, Fe levels, and transferrin saturation values between centralized and non-obese subjects. The bigger the waist, the higher the ferritin content. There was no significant correlation between waist circumference and total Fe, TIBC, and transferrin saturation levels.

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