Correlation Between Ferritin and Thyroid Hormones in Obesity

by Meita Hendrianingtyas

ORIGINAL ARTICLE

Correlation Between Ferritin and Thyroid Hormones in Obesity

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ABSTRACT

Introduction: Obesity is one of the risk factors for various metabolic diseases that will cause various kinds of complications. Continuous sub-acute chronic inflammation is characterized by increased inflammatory markers, one of which is ferritin. Low iron that can be detected with ferritin, may alter thyroid metabolism. Chronic inflammatory conditions can cause disruption of thyroid hormone production. The purpose of this study was to examine the correlation between ferritin levels and thyroid hormone levels in obese populations. **Methods:** This was a cross-sectional study enroling 41 subjects with obesity with BMI >27 in Diponegoro National Hospital Semarang. Thyroid hormone levels (TSH, T3, FT3, T4 and FT4) and ferritin were examined with an immunology analyzer. Spearman correlation test was performed. $p<0.05$ was considered as statistically significant. **Results:** There were significant weak positive correlations between ferritin levels with T3 ($r=0.38$; $p=0.02$) and with FT3 levels ($r=0.33$; $p=0.05$). There were no correlations between ferritin levels with TSH, T4, and FT4. **Conclusion:** Ferritin levels might have association with T3 and FT3 levels in obese population. If confirmed by further studies, ferritin and thyroid hormones levels could be used in therapeutic monitoring in obese population.

Keywords: Ferritin, Thyroid hormones, Obesity

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INTRODUCTION

Obesity has become a major problem in Southeast Asian countries and in Indonesia. The prevalence of overweight and obesity in Southeast Asian countries has increased into 8–30% in men and 8–52% in women (1). According to Indonesian Basic Health Research (Riset Kesehatan Dasar) in 2018, the prevalence of obesity in Indonesian patients with age of >18 years old was 21.2%. The incidence of obesity in men was 14.5%, whereas in women was 29.3% (2). The nutritional status of an adult over 18 years old was measured with body mass index (BMI) by calculating anthropometric parameters of body weight (BW) and height (H). According to Indonesian Basic Health Research (Riset Kesehatan Dasar) 2018, obesity in adults was defined as BMI 27 kg/m2 or higher, (2) while according to world health organization (WHO), obesity in adults was defined as BMI 30 kg/m2 or higher (3, 4). Diet, physical activity, genetics, environmental factors are the predisposing factors of obesity (5).

Obesity can occur continuously with chronic inflammatory state. Several studies have shown an increase in inflammatory markers in patients with obesity, including ferritin (6-8). Obesity was also thought to be associated with anaemia. This condition might be due to fat accumulation and chronic inflammation in adipose tissue that could reduce iron absorption (9, 10). There were an increase in serum ferritin levels in obese patients, and it was also thought that ferritin in obesity was more due to chronic inflammatory conditions that occured in comparison to conditions associated with iron deficiency (11-13). Meanwhile, other previous studies showed that several minerals and trace elements, including iron, were needed for thyroid hormone metabolism. Iron deficiency that can be detected with ferritin, may cause low thyroid function (14).

Chronic inflammation in obese patients can cause changes in various hormone levels in the body, including thyroid hormones. Levels of thyroid stimulating hormone (TSH), FT3, and FT4 were said to be significantly different between the obese population and controls (15-17). Study showed that TSH levels could increase with increasing BMI (17, 18). Based on previous findings that obesity could increase inflammation marker ferritin and also reduce iron absorption, our study was aimed to analyze the correlation between ferritin levels and thyroid hormones levels in obese populations.

MATERIALS AND METHODS

A cross-sectional study of 41 obese population was carried out at Diponegoro National Hospital, Semarang, Indonesia. Inclusion criteria were adult participants within productive age (20–65 years old) with BMI >27 kg/m2 and normal body temperature. Participants with a history of thyroid disease, liver disease and if there were lysis and icteric specimens would be excluded from this study.

Thyroid hormones (TSH, T3, FT3, T4, and FT4) and ferritin were examined in the Diponegoro National Hospital laboratory from March to October 2018. Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in meters square) [weight / height2 (kg/m2)] in the out-patient clinic of Diponegoro National Hospital.

Ferritin and thyroid hormones (TSH, FT3, T3, FT4 and T4) levels were measured based on the Enzyme-Linked Fluourescent Assay (ELFA) technique by a compact multiparametric immunoanalyzer (MINI VIDAS® compact multiparametric immunoanalyzer, Biomerieux clinical diagnostic, Marcy-l'Etoile, France). These measurements were automated quantitative test using VIDAS®Ferritin, VIDAS®FT3, VIDAS®T3, VIDAS®FT4, VIDAS®T4, and VIDAS®TSH. VIDAS®Ferritin/ VIDAS®FT3/ VIDAS®T3/ VIDAS®FT4/ VIDAS®T4/ VIDAS®TSH were from Biomerieux SA, Marcy-l'Etoile, France.

This study was obtaining an ethical clearance from the Health Research Ethics Commission of the Faculty of Medicine, Diponegoro University/ Dr. Kariadi General Hospital Semarang. Study subjects were providing written informed consent.

RESULTS

The baseline characteristics of all study subjects is presented in Table I. In overal, the mean age was 25.8 ± 8.17 years old. In overal, our study subjects showed waist circumference of 97.9 ± 10.15 cm, hip circumference of 107.8 ± 17.37 cm, and BMI of 32.9 ± 3.75 kg/m2 (Table I).

The baseline characteristics of the subjects stratified by sex is presented in Table II. Of 41 adult study subjects, there were 23 (56.1%) female and 18 (43.9%) male. The level of ferritin was 28.09 ± 28.29 ng/mL in female subjects and was 103.01 ± 68.76 ng/mL in male subjects (Table II).

There were 3 (16.7%) male subjects that showed low ferritin levels and 15 (83.3%) male subjects that showed normal ferritin levels or within reference value range (30–350 ng/mL). Meanwhile, there were 13 (56.6%) female subjects that showed low ferritin levels and 8 (43.4%) female subjects that showed normal ferritin level (reference value range 20–250 ng/mL).

The levels of thyroid hormones (TSH, T3, FT3, T4, and FT4) in all subjects are presented in table III. There were normal TSH, FT3, FT4, and T4 in all study subjects (Table III).

The correlations between ferritin and thyroid hormones (TSH, T3, FT3, T4, and FT4) are presented in Table IV. There was significantly weak positive correlation between ferritin and T3 (r=0.403, p=0.009). There was significantly weak positive correlation between ferritin and FT3 (r=0.338, p=0.031). There were no correlations between ferritin levels with TSH, T4, and FT4.

Table I : Baseline characteristics of subjects

PARAMETERS	Mean ± SD	Median (Min – max)
Age (years)	25.8 ± 8.17	21.0 (18.0 – 46.0)
Haemoglobin (gr/dL)	13.8 ± 1.49	14.1 (10.2 – 16.9)
Waist circumference (cm)	97.9 ± 10.15	98.5 (79.5 – 125.0)
Hip circumference (cm)	107.8 ± 17.37	107.0 (88.0 – 126.5)
BMI (kg/m^2)	32.9 ± 3.75	31.7 (27.3 – 41.6)
Ferritin (ng/mL)	61.5 ± 62.89	35.4 (9.0 – 307.4)
Thyroid hormone levels		
TSH (μIU/mL)	1.6 ± 0.97	1.44 (0.49 – 4.26)
T3 (nmol/L)	1.5 ± 0.31	1.57 (0.86 – 2.52)
FT3 (pmol/mL)	4.6 ± 0.63	4.68 (3.26 – 6.00)
T4 (nmol/L)	88.8 ± 12.63	89.20 (69.65 – 124.03)
FT4 (pmol/mL)	16.0 ± 2.27	16.32 (10.56 – 20.17)

Body mass index, BMI. Thyroid stimulating hormones, TSH.

DISCUSSION

The mean ferritin level in all subjects of this study was 61.5 ± 62.89 ng/mL. This value was lower than mean ferritin level in previous studies by Alam et al which showed a mean ferritin level in obesity of 136.15 ± 59.3

Table II : Baseline characteristics stratified by sex

	FEMALE n=23		MALE n=18	
	Mean ± SD	Median (Min-max)	Mean ± SD	Median (Min-max)
Age (years)	26.35±8.75	21(18-46)	24.78±7.39	20.50(18-39)
Hb (gr/dL)	12.93±1.20	13.3(10.2-14.7)	15.02±0.89	15(13.7-16.9)
WC (cm)	92.58±8.14	91(79.5-110)	104.03±9.26	104.25(89-125)
HC (cm)	108.74±8.43	107(88-126)	111.17±8.43	108(100-126.5)
BMI (kg/m^2)	32.43±3.73	31.73(27.3-41.6)	33.21±3.94	31.65(28.3-40.5)
Ferritin (ng/mL)	28.09±28.29	19.68(9-113.52)	103.01±68.76	83.79(20.52-307.45)
Thyroid hormone				
TSH (μIU/mL)	1.62±2.03	1.44(0.49-4.17)	1.81±1.01	2.31(0.61-4.26)
T3 (nmol/L)	1.45±0.27	1.43(0.86-1.94)	1.68±0.32	1.61(1.13-2.52)
FT3 (pmol/mL)	4.42±0.37	4.62(3.66-5.00)	4.97±0.76	4.97(3.26-6.00)
T4 (nmol/L)	89.38±13.16	89.47(69.65-124.03)	88.28±11.91	89.34(72.50-107.62)
FT4 (pmol/mL)	16.09±2.34	16.23(10.88-20.99)	16.31±2.47	16.91(10.56-19.59)

Hb=haemoglobin, WC= Waist circumference, HC= Hip circumference, BMI=body mass index

Table III : Thyroid hormone levels in all subjects

Variable		n	%
TSH	High	0	0
	Normal	41	100
	Low	0	0
T3	High	0	0
	Normal	39	95.2
	Low	2	4.8
FT3	High	0	0
	Normal	41	100
	Low	0	0
T4	High	0	0
	Normal	41	100
	Low	0	0
FT4	High	0	0
	Normal	41	100
	Low	0	0

ng/mL and also by Khan et al with mean ferritin levels of 163.48 ± 2.23 ng/mL (19, 20). However, the study by Khan et al was carried out at an older age compared to our study.

In our study, the mean ferritin level of female subjects (28.09 ± 28.29 ng/mL) was lower than of male subjects (103.01 ± 68.76 ng/mL). This was similar with the previous study by Kim JW et al which showed that ferritin levels in female subjects were significantly lower than in male subjects ($p<0.001$) (21). Previous study from Shim YS et al also showed similar results in which the ferritin level in male subjects was higher than in female subjects (122.30 ng/mL vs 64.61 ng/mL, $p<0.001$) (22). Likewise, the study by Kim YE et al stated that ferritin levels in girls were significantly lower than boys ($p<0.001$) (23). The low ferritin level could

Table IV : The correlation between ferritin and thyroid hormones

PARAMETER	Ferritin [sp]	
	r	*p*
TSH	0.207	0.193
T3	0.403	0.009*
FT3	0.338	0.031*
T4	0.196	0.281
FT4	0.021	0.897

*$p<0.05$ was considered as statistically significant

sp Spearman Correlation Test

be affected with sex, intake pattern, and nutrition status of study population (24). A study showed that, from 13 (81.3%) female subjects, there were 1 (6.3%) female subjects with mild anemia (Hb 11.0 – 11.9 mg/dL) and 3 (18.8%) female subjects with moderate anemia (10.0 – 10.9 mg/dL), and the rest female subjects were at the lower limit Hb reference value with low MCV value. All female subjects in our study were in reproductive age, and their low Hemoglobin value can be caused by their menstrual period. We did not explore further about their menstrual cycle and nutrient intake in all subjects.

Most of thyroid hormone levels in our study subjects were still within the range of reference values, including TSH, T4, FT4 and FT3 levels. Meanwhile there were 2 (4.8%) subjects showing that T3 level was less than the reference value range. This finding was similar with previous studies by Ozer et al which showed that there were no significant differences in TSH levels in several criteria for obesity (25).

The mean TSH levels in our study was 1.68 ± 0.97 μU/mL; this was similar with the mean TSH levels in obesity in study by Kitahara which was 1.69 μIU/mL (26) and also in the Solanki study which was 2.64 mIU/L

(18). Both studies by Solanki and Kitahara also stated that the higher the BMI, the higher TSH levels will be (18, 26).

The mean FT4 level in our study was 16.07 ± 2.27 pmol/mL, which was higher than that in study by Al-Musa which was 10.3 ± 4.5 pmol/mL and also in obesity study by Kitahara which was 0.76 ng/dL (9.78 pmol/L) (18, 26). The mean FT3 level in our study (4.6 ± 0.63 pmol/mL) was comparable with study by Al Musa (4.19 ± 1.38 pmol/mL) and also by Kitahara (3.21 pg/mL) (4.93 pmol/L) (18, 26). Thyroid hormones levels in patients with obesity can be normal, increased or decreased with respect to different examination time, degrees of obesity and different types of obesity and their relation to insulin sensitivity (27).

Our study showed that most subjects [n=25; (60%)] had ferritin levels within the range of reference values, while the remaining [n=16; (40%)] had ferritin levels below the reference value, in which 13 of these 16 subjects were female in reproductive age (childbearing age). In the other hand, study from Lecube showed that ferritin levels in obese patients with metabolic syndrome were higher than obese patients without metabolic syndrome. The different finding between study by Lecube and our study was due to the difference in study population, in which the previous study was involving obese patients with metabolic syndrome and diabetes mellitus, while our study did not observe the glucose levels in each subject (28).

Our study showed significant correlations between ferritin to T3 (r=0.403; p=0.009) and between ferritin to FT3 (r=0.338; p=0.031). However, there was no correlation between ferritin and TSH, T4, and FT4. This was similar with previous study which showed that there was no significant correlation between serum ferritin and TSH in patients with iron deficiency (29). Studies by Dahiya and Araque showed similar results in which there was no significant correlation between ferritin and TSH, (30,31) but they could reveal significant correlation between ferritin and FT4 levels in the diabetic population. This might be due to a higher inflammatory state in obesity with diabetes than in obesity without diabetes.

Almost all obese subjects in our study showed normal HbA1c value (<6.5%), except one subject who showed HbA1c >6.5%. This subject also showed the highest ferritin level (307.45 ng/mL). This finding might imply that there would be higher ferritin level in subjects with obesity and diabetes caused by chronic inflammation. In female subjects, low ferritin level caused by anemia can conceal inflammatory state in obese population.

The correlation between ferritin level with T3 and FT3, but not between ferritin with TSH, T4, and FT4, could be mediated by a theory in which the chronic inflammatory state might cause a disruption in conversion of T4 to T3. Our study showed that T4 and FT4 levels were still within the reference range, whereas T3 level decreased in some subjects. This finding showed that although there might be disruption of T4 conversion to T3, but it has not affected the pituitary so that TSH levels were still within normal limits. Hence, it can be further examined by reverse T3 (rT3) examination to find out whether T4 is not converted to active T3. Moreover, further studies are still needed to examine other inflammatory markers.

CONCLUSION

Ferritin levels might have association with T3 and FT3 levels in obese population, but not with TSH, T4, and FT4. If confirmed by further studies, ferritin and thyroid hormones levels could be used in therapeutic monitoring in obese population.

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PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5