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한국 성인의 비만과 과체중에 따른 혈청 페리틴과 백혈구의 차이

이혜순
한남대학교 간호학과

The Difference in Serum Ferritin and Leukocyte Regarding Overweight and Obese South Korean Adults

Lee, Hea Shoon
Department of Nursing, College of Life Science and Nano Technology, Hannam University, Daejeon, Korea

Purpose: The purpose of this study was to investigate the difference in serum ferritin and leukocyte regarding overweight and obese South Korean adults. **Methods:** This study was conducted on 5,281 subjects older than 19, according to data from the Fifth Korea National Health and Nutrition Examination Survey (KNHANES V-3), 2015. Data were analyzed using descriptive statistics, t-test, ANOVA, Scheffe's test, Pearson's correlation coefficient, and stepwise multiple regression analysis (SPSS 24.0). **Results:** First, serum ferritin and leukocyte were higher regardubg obesity, followed by being overweight and within normal weight. Second, body mass index (BMI) was positively correlated with serum ferritin and leukocyte. Third, factors affecting serum ferritin were gender, and being obese and overweight. Explanatory power of the model was 26.2%. Factors affecting leukocyte were gender, obesity, being overweight, and weight change over the past year (weight gain). Explanatory power of the model was 10.2%. **Conclusion:** Obesity and being overweight were factors affecting serum ferritin and leukocyte, and obesity was more affected than being overweight in Koreans older than 19. In conclusion, serum ferritin was a marker of inflammation, rather than iron status, in overweight and obese Korean adults.

Key Words: *Adult; Body mass index; Ferritin; Leukocytes*
국문주요어: 성인, 체질량지수, 페리틴, 백혈구

Introduction

Obesity is a global health problem, In 2016, more than 1.9 billion adults, 18 years and older, were overweight. Of these over 650 million were obese [1]. The obesity is classified as a "disease" in 2013 by the American Medical Association [2]. Obesity and overweight people persist in sub clinical inflammation, leading to of iron deficiency (ID) and iron deficiency anemia (IDA), malignancy, and so forth [3]. Serum ferritin is used as a marker of iron deficiency [4]. Serum ferritin levels are present in abnormal conditions because they are acute phase reactants, serum ferritin levels are high in overweight and obesity, which are generalized inflammatory conditions [5]. For this reason, the use of serum fer-

Corresponding author: **Lee, Hea Shoon**
Department of Nursing, College of Life Science and Nano Technology, Hannam University 70, Hannam-ro, Daedeok-gu, Daejeon 34430, Republic of Korea
Tel: +82-42-629-8474 Fax: +82-42-629-8883 E-mail: lhs7878@hanmail.net

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ritin as a marker of ID or IDA in overweight or obese is controversial [6].

The inflammation caused by the increase of the adiposity will be suggested as a link between iron status and obesity [7]. Among the many metabolic activities of obesity, high Body mass index (BMI) is associated with incompatibility of iron parameters [8]. Chronic inflammation caused by obesity led to low iron status and showed low iron status in 38.8% of obesity and 12.1% of overweight [9]. Physical activity and weight gain are inversely related, thus, physical activity may reduce body iron deficiency in obesity [10].

When ID/IDA and obesity coexist, they double the adverse health effects of obesity itself. Chronic inflammation caused by excessive fat tissue, rather than diet, provides an explanation for obesity's ID/IDA, but the presence of acute and chronic infections should also be considered and inflammatory diseases should be considered [11]. As a result, ferritin is an indicator of inflammation in overweight and obesity than iron status. Higher ferritin levels secondary to asymptomatic inflammation of overweight and obese people can conceal iron deficiency because they are acute-phase responders [12].

In a study of Korean adults, serum ferritin is a positive associated with metabolically obese normal weight [6], and serum ferritin is the highest in obesity and lowest in normal weight [12]. Serum ferritin levels are associated with incidence of obesity in Korean men [13] and had a positive correlation with BMI and negative correlation with iron [12].

On the other hand, obesity is associated with decreased anemia, high hemoglobin and platelets [14,15]. Platelets are correlated with body fat mass and body fat percentage, and chronic inflammation is the cause of platelet activation [15].

The leukocyte is a hematological parameter that could provide useful information about health condition, leukocyte is needed to protect against invading organisms and the immune system [16]. There is strong evidence for a link between obesity and increased leukocyte [17]. Also, serum ferritin is positive correlated with C-reactive protein (CRP) as an indicator of inflammation [12].

In previous studies, there is a difference in serum ferritin and leukocyte according to obesity level of foreigners [10,17], but there are few studies of obesity in Korea. In particular, studies investigating the difference in serum ferritin and leukocyte in overweight and obese groups are rare. Also, the effects of obesity have shown contradictory results for iron reduction [3,7-9] or iron gain [14,15]. Serum ferritin, which reflects iron status, is used as a variable in this study.

The Fifth Korea National Health and Nutrition Examination Survey is representative of nationwide survey data. Therefore, it is appropriate sample data to construct domestic reference value. In this study, we suggested a fundamental data of adult obesity prevention and management program by identifying the difference in serum ferritin and leukocyte according to overweight and obesity in Korean adults. We suggested a fundamental data of Korean adult obesity prevention and management program.

Methods

1. Research design

This study is a descriptive survey study which attends a secondary analysis of The Fifth Korea National Health and Nutrition Examination Survey's raw data to investigate the difference in serum ferritin and leukocyte according to overweight and obesity in South Korean adults.

2. Samples and setting

Subject of this study is adult (over 19 years) and data was based on 'The Fifth Korea National Health and Nutrition Examination Survey (KNHANES V-3), 2015' which Ministry of Health and Welfare and Korea Centers for Disease Control and Prevention conducted.

According to classification standard of BMI groups were divided in normal weight 2,303 (43.6%), overweight 1,282 (24.3%) and obesity 1,696 (32.1%). The total 5,281 subjects were analyzed as the data of this study.

3. Instruments

1) BMI

The subject's height and weight were measured after overnight fasting with participants shoe less and wearing a lightweight gown. World Health Organization (WHO) classified BMI over 25 kg/m^2 as overweight and over 30 kg/m^2 as obesity [1]. However, it was not appropriate to apply it to Asians because it was developed based on the results of research on westerner [18]. In the World Health Organization Western Pacific region [19], classified BMI as normal weight less than 23 kg/m^2, overweight as 23-24.9 kg/m^2 and obesity as 25 kg/m^2 or more. This criterion was applied in this study as well.

2) Blood measurement

Blood sampling was collected in the morning after fasting for 8 hours

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or more, and median cubital vein was punctured using a vacutainer needle and blood was drawn into a vacuum tube.

Serum ferritin was measured by immuno-radiometric assay using a 1470 Wizard Gamma Counter (Perkin-Elmer, Finland). Leukocyte was measured by laserflow cytometry using a Sysmex XE2100D (Sysmex, Japan).

4. Ethical consideration

The Korea National Health and Nutrition Examination Survey which was used in this study was reviewed from Korea Centers for Disease Control and Prevention Institutional Review Boards (IRB)(2012-01EXP-01-2C), and subject's anonymity and confidentiality were guaranteed by collecting their private information in serial number which was unable to distinguish, and we conducted an annual survey. In this study, according to the raw data open and care regulation of Korea Centers for Disease Control and Prevention, after the researcher got confirmation for using data (Dec 7th, 2017), the data was provided, and we used them.

5. Data analysis

The data was analyzed by SPSS WIN 24.0 program (SPSS Inc. Chicago, IL, USA). The general characteristic of subject was analyzed by descriptive statistics. Difference of serum ferritin and leukocyte depends on subject's obesity degree was analyzed by t-test, ANOVA, Scheffe's test, Correlation among subject's BMI, serum ferritin and leukocyte were analyzed by Pearson correlation coefficient. The predictive variables for serum ferritin and leukocyte were analyzed by stepwise multiple regression. All significance were analyzed using a 2-tailed method, and a P-value < 0.05 was considered statistically significant.

Results

1. General characteristics of subject

The average age of the subjects were 50.80 years old. The average BMI was 23.76 kg/m^2, specifically, normal weight was 43.6%, overweight was 24.3%, and obesity was 32.1%. The average serum ferritin was 81.88 (ng/mL) and the average leukocyte was 5.87 (x10^3/uL) (Table 1).

2. Differences of serum ferritin and leukocyte according to subject's BMI.

The serum ferritin was higher in males than females (t = 38.69, p < .001). According to BMI classification, serum ferritin was highest in obesity, followed by overweight and normal weight (F = 181.15, p < .001). The leukocyte was higher in males than in females (t = 15.27, p < .001). In weight change over the past year, weight gain was higher than no change (within 0-3 kg) and weight loss (F = 9.06, p < .001). According to the BMI classification, leukocyte was the highest in obesity, followed by overweight and normal weight (F = 76.82, p < .001) (Table 2).

3. Correlation among subject's BMI, serum ferritin and leukocyte

The subject's BMI was positively correlated with serum ferritin

Table 1. General Characteristics of Subject (N = 5,281)

Variables	Category	Mean ± SD n (%)	Acquired score range
Age (years)		50.80 ± 16.39	19-88
Gender	Male	2219 (42.0)	
	Female	3062 (58.0)	
Education level	Under elementary school	1314 (24.9)	
	Middle School	565 (10.7)	
	High school	1787 (33.9)	
	Above college	1607 (30.5)	
Weight change over the past year	No change (within 0-3Kg)	3568 (67.6)	
	Weight loss	747 (14.1)	
	Weight gain	966 (18.3)	
BMI (kg/m^2)		23.76 ± 3.40	14.42-53.54
	Normal weight (< 23)	2303 (43.6)	
	Overweigh (23-24.9)	1282 (24.3)	
	Obese (≥ 25)	1696 (32.1)	
Serum ferritin (ng/mL)		81.88 ± 48.23	12.00-450.40
leukocyte (× 10^3/uL)		5.87 ± 1.65	2.00-24.00

SD = Standard deviation; BMI = Body mass index.

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Table 2. Differences of Serum ferritin and Leukocyte according to Subject's BMI (N = 5,281)

Variables	Category	Serum ferritin		Leukocyte	
		Mean ± SD	t/ F (*p*-value)	Mean ± SD	t/ F (*p*-value)
Gender	Male	122.71 ± 52.83	38.69 (< .001)	6.27 ± 1.68	15.27 (< .001)
	Female	49.84 ± 28.45		5.58 ± 1.55	
Education level	Under elementary school[1]	78.47 ± 25.07	2.26 (.105)	5.80 ± 1.72	1.53 (.203)
	Middle School[2]	81.61 ± 38.60		5.91 ± 1.64	
	High school[3]	77.45 ± 37.98		5.92 ± 1.59	
	Above college[4]	81.14 ± 36.51		5.86 ± 1.63	
Weight change over the past year	No change (within 0-3Kg)[1]	80.31 ± 25.75	0.97 (.378)	5.81 ± 1.60	9.06 (< .001)
	Weight loss[2]	83.53 ± 21.63		5.90 ± 1.76	
	Weight gain[3]	78.32 ± 32.60		6.06 ± 1.69	1,2 < 3
BMI (kg/m^2)	Normal weigh (< 23.0)[1]	60.50 ± 24.30	181.15 (< .001)	5.59 ± 1.62	76.82 (< .001)
	Overweigh (23-24.9)[2]	82.94 ± 38.22		5.90 ± 1.53	
	Obesity (≥ 25)[3]	105.46 ± 47.67	1 < 2 < 3	6.23 ± 1.68	1 < 2 < 3

SD = Standard deviation; BMI = Body mass index.

Table 4. Predictive Variables for Serum ferritin and Leukocyte (N = 5,281)

Variables	Serum ferritin			Leukocyte		
	β	t	p	β	t	p
Gender (female)	-.455	-37.55	< .001	-.191	-14.19	< .001
BMI (kg/m^2)						
Obesity (≥ 25)	.209	16.01	< .001	.149	1.12	< .001
Overweigh (23-24.9)	.075	5.78	< .001	.06	4.15	< .001
Weight change over the past year (weight gain)				.047	3.46	.001
Constant		42.242	< .001		73.587	< .001
Adjusted R^2		.262			.102	
F (p)		468.55 (< .001)			36.42 (< .001)	

BMI = Body mass index.

(r = 0.20, p < .001) and leukocyte (r = 0.17, p < .001) (Table 3).

4. Predictive variables for serum ferritin and leukocyte

To determine the factors affecting serum ferritin and leukocyte, gender, weight change over the past year and BMI (obesity, overweight, normal weight), which showed significant differences in serum ferritin and leukocyte were regarded as independent variables. A stepwise multiple regression analysis was performed and the nominal scale was converted to a dummy variable.

Serum ferritin regression model was significant (F = 468.55, p < .001) and the explanatory power of the model was 26.2%. Factors affecting serum ferritin were gender (female) (β = -.455, p < .001), obesity (β = .209, p < .001), and overweight (ß = .075, p < .001).

The leukocyte regression model was significant (F = 36.42, p < .001) and the explanatory power of the model was 10.2%. Factors affecting leukocyte was gender (female) (β = -.191, p < .001), obesity (β = .149, p < .001), overweight (β = .060, p < .001), and weight change over the past year (weight gain) (β = .047, p = .001) (Table 4).

Table 3. Correlation among Subject's BMI, Serum ferritin and Leukocyte (N = 5,281)

Variables	BMI	Serum ferritin	Leukocyte
	r (*p* value)		
BMI	1		
Serum ferritin	0.20 (< .001)	1	
Leukocyte	0.17 (< .001)	0.14 (< .001)	1

BMI = Body mass index.

Discussion

The study is performed to investigate the difference in serum ferritin and leukocyte according to overweight and obesity in South Korean adults. In this study, BMI and serum ferritin are positive correlation, and serum ferritin is the highest in obesity, followed by overweight and normal weight. In addition, factors affecting serum ferritin is gender, obesi-

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ty, and overweight.

The study second, third and fourth quartiles of serum ferritin levels are incident obesity 1.08 times, 1.14 times, and 1.24 times as compared with the first quartile, also there is a consistent association with severe obesity (BMI ≥ 30 kg/m^2) [13]. Serum ferritin is a marker of inflammation in obese subjects, the high BMI is to have a high level of serum ferritin, which can be caused because of the dominant inflammatory conditions, in the presence of an increased adipose tissue [12]. Increased body fat tissue appears to be associated with an increased risk of iron deficiency that can be masked by elevated serum ferritin levels, perhaps the increased cytokines results in increased acute phase reactant synthesis leading to a decrease in macrophages sequestration and / or intestinal iron uptake [20].

The expression of serum ferritin, a prime indicator of iron status, is stimulated by a number of factors, including cytokines released during inflammation and liver disease. Inflammation in turn leads to hepatic synthesis of acute-phase proteins and obesity is one of the most common and prevalent conditions promoting low-level inflammation [21]. ID commonly observed in overweight and obese people is most likely due to inflammatory mechanisms [22].

IDA occurs most often due to malnutrition. Obesity, on the other hand, is often caused by excessive nutrition. Therefore, the coexistence of IDA and obesity in the same person indicates malnutrition and hyper nutrition. Among the factors responsible for mutual co-existence, such as diluted hypoferremia, lack of dietary iron intake, increased iron demand, and/or iron absorption disorder, hepcidin has recently been identified as a major cause of obesity ID or IDA [23].

In this study, BMI and leukocyte were positive correlation, and leukocyte was the highest in obesity, followed by overweight and normal weight. In addition, factors affecting leukocyte were gender, obesity, overweight and weight change over the past year (weight gain). The study found a positive correlation between BMI and leukocyte in the obese group [24] and cross-sectional studies reported a positive association between obesity and leukocyte count [17]. The number of leukocyte in overweight and obesity was 1.06 times (95% CI = 0.9-1.2) and 1.11 times (95% CI = 0.9-1.3), respectively [14]. A previous study showed some factors that cause continuous increase in leukocyte in obese patients [25]. Obesity is the only identified cause in patients with leukopenia. In another study, people with central fat had higher levels of some inflammatory markers, including leukocyte counts, 17% higher than those with normal body fat distribution [26]. Leukocytes increased with increasing waist circumference(WC), and the number of leukocytes are the most consistent between BMI and WC [25].

It has been shown that there is some association between increased numbers of immune cells and obesity as a result of chronic inflammatory conditions resulting from increased cytokines production by adipose tissue, obesity has also been demonstrated to be associated with low-grade sub clinical and smoldering inflammation [27], supporting the results of this study. The previous findings are positive correlation between cell number and obesity have been reported in cross-over study [16]. Measurements of central fat accumulation have been found to be more closely related to the various diseases and health conditions of BMI in both gender [25]. It is necessary to study the difference of serum ferritin and leukocyte including WC and BMI.

The sampling framework of the National Health and Nutrition Survey used in this study was designed to extract representative samples. So, the results of this study, it was meaningful that it can represent the characteristics of Korean adults.

As a limitation of this study, the increase of leukocyte in obesity may be due to hypervolemic in obese people, resulting in a naturally increasing number of blood cells. In addition, the correlation between obesity and chronic inflammation requires implementation of not only leukocyte but also inflammatory markers (for example, CRP).

Conclusions

In this study, obesity and overweight is a factor affecting serum ferritin and leukocyte, and obesity is more affected than overweight in Korean aged over 19 years. In conclusion, Serum ferritin is a marker of inflammation rather than iron status in overweight and obese Korean adults. Because of acute-phase reactions, high ferritin levels secondary to asymptomatic inflammation of both overweight and obesity can mask underlying iron deficiency. It is recommended to request an iron studies including transferrin saturation, total iron binding capacity, and the like.

CONFLICT OF INTEREST

The authors declared no conflict of interest.

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