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Iron status and Hepcidin Level of normal and obese adolescents

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ABSTRAK

Latar Belakang: *Faktor risiko anemia pada remaja obesitas meningkat dengan adanya gangguan homeostasis besi yang terjadi, ditandai dengan kadar feritin dan kadar hepcidin tinggi namun kadar hemoglobin rendah yang disebabkan oleh adanya inflamasi kronik derajat ringan terkait obesitas.*
Tujuan: *Penelitian ini dilakukan untuk mengetahui hubungan antara obesitas, faktor perantara yang memengaruhi, dan kejadian anemia pada remaja usia 12-15 tahun di SMP di Kota Yogyakarta.*
Metode: *Penelitian yang dilakukan adalah penelitian observasional dengan rancangan penelitian potong lintang pada 68 siswa SMP di Kota Yogyakarta yang mempunyai status gizi normal dan obesitas. Pengukuran tinggi badan, berat badan, indeks massa tubuh, kadar hepcidin, kadar feritin, kadar hemoglobin, dan penilaian asupan zat gizi responden dilakukan dalam satu kurun waktu yang hampir bersamaan.*
Hasil: *Persentase anemia pada kelompok normal sebesar 15,15% sedangkan pada kelompok obesitas sebesar 2,85%. Pada penelitian ini, tidak terdapat perbedaan secara signifikan pada prevalensi anemia antara remaja status gizi normal dan obesitas (p=0,074). Median data kadar hemoglobin pada kelompok normal 14,2 g/dl dan kelompok obesitas 14,5 g/dl. Kadar feritin pada kelompok obesitas lebih tinggi secara signifikan dibandingkan dengan kelompok normal, masing-masing 9,7 ng/ml pada kelompok normal, 11,59 ng/ml pada kelompok obesitas sedang dan 15,81 ng/ml kelompok obesitas berat. Terdapat perbedaan signifikan pada kadar leukosit pada kedua kelompok responden (p=0,0443), namun tidak terdapat perbedaan signifikan pada kadar hepcidin (p=0,511). Tidak terdapat korelasi antara kadar hepcidin dan feritin pada seluruh responden (p=0,396), serta terdapat korelasi positif tingkat rendah antara kadar feritin dan hemoglobin pada seluruh responden (p=0,0008).*
Kesimpulan: *Terjadi proses inflamasi kronis derajat ringan pada kelompok obesitas, namun tidak terjadi gangguan metabolisme besi akibat inflamasi. Penelitian lebih lanjut dibutuhkan untuk menggali hubungan anemia dengan obesitas di masa dewasa.*

KATA KUNCI*: anemia; gizi remaja; Hemoglobin; obesitas*

ABSTRACT

Background: *The risk factor for anemia in obese adolescents is increased by the presence of iron homeostatic disorder that occurs, characterized by high levels of ferritin and hepcidin levels but low hemoglobin levels which is caused by mild chronic inflammation associated with obesity.*
Objectives: *This study was conducted to determine the relationship between obesity and intermediary factors that affect the incidence of anemia in adolescents aged 12-15 years in Junior High School, Yogyakarta*
Methods: *This study was observational research with a cross-sectional study design on 68 junior high school students in Yogyakarta City who had normal and obese nutritional status. Measurement of height, weight, body mass index, hepcidin levels, ferritin levels, hemoglobin levels, and assessment of nutrient intake of respondents performed in a period of time.*
Results: *The percentage of anemia in the Normal Group (NG) was 15.15% meanwhile in the Obese Group (OG) was 2.85%. In this study, there was no significant difference in the prevalence of anemia between NG and OG (p=0.074). Median data hemoglobin levels in the NG were 14.2 g/dl and in the OG was 14.5 g/dl. Surprisingly, there was a significantly higher level of ferritin found in the OG than NG, respectively*

9,7 ng/ml in NG, 11.59 ng/ml in the moderately obese group, and 15.81 ng/ml severe obese. There was a significant difference in leukocyte levels between groups (p = 0.0443), however, there was no significant difference in hepcidin levels (p=0.511). There was no correlation between hepcidin and ferritin levels in all respondents (p=0.396), and there was a low positive correlation between ferritin and hemoglobin levels in all respondents (p=0.0008).

***Conclusions:** Low-grade chronic systemic inflammation occurs in the OG, but no iron metabolism disorder occurs due to inflammation. Further study is needed to explore the correlation between anemia and obesity in adulthood.*

KEYWORDS*: adolescents; anaemia; Haemoglobin; obesity*

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INTRODUCTION

Iron deficiency and obesity are two nutritional problems that are globally experienced by billion of humans over the world. Iron deficiency and obesity are known to be related and often occur together. Based on Basic Health Survey 2013 data, the prevalence of obesity in Indonesia in the adult age group (above 18 years) was 13.3% while in the 13-15 year age group was 2.5%. In the Special Region of Yogyakarta, the prevalence of obesity in the adult age group was 15.8% with the highest prevalence in Yogyakarta City (22.8%), while in the 13-15 year age group was 4.2% with prevalence in Yogyakarta City was 2.0% (1).

Obesity is associated with a low-grade degree of chronic inflammation. Obesity and inflammation are often associated with the incidence of anemia in obese individuals with hepcidin as a key mediator (2-5). Hepcidin can control the amount of iron in blood circulation by increasing the amount of stored iron. Expression of hepcidin is influenced by several conditions, such as levels of iron in the circulation, the process of erythropoietic, inflammation, and hypoxia (6).

Hepcidin may affect elevated levels of ferritin under conditions of chronic inflammation as a defense mechanism to minimize iron serum (functional iron) in the blood used by bacteria or other infectious agents. The iron serum will be converted into iron storage in the form of ferritin so that there will be an increase in ferritin levels (6, 7).

Children and adolescents are at risk for iron deficiency due to iron requirements increasing during growth periods. Iron requirements decrease from age 6 months to 3 years but gradually increase until puberty age (8). Factors that may increase the risk of anemia in adolescents are inadequate iron intake, increased body mass, increased iron requirement, and do unhealthy diet (9). Although, some interventions are already conducted to overcome anemia in adolescents, such as nutrition education and school-based intervention (10, 11), but the prevalence of anemia remains high.

Based on the age group, the prevalence of anemia in the age group of 5-14 years was 26.4% and as much as 18.4% in the 15-24 age group (1). The occurrence of anemia and obesity is often associated with inflammation in obese adolescents. The risk factors for anemia in obese adolescents increase with the presence of iron metabolism disorder, characterized by low iron serum levels, low saturation transferrin levels but high ferritin levels (4,8,9,12).

This study was conducted to determine the correlation between obesity and anemia, also its intermediary factors in adolescents aged 12-15 years in junior high school, Yogyakarta. This study could describe the prevalence of anemia in the obese adolescent population in Indonesia, add the theoretical basis to overcome anemia of inflammation in obese adolescents, and can describe

the urgency of overcoming anemia of inflammation in obese adolescents in Indonesia.

MATERIALS AND METHODS

This study was an observational study with a cross-sectional design. Body mass index, serum ferritin, hepcidin, and hemoglobin levels were measured over the same period. The study was conducted for 5 months (December 2016 - April 2017).

Data collection on subjects was conducted in 4 junior high schools in Yogyakarta, namely State Junior High School 1 Yogyakarta, State Junior High School 2 Yogyakarta, Muhammadiyah 3 Junior High School Yogyakarta, and Masjid Syuhada Islamic Junior High School, Yogyakarta. Measurements of body mass index and blood sampling were done at school. Examination of serum ferritin and hepcidin levels was performed at the Biochemistry Laboratory, Faculty of Medicine, Universitas Gadjah Mada (UGM). Complete blood count analysis was analyzed at Clinical Pathology Laboratory, Faculty of Medicine, UGM.

The population of this study was adolescents in Yogyakarta City. The subjects of this study are adolescents aged 12-15 years in Yogyakarta Junior High School with the following inclusion criteria:

a. Obtaining parental consent by filling out and signing informed consent and being willing to be the subject of the study by filling out and signing informed consent.
b. Having BMI/A (Body Mass Index per Age) which was normal or obese.

Exclusion criteria of research subjects were:

a. Suffering from chronic illness (based on medical history).
b. Suffer from infectious diseases (leukocyte level > 10.8×10^9/L).
c. Consume iron supplements within the last 3 months.
d. Have severe bleeding within the last 3 months.

The sample size was calculated by the sample formula for the cross-sectional study of the proportion of 2 populations with a 95% confidence level and 92% power. The estimated proportion of anemia in the obese adolescent population was 8.7% and the estimated proportion of anemia in the normal nutritional status adolescent population was 3.2% (10). From the calculation, the obtained sample size minimum was 68 subjects.

The subject's selection was done by cluster sampling based on their school. The selection of schools was done by simple random sampling to determine which schools will be screened. Four schools were taken as research locations of all junior high schools in Yogyakarta. Subjects selection was preceded by nutritional status screening in all schools. The selection of subjects was using randomization methods which were differentiated by sex to obtain a proportionate amount between the male and female subjects.

Characteristic of subjects was taken by using characteristic from which self-filled by subjects. Height measurement was done by using microtoise with a precision level of 0.1 cm. Weight measurement was performed using calibrated digital body scales with a precision level of 0.1 kg. Assessment of subjects' nutrient intake was done using a validated SQ-FFQ form. Measurement of height, weight, and assessment of nutrient intake was carried out by nutritionists.

Blood sampling was done by a health analyst. Analysis of hepcidin and ferritin levels was performed by ELISA using ELISA kit (DRG EIA-1872 for ferritin and Fine Test EH-3221 for hepcidin), whereas hemoglobin level was analyzed using Sysmex Hematology Analyzer. Hemoglobin levels were categorized as normal if the value was ≥12 g/dl and if the hemoglobin level of subjects was <12 g/dl, subjects were categorized as anemic (13).

Calculation of z-score values from anthropometric data was analyzed using WHO Anthro Plus software. Data analysis was performed using STATA 12. Data analysis was analyzed by univariate analysis that was by displaying data descriptively. Furthermore, the data were analyzed by bivariate analysis to know the relationship between two variables. Data analysis was done by non-parametric test because of abnormal data distribution. This research has obtained the ethical license from the Ethical Commission, Faculty of

Medicine, Public Health and Nursing UGM with the number: KE/FK/0154/EC/2017.

RESULTS AND DISCUSSIONS

Measurement of nutritional status was performed on all grade 8 students at the four schools. Nutritional status was categorized into 4 categories based on WHO 2007 Growth References.

From the data of nutritional status measurement in all grade 8 students in four junior high schools, 68 students were eligible as subjects according to the inclusion and exclusion criteria. The characteristics of the subjects of this study can be seen in **Table 1.**

Table 1. Characteristics of Subjects

Characteristics	Mean or n(%)
Age (years)[a]	13.81 ± 0.39
Gender[b]	
Male	34 (50)
Female	34 (50)
Body weight (kg)[c]	62.5 (50.05 ; 75.4)
Height (cm)[c]	159 (155.63 ; 164.25)
Mother's Occupation[b]	
Housewife	25 (36.76)
Civil Servant	10 (14.71)
Private Sector	12 (17.65)
Enterpreuner	7 (10.29)
Farmer	8 (11.76)
Merchant	3 (4.41)
Labour	2 (2.94)
Honorary Staff	1 (1.47)
Father's Occupation[b]	
Civil Servant	18 (26.47)
Private Sector	22 (32.35)
Enterpreuner	14 (20.59)
Merchant	9 (13.24)
Labour	2 (2.94)
Unemployed	3 (4.41)
Total Family Income[b]	
< Rp1.000.000	4 (5.88)
Rp1000.000-Rp3.000.000	19 (27.94)
Rp3.000.000-Rp5.000.000	18 (26.47)
Rp5.000.000-Rp7.000.000	5 (7.35)
Rp7.000.000- Rp10.000.000	15 (22.06)
Rp10.000.000-Rp20.000.000	3 (4.41)
> Rp20.000.000,00	4 (5.88)

[a] Data presented by mean ± SD, [b] Data were presented by n (%), [c] Data were presented by median (Q1;Q3)

Data of the total leukocyte count of subjects can be seen in **Table 2**. Data of measurement of nutritional status of subjects can be seen in **Table 3**.

Table 2. Mean of Total Leukocyte Count of Subjects

Nutrition Status	Mean ± SD (x 10^9/L)	P-*Value*
Normal	7.49 ± 1.72	0.0443*
Obese	8.34 ± 1.69	

*Independent t-test, p<0,05

Table 3. Nutritional Status of Subjects

Indicator	Normal Median (Q1;Q3)	Obese Median (Q1;Q3)
BMI/A (kg/m^2)	19.8 (18.6 ; 20.7)	28.7 (28 ; 32.1)
z-score BMI/A	0.17 (-0.255 ; 0.47)	2.19 (2.37 ; 2.87)

To see the differences in hepcidin, ferritin, and hemoglobin levels in the subjects with moderate and severe obesity, data were then grouped into 3 groups. Subjects with BMI <100% 95th percentiles were categorized as a normal group, subjects with BMI 100%-119% 95th percentiles were categorized as moderate obese and subjects with BMI ≥ 120% 95th percentile were categorized as a severe obese group (12). Data of hepcidin, ferritin and hemoglobin based on normal, moderate and severe obesity can be seen in **Table 4**.

Table 4. Hepcidin, Ferritin, and Hemoglobin Levels of Subjects Based on Normal, Moderate and Severe Obese Groups

Indicator	Nutritional Status		
	Normal Median (Q1;Q3)	Moderate Obese Median (Q1;Q3)	Severe Obese Median (Q1;Q3)
Hepcidin (ng/ml)	29.23[a] (18.99 ; 38.05)	29.8[a] (20.26 ; 41.31)	28.88[a] (22.27 ; 40.93)
Feritin (ng/ml)	9.7[a] (1.91 ; 19.47)	11.59[ab] (2.91 ; 17.56)	15.81[b] (11.44 ; 34.71)
Hemoglobin (g/dl)	14.2[a] (13.25 ; 15)	14.35[a] (13.45 ; 15.2)	14.5[a] (13.4 ; 15.2)

Data analysis were performed using the *Mann-Whitney test*
[a,b] different font within rows showed significant different (p<0,05)

The result of analysis of the relationship between obesity and the incidence of anemia was analyzed by Fisher Exact test can be seen in Table 5.

Table 5. Prevalence of Anemia

Anemia Status	Nutritional Status		Total	P-*Value*
	Normal	Obese		
Anemia	5 (15.15%)	1 (2.85%)	6 (8.82%)	0.074
Non Anemia	28 (84.84%)	34 (97.14%)	62 (91.17%)	
Total	33 (100%)	35 (100%)	68 (100%)	

The relationship between hepcidin and ferritin levels was analyzed by the Spearman test. From the outlier identification. found that there was outlier data (outlier was found on hepcidin and ferritin level data) so that data transformation was performed before data analysis. Data transformation was performed by square root data transformation The data transformation was chosen based on skewness type of data which was positive.

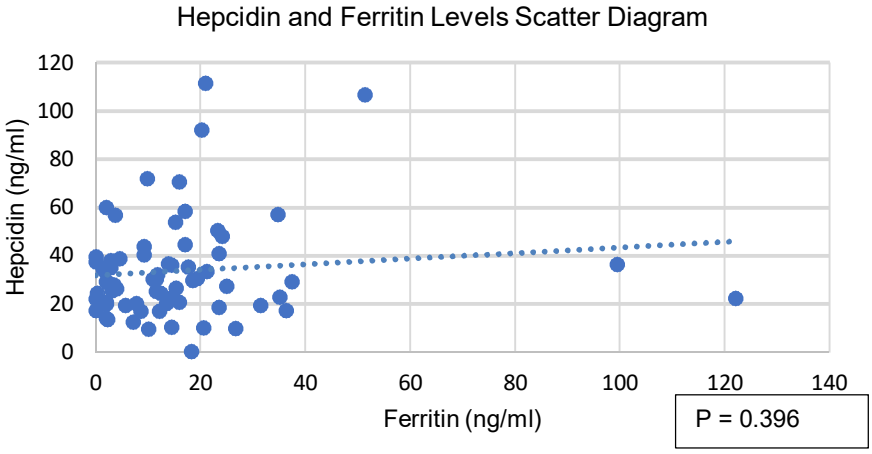

Figure 1. Hepcidin and Ferritin Levels Scatter Diagram

The relationship between ferritin levels and hemoglobin levels was analyzed by the Spearman test. Data of hemoglobin levels were transformed by inverse square root transformation in accordance with the negative skewness type of data.

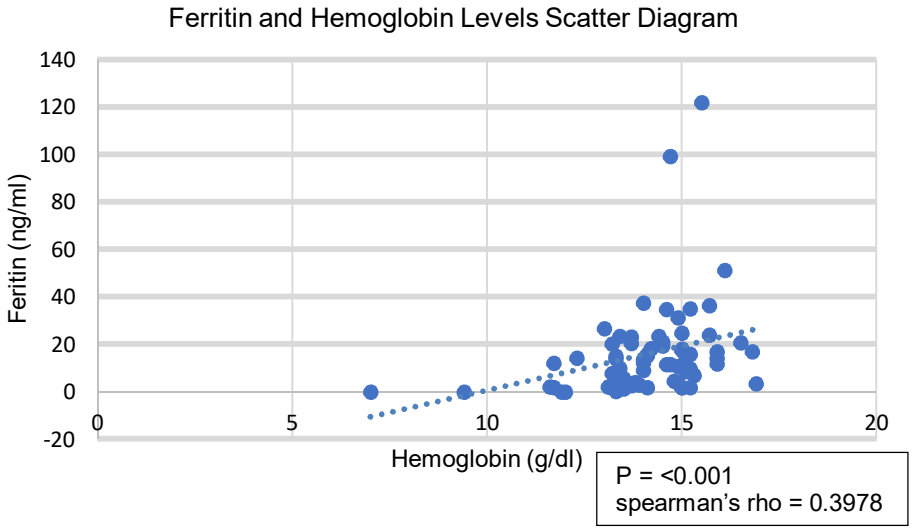

Figure 2. Ferritin and Hemoglobin Levels Scatter Diagram

Total leukocytes count between subjects with normal and obese nutritional status were significantly different (p = 0.0443) with the average total leukocyte on normal nutritional status was 7.49±1.72 × 10^9/L and on obese subjects was 8.34±1.69 × 10^9/L. The results of data analysis showed a significant difference. Levels of inflammatory markers in obese adolescents were higher than those with normal nutritional status. although leukocyte count in both groups remained within the normal range of <10.8 × 10^9/L.

Leukocytes are positively correlated with CRP levels. which is one of the most sensitive inflammatory markers (1). Leukocytes are elevated during inflammation. The increase in total leukocytes in the blood shows a low grade of systemic inflammation that occurs in obese individuals (1-4).

Hepcidin levels are associated with inflammation in the human body. Inflammation can lead to an increase in hepcidin levels. In this study. hepcidin levels in subjects with normal nutritional status and obesity were not significantly different (p = 0.511). The median of hepcidin levels in the subjects with normal nutritional status was 29.23 mg/mL meanwhile in the obese group was 29.32 ng/mL. In this study. inflammatory markers of total leukocyte count in the obese group were significantly higher compared with those with normal nutritional status. This illustrates the occurrence of inflammation in obese adolescents. but the inflammation does not affect hepcidin levels shown by the analysis of hepcidin levels relationship between the subjects with normal nutritional status and obese which was not significantly different.

The results are consistent with the research of Ridha & Daud who found no significant difference in hepcidin levels among adolescents with normal and obese nutritional status (5). In that study. found significant differences in hepcidin levels in subjects with normal nutritional status and superobese. Compared with obese individuals. individuals with superobese conditions experienced differences in the degree of inflammation. greater exposure. and long processes to stimulate the release of hepcidin. Thus. it may be concluded that although the obese subjects have been experienced by inflammation. but not enough to stimulate the release of hepcidin by hepatocytes.

The impact of increased leukocytes may not affect hepcidin levels due to changes in body composition and age group. The degree of chronic inflammation experienced by obese adolescents is related to the fat mass in the body. Fat mass in the adolescent body is very easy to change because they are still in their growth periods. The growth and development of children will accelerate during puberty and affect the body composition (6-8). At the age of 13 years. an increase in the percentage of fat mass is due to physiological changes associated with puberty in adolescent girls. At the age of 13-17 years. adolescent males experience increased fat-free body mass due to puberty (9).

Inflammation that occurs in the body of obese individuals is also affected by age. As humans get older. CRP levels will increase. In a 15-year cohort study. there was found an increase in CRP levels in both male and female subjects. The impact of BMI increase as age increases can increase oxidative stress and inflammation characterized by elevated levels of CRP. glutamyltransferase. and uric acid (10).

In this research. the median data of ferritin levels of subjects with normal nutritional status was 9.7 ng/mL while the obese was 14.35 ng/mL. The results of statistical analysis showed no relationship between hepcidin levels and ferritin levels in the respondents (p = 0.39). This is in line with the results of leukocyte level relationship analysis with hepcidin levels that are not significantly related. This illustrates the inflammatory outcomes that occur in obese subjects not seen in hepcidin levels or ferritin levels of subjects.

Based on Ridha & Daud. the absence of significant difference of ferritin level in adolescents with normal and obese nutritional status and adolescents with normal nutritional status and superobese because hepcidin released by hepatocytes is not enough. the intensity is strong enough and exposure has not been experienced for a long time (5).

Hepcidin may affect elevated levels of ferritin under conditions of chronic inflammation in the body as a body's defense mechanism to minimize serum iron (functional iron) in the blood used by bacteria. The iron serum will be converted into iron storage in the form of ferritin so that there will be an increase in ferritin levels. Hepcidin can cause a decrease in ferritin levels in iron deficiency conditions and there is no interruption of iron metabolism disorder related to inflammation. Hepcidin will respond to iron deficiency to convert iron reserves in the form of ferritin into functional iron in the form of iron serum (11-12).

The level of ferritin is indicated by iron storage in the body. When the body has iron deficiency. serum ferritin levels will decrease due to iron changes in the form of ferritin into functional iron. Functional iron will be used as a synthesis component of various compounds in the body. one of them is hemoglobin.

In this study obtained median data hemoglobin levels on the subjects with normal nutritional status was 14.2 g/dL while on obese was 14.5 g/dL. The result of data analysis showed a positive correlation with the low strength level between ferritin level and hemoglobin level on the subjects (p = 0.0008. r = 0.3978). This indicates the absence of iron metabolism disturbance on obese subjects.

In anemia caused by inflammation. ferritin levels show a negative correlation with hemoglobin levels. Anemia that is found in this study was iron deficiency anemia characterized by a positive correlation between ferritin and hemoglobin levels.

The prevalence of anemia in all subjects was 8.82%. Subjects who experienced anemia in the group of normal nutritional status were 5 people (15.15%) while in a group of obese there was only 1 person (2.85%). The median hemoglobin level in the normal nutritional status group was slightly lower than the median hemoglobin level in the obese group. namely 14.2 and 14.5 g/dL respectively. The prevalence difference of anemia in both groups was not significant (p=0.074).

The result of this study is also in line with the study conducted by Viana *et al*. in 707 adolescents aged 11-19.9 years who found no association between BMI on hemoglobin levels. although hemoglobin levels in overweight women were significantly lower when compared with adolescent girls with normal nutritional status (13).

Similar results were also found by Ausk &

Ioannou who examined the association of obesity with anemia in adults with normal nutritional status. overweight. mild. moderate. and severely obese (14). The results showed lower serum levels of iron and transferrin. higher CRP. and serum ferritin levels in adult individuals with moderate and severe obese nutrition status compared with normal adult individuals. Hemoglobin levels and percentage of anemia did not differ significantly in the five groups of subjects. It shows that obesity is not a single factor as a risk factor for obese individuals.

A study conducted by Ridha & Daud also showed no difference in levels of ferritin and serum transferrin in obese and superobese adolescents compared with normal nutritional status (5). In the study. there was a difference in mean hepcidin and CRP levels in the superobese group compared with the normal nutritional status group. This suggests that superobese and obese conditions differ in degree of inflammation. greater exposure and inflammatory processes have lasted longer to stimulate the release of hepcidin.

The result of this study was in contrast with several studies. Based on Nazif *et al*.. there was a significant decrease in hemoglobin. iron serum. serum ferritin. and transferrin in obese teenagers compared with non-obese teenagers (15). The hepcidin level was positively correlated with BMI and CRP levels but negatively correlated with iron status in obese adolescents. A study conducted by Newfield *et al*. showed a proportion of iron deficiency (iron serum <8 µmol/L) greater in obese children and adolescents than normal (16).

Similar results were also found by Keikhaei *et al*. which suggests a greater risk of anemia in adolescents with abnormal nutritional status (thin. overweight. and obese) compared with adolescents with normal nutritional status (17). A study conducted by Peter *et al*. showed a negative correlation between hemoglobin and BMI levels in overweight and obese women aged 16-30 years old (18).

Iron deficiency in obese adolescents can be caused by metabolic disorders due to hepcidin mediation in decreased iron absorption and increased iron storage formation. Obesity can not be the single cause of anemia associated with inflammation in obese adolescents. Intake of iron. body fat mass. inflammation rate (obesity comorbidity). age. and sex into other factors that can cause anemia associated with inflammation in obese individuals (5. 13-19).

In this study. there was no significant difference in the prevalence of anemia between adolescents of normal nutritional status and obesity. There were significant differences in leukocyte levels (higher in the obese group) in both groups of respondents. but no significant difference in hepcidin levels. Levels of leukocytes in all subjects were still within normal levels. There was no correlation between hepcidin and ferritin levels in all subjects. and there was a positive correlation between ferritin and hemoglobin levels in all subjects. This suggests a low-grade degree of chronic inflammation in the obese group. but no metabolic disorders of iron due to inflammation in the obese group. A positive correlation between ferritin and hemoglobin levels showed that the anemia found in this study was iron deficiency anemia and unrelated to inflammation.

CONCLUSIONS AND RECOMMENDATIONS

There was a low-grade degree of the chronic inflammatory process in the obese group. but there was no disturbance of iron metabolism due to inflammation in the obese group. Further study is needed to explore more about the correlation of anemia. iron status. and obesity in another stage of life.

In the next research. it is better to consider the variable of comorbidity degree of obesity. fat mass. and long exposure of inflammation due to obesity. This study can be performed on obese adult women and conducted with a balanced proportion of anemic and non-anemic subjects. Anemia elimination program in adolescents is appropriate which is to overcome iron deficiency anemia due to inadequate intake of iron.

REFERENCES

1. Farhangi M. S K. Eshraghian M. Ostadrahimi A. White Blood Cell Count in Women : Relation

to Inflammatory Biomarkers . Haematological Profiles . Visceral Adiposity . and Other Cardiovascular Risk Factors. J Heal Popul Nutr. 2013; 31(1): p. 58-64.
2. Reyes M. Quintanilla C. Burrows R. Blanco E. Cifuentes M. Gahagan S. Obesity is associated with acute inflammation in a sample of adolescents. Pediatr Diabetes. 2015; 16: p. 109-116.
3. Nascimento H. Rocha S. Rego C. Mansilha H. Santos-silva A. Belo L. Leukocyte Count versus C-Reactive Protein Levels in Obese Portuguese Patients Aged 6-12 Years Old. Open Biochem J. 2010; 4: p. 72-76.
4. Ala-korpela M. Bloigu A. Canoy D. Pirkola J. Va M. Hartikainen A. Original Contribution Low-Grade . Systemic Inflammation in Adolescents : Association With Early-Life Factors. Gender. and Lifestyle. Am J Epidemiol. 2010; 171(1): p. 72-82.
5. Ridha N. Daud D. Hubungan Kadar Hepcidin dengan Status Besi pada Inflamasi Akibat Obesitas. Sari Pediatr. 2014; 16(3): p. 161-166.
6. Jun M. Ning F. Shiei Z. Yonging P. Yongo H. Comparison of Changes in Body Composition during Puberty Development of Obese and Normal-weight Children in China. Biomed Environ Sci. 2009; 22(5): p. 413-418.
7. Moreno L. Blay M. Blay V. Garagorri J. Sarrı A. Body composition in adolescents : measurements and metabolic aspects. Int J Obes. 2004; 28: p. 554-558.
8. Wardle J. Brodersen N. Cole T. Jarvis M. Boniface D. Development of adiposity in adolescence: five year longitudinal study of an ethnically and socioeconomically diverse sample of young people in Britain. BMJ. 2006; 332(1130): p. 5-10.
9. Araújo J. Barros H. Severo M. Lopes C. Ramos E. Longitudinal changes in adiposity during adolescence : a population-based cohort. BMJ Open. 2014; 4(6).
10. Hulsegge G. Herber-Gast G. Spijkerman A. Susan H. Picavet J. Schouw Y. et al. Obesity and Age-Related Changes in Markers of Oxidative Stress and Inflammation Across Four Generations. Obesity. 2016; 24(6): p. 1389-1396.
11. Perdana W. Jacobus D. Hepcidin dan Anemia Defi siensi Besi. CDK. 2015; 42(12): p. 919-926.
12. Cullis J. Diagnosis and management of anaemia of chronic disease : current status. Br J Haematol. 2011; 154(3): p. 289-300.
13. Viana U. Raggio R. Valeria G. Overweight is associated with low hemoglobin levels in adolescent girls. Obes Res Clin Pract. 2013; 7(3): p. 218-229.
14. Ausk K. Ioannou G. Is obesity associated with anemia of chronic disease? A population-based study. Obesity. 2008; 16(10): p. 2356-2361.
15. Nazif H. El-shaheed A. Mohsen M. Fadl N. Moustafa R. Study of Serum Hepcidin as a Potential Mediator of the Disrupted Iron Metabolism in Obese Adolescents. Int J Health Sci (Qassim). 2015; 9(2).
16. Newfield R. Koren I. Agmon A. Lilos P. Phillip M. Greater prevalence of iron deficiency in overweight and obese children and adolescents. Int J Obes. 2003; 27: p. 416-418.
17. Keikhaei B. Askari R. Aminzadeh M. Adolescent with Unfeasible Body Mass Index : A Risk Factor for Iron Deficiency Anemia. J Heal Med Informat. 2012; 3(1): p. 1-4.
18. Peter R. Kumar R. Sangwan L. Pandey S. Prevalence of Anemia and Its Correlation to Body Mass Index: Study Among Unmarried Girls. Int J Basic Appl Med Sci. 2012; 2(3): p. 58-62.
19. Cheng H. Bryant C. Rooney K. Steinbeck K. Griffin H. Petocz P. Iron. Hepcidin and Inflammatory Status of Young Healthy Overweight and Obese Women in Australia. PLoS One. 2013; 8(7): p. 1-6. x