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Dietary iron intake and serum interleukin-6 levels of obese children with and without iron deficiency



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ABSTRACT

Background: Iron deficiency is more common in obese children. Low dietary iron intake and inflammation are suspected as the cause. This study investigates the dietary iron intake and serum IL-6 levels relationship with the obese children iron status.

Methods: Seventy obese children were recruited. Dietary iron intake was calculated using three days' food record. Serum IL-6 was measured using sandwich ELISA. Iron deficiency was confirmed if iron serum <60 mcg/dl and/or saturation of transferrin <20%. Independent t-test was used to analyze the mean difference of the dietary iron intake between the with and without iron deficiency groups, $\alpha=0.05$.

And, Mann-Whitney for the median difference of the serum IL-6 between the two groups.

Results: Forty-six subjects (65.7%) had iron deficiency. Dietary iron intake of the with and without iron deficiency groups were 6.8 mg (SD 3.3) and 6.6 mg (SD 3.8), respectively ($p>0.05$). The interleukin-6 was 2.7 pg/ml (0.3-16.8) and 1.7 pg/ml (0.8-4.9), respectively ($p<0.05$).

Conclusion: Iron deficiency in obese children was high. It was not associated with low dietary iron intake, but associated with inflammation.

Keywords: iron, obesity, inflammation

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INTRODUCTION

Iron deficiency (ID) and obesity in children are two common nutritional problems in the developed and the developing countries. Several studies reported ID prevalence of 26-45% and obesity in children was 6.7%.^{1,2} In Indonesia, the prevalence of ID was 12-27%.³ And, the obesity in children was 9.5%-18.8%.⁴ Both of them impact negatively on child health. Iron deficiency causes behavioral disturbances and impaired cognitive function.⁵ Some literatures show obesity associated with several diseases such as hypertension, coronary heart disease, diabetes type 2, dyslipidemia, and premature death.^{6,7}

Recently, ID was reported in obese children more frequently than in the normal weight counterparts.^{8,9} It is suspected that a reduced dietary iron intake associates with a poor iron status. On the other hand, inflammation has also been suspected to contribute to poor iron status after hepcidin, a key role of body iron homeostasis was found. Increased pro-inflammatory cytokines, such as interleukin-6 (IL-6) in obese children, stimulates hepcidin expression and reduces iron availability.¹⁰

Our study aimed to find the prevalence of ID in obese children, and to compare the dietary iron intake and IL-6 levels between obese children with and without ID.

METHODS

Our study was a cross sectional study, enrolled from January to June 2014. The study involved 7 (seven) primary schools in Denpasar, Bali. The ethical approval was issued by the ethics committee of Udayana University Faculty of Medicine in conjunction with the teaching hospital, Sanglah General Hospital, Denpasar, Bali. The inclusion criteria were obese children 6-10-year-old and their parents agreed to enroll them and participate in this study and sign the informed consent. The obese children were excluded from the study if they had a major congenital defect, chronic diseases, malignancies, liver and kidney disease, or they had been joining weight loss programs, getting iron therapy and if the obesity was caused by chromosomal or hormonal defects.

We asked the physical education teachers who attended the school health unit (*usaha kesehatan sekolah*/UKS) of each school for the 6 to 10-year-old students who were recorded as overweight or obese. The parents were sent a letter by the school principle to invite them to the school, where the researcher explained the study in details. The children whose parents agreed to enroll them in the study were examined to determine whether they are obese or not. The body weight was measured using digital scale (Seca® 881). Subjects were measured in

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standing position, wearing minimal clothes without shoes. The body height was measured using stadiometer (Seca® 206). The subject stood erect on the floorboard of the stadiometer with his or her back to the vertical backboard of the stadiometer. Body mass index (BMI) was calculated based on the result of body weight in kilogram divided by the square body height in meter (kg/m²). Next, the BMI was plotted into the age-and-gender-specific BMI percentiles from the CDC-2000 growth chart. The child was classified as obese when the BMI ≥ 95th percentile.¹¹

The parents of the students who were obese were given a dietary assessment. The assessment was made using a three-days food record. The parents recalled all food consumed by their children on Monday, Wednesday and Sunday last week. The macro and micronutrients contents of the recorded food were analyzed using a *nutri-survey* software by a trainee dietician.

Then, subjects were invited to go to Prodia Laboratory in the next morning, after fasting 10 hours overnight. A venipuncture to gain 15 ml

of blood was done. Next, the blood was centrifuged. The serum was stored at -20°C until the analysis. Serum iron was measured using Ferozine method (ADVIA® Chemistry System), while serum TIBC used Sequential release and uptake of iron method (ADVIA® Chemistry System), and serum ferritin used the electrochemiluminescence immunoassay method (COBAS® ECLIA), and serum IL-6 used quantitative sandwich enzyme immunoassay method. Percent transferrin saturation was calculated as serum iron divided by TIBC (SI/TIBC × 100). The subjects were considered suffering from ID if serum iron less than 60 mcg/dl and/or transferrin saturation less than 20%.¹²

The data were analyzed using SPSS 20. The minimum sample size was 66 subjects to detect 0.9 pg/ml difference of IL-6 between groups, $\alpha=0.05$, $\beta=80\%$. The study used the logistic regression for multivariable analysis, while X^2 test was to analyze the difference in proportions, and independent t-test for mean difference (parametric) and Mann-Whitney test for median difference (non-parametric), $\alpha=0.05$.

RESULTS

The total number of sample is 70. The characteristics of the sample according to the demographic, anthropometric, dietary intake and biochemist characteristics of the subjects are presented in Table 1. Forty-six subjects (65.7%) had ID. Iron deficiency was more prevalent among the female (78.8%) compared to the male (54.1%), $p<0.05$. Dietary food intake, including iron intake was not significantly different between the group with and without ID ($p>0.05$). Similar with the dietary food intake, the anthropometric status was also not significantly different between two groups ($p>0.05$). However, the serum IL-6 level was significantly higher in the ID group than in the group without ID (2.7 pg/ml vs 1.7 pg/ml, $p<0.05$).

Logistic regression analysis was performed to evaluate the independent association of age, gender, dietary iron intake, serum IL-6 levels and ID (Table 2). The ID group had a higher serum IL-6 level than the group without ID, OR=2.0 (95% CI: 1.2-3.3, $p<0.05$). But, the dietary iron intake was similar between the two groups.

DISCUSSION

The prevalence of ID in obese children in this study was 65.7%. This finding was higher than other studies, which recorded around 5.5% to 58.5%.^{8,9,13} Because, we used different criteria. Apart from the prevalence differences among the studies, they still

Table 1 Demographic, Anthropometric, Dietary Intake and Biochemistry Characteristics

	With ID n=46 mean ± SD or median (min-max)	Without ID n=24 mean ± SD or median (min-max)
Male/female	20/26	17/7
Age (year)	9.5 ± 1.1	9.4 ± 1.1
Body weight (kg)	52.5 ± 9.1	55.1 ± 11.0
Body height (m)	1.39 ± 0.06	1.40 ± 0.1
BMI (kg/m ²)	26.9 ± 3.6	27.8 ± 3.2
Energy (kcal)	1725 ± 333	1805 ± 304
Protein (g)	67.9 ± 19.0	72.8 ± 20.7
Lipid (g)	57.5 ± 25.1	60.5 ± 25.9
Iron intake (mg)*	6.8 ± 3.3	6.6 ± 3.8
Serum iron (mcg/dL)	46.5 (15.0-70.9)	86.5 (57.0-139.0)
TIBC	336.4 ± 32.5	338.3 ± 37.9
Serum ferritin (ng/mL)	64.3 (27.8-143.0)	96.3 (39.5-426.0)
Transferrin saturation (%)	14.6 (4.8-19.2)	25.6 (20.1-39.1)
IL-6 (pg/mL)*	2.7 (0.3-16.8)	1.7 (0.8-4.9)

* $p>0.05$ by t-test analysis; * $p<0.05$, by Mann-Whitney.

Table 2 Logistic Regression Predicting Iron Deficiency

	OR	95% CI	p value
Age (years)	1.1	0.6-1.8	0.703
Gender	0.2	0.1-0.9	0.037
Iron intake (mg)	1.0	0.9-1.2	0.379
IL-6 (pg/ml)	2.0	1.2-3.3	0.008

showed that ID more frequent in obese children than in the normal weight counterparts.

The risk factors of ID in children include poor iron-rich foods intake, poor intake of iron absorption enhancers such as vitamin C, or a diet rich of iron absorption inhibitors such as polyphenols, tannins, phytates, and calcium.¹⁴ In our study, the dietary intake including the iron intake was documented. We compared the dietary iron intake between the ID and non-ID groups. There was no significant difference of the dietary iron intake between the groups. It means that ID in obese children was not caused by a low dietary iron intake. The result was consistent with other studies previously.^{13,15-17}

Obesity is related to chronic low-grade inflammation. Several pro-inflammatory cytokine are produced by the obese adipose tissue and adipose tissue macrophage (ATM) such as Tumor Necrosis Factor- α (TNF- α), Interleukin-6 (IL-6) and Interleukin-1 β (IL-1 β).¹⁸ All of this pro-inflammatory cytokines are released chronically into the blood circulation. IL-6 is directly stimulating the production of hepcidin by the liver. A high circulation of hepcidin induces an internalization and a degradation of ferroportin, an iron exporter protein that blocks the iron absorption in the intestinal membrane and inhibits the iron release from macrophage into the blood circulation. Thus, it results in a low serum iron levels and a low transferrin saturation.¹⁹ Therefore, inflammation is suspected as the cause of ID in obese children.²⁰

In this study, the level of IL-6 serum in obese children with ID was higher than in obese children without ID. Our data indicated that ID in obese children related to inflammation, rather than a low dietary iron intake. Many studies reported the relationship between inflammation and obesity using other inflammation marker such as CRP.^{13,15,21,22} They concluded that the increased risk of ID might be due to the effects of obesity-related-inflammation on dietary iron absorption.

Iron deficiency is associated with impaired learning, lower score of mental, and motor development in children.⁵ Moreover, obesity is associated with chronic diseases such as diabetes type 2, hypertension, dyslipidemia, heart diseases, and stroke.^{6,7} Given the long-term impact on a child health, its prevention and the comprehensive treatment are important public health issues.

CONCLUSION

Iron deficiency in obese children is high and it may be more related to a chronic inflammation than a low dietary iron intake. The data confirmed that

a guideline to screen ID may be needed in obese children. And, the treatment should be focused on decreasing the inflammation process.

STUDY LIMITATIONS

Some potential limitations may be found in this study. This study relied on the parent recall on the last week diet of the children. Thus, making a recall bias inevitable. Our study sample was also small in number. However, this study was intended to serve as a pilot for a more advance study. Because our study was a cross sectional by design, we could not determine the causal relationship between the dietary iron intake and the inflammatory marker with the iron status.

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