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Original Article

Soluble transferrin receptor levels in obese and non obese adolescents

Zul Febrianti, Fadil Oenzil, Firman Arbi, Gustina Lubis

Abstract

Background Iron deficiency in children and adolescents maybe due to an inadequate supply of iron as well as increased iron requirements for growth and developmental processes. The increasing prevalence of obesity puts children at risk of iron deficiency. Studies on the effects of obesity on iron deficiency have focused on low grade systemic inflammation as well as examining soluble transferrin receptor levels (sTfR) as an indicator of iron deficiency.

Objective To compare sTfR levels in obese and non-obese adolescents, assess for correlations between BMI, sTfR and obesity, and determine the risk of iron deficiency in obese adolescents.

Method This cross sectional study was conducted on 20 obese and 20 non-obese adolescents aged 15-17 in East Aceh District, from September to December 2011. Subject were chosen through cluster sampling. The obese subjects had BMI >95th percentile and the non-obese subjects had BMI ≤85th percentile based on the 2000 National Center for Health Statistics (NCHS). Exclusion criteria were blood disorders, chronic diseases, and a history of bleeding. Data were analyzed by Chi-square test and T-test with a significance level of P <0.05, and Pearson's correlation.

Results The mean sTfR levels in obese adolescents was higher than in non-obese adolescents, [2.59 (SD 0.76) vs 2.14 (SD 0.45) μg/mL (P = 0.030)]. Iron deficiency (sTfR>2.5 μg/mL) was more common in obese than in non-obese adolescents [(55% vs. 15%, respectively, (P = 0.019)]. Analysis of the relationship between obesity according to BMI and sTfR revealed an OR of 6.93; 95% CI 1.53 to 31.38. The relationship between the BMI and sTfR levels indicated a positive, moderate strength of association (r = 0.392).

Conclusion The mean sTfR levels in obese adolescents is significantly higher than in non-obese individuals. Obese adolescents have a 6.93 times higher risk of iron deficiency than non-obese adolescents. Body mass index has a positive and moderate association with sTfR. **[Paediatr Indones. 2014;54:77-81.]**

Keywords*: soluble transferrin receptor, obese adolescents, body mass index, iron deficiency.*

Iron is one of the most important trace elements for optimal physical performance and cognitive function.[1] In children and adolescents, iron deficiency occurs because of inadequate iron supply (decreased intake or low availability in the diet) and the increased need for iron due to growth and development.[2] Iron deficiency can occur at any age and is mostly caused by nutritional factors.[3,4]

Data from the National Center for Health Statistics (NCHS) showed that nearly 1 in 5 children in the United States is overweight, with a steadily rising prevalence in the past 20 years.[5,6] Increased incidence of obesity in children has been noted in both developed and developing countries.[5]

In the early 1960's, researchers observed a strong correlation between low iron status and obesity in male and female adolescents.[7] The prevalence of obesity in Indonesia according to data from the National Socioeconomic Survey (SUSENAS) showed an increase both in urban and rural.[8]

It has been theorized that there are associations involving low dietary iron, increased iron need due to increased body size and blood volume, decreased

From the Department of Child Health, Andalas University Medical School, Padang, Indonesia.

Reprint requests to: E.S Zul Febrianti, Department of Child Health, Andalas University Medical School, Jl. Perintis Kemerdekaan No.l 49, PO BOX 49, Padang, Indonesia. Tel. +62-75131746, Fax. +62-75132838. E-mail: febriyo@yahoo.com.

physical activity, menstrual irregularity, and obesity to inflammatory processes involving hepcidin, peptide hormone that regulates iron homeostasis.[9-11] Recent study has focused on the impact obesity on low grade systemic inflammation, due to the release of proinflammatory cytokines interleukin-6 (IL-6) from adipose tissue that stimulates hepcidin production.[9]

In order to determine the type of iron deficiency, several laboratory tests are required. Evaluation of sTfR has been widely used as a diagnostic tool to differentiate iron deficiency anemia from anemia of chronic diseases.[10,12,13] Soluble transferrin receptor (sTfR) is useful as a measurement of body iron availability, as it is a clinical marker of erythropoietic activity, requires only a few serum samples, and has been shown to be comparable to bone marrow puncture for describing iron availability. Another advantage of sTfR measurements is that sTfR level is not influenced by inflammation or infection, hence, iron defieciency that has increased to the 2nd or 3rd stages can be detected and attributed to iron deficiency anemia.[14-16] This study was undertaken to assess sTfR levels in obese and non-obese adolescents, evaluate the possible correlation levels of sTfR to body mass index (BMI), and determine the risk of iron deficiency in obese adolescents.

Methods

This cross sectional study was conducted on 20 obese and 20 non-obese adolescents aged 15-17 years in the East Aceh District, from September to December 2011. Participants were chosen through cluster sampling. Obese subjects had BMI ≥95th percentile and non-obese subjects had BMI <85th percentile on the 2000 NCHS curve.[6] Data were analyzed by Chi-square test and T- test with significance level of P <0.05, and Pearson's correlation. This study was approved by the Research Ethics Committee of Medical Faculty Andalas University.

We included high school students who were willing to join the study and provide blood specimens. Informed consent was obtained from subject's parents. We excluded those who experience trauma/accidents during the study, those who had heart defects or chronic diseases, such as tuberculosis, dental caries, chronic tonsillitis, or kidney failure, those with blood disorders, history of severe bleeding during menstruation (for girls).

The required minimum sample-size was calculated to be 15 subjects per study group. All students underwent weight and height measurements, BMI was then determined by calculating body weight/body height (kg/m^2). Subjects in the two groups were matched for age. Up to 3 mL of venous cubital blood was taken for haemoglobin (Hb), hematocrit (Ht) and sTfR levels. Data was analyzed with SPSS version 17.0 using Chi-square test and T-test with significance level of P <0.05. We also performed regression and correlation analysis.

Results

There were 40 participants with 20 subjects in each group. Subjects' characteristics are shown in **Table 1**.

There were no significant differences in age or gender between the two groups (P= 0.317 and P= 1, respectively). The mean weights in non-obese and obese groups were 49.70 (SD 6.28) and 78.20 (SD 13.25) kg, respectively, while the mean BMIs in the non-obese and obese groups were 20.32 (SD 1.28) and 32.74 (SD 2.64) kg/m^2, respectively (**Figure 1**), but

Table 1. Subject characteristics

Characteristics	Non-obese (n=20)	Obese (n=20)	P value
Mean age (SD), years	16.16 (0.82)	16.43 (0.89)	0.317*
Mean body weight (SD), kg	49.70 (6.28)	78.20 (13.25)	0.000*
Mean body height, (SD), m	1.56 (0.74)	1.58 (0.75)	0.452*
Mean BMI (SD), kg/m^2	20.32 (1.28)	32.74 (2.64)	0.000*
Gender, n			1.00**
Male	11	12	
Female	9	8	

* Independent T- test

** Chi-square test

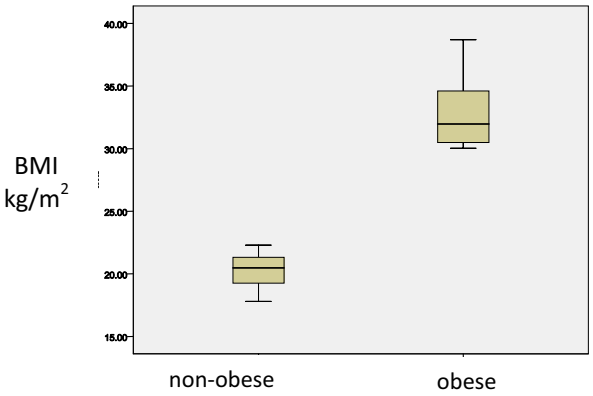

Figure 1.Boxplot of the mean BMI of the non-obese and obese groups

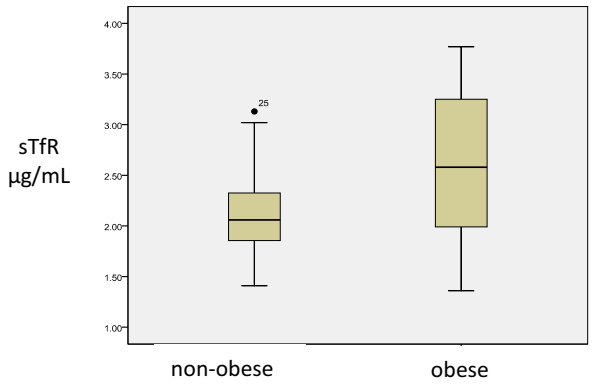

Figure 2.Boxplot of the mean sTfR levels in the non-obese and obese groups

there was no significant differences in height between the groups (P= 0.452).

Table 2 shows that mean hemoglobin and hematocrit levels in each group were within the normal limits for age. Statistical analysis revealed highger mean sTfR level in obese group compared to those in non-obese group (P=0.03).

The correlation between BMI and sTfR is shown in **Figure 3**. Body mass index had a positive, moderate correlation with sTfR level (r=0,392) as higher BMI was significantly associated with higher sTfR level. Subject's sTfR levels are shown in **Table 3**. Obese adolescents had higher risk of iron deficiency (OR=6.93; 95% CI 1.53 to 31.38) compared to non obese group.

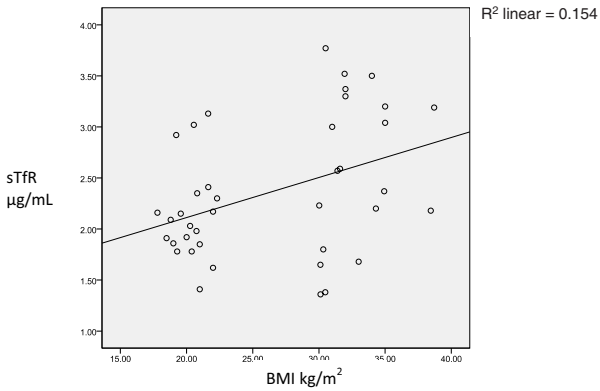

Figure 3. Soluble transferrin receptor (sTfR) correlation with BMI

Discussion

There were no differences in age or gender between the two groups of 20 obese and 20 non-obese adolescents in this study. Previous studies reported that age and gender were not significantly different between obese and non obese children.[7,17,18] In Iranian children and adolescents, gender also was not significantly

Table 2. Laboratory parameters results

Blood parameters	Non-obese group (n=20)	Obese group (n=20)	P value*
Mean hemoglobine(SD), g/dL	14.41 (1.04)	14.36 (1.41)	0.879
Mean hematocrit(SD), %	42.99 (0.61)	40.08 (3.68)	0.293
Mean sTfR (SD), µg/mL	2.14 (0.45)	2.59 (0.77)	0.030

* Independent T-test

Table 3. Distribution of sTfR levels of obese and non-obese adolescents

	sTfR ≥2,5 µg/mL	sTfR<2,5 µg/mL	Total	OR 95%CI	P value*
Obese, n	11	9	20	6.93	0.019
Non-obese, n	3	17	20	(1.53-31.38)	

*Chi-square test

related to overweight and obesity.[18] Another study of obese children and adolescents found no significant differences between genders.[19] In line with previous study,[7] we also found iron deficiency to be more common in obese than non-obese adolescents (11/20 vs. 3/20, respectively, P = 0.019; **Table 3**). Similarly, a study of 321 Israeli adolescents reported a 175 times more nutritional iron deficiency in obese, using serum iron parameter. In addition, obese children aged 11-17 years in Iran had 3 times more iron deficiency than the normal weight.[22,23] Another study also found more iron deficiency in obese than in non-obese adolescents (58.3% vs 6.7%).[17] Nead *et al*. reported that overweight children and adolescents were at higher risk of iron deficiency than normal weight ones, as >15% of overweight, female adolescents had iron deficiency, based on 2 out of 3 laboratory parameters, iron level, FEP, and ferritin.[20] We did not examine iron and ferritin leves but performed sTfR levels measurement as a parameter of iron deficiency which is more stable, not influenced by inflammatory process and requires a bit of blood sample. A study also shows that iron deficiency, determined through sTfR levels, were more common in overweight than normal weight (20% vs 6%).[19] We jound similar results in this study, more over we found that adolescents in the obese group had higher level of sTfR compared to the non-obeser (mean difference of 0.45 μg/mL.

A study reported that hemoglobin (Hb) and hematocrit (Ht) levels were significantly different in young men, which increasing in accordance with increasing age, but not in female adolescents.[7] We also examined Hb and Ht levels as other parameters for iron deficiency, and found that obese subjects had lower levels than non-obese, although the differences were not significant. We also found no anemia, based on the Hb and Ht results, suggesting that obesity may be correlated to a latent stage of iron deficiency or erythropoesis occurring at an iron deficient stage of iron erythrocytes, but iron reserves were dwindling.

Aeberli *et al* compared the iron status of overweight to normal weight children based on hepcidin, leptin, and IL-6 levels in the blood. They found that BMI was significantly associated with sTfR, the inflammatory marker hepcidin and three other parameters examined, the C-reactive protein, IL-6, and leptin levels. Multiple regression analysis revealed a correlation between serum levels of hepcidin and BMI with sTfR.[21] It is clear that the theory of low-level systemic inflammation in obesity, leading to macrophage infiltration into adipose tissue and stimulates IL-6 and CRP to increase hepcidin production so that the degradation of ferroportin will increase and there was a decrease in iron uptake in enterocytes.[22-24] Limitations of this study include not doing bone marrow puncture (BMP) as gold standard examinations, for evaluation of iron status of patients. Examination of hepcidin levels and inflammatory factors also were not done in this study because of the limited tools of investigation.

In conclusion, there is a significant different of sTfR level as iron deficiency parameter, in which sTfR level is higher in obese than non-obese adolescents.

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