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Original Article

Mentzer index as a screening tool for iron deficiency anemia in 6-12-year-old children

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Abstract

Background There is a high prevalence of iron deficiency anemia (IDA) in Indonesia. Iron deficiency anemia impairs the growth and development process in children. The reference standard to diagnose IDA is serum ferritin level. Since this test is expensive and rare not widely available, an inexpensive, simpler test is needed. The Mentzer index (mean corpuscular volume/red blood cell or MCV/RBC) has been used to identify hypochromic-microcytic anemia with good validity.

Objective To assess the validity of the Mentzer index for diagnosing IDA by comparing Mentzer indexes to serum ferritin and to define an optimal Mentzer index cut off point with good sensitivity and specificity.

Methods The study was a diagnostic test with cross-sectional design. Subjects were collected by multistage, random sampling, from April to May 2013 at 18 elementary schools in Palembang. The study had a survey phase and diagnostic test phase. Subjects were aged 6-12 years with hypochromic-microcytic anemia. We examined complete blood counts to diagnose hypochromic-microcytic anemia, calculated Mentzer indexes, and measured serum ferritin levels of our subjects. We analyzed the validity of Mentzer index compared to serum ferritin level for diagnosing IDA.

Results There were 100 children in our study, consisting of 51 boys and 49 girls with a mean age of 9.1 (SD 2.02) years. From the receiver-operator curve (ROC) curve analysis, the area under the curve (AUC) was 91.9% for a Mentzer index cutoff point of 13.51. Diagnostic test analysis revealed a sensitivity of 93%, specificity 84%, and accuracy 90%.

Conclusion Mentzer index has good validity as an inexpensive and simple screen for IDA in 6-12-year-old children with hypochromic-microcytic anemia.

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Keywords: *IDA, Mentzer index, serum ferritin*

Iron deficiency anemia (IDA) is a major public health problem in Indonesia. The high prevalence is of concern because untreated IDA may lead to impaired childhood growth and development, as well as increased susceptibility to infection.[1,2] The 2007 *Basic Health Research Report* (*Riset Kesehatan Dasar*/Riskesdas) reported that in South Sumatera, the IDA prevalence was 16.5%. Of the IDA cases, 70.1% had hypochromic-microcytic anemia. The IDA prevalence in school-aged children in Palembang was 33.7%.[1]

Iron deficiency anemia (IDA) is diagnosed by fulfilling the following criteria: hemoglobin level below normal according to age, peripheral blood smear reveals microcytic and/or hypochromic red blood cells, and hemoglobin level rises after two months of iron supplementation; in addition, one or more the following criteria must be met: red cell distribution width (RDW) > 14% and Mentzer index > 13.[2] The diagnostic tests widely used for IDA are complete blood count (CBC), serum iron (SI), total iron binding capacity (TIBC), and serum ferritin level.

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Those examinations have mainly been used in clinical practice. However, these tests are expensive and not widely available in Indonesia. Because of the high prevalence of IDA in children, especially in school-aged children, early screening is needed to detect IDA. The screening tool should be easy-to-use, affordable and sensitive enough to screen for IDA in school-aged children. Tests previously shown to be sensitive were Mentzer, erythrocyte, England-Fraser, Shine and Lal, and Srivastava indexes. Among these tests, the Mentzer index had the highest sensitivity and specificity.[3] To date, there has been no report on using the Mentzer index to screen for IDA in school-aged children in Palembang.

The aims of this study were to compare the Mentzer index to the serum ferritin level test for diagnosing IDA in children aged 6-12 years with hypochromic-microcytic anemia, and to define an optimal Mentzer index cut off point with good sensitivity and specificity in this study population.

Methods

We conducted a diagnostic study with cross-sectional design from April to May 2013 at 18 elementary schools in Palembang. All 6-12 year-old elementary students who fulfilled inclusion criteria were obtained in this study. We did a multistage randomized sampling to obtained subjects from 18 elementary schools in 10 of 16 districts in Palembang. We estimated a required sample size of 100 subjects, based on α = 0.05 and power = 95%. The subject were 100 elementary students aged 6-12 years in Palembang who were found with hypochrom-microcytic anemia in their complete blood count (CBC) examination which fulfilled inclusion criteria. The inclusion criteria was agreed to follow this study and their parent had sign up the agreement. We exluded student with blood disease history (pale or icteric history), severe anemia, chronic infection (prolonged fever), inflamation diseases, severe malnourished, and or body temperature above 37.5°C, or blood specimens were lysis.

Data collected included history, physical examination, and laboratory tests. An assistant and an author interviewed parents to obtain informed consent and the needed information. Data included age, gender, parental education level, socioeconomic status and child's history of disease. Physical examinations were performed to assess for clinical manifestations of anemia, infection, inflammation, as well as anthropometric measurements comprising of weight (kg) and height (cm). Based on CDC 2000, nutritional status was classified as well-nourished (weight for height index <85%) or undernourished (weight for height index ≥85%).[4] Blood specimens were obtained twice from subjects. The first blood specimen was used for CBC and Mentzer index (MCV/RBC). Children with hypochromic-microcytic anemia provided a second blood specimen for serum ferritin measurements performed at a reference laboratory. Serum ferritin was measured by enzyme-linked immunosorbent assay (ELISA) using a Mini Vidas kit by Biomeriuex.

Anemia was defined as having a hemoglobin level < 11.5 g/dL (for 6-12 year-olds). Hypochromic-microcytic anemia was defined as anemia with MCV < 77 fl and MCH < 25 ρg. Iron depletion was defined as serum ferritin < 30 μg/L.[5] Mentzer index was calculated from MCV divided by RBC count; IDA was considered to be the diagnosis for those with Mentzer index > 13.[3] Clinical manifestations of anemia were considered to be palmar and or conjunctival palpebrae pallor, cheilitis, stomatitis, tongue mucous atrophy.

We performed validity tests (sensitivity, specificity, positive predictive value/PPV, negative predictive value/NPV, positive likelihood ratio, negative likelihood ratio, and accuracy) to assess the diagnostic value of Mentzer index to screen for IDA in subjects with hypochromic-microcytic anemia. A receiver operator curve (ROC) was used to define the best Mentzer index cut off point for IDA diagnosis.

Statistical analyses were performed by using the statistical product and services solutions *(SPSS) version 15.0.* This study was approved by the Ethics Committee of the Sriwijaya University Medical School and Dr. Moh. Hoesin Hospital, Palembang, Indonesia.

Results

Subject recruitment process in this study consisted of two phases (**Figure 1**). In the first phase, we screened 4740 children aged 6-12 years from 18 elementary schools. Four hundred and twenty children out of them had clinical manifestation of anemia, and these children performed hemoglogin test which revealed 260 children with anemia. A complete blood count examination was performed in those anemic children and revealed 100 children with hypochrome mycrocytic anemia. All of these children were enrolled into this diagnostic study. Both, Mentzer index and serum ferritin level, were performed in all subjects.

Subjects' characteristics are shown in **Table 1**. The CBCs revealed the following: mean hemoglobin of 9.9 (SD 0.97) g/dL, red blood cell (RBC) count 4.4 (SD 1.02) $10^6/mm^3$, MCV 67.7 (SD 5.1) fl and MCH 21.3 (SD 2.52) ρg. From the 100 subjects, there were 68 (68%) with serum ferritin level <30 μg (iron depletion) and 32 (32%) with ≥30 μg (iron sufficient).

Table 1. Baseline characteristics of subjects

Characteristics	n (100)	%
Gender		
Male	59	59
Female	41	41
Age group		
6-9 years	48	48
10-12 years	52	52
Nutritional status		
Undernourished	51	51
Well-nourished	49	49

Iron status profile according to sex, age and nutritional status is shown in **Table 2**.

Of 100 subjects, there were 68 (68%) with Mentzer index ≥13 and 32 (32%) below 13. Subjects' mean Mentzer index was 16.3 (SD 3.76). The ROC revealed that the best Mentzer index value cut off point was 13.51, with sensitivity of 93%, specificity of 84%, and AUC of 91.9% [P<0.001; 95%CI 85.5 to 98.3]. Cross-tabulation between Mentzer index values and serum ferritin level are shown in **Table 3**.

Discussion

Iron deficiency anemia (IDA) is common in children, especially in school-aged children.[6] It can impair many aspects of children's growth and development, such as by reducing immunity, cognitive function, as well as the function of multiple organs.[7] We aimed to find a simple and affordable screening tool to identify IDA in an effort prevent these impairments. In clinical practice, serum ferritin level is the reference standard for IDA diagnosis.[8,9] Some sensitive previously reported screening tools are the Mentzer, erythrocyte, England-Fraser, Shine and Lal, and Srivastava indexes. Among these indexes, the Mentzer index reportedly

Table 2. Serum ferritin level according to gender, age, and nutritional status

Variables \ Serum ferritin	Mean (SD), µg/mL	Min-max, µg/mL	P value*
Gender			
Male	43.2 (35.73)	7.1-180.2	0.004
Female	42.9 (45.29)	1.7-189.6	
Age group			
6-9 years	38.8 (36.66)	7.1-180.2	0.063
10-12 years	46.9 (42.30)	1.7-189.6	
Nutritional status			
Well-nourished	45.0 (40.95)	1.7-180.2	0.720
Undernourished	41.1 (38.78)	10.7-189.6	

*T-test

Table 3. Cross-tabulation between Mentzer index and serum ferritin level

Mentzer index	Serum feritin level		Total
	< 30 µg/mL	≥30 µg/mL)	
≥13.51	63	5	68
<13.51	5	27	32
Total	68	32	100

Sensitivity 93%; specificity 84%; positive predictive value 93%; negative predictive value 84%; positive likelihood ratio 5.81; negative likelihood ratio 0.08)

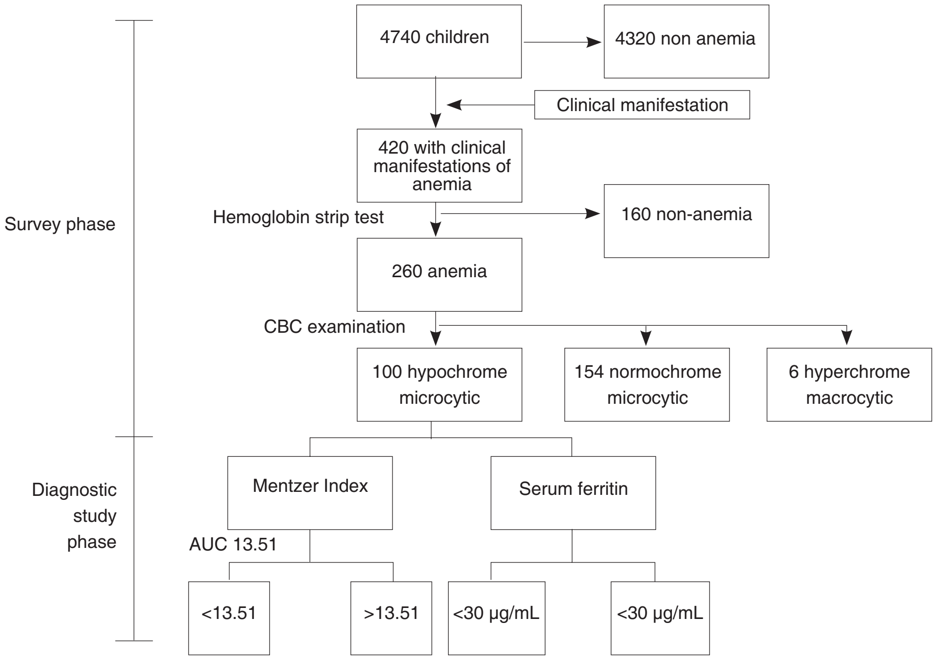

Figure 1. Subject recruitment process

had highest sensitivity and specificity.[3]

In our subjects, we found that 51 (51%) subjects were undernourished and 49 (49%) were well-nourished, indicating no significant differences between groups. Soemantri reported that in 5-14-year-old children of low socioeconomic background, the prevalence of anemia was 47-64% in well-nourished children and 38-67% in undernourished children, in several Indonesian cities.[10]

Serum ferritin level is a sensitive and reliable parameter to assess iron storage in normal individuals.[9] Normal values of serum ferritin for children aged 6 months to 15 years are 12-140 μg/L. Interpretation of serum ferritin must be looked at closely. Ferritin is an acute-phase reactant that can become elevated in settings of inflammation, chronic infection and malignancy.[11,12]

In order to prevent false negatives for IDA using serum ferritin measurements, we excluded the children who suffered from infection and inflammation based on history-taking, physical examination and performing semi-quantitative C-reactive protein (CRP) exams, although we did not show these CRP value results. C-reactive protein (CRP) rises rapidly two hours after the onset of infection, reaches its peak at 48 hours, and declines after the resolution of acute-phase reactant, with a half-life of 18 hours.[13]

In this study, we used a serum ferritin level of 30 μg/L as the reference standard for IDA. It was based on median value of serum ferritin level at age 6 months-15 years.[5]

In our study, we found 68 (68%) subjects with iron depletion (ID) and 32 (32%) subjects with iron sufficiency. Iron depletion (ID) differed in males and females, with female having lower mean serum ferritin than males. In contrast, Domellof *et al*. reported lower serum ferritin in male infants than in females.[14] Gender differences reportedly only affect ID in adolescents, as females are at higher risk due to menstruation and rapid growth. In developing countries, ID has also been attributed to chronic blood loss due to parasitic infections.[11] A limitation of our study was that we did not perform stool examinations to detect parasitic infection.

Serum ferritin level reportedly differ according to age.[15] However, we found no differences in mean serum ferritin level according to age groups, similar to that of Glader's study who found no differences in median serum ferritin in children aged 6 months-15 years.[5]

We constructed a ROC in order to choose the best Mentzer index cut-off point, which was ≥13.51. The sensitivity and specificity of this cut off were 93% and 84%, respectively, with AUC of 91.9%, indicating that the Mentzer index was valid for use as a screening tool for IDA. A good screening tool is defined as having sensitivity ≥80%, despite the presence of low specificity.[16,17]

In conclusion, Mentzer index is valid to use as a screen for iron deficiency anemia in 6-12-year-old children with hypochromic-microcytic anemia using a Mentzer index value of ≥13.51 to screen iron deficiency anemia.

Based on this study, we recommend using the Mentzer index to screen for IDA in children aged 6-12 years with hypochromic-microcytic anemia in community-based clinics. For more accurate diagnosis of IDA in hospitals, other tests should still used for iron status examination and iron supplementation response. Lastly, to confirm the screening benefit of the Mentzer index, further studies with a larger and more diverse subjects should be undertaken.

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