Screening of Iron Deficiency Anemia in Children Using Mentzer Index in Pakistan: A Cross Sectional Study

Global Pediatric Health
Volume 10: 1–5

DOI: 10.1177/2333794X221130986
journals.sagepub.com/home/gph
SAGE

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Abstract

The objective of the study was to determine the diagnostic accuracy of Mentzer Index in children with hypochromic microcytic anemia by taking serum ferritin levels as a gold standard. This cross-sectional study was conducted in the Department of Pediatric Medicine, Liaquat National Hospital Karachi, from 1st January to 30th June 2022. Children age 1 to 5 years and both genders were included in this study. Children who have had a history of blood transfusion in the past 3 months or Thalassemia or blood disorders, chronic liver disease or kidney diseases, and children with malignancy and congenital abnormalities were excluded. Eligible children were enrolled after taking written informed consent. Complete blood count (CBC) and serum ferritin were sent to the laboratory. Sensitivity, specificity, diagnostic accuracy, and likelihood ratio were calculated taking serum ferritin levels as a gold standard. A total of 347 subjects were enrolled. The median age was 26 (IQR-18) months and 42.9% were males. The most common symptom was fatigue 40.9%. The sensitivity of the Mentzer index was 80.7% while the specificity was 77.7%. Similarly, the positive predictive value (PPV) was 56.8% while the negative predictive value (NPV) was 91.6%. Finally, the accuracy of the Mentzer index in determining iron deficiency anemia was 78.4%. Diagnostic accuracy was 78.4% and the likelihood ratio was 3.6. Mentzer index is a valuable tool in the early detection of IDA in children. It has got high sensitivity, specificity diagnostic accuracy, and likelihood ratio.

Keywords

anemia, iron-deficiency, ferritin, sensitivity, specificity, accuracy, likelihood ratio

Received August 20, 2022. Accepted for publication September 19, 2022.

Introduction

World health Organization (WHO) defines anemia as a hemoglobin level of <11 g/dl. Most common cause of anemia in children is nutritional anemia. WHO estimates that 42% of under 5 children worldwide anemic and half of them are attributable to iron deficiency.[1] Prevalence of nutritional anemia in children is high in low- and middle-income countries. About 51% of the young children are affected due to nutritional anemia,[2] which is more prevalent in South Asia and Africa.[3] In Pakistan, nutritional anemia has been recognized to be the most common type of anemia in under nourished children.[4] According to National Nutritional Survey of Pakistan, the prevalence of nutritional anemia increased from 38% to 53.7% from 1977 to 2018 respectively.[3,4]

Iron deficiency anemia (IDA) in children is a major cause of nutritional anemia is one of the major public health issues in Pakistan.[5] The reported prevalence of IDS in, under-five children of Pakistan is 40% to 70%.[6] However, according to National Nutritional Survey 2018, the prevalence of IDA in children is 28.6%.[6] The proportion of IDA in urban boys was 29.1% and 28.9% in rural areas.[7]

IDA is the third leading cause of disability around the world and 13th leading risk factor for globally disability adjusted life years.[8] IDA in under-five children in associated with poor growth, mental and intellectual impairment due to impaired brain development. It is also

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claimed to be associated with high infant mortality in Pakistan.[1,9,10]

For the diagnosis of IDA; complete blood count, serum iron, total iron binding capacity and serum ferritin levels are routinely performed. In low resource settings, IDA can be measured by low hemoglobin levels, microcytic and hypochromic red cells on peripheral smear and increase in hemoglobin levels after 2 months of iron therapy.[11] However, these tests are very expensive and not readily available in every laboratory. Other tests suggest IDA is red cell distribution width of >14% and Mentzer index >13%.[12] Mentzer index (MI) is a simplified diagnostic tool to screen children with possible IDA. MI is the ratio between mean corpuscular volume and red cell count (red blood cells in million per micro liter). MI of >13 is highly suggestive of IDA.[13]

Previously, tests such as England-Fraser, Shine and Lal, Shrivastava index, Youden index[14] are shown to be sensitive screening tools to detect IDA in children. However, MI has high sensitivity and specificity. The reported sensitivity of MI in suggesting IDA ranges from 85% to 90% and specificity ranges from 80% to 93%.[15,16]

In Pakistan the diagnostic accuracy of MI as a screening tool for detecting IDA is not reported. The objective of the study was to determine the diagnostic accuracy of MI in children with hypochromic microcytic anemia by taking serum ferritin levels as a gold standard.

Material and Methods

Study Setting and Design

A cross-sectional study was conducted in the Department of Pediatric Medicine, Liaquat National Hospital Karachi from 1st January to 30th June 2022. Liaquat National Hospital is one of the largest private sector hospitals that provide all health facilities, diagnostics, and tertiary level management of all health-related issues. Department of Pediatrics had consisted of 7 bedded pediatric intensive care unit, 13 bedded neonatal intensive care unit, 10 bedded high-dependency units and 25 bedded general ward.

Study Population

Children age 1 to 5 years and both genders presented either out-patients department OPD or admitted patients with complaints of pallor, easy fatigability, and breathlessness were included in this study. Children who have had a history of blood transfusion in the past 3 months or chronic illness associated with anemia such as Thalassemia, blood disorders, chronic liver disease or kidney disease, and children with syndrome/congenital anomalies or present with an inborn error of metabolism were excluded.

Data Collection

Eligible children were enrolled after informed consent from parents or caretakers. Patients were assigned a unique identification number. A trained resident collected demographic and clinical data and examine the child. Data were recorded in a structured questionnaire. A 5 ml blood was collected by trained phlebotomists in the EDTA bottle for complete blood count, using automated hematology analyzer SAPHARE® by Abbot, and 5 ml blood in yellow top vacutainer for serum ferritin level, using the immunoturbidimetric technique on 3501COBAS by Roche. Mentzer index was calculated by dividing mean corpuscular volume (MCV) femtoliter (Fl) by red blood cell (RBC) count (Millions per micro Liter). IDA was considered if MI is >13.

Statistical Analysis

A sample size of 347 was needed by taking confidence level 95% with desired precision (d) of 0.07, expected sensitivity (82.3%), and specificity (98.7%) with an approximate population estimation of 33.2%.[17,18] All questionnaires were checked for errors, inconsistencies, and missing values by a data editor. Data were entered and analyzed SPSS version 20 for windows. Mean and standard deviation was calculated for quantitative variables like age, weight, height, duration of illness, and frequencies, and percentages were computed for qualitative variables like gender. Age was categorized children into 3 categories: (1) toddlers (12-24 months), (2) preschoolers (25-48 months), and (3) school-going children (>48-60 months). MI is categorize to ≤13 and >13 and serum ferritin to <12 ng/ml ≥12 ng/ml. The sensitivity, specificity, positive predictive values (PPV), negative predictive values (NPV), accuracy, and positive likelihood ratio (LR) of the MI was calculated taking serum ferritin as the gold standard. Effect modifiers were controlled through stratification of age groups, gender, and socioeconomic condition to see the effect of these on sensitivity, specificity, PPV, NPV, accuracy, and LR. Point estimates and 95% Confidence interval (CI) was calculated sensitivity, specificity, PPV, NPV, accuracy, and LR.

Ethical Consideration

This study was approved by the Ethical Review Committee of Liaquat National University, Karachi. Written informed consent was taken from all enrolled participants.

Table 1. Characteristics of Study Participants.

Characteristics	Frequency(n-347)
Age *median (IQR)*	26 (18)
Weight *median (IQR)*	12 (3)
Height *median (IQR)*	84 (13)
Age groups (%)	
Pre-school	172 (49.6)
Toddler	140 (40.3)
School going	35 (10.1)
Gender (%)	
Female	198 (57.1)
Male	149 (42.9)
Clinical features (%)	
Fatigue	142 (40.9)
Headache	93 (26.8)
History of PICA	87 (25.1)
Irritability	96 (27.7)
Socioeconomic status (%)	
Low	143 (41.2)
Middle	122 (35.2)
High	82 (23.6)
Ferritin level (%)	
<12 ng/ml	254 (73.2)
≥ 12 ng/ml	93 (26.8)
Mentzer index (%)	
≤ 13	215 (62.0)
>13	132 (38.0)

Results

Of 347 subjects enrolled in the study, the median age of children was 26 (IQR-18) months, 149 (43%) were males. Median weight and height were found to be 12 (IQR 3) kg and 84 (IQR-13) cm respectively. A total of 172 (49.6%) were preschoolers, and 10% were school-going children. The most important symptom was fatigue 142 (41%), followed by irritability and headache. Only 13 (3.7%) children were wasted and none were stunted. Most of the participants belonged to low socioeconomic strata (SES) 143 (41%), 254 (73.2%) has serum ferritin level <12 ng/ml (low iron stores) and 132 (38%) has MI >13 (suggestive of IDA) (Table 1).

Table 2 showed the characteristics of the study participants by serum ferritin level <20 ng/ml and MI >13. The proportion of MI >13 in preschool children was 8 (6.1%) while serum ferritin level <12 ng/ml in preschool children was 10 (10.8%) cases. The proportion of MI >13 in females was 74 (56.1%) while serum ferritin level <12 ng/ml in females was 59 (63%) cases. The proportion of MI >13 in preschool children was 8 (6.1%) while serum ferritin level <12 ng/ml in preschool children was 10 (10.8%) cases. The proportion of MI >13 in children with a history of PICA was 32 (24.2%) while serum ferritin level <12 ng/ml in children with a history of PICA was 17 (18.3%) cases.

The sensitivity of MI was 80.7% (95% CI 71.2%-88.1%) while the specificity was 77.7% (95% CI 71.9%-82.5%), PPV was 56.8% (95% CI 50.6%-62.8%), NPV was 91.6% (95% CI 87.8%-94.3%), accuracy 78.4% (95% CI 73.7%-82.6%), positive LR 3.6 (95% CI 2.8-4.6%) Table 3.

Stratified analysis did not show differences in sensitivity, specificity, PPV, NPV, accuracy, and LR across age groups except school-going children where the sensitivity of the MI in diagnosing IDA was 50% (95% CI 18.7%−81.3%). However, specificity was 88% (95% CI 68.8%−81.3%). No difference found when stratified by sex and socioeconomic strata (Table 3).

Discussion

This study aims to find a simplified screening tool to detect IDA. It was found that the sensitivity of MI is 80.64% while the specificity is 77.5%; Positive predictive value is 56.8%, negative predictive value (NPV) is 91.6%; accuracy is 78.4% and positive LR is 3.6%.

Serum ferritin level was a reference to diagnose IDA. However, serum ferritin is not cost effective to diagnose IDA in children. Therefore, MI is a screening tool with high with a NPV and a positive LR of 3.6; it means MI >13 is 3.6 times more likely to detect IDA as compared to serum ferritin levels.

In this study, the proportion of anemia is most in preschool children. However, other studies showed that anemia is most common in school going children.[4] This could be attributable to the nutritional status of pregnant women, faster growth, top feeding, usually cow milk which is low in iron, feeding with bottle, and early weaning. Fatigue is the most common is the most complaint that was recorded in this study secondary to the decreasing oxygen-carrying capacity of red blood cells which need iron for enough to produce hemoglobin.

Conflicting results have been shown on the influence of anemia on gender. In this study and other studies, there is no association between sex and anemia.[19,20] However, some authors reported a high proportion of anemia in boys.[21,22] Females are most affected compared to males in this study accounting for 57.1% of cases. In a Brazilian study similar results reported according to Brazilian study 54.3% girls had anemia. In this study iron deficiency is most common in low socio-economic group. This is due to poverty, a diet deficient in iron and other micronutrients.

Both IDA and beta Thalassemia trait presented with microcytic and hypochromic anemia. However, the MI

Table 2. Characteristics of Participants with Serum Ferritin <12 ng/ml and Mentzer Index >13.

	Mentzer index(n-132) (%)	Serum ferritin(n-93) (%)
Age groups		
Pre-school	65 (49.2)	39 (41.9)
Toddler	59 (44.7)	44 (47.3)
School going	8 (6.1)	10 (10.8)
Gender		
Female	74 (56.1)	59 (63)
Male	58 (43.9)	34 (36.6)
Clinical features		
Fatigue	60 (45.5)	43 (46.2)
Headache	34 (25.8)	20 (21.5)
PICA	32 (24.2)	17 (18.3)
Irritability	39 (29.5)	28 (30.1)
Socioeconomic status		
Low SES	61 (46.2)	43 (46.2)
Middle SES	36 (27.3)	28 (30.1)
High SES	35 (26.5)	22 (23.7)
Wasting	7 (5.3)	7 (7.5)

Table 3. Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value, Accuracy and Likelihood Ration of Mentzer Index in Diagnosing Iron Deficiency Anemia Keeping Serum Ferritin as Gold Standard.

	Sensitivity	Septicity	PPV	NPV	Accuracy	Likelihood ratio
Overall	80.7 (71.2-88.1)	77.7 (71.9-82.5)	56.8 (50.6-62.8)	91.6 (87.8-94.3)	78.4 (73.7-82.6)	3.6 (2.8-4.6)
Female	76.3 (63.4-86.4)	79.1 (71.4-85.6)	60.81 (52.1-68.8)	88.7 (83.2-92.6)	78.2 (71.9-83.8)	3.6 (2.6-5.2)
Male	88.2 (72.6-96.7)	75.7 (66.8-83.2)	51.7 (43.2-60.2)	95.6 (89.6-98.2)	78.5 (71.1-84.8)	3.5 (2.5-5.0)
School going	50 (18.7-81.3)	88 (68.8-81.3)	62.5 (32.8-85.1)	81.5 (70.0-89.3)	77.1 (59.9-89.6)	4.2 (1.2-14.2)
Toddler	84.1 (70.0-93.4)	77.1 (67.4-85.1)	62.7 (53.3-71.3)	91.4 (84.2-95.6)	79.3 (71.6-85.7)	3.7 (2.5-5.4)
Pre-school	84.6 (69.5-94.1)	75.9 (678-82.9)	50.8 (42.6-58.9)	94.4 (88.9-97.3)	77.9 (70.9-83.9)	3.5 (2.5-4.9)
High SES	91.0 (70.8-98.9)	75.0 (62.1-85.3)	57.1 (45.8-67.8)	95.7 (85.6-98.8)	79.3 (68.9-87.4)	3.6 (2.3-5.8)
Middle SES	71.4 (51.3-86.8)	83.0 (73.8-90.0)	55.6 (43.0-67.4)	90.7 (84.4-94.6)	80.3 (72.2-87.0)	4.2 (2.5-6.9)
Low SES	81.4 (66.6-91.6)	74.0 (64.3-82.3)	57.4 (48.4-65.9)	90.2 (83.0-94.6)	76.2 (68.4-82.9)	3.1 (2.2-4.5)

Abbreviations: NPV, negative predictive value; PPV, positive predictive value.

can be used to differentiate between IDA and beta thalassemia trait. MI < 13 is suggestive of beta thalassemia trait.

This study has some strength; to the best of my knowledge, this is the first study from Pakistan who studied the accuracy of MI as the diagnostic tool to screen IDA. This study not only reported sensitivity and specificity but also the accuracy as well as positive LR. LR not only uses to assess the efficacy of MI as well as how likely patients have the disease.

This study has some limitations; serum ferritin is also an acute phase reactant so its interpretation must be cautiously interpreted. So, to prevent false negatives, serum ferritin was collected in children without fever or suspected infection. Also, children with chronic inflammatory diseases and malignancies were excluded. The MI was not compared with other indices such as English-Fraser, Shina and Lal and Srivastava indices. However, studies have found among these indices, the Mentzer is the most sensitive and specific for the detection of IDA. The helminthic infestation was not studied in this study, which is one of the most common cause of chronic blood loss hence can contribute in IDA.

Author Contributors

AS, AA conceptualize and implement the study. AS wrote the first draft. AS, AA SST did data analysis and interpretation. SS is the study coordinator. All authors read and approved the manuscript.

Data Availability Statement

Data are available on reasonable request.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The cost of the study bared by AS and AA. The study was not funded.

Ethical Approval

This study was approved by the Liaquat National Medical University, Karachi, Pakistan (Ref:App.# RC – LNH-Pds M – 12/2022/08).

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