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Research Article

Diagnostic Accuracy of Mentzer Index in Diagnosis of Iron Deficiency Anemia Keeping Serum Ferritin Levels as Gold Standard

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ABSTRACT

Background: The diagnostic tests widely used for iron deficiency anemia are complete blood count, serum iron, total iron binding capacity and serum ferritin level. These examinations have mainly been used in clinical practice. One of the laboratory examination parameters that can be used for thalassemia carrier screening test is Mentzer index. Mentzer index is an MCV/RBC ratio calculation.

Methods: This cross-sectional study was conducted during 26th July 2021 to 25th January 2022 in the Pediatrics department, Jinnah Hospital, Lahore. A total of 160 children age 6 – 59 months, of either gender presenting to opd for routine checkup were included. Children with history of blood diseases, chronic infection, inflammatiory diseases and malnourished were excluded. Blood specimens were obtained twice form subjects. The first specimen was used for CBC and Mentzer index. Children with hypochromic microcytic anemia was provided a second blood specimen for serum ferritin measurements. Serum ferritin was measured by ELISA using a Mini Vidas kit. IDA was considered to be diagnosed by Mentzer index, serum ferritin.

Results: Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of Mentzer index in diagnosis of iron deficiency anemia keeping serum ferritin levels as gold standard was 78.26%, 86.81%, 81.82%, 84.04% and 83.13% respectively.

Conclusion: This study has shown that diagnostic accuracy of Mentzer index in diagnosis of iron deficiency anemia is quite high.

Keywords: Iron Deficiency Anemia, Mentzer Index, Sensitivity.

INTRODUCTION

Pediatric anemia refers to a hemoglobin or hematocrit level lower than the age-adjusted reference range for healthy children. Physiologically, anemia is a condition in which reduced hematocrit or hemoglobin levels lead to diminished oxygen-carrying capacity that does not optimally meet the metabolic demands of the body. Anemia is not a specific disease entity but is a condition caused by various underlying pathologic processes. It may be acute or chronic. [1]Causes of anemia are either inherent in the RBCs or related to an external factor. The underlying pathologic processes that cause anemia can be broadly categorized as (1) decreased or ineffective red cell production, (2) increased red cell destruction (hemolysis), and (3) blood loss, although more than 1 mechanism may be involved in some anemias.

Iron deficiency anaemia (IDA) is one of the common micronutrient deficiencies all over the world especially young children are at risk because of their rapid growth, they have high iron requirements.[1-2] Various risk factors are considered for high prevalence of IDA that include, prematurity, low birth weight, low intake of iron-rich complementary foods, high cow's-milk intake, immigrant status and low socioeconomic status.[1] A local study reported

prevalence of IDA among 6 – 59 months old children as 33.2%.[3]

Iron is very essential element for almost all living organisms as it participates in a wide variety of metabolic procedures, haemoglobin measurement, DNA synthesis, and electron transport.[4] However, as iron can form free radicals, its concentration in body tissues must be tightly regulated because in excessive amounts, it can lead to tissue damage.[5] Such disorders of iron metabolism are among the most common diseases of humans and include a broad range of diseases with diverse clinical appearances, ranging from anaemia to iron overload, and possibly to neurodegenerative illnesses.[5]

The diagnostic tests widely used for iron deficiency anemia are complete blood count, serum iron, total iron binding capacity and serum ferritin level. These examinations have mainly been used in clinical practice. Because of the high prevalence of IDA in children, especially in school-aged children, early screening is needed. The screening tool should be easy to use, affordable and sensitive enough to screen for IDA in children. One of the laboratory examination parameters that can be used for thalassemia carrier screening test is Mentzer index. Mentzer index is an MCV/RBC ratio calculation.[6-7]

In a study, sensitivity and specificity of Mentzer index as a diagnostic modality in evaluation of iron deficiency anemia were 93% and 84% respectively.[8] In another study, sensitivity and specificity of Mentzer index as a diagnostic modality in evaluation of iron deficiency anemia were 36% and 81% respectively.[9] The demand of the patient and clinician to provides a rapid and accurate diagnosis with a minimum of investigation, invasive procedure and by economic constraints of patient admission. This led us to study to determine the diagnostic accuracy of Mentzer index in diagnosis of iron deficiency anemia.

By the result of this study, we will be able to confirm the accuracy of Mentzer index in the evaluation of IDA and also to outline a better management plan. Furthermore, no local study is available and there is conflict among existing international literature.

METHODOLOGY

This cross-sectional study was conducted during the period of 26th July 2021 to 25th January 2022 in the Pediatrics department, Jinnah Hospital, Lahore. Ethical permission was taken from head of the department. After proper written informed consent children age 6 – 59 months, of either gender presenting to opd for routine checkup were included. Sample size of 160 cases was calculated by 95% confidence level with expected percentage of IDA as 33.2%[3] with sensitivity as 36% with 8% margin of error and specificity as 84% with 13% margin of error. Non-probability, consecutive sampling technique was applied. Children with history of blood diseases, chronic infection, inflammatiory diseases, body temperature above 37.50^{C} and malnourished children were excluded. Physical examination was performed to assess for clinical manifestations of anemia, infection and inflammation. Blood specimens were obtained twice form subjects. The first specimen was used for CBC and Mentzer index. Children with hypochromic microcytic anemia was provided a second blood specimen for serum ferritin measurements. Serum ferritin was measured by enzyme-linked immunosorbent assay (ELISA) using a Mini Vidas kit. IDA was considered to be diagnosed by Mentzer index, serum ferritin, and bone marrow iron staining as per operational definitions. All the data was collected through a pre-designed proforma.

Data was analyzed by SPSS v25.0. Quantitative variables like age were presented as Mean±S.D. Qualitative variables like IDA on histopathology, serum ferritin and Mentzer index were presented as frequency and percentages. A 2x2 contingency was generated to calculate sensitivity, specificity, PPV, NPV and accuracy. Data was stratified for age, socio-economic status and gender to address the modifier effect. Post stratification, 2x2 table was computed to calculate sensitivity, specificity, PPV, NPV and accuracy. A p-value of ≤ 0.05 was taken as significant.

RESULTS

Age range in this study was from 6 months-5 years with mean age of 2.18 ± 0.89 years. Majority of the patients 114 (71.25%) were between 6 months to 2 years of age as shown in Table I. Distribution of patients according to gender & socioeconomic status is also shown in Table I.

In 66 Mentzer index positive patients, 54 (True Positive) had iron deficiency anemia and 12 (False Positive) had no iron deficiency anemia on serum ferritin levels. Among, 94 Mentzer index negative patients, 15 (False Negative) had iron deficiency anemia on serum ferritin

levels whereas 79 (True Negative) had no iron deficiency anemia on serum ferritin levels as shown in Table II. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of Mentzer index in diagnosis of iron deficiency anemia keeping serum ferritin levels as gold standard was 78.26%, 86.81%, 81.82%, 84.04% and 83.13% respectively.

Table-I: Showing Distribution of Patients According tto Age, Gender & Socio-Economic Status

Age (years)	**No. of Patients**	**%age**
6 months-2 years	114	71.25
3-5 years	46	28.75
Total	160	100.0
Gender		
Male	79	49.38
Female	81	50.62
Socio-economic status (Monthly income)		
<20000	58	36.25
20001-50000	75	46.88
>50000	27	16.87

Table-II: Diagnostic Accuracy Of Mentzer Index In Diagnosis Of Iron Deficiency Anemia Keeping Serum Ferritin Levels As Gold Standard.

	Positive result on serum ferritin levels	**Negative result on serum ferritin levels**	**P-value**
Positive result on Mentzer index	54 (TP)*	12 (FP)***	0.0001
Negative result on Mentzer index	15 (FN)**	79 (TN)****	

*-TP=True positive **-FP=False positive ***-FN=False negative ****-TN=True negative

Sensitivity: 78.26%
Specificity: 86.81%
Positive Predictive Value (PPV): 81.82%
Negative Predictive Value (NPV): 84.04%
Diagnostic Accuracy: 83.13%

DISCUSSION:

In IDA, the bone marrow cannot produce enough RBCs and also they are smaller (microcytic) in size, the result of which is low RBC count and low MCV, the Mentzer index will be more than 13. In thalassemia, the number of RBC's produced is normal as the defect is in synthesis of globin chain, the RBCs are smaller in size and with increased fragility. The RBC count is normal, but with low MCV, the Mentzer index will be lower than 13.[10]

I have conducted this study to find the diagnostic accuracy of Mentzer index in diagnosis of iron deficiency anemia keeping serum ferritin levels as gold standard. In my study, sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of Mentzer index in diagnosis of iron deficiency anemia keeping serum ferritin levels as gold standard was 78.26%, 86.81%, 81.82%, 84.04% and 83.13% respectively. In a study, sensitivity and specificity of Mentzer index as a diagnostic modality in evaluation of iron deficiency anemia were 93% and 84% respectively.[8] In another study, sensitivity and specificity of Mentzer index as a diagnostic modality in evaluation of iron deficiency anemia were 36% and 81% respectively.[9]

Mentzer WC et al from Turkey assessed 290 children aged 1 - 16 years and used the red blood cell count, RDW and Mentzer index (mean corpuscular volume/red blood cell count ratio) to differentiate β thalassemia trait from iron deficiency anemia. These results indicated that the Mentzer index was the most reliable indicator, with a sensitivity of 98.7% and specificity of 82.3%.[11] In 2009, Ehsani et al showed that the best discrimination index according to Youden's criteria was the Mentzer index (90.1%), followed by the Ehsani et al

index (85.5%). In their study, the Mentzer and Ehsani et al were able to correctly diagnose 94.7% and 92.9% of cases, respectively.[12] Similar results (Mentzer index: sensitivity, 90.9%; specificity, 80.3%) were found by Ghafouri et al.[13] Batebi et al[14] reported sensitivity and specificity of the Mentzer index as 86.3% and 85.4% respectively. Some have reported a lower sensitivity of 67% in Mentzer's index while other studies have shown higher sensitivity with this index (82-95%).[15-16]

Various indices have been used in an attempt to differentiate between iron deficiency anemia (IDA) and beta thalassemia by using simple blood counts parameters but none has so far been found to be 100% sensitive and 100% specific. It is found that Mentzer Index has got maximum sensitivity and specificity among all relevant indices.[17] This was also verified by Munir AH et al in their study.[18] Those with Mentzer Index > 13 are most probably having IDA with a sensitivity of 91% and having non probability of beta thalassemia with a specificity of 91%. Contrarily, patients with microcytic hypochromic anemia, whose Mentzer Index is < 13 are more probably having βTT with a sensitivity of 83% and having non-probability of IDA with a specificity of 83%. Thus, Mentzer Index is more reliable in diagnosing IDA and excluding βTT. This was also concluded in a study conducted by Bose S et al. in India.[19] Similar results were reached by D Lawrie in his study conducted in South Africa.[20]

Vehapoglu et al[21] also found that Mentzer index had the high sensitivity 98.7%, specificity 82.3% for correctly distinguishing BTT and IDA. When the Mentzer index was calculated, 91% of children with microcytic anemia were correctly diagnosed. Rahim and Keikhaei,[22] also found that, Mentzer index had 85% sensitivity and 93% specificity. Similar results of Mentzer index sensitivity 90.9% and specificity 80.3% were found by Ghafouri et al.[23] In contrast Demir et al[24] found that, sensitivity of Mentzer index (62% and 86%) and it is specificity (86% and 62%) for BTT and IDA respectively, and according to their results Mentzer index cannot be considered as one of the reliable indices and RDW index followed by RBCs count are better than it. Also, Sirdah et al[25] found that the most reliable indices for differentiation between BTT and IDA are Green and King index followed by RDW index. According to Ntaios et al[26] Green and King shows the highest reliability, followed by England and Fraser, RBC count, Mentzer index, and RDW index.

In another study conducted by W Siswandari found that Mentzer index Odd Ratio value was 2.4 (0.5 - 11.5, CI95%). Mentzer Index sensitivity (Sn) was 0.36 with specificity (Sp) at 0.81, positive predictive value (PPV) at 0.44 and negative predictive value (NPV) at 0.75. Mentzer index could be used to predict the diagnosis of beta-thalassemia carrier.[27] Mentzer index can be calculated using MCV and RBC count and can be used to differentiate between beta thalassemia trait and iron deficiency anemia. Many studies have found it to be one of the most reliable indices to differentiate between these 2 conditions. Differentiating these conditions is important because of the obvious implications such a differentiation may have on the management of the patients.

CONCLUSION

This study has shown that diagnostic accuracy of Mentzer index in diagnosis of iron deficiency anemia is quite high. So, we recommend that public awareness programs should be arranged to enhance our public for timely and appropriate treatment of iron deficiency anemia among children under 5 years age in order to reduce the complications of anemia.

List of Abbreviations:

Iron deficiency anemia (IDA), enzyme-linked immunosorbent assay (ELISA), Red blood cells (RBCs), mean corpuscular volume (MCV), red cell distribution width (RDW).

Conflict of Interest

The authors declare that they have no competing interests.

Authors' Contributions: US: Conceptualization, methodology, supervision; JA: Data curation, formal analysis; FT: Investigation, writing—original draft; IS: Visualization, project administration; AH: Writing—review and editing.

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Ethical Considerations:

The study was conducted in accordance with the Declaration of Helsinki. Ethical permission was taken from head of the department. All protocols were carried by with college guidelines and regulations.

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