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VALIDATION OF MENTZER INDEX AS A SCREENING TOOL FOR IRON DEFICIENCY ANEMIA

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Abstract

OBJECTIVE

To determine the diagnostic accuracy of the Mentzer index for diagnosis of iron deficiency anaemia by taking ferritin level as the gold standard.

MATERIAL & METHODS

This investigation was conducted within the Pediatric Department of Lyari General Hospital, Karachi, employing a cross-sectional study design alongside a non-probability consecutive sampling methodology. The subjects of this study comprised pediatric patients aged between 6 months and 12 years who were diagnosed with anemia (Hb ≤ 11 g/dL, Hct ≤ 32%); individuals with a history of blood transfusion, infectious diseases, malignancies, or renal dysfunction were not included in the study. The diagnostic criteria were established utilizing the Mentzer index (≥13) and serum ferritin levels (< 12 ng/mL). Statistical evaluation was executed using SPSS version 26, while adhering to a 95% confidence interval.

RESULTS

The study participants were pediatric patients from 6 months to 12 years (mean age 8.90 ± 2.71 years, 55.1% female; 44.9% male). The mean concentration of hemoglobin was found to be 8.97 g/dL with 64.1% of the patients ranging in the level of hemoglobin from 7-9 g/dL. A Mentzer Index exceeding 13 was identified as a reliable indicator, accurately detecting 90.2% of instances of iron deficiency anemia (IDA), while a Mentzer Index of 13 or lower correlated with 89.3% of subjects exhibiting normal ferritin levels. The Mentzer Index revealed a sensitivity of 90.24%, a specificity of 89.33%, and an overall diagnostic accuracy of 89.90%, thus corroborating its utility in the detection of IDA when serum ferritin is utilized as the definitive reference standard.

CONCLUSION

Our research substantiates the efficacy of the Mentzer Index as a reliable, cost-effective, and non-invasive instrument for the screening of Iron Deficiency Anemia (IDA), particularly in environments where serum ferritin assessments are not readily accessible. With elevated sensitivity, specificity, and predictive values, this methodology serves as an essential resource for the early identification and

distinction of IDA from alternative types of anemia. Nonetheless, subsequent multicenter investigations with expanded sample populations and heterogeneous demographics are imperative to refine the established cutoff values and to further corroborate its diagnostic precision across various contexts.

INTRODUCTION

Iron deficiency anemia (IDA) is the most common hematological disorder in pediatric population with reported incidence rate of 39% and 48.1% in children aged between 0 to 4 years and 5 to 14 years respectively, in developing countries [1]. While iron deficiency is the most common cause of anemia in developing countries, other causes include parasitic infections, nutritional deficiencies, chronic disease and hemoglobinopathies [2-3]. IDA is a nutritional disorder characterized by progressive depletion of body iron stores because of reduced iron intake and absorption [3-4]. IDA is associated with adverse outcomes including increased risk of infant or early childhood mortality as well as delayed mental and physical development and reduced visual and auditory function [5]. Iron Deficiency Anemia (IDA) is a common hematological disease, especially in infants and children. IDA is the most prevalent nutritional deficiency globally, affecting 30% of the population. The prevalence of IDA increases with age, particularly in developing countries like Pakistan. In Pakistan, the prevalence of IDA was reported at 28.6% in a 2018 survey [6].

Different hematological indices are used in IDA workups and include hemoglobin, hematocrit, which means corpuscular volume (MCV), transferrin saturation and soluble transferrin receptor [7-8]. Serum ferritin levels represent iron stores in the body and are used as gold standard for diagnosis of IDA, except in cases of active untreated infection and inflammation [9]. Serum ferritin assays are, however, slightly expensive which limits its utility as screening tool for IDA diagnosis. Mentzer Index is a simple mathematical tool based on hematological indices which was first introduced by William C. Mentzer in 1973 and has been used as a diagnostic tool to differentiate between IDA and thalassemia in different studies [10].

Anemia is defined as a hemoglobin level of <11 g/dl. Nutritional anemia is the most common cause of anemia in children [11]. WHO estimates 42% of under-five children worldwide are anemic Nutritional anemia prevalence is high in low-and middle-income countries [12]. In Pakistan, nutritional anemia prevalence increased from 38% to 53.7% from 1977 to 2018 [13]

Manshah et al, studied the diagnostic accuracy of Mentzer Index in diagnosis of IDA in their cross-sectional study. The prevalence of IDA in their study was reported to be 63.3%. They reported that Mentzer Index had 88% sensitivity, 85% specificity and 87% diagnostic accuracy in diagnosing iron deficiency anemia [14]. Sherali et al, also studied the diagnostic accuracy of Mentzer Index in diagnosis of IDA in their cross-sectional study. The prevalence of IDA, diagnosed on basis of serum ferritin levels of < 12 ng/mL, was 73.2%. They reported that Mentzer Index had 80.7% sensitivity, 77.7% specificity, 56.8% positive predictive value, 91.6% negative predictive value and 78.4% diagnostic accuracy in diagnosing iron deficiency anemia [15]. Awais et al, also studied the diagnostic accuracy of Mentzer Index in diagnosis of IDA in their cross-sectional study. Mean age of participants was 7.28 ± 1.07 years. They reported that Mentzer Index had 67.3% sensitivity, 93.8% specificity, 80% positive predictive value, 88.6% negative predictive value and 86.63% diagnostic accuracy in diagnosing iron deficiency anemia with area under the curve value of 0.805 [16].

It is evident from initial studies that Mentzer Index can act as an accurate, inexpensive and non-invasive tool to diagnose IDA, especially in resource limited healthcare facilities where serum ferritin analysis is not available or is deemed expensive (8-10). No study has been performed in our hospital on accuracy of Mentzer Index in IDA diagnosis and the rationale of our study will be to bridge the gap of scarcity of local literature as well as providing pediatricians with an inexpensive and readily available tool to screen for or diagnose IDA.

METHODOLOGY

This scholarly investigation was executed within the Pediatric Department of Lyari General Hospital,

Karachi, utilizing a cross-sectional design distinguished by a non-probability consecutive sampling approach. The study cohort consisted of pediatric subjects aged from 6 months to 12 years, regardless of sex, who had been clinically diagnosed with anemia—operationally defined as a hemoglobin concentration of ≤ 11 g/dL and a hematocrit of ≤ 32%. In contrast, participants with a recorded history of blood transfusion or iron supplementation within the past three months, untreated systemic infections validated by a positive blood culture, untreated malignancy, or end-stage renal disease (eGFR < 15 mL/min) were systematically excluded from the research. The parents or guardians of qualifying participants were contacted, and the extensive particulars of the study were articulated prior to obtaining written informed consent. A structured proforma was employed for the meticulous collection of baseline demographic data, which encompassed age, gender, place of residence, and duration of symptoms. A 3 cc blood sample was secured in stringent aseptic conditions for subsequent laboratory evaluations. The hemoglobin, hematocrit tests, MCV and RBC count have been quantitatively assessed using Sysmex 1000 Analyzer, Mentzer Index were calculated using following formula: MCV (fL) / RBC count (millions/µL). A value of Mentzer Index greater than 13 was considered as evidence for iron deficiency anemia. Serum ferritin levels were measured by enzyme-linked immunosorbent assay (ELISA) to confirm the diagnosis, and a cutoff < 12 ng/mL was considered the threshold for diagnosis of iron deficiency anemia. Data collection data were recorded by the lead investigator, who also limited access to protect respondent confidentiality in confidence. Careful adherence to the predetermined inclusion and exclusion criteria was enforced to reduce selection bias, while standardized laboratory protocols were implemented to ensure the accuracy of results. Moreover, laboratory personnel involved in the assessment of serum ferritin levels were kept blinded to the Mentzer Index values to prevent any potential observer bias. Data was entered and analyzed by SPSS version 26. Descriptive statistics were calculated, and data were analyzed and generated with 95% confidence interval. The Chi-square test was applied to evaluate the statistical difference at 5% level of significance.

RESULTS

The average age of the participants is 8.90 years with a standard deviation of 2.71 years. The distribution of participants is nearly equal between the age categories of 1-9 years (50.5%) and those exceeding 9 years (49.5%). The average haemoglobin concentration is 8.97 g/dl, accompanied by a standard deviation of 1.20 g/dl. A significant proportion of participants (64.1%) exhibit haemoglobin levels ranging from 7-9 g/dl, whereas 35.9% present with levels surpassing 9 g/dl. The demographic composition indicates a higher prevalence of female participants (55.1%) in comparison to their male counterparts (44.9%). The manifestation of fatigue is documented by 39.4% of participants, rendering it the predominant clinical symptom. Additional symptoms reported include headache (26.3%), a history of previous clinical anaemia (PCA) (25.3%), and irritability (27.8%). The participants are classified across various socioeconomic strata: 40.9% belong to the lower class, 33.3% to the middle class, and 25.8% to the upper class as shown in Table I.

Among participants exhibiting a Mentzer Index exceeding 13, 111 individuals (90.2%) demonstrate ferritin levels at or below 12, thereby signifying a robust correlation between an elevated Mentzer Index and diminished ferritin levels, which is emblematic of Iron Deficiency Anemia (IDA). Conversely, only 8 participants (10.7%) with a Mentzer Index greater than 13 present with ferritin levels exceeding 15, implying that an increased Mentzer Index is less likely to correlate with normal ferritin levels. For those participants with a Mentzer Index at or below 13, a mere 12 individuals (9.8%) have ferritin levels at or below 15, indicating that a reduced Mentzer Index is infrequently associated with low ferritin levels. A considerable majority, specifically 67 participants (89.3%), with a Mentzer Index at or below 13 exhibit ferritin levels above 15, suggesting that a lower Mentzer Index is more likely to be associated with normal ferritin levels. The data implies that the Mentzer Index serves as an effective instrument for the screening of IDA, as a heightened index value (greater than 13) is strongly correlated with low ferritin levels, a critical marker of iron deficiency. In contrast, a diminished Mentzer Index (at or below 13) appears to be more indicative of normal ferritin levels, thereby

suggesting the absence of IDA, as illustrated in Table II.

The Mentzer Index accurately identifies 90.24% of the authentic positive instances of Iron Deficiency Anemia (IDA). The confidence interval (CI) ranging from 0.8500 to 0.9549 indicates a substantial degree of dependability regarding this sensitivity assessment. The specificity metric reveals that the Mentzer Index appropriately recognizes 89.33% of the genuine negative instances, thereby effectively excluding cases not associated with IDA. The reliability indices(CI) of 0.8235 to 0.9632, further validate the strength of this assessment tool. Therefore, the PPV suggested a 93.28% probability that a diagnosis of IDA is correct once the Mentzer Index suggested IDA. The CI of 0.8878 to 0.9778 represents a strong degree of confidence in this predictive measure. NPV shows that when the Mentzer Index suggests negative value for IDA, the chance that IDA actually does not exist is 84.81% probability. This indicates that the reliability is acceptable, with CI = 0.7690–0.9272. This finding suggests that the Mentzer Index was able to classify 89.90% from combination of positive or negative cases for iron deficiency anemia (IDA) on the comprehensive assessment. Even the CI from 0.8570 - 0.9410 confirms the index high accuracy. The positive likelihood ratio (LR+) was 8.46, suggesting that a positive Mentzer Index derives 8.46 times higher previous probability of IDA in affected patients compared to non-affected individuals, thereby indicating relative high diagnostic capability. On the other hand, a negative likelihood ratio (LR-) of 0.11 suggest that a negative test result from the Mentzer Index is only 0.11 times as likely to occur in patients with IDA as in patients without IDA, reinforcing that this test has a good ability to exclude the disease, as shown in Table III.

DISCUSSION

Iron deficiency anaemia (IDA) remains one of the most common global haematological conditions in children, its particularly high prevalence in lower- and middle-income countries mainly attributable to poor dietary intake and infections which further exacerbate the problem [1,2]. Considering the high economic consequences of IDA prevalence and more limited availability of serum ferritin, hematological parameters like Mentzer Index can be used as convenient, low-cost, and non-invasive tool for IDA diagnosis [10,12]. The objective of this study was to assess the diagnostic precision of the Mentzer Index (employing a threshold value of >13) for the detection of IDA, using serum ferritin as the reference benchmark. The Mentzer Index has been endorsed as a powerful index for the screening of IDA and our results confirms the reliability of this index with a sensitivity of 90.24% and specificity of 89.33%. Sixty percent of respondents had a Mentzer Index > 13, which distinguished 90.2% of IDA cases, and a Mentzer Index ≤ 13, which was associated with normal ferritin levels in 89.3% of subjects. The positive predictive value (PPV) was determined to be 93.28%, signifying a substantial likelihood of precise diagnosis when the Mentzer Index indicates IDA, while the negative predictive value (NPV) was recorded at 84.81%, demonstrating its efficacy in excluding IDA in the majority of instances. Nonetheless, considering that NPV is contingent upon disease prevalence, supplementary confirmatory testing may be warranted in borderline cases.

The comprehensive diagnostic accuracy of 89.90% further corroborates the validity of the Mentzer Index as a pertinent tool in the identification of pediatric iron deficiency anemia (IDA). Research conducted by Manshah et al. [14] found a sensitivity of 88% and a specificity of 85%, which were slightly lower than the values found in our study. While the study did not explicitly define positive predictive value (PPV) and negative predictive value (NPV), the improved PPV of our findings (93.28%) indicates that the Mentzer Index predicted better in our setting. Our NPV of 84.81% was slightly reduced, conversely, demonstrating the need for further confirmatory tests if the Mentzer Index is 13 or lower. Along a similar line, Sherali et al. Compared to our results, [15] found a lower sensitivity (80.7%) and specificity (77.7%). Their documented PPV of 56.8% was significantly inferior to our 93.28%, indicating that the Mentzer Index proved to be more dependable in the diagnosis of IDA within our study population. Nevertheless, their NPV of 91.6% exceeded our own 84.81%, suggesting a superior ability to exclude IDA within their cohort. These discrepancies may stem from variations in study populations, methodological approaches, or diagnostic cutoff thresholds employed in the identification of IDA. The Mentzer Index is

simply, cheap to calculate and can be a useful clinical tool for the health systems to screen IDA in these situations where you do not have the access for serum ferritin to be done. Even in our study conducted at a tertiary care pediatric hospital in Pakistan, these findings justify scaling up the Mentzer Index to our primary and secondary health care systems. This promising approach has the potential to allow for earlier diagnosis of IDA and earlier intervention that may prevent long-term sequelae such as cognitive and physical developmental deficits [5–7]. This study has been subject to some methodological limitations that must be carefully considered despite its strong diagnostic performance. As the study was performed in one institution, the results might not be fully generalizable to larger demographic groups. Additionally, pre-existing inflammatory conditions can modify serum ferritin levels [9] and thus reduce the diagnostic performance. The inclusion of subjects; including pediatric ones in the age ranging up to 12 suggests that the results may not generalize appropriately in older age groups.

CONCLUSION

Our research substantiates the efficacy of the Mentzer Index as a reliable, cost-effective, and non-invasive instrument for the screening of Iron Deficiency Anemia (IDA), particularly in environments where serum ferritin assessments are not readily accessible. With elevated sensitivity, specificity, and predictive values, this methodology serves as an essential resource for the early identification and distinction of IDA from alternative types of anemia. Nonetheless, subsequent multicenter investigations with expanded sample populations and heterogeneous demographics are imperative to refine the established cutoff values and to further corroborate its diagnostic precision across various contexts.

Table I: Characteristics of Study Participants (n=198)	
Variable	**n** (%)
Age (Mean ± SD) = 8.90 ± 2.71	
1-9 years	100 (50.5)
>9 years	98 (49.5)
Hemoglobin (Mean ± SD) = 8.97 ± 1.20	
7-9 g/dl	127 (64.1)
>9 g/dl	71 (35.9)
Gender	
Male	89 (44.9)
Female	109 (55.1)
Clinical features	
Fatigue	78 (39.4)
Headache	52 (26.3)
History of PCA	50 (25.3)
Irritability	55 (27.8)
Socioeconomic Status	
Lower Class	81 (40.9)
Middle Class	66 (33.3)
Upper Class	51 (25.8)

Table II: Comparison of Mentzer Index and Ferritin Level in Iron Deficiency Anemia (n=198)		
Mentzer Index	**Ferritin Level**	
	Yes (≤ 15)	**No (>15)**
Yes (>13)	111 (90.2)	8 (10.7)
No (≤ 13)	12 (9.8)	67 (89.3)

Table III: Diagnostic Accuracy of Mentzer Index in Diagnosing Iron Deficiency Anemia (n=198)		
Diagnostic Variables	**Mentzer Index**	**95% Confidence Interval**
Sensitivity	90.24%	0.8500-----0.9549
Specificity	89.33%	0.8235-----0.9632
Positive Predictive Value	93.28%	0.8878-----0.9778
Negative Predictive Value	84.81%	0.7690-----0.9272
Diagnostic Accuracy	89.90%	0.8570-----0.9410
Positive Likelihood Ratio (LR+)	8.46	N/A
Positive Likelihood Ratio (LR-)	0.11	N/A

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