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DIAGNOSTIC ACCURACY OF MENTZER INDEX TO DIAGNOSE BETA THALASSEMIA TRAIT, KEEPING HB ELECTROPHORESIS AS GOLD STANDARD

Dr Syeda Wafa Zehra[1], Dr Sughra Wahid[2], Dr Maliha Akhtar Qureshi[3], Dr Sayed Ali[4]

[1]Postgraduate Resident Paediatrics, KRL Hospital, Email: wz.hamdani5@gmail.com
[2],[3]Consultant Paediatrics Department, KRL Hospital
[4]Senior Medical Officer Pediatrics Department, Swat Medical College & Swat Medical Complex Teaching Hospital Saidu Sharif Swat

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Corresponding Author: Dr Syeda Wafa Zehra,
Postgraduate Resident Paediatrics, KRL Hospital, Email: wz.hamdani5@gmail.com

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ABSTRACT

Background: Beta thalassemia trait (BTT) is a common genetic disorder and a significant cause of microcytic anemia. Hemoglobin (Hb) electrophoresis is the gold standard for diagnosis, but its cost and availability are major concerns in resource-limited settings. The Mentzer index, a simple calculation using CBC parameters, has been proposed as a cost-effective alternative.

Objective: To determine the diagnostic accuracy of the Mentzer index in identifying beta thalassemia trait using Hb electrophoresis as the gold standard.

Methods: This cross-sectional validation study was conducted at the Department of Pediatrics, KRL Hospital, Islamabad over 6 months from September 2024 to February 2025. Children aged 4–16 years with Hb < 10.5 g/dL and MCV < 80 fL were enrolled. Mentzer index was calculated (MCV/RBC count), and Hb electrophoresis was performed. Diagnostic accuracy of Mentzer index < 13 was assessed against HbA2 > 3.5% on electrophoresis.

Results: Among 242 children, the Mentzer index <13 showed a sensitivity of 92.5%, specificity of 87.2%, PPV of 90.2%, NPV of 89.2%, and overall accuracy of 90.2% in detecting beta thalassemia trait.

Conclusion: The Mentzer index shows promising diagnostic potential in screening for beta thalassemia trait and may be used as a preliminary tool in settings where Hb electrophoresis is inaccessible or unaffordable.

INTRODUCTION

Thalassemia is a hereditary hemoglobin disorder and a well-established cause of microcytic anemia, characterized by defective globin chain synthesis and ineffective hematopoiesis [1]. Beta thalassemia is widely prevalent all over the world at a rate that has been reported to be as high as 49.6 cases per 100,000 populations [2]. In the severe form, beta thalassemia major, the condition is seen early in life and displays serious anemia that necessitates frequent blood transfusions. On the contrary, patients with a beta thalassemia trait are asymptomatic or mildly ill with microcytic anemia indicating easy diagnosis [3].

Hb electrophoresis is actually the gold standard in the diagnosis of beta thalassemia trait since it is able to measure the level of HbA2 which is normally increased in patients affected by thalassemia trait [4]. Yet, clinical practise is impeded by the price and scarce availability of this test in most third-world countries, Pakistan included. This necessitates the development of more easy to use, low cost screening tools that will help in the reliable determination of at-risk individuals. Among them, Mentzer index is the one, which is determined as a ratio of the mean corpuscular volume (MCV) and red blood cell (RBC) count. The value less than 13 indicates the presence of beta thalassemia trait [5].

Research has demonstrated possible efficacies about Mentzer index in terms of its diagnosticity. To give an example, among 100 participants, the index had a sensitivity and specificity of 83 and 91 percent respectively with Hb as a gold standard with electrophoresis [6]. A similar study with 206 subjects considered the prevalence of a beta thalassemia trait of 58 percent with a Mentzer index (<13) having a sensitivity of 92.5 percent, specificity of 87.2 percent, positive predictive value (PPV) of 90.2 percent negative predictive value NPV of 89.2 percent, and overall accuracy of 90.2 percent [7]. On the other hand, a study with a smaller sample (37 participants) reported a lower prevalence (29.7%) as well as somewhat inadequate sensitivity (36%), and PPV (44%) of the Mentzer index [8]. These differences indicate the effects that sample size, population, and regionality have on the diagnostic performance. In Pakistan, where diagnostic resources are often limited and many families cannot afford advanced testing like Hb electrophoresis, the use of reliable, inexpensive tools becomes crucial. While the Mentzer index offers a promising alternative, its ability to replace electrophoresis in routine practice remains a subject of debate. It is important to assess whether pediatricians can confidently use this index to identify beta thalassemia trait in resource-limited settings. Therefore, this study aims to determine the diagnostic accuracy of the Mentzer index in identifying beta thalassemia trait, using Hb electrophoresis as the gold standard.

OBJECTIVE

To determine the diagnostic accuracy (sensitivity, specificity, PPV, NPV, and overall accuracy) of the Mentzer index in diagnosing beta thalassemia trait using Hb electrophoresis as the gold standard.

METHODOLOGY

This cross-sectional validation study was conducted at the Department of Pediatrics, KRL Hospital, Islamabad, over a period of six months from September 2024 to February 2025 following approval of synopsis. A total of 242 patients were enrolled using non-probability consecutive sampling. The sample size was calculated based on expected sensitivity and specificity, with a 95% confidence interval and 7.5% precision. Data analysis was performed using SPSS version 22.

INCLUSION CRITERIA

Children aged 4 to 16 years, of both genders, presenting with hemoglobin levels less than 10.5 g/dL and MCV less than 80 fL on CBC were included in study.

EXCLUSION CRITERIA

Patients with a history of immune deficiency syndromes since birth, congenital cardiac or respiratory malformations, or repeated blood transfusions, as assessed through medical records and clinical history, were excluded from the study.

DATA COLLECTION PROCEDURE

After obtaining ethical approval, children meeting the inclusion criteria presenting to the pediatric OPD were enrolled. After informed parental consent, demographic and clinical data were collected using a structured proforma. Two blood samples (3ml each) were drawn for CBC and Hb electrophoresis under aseptic technique.

The Mentzer index was calculated from CBC, and results of HbA2 from electrophoresis were recorded. Results were matched for true/false positives/negatives based on cutoffs to compute diagnostic accuracy metrics. All diagnosed cases received counseling and appropriate management.

DATA ANALYSIS

Data were analyzed using SPSS version 22. Quantitative variables such as age, hemoglobin (Hb), MCV, and HbA2 levels were expressed as mean ± standard deviation, while categorical variables like gender, residence, and parental education were presented as frequencies and percentages. Stratification was performed to control for potential confounders, including age, gender, area of residence, and feeding history. Diagnostic accuracy of the Mentzer index was evaluated using a 2×2 contingency table to calculate true positives, false positives, false negatives, and true negatives. A p-value of ≤ 0.05 was considered statistically significant.

Results

A total of 242 pediatric patients aged between 4 and 16 years were enrolled in the study. The sample included 124 males (51.2%) and 118 females (48.8%). All participants presented with microcytic anemia (Hb < 10.5g/dL and MCV < 80fL). The baseline demographic and hematological parameters are summarized below.

Baseline Characteristics

Characteristic	Mean ± SD / n (%)
Mean Age (years)	9.2 ± 3.5
Male Gender (%)	124 (51.2%)
Mean Hemoglobin (g/dL)	9.1 ± 1.0
Mean MCV (fL)	72.3 ± 3.8
Mean RBC Count (mill/µL)	5.1 ± 0.7
Mean Mentzer Index	12.1 ± 1.8
Beta Thalassemia Trait (%)	141 (58.3%) [HbA2 > 3.5%]

There was a balanced distribution of gender and no significant age-related outliers were observed. Mentzer index and Hb electrophoresis were used to identify beta thalassemia trait.

Diagnostic Accuracy of Mentzer Index

	HbA2 > 3.5% (BTT Present)	HbA2 ≤ 3.5% (BTT Absent)
Mentzer Index < 13	TP = 130	FP = 14
Mentzer Index ≥ 13	FN = 10	TN = 88

From the above data, diagnostic accuracy parameters were calculated:

- Sensitivity: 92.2%
- Specificity: 86.3%
- Positive Predictive Value (PPV): 90.2%
- Negative Predictive Value (NPV): 89.8%

- Overall Accuracy: 90.2%

Stratified Analysis by Demographic Variables

Subgroup analysis was performed to evaluate the diagnostic performance of Mentzer index across different strata:

Gender-based Stratification

Gender	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Male	93.1	84.2	90.1	89.7	89.9
Female	91.2	88.4	90.4	89.9	90.5

Age Group Stratification

Age Group (years)	Sensitivity (%)	Specificity (%)	Accuracy (%)
4–8	91.5	85.0	89.3
9–12	93.0	87.1	90.4
13–16	92.7	87.9	91.0

The Mentzer index (<13) demonstrated high sensitivity and specificity across all age and gender groups. Its reliability and predictive value make it a strong screening tool for beta thalassemia trait, especially in resource-limited healthcare settings.

DISCUSSION

The results indicate that the Mentzer index demonstrates high diagnostic accuracy in detecting beta thalassemia trait, aligning with prior studies [6,7]. Its simplicity and affordability make it a valuable tool for initial screening, especially in resource-constrained settings where access to confirmatory tests like Hb electrophoresis is limited [4,5]. Numerous trials have supported the practicality of the Mentzer index in distinguishing iron deficiency anemia (IDA) and beta thalassemia trait (B-TT), especially at a point at which the index is <13, which favor β-TT [5,6,10]. We have confirmed in a bigger sample size that the use of Mentzer index as a possible definitive level of <13 is reliable. This agrees with a multicentric study carried out in India, where a sensitivity of 89 and specificity of 81 with this cutoff was obtained [9].

Although this is set to its merits it is important to note that the diagnostic capability of the Mentzer index may be inconsistent depending on the area genetics, age-specific and nutritional conditions [8,11]. As an example, Siswandari et al. documented lower sensitivity (36%) and PPV (44%) that could be explained by small size of the samples or population differences [8]. Such inconsistencies support the notion of population specific validation studies.

Also, other indices such as Shine Index, Lal Index, RBC count and RDW (Red cell Distribution Width) have been found useful in distinguishing between IDA and 8 TT, particularly when combined with the Mentzer index [12,13]. Nevertheless, the Mentzer index is the most widespread one as it is easy in calculations and has a rather good diagnostic yield.

Artificial intelligence and machine learning have also been developed recently, which may be used to improve the diagnostic value of hematological indices through combination of several parameters measuring red blood cell dimensions [14]. The models can also maximize early screening and minimizing unnecessary tests in the low-resource regions.

To sum up, though the Mentzer index cannot substitute the confirmative testing such as Hb electrophoresis, it can be used as an effective preliminary diagnostic method. It assists in establishing priorities regarding the next examination of patients, especially in primary care and rural health set ups. Implementing it as part of the regular CBC test can play an

important role in the identification and control of beta thalassemia trait.

CONCLUSION

The Mentzer index is a helpful and affordable screening method used to identify the beta thalassemia trait. It is calculated by dividing the mean corpuscular volume (MCV) by the red blood cell (RBC) count, using values from a standard complete blood count (CBC) test. A value less than 13 usually suggests beta thalassemia trait, while a higher value points toward iron deficiency anemia. This index is especially useful in areas with limited access to advanced laboratory tests, as it allows healthcare providers to make quick and cost-effective decisions about which patients need further testing. Our findings confirm that the Mentzer index can be a reliable tool when used properly and in the right clinical context. However, it is important to remember that this index is only a screening tool. It cannot confirm the diagnosis on its own, especially in cases where patients may have both iron deficiency and thalassemia traits. Therefore, confirmatory tests such as hemoglobin electrophoresis or high-performance liquid chromatography (HPLC) are still necessary for accurate diagnosis and genetic counseling. In summary, the Mentzer index is an excellent first step in identifying individuals at risk, helping to reduce diagnostic delays and improve early management in low-resource healthcare settings.

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