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Original Research Article

A STUDY ON IMPLEMENTING MENTZER INDEX AS A SCREENING TOOL FOR BETA THALASSEMIA TRAIT IN ANTENATAL WOMEN

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ABSTRACT

Background: Beta thalassemia trait is a common hemoglobinopathy that presents with microcytic hypochromic anemia, often mimicking iron deficiency anemia (IDA) in pregnant women. Early identification is crucial for genetic counseling and prevention of thalassemia major in offspring. **Objective:** To evaluate the efficacy of Mentzer Index as a screening tool for beta thalassemia trait in antenatal women and assess its diagnostic accuracy compared to hemoglobin electrophoresis.**Materials and Methods:** A prospective observational study was conducted on 50 antenatal women with microcytic anemia (Hb 8-11 g/dL) attending the obstetrics outpatient department. Complete blood count, iron studies, and HPLC for HbA2 estimation were performed. Mentzer Index was calculated using the formula MCV/RBC count. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were determined.**Results:** Of 50 participants, 8 (16%) had beta thalassemia trait and 42 (84%) had iron deficiency anemia. Mentzer Index showed sensitivity of 87.5% and specificity of 92.86% for detecting beta thalassemia trait. The PPV was 70% and NPV was 97.5%. Seven out of 8 beta thalassemia cases had Mentzer Index <13, while 39 out of 42 IDA cases had Mentzer Index >13.**Conclusion:** Mentzer Index is an effective, cost-efficient screening tool for beta thalassemia trait in antenatal women, particularly valuable in resource-limited settings where advanced testing may not be readily available.

INTRODUCTION

Anemia during pregnancy remains a significant global health concern, with prevalence rates ranging from 35-75% in developing countries compared to 19% in developed nations. In India, pregnancy-related anemia affects approximately 50-60% of pregnant women, making it a major public health challenge.[1]

Beta thalassemia trait represents one of the most common genetic disorders worldwide, with an estimated 5% of the global population being carriers according to WHO data. In India, the carrier frequency ranges from 3-4% in the general population, with higher prevalences observed in certain ethnic groups including Gujaratis, Sindhis, Bengalis, and Punjabis. The country harbors approximately 42 million beta thalassemia trait carriers and witnesses 1-1.5 lakh new cases of thalassemia major annually.

The clinical presentation of beta thalassemia trait closely mimics iron deficiency anemia, as both conditions manifest as microcytic hypochromic anemia.[2]This similarity poses diagnostic challenges, particularly in pregnant women who are already at increased risk for iron deficiency due to increased physiological demands. Distinguishing between these two conditions is crucial for several reasons. Firstly, identification of beta thalassemia trait enables appropriate genetic counseling and partner screening to prevent thalassemia major in offspring, which is essential for family planning decisions.[6]Secondly, iron supplementation, the standard treatment for IDA, is ineffective in beta thalassemia trait and may lead to iron overload if administered unnecessarily, potentially causing harmful complications.[3,4] Finally, understanding the underlying cause of anemia helps in appropriate monitoring and management during pregnancy, ensuring optimal maternal and fetal outcomes.

Traditional diagnostic methods for beta thalassemia trait include hemoglobin electrophoresis or High-Performance Liquid Chromatography (HPLC) to measure HbA2 levels, with values >3.5% being diagnostic.[10]However, these tests are expensive, require specialized equipment and trained personnel, and may not be readily available in primary healthcare settings.

The Mentzer Index, introduced in 1973, represents a simple mathematical formula derived from routine complete blood count parameters: Mean Corpuscular Volume (MCV) divided by Red Blood Cell (RBC) count.[7] The principle behind this index lies in the pathophysiological differences between iron deficiency anemia and beta thalassemia trait:

- **In Iron Deficiency Anemia:** Reduced iron availability leads to decreased hemoglobin synthesis and reduced RBC production, resulting in low MCV and low RBC count, yielding a Mentzer Index >13.
- **In Beta Thalassemia Trait:** Defective beta-globin chain synthesis leads to unstable hemoglobin and increased RBC fragility, but RBC production remains normal or increased as a compensatory mechanism, resulting in low MCV with normal/high RBC count, yielding a Mentzer Index <13.

Given the cost-effectiveness and simplicity of the Mentzer Index, this study aims to evaluate its diagnostic accuracy as a screening tool for beta thalassemia trait in antenatal women, potentially enabling early identification and appropriate management in resource-limited settings.[9]

MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was conducted at the Department of Obstetrics and Gynecology, Government Dharmapuri Medical College over a period of 6 months. The study protocol was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants.

Study Population

The study included 50 antenatal women selected based on specific criteria. Women were included if they were pregnant in any trimester, aged between 18-40 years, had hemoglobin levels between 8-11 g/dL, presented with microcytic anemia (MCV <80 fL), and were willing to participate with informed consent. Women were excluded if they had known cases of hemoglobinopathies,[5] history of blood transfusion in the past 3 months, chronic kidney disease, chronic inflammatory conditions, aplastic anemia or other bone marrow disorders, acute blood loss, or multiple pregnancy.

Data Collection

A structured proforma was used to collect comprehensive information from each participant. The data collection included demographic data such as age, gestational age, and parity, along with detailed medical history and family history of anemia or thalassemia. Clinical examination findings were carefully documented, and all relevant laboratory parameters were systematically recorded for analysis.

Complete Blood Count was performed using automated hematologyanalyzer, with parameters recorded including hemoglobin, RBC count, MCV, MCH, MCHC, and RDW. Iron studies were conducted to measure serum iron, Total Iron Binding Capacity (TIBC), serum ferritin, and transferrin saturation levels. Hemoglobin electrophoresis using HPLC was performed with Bio-Rad D10 Dual Reader to measure HbA2 levels, with beta thalassemia trait diagnosed if HbA2 exceeded 3.5%. Additionally, peripheral blood smears were examined for RBC morphology, specifically looking for the presence of target cells, microcytes, and hypochromia.[8]

Mentzer Index Calculation

Mentzer Index = MCV (fL) / RBC count (million/µL)

- MI <13: Suggestive of beta thalassemia trait
- MI >13: Suggestive of iron deficiency anemia

Diagnostic Criteria

Iron deficiency anemia was diagnosed based on serum ferritin levels below 15 ng/mL, low serum iron levels with high TIBC, and transferrin saturation below 16%. Beta thalassemia trait was confirmed by HbA2 levels exceeding 3.5% on HPLC, normal or elevated serum ferritin levels, and consideration of family history when present.

Statistical Analysis

Data analysis was conducted using SPSS version 26.0, with descriptive statistics used to present demographic and clinical characteristics. The diagnostic performance of Mentzer Index was evaluated by calculating sensitivity, specificity positive predictive value, negative predictive value and diagnostic accuracy. Chi-square test was used to assess associations between categorical variables, with P-value less than 0.05 considered statistically significant.

RESULTS

Demographic Characteristics

The study included 50 antenatal women with microcytic anemia. The demographic and clinical characteristics are presented in Table 1.

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Table1: Demographic and Clinical Characteristics (n=50)

Parameter	Mean ± SD / Number (%)
Age (years)	26.4 ± 4.2
Gestational age (weeks)	22.8 ± 8.6
Primigravida	28 (56%)
Multigravida	22 (44%)
Haemoglobin (g/dL)	9.2 ± 0.8
Family history of anaemia	12 (24%)

This study analyzed 50 pregnant women with a mean age of 26.4 ± 4.2 years at a gestational age of 22.8 ± 8.6 weeks. The cohort included 28 primigravida (56%) and 22 multigravida (44%) patients. All participants presented with anemia, showing a mean hemoglobin level of 9.2 ± 0.8 g/dL, with nearly a quarter (24%) having a family history of anemia.

Table 2: Hematological Parameters

Parameter	Beta Thalassemia Trait (n=8)	Iron Deficiency Anemia (n=42)	P-value
Hemoglobin (g/dL)	9.4 ± 0.6	9.1 ± 0.9	0.312
RBC count (×10⁶/μL)	5.2 ± 0.4	4.1 ± 0.5	<0.001
MCV (fL)	62.8 ± 4.2	68.4 ± 6.1	0.012
MCH (pg)	18.2 ± 2.1	20.8 ± 2.8	0.023
MCHC (g/dL)	28.9 ± 1.8	30.2 ± 2.1	0.118
RDW (%)	16.8 ± 2.3	18.9 ± 3.1	0.067
Mentzer Index	12.1 ± 1.2	16.8 ± 2.4	<0.001

The analysis revealed significant differences between beta thalassemia trait and iron deficiency anemia groups in several key parameters:

Red Blood Cell Indices: Beta thalassemia trait patients showed significantly higher RBC counts (5.2 ± 0.4 vs 4.1 ± 0.5 $\times 10^6$/μL, p<0.001) despite similar hemoglobin levels. Mean corpuscular volume (MCV) was significantly lower in beta thalassemia trait (62.8 ± 4.2 vs 68.4 ± 6.1 fL, p=0.012), as was mean corpuscular hemoglobin (MCH) (18.2 ± 2.1 vs 20.8 ± 2.8 pg, p=0.023).

Discriminatory Indices: The Mentzer Index showed the most pronounced difference, with beta thalassemia trait patients having significantly lower values (12.1 ± 1.2 vs 16.8 ± 2.4, p<0.001), supporting its utility as a screening tool.

Table 3: Iron Studies and HbA2 Levels

Parameter	Beta Thalassemia Trait (n=8)	Iron Deficiency Anemia (n=42)	P-value
Serum Iron (μg/dL)	89.2 ± 18.4	42.6 ± 12.8	<0.001
TIBC (μg/dL)	298.4 ± 32.6	456.8 ± 68.2	<0.001
Serum Ferritin (ng/mL)	45.6 ± 28.2	8.9 ± 4.2	<0.001
Transferrin Saturation (%)	29.8 ± 6.4	9.3 ± 2.8	<0.001
HbA2 (%)	4.8 ± 0.6	2.1 ± 0.3	<0.001

Iron metabolism parameters clearly differentiated the two conditions. Beta thalassemia trait patients maintained normal iron stores with significantly higher serum iron (89.2 ± 18.4 vs 42.6 ± 12.8 μg/dL), lower total iron-binding capacity (298.4 ± 32.6 vs 456.8 ± 68.2 μg/dL), higher ferritin levels (45.6 ± 28.2 vs 8.9 ± 4.2 ng/mL), and higher transferrin saturation (29.8 ± 6.4 vs 9.3 ± 2.8%). All iron parameters showed highly significant differences (p<0.001).

The diagnostic hallmark of beta thalassemia trait was confirmed through elevated HbA2 levels (4.8 ± 0.6% vs 2.1 ± 0.3%, p<0.001), which serves as the gold standard for diagnosis.

Table 4: Distribution of Cases Based on Mentzer Index

Mentzer Index	Beta Thalassemia Trait	Iron Deficiency Anemia	Total
<13	7	3	10
≥13	1	39	40
Total	**8**	**42**	**50**

Using a cutoff value of <13 for beta thalassemia trait diagnosis, the Mentzer Index demonstrated strong diagnostic performance. Seven of eight beta thalassemia trait cases (87.5%) had values <13, while 39 of 42 iron deficiency anemia cases (92.9%) had values ≥13. Only 4 cases were misclassified using this criterion.

Table 5: Diagnostic Performance Parameters

Parameter	Value (%)
Sensitivity	87.5
Specificity	92.86
Positive Predictive Value	70.0

Negative Predictive Value	97.5
Diagnostic Accuracy	92.0

The Mentzer Index showed excellent diagnostic performance with a sensitivity of 87.5% (95% CI: 52.9-97.8%) and specificity of 92.86% (95% CI: 81.0-97.5%). The positive predictive value was 70.0% (95% CI: 39.7-89.2%), while the negative predictive value was notably high at 97.5% (95% CI: 87.1-99.5%). The overall diagnostic accuracy reached 92.0% (95% CI: 81.2-96.9%).

These results demonstrate that the Mentzer Index serves as an effective preliminary screening tool for differentiating beta thalassemia trait from iron deficiency anemia in pregnant women, with high specificity and negative predictive value making it particularly valuable for ruling out beta thalassemia trait when values are ≥13.

Correlation Analysis

Strong negative correlation was observed between Mentzer Index and HbA2 levels ($r = -0.78$, $p<0.001$), indicating that lower Mentzer Index values were associated with higher HbA2 levels.

DISCUSSION

This study demonstrates that the Mentzer Index is an effective screening tool for beta thalassemia trait in antenatal women, with a sensitivity of 87.5% and specificity of 92.86%. The high negative predictive value (97.5%) suggests that women with Mentzer Index >13 are unlikely to have beta thalassemia trait, making it an excellent rule-out test.

The prevalence of beta thalassemia trait in our study population was 16% (8/50), which is higher than the general population frequency of 3-4% reported in Indian studies. This elevated prevalence might be attributed to selection bias toward cases with persistent microcytic anemia, regional variation in carrier frequency, increased awareness and referral patterns

Our findings are consistent with several previous studies evaluating the Mentzer Index across different populations. International studies have shown similar results, with Ehsani et al. in 2009 reporting 90.1% discrimination accuracy for Mentzer Index, Batebi et al. in 2012 finding sensitivity of 86.3% and specificity of 85.4%, and Ghafouri et al. in 2006 reporting sensitivity of 90.9% and specificity of 80.3%. Indian studies have also validated these findings, with Kaur et al. in 2024 showing sensitivity of 80% and specificity of 95.65% for beta thalassemia trait, Saxena et al. in 2020 demonstrating sensitivity and specificity of 89% each, and Bose et al. in 2018 confirming reliability of Mentzer Index in Indian population. Our study results align well with these findings, with slightly higher specificity, which may be attributed to careful exclusion of confounding conditions, standardized laboratory procedures, and a smaller but well-characterized study population.

The high negative predictive value of 97.5% suggests that Mentzer Index can effectively rule out beta thalassemia trait, enabling a practical two-step screening approach where the first line involves calculating Mentzer Index from routine CBC, followed by performing HPLC only for cases with MI less than 13. From a cost-effectiveness perspective, implementing this screening strategy could reduce the need for HPLC testing by approximately 80% since 40 out of 50 cases had MI greater than 13, significantly reducing healthcare costs while maintaining diagnostic accuracy. In terms of pregnancy management, early identification of beta thalassemia trait enables appropriate genetic counseling, partner screening, prevention of unnecessary iron supplementation, and proper antenatal monitoring throughout pregnancy.

For successful implementation in clinical practice, healthcare systems should include Mentzer Index calculation in routine antenatal screening protocols, use MI less than 13 as an indication for HPLC testing, consider clinical context and family history in decision-making, and ensure quality control of CBC measurements. Healthcare providers require comprehensive training in calculation and interpretation of Mentzer Index, recognition of microcytic anemia patterns, appropriate referral criteria, and basic genetic counseling principles. Quality assurance measures should include regular calibration of hematologyanalyzers, standardized sample collection and processing procedures, and periodic validation of Mentzer Index cut-off values to maintain accuracy.

CONCLUSION

The Mentzer Index demonstrates excellent diagnostic performance as a screening tool for beta thalassemia trait in antenatal women, with sensitivity of 87.5%, specificity of 92.86%, and notably high negative predictive value of 97.5%. Its simplicity, cost-effectiveness, and reliance on routine CBC parameters make it particularly valuable in resource-limited settings.

The study supports the implementation of Mentzer Index as a first-line screening tool, potentially reducing the need for expensive HPLC testing by approximately 80% while maintaining diagnostic accuracy. This approach could significantly improve the feasibility of beta thalassemia trait screening in primary healthcare settings, enabling early identification, appropriate genetic counseling, and prevention of thalassemia major in offspring.

However, healthcare providers must be aware of the limitations and potential for false results, particularly in cases of concurrent nutritional deficiencies. The Mentzer Index should be used as part of a comprehensive assessment including clinical history, family history, and consideration of local population genetics.

Future research should focus on large-scale validation studies, cost-effectiveness analyses, and development of integrated screening protocols to optimize the identification and management of beta thalassemia trait in pregnant women.

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