Evidence Based Case Report: Can the Mentzer Index Guide Diagnosis of Microcytic Anemia in Rural Indonesia?

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Abstract

***Introduction**: Indonesia, part of the "Thalassemia Belt," carries a significant burden of hemoglobinopathies, with β-thalassemia trait (BTT) affecting up to 10% of the population. In rural settings with limited access to advanced diagnostics, distinguishing between BTT and iron deficiency anemia (IDA) using clinical and hematologic indices such as the Mentzer Index may aid early management.*
***Method**: A structured literature search was conducted in MEDLINE and EBSCO to identify diagnostic or cross-sectional studies comparing red blood cell indices, particularly the Mentzer Index, in differentiating IDA from BTT. Studies were selected based on inclusion and exclusion criteria, and full texts were critically appraised by three reviewers using criteria of validity, importance, and applicability.*
***Results**: Six studies with Level 4 evidence were included. The Mentzer Index was evaluated in all studies, with sensitivity ranging from 66% to 100% and specificity from 47.1% to 100%. Rashwan et al. and Jasim et al. reported perfect or near-perfect accuracy, while Indrasari et al., an Indonesian study, found more modest results (sensitivity 66%, specificity 62.5%). Variability in diagnostic performance may be influenced by population genetics, disease spectrum, and laboratory techniques.*
***Conclusion**: The Mentzer Index demonstrates promising diagnostic value, particularly in settings where advanced testing is unavailable. However, variability in its accuracy across populations suggests that clinical judgment remains essential. The Mentzer Index can be a useful preliminary tool but should not replace confirmatory tests when available.*

***Keywords:** Anemia, Thalassemia, Hemoglobinopaties, Splenomegaly.*

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Laporan Kasus Berbasis Bukti: Dapatkah Indeks Mentzer Membimbing Diagnosis Anemia Mikrositik di Daerah Rural Indonesia?

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Abstrak

***Pendahuluan**: Indonesia yang merupakan bagian dari "Thalassemia Belt" memiliki beban hemoglobinopati yang tinggi, dengan prevalensi pembawa sifat β-thalassemia (BTT) diperkirakan mencapai hingga 10% dari populasi. Di daerah terpencil dengan keterbatasan akses terhadap pemeriksaan diagnostik lanjutan, penggunaan indeks hematologis seperti Mentzer Index dapat membantu penegakan diagnosis awal untuk membedakan antara BTT dan anemia defisiensi besi (ADB).*
***Metode**: Penelusuran literatur dilakukan secara sistematis melalui basis data MEDLINE dan EBSCO untuk menemukan studi diagnostik atau potong lintang yang membandingkan indeks sel darah merah, khususnya Mentzer Index, dalam membedakan ADB dan BTT. Studi yang sesuai dengan kriteria inklusi dan eksklusi diseleksi dan kemudian dilakukan telaah kritis oleh tiga penelaah berdasarkan aspek validitas, pentingnya hasil, dan aplikabilitas.*
***Hasil**: Enam studi dengan level of evidence 4 disertakan dalam telaah ini. Mentzer Index dievaluasi pada semua studi, dengan nilai sensitivitas berkisar antara 66% hingga 100% dan spesifisitas antara 47,1% hingga 100%. Studi oleh Rashwan et al. dan Jasim et al. menunjukkan akurasi yang sangat tinggi, sementara studi lokal oleh Indrasari et al. di Indonesia menunjukkan hasil yang lebih rendah (sensitivitas 66%, spesifisitas 62,5%). Variabilitas performa diagnostik ini dapat dipengaruhi oleh faktor genetik populasi, spektrum penyakit, dan metode laboratorium yang digunakan.*
***Kesimpulan**: Mentzer Index menunjukkan potensi sebagai alat diagnostik awal yang menjanjikan, khususnya di daerah dengan keterbatasan fasilitas pemeriksaan lanjutan. Namun, mengingat adanya variasi akurasi antar populasi, penilaian klinis tetap diperlukan. Mentzer Index dapat digunakan sebagai alat skrining awal, namun tidak dapat menggantikan pemeriksaan konfirmasi jika tersedia.*

***Kata Kunci:** Anemia, Talasemia, Hemoglobinopati, Splenomegali*

Clinical Scenario

A 2-year-6-month-old boy presented with abdominal distension since infancy, worsening pallor, weakness, and difficulty walking. Physical exam revealed Cooley's facies and massive splenomegaly. Lab tests showed severe microcytic hypochromic anemia (Hb 3.1 g/dL, MCV 62.7 fL, MCH 16.8 pg), and the Mentzer Index was 33.9—suggestive of IDA. However, the clinical presentation, transfusion dependence, and peripheral smear (showing target cells and normoblasts) were more consistent with thalassemia. Due to the unavailability of hemoglobin electrophoresis, diagnosis and management were guided by clinical judgment.

Introduction

Anemia remains a significant global public health problem, affecting up to 50% of children under five years of age worldwide.[1] The World Health Organization (WHO) defines anemia in children aged 24–59 months as a hemoglobin concentration below 11 g/dL.[2] The consequences of childhood anemia are profound, including growth retardation, impaired cognitive and motor development, and increased susceptibility to infections.[3] Its prevalence is disproportionately higher in low- and middle-income countries, particularly among women and young children. The causes are multifactorial, ranging from nutritional deficiencies (especially iron), chronic infections, and socioeconomic deprivation, to

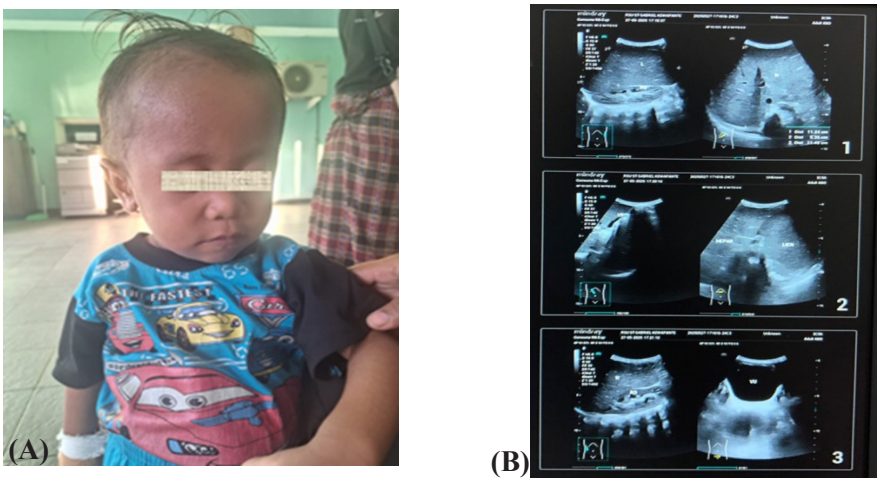

Figure 1. (A) Clinical appearance showing Cooley Facies, characterized by frontal bossing, maxillary prominence, and depressed nasal bridge, commonly seen in thalassemia major.
(B) Abdominal ultrasound showing splenomegaly and mild hepatomegaly.

genetic hemoglobin disorders such as thalassemia and sickle cell disease.[4]

Iron deficiency anemia (IDA) is the most common cause, accounting for approximately 20% to 25% of anemia cases in preschool children, particularly in regions with high rates of malnutrition.[5] However, in areas such as South and Southeast Asia, hemoglobinopathies like β-thalassemia and α-thalassemia are also major contributors to the anemia burden, with over 300,000 children born annually worldwide with severe genetic anemias. In Indonesia—situated within "Thalassemia Belt"—carrier rates are estimated at 3–10% for β-thalassemia and 2.6–11% for α-thalassemia, with ethnic clusters such as the Sumbanese exhibiting even higher prevalence.[6]

In rural Indonesian settings, diagnostic limitations—including the lack of hemoglobin electrophoresis, ferritin testing, or molecular diagnostics—frequently hinder accurate diagnosis.[7] As a result, healthcare providers must rely on clinical signs and basic hematologic indices, such as the Mentzer Index, to differentiate between IDA and thalassemia. However, these indices have variable diagnostic accuracy, especially in children with mixed etiologies.[8]

Clinical Question

Does the Mentzer Index have sufficient diagnostic accuracy to distinguish between iron deficiency anemia (IDA) and thalassemia in children presenting with microcytic hypochromic anemia, particularly in rural areas where advanced diagnostic tools such as hemoglobin electrophoresis are unavailable?

Search Strategy

A structured literature search was conducted to explore the diagnostic value of the Mentzer Index in differentiating iron deficiency anemia (IDA) from thalassemia trait in children, especially in rural areas where diagnostic resources such as hemoglobin electrophoresis are unavailable. The search was performed using three major databases: PubMed, EBSCOhost, and Google Scholar.

The initial search yielded a total of 106 articles: 4 from PubMed, 8 from EBSCOhost, and 94 from Google Scholar. After removing one duplicate, 105 unique articles remained. These articles underwent an initial screening based on titles and abstracts, resulting in 13 studies that appeared relevant to the clinical question. Full-text screening was then conducted, during which 6 articles were excluded due to incomplete diagnostic data or unavailability of full text. This left 7 eligible studies. An additional 2 articles were identified through a manual search of the reference lists from included studies, resulting in a final total of 9 articles.

These 9 articles were included for critical appraisal to assess their validity, clinical relevance, and applicability to settings with limited diagnostic tools, such as rural healthcare environments. The overall article selection process is illustrated in the PRISMA flow diagram (Figure 2).

Table 1. Literature Search Strategy

Database	Search Strategy	Hits
PubMed	("Mentzer Index"[All Fields] OR "Red Cell Indices"[All Fields]) AND ("Iron-Deficiency Anemia"[MeSH Terms] OR "IDA"[All Fields]) AND ("Thalassemia"[MeSH Terms] OR "Hemoglobinopathies"[MeSH Terms]) AND ("Child"[MeSH Terms] OR "Pediatrics"[MeSH Terms]) AND ("Diagnosis"[MeSH Terms] OR "Screening"[All Fields])	4
EBSCOhost	"Mentzer Index" AND "iron deficiency anemia" AND thalassemia AND children AND (sensitivity OR specificity)	8
Google Scholar	"Mentzer Index" AND ("iron deficiency anemia" OR IDA) AND (thalassemia) AND (children OR pediatric) AND (sensitivity OR specificity)	94

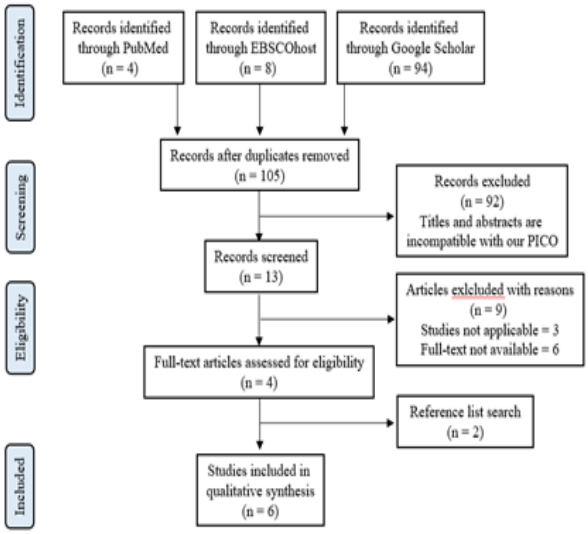

Figure 2. Prism Flowchart

Critical Appraisal

The critical appraisal was conducted by assessing the validity, importance, and applicability using a checklist of questions presented in Table 2.

Result

The results of the journal search were summarized and recorded systematically in the form of a PRISMA flowchart in Figure 1. Based on the search conducted through PubMed, EBSCO, and Google Scholar, six eligible studies were selected for critical appraisal. From the assessment of validity, there were two studies (Alqarni et al. and Ahmed et al.) with an unclear answer for V1; however,

Table 2. Checklist Questions to Assess Validity, Importance, and Applicability

Aspect	Question Code	Explanation
Validity	V1	Was blinding independently applied against the gold standard?
	V2	Were the patient characteristics appropriate?
	V3	Was a reference standard applied?
Importance		Sensitivity, specificity, prevalence, positive likelihood ratio, pretest odds, post-test odds, and post-test probability
Applicability	A1	Is the diagnostic index affordable, accessible, and practical in rural area?
	A2	Can the index be used to estimate likelihood of IDA or thalassemia bas pre-test probability?
	A3	Does the result of post-test probability influence patient management?
	A4	Are the study results relevant and beneficial for improving diagnostic accuracy and patient outcomes in children in rural healthcare settings?

in diagnostic accuracy studies, blinding may not be necessary when the outcome measure is objective laboratory data. Therefore, based on Table 3, it can be concluded that all studies are valid, important, and applicable.

Discussion

The diagnosis of microcytic anemia in pediatric patients—particularly in thalassemia-endemic regions like Indonesia—requires a careful, structured approach. In resource-limited settings where confirmatory tests such as hemoglobin electrophoresis are unavailable, clinicians often rely on a combination of clinical signs, red cell indices, and peripheral smear findings.[7]

Among the six analyzed studies, the Mentzer Index showed consistently strong diagnostic performance in differentiating between iron deficiency anemia (IDA) and beta-thalassemia trait (BTT) among children with microcytic hypochromic anemia. Sensitivity values ranged from 66% to 100%, while specificity ranged from 47.1% to 100%. Several studies supported the reliability of the Mentzer Index. Rashwan et al. demonstrated 100% sensitivity and specificity, while Ahmed et al. reported similarly high accuracy with 95.24% sensitivity and 93.1% specificity. Uzunoğlu et al. found 93.4% sensitivity and 47.1% specificity using the conventional cut-

Table 3. Critical Appraisal Based on Validity, Importance, and Applicability

Author	Design	Sample size	V1	V2	V3	Importancce	A1	A2	A3	A4
Uzunoğlu et al.[9]	Cross-sectional	273	Yes	Yes	Yes	Sens: 93.4%, Spec: 47.1%, PPV: 64%, NPV: 87.7%, AUC: 0.869, Revised Cut-off: 11.87 (Sens: 72.1%, Spec: 88.3%)	Yes	Yes	Yes	Yes
Indrasari et al.[10]	Cross-sectional	223	Yes	Yes	Yes	Sens: 66%, Spec: 62.5%, PPV: 81.4%, NPV: 42.6%, Accuracy: 65.02%	Yes	Yes	Yes	Yes
Jasim & Aouda[11]	Cross-sectional	114	Yes	Yes	Yes	Sens: 95.6%, Spec: 72.7%	Yes	Yes	Yes	Yes
Rashwan et al.[12]	Cross-sectional	300	Yes	Yes	Yes	Sens: 100%, Spec: 100%,	Yes	Yes	Yes	Yes
Alqarni et al.[13]	Cross-sectional (secondary data)	434	No	Yes	Yes	Accuracy 100% Sens: 74%, Spec: 63% (β-TT) Sens: 61%, Spec: 36% (IDA) NPV: 98%, PPV: 79%	Yes	Yes	Yes	Yes
Ahmed et al.[14]	Cross-sectional	65	No	Yes	Yes	Sens: 95.24%, Spec: 93.1%	Yes	Yes	Yes	Yes

off, which improved to 72.1% sensitivity and 88.3% specificity when revised. These findings affirm that the Mentzer Index can serve as a useful and affordable diagnostic screening tool in various populations. Similarly, Jasim & Aouda found it had 95.6% sensitivity and 72.7% specificity in Iraq. This consistency strengthens the case for using the Mentzer Index in pediatric populations across different settings.[9,11,12,14]

However, these findings are not universally replicated. Alqarni et al. (2024) found notably lower performance of the Mentzer Index in a Saudi pediatric cohort, with sensitivity of 74% and specificity of 63% for BTT, and even lower diagnostic power for IDA (sensitivity 61%, specificity 36%). They concluded that the Mentzer Index was not highly reliable, and emphasized its limitations. They hypothesized that genetic variation, age-related red cell changes, severity of iron deficiency, and variability in laboratory techniques might explain these discrepancies.[13]

In Indonesia, Indrasari et al. evaluated several indices in children with hypochromic microcytic anemia and concluded that none provided perfect accuracy. For the Mentzer Index specifically, they found sensitivity of 66%, specificity of 62.5%, PPV 81.4%, NPV 42.6%, and accuracy 65.02%—inferior to the Green & King formula, which performed better with 78.6% sensitivity, 76.6% specificity, and accuracy of 78.03%. These findings suggest that, in low-resource and high-thalassemia-burden settings like Indonesia, the Mentzer Index may be helpful for initial screening, but not as robust as other indices such as Green & King.[10]

Taken together, while studies like those by Rashwan, Ahmed, Uzunoğlu, and Vehapoglu support the high diagnostic value of the Mentzer Index, other studies in different populations demonstrate inconsistent results, underscoring the need to consider local epidemiology, patient characteristics, and laboratory capacity when interpreting these indices. In settings where confirmatory tests like hemoglobin electrophoresis are not readily available, indices like Mentzer, Green & King, and Ehsani may serve as valuable preliminary screening tools, but should not be used in isolation for definitive diagnosis.

Conclusion

This case underscores the limitations of relying solely on red cell indices such as the Mentzer Index in differentiating thalassemia from iron deficiency anemia, especially in settings without access to confirmatory tests. In resource-limited environments, clinical judgment—supported by morphological evaluation—remains crucial for provisional diagnosis, guiding timely intervention and appropriate follow-up until definitive testing can be performed.

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