Mentzer Index and Red Cell Distribution Width Index in differentiating iron deficiency anemia and β-thalassemia trait

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ABSTRACT

The differentiation between iron deficiency anemia (IDA) and β-thalassemia trait (βTT) is essential for managing microcytic hypochromic anemia. Indices such as the Mentzer Index (MI) and Red Cell Distribution Width Index (RDWI) serve as cost-effective preliminary diagnostic tools. This study evaluates the reliability and diagnostic accuracy of these indices. This cross-sectional study included 200 patients with microcytic hypochromic anemia at Khartoum public hospitals in 2021. MI was calculated as mean corpuscular volume (MCV)/red blood cell (RBC) count, and RDWI as (MCV×RDW)/RBC. Sensitivity, specificity, and the Youden Index were determined. Results revealed that among 200 patients, 100 had IDA and 100 had βTT. Both groups showed microcytic hypochromic features, though RBC was slightly elevated in βTT. IDA patients had decreased serum iron, while hemoglobin (Hb) electrophoresis revealed increased HbA2 and HbF in βTT. MI showed a sensitivity of 90% (βTT) and 95% (IDA), with a specificity of 95% and 90%, respectively. RDWI had a sensitivity of 83% (βTT) and 96% (IDA), with a specificity of 96% and 83%. MI had a higher Youden Index (0.85 for βTT). In conclusion, both indices effectively differentiate IDA and βTT, but MI is the most reliable and cost-effective tool.

Introduction

Iron deficiency anemia (IDA) arises from insufficient iron to support hemoglobin (Hb) synthesis, making it the most common hematological disorder in infants and children. Globally, IDA is the leading cause of hypochromic microcytic anemia, predominantly resulting from depleted iron stores in the body. According to the World Health Organization, nearly half of the estimated 1.62 billion anemia cases

worldwide are attributed to iron deficiency.[1] Common causes of IDA include blood loss, poor iron absorption, menstrual bleeding, malabsorption, and epistaxis. In Sudan, IDA is the predominant microcytic anemia, with prevalence rates reported between 23.46% and 76%.[2,3]

Thalassemia, a genetically inherited group of blood disorders, is characterized by microcytic hypochromic anemia due to reduced synthesis of α or β Hb chains.[4] The global prevalence of α- and β-thalassemia gene mutations ranges from 1% to over 80% in malaria-endemic regions.[2] β-thalassemia, caused by point mutations in the β-globin gene, is classified into three types based on the zygosity of the mutation: major (Cooley's anemia), intermediate, and minor [β-thalassemia trait (βTT)]. Major β-thalassemia, resulting from homozygous mutations, leads to a complete absence of β-chains, whereas the trait form is linked to heterozygous mutations with partial β-chain production. Intermediate β-thalassemia lies between the major and minor forms in severity.[5]

Major β-thalassemia typically presents at an early age. Affected infants often exhibit failure to thrive, pallor, recurrent fevers, irritability, feeding difficulties, diarrhea, growth abnormalities, bone deformities, and splenomegaly. It is one of the most prevalent, with an estimated 1.5% of the global population and approximately 60,000 symptomatic births annually, primarily in developing countries. The diagnosis of microcytic hypochromic anemia involves complete blood count (CBC) analysis, peripheral smear evaluation, and specific confirmatory tests like iron profiles, Hb electrophoresis, and molecular studies.[6,7] IDA and βTT share overlapping features such as decreased Hb levels and altered red blood cell (RBC) indices, making it challenging to differentiate them based solely on peripheral blood smears. Effective differentiation requires additional tests, including serum ferritin, serum iron, and HbA2 estimation. βTT typically exhibits elevated HbA2 levels and occasionally increased HbF levels. The utility of various RBC indices, such as the Mentzer Index (MI), distinguishes between these conditions. MI is calculated by dividing the mean corpuscular volume (MCV) by the RBC count; a value greater than 13 typically suggests IDA, while a value less than 13 indicates thalassemia trait.[8,9]

β-thalassemia carriers are often undiagnosed until adolescence or adulthood, detected through hematological screenings that rely on expensive diagnostic methods available in limited facilities. To minimize the cost, time, and complexity of differentiating βTT from IDA, simpler and more accessible diagnostic parameters are crucial. These parameters assist in identifying carriers and avoiding misdiagnosis. A definitive diagnosis of βTT and IDA relies on HbA2 electrophoresis, iron profiles, and molecular analysis. Developing and employing simpler, cost-effective diagnostic methods can significantly reduce the need for expensive and time-intensive procedures.[10,11]

Various formulas have been developed to differentiate between IDA and βTT based on RBC indices. These formulas use parameters such as MCV, RBC count, Hb, mean corpuscular hemoglobin (MCH), MCH concentration, and red cell distribution width (RDW). The goal is to find cost-effective, simple, and easily accessible methods for distinguishing these two conditions, especially in settings with limited resources. Numerous studies have tested these formulas with different cut-off values; However, none have demonstrated ideal sensitivity, specificity, or reliability, indicating the challenge of accurately differentiating between IDA and βTT using RBC indices alone. This cross-sectional study aimed to assess the sensitivity, specificity, and reliability of the Red Cell Distribution Width Index (RDWI) and MI, and evaluate the most reliable for diagnosis.[12,13]

Materials and Methods

This cross-sectional study included 100 known βTT and 100 IDA patients who attended public health hospitals in Khartoum (Sudan) in 2021 and presented with microcytic hypochromic anemia. CBC was performed by a Sysmex machine, followed by serum iron (Roche Cobas 600 analyzer, Mannheim, Germany) and Hb electrophoresis by a TOSHO HPLC machine (Tokyo, Japan) for confirmation. MI was calculated by dividing the MCV by the RBC count, and then compared with the cut-off. A value <13 indicated βTT, while >13 suggested IDA.[12] The study also examined the diagnostic accuracy of RDWI using the formula MCV× RDW/RBC.[13] To evaluate the reliability, sensitivity, specificity, and Youden Index were calculated, statistical analysis was performed, and results were tabulated.[14]

Results

This study highlights the utility of CBC, RBC indices, and newly calculated indices in differentiating βTT from IDA, characterized by microcytic hypochromic anemia (Table 1). In CBC results, the mean Hb, hematocrit (HCT),

Table 1. Formulas used in this study.

Index	Formula
RDWI	MCV × RDW/RBC (1987)[1,13]
MI	MCV/RBC count (1973)[1,12]
PPV	true positive / (true positive + false positive) × 100
NPV	true negative/ (true negative + false negative) × 100[1]
Sensitivity	[true positive/(true positive + false negative)] × 100[14]
Specificity	[true negative/(true negative + false positive)] × 100[14]
The Youden index	sensitivity + specificity – 1[14] The maximum value of the Youden Index is 1 (perfect test) and the minimum is 0 when the test has no diagnostic value[(1)]

MCV, mean corpuscular volume; RDW, red cell distribution width; RBC, red blood cell count; MI, Mentzer Index; RDWI, Red Cell Distribution Width Index; NPV, negative predictive value; PPV, positive predictive value.

and MCV values were lower in IDA compared to βTT, confirming microcytic hypochromic anemia. However, RBCs are more increased in βTT than in IDA (3.9 and 5.77, respectively) (Table 2). Electrophoresis results show higher HbA2 (6.4%) and HbF (1.95%) in βTT with decreased HbA (78.2%) (Table 3). The mean serum iron was decreased in IDA, confirming the iron deficiency group (Table 4). For reliability evaluation using the Youden Index, MI emerged as the most reliable (0.85), followed by RDWI (0.79). MI and IDA demonstrated high sensitivity and specificity (90-95%/83-96%, respectively), making them effective for screening both conditions (Table 5).

Discussion and Conclusions

This research highlights the critical role of CBC, RBC indices, and newly calculated indices in distinguishing βTT from IDA. The results are consistent with previous studies, showing that specific hematological parameters, especially RBC indices and Hb electrophoresis, are essential for differentiating these conditions.

The CBC results reveal expected differences in hematological parameters between IDA and βTT. Mean Hb, HCT, and MCV are significantly lower in IDA compared to βTT, confirming the typical microcytic hypochromic profile of IDA. In contrast, RBC counts are significantly higher in βTT than in IDA, supporting the characteristic erythrocytosis seen in thalassemia carriers.

Hb electrophoresis further differentiates βTT from IDA, with elevated HbA2 and HbF in βTT, along with a relative decrease in HbA. This aligns with the known pathophysiology of β-thalassemia, where reduced β-globin chain synthesis leads to increased compensatory Hb fractions. Conversely, serum iron levels are notably reduced in IDA, confirming iron depletion as the primary cause.

Among the diagnostic indices evaluated, MI and the RDWI are the most reliable in differentiating IDA from βTT. The Youden Index analysis identifies MI (0.85) and RDWI (0.97) as the most effective tools, with high sensitivity and

Table 2. Complete blood count parameters between the study group.

CBC parameters	HB		MCV		HCT		MCH		RBCs	
Disease	IDA	βTT	IDA	βTT	IDA	βTT	IDA	βTT	IDA	βTT
Mean	8.5	10.9	68	59.11	26	33.96	22.2	19.1	3.9	5.77
Minimum	4.9	6.8	44	44.2	15	23.4	12.7	13.3	2	4.1
Maximum	12	15	79	81.8	37	46	28.4	31.8	5.3	7.5
SD	2.1	1.82	7.4	6.52	5.8	4.964	3.27	2.931	0.8	0.81

Hb, hemoglobin; MCV, mean corpuscular volume; HCT, hematocrit; MCH, mean corpuscular hemoglobin; RBCs, red blood cells; IDA, iron deficiency anemia; βTT, β-thalassemia trait.

Table 3. Hemoglobin electrophoresis for the β-thalassemia trait group.

Parameters	HbA	HbA2	HbF
Mean	78.29	6.4	1.948
Minimum	70.1	3.6	0.4
Maximum	87.1	12	10.4
SD	3.076	1.5	1.848

Hb, hemoglobin; SD, standard deviation.

Table 4. Red cell distribution width between the study group and serum iron for the iron deficiency anemia group.

Index	RDW		Serum iron for IDA
Disease	IDA	βTT	Result
Mean	17.7	18.565	32
Minimum	11.7	12.5	13
Maximum	38.1	28.9	42
SD	4.36	2.8235	

RDW, red cell distribution width; IDA, iron deficiency anemia; βTT, β-thalassemia trait; SD, standard deviation.

Table 5. Sensitivity, specificity, and reliability of indices for diagnosis of iron deficiency anemia and β-thalassemia trait.

Index	Cut off	βTT	IDA	Sensitivity	Specificity	NPV%	PPV%	Youden Index
RDWI	<220>220	8317	496	8396	9683	8594.5	95.485	0.79
MI	<13>13	9010	595	9095	9590	90.594.7	94.790.5	0.85

MI, Mentzer Index; RDWI, Red Cell Distribution Width Index; IDA, iron deficiency anemia; βTT, β-thalassemia trait; NPV, negative predictive value; PPV, positive predictive value.

specificity (90-95% and 83-96%, respectively). These findings suggest that MI and RDWI are valuable, cost-effective screening tools for the initial assessment of microcytic hypochromic anemia, especially in resource-limited settings.

In conclusion, both indices showed good discrimination between the two microcytic anemias. However, the MI proved to be the most reliable tool for distinguishing between IDA and βTT, as per the Youden Index. It is preferable to use MI and RDWI together; in combination, they offer a cost-effective approach to diagnosing and managing microcytic hypochromic anemia.

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