Clin. Lab. 2026;72:XXX-XXX
©Copyright

ORIGINAL ARTICLE

Hematological Indices in the Differential Diagnosis of Anemia in Adults

Zeynep Asik, Muhteşem E. Yayla

Adana City Training & Research Hospital, Family Medicine Clinic, Adana, Türkiye

ABSTRACT

Background: **Many different tests are used in the screening and differential diagnosis of anemia, a public health problem that affects approximately one-quarter of the world. The aim of this manuscript was to investigate the effectiveness of hematological indices, which are especially easy to use in community screenings; the Mentzer Index, Green King Index, England Fraser Index, RDW Index, Ricarca Index, Srivastava Index, Shine Lal Index, Ehsani Index, Yau Zhai Wang Index, Matos Carvalho Index, Sirdah Index, and RBC Index.**

Methods: **Patients with beta thalassemia trait, iron deficiency anemia, and sickle cell anemia were retrospectively determined using hemoglobin electrophoresis, ferritin, hemogram, and health records. Then, 12 hematological indices were evaluated in the differentiation of iron deficiency anemia - beta thalassemia trait and in the differential diagnosis of sickle cell anemia. For the distinction between iron deficiency anemia and beta thalassemia trait, region-specific revised cutoff, sensitivity, specificity, AUC, and Youden Index values were calculated. Similarly, indices were evaluated to distinguish patients with sickle cell disease from those without sickle cell disease.**

Results: **Participants were 1,115 people, aged between 18 and 96. Out of them, 55.4% were female and 44.5% were male, and 17.1% (n = 191) of our participants had iron deficiency anemia, 13.9% (n = 155) had beta thalassemia trait, and 16.4% (n = 183) had sickle cell anemia. Mentzer Index, England Fraser Index, RDW Index, Ricarca Index, Srivastava Index, Shine Lal Index, Ehsani Index, Yau Zhai Wang Index, Matos Carvalho Index, Sirdah Index, and RBC Index were found to be successful in the differentiation of iron deficiency anemia, beta thalassemia trait, and in the differential diagnosis of sickle cell anemia (p = 0.000). According to the AUC and Youden Index, the Sirdah Index was the most successful index in differentiating iron deficiency anemia and beta thalassemia trait; the RDW Index and Ricarca Index were the most successful indexes in the differential diagnosis of sickle cell anemia.**

Conclusions: **None of the hematological indices evaluated had 100% sensitivity and specificity. However, most of the indexes were statistically significantly successful. If multiple indices are used in community screening and region-specific revised cutoff values are selected, high-risk individuals can be identified rapidly, with high accuracy, and cost-effectively.**

(Clin. Lab. 2026;72:xx-xx. DOI: 10.7754/Clin.Lab.2025.251202)

Correspondence:
Zeynep Asik
Adana City Training & Research Hospital
Family Medicine Clinic
Dr. Mithat Özsan Bulvari Kişla Mah. 4522 Sok. No.: 1
Yüreğir, Adana
Türkiye
Phone: + 90 5057616415
Email: zynpask@gmail.com
ORCID: 0000-0002-1883-0761

Manuscript accepted December 10, 2025

KEYWORDS

iron deficiency anemia, beta thalassemia trait, sickle cell anemia, hematological indices, differential diagnosis

INTRODUCTION

Anemias are a common group of disorders affecting approximately one-fourth of the world. The global prevalence of anemia is 24.3% (31.2% in women, 17.5% in

men) [1]. Iron deficiency anemia is more frequently observed in developing countries where nutritional problems may occur, while thalassemias and sickle cell anemia are more common in specific geographic regions as genetic mutations play a role in their etiology. Both thalassemia and sickle cell anemia are more frequently seen in the Mediterranean Basin, the Middle East, certain regions of Africa, and India [2,3].

Adana, where the study was conducted, is considered a high-risk region for all of these anemias due to it being a developing area, it being located in a malaria-endemic zone, and it being part of the Mediterranean region where thalassemia is commonly encountered. For this reason, screening the population for anemias, implementing preventive measures, and initiating treatment early when necessary are of vital importance.

There are numerous gold-standard tests used in the differential diagnosis of anemias. Hemoglobin electrophoresis, prenatal and/or postnatal genetic tests, and hemoglobinopathy screening programs are among these. However, challenges may arise regarding cost, turnaround time, and accessibility, preventing adequate population-level screening. Indices used in the differential diagnosis of anemia, on the other hand, are derived from hemogram parameters, making them less expensive, faster, and more accessible. However, none of these indices are used for definitive diagnosis, and their performance varies.

In this study, we planned to compare hematologic indices (Mentzer Index, Green King Index, England Fraser Index, RDW Index, Ricarca Index, Srivastava Index, Shine Lal Index, Ehsani Index, Yau Zhai Wang Index, Matos Carvalho Index, Sirdah Index, RBC Index) [4-15] in distinguishing iron deficiency anemia and beta-thalassemia trait, which are among the most common microcytic anemias, and planned to evaluate the indices in relation to sickle cell anemia, which is also frequently encountered in our region.

Our aim in this research was to analyze 12 indices that can be used in the differential diagnosis of anemia, to determine revised cutoff values specific to our geographic region, and to provide a new perspective regarding their use in clinical practice based on sensitivity, specificity, area under the curve (AUC), and Youden Index (YI).

MATERIALS AND METHODS

The study is a retrospective archive review. The archive of SBÜ Adana City Training and Research Hospital was screened between 01-01-2021 and 04-30-2025. All patients aged 18 years and older who presented to the hospital outpatient clinics for any reason, who had hemogram, hemoglobin electrophoresis, and ferritin values evaluated at the same visit, and who had no known pregnancy were included in the study. The absence of any of these criteria was considered an exclusion criterion. The number of individuals included in the study is 1,115.

To reduce the possibility of bias, all individuals who met the inclusion criteria were included in the study.

Ethics committee approval was obtained for the study from the Scientific Research Ethics Committee of SBÜ Adana City Training and Research Hospital on 05-08-2025 with decision number 499, and the study complied with the Declaration of Helsinki.

IBM SPSS 22.0 software was used for statistical analysis, and $p < 0.05$ was accepted as the level of significance.

The descriptive statistics used were number, percentage, range, mean, and standard deviation. Compliance with normal distribution was assessed using the Kolmogorov-Smirnov test. Fisher's exact test was used for the analysis of categorical variables, and the Mann-Whitney U test and Kruskal-Wallis test were used for the analysis of numerical variables. Additionally, receiver operating characteristic (ROC) curves of the indices examined, revised cutoff values, sensitivity, specificity, area under the curve, and Youden index values were calculated.

In the study, the values of hemoglobin (g/dL), hematocrit (%), RBC (10^6/µL), RDW (%), MCV (fL), MCH (pg), MCHC (g/dL), ferritin (ng/mL), HbA (%), HbA2 (%), HbF (%), HbE (%), and HbS (%) were determined for the participants. The hematologic disorders investigated were first identified using the examined blood markers and were then verified through hospital records.

Validity and reliability studies of all the evaluated indices were conducted, and they have been in use since the 1970s. The indices and their formulas, arranged according to the units used in the study, are as follows [4-15]:

1) Mentzer Index (MCV/RBC)
2) Green & King Index (MCV^2.RDW/100.Hb)
3) England & Fraser Index (MCV-RBC-5Hb-3,4)
4) RDW Index (MCV.RDW/RBC)
5) Ricarca Index (RDW/RBC)
6) Srivastava Index (MCH/RBC)
7) Shine & Lal Index (MCV^2.MCH/100)
8) Ehsani Index (MCV-10.RBC)
9) Yau & Zhai & Wang Index (Hb/MCV)
10) Matos & Carvalho Index
    ((1.91.RBC) + (0.44.MCHC))
11) Sirdah Index (MCV-RBC-3.Hb)
12) RBC Index (RBC)

RESULTS

A total of 1,115 patients aged 18 - 96 years, with a mean age of 41.30 ± 15.62, were included in the study. Out of the participants, 618 (55.42%) were female and 496 (44.48%) were male.

A total of 319 participants (28.61%) had at least one mi-

Table 1. Distribution of hematological parameters and anemias according to mean ± standard deviation.

	All participants (n = 1,115)	Beta thalassemia trait (n = 155)	Iron deficiency anemia (n = 191)	Sickle cell anemia (n = 183)	p *
Hemoglobin	12.037 ± 2.996	11.030 ± 1.801	10.488 ± 1.481	9.511 ± 2.409	0.000
Hematocrit	36.781 ± 8.619	35.035 ± 5.226	33.281 ± 4.129	28.201 ± 6.843	0.000
RBC	4.698 ± 1.082	5.430 ± 0.883	4.748 ± 0.665	3.472 ± 1.195	0.000
RDW	17.079 ± 5.398	17.229 ± 3.674	17.947 ± 4.161	20.042 ± 6.518	0.000
MCV	79.512 ± 11.981	65.130 ± 6.593	70.682 ± 7.877	85.489 ± 13.981	0.000
MCH	26.269 ± 4.956	20.645 ± 2.581	22.425 ± 3.271	29.094 ± 5.745	0.000
MCHC	32.853 ± 1.989	31.635 ± 1.360	31.579 ± 2.046	33.873 ± 1.962	0.000
HbA (n = 1095)	88.347 ± 21.536	93.809 ± 3.189	96.386 ± 5.047	44.463 ± 25.769	0.000
HbA2 (n = 1115)	3.075 ± 1.345	4.829 ± 0.681	2.622 ± 0.990	4.104 ± 2.039	0.000
HbF (n = 403)	3.82 ± 7.792	2.38 ± 3.627	1.16 ± 1.674	6.78 ± 6.614	0.000
HbE (n = 7)	28.43 ± 13.167	-	-	-	-
HbS (n = 183)	48.92 ± 24.615	-	-	48.92 ± 24.615	0.000
Ferritin	144.92 ± 430.771	90.41 ± 139.958	7.67 ± 6.783	426.29 ± 783.180	0.000

*** Beta thalassemia trait, iron deficiency anemia, and sickle cell anemia were compared using the Kruskal Wallis test according to the hematological data examined.**

Table 2. Distribution of hematological indices and anemias according to mean ± standard deviation.

Index	Beta thalassemia trait (n = 155)	Iron deficiency anemia (n = 191)	Sickle cell anemia (n = 183)	p *
Mentzer Index	12.450 ± 3.220	15.322 ± 3.523	28.521 ± 13.802	0.000
Green King Index	117.970 ± 98.795	99.271 ± 64.555	107.348 ± 75.793	0.253
England Fraser Index	1.146 ± 10.689	10.092 ± 8.629	31.059 ± 20.473	0.000
RDW Index	213.307 ± 74.753	271.630 ± 77.176	582.885 ± 357.977	0.000
Ricarca Index	3.272 ± 1.022	3.849 ± 1.026	6.614 ± 3.470	0.000
Srivastava Index	3.949 ± 1.057	4.874 ± 1.302	9.757 ± 4.937	0.000
Shine Lal Index	907.019 ± 341.836	1,167.085 ± 402.543	2,319.85 ± 1,276.160	0.000
Ehsani Index	10.823 ± 13.141	23.197 ± 12.729	50.763 ± 22.559	0.000
Yau Zhai Wang Index	1.704 ± 0.028	1.492 ± 0.020	1.146 ± 0.035	0.000
Matos Carvalho Index	24.92 ± 1.711	22.964 ± 1.324	21.537 ± 2.238	0.000
Sirdah Index	26.607 ± 8.297	34.469 ± 7.663	53.482 ± 17.385	0.000
RBC Index	5.430 ± 0.883	4.748 ± 0.665	3.472 ± 1.195	0.000

*** Beta thalassemia trait, IDA, and sickle cell anemia were compared using the Kruskal Wallis test according to the evaluated indices.**

crocytic anemia. The distribution of disorders identified for the study is shown in Figure 1.

Forty-one (3.67%) of the participants were refugees who had migrated from Syria to Türkiye. The pathologies identified in this group were as follows: 7.31% (n = 3) iron deficiency anemia, 19.51% (n = 8) thalassemia trait, 7.10% (n = 3) sickle cell anemia, and 14.63% (n = 6) polycythemia.

Participants with iron deficiency anemia were identified based on Hb < 12 in women, Hb < 13 in men; MCV < 80; and ferritin < 15 [16]. Out of those with iron deficiency anemia, 83.8% (n = 160) were female and 16.2% (n = 31) were male (p = 0.000). The age range of patients with iron deficiency was 18 - 79 years, with a mean of 37.492 ± 13.419. Twenty-seven individuals

Table 3. Revised cutoff, AUC, and YI distribution for differentiation of beta thalassemia trait and iron deficiency anemia.

Test result variable(s)	Revised cutoff (for TT)	Sensitivity	Specificity	Area under the curve	Std. error	Youden Index	p *
Mentzer Index	< 13.487	82.9	72.9	0.824	0.024	55.8	0.000
Green King Index	< 98.45	76.8	38.7	0.554	0.032	15.5	0.097
England Fraser Index	< 5.470	87.2	69.7	0.812	0.025	56.9	0.000
RDW Index	< 224.272	74.2	72.3	0.836	0.024	46.5	0.000
Ricarca Index	< 3.179	63.2	84.8	0.775	0.027	48.0	0.000
Srivastava Index	< 4.548	79.4	70.1	0.800	0.025	49.5	0.000
Shine Lal Index	< 99.442	78.1	73.8	0.779	0.027	51.9	0.000
Ehsani Index	< 16.35	71.0	84.1	0.831	0.023	55.1	0.000
Yau Zhai Wang Index	> 1.62	65.8	88.4	0.790	0.026	54.3	0.000
Matos Carvalho Index	> 23.801	66.5	84.1	0.787	0.026	50.6	0.000
Sirdah Index	< 29.76	71.0	87.2	0.836	0.023	58.2	0.000
RBC Index	> 5.09	65.8	86	0.788	0.026	51.8	0.000

*** Participants with beta thalassemia trait and iron deficiency anemia were compared using the Mann Whitney U test, respectively, according to the indices listed in the table.**

Table 4. Revised cutoff, AUC, and YI distribution for differential diagnosis of sickle cell anemia.

Test result variable(s)	Revised cutoff	Sensitivity	Specificity	Area under the curve	Std. error	Youden Index	p *
Mentzer Index	> 19.865	66.1	85.3	0.807	0.020	51.4	0.000
Green King Index	> 98.325	33.3	74	0.475	0.024	7.3	0.278
England Fraser Index	> 19.690	68.3	87.3	0.831	0.018	55.6	0.000
RDW Index	> 357.08	70.5	88.4	0.842	0.017	58.9	0.000
Ricarca Index	> 4.234	76	82.9	0.836	0.018	58.9	0.000
Srivastava Index	> 6.487	67.8	82.7	0.808	0.020	50.5	0.000
Shine Lal Index	> 2,212.210	51.4	74.9	0.660	0.023	26.3	0.000
Ehsani Index	> 42.75	60.1	85.1	0.779	0.021	45.2	0.000
Yau Zhai Wang Index	< 1.23	66.7	91.1	0.834	0.018	57.8	0.000
Matos Carvalho Index	< 21.61	63.9	89.1	0.805	0.019	53	0.000
Sirdah Index	> 46.315	61.2	88.4	0.805	0.019	49.6	0.000
RBC Index	< 3.985	67.2	89.2	0.838	0.017	56.4	0.000

*** Participants with and without sickle cell anemia were compared using the Mann Whitney U test, respectively, according to the indices listed in the table.**

(14.1%) with iron deficiency anemia also had thalassemia trait.

Patients with beta-thalassemia trait were identified based on hemoglobin electrophoresis. Participants with HbA2 levels of 3.5 - 8%, HbF levels of 1 - 5%, and HbS of 0% on electrophoresis were accepted as having beta-thalassemia trait. Among participants with beta-thalassemia trait, 58.1% (n = 90) were female and 41.9% (n = 65) were male (p = 0.274). Their age range was 18 - 92 years, with a mean age of 45.200 ± 19.089. Twenty-seven participants (2.42%) had both beta-thalassemia trait and iron deficiency anemia.

Diagnoses of sickle cell anemia were determined based on hemoglobin electrophoresis and medical records. Participants who carried HbS together with other hemoglobins on electrophoresis, who were genetically confirmed to be homozygous for HbS, and whose medical records reflected this condition were accepted as having

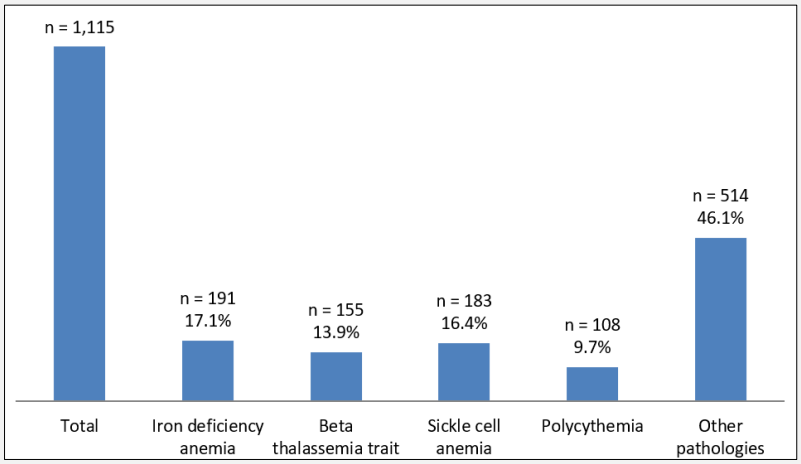


Figure 1. Disease distribution of the participants.

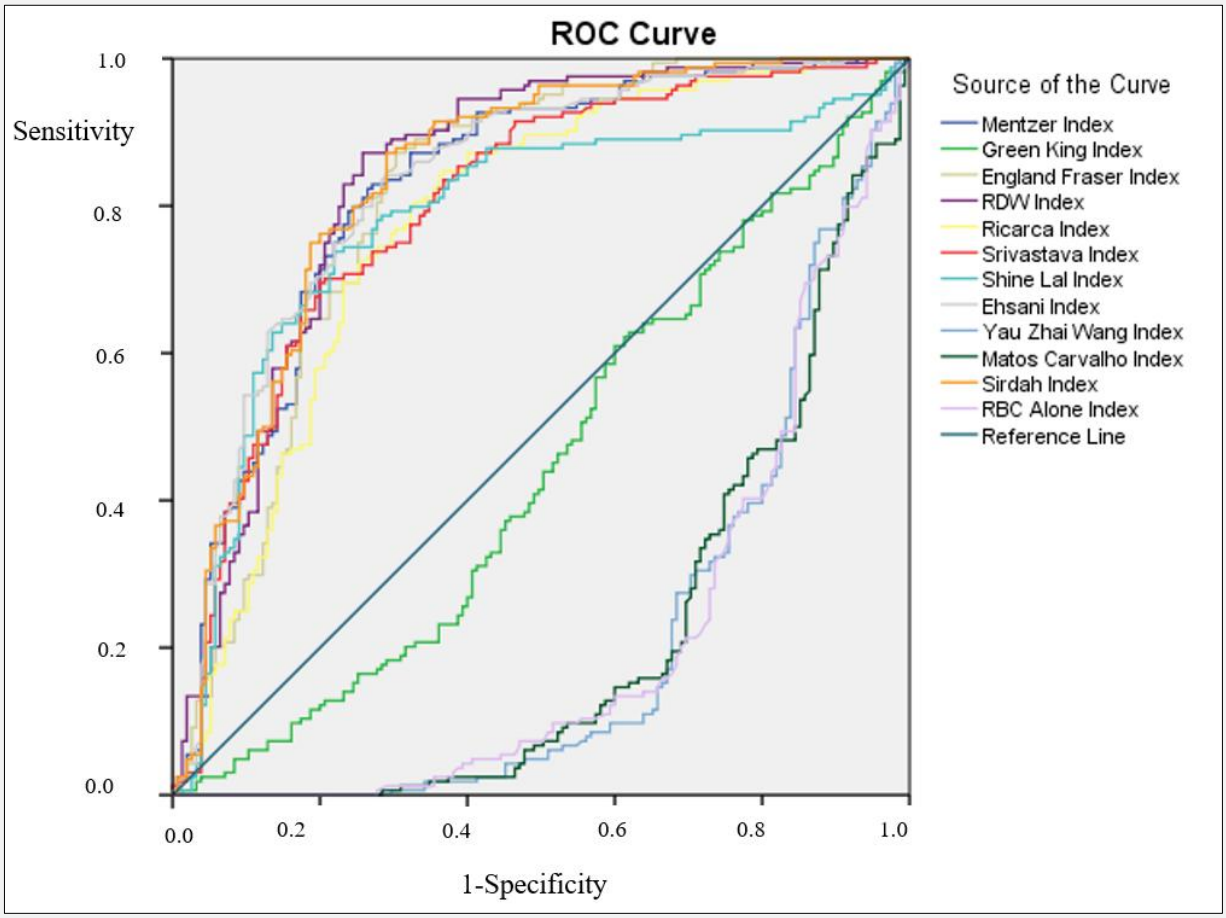


Figure 2. Indices and ROC curves in the differentiation of thalassemia trait and iron deficiency anemia.

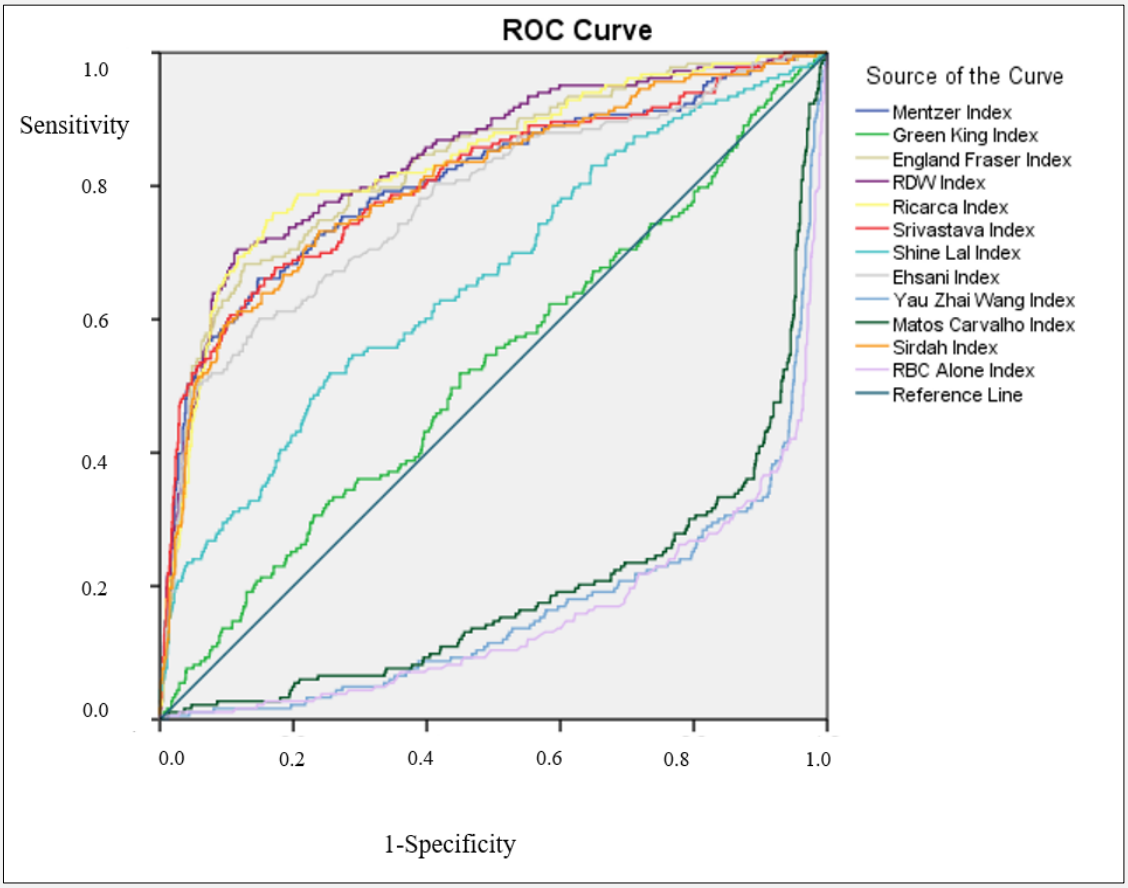


Figure 3. Indices and ROC curves in the differential diagnosis of sickle cell anemia.

sickle cell anemia. Among participants with sickle cell anemia, 59% (n = 108) were female and 41% (n = 75) were male (p = 0.000). No participant with sickle cell anemia had iron deficiency, beta-thalassemia trait, or polycythemia. The mean age of patients with sickle cell anemia was 41.114 ± 12.605.

Polycythemia was evaluated based on the hemogram, and Hb > 18.5 g/dL in men and Hb > 16.5 g/dL in women were accepted as polycythemia. Out of the participants with polycythemia, 97.2% were male (n = 105) and 2.8% (n = 3) were female (p = 0.000). The mean age of patients with polycythemia was 42.925 ± 15.385.

The mean and standard deviations of the participants evaluated blood values are presented in Table 1.

The mean ± standard deviation results of the indices evaluated in the study according to the examined anemic disorders are presented in Table 2.

The revised cutoff values of the indices evaluated in the study for differentiating beta thalassemia trait-iron deficiency anemia and for the differential diagnosis of sickle cell anemia were calculated separately, and the Youden indices were determined. The formula {Youden index = Sensitivity (%) + Specificity (%) - 100} was used in the calculation. In addition, the area under the curve values were calculated.

The results are presented in Tables 3 and 4.

In Table 3, participants with microcytic anemia (n = 319) were evaluated according to the indices for differentiating beta thalassemia trait from iron deficiency anemia. All 12 indices examined were statistically significantly successful in microcytic anemias.

According to the Youden Index, the index with the highest score in distinguishing beta thalassemia trait from iron deficiency anemia was the Sirdah Index. It was followed by the England Frasher Index and the Mentzer Index. The revised cutoff values, AUC, and Youden indices we identified are presented in Table 3. According to this evaluation, values below the cutoff for the Mentzer Index, Green King Index, England Fraser Index, RDW Index, Ricarca Index, Srivastava Index, Shine Lal Index, Ehsani Index, and Sirdah Index favor beta thalassemia trait, whereas values above the cutoff

favor iron deficiency anemia. In addition, for the Yau Zhai Wang Index, Matos Carvalho Index, and RBC Index, values below the cutoff favor iron deficiency anemia, whereas values above the cutoff favor thalassemia trait (Table 3, Figure 2).

Sickle cell anemia is not a microcytic anemia type, and therefore indices such as the Mentzer Index are not frequently used in its differential diagnosis. However, in our study, the second most common anemia type among the participants was sickle cell anemia, and for this reason, the indices commonly used in the differential diagnosis of microcytic anemias were also evaluated for their performance in distinguishing participants with and without sickle cell anemia.

The findings showed that 11 out of the 12 indices examined in the study were statistically significantly successful in distinguishing individuals with sickle cell anemia from those without sickle cell anemia (Mentzer Index, England Fraser Index, RDW Index, Ricarca Index, Srivastava Index, Shine Lal Index, Ehsani Index, Yau Zhai Wang Index, Matos Carvalho Index, Sirdah Index, RBC Index) (Table 4). According to the Youden Index, the indices that best distinguished sickle cell anemia were, respectively, the RDW Index, Ricarca Index, and RBC Index. The revised cutoff values, AUC, and Youden Indices we determined are presented in Table 4. Accordingly, for the Mentzer Index, Green King Index, England Fraser Index, RDW Index, Ricarca Index, Srivastava Index, Shine Lal Index, Ehsani Index, and Sirdah Index, values above the cutoff favor sickle cell anemia; for the Yau Zhai Wang Index, Matos Carvalho Index, and RBC Index, values below the cutoff favor sickle cell anemia (Table 4, Figure 3).

The ROC curves of some of the indices we evaluated for the differentiation between beta thalassemia trait and iron deficiency anemia and for the assessment of sickle cell anemia are shown in Figures 2 and 3.

DISCUSSION

The participants in our study were adults aged 18 years and older. The most frequent hematologic pathologies, in descending order, were iron deficiency anemia at 17.1%, sickle cell anemia at 16.4%, beta thalassemia trait at 13.9%, and polycythemia at 9.7%.

In a study conducted in Türkiye in 2023 [17], the rate of iron deficiency was 20.3%, in a study carried out among elderly individuals in Switzerland [18] it was 28.3%, and in another study evaluating individuals aged 20 - 65 years in Iran [19] it was 10.86%. As seen, iron deficiency anemia, which may result from inadequate nutrition and/or absorptive pathologies, is a common disease, and its prevalence varies by region. The prevalence of iron deficiency anemia in our study is consistent with the literature.

According to the World Health Organization, the prevalence of thalassemia trait is 2% in Bahrain, 9% in Egypt, and 3% in Lebanon [20]. In our study, the rate of beta thalassemia trait was considerably higher than these rates. Adana being a city located on the Mediterranean coast may have an influence on this situation.

Sickle cell anemia affects approximately 100,000 individuals in the USA and 20,000 individuals in Europe [21]. The high rates observed in our study also provide insight into the prevalence of sickle cell anemia (16.4%) in the region where we conducted the research and highlight the importance of the disease for the community.

The differentiation between iron deficiency anemia and beta thalassemia, two of the most commonly encountered microcytic anemias, was evaluated through 12 indices. According to our data, beta thalassemia carriers scored 12.45 ± 3.22 and individuals with iron deficiency anemia scored 15.32 ± 3.52 based on the Mentzer Index. In a similar study conducted in India, female beta thalassemia carriers scored 12.4 ± 0.9 and those with iron deficiency anemia scored 15.6 ± 0.8 based on the Mentzer Index [22]. Our results are parallel to each other.

According to the YI, in our study the indices with the highest scores in distinguishing iron deficiency anemia and beta-thalassemia were, respectively, the Sirdah Index, the England Frasher Index, and the Mentzer Index. In another study examining hematologic indices, the YI ranking was RBC Index, RDWI, and Mentzer [23]. The results differ from each other, but all of these indices (Sirdah Index, England Frasher Index, Mentzer Index, RBC Index, RDWI Index) were found to be statistically significantly successful in distinguishing iron deficiency anemia and beta-thalassemia trait (Table 3). According to another study published in Adana in 2021 (n = 92), the indices with the highest YI for distinguishing iron deficiency anemia and beta-thalassemia trait were, respectively, the Sirdah Index, the Ehsani Index, and the Mentzer Index [24]. It is noteworthy that studies conducted in the same region at different times and with different sample sizes yielded similar results. These findings suggest that the indices to be used may appropriately be selected according to the local characteristics of the region.

In the study, revised cutoff values were calculated for all indices to be used in distinguishing iron deficiency anemia and beta-thalassemia (Table 3). Similarly, revised cutoff values for the indices were calculated in a study conducted in China [25]. Although the cutoff values from the period when the indices were first published and the revised cutoff values are close to each other, there are differences [4-15]. These differences may result from the time the studies were conducted, the study setting, sample size, and regional characteristics. Therefore, using local revised cutoffs in differential diagnosis may be beneficial, when possible.

The second most common anemia encountered in the study was sickle cell anemia (16.4%). We first identified these patients according to hemogram electrophoresis and then confirmed the accuracy of the diagnosis from medical records. Sickle cell anemia is a type of

anemia caused by an HbS point mutation and has protective effects against malaria [26]. Various screening programs have been implemented at different times to prevent complications of sickle cell anemia [26]. However, these screenings have sometimes been disrupted due to fear of stigmatization. In our study, we analyzed the effectiveness of the indices we evaluated in the differential diagnosis of sickle cell anemia. We sought to answer the question, "Can these hematological indices be used in sickle cell anemia screening?" Our results are presented in Table 4. Particularly the RDW Index, the Ricarca Index, and the You Zhai Wang Index were found to be successful in distinguishing individuals with sickle cell anemia from those without anemia.

According to a study published in Egypt, Mentzer Index, RDW Index, Shine Lal Index, Srivastava Index, Ricerca Index, and Huber-Herclotz Index were found to be statistically significant in the comparison of sickle cell anemia and control group [27]. Our results are similar (Table 4). In sickle cell anemia screenings, we think it may be useful to use the Mentzer index, RDW Index, Ricarca Index, Srivastava Index, Shine Lal Index, Yau Zhai Wang Index, and Matos Carvalho Index with cut-off values revised according to the characteristics of the study region, as they may help identify individuals in the at-risk group.

According to the October 2025 price list of a private laboratory, hemoglobin electrophoresis costs 11.54 Euros, while a complete blood count costs 1.73 Euros. The difference between the fees is approximately sevenfold. Therefore, in population-based screenings, utilizing the complete blood count and indices, and performing hemoglobin electrophoresis only if the individual is symptomatic or falls into the at-risk group according to the indices used, is cost-effective.

None of the indices we investigated have 100% sensitivity and specificity either in the differentiation of beta thalassemia trait and iron deficiency anemia or in the differential diagnosis of sickle cell anemia. Nevertheless, statistically significant results were obtained.

Although the indices do not replace electrophoresis in definitive diagnosis, Sirdah Index, England Fraser Index, and Mentzer Index were found to be the most successful in differentiating beta thalassemia trait and iron deficiency anemia. In the differential diagnosis of sickle cell anemia, RDW Index, Ricarca Index, and RBC Index were the most successful indices.

In patients for whom anemia differential diagnosis will be performed, especially after the detection of microcytic anemia, evaluation using multiple indices will increase sensitivity and specificity. In addition, using cut-off values determined specifically for the patient's region and age group will be cost-effective and will strengthen the diagnosis. Such an approach can be used for screening purposes, particularly in areas with a high prevalence of anemia.

Source of Support:
The research did not receive any grant, equipment, nor drug support.

Declaration of Generative Artificial Intelligence in Scientific Writing:
The authors declare that generative artificial intelligence was not used in their scientific writing.

Declaration of Interest:
The authors declare that they have no conflicts of interests.

References:

1. GBD 2021 Anaemia Collaborators. Prevalence, years lived with disability, and trends in anaemia burden by severity and cause, 1990-2021: findings from the Global Burden of Disease Study 2021. Lancet Haematol 2023 Sep;10(9):e713-e734. (PMID: 37536353)

2. Sicle Cell Disease, World Health Organisation. https://www.who.int/news-room/fact-sheets/detail/sickle-cell-disease

3. CDC Thalassemia, About Thalassemia. https://www.cdc.gov/thalassemia/about/index.html#:~:text=Traits%20for%20thalassemia%20are%20more,out%20if%20you%20have%20thalassemia

4. Mentzer WC Jr. Differentiation of iron deficiency from thalassemia trait. Lancet 1973 Apr 21;1(7808):882. (PMID: 4123424)

5. Green R, King R. A new red cell discriminant incorporating volume dispersion for differentiating iron deficiency anemia from thalassemia minor. Blood Cells 1989;15(3):481-91; discussion 492-5. (PMID: 2620095)

6. England JM, Fraser PM. Differentiation of iron deficiency from thalassaemia trait by routine blood-count. Lancet 1973 Mar 3;1(7801):449-52. (PMID: 4120365)

7. Jayabose S, Giamelli J, Levendoglu-Tugal O, Sandoval C, Özkaynak F, Visintainer P. #262 Differentiating iron deficiency anemia from thalassemia minor by using an RDW-based index. J Pediatr Hematol Oncol 1999;21(4):314. https://journals.lww.com/jpho-online/citation/1999/07000/_262_differentiating_iron_deficiency_anemia_from.40.aspx

8. Ricerca BM, Storti S, d'Onofrio G et al. Differentiation of iron deficiency from thalassaemia trait: a new approach. Hematologica. 1987 Sep-Oct;72(5):409-13. (PMID: 3121463)

9. Srivastava PC. Differentiation of thalassemia minor from iron deficiency. Lancet 1973 Jul 21;2(7821):154-5. (PMID: 4124080)

10. Shine I, Lal S. A strategy to detect beta-thalassaemia minor. Lancet 1977 Mar 26;1(8013):692-4. (PMID: 66486)

11. Ehsani MA, Shahgholi E, Rahiminejad MS, Seighali F, Rashidi A. A new index for discrimination between iron deficiency anemia and beta-thalassemia minor: results in 284 patients. Pak J Biol Sci 2009 Mar 1;12(5):473-5. (PMID: 19579993)

12. Yao QC, Zhai HL, Wang HC. Ratio of hemoglobin to mean corpuscular volume: A new index for discriminating between iron deficiency anemia and thalassemia trait. World J Clin Cases 2023 Dec 16;11(35):8270-5. (PMID: 38130603)

13. Matos JF, Dusse LM, Borges KB, de Castro RL, Coura-Vital W, Carvalho Md. A new index to discriminate between iron deficiency anemia and thalassemia trait. Rev Bras Hematol Hemoter 2016 Jul-Sep;38(3):214-9. (PMID: 27521859)

14. Sirdah M, Tarazi I, Al Najjar E, Al Haddad R. Evaluation of the diagnostic reliability of different RBC indices and formulas in the differentiation of the beta-thalassaemia minor from iron deficiency in Palestinian population. Int J Lab Hematol 2008 Aug;30(4): 324-30. (PMID: 18445163)

15. Klee GG, Fairbanks VF, Pierre RV, O'Sullivan MB. Routine erythrocyte measurements in diagnosis of iron-deficiency anemia and thalassemia minor. Am J Clin Pathol 1976 Nov;66(5):870-7. (PMID: 983994)

16. World Health Organisation. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and Mineral Nutrition Information System 2011. https://www.who.int/publications/i/item/WHO-NMH-NHD-MNM-11.1

17. Kaplanoğlu E, Özbalcı D, Alanoğlu EG, Gürdal O. The Prevalance of Iron Deficiency Anemia in Adults in Hospital of Isparta Suleyman Demirel University And Evaluation of Etiological Factors. Med J SDU 2023;30(1):1-9. https://dergipark.org.tr/en/pub/sdutfd/issue/76153/1264115

18. Nilsson-Ehle H, Jagenburg R, Landahl S, Svanborg A. Blood hemoglobin declines in the elderly: implications for reference intervals from age 70 to 88. Eur J Haematol 2000 Nov;65(5):297-305. (PMID: 11092459)

19. Akbarpour E, Paridar Y, Mohammadi Z et al. Anemia prevalence, severity, types, and correlates among adult women and men in a multiethnic Iranian population: the Khuzestan Comprehensive Health Study (KCHS). BMC Public Health 2022 Jan 25;22(1): 168. (PMID: 35073904)

20. World Health Organization and Thalassaemia International Federation. Management of haemoglobin disorders - report of Joint WHO-TIF meeting 2007. https://iris.who.int/items/0baf2cb8-2534-41ef-95f1-5ca6488c2e32

21. Matte A, Zorzi F, Mazzi F, Federti E, Olivieri O, De Franceschi L. New Therapeutic Options for the Treatment of Sickle Cell Disease. Mediterr J Hematol Infect Dis 2019 Jan 1;11(1):e2019002. (PMID: 30671208)

22. Odhwani J, Dholakia MK, S, Kangad G et al. Differentiating iron deficiency anaemia and β thalassemia trait based on red cell indices- an economic way to health care in a resource limited setup. International Journal of Research in Medical Sciences 13(5), 2036-2041. https://www.msjonline.org/index.php/ijrms/article/view/15021

23. Miri-Aliabad GH, Asgarzadeh L, Sedaghatyan S. Diagnostic Value of Red Blood Cell Indices in Differentiating Iron Deficiency Anemia From Beta Thalassemia Trait. Journal of Pediatrics Review 2025;13(3):249-56. https://jpr.mazums.ac.ir/article-1-695-en.pdf

24. Balci T, Ayan D, Türkyürek C, E Yaylagül E. Evaluation of diagnostic accuracy tests of erythrocyte indexes in the differential diagnosis of beta thalassemia minor and iron deficiency anemia: A preliminary report. Cukurova Med J 2021;46(3):1009-1017. https://dergipark.org.tr/en/pub/cumj/issue/62102/905007

25. Xiao H, Wang Y, Ye Y et al. Differential diagnosis of thalassemia and iron deficiency anemia in pregnant women using new formulas from multidimensional analysis of red blood cells. Ann Transl Med 2021 Jan;9(2):141. (PMID: 33569443)

26. Naik RP, Haywood C Jr. Sickle cell trait diagnosis: clinical and social implications. Hematology Am Soc Hematol Educ Program 2015;2015(1):160-7. (PMID: 26637716)

27. Khaled SAA, Ahmed HA, Elbadry MI, NasrEldin E, Hassany SM, Ahmed SA. Hematological, Biochemical Properties, and Clinical Correlates of Hemoglobin S Variant Disorder: A New Insight Into Sickle Cell Trait. J Hematol 2022 Jun;11(3):92-108. (PMID: 35837371)