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EVALUATION OF THE UTILITY OF HEMATOLOGICAL INDICES FOR DIFFERENTIAL DIAGNOSIS OF BETA THALASSEMIA TRAIT AND IRON DEFICIENCY ANEMIA: A META ANALYSIS

Immunohematology

Dr. Nidhi Bhatnagar	Professor & Head, Dept. of IHBT, B.J. Medical College , Ahmedabad.
Dr. Mamta Shah	Assistant professor, Dept. of IHBT, B.J. Medical College , Ahmedabad.
Dr. Sangita Shah	Assistant professor, Dept. of IHBT, B.J. Medical College , Ahmedabad.
Dr. Drashti Gajera	Resident doctor, MD IHBT, Dept. of IHBT, B.J. Medical College , Ahmedabad.
Dr. Anu Patel	Resident Doctor, MD IHBT, Dept. of IHBT, B.J. Medical College, Ahmedabad.
Dr. Vaishnavi. P	Resident Doctor, MD Pathology, Dept. of Pathology, B.J. Medical College, Ahmedabad.

ABSTRACT

Background/Objectives: β-thalassemia trait (βTT) and iron deficiency anemia (IDA) are most regularly reported microcytic anemia disorders. We aimed at evaluating the utility of various hematological indices in the differentiation of iron deficiency anemia and beta-thalassemia trait. **Methods:** In this study, a total of 70 Patients aged between 3-52 years diagnosed with IDA (supported by iron studies) or βTT (supported by HPLC) were included. The Hemoglobin values ranged 7.5-11.6gm/dl. Hematological parameters like Hemoglobin, Mean Corpuscular Volume, Mean Corpuscular Hemoglobin, Red Blood Cell Distribution Width, Mean Corpuscular Hemoglobin Concentration and Red Blood Cell count which were measured by Horiba pentra XLR automated hematology analyzer for each case. 12 discrimination indices(DIs) namely Red blood distribution width index(RDWI),Red blood cell count, Mentzer index, Shine and Lal, England and Fraser(E&FI), Srivastava, Green and King(G&KI), Ricerca, Sirdah, and Ehsani indices; Mean density of hemoglobin/ litre of blood; Mean cell density of hemoglobin in all patients were calculated using above hematological parameters. We also calculated sensitivity, specificity, positive & negative predictive value and yoden's index of each DIs to assess the diagnostic accuracy of DIs. **Results:** RBC count, Mentzer index and RDWI were the most sensitive and specific for both IDA and TT. **Conclusion:** All twelve DIs have variable sensitivity and specificity. However, these hematological indices which are routinely performed offer rapid, reliable and cost effective method in distinguishing βTT and IDA.

KEYWORDS

β-Thalassemia trait, Iron deficiency anemia, Mentzer index.

INTRODUCTION:

βTT and IDA are among the most regularly reported microcytic anaemia. A definitive differential diagnosis between beta thalassemia trait (βTT) and IDA is based on the HbA2 electrophoresis, serum iron levels and ferritin. However, these tests are expensive and time consuming. Several Discrimination Indices (DI's) have been proposed by number of workers using the possibility of RBC indices to overcome these short comings. Various CBC based discrimination indices like Mentzer's index, Green and King index, Shine and Lal index, etc., have been published and evaluated for screening of BTT. These indices can be used as preliminary screening tools which can help distinguish between IDA & BTT. The purpose of using indices in anemia is to detect patients who have a high probable diagnosis of βTT and IDA and appropriate follow up.

BACKGROUND/OBJECTIVES:

We aimed at evaluating the utility of various hematological indices in the differentiation of iron deficiency anemia and beta-thalassemia trait.

METHODS:

- Retrospective study
- Sample size: 70
- Patients Age range: 3-52 years.
- Inclusion criteria: **1.** Hemoglobin range: 7.5-11.6 gm/dl. **2.** MCV : < 80 fl ; MCH: < 27 pg **3.** Patients diagnosed with IDA (supported by iron studies) or βTT (supported by HPLC).

Discrimination Indices(DI's) /Hematological Indices :

1) Red blood distribution width index (RDWI) **2)** Red blood cell count **3)** Mentzer index **4)** Shine and Lal **5)** England and Fraser (E&FI) **6)** Srivastava **7)** Green and King (G&KI) **8)** Ricerca **9)** Sirdah **10)** Ehsani indices **11)** Mean density of hemoglobin/litre of blood **12)** Mean cell **2)** density of hemoglobin

Table 1 : Different RBC Indices And Their Mathematical Formulas[1-10]

Hematological index	Formula
Mentzer Index	MCV/ RBC
RDWI	MCV × RDW/RBC
Shine and Lal	MCV × MCV × MCH/100
Srivastava	MCH/RBC
Green and King	MCV × MCV × RDW/Hb × 100
Sirdah	MCV − RBC − (3 × Hb)
Ehsani	MCV − (10 × RBC)
England and Fraser	MCV − (5 × Hb) − RBC − 3.4
Ricerca	RDW/RBC
MDHL	(MCH/MCV) × RBC
MCHD	MCH/MCV

Peripheral Smear :

A. Iron Deficiency Anemia B. Beta Thalassemia Trait

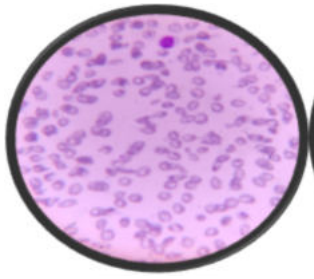

Figure: 1 **Figure: 2**

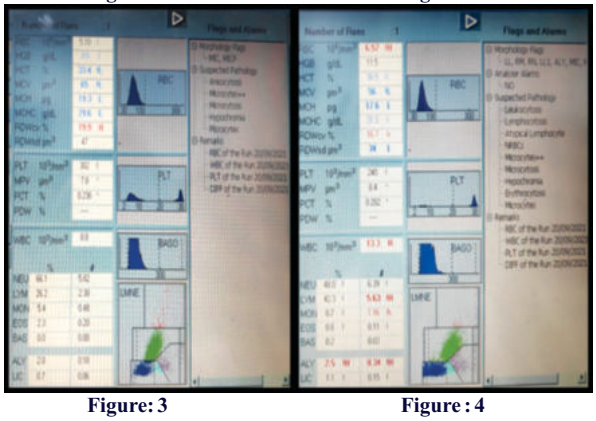

Figure: 3 **Figure : 4**

HPLC GRAPH

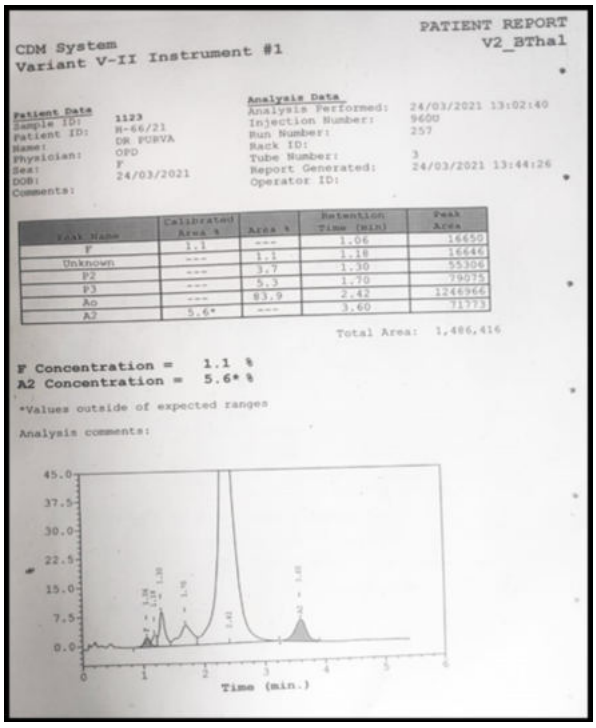

Figure:5

RESULT

Data were analyzed with computerized statistical package for social sciences (SPSS) version 15.0. 12 . The 12 discrimination indices used in the evaluation are calculated and summarized in **Table 2**.

Table 2: Results Obtained From Each Discrimination Index With Their Cutoff's And Correctly Identified Number Of Cases.

INDICES		βTT (n=37)	IDA (n=33)	No. correctly diagnosed	No. correctly diagnosed
MENTZER	βTT<13 IDA>13	26 11	11 22	48(26+22)	68.57
RBC COUNT	βTT <5 IDA>5	9 24	9 24	51(27+24)	72.85
RDWI	βTT <220 IDA>220	24 9	24 9	25(16+9)	35.71
SHINE AND LAL	βTT <1530 IDA>1530	32 1	32 1	32(31+1)	45.71
SHRIVASTAVA	βTT <3.8 IDA>3.8	9 24	9 24	34(10+24)	48.57
GREEN AND KING	βTT <65 IDA>65	21 12	21 12	22(10+12)	31.42
SRIDAH	βTT <27 IDA>27	10 23	10 23	33(10+23)	47.14
EHSANI	βTT <15 IDA>15	11 22	11 22	36(9+27)	47.14
E & F	βTT <0 IDA>0	6 27	6 27	36(18+18)	51.42
RICERCA	βTT <4.4 IDA>4.4	15 18	15 18	36(18+18)	51.42
MDHL	βTT >1.63 IDA<1.63	7 26	7 26	39(13+26)	55.71
MCHD	βTT >0.3045 IDA<0.3045	25 8	25 8	30(22+8)	42.85

Table 3 : Statistical Results Obtained From Each Discrimination Index To Discriminate Between βTT And IDA In 70 Patients.

INDICES	βTT IDA	SENSITIVITY	SPECIFICITY	PPV	NPV	YI
MENTZER	βTT	70.27	66.66	70.27	66.66	36.93
	IDA	66.66	70.27	66.66	70.27	36.93
RBC COUNT	βTT	72.97	72.72	75	70.5	45.7
	IDA	72.72	72.97	70.58	75	45.7
RDWI	βTT	43.24	27.27	40	30	29.48
	IDA	27.27	43.24	30	14.28	29.48
SHINE AND LAL	βTT	83.78	3.03	49.2	49.2	13.18
	IDA	3.03	83.78	14.28	47.05	13.18
SHRIVASTAVA	βTT	27.02	72.72	52.63	52.63	0.24
	IDA	72.72	27.02	47.05	30.7	0.24
GREEN AND KING	βTT	27.02	36.36	32.25	32.25	36.6
	IDA	36.36	27.02	30.76	46	36.6
SRIDAH	βTT	17.02	69.69	50	46	3.27
	IDA	69.69	27.02	46	50	3.27
EHSANI	βTT	29.72	66.66	50	45.83	3.6
	IDA	66.66	29.72	45.83	50	3.6
E & F	βTT	24.32	81.81	60	49.09	6.14
	IDA	81.81	24.32	49.09	60	6.14
RICERCA	βTT	48.64	54.54	54.54	48.64	3.19
	IDA	54.54	48.64	48.64	54.54	3.19
MDHL	βTT	78.78	78.78	65	52	13.92
	IDA	35.13	35.13	52	65	13.92
MCHD	βTT	24.24	24.24	48.8	34.78	16.29
	IDA	59.45	59.45	34.78	46.8	16.27

DISCUSSION:

Thalassemia is a group of inherited anemia caused from mutations in the β-globin gene (β-thalassemia) or α-globin gene (α-thalassemia) that cause the defective in hemoglobin (Hb) synthesis[12]. Beta-thalassemia syndromes are the group of hereditary anemia characterized by a genetic lack or deficiency in the synthesis of β-globin chains, [13]. Heterozygous state or β-thalassemia minor or β-thalassemia trait, cause mild to moderate microcytic anemia, resulting in a decrease in the β-globin protein synthesis by approximately 50%[12].

Iron-deficiency anemia is the most type of anemia.It is more prevalent in women and children in India. Iron deficiency may occur due to inadequate dietary iron intake, malabsorption of iron, chronic blood loss, diversion of iron to fetal and infant erythropoiesis during pregnancy and lactation, intravascular hemolysis with hemoglobinuria, diversion of iron to nonhematopoietic tissues such as the lung, genetic factors, or a combination of these factors.

Distinguishing βTT from IDA has important clinical implications since cause, prognosis, and treatment differ in each disease. Misdiagnosis of βTT has consequences for potential homozygous offspring. The HbA2 analysis is considered the gold standard for diagnosing thalassemia. However, concomitant vitamin B12 or folic acid deficiency and double heterozygous δβ-thalassemia alter HbA2 levels in βTT . If a discrimination index have high sensitivity, specificity, positive and negative predictive value and Youden's index, then that discrimination index has better differential performance. In studies by Demir et al [10] and Beyan et al [11] RBC count was the reliable index ,similar to the present study.

In a study by Ferrara et al.[14] RDWI had the highest sensitivity , that the England and Fraser index had the highest specificity and highest Youden's index, and that the Green and King index had the highest efficiency.

All twelve DIs have variable sensitivity and specificity. However, these hematological indices which are routinely performed offer rapid, reliable and cost effective method in distinguishing βTT and IDA. In places where the incidence of thalassemia is high, Identifying carriers and counselling them about the genetic implications of marrying another carrier is the most effective method for preventing β-thalassemia major.

CONCLUSION:

The overall most useful index was found to be RBC count followed by Mentzer index . The Shine and Lal had sensitivity of (83.78 %) had low specificities for correctly identifying IDA (3.03 %). None of the indices studied, demonstrated 100 % precision in recognizing Btt. Youden's index showed the following ranking with respect to the indices's ability to distinguish between BTT and IDA **RBC Count > Mentzer index > Green and King > RDWI > MCHD > MDHL > Shine and Lal > Ehsani > Sirdah > England and Fraser > Ricerca > Srivastava index.**

Conflicts Of Interest: There are no conflicts of interest.

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