



TO DISTINGUISH BETA THALASSEMIA TRAIT FROM IRON DEFICIENCY ANEMIA USING HAEMATOLOGICAL INDICES – A CROSS SECTIONAL STUDY

Paediatrics

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ABSTRACT

The difference between iron deficiency anaemia and Beta thalassemia trait (BTT) is confounded since the symptoms of anaemia are similar. Thus, it is important to differentiate between iron deficiency anaemia and thalassemia trait. Nowadays, differential diagnosis is done through time- and money-consuming laboratory procedures. The objective of the study was to differentiate beta thalassemia trait from IDA by reliable parameter based on haematological indices with cost effective routine CBC parameters in paediatric population. A cross sectional study was done among the 150 patients suffering from beta thalassemia trait and Iron deficiency Anemia, admitted in a tertiary care hospital at West Godavari district, Andhra Pradesh. Various indices were used in this study - Mentzer, Srivastava, Ricerca, Green and King, Sirdah and Ehsani indices for differentiating BTT from IDA. Among all the Indices, diagnostic accuracy by Ehsani and Mentzer indices were found to be the highest Area under Curve (AUC). The data shows that Srivastava and Sirdah indices presents the highest sensitivity. Ehsani and Mentzer indices presents the highest specificity. The study concluded that the CBC-based indices, particularly those developed by Mentzer, Ehsani, Green and King, Ricerca, Sirdah, and Sirvistava, were valid diagnostic tools for differentiating BTT from IDA in developing nations with scarce healthcare resources

KEYWORDS

INTRODUCTION:

The heterozygous disease known as beta-thalassemia trait (BTT), also known as beta-thalassemia minor, which affects only one beta-globin gene. Majority of BTT patients exhibit no symptoms, and their microcytosis is identified incidentally when their complete blood count (CBC) is performed. Iron deficiency anaemia (IDA), BTT, anaemia of chronic disease (ACD), lead poisoning, and sideroblastic anaemia are common causes of microcytosis. More than 3.5 billion people in developing nations suffer from iron deficiency anaemia, reducing vitality for the young and hinders children's cognitive development. (1)

The difference between iron deficiency anaemia and Beta thalassemia trait (BTT) is confounded since the symptoms of anaemia are similar. Thus, it is important to differentiate between iron deficiency anaemia and thalassemia trait. Nowadays, differential diagnosis is done through time- and money-consuming laboratory procedures. Complete blood count (CBC), Hemoglobin A2 (HbA2), and electrophoresis techniques are used to diagnose BTT. Simple tests like the CBC or measures of iron and serum ferritin can be used to diagnose IDA(2)

Many indices and equations, such as red cell indices generated from automated red cell analyzers, such as RBC, haemoglobin (Hb), mean cell volume (MCV), and red cell distribution width (RDW) have been published to differentiate between IDA and BTT patients. However, none of these indices, in contrast to IDA and TT, have 100% sensitivity (SENS) and 100% specificity (SPEC). Also, there aren't many research evaluating the validity of various approaches in the paediatric age group.

The measurement of serum ferritin, serum iron, and HBA2 is the gold standard for the diagnosis of IDA and BTT. Nevertheless, especially in developing nations like India, these criteria are expensive and time-consuming for the public health financial system. Hence, the diagnosis of IDA and BTT can be made utilising a variety of affordable and cost effective haematological indices. So the objective of this study was to differentiate beta thalassemia trait from IDA by reliable parameter based on haematological indices with cost effective routine CBC parameters in paediatric population. (6)

METHODOLOGY:

A cross sectional study was conducted from August 2021 – March 2022 among the patients suffering from beta thalassemia trait and Iron deficiency Anemia, admitted in a tertiary care hospital at West Godavari district, Andhra Pradesh. The study was done in the

paediatric department of ASRAM hospital, Eluru. Children of 5-18 years age group with Hb levels between 8.7 – 11.4 g/dl, MCV 70 FL in children above 6 years of age and MCV 70 under the age of 6 years were included in the study. Children who were resistant to iron replacement, receiving iron replacement for three months or longer without clinical or laboratory improvement, who had stopped iron therapy for at least one month, children with acute or chronic inflammation, infectious disease, acute bleeding, or children who had received a blood transfusion in the previous three months, children with lead poisoning were all excluded from the study.

Data was collected using a pretested semi structured questionnaire for general information and calculation of the various indices. The blood samples of the patients were taken for complete blood picture analysis and red cell indices were noted. Various indices used in this study are Mentzer, Srivastava, Ricerca, Green and King, Sirdah and Ehsani indices (Table 1)

Table 1: Indicators for distinction between β -TT and IDA (6)

Indices	Calculation	Cut-off β -TT	Cut-off IDA
Mentzer	MCV/RBC	<13	>13
Srivastava	MCH/RBC	<3.8	>3.8
Ricerca	RDW/RBC	<4.4	>4.4
Green and King	$(MCV \times RDW) / (100 \times HB)$	<65	>65
Sirdah	$MCV - (3 \times Hb)$	<27	>27
Ehsani	$MCV - (10 \times RBC)$	<15	>15

Data was entered in a Microsoft Excel spreadsheet and analysed using Statistical Package for social sciences (SPSS) software version 17. The socio-demographic data and indices were expressed in terms of means and proportions. Test of significance was done using an independent T-test for two groups BTT and IDA. Sensitivity and specificity were determined using ROC Curves. A p-value of less than 0.05 was considered significant.

RESULTS:

A total of 150 children of which 100 are suffering from beta thalassemia trait and 50 from Iron deficiency Anemia were included in the study. Majority of the study population were found between 6-10 years age group for BTT and <5 years for IDA (Table 2). All the red cell parameters and indices were found to be significant for the two groups BTT and IDA (Table 3 & 4)

Table 2: Socio demographic factors of the two groups

Socio demographic factors	BTT (N=100)	IDA (N=50)
Age		
<5 years	29% (29)	76% (38)
6-10 years	68% (68)	24% (12)
>10 years	3% (3)	0
Gender		
Boys	45% (45)	40% (20)
Girls	55% (55)	60% (30)

Table 3: Association between the groups and the parameters

Parameters	Group	N	Mean	Std. Deviation	P value
RBCs	BTT	100	5.077	.4684	<0.001
	IDA	50	3.624	.5097	
Hb	BTT	100	9.292	.7687	<0.001
	IDA	50	8.336	.3999	
MCV	BTT	100	57.8122	3.32360	<0.001
	IDA	50	65.5418	2.49448	
MCH	BTT	100	19.2965	2.26997	<0.001
	IDA	50	22.1580	1.74626	
MCHC	BTT	100	30.671	1.4504	<0.001
	IDA	50	33.042	3.8147	
RDW	BTT	100	19.683	3.7085	0.88
	IDA	50	19.598	2.3064	
SI	BTT	100	80.2183	31.86575	<0.001
	IDA	50	44.3862	25.04320	
SF	BTT	100	46.8025	28.34604	<0.001
	IDA	50	10.3230	4.24798	
TIBC	BTT	100	318.7250	57.60100	<0.001
	IDA	50	463.3910	36.59797	

Table 4: Association between the groups and the various indices.

Indices	Group	N	Mean	Std. Deviation	t	df	P-value
Mentzer	BTT	100	11.48	1.25	-23.094	148	<0.001
	IDA	50	18.40	2.41			
Srivastava	BTT	100	3.82	0.55	-21.198	148	<0.001
	IDA	50	6.20	0.80			
Ricerca	BTT	100	3.91	0.82	-10.711	148	<0.001
	IDA	50	5.49	0.92			
Green and King	BTT	100	71.69	17.21	-10.468	148	<0.001
	IDA	50	101.21	14.20			
Sirdah	BTT	100	29.93	3.81	-17.371	148	<0.001
	IDA	50	40.53	2.83			
Ehsani	BTT	100	7.04	5.77	-22.481	148	<0.001
	IDA	50	29.30	5.60			

Among all the Indices, diagnostic accuracy by Ehsani and Mentzer indices were found to be the highest Area under Curve (AUC). The data shows that Srivastava and Sirdah indices presents the highest sensitivity. Ehsani and Mentzer indices presents the highest specificity.

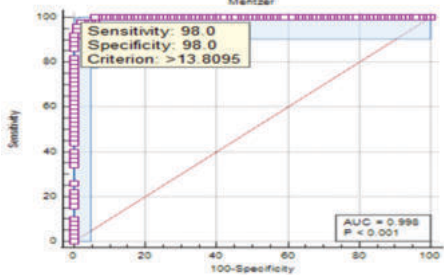


Figure: 1

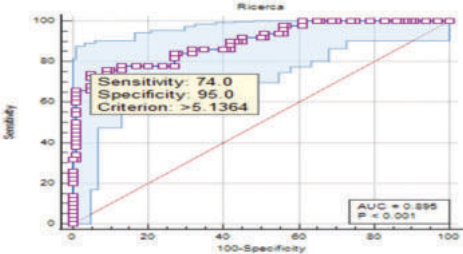


Figure: 2

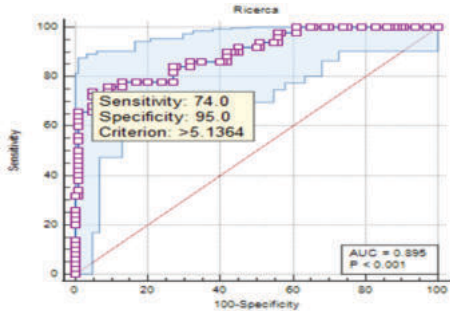


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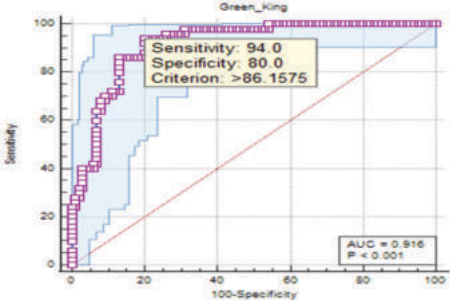


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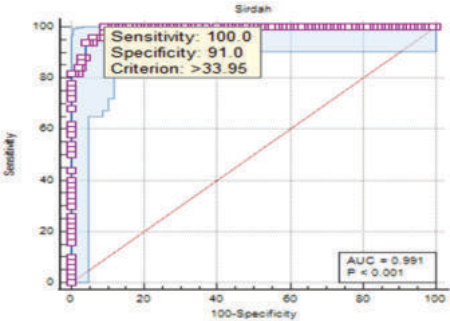


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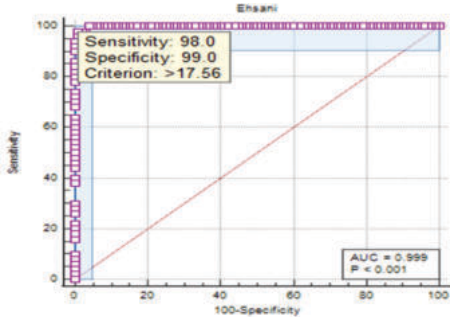


Figure: 6

DISCUSSION:

Among paediatric population, IDA and BTT are two common causes of microcytic anaemia. There are various clinical and scientific characteristics of these two hematologic disorders that are comparable. Misdiagnosis of BTT has consequences for potential homozygous offspring. Until date, diagnosing BTT has relied on a rise in HbA2, whereas diagnosing IDA has relied on an increase in TIBC, a drop in blood iron, and an increase in serum ferritin. The importance of distinguishing between IDA and BTT led to the market's suggestion of a multitude of different indices using just a complete blood count. (6)

The clinical relevance of these indices varied, but none of them had a verified diagnosis in any of the trials, and in particular, no study has established the reliability of any of these RBC indicators. Six haematological indices that distinguish between IDA and BTT using CBC and iron profile characteristics were proposed by us. These tests allowed us to identify children who were at high risk of developing these anaemias and prevent spending money on unnecessary

investigations. A reliable discrimination index becomes essential in this scenario. (6)

With the exception of RDW, which agrees with Vehapoglu et al., our study revealed significant differences in the haematological parameters of the BTT and IDA categories, demonstrating that it is possible to distinguish between BTT and IDA instead of using expensive procedures and high-performance indices.(3)

When compared to the sensitivity (73.5%) and specificity (94.8%) of Mentzer's index by Shaily Garg et. al., the present study found that Mentzer's index had an equivalent sensitivity and specificity of 98%. 100% sensitivity by the Mentzer and Ehsani indices and 100% specificity by all six indices, which is higher than our current study, were reported in a study by Nagwan I. Rashwan et al. (4)

RDW is a sign of anisocytosis. In IDA, it has a higher value, and in TT, it is either close to normal or somewhat higher. Even though RDW is a highly regarded discriminating indicator for distinguishing between TT and IDA(4)Our findings revealed that RDW is nearly similarly increased in both TT and IDA, indicating that it is not a good indicator of TT and IDA.

The results of the current research found that the Mentzer and Ehsani indices had excellent sensitivity, specificity, and AUC for both and were much better at discriminating between TT and IDA. Demir et al. (17), in contrast to our findings, demonstrated that the Mentzer index had limited validity in paediatric patients.(5)

Small sample size and absence of analysis of all red cell indices were the study's limitations. The differentiating ability of all prospective red cell indices that have been previously reported has to be tested; however, the current study only permits us to use six of them, and the results cannot be generalised to the entire community. There are no conflicts of interest.

CONCLUSION:

On the basis of the results, it can be said that CBC-based indices, particularly those developed by Mentzer, Ehsani, Green and King, Recierca, Sirdah, and Sirvistava, were valid diagnostic tools for differentiating BTT from IDA in developing nations with scarce healthcare resources. These indices were discovered to be the most precise, sensitive, and highly specific way to identify the Beta thalassemia trait from IDA.

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