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## A New Index for Discrimination Between Iron Deficiency Anemia and Beta-Thalassemia Minor: Results in 284 Patients

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**Abstract:** The present study reports the results in 284 patients of applying a recently developed index,  $MCV - (10 \times RBC)$ , for discrimination between beta-thalassemia trait ( $\beta$ -TT) and Iron Deficiency Anemia (IDA), the two most common causes of microcytic hypochromic anemias. A total of 284 carefully selected patients (130 patients with IDA and 154 with  $\beta$ -TT) were studied. Sensitivity, specificity and Youden's index were compared between the proposed index and four other indices, namely England-Fraser, Mentzer, Srivastava and RBC count. The new index correctly identified 263 (92.96%) patients, standing inferior only to Mentzer which correctly diagnosed 269 (94.71%) patients. The best discrimination index according to Youden's criteria was Mentzer (Youden's index = 90.1) followed by the new index (Youden's index = 85.5). There are remarkable inconsistencies among the results obtained in different studies. Larger studies are needed to establish the optimal discrimination index as well as to confirm the results obtained in the present study. Nevertheless, the epidemiological indices of the proposed discrimination index and the simplicity of its calculation make it acceptable for use in Iran.

**Key words:** Beta-thalassemia, iron deficiency anemia, discrimination index

### INTRODUCTION

Iron Deficiency Anemia (IDA) and beta-thalassemia trait ( $\beta$ -TT) are the most common causes of hypochromic microcytic anemias (Wharton, 1999; Olivieri, 1999). Several indices, e.g., England and Fraser (1973), Mentzer (1973), Srivastava and Bevington (1973), Shine-Lal (1977) and Green-King (1989) have been proposed during the past 35 years to discriminate between the two (Sirdah *et al.*, 2008). An ideal discrimination index has a high sensitivity and specificity and is easy to calculate.

Recently researchers developed a new index with such properties (Ehsani *et al.*, 2005). However, before any new index can be safely applied in practice, it should be carefully evaluated and compared with the already existing indices. Here the results of study on 284 patients (130 patients with IDA and 154 with  $\beta$ -TT) are briefly reported.

### MATERIALS AND METHODS

A total of 284 patients (96 males) aged  $24.2 \pm 13.5$  (range: 10-38) years were studied. All patients had hypochromic ( $MCHC < 30 \text{ g dL}^{-1}$ ) microcytic ( $MCV < 80 \text{ fL}$

for ages over 6 years and  $MCV < 70 \text{ fL}$  otherwise) anemia. Anemia was defined as a hemoglobin concentration of at least 2 standard deviations lower than age- and sex-specific average. Red blood cell count and red blood cell distribution width (RDW) were obtained with Coulter Counter (London, UK). Serum Iron (SI) and Total Iron Binding Capacity (TIBC) were determined calorimetrically and ferritin was measured turbidimetrically by using a Hitachi-911 automatic analyzer (Boehringer Mannheim, Tokyo, Japan) and commercially available kits. HbA2 levels were measured by alkaline cellulose acetate electrophoresis (Marengo-Rowe, 1965). Transferrin Saturation (TS) was calculated by the ratio of SI to TIBC. IDA was diagnosed based on the presence of iron-responsive hypochromic microcytic anemia, serum ferritin  $< 12 \text{ ng mL}^{-1}$  and TS  $< 16\%$ .  $\beta$ -TT was diagnosed with  $HbA2 > 3.5\%$  plus  $MCV < 80 \text{ fL}$  and/or  $MCH < 27 \text{ pg cell}^{-1}$ , as recommended by national guidelines (Samavat, 2004).

Pregnant women as well as patients with a known chronic disease, acute or chronic infections, hemoglobinopathies other than  $\beta$ -TT, or concurrent IDA/ $\beta$ -TT were not included. The new index was calculated by  $MCV - (10 \times RBC)$  and its sensitivity and

specificity was compared with the following 4 indices: England-Fraser =  $MCV-RBC-(5 \times Hb)-k$ , Mentzer =  $MCV/RBC$ , Srivastava =  $MCH/RBC$  and RBC count. Youden's index was calculated by sensitivity+ specificity-100 (Lin *et al.*, 1992; Pekkanen and Pearce, 1999). Informed consent was obtained from all patients and the study protocol was approved by the ethics committee of our university.

## RESULTS AND DISCUSSION

Table 1 shows hematological findings of patients. The new index correctly identified 263 (92.96%) patients, standing inferior only to Mentzer which correctly diagnosed 269 (94.71%) patients. The best discrimination index according to Youden's criteria was Mentzer (Youden's index = 90.1) followed by the new index (Youden's index = 85.5) (Table 2, 3).

The discrimination between IDA and  $\beta$ -TT is important because MCV will not normalize in  $\beta$ -TT if misdiagnosed as IDA and treated with iron (Olivieri, 1999). Iran, a country located on the thalassemia belt, is one of the areas with a high prevalence of beta-thalassemia (Lee *et al.*, 1999). On the other hand, iron deficiency anemia is a common problem in Iran, affecting up to 30% of the population by recent estimates (Keikhaei *et al.*, 2007; Kadivar *et al.*, 2003; Karimi *et al.*, 2002; Djazayeri *et al.*, 2001). Therefore, the confusion between IDA and  $\beta$ -TT is not uncommon in this country. This

Table 1: Hematological findings of patients

Parameters	IDA (n = 130)	$\beta$ -TT (n = 154)
RBC ( $\times 10^6$ mL <sup>-1</sup> )	4.41 $\pm$ 0.55	5.89 $\pm$ 0.59
Hb (g dL <sup>-1</sup> )	9.30 $\pm$ 1.89	11.24 $\pm$ 1.37
Hct (%)	31.11 $\pm$ 5.25	36.45 $\pm$ 4.20
MCV (fL)	70.04 $\pm$ 7.94	62.02 $\pm$ 4.57
MCH (pg cell <sup>-1</sup> )	21.30 $\pm$ 3.52	19.68 $\pm$ 1.53
MCHC (g dL <sup>-1</sup> )	29.88 $\pm$ 2.86	30.93 $\pm$ 1.71

Table 2: Results obtained from each discrimination index

Parameters	IDA (n = 130)	$\beta$ -TT (n = 154)	Total No. of correctly diagnosed patients (n = 284)	Correctly diagnosed (%)
England-Fraser				
IDA > 0	129	47	236 (129+47)	83.09
$\beta$ -TT < 0	1	107		
Mentzer				
IDA > 13	122	7	269 (122+147)	94.71
$\beta$ -TT < 13	8	147		
Srivastava				
IDA > 3.8	115	22	247 (115+132)	86.97
$\beta$ -TT < 3.8	15	132		
RBC count ( $\times 10^6$ )				
IDA < 5	112	3	263 (112+151)	92.61
$\beta$ -TT > 5	18	151		
New index				
IDA > 15	117	7	264 (117+147)	92.96
$\beta$ -TT < 15	13	147		

problem urged us to compare the value of popular discrimination indices and try to develop a new index which is sensitive, specific and easy to calculate. Based on the above results, the new index and the Mentzer index have high Youden's indices and are able to correctly diagnose 93-95% of cases while both are easy to calculate.

Table 4 provides a brief summary of the results of relevant studies to date. Unlike our study, the Mentzer index was not among the two best discrimination indices in the other five reports. Here, sample size of 284 patients and the fairly small difference between the performance of the Mentzer index and that of the new index do not allow us to draw a firm comparative conclusion. However, the new index may be a suitable alternative, if not a replacement, to the Mentzer index because the difference between the performance of these two indices in our series was attributable to the lower sensitivity of the new index in diagnosing IDA, a problem which can be partly resolved by IDA patients' suggestive history and manifestations in physical examination. Also, the two indices may work together to provide a more accurate

Table 3: Sensitivity, specificity and Youden's index of five indices to discriminate between IDA and  $\beta$ -TT in 284 patients

Parameters	Sensitivity (%)	Specificity (%)	Youden's index
England-Fraser			
IDA	99.2	69.5	68.7
$\beta$ -TT	69.5	99.2	
Mentzer			
IDA	94.6	95.5	90.1
$\beta$ -TT	95.5	94.6	
Srivastava			
IDA	88.5	85.7	74.2
$\beta$ -TT	85.7	88.5	
RBC count			
IDA	86.2	98.1	84.3
$\beta$ -TT	98.1	86.2	
New index			
IDA	90.0	95.5	85.5
$\beta$ -TT	95.5	90.0	

Table 4: Summary of recent relevant studies

References	Sample size	Best two indices	Youden's index
Demir <i>et al.</i> (2002)	63	RBC count	82.0
		RDWI	80.0
Ntaios <i>et al.</i> (2007)	493	Green-King	70.9
		England-Fraser	63.2
Beyan <i>et al.</i> (2007)*	111	RBC count	73.7
		Green-King	65.5
Sirdah <i>et al.</i> (2008)*	2196	Green-King	68.6
		RDWI	68.4
Urrechaga <i>et al.</i> (2008)	318	Green-King	80.9
		Microcytic%/hypochromic%	76.3
Ehsani <i>et al.</i> (present study)*	284	Mentzer	90.1
		Present formula	85.5

RDWI: Red blood cell distribution width index, \*:Studies that considered our index

discrimination decision. The present study is the third to apply the new index to a large sample of patients and also the first report from Iran. Due to remarkable inconsistencies between the results obtained so far, it is not possible to choose one discrimination index as the most appropriate and the issue awaits future large studies.

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