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Value of the Matos and Carvalho index for thalassemia trait detection, experience of single hematological center in Iraq

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Abstract:

BACKGROUND: Thalassemia trait and other low red cell index (LRCI) diseases commonly have same presentation with microcytic hypochromic anemia. Most of beta thalassemia minor (TM) people are subclinical and without specific investigation may be undiagnosed or treated as iron-deficiency anemia. Thalassemia carriers may be undiagnosed, which in turn leads to severe forms of thalassemia syndromes with poor premarital counseling in high-prevalence areas. Many trials tried to find simple diagnostic tools to differentiate between thalassemia traits and other microcytic anemia depending on blood discriminative indices that can be found in limited resource places and routine clinics using blood cell count parameters. The aim was to assess the value of Matos and Carvalho index (MCI) in detecting TM from patients presented with microcytic anemia.

PATIENTS AND METHODS: The study was carried out on 171 patients who were diagnosed as cases of hypochromic microcytic anemia in Kut Hemato-oncology Center. By Measuring hematological parameters using five automated red cell discriminative indices (red blood cell (RBC) count, RBC distribution width, Shine and Lal index, MCI index, and Mentzer index [MI]) with measuring hemoglobin (Hb) A2 levels using Hb variant B thalassemia short arm program.

RESULTS: Of 171 patients screened for TM, 108 patients were diagnosed as TM by Hb electrophoresis. Patients with TM presented with the mean age of 25.3 years, while the mean of age in patients with other LRCI anemia was 6.2 years. RBC count was the best index of correctly identifi ed patients as 84%, followed by MI and MCI with 74% and 72%, respectively. Furthermore, the RBC count was the best indicator Youden's indices (58.2), with high sensitivity for BT (96.3%) followed by MI with Youden's index (38). Wide thalassemia mutation play important role in this issue.

CONCLUSION: RBC count are simply accessible and dependable ways for identifying beta thalassemia trait, but there are no red cells indices and methods have 100% specificity, efficacy, and sensitivity for the differentiation beta TM from other hypochromic microcytic anemia which may be due to wide thalassemia mutations.

Keywords:

Anemia, beta thalassemia minor, Matos and Carvalho index

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Introduction

Microcytic anemia is usually due to iron deficiency, thalassemia minor (TM), or both of the conditions. Iron deficiency anemia is a common condition, in area of developing countries because of a defect in nutrition supply, even so in the developed countries, where female of gestational age are usually detected with iron deficiency anemia because of loss of blood in combination with inadequate iron intake.[1] Hemoglobinopathies impose an important load on worldwide health system. Around 5%–7% of the worldwide

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population have a pathological hemoglobin (Hb) gene. It essentially contains the basic Hb variations and special type of thalassemia.[2] Precise and suitable recognition of several Hb variations involving Beta thalassemia can avoid the occurrence of severe illnesses such as thalassemia major in newborns.[3] Hoffman stated that "Thalassemia conventionally has an extreme occurrence in the Mediterranean region, people in the Arabic peninsula, the Middle East, and Southeast Asia, however now people movement has to distribute thalassemia genetic factor around approximately the the whole world, Obviously a correct diagnosis in patients with microcytic anemia is important: it gives a sign for adding iron to iron deficiency anemia patients, for preventing avoidable iron treatment in TM, and moreover for avoiding fatal forms of thalassemia diseases in the skeleton of premarital advising in extreme predominance zones."[4] Hb analysis with high-performance liquid chromatography (HPLC) and iron study is expensive for community health budget, particularly in nations with a significant incidence of thalassemia and not presented usually in little Supply conditionsYears. Complete blood count analysis; however, computerized blood cell counter is commonly used in the daily work.[5] Regions where thalassemia is endemic often have low health care supplies and these assays may not be mostly available. Thus, numerous easy assessment keys have been established for differentiating TM and other microcytic anemia.[6] It is extensively approved that none of these indicators is 100% sensitive or 100% specific. Even more complex styles, including combinations of different simple indices, multivariate discriminant analysis or artificial neural network computing are unable to reach absolute sensitivity and specificity.[7]

Hoffman reported that although the reason is not apparent, the difference in gene according to ethnic groups may play a role in the fact that there is no screening indices have a superior function to detection TM.[4] By this article, especially in countries with limited resources, the physician should Use available facilities to reach a diagnosis. Red blood cell (RBC) indices which can be obtained by blood coulter are essential to make the mind of them more oriented regarding the differentiation between beta TM and other microcytic anemia.

Patients and Methods

This study is a cross-sectional analysis was done on 171 patients who were diagnosed as cases of hypochromic microcytic anemia in Kut Oncology Center, Wasit, Iraq, during the period from the first of January 2011 to the end of December 2011. Microcytic anemia.

Blood samples were collected from all patients who were referred to hematology center as cases of anemia. The mean age of the patients was 18.2 (range 0.8–72) years old. The hematological considerations, containing red cell manifestations, were calculated by a computerized blood counter (Sysmex KX-21).

Low red cell indices (LRCI) was defined as a microcytic anemia (mean corpuscular volume [MCV] <80 femtoliter [fL] at age ≥6 years or MCV <70 fL for age <6 years. The HPLC assessment was done in Bio-Rad variant Hb assessment technique with B-thalassemia short program using a variant beta-thalassemia short program pack. The patients with an Hb A2 level among four to nine were diagnosed as beta thalassemia trait (BTT).[8]

Five discrimination indices used in the evaluation were calculated. Positive predictive value (PPV sensitivity, specificity), negative predictive value (NPV), and Youden's index were analyzed for individual measure.

The values for each discrimination index were applied as used in the original published reports: Mentzer index,[9] the Shine and Lal index,[10] MCI,[11] and RBC count and RDW were evaluated and compared.

The data were presented as mean ± standard deviation. SPSS version 20.0 (SPSS, Chicago, IL, USA) program was used for data analysis. An independent sample *t*-test was performed to detect differences between both groups of patients with pallor. *P* values <0.05 were considered statistically significant.

Results

From 171 patients screened for TM, 108 patients were diagnosed with TM by Hb electrophoresis. Table 1 shows the cutoff point of blood indices which were used in this thesis.

Table 2 shows age as well as the hematological difference between patients with TM and patients with other LRCI; there was a significant difference in the age of presentation, as in patients with TM the mean age was 25.3 years, while the mean of age in patients with LRCI was 6.2 years. There was a significant statistical difference between patients with TM and other LRCI anemia regarding hematological parameter. The mean of MCI in TM patients was 24.3, while in patients with LRCI, anemia was 21.4 with $P = 0.001$.

Table 3 shows the discrepancy value of the index and appropriately known number of the patients with percent. RBC count was the best index as the percent of correctly identified percent was 84%, followed by MI and MCI with 74% and 72%, respectively.

Table 1: Cutoff point of blood indices in patients with BT and other low red cell index anemia

Indices	Other LRCI	BT
RBC ($\times 10^{12}$/L)	<5	>5
RDW (%)	>16	<16
MI=MCV/RBC	>13	<13
S and L index=$MCV^2 \times MCH \times 0.01$	>1530	<1530
MCI = (1.91 × RBC) + (0.44 × MCHC)	<23.85	>23.85

MI=Mentzer index, RBC=Red blood cell, RDW=RBC distribution width, MCI=Matos and Carvalho Index, LRCI=Low red cell indices, BT=Beta thalassemia, MCV=Mean corpuscular volume, S and L=Shine and Lal, MCHC=Mean corpuscular hemoglobin concentration, MCH=Mean corpuscular hemoglobin

Table 2: Age and hematological parameters of patients with BT and other low red cell index anemia

Item	Diagnosis sorting	*n*	Mean±SD	*P*
Age in months	BT	108	304.1 (190.1)	0.00
	Other LRCI	63	75.0 (60.0)	
RBCs	BT	108	5.8 (0.5)	0.00
	Other LRCI	63	4.8 (0.75)	
HCT	BT	108	37.9 (4.8)	0.00
	Other LRCI	63	29.6 (5.4)	
Hb	BT	108	11.5 (1.8)	0.00
	Other LRCI	63	8.4 (2.2)	
MCV	BT	108	66.0 (5.9)	0.00
	Other LRCI	63	62.4 (7.3)	
MCHC	BT	108	29.9 (1.9)	0.00
	Other LRCI	63	27.9 (3.6)	
MCH	BT	108	19.6 (2.5)	0.00
	Other LRCI	63	17.7 (4.0)	
RDW	BT	108	12.4 (1.7)	0.00
	Other LRCI	63	14.4 (3.6)	
MI index	BT	108	11.4 (1.4)	0.00
	Other LRCI	63	13.3 (3.2)	
S and L	BT	108	878 (256.1)	0.00
	Other LRCI	63	720 (296.7)	
MCI	BT	108	24.3 (1.3)	0.00
	Other LRCI	63	21.4 (2.2)	

LRCI=Low red cell indices, BT=Beta thalassemia, MI=Mentzer index, RBC=Red blood cell, RDW=RBC distribution width, MCI=Matos and Carvalho Index, MCV=Mean corpuscular volume, SD=Standard deviation, S and L=Shine and Lal, Hb=Hemoglobin, HCT=Hematocrit, MCHC=Mean corpuscular hemoglobin concentration, MCH=Mean corpuscular hemoglobin

The NPV sensitivity, specificity, PPV, and Youden's index of each discrimination index are shown in Table 4. RBC count was the best indicator with Youden's indices 58.2, the sensitivity of it for BT was 96.3%, the best Youden's index after RBCs count is MCI which was 50.3, followed by Youden's index of MI which was 38.

Discussion

Ebrahim Miri stated "BTM is the most common cause of microcytic anemia. To reduce the cost, time and complicated procedures for their discrimination, various RBC indices and formulas have been used. It has been reported that the RBC indices MCV, MCH and MCHC show remarkably small differences over the globe, enabling using them for internal quality control purposes. It is crucial to select which formula is more accurate in the differentiation of BTT from Other LRCI cases. The most of BTT cases are asymptomatic and without specialized tests may be missed or sometimes misdiagnosed as IDA."[12] Expectation of these parameters might be equal over the world because several of blood indices depend on other standard red cell indices.[4]

Specialized tests such as Hb electrophoresis may be not available in all hospitals, especially in developing countries.

For that reason, the clinician should have knowledge about indexes that can help him to differentiate between BTT and other LRCI anemia. In this study, we tried to detect better RBC indices and formula which are more applicable in our situation as compared with other studies. The percentage of correctly identified patients' value for MCI was 72%, which lower than what reported in Matos *et al*.'s study (99.6%).[11] There is limitation in the use of MCI index as screening test for BTT; this limitation was reported in Hoffmann study; Hoffman suggested that" use of MCI index can use after further justification according to the patient population.[13]

The limitation of the MCI use supported by Youden's indices which was 50.3.

In this study, the highest percent of correctly identified patients was reported for RBC count index (84%), followed by MI and MCI, 74% and 72%, respectively. The highest value of Youden's indices was reported in RBC index followed by MI (58.2, 50.3), respectively

RBC index with high Youden's indices was reported in Fakher study (82), Vehapoglu *et al*.'s study (65.3), and George study (63.4).[14-16]

Ebrahim stated that "Cell counting devices easily obtain RBCs count, facilitate the diagnosis process. At present, cell counters are widely used in routine practice so that screening can be done without additional costs to medical systems. (Successful prevention programs for BTT in Greece and Italy have relied on detection by RBC indices and HbA2 concentration."[12]

Many other important readings can be obtained from cell counting devices, such as RDW. In this study, the Youden's index was 15, which is lower than what was reported in Vehapoglu *et al*.'s study which was 59.6.[15] However, it is higher than what was reported in Gorge natali study (3.4).[16] While in Nesa *et al*.'s study, the Youden's index of RDW is 2.3, Nesa reported that "in both beta thalassemia minor and iron deficiency anemia, the RDW may be equally elevated."[17] The variation of RDW values explained by Hoffmann *et al*., where

Table 3: The differential values of each discrimination index and correctly identified number of patients

Differential values			Other LRCI (*n*=63)	BT (*n*=108)	TCIP (*n*=171)	PCIP (%)
	Other LRCI	BT				
RBC ($\times10^{12}$/L)	<5	>5	+ 39	- 4	143 (39+104)	84
			- 24	+ 104		
MI	>13	<13	+ 32	- 14	126 (32+94)	74
			- 31	+ 94		
MCI	<23.85	>23.85	+ 55	- 40	123 (55+68)	72
			- 8	+ 68		
RDW (%)	>16	<16	+ 18	- 15	111 (18+93)	65
			- 45	+ 93		
S and L	>1530	<1530	+ 1	- 0	109 (1+108)	64
			- 62	+ 108		

TCIP=Total correctly identified patients, PCIP=Percentage of correctly identified patients, RBC=Red blood cell, RDW=RBC distribution width, MI=Mentzer index, MCI=Matos and Carvalho Index, S and L=Shine and Lal, LRCI=Low red cell indices, BT=Beta thalassemia, +=Ture positive, -=False negative

Table 4: Sensitivity, specificity, positive predictive value, negative predictive value, and Youden's index of each discrimination index

Index	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Efficiency (%)	Youden's indices
RBC$\times10^{12}$/L						
Other LRCI	62	96.3	91	81.3	84	58.2
BT	96.3	62	81.3	91		
MCI						
Other LRCI	87.3	63	58	90	72	50.3
BT	63	87.3	90	58		
MI						
Other LRCI	51	87	70	75.2	74	38
BT	87	51	75.2	70		
RDW (%)						
Other LRCI	29	86.1	55	67.4	65	15
BT	86.1	29	67.4	55		
S and L						
Other LRCI	2	100	100	64	64	2
BT	100	2	64	100		

PPV=Positive predictive value, NPV=Negative predictive value, LRCI=Low red cell indices, BT=Beta thalassemia, RBC=Red blood cell, RDW=RBC distribution width, MI=Mentzer index, MCI=Matos and Carvalho index, S and L=Shine and Lal

he reported that the low diagnostic importance of red distribution width parameter may be explained by not well standardization between analyzers.[4] Shen *et al*. and Miri-Moghaddam and Sargolzaie concluded that the mutation of thalassemia will effect on RBC parameter, this fact make determine the standard value of each the population is necessary[12,18] Sakorn found that the the difference in mutation gene of thalassemia can be an essential issue for differentiation between TM and iron deficiency anemia, the level of iron that causes anemia, range of age, as well as the size of the sample.[19]

Conclusion

According to this study, MCI is not the best index that helps the physician to detect TM; there are no red cell indices and formulas that provided 100.0% sensitivity, specificity, and efficacy for the discrimination of beta TM from other hypochromic microcytic anemia. Wide thalassemia mutation plays an important role in these differences. The RBC count is an available and easy method for detection of TM.

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Conflicts of interest

There are no conflicts of interest.

References

1. Milman N. Anemia – Still a major health problem in many parts of the world! Ann Hematol 2011;90:369-77.
2. Gorakshakar AC, Colah RB. Is RBC discrimination index suitable for differentiating between α- and β- thalassemias? Indian J Hum Genet 2011;17:115-6.
3. Sachdev R, Dam AR, Tyagi G. Detection of Hb variants and hemoglobinopathies in Indian population using HPLC: Report of 2600 cases. Indian J Pathol Microbiol 2010;53:57-62.
4. Hoffmann JJ, Urrechaga E, Aguirre U. Discriminant indices for distinguishing thalassemia and iron deficiency in patients with microcytic anemia: A meta-analysis. Clin Chem Lab Med

2015;53:1883-94.
5. Ferrara M, Capozzi L, Russo R, Bertocco F, Ferrara D. Reliability of red blood cell indices and formulas to discriminate between beta thalassemia trait and iron deficiency in children. Hematology 2010;15:112-5.
6. Green R, King R. A new red cell discriminant incorporating volume dispersion for differentiating iron deficiency anemia from thalassemia minor. Blood Cells 1989;15:481-91.
7. Barnhart-Magen G, Gotlib V, Marilus R, Einav Y. Differential diagnostics of thalassemia minor by artificial neural networks model. J Clin Lab Anal 2013;27:481-6.
8. Pornprasert S, Kasemrad C, Sukunthamala K. Diagnosis of thalassemia on dried blood spot samples by high performance liquid chromatography. Hemoglobin 2010;34:486-94.
9. Mentzer WC Jr. Differentiation of iron deficiency from thalassaemia trait. Lancet 1973;1:882.
10. Shine I, Lal S. A strategy to detect beta-thalassaemia minor. Lancet 1977;1:692-4.
11. Matos JF, Dusse LM, Borges KB, de Castro RL, Coura-Vital W, Carvalho MD, *et al.* A new index to discriminate between iron deficiency anemia and thalassemia trait. Rev Bras Hematol Hemoter 2016;38:214-9.
12. Miri-Moghaddam E, Sargolzaie N. Cut off determination of discrimination indices in differential diagnosis between iron deficiency anemia and β- thalassemia minor. Int J Hematol Oncol Stem Cell Res 2014;8:27-32.
13. Matos JF, Dusse LM, Borges KB, de Castro RL, Coura-Vital W, Carvalho MD, *et al*. Response to the assessment of the matos and amp; amp; carvalho index by hoffmann and urrechaga. Rev Bras Hematol Hemoter 2017;39:290-1.
14. Rahim F, Keikhaei B. Better differential diagnosis of iron deficiencyanemia from beta-thalassemia trait. Turk J Haematol 2009;26:138-45.
15. Vehapoglu A, Ozgurhan G, Demir AD, Uzuner S, Nursoy MA, Turkmen S, *et al.* Hematological indices for differential diagnosis of beta thalassemia trait and iron deficiency anemia. Anemia 2014;2014:576738.
16. Ntaios G, Chatzinikolaou A, Saouli Z, Girtovitis F, Tsapanidou M, Kaiafa G, *et al*. Discrimination indices as screening tests for beta-thalassemic trait. Ann Hematol 2007;86:487-91.
17. Nesa A, Tayab MA, Sultana T, Khondker L, Rahman MQ, Karim MA, *et al*. RDWI is better discriminant than RDW in differentiation of iron deficiency anaemia and beta thalassaemia trait. Bangladesh J Child Health 2009;33:100-3.
18. Shen C, Jiang YM, Shi H, Liu JH, Zhou WJ, Dai QK, *et al*. Evaluation of indices in differentiation between iron deficiency anemia and beta-thalassemia trait for Chinese children. J Pediatr Hematol Oncol 2010;32:e218-22.
19. Pornprasert S, Panya A, Punyamung M, Yanola J, Kongpan C. Red cell indices and formulas used in differentiation of β-thalassemia trait from iron deficiency in Thai school children. Hemoglobin 2014;38:258-61.