SUGGESTION OF NEW FORMULAE TO BE USED IN DISTINGUISHING BETA THALASEMIA TRAIT FROM IRON DEFICIENCY ANEMIA

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ABSTRACT

Introduction: Clinical findings of thalasemia trait is similar with iron deficiency anemia. It is important to discriminate both from each other. Because treatment approaches are different for the each entities. But, it is not always possible to reach enough laboratory sufficiency for discriminating the two entities everywhere. Some practical and easy formulae could help for the discrimination in such insufficient technical possibilities.

Materials and method: 40 patients included in the study. The formula (RDW(Red blood cell distribution width) X RBC(Red blood cell count) X HGB(Hemoglobin))/MCV(Mean corpuscular volume) was evaluated for the discrimination of the two entities. The formula log_{10} (MCH(Mean corpuscular hemoglobin) X MCHC(Mean corpuscular hemoglobin concentration) X RDW / RBC ) was also evaluated for the differentiation of these two entities. The latter formula was identified as “Alparslan index”. These formulae were compared with the well known indices such as Mentzer index. Youden Index was calculated for each index for comparing the reliability and validity of the indices.

Results: The study showed no difference between the compared indices according to the sensitivity. Youden Index were found 94.73 for the Alparslan Index and 89.96 for the Mentzer Index.

Discussion: There are many formulae and indices to help have an opinion for the discrimination of beta thalasemia trait from IDA(Iron deficiency anemia). Simply calculable valid formulae could be more commonly and easily used according to the complex calculation formulae. RDWI(Red Blood Cell Distribution Width Index) was found to provide more reliability than Mentzer Index in the study. In the study, Alparslan Index and RDWI were also found to provide same reliability according to Youden Index.

Keywords: Thalasemia trait, iron deficiency anemia, discrimination index.

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Introduction

Thalasemia is an inherited abnormal hemoglobin disease. The molecular defects in the hemoglobin synthesis result in anemia and cause decreased oxygen transport to tissues. Thalasemia related genes are commonly expressed in the Mediterranean region. Beta thalasemia trait is the frequent and mostly asymptomatic form of the genetic expression of the minor thalasemic gene defects. Clinical findings of thalasemia trait is similar with IDA. And it is important to discriminate both from each other. Because treatment approaches are different for the each entities.

Hemoglobin electrophoresis is the most widely used test for an accurate diagnosis of beta thalasemia. On the other hand, genetic testing is needed to diagnose alpha thalasemia, which is rare according to beta thalasemia. Beta thalasemia trait is a common reason of anemia in the Mediterranean countries. And it is not always possible to reach enough laboratory sufficiency for discriminating the two entities everywhere. Mentzer introduced a simple formula using the complete blood count test to differentiate thalasemia trait and iron deficiency anemia(6). This formula which is called Mentzer Index (MI) is commonly used in the clinic. And “RDWI” index, “Green and King” index,
“Sristava” index are some other well known indices for the discrimination of thalasemia minor and iron deficiency anemia\(^{\text{2,3,4}}\).

Mean corpuscular hemoglobin gives the average amount of hemoglobin per red blood cell in a complete blood count test. And mean corpuscular hemoglobin concentration gives the average hemoglobin concentration per red blood cell in a complete blood count test. Hereby, it is aimed to evaluate alternative formulae to be used in the discrimination of IDA and thalasemia trait (TT).

**Materials and method**

40 patients included in the study. 21 patients had IDA and 19 patients had beta thalasemia trait. The patients who had hemoglobin levels below 12 mg/dl and who had low ferritin levels were putted into the IDA group. The patients who had incresed HbA2 levels in hemoglobin electrophoresis were putted into thalasemia trait group. The patients had been evaluated in the period of the February-May 2016 in Aksu District Internal Medicine Outpatient Unit of the University of Health Sciences Antalya Education and Research Hospital. The datas of the patients were analysed retrospectively from the records.

Only, the patients whose records were accurate and exactly reachable were included in the study. The patients’ CBC(Complete Blood Count) tests had been done by one of the three CBC analyzers used in the hospital laboratories. These were HORIBA ABX Pentra XL 80, HORIBA ABX Micro ES 60, Beckmann Coulter LH780 CBC analyzers. Hemoglobin was expressed in grams per deciliter (g/dL) of blood. And RBC was expressed as a number(n) of cells in millions per cubic millimeter (nx10\(^6\)/mm\(^3\)) of blood.

Firstly, the formula “\((\text{RDW X RBC)/MCV}^\)" was evaluated to use in the discrimination of beta thalasemia trait and iron deficiency anemia. The other formula “\((\text{RDW X RBC X HGB)/MCV}^\)" was evaluated for the discrimination of the two entities. This latter formula was identified as “Merdin Index”. The third formula “\(\log_{10} (\text{MCH X MCHC X RDW / RBC})\)" was also evaluated for for differentiation of these two entities. And this third formula was identified as “Alparslan Index”. We compare these three indices with the mostly used well known index the Mentzer Index\(^{\text{1}}\). We also compare the formulae with the index reported by the Jayabose et al\(^{\text{2}}\). The index reported by Jayabose et al. is also named as RDWI index\(^{\text{2}}\). Mentzer index is the quotient of the mean corpuscular volume divided by the red blood cell count\(^{\text{1}}\). Quotient more than 13 suggests IDA, less than 13 suggests thalasemia trait\(^{\text{1}}\). RDWI is the quotient of the (MCV X RDW)/RBC\(^{\text{2}}\). Quotient more than 220 suggests IDA, less than 220 suggests beta thalasemia trait\(^{\text{2}}\).

RDWI and the first formula uses the same hemogram parameters; but they are different formulae. ROC (Receiver operating characteristic) analysis was done to detect the cut off values for the formulae (PASW Statistics 18). Youden Index (YI) was calculated for each index\(^{\text{5}}\). YI was used to compare the validity and reliability of the each index\(^{\text{3,5}}\). YI is equal to sum of sensitivity plus specificity minus 100 (sensitivity+specificity-100). Two patients were not included in the study (one with RDWI value equal to 220, and the other with the Mentzer index equal to 13).

The study was approved by the Clinical Research Ethics Committee of the University of Health Sciences Antalya Education and Research Hospital.

**Results**

The most sensitive and specific cut-off level for the formula “\((\text{RDWXRBC)/MCV}^\)" was found to be 1,27 by the ROC analysis. The values less than 1,27 suggest that the patient has IDA, and the values more than 1,27 suggest that the patient has beta thalasemia trait. In addition to this formula, the most sensitive and specific cut-off level for the formula “Merdin Index” was found to be 14,7 by the ROC analysis. The values less than 14,7 suggest that the patient has IDA, and the values more than 14,7 suggest that the patient has beta thalasemia trait. Lastly, the most sensitive and specific cut off level for the formula “Alparslan Index” was found to be 3,34 by the ROC analysis. The values less than 3,34 suggest that the patient has beta thalasemia trait, and the values more than 3,34 suggest that the patient has IDA.

The study showed no difference between MI, RDWI, Merdin Index, Alparslan Index and “\((\text{RDWXRBC)/MCV}^\) according to the sensitivity (Table 1). It was also found equal values of YI for the Alparslan index\(^{94.73}\), RDWI \(^{94.73}\), and “\((\text{RDWXRBC)/MCV}^\) formulae (Table 1). And lower values of YI were found for the MI \(^{89.96}\) and Merdin index \(^{89.96}\) (Table 1). PPV and specificity of the Alparslan index, RDWI and
“(RDWxRBC)/MCV” formulae were found as 100% (Table 1). Lastly, NPV of the MI, RDWI, Merdin Index, Alparslan Index and “(RDWxRBC)/MCV” were found as 95.23%, 95.45%, 95.23%, 95.45% and 95.45%, respectively (Table 1).

<table>
<thead>
<tr>
<th>Index</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Youden Index</th>
</tr>
</thead>
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<tr>
<td>Mentzer Index</td>
<td>94.73%</td>
<td>95.23%</td>
<td>94.73%</td>
<td>95.23%</td>
<td>89.96</td>
</tr>
<tr>
<td>RDW Index(RDW1)</td>
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<td>100%</td>
<td>100%</td>
<td>95.45%</td>
<td>94.73</td>
</tr>
<tr>
<td>Merdin Index</td>
<td>94.73%</td>
<td>95.23%</td>
<td>94.73%</td>
<td>95.23%</td>
<td>94.73</td>
</tr>
<tr>
<td>(RDWxRBC)/MCV</td>
<td>94.73%</td>
<td>100%</td>
<td>100%</td>
<td>95.45%</td>
<td>94.73</td>
</tr>
<tr>
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<td>94.73%</td>
<td>100%</td>
<td>100%</td>
<td>95.45%</td>
<td>94.73</td>
</tr>
</tbody>
</table>

Table 1: Sensitivity, specificity, PPV, NPV and Youden Index of the formulae.

Discussion

There are many formulas and indices to help have an opinion for the discrimination of beta thalassemia trait from IDA. Vehapoglu A et al. analysed 12 discrimination indices in all patients with hematocrit values of 8.7-11.4 g/dL in their study and reported that the Mentzer index provided the highest reliabilities for differentiating beta thalassemia trait from IDA (7,8). Ntaios G et al. also compared some well known indices in their study and reported that Green & King Index (9) proved to be the most reliable index (9). Demir A et al. compared eight indices and they found that red blood cell count and RDWI were the most reliable discrimination indices in differentiation between beta TT and IDA in their study (9). Sirdah M et al. also analysed some well known discrimination indices with their formula and reported that their formula, Green-King Index and the RDWI provided the highest reliabilities in differentiating beta-thalassaemia minor from iron deficiency (10).

In this study, it is showed that RDWI provided more reliability than Mentzer Index. And findings of this study fit in with the literature (7,8). In this study, it is also found that Alparslan Index, RDWI and the formula “(RDW x RBC) / MCV” provided same reliability according to Youden Index. In addition to this, it is showed that Merdin Index had the same reliability with Mentzer Index according to Youden Index.

The formulae helping for the discrimination of beta thalassemia trait from iron deficiency anemia should be made of easier calculations. Simply calculable valid formulae could be more commonly and easily used according to the complex calculation formulae. Hereby, new simple formulae are suggested to be used in the discrimination of thalassemia trait from iron deficiency anemia. These formulae would be easily calculated and might help to have opinion in the in differential diagnosis of IDA and thalassemia trait. These indices might also be used in rural areas and in the underdeveloped countries for the discrimination of thalassemia trait and iron deficiency anemia. Besides, further larger studies would help to find the most accurate discriminative index.

References


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