RESEARCH ARTICLE

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The role of erythrocyte indices in the differential diagnosis of microcytic anemia disorders

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ABSTRACT: The survival of the cells in the tissue depends on the delivery of sufficient oxygen. A small decrease in the erythocyte mass responsible for carrying blood to tissues causes hematological problems called anemia. Anemia cases are often considered as predictor of important diseases. In this respect, anemic diseases should be taken seriously and their causes should be investigated and evaluated. Iron deficiency anemia (IDA) and beta thalessemia minor (BTM) consititute the most of microcyter anemia. In this study, the role of erythrocyte indexes drived from hemogram parameters that can be made each center and easily accessible, in the diagnosis of IDA and BTM searched. Patients who apply to Kahramanmaras Sutcu Imam Hospital between January 2019 and March 2019 dates were included to research. Patients who have beta thalessemia minor and iron deficiency included in this study. 25 patients diagnosed IDA, 5 patients diagnosed BTM and 22 patients diagnosed beta thalessemia with iron deficiency anemia (DETMER) including in a total of 52 patients, were enrolled in this study. It has been calculated with the red blood cell indexes that are Mentzer Index (MI), Green & King Index (G&K), England & Fraser Index (E&F), RDW Index, Ricerca Index (RI), Srivastava Index (SI) ve Shine & Lal Index (S&L), in the differential diagnosis of patients that have iron deficiency anemia (IDA) and BTM. The red blood cell indexes'YI (Youden index) values were found as S&L (100%)>RI (84%) >E&F (%72) > RDW (64%) > G&K (64%) > RDWI (64%) > SI (56%) > MI (44%) >RBC (44%) in the differential diagnosis of IDA and BTM. YI (Youden Index) values of the red blood cell indexes were found as RDW (100%) > S&L (96.29%) RI (72.8%) > G&K (54.37%) >E&F (51.25%) > RDWI (50.6%) > SI (50.07%) > RBC (49.18%) > MI (45.18%) in the differential diagnosis of ''IDA'' diagnosed patient group and ''BTM with DETMER'' diagnosed patient group. S&L, RI and E&F has the highest index value in the differential diognosis of BTM and IDA. It is required to measure the level of ferritin, Hb electrophoresis, mutation analysis and HPLC analysis for the definitive diagnosis of patients who are considered iron deficiency and thalassemia minor as a result of the red blood cell indexes.

Keywords: Iron deficiency anemia, beta thalessemia minor, red cell indices

INTRODUCTION

The most common form of anemia is microcytic anemia. Microcytic anemia often arise due to iron deficiency. In addition, another factor that causes microcytic anemia is thalassemias (Turgeon, 2005). Beta thalassemia minor, which is common in Mediterranean countries, is also seen in our country by 2.1% (Çavdar and Arcasoy, 1971). But, this rate is higher in the provinces of the Mediterranean Region in our country. For example, 7.6% in Hatay, 12% in Antalya, 5.5% in Adana and 9.9% in Mugla province are evaluated (Arcasoy, 1994). In terms of incidence, Microcytic anemia needs to be clinically evaluated urgently.

Anemia is the condition, in which the value of hemoglobin or hematocrit is below normal depending an age and gender. Anemia occurs in cases when the hemoglobin value is below 13 g/dL in adult men and 12 g/dL in adult women (Kern, 2002). Iron deficiency anemia and thalassemia constitute the majority of microcytic anemia. In addition, chronic disease anemia, copper deficiency, lead poisoning are other kinds of microcytic anemia (Haznedar, 2003). Depending on the iron deficiency anemia, clinical findings such as fatique, palpitations, and pale skin can be seen. In addition, developmental delay in children and weakness in perception in adults are causes of anemia due to iron deficiency. In laboratory findings of iron deficiency anemia, Hb value and MCV value are often low in whole blood count. Iron deficiency anemia is also present where MCH and MCHC values are low. An increase in RDW value is observed (Hoffbrand et al., 2006).

Thalassemias are autosomal recessive inherited syndromes and have a widely distributed all over the world (Cooley et al., 1984). It manifests as disorders in globin synthesis. Clinically the most common are alpha and beta thalessemia. Beta thalassemia is in the group of minor microcytic anemia and is detected by increases in HbA2. Thalessemia minor does not show clinical sings but symptons can be observed in cases such as pregnancy, stress and infection (Cooley et al., 1984). Differantial diagnosis of iron deficiency anemia and beta thalessemia minor can be made by laboratory study. Differential diagnosis between these two syndromes can be made by using erythrocyte indices. In our study, the differential diagnosis of iron deficiency anemia and beta thalessemia minor was made using erythrocyte indices.

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MATERIALS AND METHOD

Patients who were diagnosed with iron deficiency anemia (IDA) and beta thalessemia minor (BTM) at the hematology outpatient clinic of Kahramanmaras Sutcu Imam Hospital between January 2019 and March 2019 were included in our study. A total of 52 patients were included in our study, of which 25 were diagnosed with IDA, 5 were diagnosed with BTM and 22 were with iron deficiency beta thalassemia minor. To our research; patients with hemoglobin levels between 9-12 g/dL for women, 9-14 g/dL for men and MCW values below 80 fl were included. All hemogram values used in the study were obtained from ‘‘cell-dyn sapphire’’ devices as standard. Ferritin values were obtained from ‘‘Architect-ci 8200’’ device.

Table 1. *Calculation of erythrocyte indices*

Mentzer Index (MI)	MCV/RBC
Green & King Index (G&K)	MCV2 x RDW /100x Hb
England & Fraser Index (E&F)	MCV- RBC-5Hb-3.4
RDW Index (RDWI)	MCVxRDW/RBC
Ricerca Index (RI)	RDW/RBC
Srivastava Index (SI)	MCH/RBC
Shine & Lal Index (S&L)	MCV2 x MCH /100

Hemoglobin, RBC, MCV and RDW values were recorded in all patients group respectively. With the help of these values, Mentzer Index (MI), Green & King Index (G&K), England & Fraser Index (E&F), RDW Index , Ricerca Index (RI), Srivastava Index (SI) ve Shine & Lal Indexes (S&L) values of the patients calculated according to Table-1. With the decision dated 12/07/2019 and numbered 5, the necessary ethics committee permission was obtained from the Medical Faculty of Kahramanmaras Sutcu Imam University. In addition informed consent was obtained from the patients included in our study.

RESULTS

The red blood cell indexes’YI (Youden index) values were found as S&L (100%)>RI (84%) >E&F (72%) > RDW (64%) > G&K (64%) > RDWI (64%) > SI (56%) > MI (44%) >RBC (44%) in the differential diagnosis of IDA and BTM. YI (Youden Index) values of the red blood cell indexes were found as RDW (100%) > S&L (96.29%) RI (72.8%) > G&K (54.37%) >E&F (51.25%) > RDWI (50.6%) > SI (50.07%) > RBC (49.18%) > MI (45.18%) in the differential diagnosis of ‘‘IDA’’ diagnosed patient group and ‘‘BTM with DETMER’’ diagnosed patient group. The hemalotogical parameters of the patients are shown in table-2.

Table 2. *Results of hematological parameters in iron deficinecy anemia (IDA) and beta thalessemia minor (BTM)*

	DEA	BTM
RBC (x106 /µL)	4.37±0.5	5.67±0.6
Hb (g/dL)	10.23±1.7	11.52±1.3
MCV (fL)	69.31±6.9	64.21±5.0
MCH (pg)	21.77±3.9	20.51±1.8
RDW (%)	17.85±3.1	16.92±1.7
Ferritin (ng/dL)	4.02±1.9	89.6±1.34

Results are given as mean ± standard deviation (SD).

DISCUSSION

Various differentiator methods have been used between IDA and BTM. These methods developed are not ability to be applied everywhere and they are quite high in cost. Differential diagnosis can be made easily by using erythrocyte parameters. When looking at the erythrocyte index in simple way, it can be seen that there are differences in 3 basic parameters and a diagnosis can be made. Unlike iron deficiency anemia in beta thalassemia minor; erythrocyte count is higher, RDW, which is an indicator of anisocytosis is lower , and the MCV is disproportionately low with the Hb level (Mentzer, 1973). Kahramanmaras is a city located in the Mediterranean Region. Our study was conducted to investigate the roles of nine erythrocyte indices (MI, RBC, G&K, E&F, RDW, RI, SI, RDW1 and S&L) in the differential diagnosis of iron deficiency and thalassemia minor patients in our province with high beta thalassemia density.

In our study, patients were evaluated by dividing into 3 groups. Patients with IDA in our first group and patients with BTM were included in our second group. Finally, patients with beta thalassemia in addition to iron deficiency (DETM) were included in our third group. Youden index is a correct method in terms of selectivity. When the erythrocyte indices of iron deficiency anemia and beta thalassemia minor patient groups were compared, the highest values in terms of YI S&L (100%)>RI (84%)

>E&F (72%) > RDW (64%) > G&K (64%) > RDWI (64%) > SI (56%) > MI (44%) >RBC (44%) were found to be respectively. Hematological parameters in IDA and BTM are shown in Table-2. The E&F formula with a high Youden index value uses the erythrocyte count and MCV values. This situation indicates that erythrocytes count is an important parameter in the differentiation of iron deficiency anemia and beta thalassemia. In addition, erythrocyte indexes of BTM and DETM and IDA were evaluated together with patients in our study. When we compare the DETM patient group and BTM patient group with the patients with IDA the YI values of the erythrocyte indices RDW (100%) > S&L (96.29%) RI (72.8%) > G&K (54.37%) >E&F (51.25%) > RDWI (50.6%) > SI (50.07%) > RBC (49.18%) > MI (45.18%) were found to be respectively. When we compare the DETM patient group with the IDA group, it is seen that high YI values are formed in detecting the presence of BTM. This phenomenon has not been shown in literature studies. It can be said that this situation adds a different originality to our work. Although there was IDA in the DETM patient group, it was observed that the erythrocyte indices were different.

Erythrocyte distribution width (RDW) is an indicator of anisocytosis (Keskin et al., 2000). Therefore, it is higher than normal in iron deficiency anemia. It has been shown many studies that RDW is high (Akgüneş et al., 2005). RDW's efficiency was found to be high in our study. While RDW activity was found to be low for differential diagnosis in some studies, it was evaluated as normal value in our studies (Adamson, 2005; Ntaios et al., 2007). S&L, E&F and RI were found to be the indexes with the highest YI value in our research.

Among the values we find high the E&F index is observed to be high in many studies (Demir et al., 2002). In our study, the index with a YI value of 72% (E&F) took the third place in the activity. When previous studies are reviewed, it is seen that the YI value of E&F varies between 57.6% and 75% (Beyan, 2007). In our study, the average YI value of MI was found to be 44.75%. Its distinctiveness is rated low. In literature studies, the mean YI value of MI ranges between 42% and 75% (Okan, et al., 2009; Rahim, et al., 2009). In our research, it is seen that the average value of RBC index is 47.5%. In literature studies, the mean YI value of the RBC index is between 50% and 82% (Gülez, 1998).

The red blood cell indexes'YI values were found as S&L (100%)>RI (84%) >E&F (72%) > RDW (64%) > G&K (64%) > RDWI (64%) > SI (56%) > MI (44%) >RBC (44%) in the differential diagnosis of IDA and BTM in our study. When evaluated together with other studies, the E&F value is similar. RBC and MI values appear to be lower than other studies.

CONCLUSION

Erytrocyte indices can be used in differential diagnosis. Although there are similar results in literature studies, it would be wrong to make a definite diagnosis by only looking at the erytrocyte index. It will be diffucult to calculate these values in practice and keep them in mind in outpatient clinic conditions. Based on the indexes, patients who are thought to have IDA should be followed up with iron treatment, and patients who do not improve should be referred to a higher center and serum ferritin analysis should be performed. In addition, with the help of indices hemoglobin electrophoresis should be performed and the diagnosis should be confirmed.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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***Ethical Considerations*:** Research study participants were approved by the Kahramanmaraş Sütçü İmam University Ethic Committee for Non- interventional Studies (Number: 2019/5, Date:12/07/2019).

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