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Red cell distribution width as a differential parameter between iron deficiency anemia and α-thalassemia: an empirical approach

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Iron deficiency anemia (IDA) and thalassemia minor are the most common hypochromic microcytic anemias in the world. Different formulas have been proposed to differentiate IDA from beta thalassemia minor. However, yet no formula has been proposed to differentiate IDA from alpha thalassemia minor, and Hb electrophoresis is not helpful in this hemoglobinopathy. Red cell distribution width (RDW) as indicator of changes in red blood cell size is primarily employed to differentiate IDA from other microcytic anemias. An empirical approach involving iron therapy over 1 month has shown that an increase in Hb concentration by 1 g/dL over this period is indicative of IDA, while no changes in Hb concentration are suggestive of alpha thalassemia. RDW measured after iron therapy in order to differentiate IDA and related disorders from alpha thalassemia is a better index than an increased reticulocyte count. Due to the high prevalence of IDA and costly and time-consuming nature of specific diagnostic tests, the RDW index is considered as a very sensitive and cost-effective tool in the differential diagnosis of IDA.

Key words: *iron deficiency anemia, α-thalassemia, red cell distribution width, hypochromic microcytic anemias, β-thalassemia*

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Iron deficiency anemia (IDA) and thalassemia minor are the most common hypochromic microcytic anemias in the world. IDA is essentially a nutritional disorder, while thalassemia occurs as a result of a genetic disorder in the synthesis of alpha or beta chains of hemoglobin (Hb), which is therefore divided into alpha and beta thalassemia (α-/β-thalassemia) [1]. Previous studies have shown that more than 50% of women in Khuzestan province in Iran suffer from IDA and 7–10% of them carry β-thalassemia trait (β-TT). Beta thalassemia minor has mild symptoms. Moreover, the prevalence of α-thalassemia minor and silent alpha thalassemia carriers in this province has been reported to be about 20–30% [2–4]. In silent alpha thalassemia, only one of the four genes encoding the alpha chain is deleted or disrupted, and individuals are completely asymptomatic. Premarital screening (PMS) tests are very important because of the similarity of IDA and thalassemia minor symptoms and the risk of marriage between two people with thalassemia minor. If both partners have thalassemia minor, they should have complementary tests (PMD) [5]. Different formulas have been proposed to differentiate IDA from beta thalassemia minor. For example, if an RBC count is above 5 million cells per mcL, the diagnosis is in favor of beta thalassemia minor, and if it is lower, the diagnosis is in favor of IDA. More conclusively, an increase in hemoglobin A2 (HbA2) levels on hemoglobin electrophoresis confirms the presence of β-TT [6]. However, yet no formula has been proposed to differentiate IDA from alpha thalassemia minor, and Hb electrophoresis is not helpful in this hemoglobinopathy; therefore, the diagnostic approach is to rule out other microcytic anemias. Red cell distribution width (RDW) is an indicator of changes in red blood cell size and is primarily employed to differentiate IDA from other microcytic anemias. Recent evidence, however, suggests that this indicator may help to confirm a diagnosis of such diseases as cardiovascular disease, thromboembolism, diabetes, cancer, obstructive pulmonary disease, liver and kidney disease. As mentioned above, the differentiation of thalassemia minor from IDA is very important but hampered by the similarity of symptoms between these entities. Various tests and hematological parameters, including electrophoresis and cell morphology may be applied in differential diagnosis, but cost and time are two important factors in choosing the diagnostic methods. Therefore, treatment staff needs to select a gold standard with high sensitivity and specificity [7–9]. In differentiating between beta thalassemia minor and IDA, the RDW index with a sensitivity of over 80% and a specificity of over 50% is very useful in early diagnosis. It can help differentiate IDA from other microcytic anemias along with other indicators such as RBC count, mean cell volume (MCV), mean corpuscular hemoglobin concentration (MCHC) as well as iron and ferritin levels [10–12]. An increase in RDW indicates active erythropoiesis. In a study, the RDW index was measured in a number of children with thalassemia, IDA and healthy children. The RDW values were

13.2 ± 0.9, 20.7 ± 3.2 and 15.4 ± 1.4 in healthy children, children with IDA and beta thalassemia minor, respectively. Therefore, in IDA patients, the RDW index is significantly increased but it can be normal or slightly increased in beta thalassemia minor. In people with symptoms of microcytic anemia (MCV < 80), the RDW index is very sensitive and important for the diagnosis of IDA (13). In the age groups under 10 years, other RBC indices such as the Youden's index and the Shine and Lal index are more sensitive than RDW in differentiating between IDA and beta-thalassemia minor (β-TT), but in people over 10 years old, the RDW test and RBC count are the most accurate tests [14]. In patients with IDA, iron therapy significantly improves RDW, hematocrit, hemoglobin and RBC morphological indices, but earlier changes in RDW compared to the changes in other indices confirm a high sensitivity of this index. The severity of iron deficiency can be detected by transferrin saturation level [15]. Unlike for beta thalassemia, in which RBC count can be used in differential diagnosis between beta thalassemia and IDA, no precise formula has been established for alpha thalassemia minor, as stated earlier. Similar to people with IDA, many people with alpha thalassemia minor often have an RBC count of less than 5 million cells per mcL and a high RDW. An empirical approach involving iron therapy over 1 month has shown that an increase in Hb concentration by 1 g/dL over this period is indicative of IDA, while no changes in Hb concentration are suggestive of alpha thalassemia. Empirical evidence has shown that both IDA and alpha thalassemia minor patients may initially have a high RDW. At first glance, a higher RDW is more suggestive of IDA, but on the other hand, a high RBC count would be indicative of alpha thalassemia. However, this is not always the case, as if iron therapy is performed for only one week instead of one month due to certain circumstances (e.g. cultural features of the region), an increase in RDW after one week of treatment will be considered as indicative of iron deficiency; the more severe IDA is, the greater the increase in RDW is. Patients who do not show an increase in RDW after one week of iron therapy are referred to a genetic laboratory for the verification of alpha gene mutations. In case genetic testing confirms this diagnosis, all hematological parameters usually return to normal in patients with increased RDW after three months of continuous iron therapy. The latest hematological indices to be improved in IDA patients are MCV and MCH.

CONCLUSION

Red cell distribution width (RDW) measured after iron therapy in order to differentiate iron deficiency anemia (IDA) and related disorders from alpha thalassemia is a better index than an increased reticulocyte count, because an increase in reticulocyte count firstly may not be prominent and secondly depends on the observer and there is a possibility of an individual error. Due to the high prevalence of IDA and costly and time-consuming nature of specific diagnostic tests, the RDW index is considered as a very sensitive and cost-effective tool in the differential diagnosis of IDA.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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