Hematological Indices for Differentiation of Beta Thalassemia Trait and Iron Deficiency Anemia

Beta Thalassemia Trait (β-TT) and Iron Deficiency Anemia (IDA) are among the most common types of microcytic anemias encountered by clinicians.[1,2] β-TT is the hemoglobinopathy which is transmitted by heredity and is estimated about 50% of the world's population in Southeast Asia; it is also common in the Mediterranean region, the Middle East, Southeast Asia, Southwest Europe and Central Africa.[3] The high carrier frequency of β-TT, is reported in Cyprus (14%), Sardinia (10.3%) and Southeast Asia (1-9%).[4] Individuals with the Beta Thalassemia Trait are usually asymptomatic and may be unaware of their carrier status unless diagnosed by testing. In Pakistan the frequency of β-thalassemia Trait is 5-8% and is present in all ethnic groups. It is estimated that Pakistan has 9 million carriers of β-thalassaemia, producing more than 5000 births of Transfusion Dependent Thalassemia (TDT) every year. This number is increasing day by day due to the illiteracy and lack of thalassemia awareness programmes.[5,6] According to World Health Organization (WHO) the other alarming issue in under developed countries is Iron Deficiency Anemia which resulted in 273,000 deaths and the loss of 19.7 million disability-adjusted life years, accounting for 1.3% of the global total, with 97% occurring in low and middle income countries.[7,8]

The discrimination between β-thalassemia Trait and Iron Deficiency Anemia has an important clinical implication. Therefore, a reliable diagnosis is needed in order to reduce unnecessary laboratory testing and avoid inappropriate treatment. A wide range of parameters are available to facilitate the differentiation between iron deficiency and thalassemia trait.[9] The elevation in HbA2 level is the most significant parameter for identifying β-thalassemia carriers (Normal value of HbA2 is < 3.5%).[10] Literature reveals that Iron deficiency often occurs in combination with other illnesses that complicate the differential diagnosis. It regulates the Hb A2 synthesis, resulting in reduced HbA2 levels in patients with iron deficiency. On the other hand, patients with thalassemia trait and concomitant iron deficiency may show normal or low HbA2 levels. Hence, diagnosing patients with concomitant thalassemia and iron deficiency is even more challenging.[11] The misdiagnosis can lead to homozygosity for β thalassemia resulting in birth of thalassemia major child, which is often "Transfusion-Dependent" and, rarely "Non-Transfusion Dependent" (molecular diagnosis is used to define genotypes with mild forms). Application of the Complete Blood Count (CBC) indices is recommended for screening iron deficiency and β-thalassemia trait. The main idea of using different indices in discrimination is to screen the patients having a high probability of requiring appropriate follow-up to reduce unnecessary investigations and costs. Reduction of healthcare budgets and increasing parameters available in hematological analyses make it necessary to provide support and interpretation for a correct clinical diagnosis.[12] Electronic cell counters have been used to determine red cell indices as a first indicator of β-TT.[13]

Zahid Hussain et al described the below mentioned formulae for distinguishing β-thalassemia Trait from Iron Deficiency Anemia.[14]

Formulae	Beta Thalassemia Trait	Iron Deficiency Anemia
MCV / RBC	<13	>13.3
MCH / RBC	<3.8	>3.8
MCV x MCH / 100	<1530	>1530

Shaily Garg et al focused on a comparative study between Mentzer's index and RDW to discriminate between β-TT and IDA. The Mentzer's index is defined as Mean Corpuscular Volume per Red Cell Count (MCV/RBC Count), a value < 13 states that the patient has β-thalassemia trait, while a value >13 suggests that the patient has iron deficiency. The principle involved is as follows: in iron deficiency, the bone marrow cannot produce as many RBCs and they are microcytic, so the RBC count and MCV both will be low, as a result, the value will be >13.3. Conversely, in β-thalassemia, the number of RBC's produced is normal, but the cells are smaller and more fragile. Therefore, the RBC count is normal or bit increased but the MCV is low, so the value will be < 13. Similarly, RDW critically defines microcytic hypochromic anemia where an index of >18 shows IDA.[12,13] The accuracy can be improved when read in conjunction with peripheral smears, however a definitive differential diagnosis between β-TT and IDA is based on the result of HbA_2 electrophoresis, serum iron and serum ferritin levels.[15]

Several medical centers in Pakistan lack the facility of Hb electrophoresis and instruments for special chemistry, red cell indices given by electronic counters can be reliably used there to differentiate between β-thalassaemia Trait and Iron Deficiency Anaemia. On a quick glance red cell count would be normal or raised in β-TT while MCV and MCH would be decreased. On the other hand red cell count along with MCV and MCH will be reduced in IDA.

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