

correspondence

Separating Thalassemia Trait and Iron Deficiency by Simple Inspection

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To the Editor

Recently the *Journal* has published interesting articles and correspondence on the subject of the separation of thalassemia trait (TT) from iron deficiency anemia (IDA) by the use of RBC indices. Rathod et al¹ calculated 6 previously described indexes on 200 patients and correlated the findings with the findings of hemoglobin electrophoresis and iron studies. They favored the Shine and Lal index.² Harrington et al³ used morphologic findings for the same purpose and, in the process, generated data showing red cell distribution width (RDW) to be a good discriminatory tool. Ntaios and Chatzinikolaou⁴ criticized the use of RDW as a discriminator, having previously found it of little value.

I believe it is usually easiest to separate TT and IDA by simple inspection, rather than using a mathematical index, using the following rules: (1) TT rarely causes anemia of less than 10 g/dL (100 g/L) of hemoglobin. (The hemoglobin value is usually more than 11 g/dL [110 g/L].) (2) The RBC count in TT is more than $5.0 \times 10^6/\mu\text{L}$ ($5.0 \times 10^{12}/\text{L}$) and in IDA is less than $5.0 \times 10^6/\mu\text{L}$ ($5.0 \times 10^{12}/\text{L}$). (3) The RDW in IDA is more than 17% and in TT is less than 17%.

Discordances usually indicate a combined anemia. Here are a few illustrative true patient examples. (1) A 19-year-old woman was seen in the emergency department (ED) for a urinary tract infection. Her blood indices included the following: hemoglobin, 11.9 g/dL (119 g/L); mean corpuscular volume (MCV), $64.3 \mu\text{m}^3$ (64.3 fL); RBC count, $5.77 \times 10^6/\mu\text{L}$ ($5.77 \times 10^{12}/\text{L}$); and RDW, 15.6%. All parameters indicate that she has TT, and there is no need for a hematologic workup. (2) A 37-year-old woman was seen in the ED for vaginal bleeding associated with uterine fibroids. Her blood indices included the following:

hemoglobin, 4.6 g/dL (46 g/L); MCV, $58.0 \mu\text{m}^3$ (58.0 fL); RBC count, $2.75 \times 10^6/\mu\text{L}$ ($2.75 \times 10^{12}/\text{L}$); and RDW, 27.9%. All parameters indicate IDA, and there is no need for a hematologic workup. Note that the severity of the anemia results in quite small cells. This yields a Shine-Lal index of 565, which would falsely indicate TT. Simple inspection obviates that problem. (3) A 52-year-old woman was seen in the ED for fatigue. Her blood indices included the following: hemoglobin, 8.8 g/dL (88 g/L); MCV, $54.7 \mu\text{m}^3$ (54.7 fL); RBC count, $5.83 \times 10^6/\mu\text{L}$ ($5.83 \times 10^{12}/\text{L}$); and RDW, 20.5%. The hemoglobin and RDW levels indicate IDA, but the RBC and cell size favor TT. She has TT and IDA.

As Harrington et al³ noted, morphologic examination can be quite helpful to confirm the impression. If one wishes to use an index, I favor adding the RDW to the England-Fraser method.⁵ The mean RDW for TT must, therefore, be added to the cutoff value of 3.4. In our laboratory, this sum is $3.4 + 15.5 = 18.9$. (Rathod et al¹ seem to have used a zero cutoff rather than the original 3.4, which may partially account for the failure of the England-Fraser index to perform well in their study.) The formula is then as follows: $\text{MCV} + \text{RDW} - (\text{RBC} + 5 \times \text{hemoglobin})$. Values of more than 18.9 indicate IDA, and values of less than 18.9 indicate TT.

When anemia of chronic disease (ACD) is a consideration, the total iron binding capacity or soluble transferrin receptor level will usually separate ACD from IDA.

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The Author's Reply

In response to recent articles published in the *Journal*,¹⁻³ Dr Burdick suggested that simple inspection (with the help of 3 rules concerning the degree of anemia, RBC count, and RDW value) is usually easier for differentiating TT from IDA, rather than using a mathematical index. However, in the examples that he used to support his argument, his conclusion was based not only on these 3 criteria but also on the MCV. Therefore, my first observation would be that, even if simple inspection is to be used for the discrimination between TT and IDA, 4 criteria are necessary, not 3. But actually, these 4 parameters are the ones that are also used to make up most of the indices.⁴ That means that these indices are nothing more than a mathematical expression of the rules that Dr Burdick suggested.

I agree with Dr Burdick that simple inspection is much easier compared with using mathematical indices. Moreover, in most cases, the conclusion (whether TT or IDA) is so obvious that their application seems needless. However, in daily clinical practice, we encounter many cases that are not typical and in which the results are different from expected, according to the final diagnosis. In a recent study by our

group, hemoglobin values ranged between 6.6 and 12.9 g/dL (66-129 g/L) in patients with TT. Similarly, RBC count, RDW, and MCV values ranged between 2.7 and $7.5 \times 10^6/\mu\text{L}$ (2.7 - $7.5 \times 10^{12}/\text{L}$), 10.5% and 40.4%, and 53.5 and 81.7 μm^3 (53.5-81.7 fL), respectively.⁴ It is obvious that there is considerable deviation in the range of these parameters, with a significant number of cases being "atypical."

It is my opinion that the erythrocytic indices are really reliable when a "typical" case is considered; however, it is the atypical cases that make them unreliable, not only for a definitive diagnosis but also for mass screening (owing to low sensitivity). This is the reason that, although many indices have been suggested, hemoglobin electrophoresis remains the "gold standard." In my opinion, simple inspection of these parameters has the same weakness as the indices.

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The Author's Reply

Thank you for the comments and observations. As per the suggestion, only simple findings such as RBC count and RDW can determine the β -thalassemia trait (BTT) status, but we do not think that this will help in all cases, particularly in areas with a high prevalence of BTT. We also noticed in our study¹ that a single parameter such as RBC or RDW performed poorly. This is mainly because of a high prevalence of nutritional deficiencies and chronic infection along with BTT, particularly in our country. The morphologic examination has a role in diagnosis, but it is subjective and nonspecific because it requires good technique for preparation and reporting of peripheral smears, which is not readily available in a developing country like ours.

Regarding the England and Fraser index, we used the cutoff from the original article. The modification factor is not applied in our study. Regarding the inclusion of RDW in

this index, we think that it will not increase the sensitivity. One has to study such modification to say anything. Another problem with the RDW is the different principles used by cell counters to derive it.

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