RDW for Discrimination between Iron Deficiency Anemia and Beta Thalassemia Trait among cohort of Egyptian children in Upper Egypt

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Background: Iron deficiency anemia (IDA) and beta thalassemia trait (β-TT) are most common causes of microcytic hypochromic anemia. When the diagnosis of iron deficiency anemia and thalassemia minor, is based only on hematological parameters and erythrocyte morphology, It is necessary to carry out the gold standard tests to differentiate between these two types of anemia, once the therapeutic conduct is distinct for each case.
Objective: This study aims to validate the red blood cell distribution width (RDW) for discrimination and differentiation between iron deficiency anaemia from beta thalassemia trait in Qena University Hospital.

Patients and method(s): This study is a prospective descriptive hospital based study included 30 patients (13 male and 17 female) who presented with microcytic hypochromic anemia by CBC not responding to iron therapy and suspected as β-TT at pediatric outpatient clinic of Qena University Hospital and their ages ranging from 1 year to 10.5 years from January 2018 until December 2018.

Result(s): This study is a prospective descriptive hospital based study included 30 patients with age of the patients ranges from 1 to 10.5 years .The data showed insignificant increase of red cell distribution width of RBCs among the studied cases of BTT group (18.06±3.51) compared to IDA group (18.76±2.77)withp value < 0.584.

Conclusion: Our study concluded that RDW adds useful but limited information in discrimination between β-TT and IDA. So, iron profile and HbA2arestill the gold standard for differentiation between β-TT and IDA.

Keywords:RDW, Iron Deficiency Anemia, Beta thalassemia trait, Qena.

Introduction:

Iron deficiency anemia (IDA) is the most prevalent micronutrient deficiency in the world.
Morphologically, iron deficiency anemia is microcytic and hypochromic as is beta-thalassemia trait (BTT) thereby creating a confusion on peripheral blood smear examination.**(DeMaeyer et al., 1995)**

Beta-thalassemia is the most commonly inherited hemoglobinopathy and often is presumptively diagnosed as iron deficiency anemia when based only on red blood cell (RBC) and morphologic features.**(Kotwal J et al., 1999)**

RDW represents the coefficient of variation of the red blood cell volume distribution so it has been proposed to be a more sensitive indicator to establish the possible origin of microcytic hypochromic anemia**. (RomeroArtaza J et al., 2000)**

Patient and Methods:

This prospective descriptive clinical This study included 30 patients (13 male and 17 female) who presented with microcytic hypochromic anemia by CBC not responding to iron therapy and suspected as β-TT at pediatric outpatient clinic of Qena University Hospital and their ages ranging from 1 year to 10.5 years from January 2018 until December 2018.

Inclusion criteria:-

• Any pediatric patients with microcytic hypochromic anemia not diagnosed to have

definite aetiology with haemoglobin level not less than 7 gm\dl.

• Patient refracting to iron supplementation, receive iron replacement for three months or more without clinical or laboratory improvement and stopped iron therapy for one month at least.

Exclusion criteria:

1- Acute or chronic inflammation

2**-** Infectious disease (CRP-ve).

3 - Acute bleeding or receive blood transfusion in previous three months.

4- Lead poisoning.

5- Anemia with hemoglobin less than 7 g\dl.

All patients subjected to the following:-

Medical History:-

1) Personal history (age, sex, residency and soci-economic state)
2) Present history (fatigue, school assessment, chronic blood loss and Pica)
3) Past history (receive blood transfusion)
4) Peri-natal history
5) Nutritional history
6) Developmental history
7) Vaccination
8) Family history
9) Medical History:-
10) Previous operation
11) Previous treatment
12) Full clinical examination was done for them focusing on abdominal assessment:

Clinical examination:-

1) General examination (pallor)
2) Anthropometric Measurements(weight, length, head circumference)
3) Extremities (nail changes)
4) Cardiac examination
5) Abdominal examination
6) Chest examination
7) Neurological examination

Investigations:-

All patients in this study were subjected to the following investigation :

Fasting venous blood samples were obtained after the children had a 30-minute rest in a sitting position. Two blood samples were taken from each child and used for

A).1.Complete blood count (CBC)

2. Hb-electrophorsis analysis test

B) The other sample was collected and then centrifuged for 5 minutes to get the serum. The serum was used for the Serum Iron, Serum Ferrtin, and total iron binding capacity.

Statistical analysis:

Data were analyzed using Statistical Package for Social Sciences (SPSS) software program (version 20). Qualitative variables were recorded as frequencies and percentages and were compared by chi-square test. Quantitative measures were presented as means ± standard deviation (SD).

Probability (P-value):

-P-value <0.05 was considered significant.

P-value <0.001 was considered as highly significant.-

-P-value >0.05 was considered insignificant.

Results:

This study is a prospective descriptive hospital based study included 30 patients with age of the patients ranges from 1 to 10.5 years. The data showed insignificant increase of red cell distribution width of RBCs among the studied cases of BTT group (18.06±3.51) compared to IDA group (18.76±2.77)in BTT group with p value < 0.584 (**Table.1**) with sensitivity 90% and specificity 40%.

Table (1): Values of RDWin the studied cases with microcytic hypochromic anemia between IDA and BBT

The studied parameters	Beta Thalassemia trait (n=20)	Iron Deficiency Anemia (n=10)	P. value
	Mean ± SD	Mean ± SD	
Red cell distribution width (%):			
Mean ± SD	18.06±3.51	18.76±2.77	**0.584**
Range	11.6 - 25	16.4 - 25.8	

The data showed insignificant increase of red cell distribution width of RBCs among the studied cases of BTT group (18.06±3.51) compared to IDA group (18.76±2.77) ($p < 0.584$).

Table (2):The diagnostic performance of the studied indices for detection of increased HbA2 serum level (>3.5%) among cases with microcytic hypochromic anemia between BTT and IDA groups:

	RDW
Optimal cut off value	>16.4
Sensitivity%	90
Specificity%	40
PPV %	75
NPV %	66.7
AUC	0.553
Accuracy%	65

(AUC= area under curve, ACC= accuracy, PPV = positive predictive value, NPV = negative predictive value)

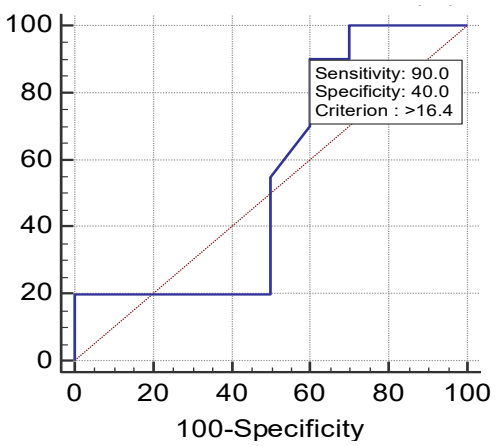

Fig (1): Receiver operating characteristic (ROC) curve to determine the diagnostic performance of RDW among the studied cases fordiscrimination between BTT and IDA group.

A ROC test was done to evaluate the diagnostic performance of RDW among the studied cases for discrimination between BTT and IDA group.it was found that the optimal cut of value of the studied parameters of RDW: was (>16.4).

Discussion:

Iron deficiency anemia (IDA) and β-thalassemia trait (β-TT)are the most frequent microcytic anemias. It is important to differentiate between these two types of anemia because it is mandatory to determine the cause of IDA and β-TT is crucial for genetic counseling.**(Lukens JN et al., 2000)**

The differentiation between them relies on measurement of serum ferritin, iron, total iron binding capacity, and hemoglobinA2 (HbA2) levels. However, these methods are money and time consuming.**(Fairbanks VF et al., 2000)**

Our study depend on value of RDW used for differentiation between IDA and β-TT through CBC and iron profile which provided us with good, rapid ,cheap and simple tools to detect subject who have a high probability of requiring appropriate follow-up and to reduce unnecessary investigative costs.

This study is a prospective descriptive hospital based study included 30 patients who %56 females and 44% males with age of the patients ranges from 1 to 10.5 years with mean age of children in β-TT is (6.1±3.23) while the

mean age in IDA group is (4.38±2.26) so, more common in school age group which similar to **Stoltzfus RJ et al., 2018** who found the prevalence of anemia ranges from 20-60% in woman and 10-35% in men with high prevalence in preschool and school children.

RDW,which is an index of anisocytosis, tends, theoretically, to be increased in IDA and normal in β-TT.

According to our results, RDW was increased (well above 14%) in both anemias so was insignificant and unreliable in discriminating between BTT and IDA with sensitivity, specificity and AUC (90% sensitivity,40% specificity and 0.553 AUC), similar to **Archana Chirag Buch et al., 2011** who founded that RDW had sensitivity67.9% and specificity25%). As well as **Zebenet al., 1990, Thompson et al.,1990** whose study showed a limited specificity of RDW that similar to **Flynn et al.,1988** and **Bagar et al.,1993** who found that RDW alone wasnot a reliable indicator to distinguish between β-TT and IDA.

In Brazil**, Lima et al.,2002; Matos et al., 2008** concluded that a correct discrimination between these disorders could not be done based on just RDW.

In contrast to our study, **Vishwanathet al., 2001**, which evaluated 100 anemic children, showed a sensitivity of 92.1% and specificity of 90.9% for RDW in detecting iron deficiency.

Conclusion:

Our study concluded that limited specificity of RDW in diagnosis of IDA among children with microcytic hypochromic children suggests that further studies like serum ferritin, serum iron, serum TIBC, bone marrow biopsy and hemoglobin electrophoresis are still necessary to make an accurate diagnosis of the cause of microcytosis.

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