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Original Article

Diagnostic Value of Red Cell Distribution Width and Red Blood Cell Distribution Width Index in Differentiating between Iron Deficiency Anemia and Beta Thalassemia Trait

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ABSTRAC

Objective: To determine the diagnostic value of red blood cell distribution width and red cell distribution width index in differentiating iron deficiency anaemia and beta-thalassemia trait.

Study Design: Cross-sectional study.

Place and Duration of Study: Pak Emirates Military Hospital, Rawalpindi Pakistan, from Dec 2021 to Feb 2022.

Methodology: A study population of 110 children with an age limit of 1.5-7 years who reported low haemoglobin was subjected to serum iron and ferritin levels with further evaluation of red cell count, blood morphology, and comparison of mean corpuscular volume. Red cell distribution width was taken from the lab report, whereas Red blood cell distribution width index value was computed for the samples.

Results: A total of 110 patients were enrolled in the study. Seventy-five (68.18%) participants were diagnosed with IDA, 26(23.63%) participants were the candidate of βTT. Nine participants were suffering from anaemia of variable etiologies such as chronic ailment and sideroblastic, etc. βTT patients presented with higher RBC counts with a mean of 5.71±1.2 x1012 /l (6.8-8.5 x1012 /l) when compared to IDA participants who deciphered values of 3.5±0.5 (2.6-4.3 x1012 /l). Mean MCV in βTT was 52.2±2.7(50.1-56.8) whereas for IDA were 72.5±1.2(61.2–78.3). In IDA low serum ferritin was recorded 4.02±1.1(2.2-9.2) as compared to mean values of βTT patients.

Conclusion: Red cell distribution width index and Red blood cell distribution width are authentic variables and inexpensive modalities in differentiating between iron deficiency anaemia and beta-thalassemia trait with reliability.

Keywords: Beta-thalassemia trait, Hemoglobin, Iron deficiency anaemia, Red cell distribution width, Red cell distribution width index.

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INTRODUCTION

Thalassemias are regarded as inherited and genetic heterogeneous hemoglobinopathy that can result in fatal anaemia, warranting sequential blood transfusions to ensure survival. In Pakistan, approximately 5000-9000 children have β-thalassemia at birth, with an estimated carrier rate of 5-7% (9.8 million carriers in the total population).[1,2] As per estimates of the World Health Organization, iron deficiency anaemia is a preeminent nutritional disorder with a 45% prevalence in Pakistan.[3] Iron deficiency anaemia (IDA) and beta-thalassemia trait (βTT) are characterized by microcytosis and hypochromia with identical morphological features.[4,5]

Previous literature concluded that derived red cell indices such as RDW, and red blood cell distribution width index (RDWI) are beneficial determinants.[6,7] RDWI is believed to have greater practical utility as all the discriminating factors, such as red blood cell (RBC) count, MCV, and RDW, are integrated with the computation.[8]

Thalassemia minor or trait present with mild anaemia refractory to pharmacotherapy. Compared to iron deficiency anaemia, Morphological RBC features are seldom seen in nucleated RBCS, normal electrophoretic mobility, and haemoglobin alkali resistance.[9]

Fetal haemoglobin and HbA2 do not increase coexistent iron deficiency. Automated blood cell counters can be conveniently used to determine RDW, leading to demarcation between two conditions. The RDW is a measure of variation in the size of average RBC with RBC histogram as a coefficient of variation of the volume distribution determined to become standard statistical value. Literature reported RDW to be a primitive deranged index in iron deficiency. An improvisation in red cell indices led to the discovery of RDWI calculated as (MCVxRDW /RBC), which is a reliable tool for the differentiation of βTT and IDA.[10] This study aims to determine the diagnostic value of red cell distribution width and red cell distribution

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width index in differentiating iron deficiency anaemia and beta-thalassemia trait.

METHODOLOGY

The cross-sectional study was carried out at Pak Emirates Military Hospital, Rawalpindi Pakistan, after getting approval from the ethical review board (ERC Number 1396/22) from December 2021 to February 2022. The sample size was calculated with the reported average prevalence for βTT was 6% as endorsed by Ansari *et al*.[11]

Inclusion Criteria: Children of either gender aged 1.5 to 7 years have MCV < 80 fl and haemoglobin < 9 g/dl on blood complete picture and no history of iron therapy during the last four weeks were included.

Exclusion Criteria: Children with chronic diseases or inflammatory conditions, those who have received a blood transfusion during the last three months and children with macrocytic or normocytic anaemia or anaemia of any other aetiology were excluded.

Participants were subjected to serum iron and ferritin levels with further evaluation of blood morphology, comparison of mean corpuscular volume and red cell count. Venous blood was collected in an EDTA tube, & CBC and RBC indices were established by Coulter Automated Cell.

Counter (LH500) in venous blood stored in an Ethylenediaminetetraacetic acid (EDTA) tube on the sampling day. Later, haemoglobin electrophoresis was performed with cellulose acetate. In the case of hypochromic microcytic presentation (haemoglobin <9 gram/dl and MCV <80fl), serum iron and ferritin levels were also measured. Various discriminant indices, as enumerated in the table-had been proposed to differentiate between two conditions; however, for the present study, only RDW and RDWI were evaluated as they are uncomplicated, inexpensive, and do not require complicated mathematical computations.[12,13]

Morphological analysis of blood, MCV comparison, RBCs no., RDW, and RDWI were also calculated. Standard Hb electrophoresis tests and serum iron levels were incorporated to differentiate IDA and βTT. Patients with HbA2 greater than 3.2% were labelled as βTT cases, whereas in the case of serum ferritin level less than 12 ng/ml, a diagnosis of IDA was made. Blood CP results with all the indices and RDW were recorded with a coulter automated analyzer LH500 for the participants, whereas the RDWI was derived from parameters obtained. Indices discriminating iron deficiency anemia and beta thalassemia trait are shown in Table-I. The cutoff values for RDW and RDWI in differentiation are given in Table-II.[14]

Table–I: Indices Discriminating Iron Deficiency Anemia and Beta Thalassemia Trait

Index	Formulae	Cut off Point
England and Fraser (E&F)	MCV–RBC–(5 Hb)–3.4	0
RBC	RBC	5.0
Mentzer	MCV/RBC	13
Srivastava	MCH/RBC	3.8
Shine and Lal (S&L)	MCV2×MCH	1.53
Bessman	RDW	15
Ricerca	RDW/RBC	4.4
Green and King (G&K)	MCV2×RDW/100 Hb	65
Jayabose (RDW index)	MCV/(RBC×RDW)	220
Sirdah	MCV–RBC–(3 Hb)	27.0
M/H ratio	Microcytic RBC %/hypochromic RBC%	3.7
Ehsani	MCV–(10 RBC)	15

** Hb in g/dL; RBC in 1012/L; MCV in fL; MCH in pg; RDW in %*

Table–II: Cutoff Points of Red cell indices for iron deficiency anemia (IDA) and beta-thalassemia trait (βTT). 14

Red Cell Indices	Iron Deficiency Anemia	Beta Thalassemia Trait
RDW(%)	<14	>14
RDWI	<220	>220

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Independent sample t-test was applied to explore the inferential statistics. The *p*-value lower than or up to 0.05 was considered as significant

RESULTS

A total of 110 patients were enrolled in the study. Seventy-five (68.18%) participants were diagnosed with IDA, 26(23.63%) participants were the candidate of βTT. Nine participants were suffering from anaemia of variable etiologies such as chronic ailment and sideroblastic, etc. βTT patients presented with higher RBC counts with a mean of 5.80±0.7 x1012 /l (5.1-6.5 x1012 /l) when compared to IDA participants who deciphered values of 3.5±0.5 (2.6-4.3 x1012 /l). Mean MCV in βTT was 52.2±2.7(50.1-56.8) whereas for IDA were 72.5±1.2(61.2–78.3).In IDA, low serum ferritin was recorded at 4.1±1.1(2.2-9.2) compared to the mean values of βTT patients. The mean RDW recorded was 13.8±2.7 and 15.4±3.31 for IDA and βTT, respectively.

The results were statistically insignificant (p=0.269) (Table–III).

Table–III: Comparison of Complete blood count (CBC) Parameters in Iron Deficiency Anemia (IDA) and Beta-Thalassemia Trait (βTT) (n=110)

Parameters	Iron Deficiency Anemia Mean±SD	Beta Thalassemia Trait Mean±SD	*p*-value
Hemoglobin(g/dl)	7.2±0.7	7.3±0.8	0.53
RBC(1012/l)	3.5±0.5	5.80±0.7	<0.001
MCV(fl)	72.5±1.2	52.2±2.7	<0.001
Mean Corpuscular Hemoglobin	23.1±2.2	17.8±1.8	<0.001
Mean Corpuscular Hemoglobin Concentration	32.3±2.1	36.1±3.4	<0.001
Ferritin (µg/l)	4.02±1.1	39.3±3.1	<0.001
Red Blood Cell Distribution Width	13.8±2.7	15.4±3.31	0.02
RDWI	21.4±3.9	11.88±2.37	<0.001

DISCUSSION

Considering the high prevalence of IDA and the significance of the diagnosis of βTT, the continuum of efforts was in the hands to establish effective, inexpensive, and easier protocols with minimal financial implications. On account of the direct effect of coexistent IDA on HbA2, thus giving ambiguous results and levels of HbA2 in βTT, discriminating outdoor laboratory evaluation is much desired as, despite intense pharmacotherapy, MCV does not show improvement in such patients.[15] To discriminate between βTT and IDA, Hb A2 evaluation is carried out by fancy procedures such as Hemoglobin electrophoresis peripheral blood film investigation and laboratory markers (serum ferritin, iron, TIBC, and transferrin saturation).RDW has an advantage in that it is already computed in complete blood counts by the automated analyzers, which are subsequently utilized to derive the value of RDWI to demarcate IDA and βTT.[16]

Sharma *et al*. studied the role of red cell distribution width for diagnosis of iron deficiency anaemia on 100 cases of microcytic anaemia (MCV <80fl), which can provide a quantitative estimation of anisocytosis, hence of great utility in the demarcation of IDA from other causes of microcytic anaemia. RDW, with a cutoff point of 14.5% along with sensitivity and specificity of 84.81% and 57.14%, was efficacious in diagnosing iron deficiency anaemia; results were in collaboration with this study.[17] Al-Numan *et al*. employed red cell indices, including RDWI, in differentiating between iron deficiency anaemia and beta-thalassemia trait among pediatric patients and concluded the largest area under the curve in the case of RDWI for detection and discrimination of IDA and βTT (p-value< 0.001).[18] Jameel *et al*. employed RDW and RDWI for discriminating beta-thalassemia traits from IDA and enrolled 135 participants of hypochromic microcytic anaemia with normal HbF and HbA2 <3.2%. They concluded that higher RBC count and lower MCV in βTT patients than IDA patients. Both batches were further evaluated with RDW and RDWI. Results for differentiation were statistically significant (p-value<0.001); however, they preferred RDWI as a diagnostic tool. [19]

LIMITATION OF THE STUDY

This study was done on a limited number of children, and more studies needed to be carried out to apply its results to the general population.

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CONCLUSION

Red blood cell distribution width index and Red cell distribution width is an authentic variable and inexpensive modality to differentiate between iron deficiency anaemia and beta-thalassemia trait with reliability.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

MBA: & FI: Conception, study design, drafting the manuscript, approval of the final version to be published.

MTN: & RA: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

SHN: Critical review, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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