ORIGINAL ARTICLE

Role of Red Cell Distribution Width and Mentzer Index in Differentiating Iron Deficiency Anemia from Anemia Due to β Thalassemia Trait

Majida Zafar[1], Arfa Tabassum[2], Quratulain A Cheema[3], Syeda B Mazhar[4]

Abstract

Objective: To determine the role of red cell distribution width (RDW) and Mentzer index in differentiating between iron deficiency anemia (IDA) and anemia secondary to β-thalassemia trait.

Materials and methods: Study design: cross-sectional study.

Setting: Department of Obstetrics and Gynecology, MCH Unit I, PIMS, Islamabad.

Duration: Six months. Primigravida with hemoglobin less than 10 mg/dL was selected. All patients were investigated with serum ferritin and Hb electrophoresis for confirmation of the thalassemia trait. Primary outcome measures were the significance of RDW and Mentzer index in differentiating IDA from anemia secondary to β-thalassemia trait. Secondary outcome measures were the prevalence of IDA and β-thalassemia trait in primigravida women.

Results: Out of the total 178 women with microcytic hypochromic anemia, 164 (92.1%) had IDA, 9 (5.1%) had coexistent IDA and β-thalassemia trait, and 5 (2.8%) had β-thalassemia trait alone. The mean RDW was 20.6 ± 5.8 in IDA category, 16.4 ± 6.7 in IDA + β-thalassemia trait, and 14.1 ± 6.5 in β-thalassemia trait alone category. RDW was significantly higher in IDA category (p value = 0.01). Similarly, the mean Mentzer index was 21.0 in IDA, 16.1 in IDA + β-thalassemia trait category. However, it was significantly low 12.2 in β-thalassemia trait alone category (p value ≤ 0.001).

Conclusion: The RDW and Mentzer index have useful significance in differentiating β-thalassemia trait and IDA, it can be used as a primary tool in low resource settings.

Keywords: Anemia, β thalassemia trait, Mentzer index, Red cell distribution width.

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Introduction

Anemia is a disorder with hemoglobin levels lower than normal or when total red blood cells are lesser than the average value.[1] Iron deficiency anemia (IDA) is the most common cause of anemia worldwide.[2] In Pakistan, the prevalence of IDA is 70–80% among the pregnant population.[3]

The loss of iron in normal pregnancy, delivery, and lactation tends to put women towards negative iron balance.[4] Serum ferritin is the most sensitive laboratory investigation to differentiate IDA from anemia due to other disorders.

β-thalassemia trait (BTT) is documented as the most common single-gene disorder transmitted by heredity.[5]

Pakistan lies in the thalassemia belt, where about 3–8% of the total population has BTT.[6] It is asymptomatic and commonly discovered during periods of stress, such as pregnancy.[3,6]

The subjects of β-thalassemia usually have normal iron stores and a microcytic hypochromic blood picture. Unfortunately, they are often erroneously treated with iron. Administration of iron to these cases can actually be harmful and produce complications of iron overload.[6] Hb electrophoresis with elevated HbA2 level is the gold standard for thalassemia screening.[3]

Iron deficiency is coexisting with BTT among individuals with lower hemoglobin levels.[7,8] Saraya et al. explained that iron deficiency in BTT leads to a lack of hemopoietic nutrients in addition to an imbalance in globin chain synthesis resulting in a further reduction in hemoglobin production.[9]

[1–4]Maternal and Child Health Care Centre, Pakistan Institute of Medical Science, Islamabad, Pakistan

Corresponding Author: Majida Zafar, Maternal and Child Health Care Centre, Pakistan Institute of Medical Science, Islamabad, Pakistan, Phone: +03335252295, e-mail: majidazafar82@yahoo.com

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The reduction in HbA_2 levels in patients with concomitant BTT and IDA has been suggested to interfere in the diagnosis of the former. There is a lack of trials that have associated the prevalence of IDA, BTT, and coexistence of both in a primigravida with hemoglobin less than 10 g/dL.[10,11]

There are concerns regarding the differentiation of IDA and BTT. Hb electrophoresis though the gold standard is an expensive test. A study was therefore undertaken to assess red cell distribution width (RDW) and Mentzer index (MI) as an indicator for differentiating between these two types of anemia.

The current study was carried out to determine the prevalence of thalassemia trait in patients with IDA in primigravida women presenting with microcytic hypochromic anemia to the Maternal and Child Health Care (MCH) centre, Pakistan Institute of Medical Sciences, Islamabad, Pakistan.

Materials and Methods

Setting and Study Design

In this cross-sectional study, all eligible pregnant women fulfilling inclusion criteria who attended antenatal clinics at the MCH centre Unit 1, Pakistan Institute of Medical Sciences (PIMS), Islamabad from June 2015 to December 2015 were enrolled. The study was approved by the Ethical Review Committee of PIMS. The laboratory services were provided with the collaboration of pathology department of Shaheed Zulfiqar Ali Bhutto Medical University (SZABMU), PIMS, Islamabad.

Sample Size

The sample size has been calculated by using the WHO calculator with the statistical assumptions of 90% power and 10% alpha error of study and magnitude of IDA 79%. A total of 178 patients were enrolled in this study through non-probability consecutive sampling technique.

Inclusion and Exclusion Criteria

All primigravida, with a singleton pregnancy, between 18 years and 49 years of age with Hb less than 10 g/dL and microcytic hypochromic anemia were enrolled in this study. Multigravida, multiple gestations, and pregnant women with Hb more than 10 g/dL were excluded from the study. Women who received blood transfusion in the last 4 weeks were also excluded from the study.

Data Collection and Analysis

Pregnant women fulfilling inclusion criteria were registered through Obstetrics and Gynecology Out Patient Department of MCH-1 PIMS, Islamabad. Demographic history including age (years), residence, occupation, family history of BTT, and family history of transfusions during pregnancy were taken. All the patients were investigated with serum ferritin and Hb electrophoresis. The blood was drawn by a trained phlebotomist. Women were followed-up after 1 week to document and save the results. All the information was collected on a specially designed pro forma. To minimize selection bias and maintain data quality of all study procedures, the data collection was performed by the researcher herself. Informed consent was taken from patients or caretakers.

The collected data was entered into SPSS version 11 and analyzed. The qualitative data like the presence of IDA (yes or no) and BTT (yes or no), occupation, residence, family history of BTT, and family history of transfusions during pregnancy were presented as frequency distribution.

Quantitative data like age and gestational age were presented as means and standard deviations. Chi-square test was applied to compare the frequency of BTT with IDA. A p value of <0.05 was considered statistically significant.

Red cell distribution width and MI was calculated from the report of blood complete picture, and the sensitivity of RDW and MI was calculated as compared to serum ferritin and Hb electrophoresis for differentiating between IDA and anemia due to BTT.

Outcome Measures

Primary outcome measures were the significance of RDW and MI in differentiating IDA from anemia secondary to BTT. Secondary outcome measures were the prevalence of IDA and BTT in primigravida women.

Operational Definitions

Anemia

Hemoglobin of less than 10.0 g/dL at any time during pregnancy in developing countries, according to WHO.[2]

Red Cell Distribution Width

The measure of the range of variation in the volume of RBC reported as a part of the standard complete blood count (CBC) is RDW. Mathematically, the red cell distribution width is calculated as (standard deviation of MCV/mean MCV) × 100. The normal range of RDW (11.5–14.5%) has a high suspicion of thalassemia trait, and high RDW often indicates IDA.[12,13]

Mentzer Index

The Mentzer index was first described by Mentzer in the year 1973. It is calculated from the CBC report. Mentzer index (MCV/RBC count) of less than 13 may represent thalassemia trait, and greater than 13 often indicates IDA.[13]

Results

Out of the total 178 primigravida women, with hypochromic microcytic anemia 164 (92.1%) had IDA, 9 (5.1%) had IDA with coexistent BTT, and 5 (2.8%) had BTT alone (Fig. 1).

The mean age of study patients was 25.1 + 3.9 years. More than 80.0% of the patients were between 21 years and 30 years of age. The mean gestational age of the patients at the time of assessment of IDA was 30.4 + 3.8 weeks. More than 90.0% had a gestational age between 26 weeks and 37 weeks. Majority 164 (92.1%) were living in the urban area, and most of the women were housewives 168 (94.3%). Nine (5.1%) patients had a positive family history of BTT. Similarly, 21 (11.8%) women were found to have a positive family history of transfusion during pregnancy.

It was found that BTT was more common among pregnant women of younger than 25 years of age ($n = 10$) compared to older women ($n = 4$), and those having a family history of BTT. Secondarily, women having a positive family history of blood transfusion during pregnancy were significantly more likely to have β-thalassemia in the present study (p value ≤ 0.001) (Table 1).

The mean hemoglobin was 8.79 + 0.60 mg/dL in the study patients. The mean RBC count was found to be 3.63 + 0.83 million/µL.

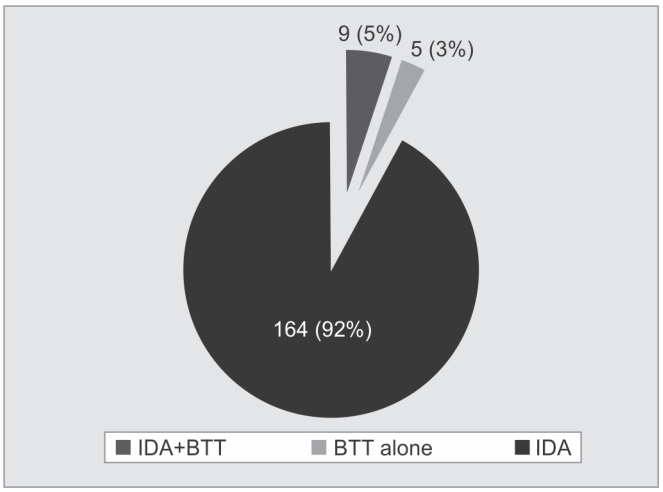

Fig. 1: Iron deficiency anemia with coexistent β-thalassemia trait ($n = 178$)

Table 1: Factors associated with β-thalassemia trait (*n* = 178)

	Total cases of β-thalassemia (n = 14)	*IDA (n = 164)*	*p value*
Age (years)			
Up to 20	1 (7.1%)	25 (15.2%)	0.02
21–25	9 (64.0%)	56 (34.1%)	
26–30	3 (21.3%)	76 (46.3%)	
31 or above	1 (7.1%)	7 (4.2%)	
Family h/o β thalassemia			
Yes	5 (35.7%)	4 (2.4%)	<0.001
No	9 (64.2%)	160 (97.6%)	
Family h/o transfusion in pregnancy			
Yes	6 (42.8%)	15 (9.1%)	<0.001
No	8 (57.2%)	149 (90.9%)	

Table 2: Average red cell distribution width and Mentzer index values in IDA and β-thalassemia categories

	IDA (n = 164)	*β thalassemia trait and coexistent IDA (n = 9)*	*β thalassemia trait alone (n = 5)*	*p value*
RDW	20.6 ± 5.8	16.4 ± 6.7	14.1 ± 6.5	0.01
Mentzer index	21.0 ± 10.5	16.1 ± 6.2	12.2 ± 5.3	<0.001

Table 3: Sensitivity and specificity of red cell distribution width and Mentzer index in diagnosis of iron deficiency anemia keeping serum ferritin as diagnostic standard (*n* = 178)

Diagnostic parameters	*RDW (%)*	*Mentzer index (%)*
Sensitivity	94.2	99.4
Specificity	50.0	00.0
Positive predictive value	98.8	97.7
Positive predictive value	16.6	00.0

The mean MCV was 68.28 + 8.54 fL, MCH was 23.31 + 15.14 pg, and MCHC was 26.91 + 5.35 mg/dL.

The average RDW and MI in different categories, i.e., IDA, coexistent BTT, and IDA and BTT, alone were calculated. The mean RDW was 18.7 in IDA category, 16.4 in IDA + BTT, and 14.7 in BTT alone (*p* value = 0.01). Similarly, the mean MI was 21.0 in IDA, 16.1 in IDA + BTT category, however, it was significantly low 12.2 in BTT alone category (*p* value = <0.001) (Table 2).

The sensitivity and specificity of RDW and MI were calculated for the diagnosis of IDA, keeping ferritin level as a diagnostic standard. The sensitivity and specificity of RDW in diagnosing IDA keeping ferritin as standard was 94.2% and 50.0%, respectively. The positive predictive value (PPV) and negative predictive value (NPV) were 98.8% and 16.6%. The sensitivity and specificity of MI in diagnosing IDA were found to be 99.4% and 00.0%, respectively (Table 3).

When Hb electrophoresis was kept gold standard for diagnosis of BTT, the sensitivity, and specificity of RDW, were found to be 64.2% and 98.1%, respectively. The PPV and NPV were found to be 75.0% and 96.9%, respectively. Moreover, the sensitivity and specificity of MI in the diagnosis of BTT keeping Hb electrophoresis as gold standard was found to be 7.1% and 100%, respectively. Similarly, the PPV and NPV of MI were found to be 100% and 92.6%, respectively (Table 4).

Table 4: Sensitivity and specificity of red cell distribution width (RDW) and Mentzer index in diagnosis of β-thalassemia trait keeping Hb electrophoresis as gold standard (*n* = 178)

Diagnostic parameters	*RDW (%)*	*Mentzer index (%)*
Sensitivity	64.2	7.1
Specificity	98.1	100
Positive predictive value	75.0	100
Negative predictive value	96.9	92.6

Discussion

The results of our study show that IDA was present in 92% of primigravida pregnant women whereas it was 78% in a national study by Toheed et al.[14] while it was 41% in a Turkish study conducted by Taner et al.[15] Study by Al-Shammari showed, by taking into account the measurement of serum iron, serum ferritin, and total iron-binding capacity, that 79% anemic pregnant women had iron deficiency. Hb electrophoresis showed an elevated HbA2 level in only 2% of cases.[3] Another study by Dolai et al. concluded that IDA is a coexisting condition in BTT.[4]

In our study, the average age of patients was 25 years, with majority between 21 years and 30 years. A slightly greater mean age of 30 years of presentation of women was reported by Chang et al.[16] Dolai from India witnessed a mean age of women presenting with IDA of 30 years.[4] Ahmed reported from UAE that majority of their cases having mild anemia were up to 30 years of age.[17] Younger age in our study could be due to the selection of primigravida women only.

The average gestational age of women was 30.4 + 3.8 weeks (third trimester) when the iron deficiency was investigated. In the study by Farzana et al., more than 75% of their women were in the 2nd and 3rd trimester when investigated for IDA.[16] Nutritional demands of fetuses increase many-fold by the third trimester, thus resulting in iron deficiency during this period in pregnant women.

In our study, the mean hemoglobin level was 8.79 g/dL and MCHC was 26.9 g/dL. In the study by Farzana, the mean values among subjects were hemoglobin 10.7 g/dL and MCHC 29.8 g/dL, shown in cases of β-thalassemia trait which was coexistent with IDA in pregnancy.[16]

Dolai et al. also witnessed a similar picture of results of blood assessments of their patients with IDA.[4] These findings were found comparable with our study results, where we also witnessed diminished parameters of blood in our patients of IDA.

In our study, the prevalence of coexistent IDA and BTT in pregnant women presenting with microcytic hypochromic anemia was (5.1%) out of the total of 178 patients. Moreover, (2.8%) patients had BTT alone. It was noticed that women with a positive family history of β-thalassemia (35.7%) and those having a family history of blood transfusions during pregnancy (42.8%) were likely to have positive BTT.

Farzana witnessed a similar proportion of BTT (6.5%) in their study women who also presented with pregnancy in Benazirabad of Sindh province. None of their patients had a family history of β-thalassemia, and there was no history of blood transfusions.[16]

Colah from India screened women, presenting for the first antenatal check-up over a period of 7 years evaluation and screened

61,935 women, they found out 1.6% of women having β-thalassemia heterozygotes.[18] This is lower than in Pakistani studies.

Sukrat reported a prevalence of 6% of IDA in their study and confirmed (2.3%) cases of BTT in their study women from Nakhon Sawan Thailand.[19]

These reports are continuous with our study findings regarding the prevalence of BTT in pregnant women having IDA. There have been many reports regarding BTTs in pregnancy. A previous World Health Organization report revealed that about 7% of pregnant women were a carrier of BTT.[20]

Study conducted by Ou et al.[21] and Shrivastav et al.[22] detected elevated hemoglobin A2 as a marker of BTT in pregnancy.

In our study, on sub-analysis of complete blood count parameters, MI and RDW were found lower in patients with BTT alone. However, they were found raised in IDA cases. These findings of RDW and MI are continuous with previous study reports and validate the results of previous studies on the topic.[12] In our study, the RDW cut-off was <15 in BTT cases, and the MI cut-off was <13 in these cases.

The RDW and MI have useful significance in differentiating BTT and IDA. In the present study, both RDW and MI had high sensitivity and average specificity in the diagnosis of IDA, while an average sensitivity and high specificity in the diagnosis of BTT. Beyan et al. reported the same findings in their study.[12] The high sensitivity for IDA is beneficial because iron deficiency is a condition not desired to be missed in an iron-deficient population. Advantageously, the study also shows a high specificity of RDW and MI for ruling out BTT that requires expensive test Hb electrophoresis for diagnosis.

However, Mazza et al. suggest that in practice, MI can not be completely used as an indicator of the type of anemia because in thalassemia RBC count is normal, and MCV is low. Practically, the RBC count has to be extremely high, and the MCV extremely low to achieve an MI of less than 13. And this is something rare to be seen, raising queries about the reliability of the index.[12,13]

The strengths of this study are that a large sample of primigravida women with microcytic hypochromic anemia was recruited. All had iron store studies as well as Hb electrophoresis was done, which is a useful data for the population of the federal capital Islamabad. A cheap readily available test complete blood count was utilized to extract the RDW and MI. These were assessed and compared with gold standard for IDA and BTT.

The limitations of this study are that spot enrollment was done using a cross-sectional observational design. Moreover, the patients were not followed up until delivery.

Conclusion

The coexistence of IDA and BTT in primigravida women is 5.1% in our study. The RDW and MI have useful significance, in differentiating BTT and IDA, it can be used as a primary tool in low resource settings. They can be used as screening to select patients for Hb electrophoresis (gold standard) and prevent unnecessary parenteral iron supplementation to the cases of BTT.

This is a baseline study revealing the existence of BTT in IDA among primigravida women with microcytic hypochromic anemia and the role of RDW and MI as less expensive modalities. Further large-scale studies are needed with a rigorous methodology to follow the affected patients and collecting information regarding their long-term outcome.

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