Original Paper

Differentiation of Beta Thalassemia Trait and Iron Deficiency Anaemia by Red Cell Indices

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Abstract

Introduction: Beta thalassaemia trait (β-TT) and iron deficiency anaemia (IDA) are the most frequent causes of hypochromic microcytic anaemia in Bangladesh. Differentiation between β-TT and IDA is important for proper treatment of patients. Red blood cell (RBC) indices obtained from automated cell counter can be used to differentiate between two.

Objective: To compare among three RBC indices; red cell distribution width (RDW), red cell distribution width index (RDWI) and Mentzer's index to differentiate between β-TT and IDA.

Materials and Methods: This cross-sectional comparative study was conducted on 50 diagnosed cases of β-TT and 50 cases of IDA at the department of pathology, Bangladesh Naval Ship, Patenga, Chattogram from January 2016 to December 2017. Patients having recent transfusion history and Hb<6.0 gm/dl were excluded. RDW, RDWI and Mentzer's index were calculated from the automated cell counter. Sensitivity, specificity, positive predictive value and negative predictive value were calculated to compare diagnostic value of the indices.

Results: Mentzer's index was found the most reliable index as it had the highest sensitivity 95.1% and specificity 84.8% for detecting IDA. RDWI showed much lower sensitivity 91.2% and specificity 66.2% while RDW showed sensitivity and specificity of 83.2% and 61.1% respectively.

Conclusion: Mentzer's index is a reliable and useful index for differentiation between β-TT and IDA compared to other two indices.

Key-words: β-Thalassemia trait, Iron deficiency anemia, RDW, RDWI, Mentzer's index.

Introduction

Iron deficiency anaemia (IDA) and Beta Thalassemia trait (β-TT) are the most common causes of hypochromic microcytic anaemia in Bangladesh[1]. It is sometimes very difficult to differentiate clinically and by routine laboratory examination especially when the underlying defect is mild, early and fluctuating. According to World Health Organization estimates in 2004, there were almost 2,73,000 deaths and 19.7 million people became disable due to iron deficiency anaemia[2]. Approximately 1.3% of world population was recorded as IDA among them 93% in developing countries like Bangladesh[1]. It is estimated that about 50% of the total β-TT cases is in Southeast Asia[2,3].

The differentiation between IDA and β-TT is important because of two main reasons, firstly Haemoglobin (Hb) won't improve in β-TT if it is misdiagnosed as IDA and unnecessary iron being prescribed by the attending physician that may causes harm to the patients. The second grave reason is that misdiagnosed β-TT as IDA may get married, resulting in homozygous or thalassaemia major in the offspring. So it became mandatory to differentiate between this two as the prognosis and treatment are distinct. Hypochromic microcytic anaemia is diagnosed microscopically in adjunction with red blood cells (RBC) indices. Due to overlapping features between IDA and β-TT, complementary lab tests are needed. Diagnosis of IDA is done by evaluating/estimating serum ferritin, serum iron and total iron binding capacity (TIBC). But in case of β-TT requires Hb electrophoresis and high performance liquid chromatography (HPLC) for the quantification of HbA_2[3,4]. Despite their great utility, gold standard test for the diagnosis of these hypochromic microcytic anaemias involve time consuming and expensive technique, moreover not available in all the laboratories as well as inaccessible to lower socio economic class of people[5-7].

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RBC indices like RDW can be calculated using the automated blood cell counters for differentiation between IDA and β-TT[8,9]. The RDW measures the average RBC size variation, calculated by the RBCs histogram and is expressed in SD (fl) and CV (%), of the volume distribution. Many studies have revealed that RDW is the first index to become abnormal in iron deficiency[10-12]. Other recently added indices RDWI and Mentzer's index have proven to be a reliable index in the differentiation of β-TT and IDA[13-15]. The aim of this study was to compare diagnostic value of RDW, RDWI and Mentzer's index in differentiation of β-TT and IDA, using very simple parameters by automated cell counters.

Materials and Methods

This cross sectional comperative study was conducted from January 2016 to December 2017 at the department of pathology, Bangladesh Naval Ship, Patenga, Chattogram. Informed consent was taken from all the study subjects and the hospital administration also granted permission for the study. Total 100 diagnosed cases were selected among them 50 cases were of IDA and rests were β-TT. Patients having recent transfusion history and Hb<6.0 gm/dl were excluded from the study because below this Hb level IDA and β-TT morphologically become very much distinguishable. Aseptically 5 ml venous blood was collected in an EDTA tube from antecubital vein of each patient. Complete blood count and RBC indices were measured by Siemens automated cell counter (Advia-2120i) on the same day of collection. This instrument was calibrated daily with normal, high and low controls provided by manufacturer before running the specimen. All the data were collected in prescribed data collection sheet. For calculating the RBC indices following cell counter based formula was used in this study and cut off value of these indices have shown in Table-I.

Table-I: Cut off values of red cell indices[16]

Red cell indices	β-TT	IDA
RDW	<17	>17
RDWI	<220	>220
Mentzer's Index	<13	>13

RDWI = MCV × RDW / RBC count, Mentzer's Index = MCV / RBC count

Collected data were analyzed by using computer software SPSS for Windows version 21.0. Data presented in frequency and percentage. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) was calculated to compare diagnostic value of RDW, RDWI and Mentzer's index in differentiation of β-TT and IDA.

Results

Mean age of the patients was 39.1±13.7 years and ranged from 1 year to 70 years. Among β-TT patients maximum (38%) belonged to 1–10 years age group and among IDA patients maximum (26%) belonged to 21–30 years age group (Table-II). In both the group number of females was much higher than male (Table-III).

Table-II: Distribution of patient by age (n=100)

Age Group (Years)	β-TT Frequency (%)	IDA Frequency (%)
1 – 10	19 (38)	11 (22)
11 - 20	11 (22)	06 (12)
21 - 30	09 (18)	13 (26)
31 - 40	04 (08)	07 (14)
41 - 50	02 (04)	09 (18)
51 - 60	04 (08)	03 (06)
61 - 70	01 (02)	01 (02)
Total	**50 (100)**	**50 (100)**

Table-III: Sex distribution of patients

Group	Frequency	
	Male	Female
β-TT	19 (38%)	31 (62%)
IDA	16 (32%)	34 (68%)

Sensitivity, specificity, PPV and NPV of three parameters in patients with βTT and IDA presented in Table-IV. For detecting IDA Mentzer's index was found the most reliable index as it showed the highest sensitivity 95.1% and specificity 84.8%.

Table-IV: Sensitivity, Specificity, PPV and NPV of RBC Indices in βTT and IDA

RBC Indices	Cases	Sensitivity % CI	Specificity % CI	PPV % CI	NPV % CI
RDW	β-TT	80.2 75.2 – 85.4	42.1 58.3 – 66.4	87.3 82.4 -90.1	66.0 58.4 – 69.1
	IDA	83.2 76.2 – 87.1	61.1 58.4 – 64.9	89.2 86.4 – 90.8	65.7 64.3 – 68.1
RDWI	β-TT	79.3 66.8 – 71.6	76.4 74.3 – 79.8	47.3 45.6 – 49.6	89.6 85.3 – 91.8
	IDA	91.2 88.4 – 93.6	66.2 63.2 – 69.1	94.1 91.5 – 95.8	54.7 51.8 – 56.7
Mentzer's lindex	β-TT	73.3 70.6 – 76.1	81.1 79.8 – 83.7	66.2 63.5 – 68.7	91.2 88.9 – 93.7
	IDA	95.1 93.4 – 97.1	84.8 71.8 – 76.2	96.3 94.6 – 98.3	65.7 62.4 – 68.1

Note: CI is 95% confidence intervals

Discussion

In this study Mentzer's index sensitivity (95.1%) and PPV (96.3%) was very high for detecting IDA. However, specificity (84.8%) and NPV of IDA was low (65.7%). Specificity (81.1%)

and NPV of the index was very high (91.2%) for detecting β-TT. Similar study by Haung TC et al[17] showed a sensitivity and specificity of 95.5% and 94.6% respectively for Mentzer's index. Ismail M and Patel NG[18] reported a sensitivity and specificity 69.7% and 99% respectively. Similar results were also found by Ehsani MA et al[19]. Hence Mentzer's index showed high validity and most important differentiating index between β-TT and IDA in this study and comparable to other also[19].

RDW is a measures of anisocytosis, increases in IDA and it is normal or mild increase in β-TT. Though RDW has been reported to be a good discrimination index to differentiate β-TT and IDA but in this study the sensitivity and specificity of RDW in detection of IDA were 83.2% and 61.1% respectively and for β-TT sensitivity was 80.2% and specificity was 42.1%. Which would not be very good discriminator of β-TT and IDA. Similar findings also reported by Haung TC et al[17] and Brancaleoni V et al[20].

RDWI also denotes anisocytosis and its value also increase in IDA and remains near normal or mild increase in β-TT. In this study, sensitivity and specificity were more than 75% in detection of β-TT and IDA. The sensitivity and specificity of RDWI in the detection of β-TT were found 79.3% and 76.4%, respectively and the sensitivity and specificity for the detection of IDA were 91.2% and 66.2%, respectively. These results are consistent with the findings of other relevant studies[21].

Conclusion

Mentzer's index found the most reliable index as it showed the highest sensitivity (95.1%) and specificity (84.8%) for initial screening and differentiating β-TT from IDA. This would result in a significant cost saving for the health system, especially in underdeveloped and developing countries with limited resources.

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