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UTILITY OF RED CELL DISTRIBUTION WIDTH IN EVALUATION OF MICROCYTIC HYPOCHROMIC ANEMIA

Pathology

Lisa Varma Resident, Dept. of Pathology, Father Muller Medical College, Mangalore

Jayaprakash CS* Professor and Head, Dept. of Pathology, Father Muller Medical College, Mangalore
*Corresponding Author

ABSTRACT

Background: The microcytic hypochromic peripheral blood smear & laboratory findings cannot distinguish iron deficiency anemia from non-iron deficiency anemia. Hence, various indices like serum ferritin, serum iron, serum transferrin and bone marrow studies are required. Bone marrow studies are invasive methods and serum ferritin, serum transferrin, and serum iron are relatively expensive and not easily available at primary health centers. RDW, alongside other red cell indices, are a part of routine blood counts in laboratories using automated hematology analyzers. If this parameter could be used with sufficient accuracy to rule in or rule out different types of microcytic hypochromic anemias, further testing would be minimized and the cost of anemia work-up would drop considerably.

Methodology: The present study was carried out in the Department of Pathology, Father Muller Medical College, Mangalore from September 2014 to January 2016. Data with regard to age, gender, clinical features, peripheral blood findings and red cell indices (Hemoglobin, RBC count, MCV, MCH, MCHC,RDW) of the patients were studied.

Results: This study included a total 101 cases of microcytic hypochromic anemia out of which 67 were females and 34 were males. The age of the patients in the study ranged from 17-91 years. The mean value for RDW in IDA is 20.7424% and 19.8357% for NON-IDA. It showed no significance between the two groups. (p=.142).

Conclusion: The present study showed that RDW when used alone for diagnosis of iron deficiency anemia, is of limited utility. Similarly, normal or increased serum ferritin values alone do not exclude IDA, as the values may be increased in individuals with iron deficiency anemia along with acute and chronic infections. However, RDW when used in systemic manner in combination with other parameters such as serum iron, serum ferritin, iron binding capacity, serum transferrin saturation , bone marrow biopsy and hemoglobin studies are still necessary to make an accurate diagnosis of the cause of microcytosis. Because of the lack of specificity, we do not feel that a patient with microcytic RBC indices can be reliably categorized using only RDW as parameter.

KEYWORDS

Microcytic hypochromic anemia, red cell distribution width, iron deficiency anemia.

Introduction:

Anemia is one of the major public health problems in India. It being an important risk factor for a number of adverse outcomes in the patients, including hospitalization, morbidity, and mortality, an appropriate evaluation and management is very important.[1] The tests commonly employed for the evaluation of the cause of anemia includes a complete blood cell count, red cell indices, peripheral smear, reticulocyte count, and serum iron studies.

The present study deals with microcytic hypochromic anemias and utility of RDW in further sub-classifying them into iron deficiency anemia, which is the most common cause of this group of anemias and non-iron deficiency anemia.

Hemoglobin estimation is by far the classical and most commonly used screening test for iron deficiency.[2] The definitive test for the diagnosis of iron deficiency anemia is assessing the iron stores in the bone marrow aspiration. But, it is an invasive and expensive procedure. Alternatively, serum ferritin levels can be estimated, which is found to be the best test for distinguishing those with IDA from those who are not iron deficient.[3] Unfortunately, serum ferritin estimation test is not available freely at many primary health care centers, especially in developing countries. Hence, one needs a screening test, which is cheap and is of high reliability and accuracy in identifying the iron deficiency.[4]

RDW, along with other red cell indices, is a parameter calculated by virtually all the modern hematology analyzers available. It has also been proposed as an additional variable that would improve the initial classification of anemia and help distinguish IDA (elevated RDW) and heterozygous thalassemia (normal RDW). [5]

If we can use these easily available tests to screen IDA with acceptably high sensitivity and specificity, the cost of anemia work-up would drop considerably. The patients with RDW suggestive of iron deficiency would not have to undergo further evaluation.[6]

MATERIALS AND METHODS:

This study was carried out in the Department of Pathology, Father Muller Medical College. Study was conducted after acquiring permission from ethical review committee. Blood samples of a total of 101 cases were taken in the present study. The samples were first aspirated into differential hematology analyzer, which analyzes the samples and provides a print out with complete blood count, RBC indices, RDW, PDW, scattergram and distribution curves. The patients with hemoglobin levels less than the WHO cut off levels for anaemia were included in the study (Children 6 months to 59 months -11.0 g/l, Children 5–11 years- 11.5 g/l, Children 12–14 years -12.0 g/l, Non-pregnant women (above 15 years of age)- 12.0g/l, Pregnant women - 11.0g/l , Men (above 15 years of age) -13.0 g/l).Red cell indices, especially MCV, were assessed and all those with MCV values <75fl were further evaluated using peripheral smear morphology. Patients were classified in two groups iron deficiency anemia (IDA) and non iron deficiency anemia (Non-IDA) based on serum ferritin levels.

Patients of all age groups fulfilling the criteria of microcytic hypochromic anemia were included in the study. Only those cases with available serum iron studies were further analyzed. Patients with anemia but MCV>75 fl ,those who had received iron therapy anytime over the past one-month and those with history of blood transfusion over the past 3 months were excluded. Patients with hematological malignancies were also not included.

RESULTS

This study includes 101 cases; out of which 59 cases were iron deficiency anemia (IDA) and 42 cases were MCHC anemia due to other causes (NON-IDA). A total of 67 cases were females and 34 were males. Among 67 females, 40(59.7%) females had IDA and 27(40.3%) females had NON-IDA. Similarly, out of 34 males, 19(55.8%) had IDA and 15(44.2%) had NON-IDA. Out of 101 cases, 25(24.8%) cases were mild MCHC anemia, 31(30.7%) were moderate MCHC anemia and 45(44.6%) were severe MCHC anemia. The mean value for S.ferritin in IDA is 8.739 and NON-IDA is 786.4295.

Table No.1Comparison of S.ferritin values between IDA and NON-IDA cases

S.Ferritin	N	Mean	Std.deviation	Median	t-value	p
NON-IDA IDA	42 59	446.63 5 8.739	786.4295 5.10425	84.400 7.120	-8.214	.000 HS

It shows high significance between the two groups. (p=.000)
The mean value for RDW in IDA is 20.7424% and 19.8357% for NON-IDA.

Table No.2 Comparison of RDW values between IDA and NON-IDA cases

RDW	N	Mean	Std.deviation	Median		
					t-value	p
NON-IDA IDA	42 59	19.8357 20.7424	3.70430 3.10535	19.5000 20.5000	-1.468	.142 NS

It shows no significance between the two groups. (p=.142).
The mean value of hemoglobin in NON-IDA cases is 7.9071 and 6.4492 in IDA cases.

Table no.3 Comparison of hemoglobin between IDA and NON-IDA cases

Hemoglobin	N	Mean	Std.deviation	Median		
					t-value	p
NON-IDA IDA	42 59	7.9071 6.4492	1.58351 2.30925	7.8000 6.8000	-3.229	.001 HS

It shows high significance between the two groups. (p=.001)
The mean value of MCV in NON-IDA cases is 70.9357 and 62.0458 in IDA cases.

Table no.4 Comparison of MCV between IDA and NON-IDA cases

MCV	N	Mean	Std.deviation	Median		
					t-value	p
NON-IDA	42 59	70.9357 62.0458	11.00975 7.35891	70.3000 60.5000	-4.317	.000 HS

It shows high significance between the two groups. (p=.000)

Discussion :

The earliest morphologic change seen in iron deficiency anemia is red cell size variation (anisocytosis). RDW is a quantitative measure of red cell size variation. It can give an idea of early iron deficiency before other tests become positive because red cell size variation is the earliest morphologic change in iron deficiency anemia. In pre-latent and latent stage of iron deficiency MCV are normal while Red Cell Distribution Width (RDW) is expected to increase in the latent stage itself because of appearance of microcytic population of cells in the blood.[52,53]

A number of studies demonstrating importance of RDW have been conducted on different age groups.In the present study, anemia was further classified according to WHO criteria into mild (Hb 9-10.9g/dl), moderate (Hb 7-8.9g/dl) and severe anemia (Hb<7g/dl).

Table no.5 Comparison of anemia between present study and other published studies

	Mild	Moderate	Severe
Choudhary et al (2015)	23%	60%	17%
Chithambaram et al (2014)	70.4%	26.5%	3.1%
Khan et al (2014)	75%	14.8%	7.0%
Vishwanath et al (2001)	55%	22.5%	22.5%
Present study	24.8%	30.7%	44.6%

Majority of the cases in present study were severe anemia while mild anemia was found to be more consistent finding in other studies.

Several studies were conducted for evaluation of sensitivity and specificity of RDW in diagnosis of iron deficiency anemia. Flynn et al in their study found sensitivity and specificity of RDW as 94% and 51% respectively. Zeben et al found similar results with sensitivity of 94% and specificity of 59%. However , these values were not consistent with other studies. In two different studies conducted by Khan et al and Chithambaram et al sensitivity was found to be 75% and 47% respectively while specificity was 14.8% and 74%.

In the present study, RDW was found to be raised in both IDA and NON-IDA groups. However, it was more in IDA (20.7±3.1) as compared to NON-IDA (19.8±3.7). The reason for the difference between the present study and other published studies was sought for. On retrospective analysis of the cases, it was found that out of 42 cases of NON-IDA, 12 cases were known cases of IDA who had come to our hospital in the present setting with complaints like fever, acute gastritis, acute bronchitis, pneumonia, ear infection etc. Their serum ferritin levels were either normal or high. Serum ferritin reflects total body iron deposits in the absence of inflammation. Thus, a low serum ferritin unequivocally means iron deficiency, which may or may not be accompanied by anemia.[54] But ferritin is also an acute phase reactant and its serum levels may be misleading in the presence of acute or chronic inflammation. Thus one cannot exclude iron deficiency as the cause of anemia when the serum ferritin is normal or even elevated in the presence of an inflammatory process. [55]

The presence of acute or chronic infection in these 12 cases in our study led to their wrong initial placement in NON-IDA group. Since these cases had fairly high RDW because of underlying IDA this led to high mean RDW in NON-IDA group resulting in similar RDW in both the groups.

Conclusion :

There is high prevalence of iron deficiency anemia in our country. Thus, it becomes important to diagnose them early to give adequate treatment with iron supplements and dietary modifications. Also, there is need to develop low cost diagnostic modalities for early detection of IDA. Currently, most automated cell counters display RDW, which aids in the diagnosis of iron deficiency anaemia. RDW, when used alone for diagnosis of iron deficiency anemia, is of limited utility. Similarly, normal or increased serum ferritin values alone do not exclude IDA, as the values may be increased in individuals with iron deficiency anemia along with acute and chronic infections. However, RDW when used in systemic manner in combination with other parameters such as serum iron, serum ferritin, iron binding capacity, serum transferrin saturation , bone marrow biopsy and hemoglobin studies are still necessary to make an accurate diagnosis of the cause of microcytosis. Because of the lack of specificity, we do not feel that a patient with microcytic RBC indices can be reliably categorized using only RDW as parameter.

However, in this study, because of the small sample size, statistically significant results could not be achieved. Further study needs to be done on a larger sample size over a longer time period to establish the significance of RDW in microcytic hypochromic anemia. Also, serum ferritin was used as a gold standard to distinguish IDA and NON-IDA in the present study. But since ferritin is an acute phase reactant, its serum levels may be misleading in the presence of acute or chronic inflammation.12 out of 42 NON-IDA cases in our study were known cases of IDA which were falsely placed in NON-IDA group due to normal or high serum ferritin levels following acute or chronic infections. Study of bone marrow iron stores still remains the gold standard, which was not done for any of the cases included in the study.

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