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Role of Red Cell Distribution Width (RDW) in the diagnosis of iron deficiency anemia

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ABSTRACT

Background: Iron deficiency anemia (IDA) is the most common nutritional deficiency worldwide. Morphologically, IDA is hypochromic and microcytic as is anemia on chronic disease (ACD) thus creating confusion on peripheral blood smear examination. Red cell distribution width (RDW) has been proposed to be a more sensitive indicator to establish the possible origin of microcytic hypochromic anemia. Various previous studies have debated the role of RDW in diagnosis of IDA, with no conclusive word on the utility of RDW in diagnosing iron deficiency anemia.

Objective. To study the utility of RDW in the diagnosis of IDA

Methods: a total of 93 patients with microcytic (MCV<80 fl) anemia were classified into iron deficient (IDA) and anemia on chronic disease (ACD/non-IDA) based on serum ferritin and total iron binding capacity (TIBC). RDW values were attained on Sysmex XN series hematology autoanalyzer. ROC was built, and the utility of RDW in the iron deficiency diagnosis was studied.

Results: RDW mean value was 20.07±7.67% in IDA group (57 patients) compared to 17.60±3.23 % in the ACD group (36 patients) (p<0.001; CI 95%: 4.14-33.42). At a 17.35% cut-off value, as found from the ROC, the sensitivity and specificity of RDW in IDA diagnosis were 85.96% and 69.44% and a positive and negative predictive value of 81.66% and 75.75% consecutively.

Conclusions: In IDA screening diagnosis, RDW has a good sensitivity in patient with hypochromic microcytic anemia.

Keywords: *Red cell distribution width; Iron deficiency anemia; Anemia on Chronic Disease, hypochromic microcytic anemia*
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INTRODUCTION

Iron deficiency anemia (IDA) is the most common nutritional deficiency worldwide.[1] Iron deficiency anemia is hypochromic and microcytic morphologically, as is anemia in chronic diseases, which often leads to confusion from peripheral blood smear examination.[2] The diagnosis of microcytic anemia is critical, especially in multi-ethnic populations such as Indonesia, since each type has different causes, pathogenesis, prognosis, and therapies. Therefore, we need a marker that can distinguish the anemia.

Red cell distribution width (RDW) has been proposed to be a more sensitive indicator to determine the possible origin of microcytic hypochromic anemia.[3] RDW represents the coefficient of variation in red blood cell volume distribution and can be considered as a heterogeneity index, equivalent to the observed anisocytosis in peripheral blood smears.[4-6]

In this current era, where there is an increase in health costs, it needs an efficient diagnostic tool that can distinguish between diseases. For IDA, Bone marrow studies are a costly, invasive method, whereas serum ferritin, serum transferrin, and serum iron sera are very expensive and not all laboratories in Indonesia have such examinations. If these easy-to-obtain tests can be used to screen IDAs with high sensitivity and specificity, the cost of anemia will drop significantly as patients with suspected RDW iron deficiency do not need to undertake further examination.[4,6]

Preceding researches have discussed the role of RDW in the diagnosis of IDA[6-11] without definite words regarding the usefulness of RDW in diagnosing iron deficiency anemia.

This research was aimed to test the wide usefulness of red blood cell distribution (RDW) in the diagnostic work of hypochromic microcytic anemia in adult patients.

MATERIALS AND METHODS

Cross-sectional analytic studies with a six-month diagnostic test were conducted at the Internal Medicine ward at a hospital in Denpasar Bali. Complete blood examination is done by using Sysmex XN series hematology autoanalyzer that has been calibrated. With anemia criteria of hemoglobin < 10 g / dl and microcytic hypochromic with MCV < 80 fl and MCH < 27 pg.[12,13]

They then classified into iron deficiency anemia and anemia due to chronic disease using the subsequent criteria:[13]

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1. Iron Deficiency Anemia (IDA) (Group 1): serum ferritin <20µg / l.
2. Anemia due to chronic disease (ACD/ non-IDA) (Group 2): serum ferritin ≥ 20 µg/l.

Serum ferritin is measured using immunochemiluminescent using Immulite 2000.

RESULTS

The study included 93 patients with 30 (32.3%) men and 63 (67.7%) women, with an average age of 46,71 ± 17,9 years. Of the 93 patients, 31 (33.3%) patients had mild anemia, 37 (39.8%) patients had moderate anemia, and 25 (26.9%) patients had severe anemia. In group 1 (IDA) included 57 people (61.29%), with 15 (26.3%) men and 42 (73.7%) women. While in group 2 (ACD/non-IDA) there were 36 (38.71%) people, with 15 (41.7%) men and 21 (58.3%) females, with an average age of 54.94 ± 15.6 years. There were no statistically significant differences between the groups with regard to age and sex distribution in both IDA and non-IDA groups. In RDW comparison between IDA and non-IDA groups, the mean RDW scores were significantly higher in the IDA group (20.07 ± 7.67%) than in the non-IDA group (17.60 ± 3.23%) in the paired t-test (p <0.001) (table 1). In the IDA group, the mean RDW scores among patients with mild, moderate and severe anemia were 16.71 ± 1.67%, 17.52 ± 1.12% and 20.75 ± 1.23%. The matching values in the non-IDA group were 16.13 ± 1.52%, 16.67 ± 1.21% and 16.74 ± 1.18%, correspondingly. ANOVA test presented a statistically significant increase in mean RDW values with an increase in the severity of anemia in patients in the IDA group (p <0,0001) contrasting the non-IDA anemia group (p <0.617).

The ROC (Figure 1) was built using the RDW values of patients between the two groups, which provided a RDW cut-off value of 17.35% as the value with the best combination of sensitivity and specificity for hypochromic microcytic anemia. At 17.35% RDW cut-off value, the sensitivity and specificity of RDW in diagnosing hypochromic microcytic anemia were 85.96% and 69.44%, respectively, with positive and negative predictive values of 81.66% and 75.75% (table 2).

Table 1 Demographic and laboratory data characteristics of the patients

Variable	Total Patient (n=93)	Group 1 (IDA) (n=57)	Group 2 (ACD/non-IDA) (n=36)	p value
Age (year) mean±SD	46.71±17.9	41.51±17.4	54.94±15.6	0.81
Gender				
Male (%)	30 (32.3%)	15 (26.3%)	15 (41.7%)	0.49
Female (%)	63 (67.7%)	42 (73.7%)	21 (58.3%)	
Hb (g/dl) mean±SD	7.22±1.74	7.07±1.80	7.45±1.62	0.03
Anemia Category				
mild (%)	31 (33.3%)	8 (14.0%)	7 (19.4%)	< 0.01
moderate (%)	37 (39.8%)	31 (54.4%)	19 (52.8%)	
severe (%)	25 (26.9%)	18 (31.6%)	10 (27.8%)	
RDW (%) mean ± SD	19.94 ± 5.60	20.07 ± 7.67	17.60 ± 3.23	<0.001

Table 2 Cut off RDW 17.35%

		Diagnosis		
		IDA	ACD	Total
RDW	Higher	49	11	60
	Lower	8	25	33
Total		57	36	93

Sensitivities: 85.96% (CI 95%: 85.67%-86.25%)
Specificities: 69.44% (CI 95%: 68.96%-69.92%)
Positive Predictive Value: 81.66% (CI 95%: 81.35%-81.98%)
Negative Predictive Value: 75.75% (CI 95%: 75.29%-76.22%)

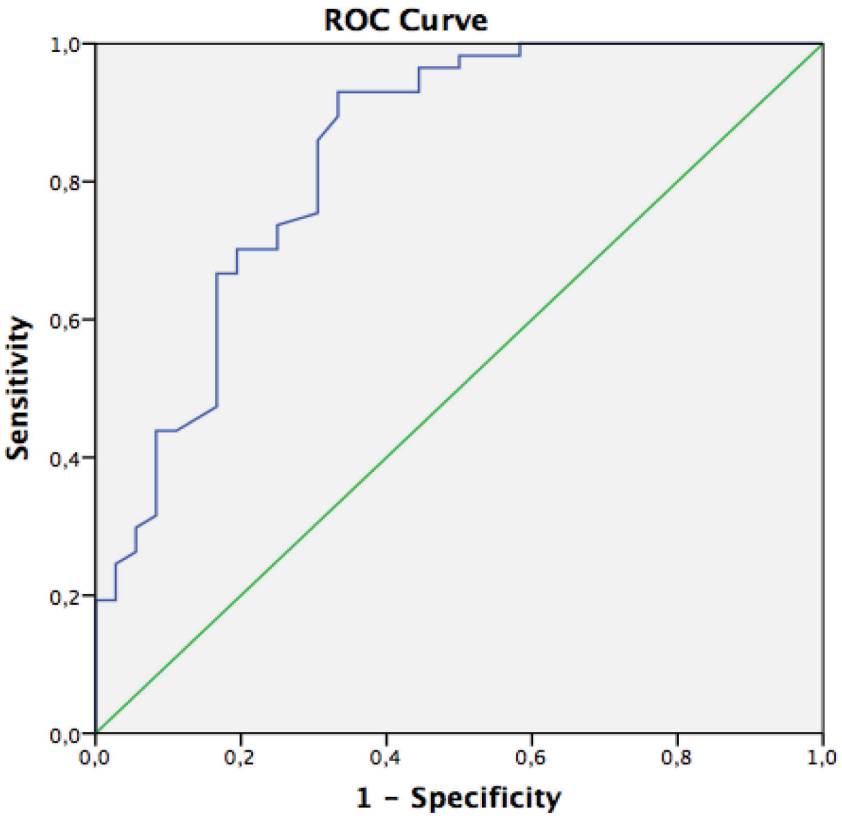

Figure 1 ROC of RDW value between 2 groups

DISCUSSION

From results above mean RDW is significantly increased among patients with iron deficiency anemia (20.07 ± 7.67) compared to the iron deficiency non-anemic group (17.60 ± 3.23). From the ROC, at a cut-off value of RDW 17.35% obtained, the sensitivity and specificity of RDW in diagnosing microcytic hypochromic anemia were 85.96% and 69.44%, correspondingly. Compared to previously published studies, these results support the studies by Zeben et al., Sultana et al. and Choudhary et al. all of the studies which show limited specificity to RDW. Whereas Sultana et al. and Mukesh et al. using serum ferritin as inclusion criteria, Zeben et al. using bone marrow iron as the gold standard. Therefore, as they suggest, an increase in RBC size heterogeneity (as measured by RDW) is seen in all microcytic categories.[4,6] While this increase in parameters is fairly sensitive for iron deficiency, it is often that increased RDW in other situations limiting its usefulness in the early diagnostic classification of microcytic anemia.[7-9] Alike to Aulakh et al., we as well found an inverse association of RDW with hemoglobin values ($p < 0.0001$, ANOVA) in iron deficiency anemia, although no correlation between non-IDA anemia ($p = 0.617$, ANOVA).[6] Also, results and advices from western countries' studies on RDW in iron deficiency anemia and ACD may not be totally applicable in countries such as a much higher percentage of IDA. In such situations, patients suffering from IDA, tend to have high RDW and are finally labeled as iron deficiency firstly. Later careful follow up after sufficient iron therapy, RDW may increase again, but the index remains low.

Limitations of the study include small sample size, we included only 93 patients, if the sample is larger in the study and correlation would have been generated, using a fixed value of hemoglobin for anemia irrespective of age, using RDW in the population that was diagnosed with IDA, lack of analysis of the patients with a fraction of RDW was helpful in the definition of iron deficiency. RDW with Hb levels and MCV and how to screen anemic patient using RDW, Hb, and MCV and use them to make the diagnosis of IDA without the need of serum iron binding capacity and transferrin saturation.

CONCLUSION

RDW has a good sensitivity for IDA screening diagnosis amongst patients with hypochromic microcytic anemia but has limited specificity in IDA diagnosis. It is recommended that the RDW can be used with other investigations like peripheral blood smear and MCV as an effective tool for the diagnosis of iron deficiency anemia. The need for further research with a larger sample size involving multi-center hospitals as a place of study.

CONFLICT OF INTEREST

Author declares there is no conflict of interest regarding all aspect of this study

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