



Determining the Association between RDW and Traditional Markers of Inflammation

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Authors' contributions

This work was carried out in collaboration between all authors. Authors HAE and HT designed the study, performed the statistical analysis, and wrote the protocol. Author ES wrote the first draft of the manuscript, managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.

Original Research Article

Received 21st February 2014
Accepted 8th April 2014
Published 26th April 2014

ABSTRACT

Objectives: Determining the association between RDW and the two widely used markers of inflammation; ESR and hs-CRP.

Materials and Methods: The laboratory tests including CBC, ESR, and hs-CRP were performed on 984 subjects, and the results were recorded. The association between RDW, ESR and hs-CRP was determined using Linear Regression Analysis and Correlation Coefficient of Pearson.

Results: There were correlation between RDW and both hs-CRP and ESR in entire study population. The result of Linear Regression Analysis and Correlation Coefficient of Pearson for determining the association between RDW and hs-CRP was $Y= 1.61x + 12.67$, and $r=0.28$ ($p<0.001$), respectively; and for RDW and ESR was $Y=0.913x + 12.74$, and $r=0.23$ ($p<0.001$).

Conclusion: According to strong association between RDW, ESR and hs-CRP, RDW can be used as potential marker of inflammation.

Keywords: RDW; ESR; hs-CRP; inflammation.

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1. INTRODUCTION

Red cell Distribution Width (RDW) is a quantitative parameter which represents the variability in size (anisocytosis) of the circulating Red Blood Cells. It is routinely measured by Hematology Analyzers and is reported as a component of the Complete blood Count. RDW is calculated by dividing the standard deviation of erythrocytes volume by MCV and the result is expressed as a percentage [1].

RDW is mainly used in differential diagnosis and classification of anemia's; For example, elevated RDW along with low MCV is indicative of iron deficiency, whereas normal RDW with low MCV is indicative of thalassemia [2].

Recent studies indicate that RDW can be used as a potential marker of inflammation and is elevated in inflammatory conditions [3], and several other studies revealed that RDW can also be used as a diagnostic and prognostic marker in various pathologic conditions; such as chronic heart failure and coronary artery disease [4, 5]. Moreover, RDW has been proposed to be associated with several pathologic conditions including liver diseases, colorectal carcinoma and neoplastic metastasis to bone marrow [6-9].

Inflammation and inflammatory conditions play an important role in the basis of many disorders such as autoimmune diseases, infections and atherosclerosis [10], and several studies indicate that RDW can be used as a potential marker for inflammatory states. [11-13]

hs-CRP and ESR are nonspecific tests for inflammatory states and are widely used for monitoring inflammatory disorders.

The aim of our study was to assessment the association between RDW and plasma markers of inflammation.

2. MATERIALS AND METHOD

2.1 Patients

From September 2012 to April 2013, 984 patients that referred to our center (Emamreza hospital of Tabriz University of Medical Sciences) were included in study. The only exclusion criteria was blood transfusion, and with the exception of blood transfusion, neither inclusion and also no any other exclusion criteria were applied to stratify the whole population. Whole blood samples were collected by venipuncture on fasting subjects. The laboratory tests including CBC, ESR and hs-CRP were performed on each sample and the results were recorded.

2.2 Laboratory Procedures

The CBC was determined using the Sysmex KX-21 automated hematology analyzer (Sysmex Corporation, kobe, Japan) and the results including Hb, Hct and RDW were recorded for each patient. The reference range for RDW was 11.5% to 14.5%.

The ESR was determined with Westergren method by using automated ESR analyzer (XC-A30A, Caretium Medical Instruments Company, China) and hs-CRP was measured by immunoturbidimetric method using fully automated biochemistry analyzers (Biotechnica BT-

3000, Biotechnica Instruments Company, USA). Through the study, the reliability and quality of assays was ensured by applying regular internal quality control programs and errors including systematic and random errors were eliminated by applying quality control programs.

2.3 Statistical Analysis

Statistical package SPSS 16 was used for the database construction and data analysis. Because hs-CRP and ESR values were not normally distributed, they were logarithmically transformed to improve normality of data prior to analysis. Statistical tests including Linear Regression Analysis and Correlation Coefficient of Pearson were used for assessment of association between RDW and plasma markers of inflammation.

3. RESULTS

From September 2012 to April 2013, 984 patients were included in study, which 464 (47.2%) of them were male and 520 (52.8%) of them were female. The age of subjects ranged from 16 to 92 years (mean: 48.2). The range of Hb was 4.7 to 20.7 (mean: 13), and based on the definition of anemia (men, Hb < 13^{g/dL} ; females, Hb < 12^{g/dL}), 428 (43.5%) of them were anemic and 556 (56.5%) of them had no anemia.

The range of ESR and hs-CRP was 2 – 145^{mm/h} , and 2 – 37^{mg/L} , respectively. RDW ranged from 11.4% to 30.7% (mean: 13.9%), and the number of subjects with elevated RDW levels (RDW > 14.5%) was 225 (22.9%). The basic information and main results are summarized in Table 1.

Table 1. The basic information and main results of the entire study population (n = 984, males= 464 , females= 520)

	Range (Min - Max)	Mean ± 2SD
Age (years)	16 - 92	48.2±37.4
Hb (g/dL)	4.7 -20.7	13±5
RDW	11.4 -30.7	13.9±4
ESR (mm/h)	2 - 145	27±62
hs-CRP (mg/L)	2 - 37	8.4±15.6

Anemia is one of the important factors which affects the value of ESR; therefore, we divided the subjects into anemic and nonanemic groups. The basic information and main results of anemic and nonanemic subjects are summarized in Table 2 and Table 3, respectively.

Table 2. The basic information and main results of the anemic patients (n = 428, males= 164 , females=264)

	Range (Min – Max)	Mean ± 2SD
Age (years)	16 - 92	51.6±40
Hb (g/dL)	4.7-12.9	10.8±3.4
RDW	11.4 -30.7	14.7±5
ESR (mm/h)	10 -145	46±72
hs-CRP (mg/L)	2 - 34	10.7±16.4

Table 3. The basic information and main results of the nonanemic patients (n = 556, males= 300, females=256)

	Range (Min – Max)	Mean ± 2SD
Age (years)	18 - 92	45.8±34.4
Hb (g/dL)	13 -20.7	14.8±2.8
RDW	11.4 -25.4	13.3±2.6
ESR (mm/h)	2 - 98	13±29.6
hs-CRP (mg/L)	2 - 37	6.6±14

For determining the correlation between RDW with ESR and hs-CRP, we used Linear Regression Analysis and Correlation Coefficient of Pearson. There were association between RDW and both ESR and hs-CRP in entire study population (Table 4).

In anemic and nonanemic groups, there were correlation between RDW and hs-CRP ($p < 0.001$), but there were no correlation between RDW and ESR at both groups (Table 4).

Table 4. Correlation between RDW with hs-CRP and ESR

		Regression equation	r	P
Entire population	hs-CRP	$Y = 1.61x + 12.67$	0.28	< 0.001
	ESR	$Y = 0.913x + 12.74$	0.23	< 0.001
Anemic group	hs-CRP	$Y = 1.05x + 13.8$	0.26	< 0.001
	ESR	$Y = 0.041x + 14.32$	0.047	0.33
Nonanemic group	hs-CRP	$Y = 1.19x + 12.48$	0.29	< 0.001
	ESR	$Y = 0.059x + 13.23$	0.019	0.25

4. DISCUSSION

RDW is Coefficient of Variation of volume of circulating erythrocytes. Elevated RDW levels indicate the increase of heterogeneity and variation in size of Red Blood Cells (Anisocytosis). RDW is elevated in conditions of ineffective erythropoiesis (such as iron deficiency, megaloblastic anemia due to vitamin B₁₂ or Folate deficiency, and hemoglobinopathies), hemolytic anemias (anemias due to increased red cell destruction) and following blood transfusions. RDW is routinely measured by automated hematology analyzers and is reported as a component of the complete blood count. Therefore, this parameter is easily available and has no additional cost for patients.

RDW can be used as a diagnostic and prognostic marker in various pathologic conditions and diseases; For example, elevated RDW levels are associated with high mortality and morbidity rates in cardiovascular diseases and chronic heart failure [11-13]. The elevated RDW levels are also seen in other conditions including liver diseases, colorectal carcinoma, and metastasis of malignant neoplasm to bone marrow [14-16].

Inflammation plays an important role in pathogenesis of various diseases such as rheumatologic disorders, autoimmune diseases and also atherosclerosis. ESR and hs-CRP are the two widely used plasma markers of inflammation. Among traditional plasma markers of inflammation, hs-CRP is one of the best and reliable markers of inflammation, because has a standardized assay, does not depend on food intake, has minimum diurnal variation, and has a long half-life [17].

ESR is another marker of inflammation and is one of the oldest laboratory tests still in use. ESR is moderately elevated in active inflammatory diseases such as rheumatoid arthritis, chronic infections, collagen vascular and neoplastic diseases. The ESR has little diagnostic value in these disorders but can be useful in monitoring disease activity. Other than inflammation, various factors and situations, such as anemia can affect the value of ESR.

In our study, RDW showed correlation with both ESR and hs-CRP in whole study population, but when study population is divided into anemic and nonanemic groups; there were correlation between RDW and hs-CRP at both groups, whereas no correlation is detected between RDW and ESR at anemic and nonanemic groups.

Several studies have reported a correlation between RDW with ESR and hs-CRP, and suggested that RDW might increase due to chronic inflammation. Lee et al. reported a potential correlation of RDW with ESR and hs-CRP in patients with rheumatoid arthritis [18], and Lippi et al. showed that there is a correlation between RDW with ESR and hs-CRP by conducting a large-scale cohort study [3].

Our study has some limitations. First, because our study is cross-sectional, it does not explain the mechanism of relation between RDW and plasma markers of inflammation. Second, we did not record any information about medications and drugs used by patients and also we have not included the background diseases and problems of participants such as iron deficiency and acute bleeding states which can affect the value of RDW. Third, in our study, we have a single measure of RDW for each patient, which can be induced by acute changes such as blood loss or hemolysis; for this reason, it is recommended to perform several measurements of RDW at different times to detect the fluctuations of RDW's levels.

Finally, additional studies are needed to reveal the mechanism of correlation between RDW and traditional markers of inflammation.

5. CONCLUSION

RDW is routinely measured by automated hematology analyzers and is reported as a component of the complete blood count. Therefore, this parameter is easily available and has no additional cost for patients. Our study and several other studies showed that there is a correlation between RDW and plasma markers of inflammation. Therefore, RDW can be used as a potential marker of inflammation.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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