

# Correlation of High Sensitive C Reactive Protein Levels as Inflammation Marker with Red Blood Cell Distribution Width Value in Regular Hemodialysis Patients at H. Adam Malik General Hospital

Anwar Sholeh<sup>1</sup>, Alwi Thamrin Nasution<sup>2</sup>, Radar Radius Tarigan<sup>2</sup>

<sup>1</sup>Department of Internal Medicine, Faculty of Medicine, Universitas Sumatera Indonesia, Medan, Indonesia

<sup>2</sup>Division of Nephrology and Hypertension, Department of Internal Medicine, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

Corresponding Author: Anwar Sholeh

## ABSTRACT

**Background:** Chronic kidney disease (CKD) is characterized by structural and functional disorder of the kidney with irreversible and gradual characteristics with one of the modalities of renal replacement therapy such as hemodialysis (HD). The role of inflammation in HD patients by uremic toxin and dialysis can be assessed by the marker of High Sensitive C Reactive Protein (HsCRP). Several studies have examined the relationship between HsCRP and red cell distribution width (RDW) in regular HD patients which leads to increase patient morbidity and mortality, but until now, there has been no study in Indonesia regarding the correlation between HsCRP and RDW in regular HD patients. This study aims to determine the correlation HsCRP as a marker of inflammation and RDW values in regular HD patients.

**Methods:** This is a cross-sectional study in Regular HD patients at Dialysis Unit-H. Adam Malik General Hospital. A total of 20 subjects were included. Bivariate and multivariate analysis was conducted to analyze the relationship of HsCRP, ureum, creatinin, hemoglobin, and eGFR to RDW.

**Results:** There were 20 Regular HD patients analyzed. The proportion of patients with increased RDW was 80%. In Pearson correlation test, there is a strong correlation between HsCRP and RDW ( $r=0.667$ ,  $p<0.001$ ).

**Discussion:** Majority of regular HD patients at H. Adam Malik General Hospital were assessed

with increased RDW. Pearson correlation analysis revealed HsCRP was significantly associated with RDW.

**Conclusion:** Increased RDW was found in 80% of regular HD patients at H. Adam Malik General Hospital. From Pearson correlation analysis, we found HsCRP was significantly associated with RDW.

**Keywords:** inflammation, high sensitive c reactive protein, red blood cell distribution width, regular hemodialysis

## INTRODUCTION

CKD is a pathological condition that occurs gradually and is irreversible, and is characterized by structural and functional abnormalities in the kidneys that last more than three months with manifestations in health and has diagnostic criteria in the form of decreased glomerular filtration rate (GFR)  $<60$  ml/minute per  $1.73$  m<sup>2</sup> for more than three months, accompanied by the presence of one or more markers of kidney damage.<sup>[1]</sup>

In the 2018 Basic Health Research, there was a reported increase in the prevalence of CKD from 2% in 2013 to 3.8% in 2018 with the lowest prevalence of 1.8% and the highest of 6.4%.<sup>[2]</sup> Based on the Indonesian Renal Registry, in 2018 it was reported that 0.03% of the Indonesian population underwent hemodialysis and it

was also reported that the number of patients undergoing hemodialysis until 2018 increased sharply in line with the increase in the number of hemodialysis units.<sup>[3]</sup>

CKD and Inflammation, along the way, have a close relationship both in terms of etiology, pathophysiology, degree of severity, and in terms of mortality. There are many markers used to detect inflammatory states in CKD patients. High sensitive C-Reactive Protein (HsCRP) is one of the known inflammatory markers and is the most frequently used for high precise inflammatory markers. Research by Kara et al. found serum HsCRP levels significantly increased in CKD patients.<sup>[4]</sup>

Recently, some markers that are known to be associated with PGK, can even be used to predict the risk of complications caused by PGK, namely red cell distribution width (RDW).<sup>[5]</sup> The dysregulation of the hormone erythropoietin induced by inflammation at PGK, leads to heterogenesis of red blood cells characterized by an increase in RDW value.<sup>[6]</sup>

From a study conducted in Turkey, there was an increase in RDW values in patients undergoing regular hemodialysis compared to controls and there was a significant correlation between HsCRP and RDW values in hemodialysis patients. A study conducted in Japan, found a significant increase in RDW values in CKD patients undergoing hemodialysis and there is a significant correlation between RDW value and HsCRP levels.<sup>[7]</sup>

We conducted a cross-sectional study to analyze the proportion of patients with increased RDW in regular HD patients at H. Adam Malik General Hospital, as well as the relationship of HsCRP, ureum, creatinine, hemoglobin and eGFR to RDW in regular HD patients.

## **MATERIAL AND METHODS**

Our study was a cross-sectional study conducted at the Dialysis Unit of H. Adam Malik General Hospital, Medan on June 2020 to July 2020. The recruited subjects were over 18 years old, had consented to

participate in the study, and had been on MHD for at least 3 months. The exclusion criteria were patients with a history liver disease, patients with infection, and also patients who have been diagnosed with malignancy. In this study, the independent variables were HsCRP, ureum, creatinine, hemoglobin and eGFR, while RDW is the dependent variable.

This study was approved by the Ethical Committee of the Medical Research Faculty of Medicine, Universitas Sumatera Uatara, and H. Adam Malik General Hospital, Medan. All subjects provided consent after receiving verbal and written explanations regarding the study.

## **Statistical Methods**

Statistical analyses were performed using the SPSS software program ver. 20.0. With respect to baseline characteristics of the subjects, continuous data with normal distribution were presented as mean SD; continuous variables with skewed data were presented as median (with minimum and maximum value), and dichotomous data were presented as proportion. Bivariate and multivariate analyses were performed to analyze relationship HsCRP, ureum, creatinine, hemoglobin and eGFR to RDW.

## **RESULTS**

Subject recruitment began in June 2020 - July 2020 at the Dialysis Unit of H. Adam Malik General Hospital, Medan, 20 samples were found that met the inclusion criteria. The characteristics of respondents are listed in the table 1.

There was a significant correlation with the positive direction between HsCRP and RDW in regular HD patients. With a p-value <0.001 and a r: 0.667. This shows that the higher the HsCRP levels, the higher the RDW values in regular HD patients.

In this study, the Pearson test was conducted also to find the correlation between RDW and hemoglobin and creatinine in 20 samples. The results show that there is a significant correlation with the positive direction between RDW and

hemoglobin and creatinine in regular HD patients.

**Table 1: Subjects' Character**

Variable	N = 20
Male, n (%)	13 (65,0%)
Female, n (%)	7 (35,0%)
Age, years (X±SD)	50.30 ± 12.57
HD duration (X±SD)	24.45 ± 20.98
Hypertension	4 (20,0%)
Diabetes Mellitus	14 (70,0%)
GN	2 (10,0%)
Hb, g/dL	9,12 ± 0,57
Ureum, mg/dL	147,1 ± 33,62
Kreatinin, mg/dL	10,1 ± 4,02
eGFR, ml/min	5,95 ± 3,11
HsCRP, mg/dL	6,78 ± 3,91
RDW, %	15,93 ± 1,87

**Abbreviation:** HsCRP, high sensitive c reactive protein; RDW, red blood cell distribution width

**Table 2: Correlation between HsCRP and RDW in regular HD patients**

Variabel	RDW	
	R	p.
HsCRP	0,667	0,001

**Abbreviation:** HD, hemodialysis; GN, glomerulonephritis; Hb, hemoglobin; eGFR, estimated glomerulus filtration; HsCRP, high sensitive c reactive protein; RDW, red blood cell distribution width

**Table 3: Correlation between RDW and Other Biochemical Characteristics in regular HD patients**

Variabel	RDW	
	R	p.
Hb	0,497	0,026*
Ureum	0,124	0,603
Kreatinin	0,519	0,019*
eGFR	0,379	0,100

**Abbreviation:** Hb, hemoglobin; eGFR, estimated glomerulus filtration; RDW, red blood cell distribution width

## DISCUSSION

From the 20 research subjects, the majority of research subjects were male, as many as 13 people (65.0%) with a mean age of  $50 \pm 12.57$ . This study is in line with the report from the IRR in 2018 where the largest proportion of patients who underwent HD was in the age range 45-64 years. The age factor, in this case aging, affects the structure and regulatory function of the kidney, which is why it causes the progression of worsening of CKD.<sup>[3]</sup>

In this study, the most comorbid diseases were Diabetes Mellitus followed by Hypertension. This is in line with data from USRDS 2015 where Diabetes Mellitus is the leading cause in the United States.<sup>[8]</sup> However, this data is inversely proportional to the data obtained from IRR, 2018,

namely that the most common cause of CKD in Indonesia is Hypertension (44%) followed by Diabetes Mellitus (22%) and other diseases.<sup>[3]</sup>

Chronic kidney disease is characterized by irreversible changes in renal function, which then lead to impaired multi-organ function in its development in the clinical syndrome of uremia. Inflammation in regular hemodialysis patients is related to RDW values caused by impaired production of the hormone erythropoietin.<sup>[9]</sup> Patients with uremia show complex renal dysfunction characterized by a decrease in erythropoietin levels resulting in an increase in cell distribution variations, namely the RDW value. Hemodialysis is associated with changes in the RDW value, where an increase in the RDW value is a parameter change that is consistent with these conditions.<sup>[10]</sup>

In this study, an increase in the RDW value was found. In line with Tekce's study, RDW levels were found to be elevated in regular hemodialysis patients.<sup>[10]</sup> This is also in line with Oh study which evaluated the RDW value in regular hemodialysis patients and obtained an increase in RDW values of 67.5% and 68.9%, respectively.<sup>[11]</sup> Another factor that has previously been described as having an effect on changes in RDW levels in hemodialysis patients besides uremia toxin and the hemodialysis process itself is the HsCRP level, which reflects the inflammatory status of the patient. Inflammation itself is influenced by many factors which will later contribute to the progression of this disease. In this study, we found a strong positive correlation between HsCRP levels and RDW values. This is in line with Tekce's research which showed a strong positive correlation between RDW values and HsCRP levels inpatients hemodialysis ( $R=0.815$ ;  $p=0.014$ ). A similar research was also expressed by Lippi, where there was a positive correlation between HsCRP levels and RDW values.<sup>[12]</sup>

There are limitations in this study in choosing the research design, in this study

using a design *cross sectional* that allows the data and the results of data analysis not entirely to describe the variation in HsCRP levels and RDW values of regular hemodialysis patients, while in previous studies conducted abroad (Turkey, Japan and Budapes) using a study design *prospective cohort*.

## CONCLUSIONS

The proportion of patients with increased RDW in regular HD patients at H. Adam Malik General Hospital was 80%. From person correlation analysis, we found HsCRP was significantly associated with RDW.

## Acknowledgement

This research was supported by the Faculty of Medicine Universitas Sumatera Utara. The authors thank colleagues from the Division of Nephrology and Hypertension, Department of Internal Medicine for providing insight, assistance and expertise that had greatly helped authors throughout this research.

**Conflict of Interest:** None

**Source of Funding:** None

**Ethical Approval:** Approved

## REFERENCES

1. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. Clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney International Supplements*. 2012; 3(1):1-150.
2. Laporan Hasil Riset Kesehatan Dasar (Riskesdas). Badan Litbangkes. 2018. Available from <https://www.litbang.kemkes.go.id/laporan-riset-kesehatan-dasar-riskesdas>.
3. 11<sup>th</sup> Report of Indonesian Renal Registry. IRR. 2018. Available from: <https://www.indonesianrenalregistry.org/data/IRR/2018>.
4. V. Kara. Relationship between red cell distribution width and serum C reactive protein levels in maintenance hemodialysis patients. *Eastern J Med*.2019;4: 497-502.
5. T. C. Evan, D. Jehle. The red blood cell distribution width. *The Journal of Emergency Medicine*.1991; 9: 71-74.
6. R. A. Savage. More on RDW. *AJCP*. 1987; 87(2): 293-294.
7. S. Yonemoto, T. Hamano, N. Fujii, K. Shimada, S. Yamaguchi, A. Matsumo, et al. Red Cell Distribution Width and renal Outcome in Patients with or Non-dialysis-dependent Chronic Kidney Disease. *PLoS ONE*.2018; 13(6):1-13.
8. System USRD. Annual Data Report: Epidemiology of Kidney Disease in The United States. 2015.
9. G. Lippi, G. Targher, M. Montagnana, G. L. Salvagno, G. Zoppini, G. C. Guidi. Relationship between Red Blood Cell Distribution Width and Kidney Function Test in a Large Cohort of Unselected Outpatients. *Scand J Clin Lab Invest*. 2008; 68(8): 745-748.
10. H. Tekce, B. K. Tekce, G. Aktas, M. Tanrisev, M. Sit. The Evaluation of Red Cell Distribution Width in Chronic Hemodilysis Patients. *Int J Nephrol*.2014: 1-6.
11. H. J. Oh, J. T. Park, J. K. Kim, D. E. Yoo, S. J. Kim, S. H. Han, et al. Red Blood Cell Distribution Width is an Independent Predictor of Mortality in Acute Kidney Injury Patients Treated With Continuous Renal Replacement Therapy. *Nephrol Dial Transplant*.2012; 27: 589-594.
12. G. Lippi, F. Pavesi, M. Bardi, S. Pipitone. Lack of Harmonization of Red Blood Cell Distribution Width (RDW): evaluation of Four Hematological Analyzers. *Clin Biochem*, 2014; 47(12):1100-1103.

How to cite this article: Sholeh A, Nasution AT, Tarigan RR. Correlation of high sensitive c reactive protein levels as inflammation marker with red blood cell distribution width value in regular hemodialysis patients at H. Adam Malik General Hospital. *International Journal of Research and Review*. 2021; 8(7): 14-17. DOI: <https://doi.org/10.52403/ijrr.20210703>

\*\*\*\*\*