# The association between red blood cell distribution width, C-reactive protein and renal function in patients with type2 diabetes mellitus

**Zehua Shao**
National Health Commission Key Laboratory of Cardiovascular Regenerative Medicine, Heart Center of Henan Provincial People's Hospital, People's Hospital of Zhengzhou University

**Yang Dong**
Department of Nephrology, Henan Provincial People's Hospital; Department of Nephrology of Central China Fuwai Hospital, Central China Fuwai Hospital of Zhengzhou University

**Shuai Huo**
Department of Nephrology, Henan Provincial People's Hospital; Department of Nephrology of Central China Fuwai Hospital, Central China Fuwai Hospital of Zhengzhou University

**Peiyuan Niu**
Department of Nephrology, Henan Provincial People's Hospital, People's Hospital of Zhengzhou University, People's Hospital of Zhengzhou University

**Fengmin Shao** ( fengminshao@126.com )
Department of Nephrology, Henan Provincial People's Hospital, People's Hospital of Zhengzhou University, People's Hospital of Zhengzhou University

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## Abstract

# Objective

Red cell distribution width (RDW) and C-reactive protein (CRP) were respectively considered as important biomarker of cardiovascular diseases and inflammatory diseases.We aimed to evaluate the association of RDW) ,CRP with renal function in patients with type2 diabetes mellitus(T2DM ).

# Methods

Patients with T2DM with a wide range of estimated glomerular filtration rate(eGFR) and proteinuria from 2019 to 2021 at Henan Provincial People's Hospital were included in this study.. Blood samples from T2DM patients with normal eGFR(n = 146) and T2DM patients with decreased eGFR(n = 246) were collected. Clinical characteristics, routine blood test results and biochemical parameters were recorded, including age, gender, red blood cell, hemoglobin, RDW, platelet, CRP, albumin, total bilirubin, glucose, high-density lipoprotein, uric acid, creatinine, urea nitrogen and cystatin C. The effect of RDW and CRP level on the renal function was evaluated by using multiple linear step.wise regression analysis.

# Results

Compared with the T2DM patients with normal eGFR,the the T2DM patients in decreased eGFR group had lower levels of hemoglobin, albumin and platelet, and higher levels of CRP, Uric acid, creatinine and cysC. Moreover, the levels of RDW levels were negatively correlated with eGFR ($r=-0.224$,$p < 0.001$), but positively related with CRP ($r = 0.211$,$p < 0.001$). Importantly, Multiple linear regression analysis showed that the levels of RDW had significant effects on decline of renal function ($\beta = 0.091$, $p = 0.002$).

# Conclusions

RDW were an independent risk factor for for decline in renal function in patients with T2DM, RDW was also positively correlated with CRP.

## Introduction

Red blood cell distribution width (RDW) is a parameter that reflecting the heterogeneity of red blood cell and routinely included in the complete blood cell count. Recently, RDW has been used for differential diagnosis of different types of anemias, higher RDW values indicate shortened erythrocyte life span due to poor erythropoiesis or enhanced RBC destruction[1]. During the decades, Overwhelming evidence implicates that RDW is an independent predictor of chronic heart failure[2],coronary heart disease[3],metabolic syndrome[4], chronic kidney disease[5] and acute kidney injury (AKI) in hospitalized patients[6]. Additionally, high RDW values predicts mortality, CV events and deterioration of renal function

in type 2 diabetes mellitus[7]. The underlying mechanisms for the above phenomenon remains unknown, but chronic inflammation, endothelial dysfunction, oxidative stress (OS) and nutritional deficiencies are postulated as possible etiologies[8]. Recently, there is interest in the identification of novel biomarkers that can predict disease progression in patients with diabetes mellitus. Although RDW has been widely investigated in in many different disease areas, there is limited literature on the possible predictive role of RDW for deterioration of renal function in T2DM. CRP has recently been suggested as an inflammatory marker for the diagnosis of gestational diabetes[9, 10]. Insulin resistance, on the other hand, appears to be caused by inflammation and increases acute phase proteins such as CRP. In addition, CRP is involved in the development of T2DM as an inflammatory marker[12]. Additionally, it has been reported that high CRP predicts deterioration of renal function in T2DM[13].

Therefore, we sought to investigate the association between RDW, CRP and renal function in patients with T2DM.

# Methods

# Patients and study design

We enrolled 392 patients with T2DM with a wide range of eGFR and proteinuria from 2019 to 2021at Henan Provincial People's Hospital. The usual clinical and analytical variables of all patients were recorded, including age, gender, CRP, ALB, WBC, RBC, HB, GLU, UA, CR, cysC, RDW. The protocol shown above was approved by the Clinical Research Ethics Committee of the Henan Provincial People's Hospital, and informed consent was obtained from all participants according to the Declaration of Helsinki.

## Statistical Analyses

SPSS 21.0 software was used for data analysis, and the mean value was used for those in accordance with normal distribution. The independent sample t test was used for comparison between for comparison of means between the groups. The non-normal distributed data was expressed by the median (25–75%), and the comparison between the two groups was performed by rank sum test. Nonparametric test was used for qualitative data. Pearson test and Spearman rank correlation test were used for correlation analysis. Multiple linear stepwise regression analysis was used for regression analysis. $P < 0.05$ was considered statistically significant.

# Results

# Clinical characteristics of the study

A total of 392 T2DM patients were enrolled. Compared with the patients in normal eGFR group, patients with decreased eGFR had lower levels of hemoglobin, albumin and platelet, and higher CRP, Uric acid, creatinine and cysC(Table 1). Briefly, mean of RDW was 13.09(13.09 ± 1.57)% of the patients with

decreased eGFR, and 12.54(12.54 ± 1.18)% in normal eGFR group. While mean of CRP was 14.44 (14.44 ± 16.17) of the patients with decreased eGFR, and 6.63(6.63 ± 11.94) of the patients in normal eGFR group. However, the differences in levels of ALB, PLT, GLU, triglyceride and total cholesterol between the two groups were not statistically significant ($p > 0.05$) (Table 1).

## Associations Of Rdw, Crp With Egfr

As shown in Table 2, the RDW levels were negatively correlated with eGFR ($r=-0.224$, $p < 0.001$), but positively related with CRP ($r = 0.211$,$p < 0.001$). the CRP levels were negatively correlated with eGFR ($r=-0.26$, $p < 0.001$).

As shown in Table 3, multiple linear regression analysis showed that the levels of RDW had significant effects on decline of renal function ($\beta = 0.091$, $p = 0.002$).

Table 1

**Comparison of clinical indicators between eGFR decreased group and eGFR normal group**

| Descriptive variables | Decreased eGFR group (n = 246) | Normal eGFR group (n = 146) | χ2/t/z | P |
|---|---|---|---|---|
| Age (years) | 67.62 ± 11.36 | 58.20 ± 12.82 | -7.331 | 0.000 |
| Gender (Male, %) | 131(53.3) | 83(56.8) | 0.478 | 0.489 |
| WBC (×109/L) | 8.25 ± 7.89 | 7.39 ± 6.93 | -1.128 | 0.260 |
| RBC (×109/L) | 4.02 ± 1.09 | 4.77 ± 3.35 | 2.616 | 0.009 |
| HB (g/L) | 114.53 ± 25.03 | 134.20 ± 18.44 | 8.260 | 0.000 |
| RDW-CV(%) | 13.09 ± 1.57 | 12.54 ± 1.18 | -3.684 | 0.000 |
| PLT (×109/L) | 214.56 ± 76.28 | 219.82 ± 72.12 | 0.683 | 0.495 |
| CRP (mg/L) | 14.44 ± 16.17 | 6.63 ± 11.94 | -5.067 | 0.000 |
| ALB (g/L) | 40.01 ± 5.70 | 43.11 ± 4.73 | 5.534 | 0.000 |
| ALT (U/L) | 27.63 ± 38.46 | 26.81 ± 30.16 | -0.235 | 0.815 |
| AST (U/L) | 25.12 ± 17.813 | 23.74 ± 20.91 | -0.666 | 0.506 |
| TBIL (umol/L) | 12.72 ± 9.28 | 14.17 ± 6.13 | 1.866 | 0.063 |
| GLU (mmol/L) | 9.41 ± 5.72 | 10.51 ± 5.25 | 1.949 | 0.052 |
| TG (mmol/L) | 1.90 ± 1.49 | 1.60 ± 1.49 | -1.914 | 0.056 |
| TC (mmol/L) | 4.80 ± 1.59 | 4.56 ± 1.27 | -1.602 | 0.110 |
| HDL-C (mmol/L) | 1.31 ± 0.39 | 1.40 ± 0.39 | 1.982 | 0.048 |
| LDL-C (mmol/L) | 3.00 ± 1.31 | 2.83 ± 1.05 | -1.354 | 0.177 |
| UA (umol/L) | 310.01 ± 132.53 | 232.87 ± 110.53 | -5.918 | 0.000 |
| CR (umol/L) | 171.93 ± 188.62 | 51.00 ± 13.25 | -7.736 | 0.000 |
| BUN (mmol/L) | 12.40 ± 8.86 | 6.30 ± 4.22 | -7.802 | 0.000 |
| cysC (mg/L) | 2.08 ± 1.18 | 0.97 ± 0.35 | -10.999 | 0.000 |

eGFR, estimated glomerular filtration rate; WBC, white blood cell; RBC, red blood cell; HB, hemoglobin; RDW, red cell distribution width; PLT, platelet; CRP, C-reactive protein; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin ; GLU, glucose; TG, triacylglycerol; TC, cholesterol; HDL-C, high-density lipoprotein; LDL-C, low density lipoprotein; UA, uric acid; CR, creatinine; BUN, urea nitrogen; cysC, cystatin C.

Table 2
Correlation analysis between eGFR and clinical and analytical variables

| Descriptive variables | r | P |
|---|---|---|
| Age | -0.414 | 0.000 |
| RBC | 0.129 | 0.011 |
| HB | 0.533 | 0.000 |
| RDW-CV | -0.224 | 0.000 |
| PLT | 0.104 | 0.041 |
| CRP | -0.260 | 0.000 |
| ALB | 0.337 | 0.000 |
| TBIL | 0.173 | 0.001 |
| GLU | 0.142 | 0.005 |
| HDL-C | 0.133 | 0.008 |
| UA | -0.278 | 0.000 |
| CR | -0.713 | 0.000 |
| BUN | -0.639 | 0.000 |
| cysC | -0.810 | 0.000 |

eGFR, estimated glomerular filtration rate; RBC, red blood cell; HB, hemoglobin; RDW, red cell distribution width; PLT, platelet; CRP, C-reactive protein; ALB, albumin; TBIL, total bilirubin ; GLU, glucose; HDL-C, high-density lipoprotein; UA, uric acid; CR, creatinine; BUN, urea nitrogen; cysC, cystatin C.

Table 3
Multiple linear regression analysis for eGFR in patients with T2DM.

| Descriptive variables | β | t | P | 95%CI | |
|---|---|---|---|---|---|
| | | | | Lower | Upper |
| Age | -0.288 | -10.566 | 0.000 | -0.882 | -0.605 |
| RDW-CV | 0.091 | 3.084 | 0.002 | 0.817 | 3.691 |
| UA | -0.104 | -3.588 | 0.000 | -0.044 | -0.013 |
| CR | -0.215 | -4.093 | 0.000 | -0.083 | -0.029 |
| UR | 0.123 | 2.575 | 0.010 | 0.140 | 1.045 |
| cysC | -0.583 | -9.224 | 0.000 | -25.425 | -16.491 |

eGFR as the dependent variable, age, RBC, Hb, rdw-cv, PLT, UA, CRP and other indicators as independent variables, multiple linear stepwise regression analysis was performed. CRP ≥ 10 was independently correlated with eGFR(β = 0.416, t = 9.045, P = 0.000 ), Age, RDW, UA, Cr, ur, CysC were independently correlated with eGFR;CI, confidence interval.

# Discussion

RDW and CRP were higher in patients with impaired renal function [14]. Our results supported previous findings, the levels of RDW and CRP were higher in T2DM patients with decreased eGFR than that in normal eGFR group, which were independent of numerous potential confounders. Chronic inflammation, endothelial dysfunction, oxidative stress (OS) and nutritional deficiencies have been considered as the explanations between elevated RDW and T2DM. [8]. Our results suggested that RDW was an independent risk factor for the decrease of eGFR in patients with T2DM, which provides further evidence for the above theoretical mechanism.Chronic inflammatory environment induces celluar OS and apoptosis, and can lead to enhanced RBC destruction [15]. In diabetics and CKD patients, several molecular pathways linking chronic inflammation and anisocytosis have been proposed: shortened erythrocyte lifespan, inhibited erythropoietin response and impaired iron metabolism[16].Furthermore, it is well-established that T2DM and diabetic-related obesity are conditions characterized by chronic inflammatory state[17]. One previous study showed that RDW was significantly associated with high-sensitivity C-reactive protein (Hs-CRP) ($r = 0.181; P < 0.001$) in coronary artery disease patients, and was still significant after adjusting for several confounding factors[18].In our study, we also found a strong linkage between RDW and CRP levels in T2DM patients. Moreover, RDW was found to be strongly correlated with high CRP levels in patients with different diseases: unselected subjects from the community[15], diabetics[19]and patients with various degrees of renal impairment, such as Peritoneal Dialysis (PD)[20]HD [21]and CKD[5].

Nevertheless, our research still has two limitations. Firstly, it is cross-sectional and can therefore only imply association and not causation. rather than causalities. Secondly, RDW and CRP detection lacks a

broader scope of participants. This study provides a new, easy, and quick measurable index. In addition, we demonstrated a significant association between elevated RDW and low eGFR in T2DM patients.

# Conclusions

After being used for the differential diagnosis of anemia for decades, the RDW has undergone a notable renaissance in recent years. Our study suggested that RDW was an independent risk factor for impairment of renal function in patients with T2DM, RDW was also positively correlated with CRP. Cohort studies or with more large sample size are needed to further establish the important role of RDW in patients with T2DM. And more related basic studies are need to explore the intrinsic mechanism..

# Declarations


### Acknowledgement

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### Statement of Ethics

### Declaration of conflicting interests

The authors have no potential or actual conflicts of interest with respect to the research, authorship, or publication of this article.


### Funding sources


### Author Contributions

### Data availability statement

No additional data available.

### Ethics approval and consent to participate

The study was approved by the Clinical Research Ethics Committee of the Henan Provincial People's Hospital(Ethical Approval No. 06. 2019). We confirm that the study was performed in accordance with the 1964 declaration of HELSINKI and later amendments. Additionally, written informed consent was obtained from all participants or their legal guardians prior to the enrollment.

### Consent for publication

Not applicable.

### Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files.

### Competing interests

The authors have no potential or actual conflicts of interest with respect to the research, authorship, or publication of this article.


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### Author Contributions

Zehua Shao wrote the main manuscript text. Yang Dong and Shuai Huo searched literature and designed manuscript. Peiyuan Niu prepared tables 1-3. Fengmin Shao reviewed manuscript, edited, and gave critics. All authors reviewed the manuscript.


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