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ORIGINAL ARTICLE

Association of Red Blood Cell Distribution Width with Diabetic Nephropathy in Type 2 Diabetes: Findings from a Cross-Sectional Study

Hairu Wang [1], Yongjin Ji [2], Peixia Yu [1]

[1] *Department of Laboratory Medicine, Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences, Tongji Shanxi Hospital, Third Hospital of Shanxi Medical University, Taiyuan, China*
[2] *Department of Otolaryngology Head and Neck Surgery, Shanxi Medical University Second Affiliated Hospital, Taiyuan, China*

SUMMARY

Background: **Diabetic nephropathy (DN) is a prevalent and significant complication associated with diabetes mellitus (DM). Although several risk factors have been established, there is still a need to explore additional indicators for the early detection and intervention planning of DN. Red cell distribution width (RDW) has been noted to play a role in cardiovascular events and metabolic syndrome. This study aimed to explore the potential association between RDW and DN in patients with type 2 DM (T2DM).**

Methods: **Data were gathered from 2011 through 2018 through NHANES, and we performed a cross-sectional study that included 3,704 T2DM patients. Logistic regression, curve fitting, and interaction effects were utilized to examine the relationship between RDW and diabetic nephropathy.**

Results: **The mean RDW values were significantly elevated in patients with diabetic nephropathy compared to those without diabetic nephropathy ($p < 0.001$). Logistic regression analysis indicated a positive correlation between RDW and DN, even after adjusting for the confounding variables (odds ratio: 1.16, 95% confidence interval: 1.12 - 1.21, $p < 0.001$). Furthermore, after accounting for all confounding variables, curve fitting demonstrateed a linear relationship between RDW and DN (p for non-linearity = 0.658). RDW was positively correlated with DN.**

Conclusions: **In conclusion, our research suggests that there is a link between higher RDW levels and the presence of DN, indicating that RDW may serve as a valuable biomarker for the early identification, prevention, and strategic intervention of this serious complication.**

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Correspondence:
Peixia Yu
Department of Laboratory Medicine
Shanxi Bethune Hospital
Shanxi Academy of Medical Sciences
Tongji Shanxi Hospital
Third Hospital of Shanxi Medical University
Taiyuan, 030001
China
Email: 627073207@qq.com

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KEYWORDS

diabetic nephropathy, type 2 diabetes mellitus, biomarker, early detection, red blood cell distribution width

INTRODUCTION

With the improvement of living standards, as a global metabolic disease, the prevalence of diabetes mellitus has risen considerably [1]. In recent years, diabetes mellitus has emerged as one of the most prevalent chronic conditions, posing considerable challenges for patients and the healthcare system, particularly for individuals

experiencing complications related to diabetes, such as diabetic nephropathy [2-4]. Diabetic nephropathy (DN) is a common complication in individuals with diabetes, primarily resulting from prolonged exposure to high glucose levels. It has the potential to shorten the lifespan of people with diabetes [5,6]. A cohort study on diabetes conducted by Livingstone and colleagues revealed that individuals with DN had a reduced life expectancy compared to those without the condition. The study suggested that DN could be a significant contributing factor to the decreased overall life expectancy of diabetic patients [7]. Due to the absence of effective pharmacological therapies, it is essential to investigate indicators that can help prevent the onset of diabetic nephropathy.

One commonly overlooked value in complete blood cell count (CBC) is red cell distribution width (RDW). While CBC is often focused on hemoglobin, white blood cell count, and platelet count, RDW can provide valuable information about the size variability of circulating red blood cells. It was reported that RDW can be an indicator of various health conditions, including anemia, nutritional deficiencies, and certain chronic diseases [8-10]. A retrospective study of 15,852 adult participants reported that individuals with a higher RDW had a greater risk of mortality. Specifically, for every 1% increase in RDW, the overall risk of death increased by 23% [11]. In a retrospective study of 4,111 patients with myocardial infarction, it was observed that there was a notable association between the level of RDW elevation and the considerably heightened likelihood of facing a subsequent nonfatal myocardial infarction, developing new symptomatic heart failure, experiencing coronary death, or having a stroke [12]. This suggests that higher levels of RDW may serve as a predictive factor for adverse cardiovascular events in patients with cardiovascular disease. However, there are limited reports and no substantial evidence from large population studies regarding the association between RDW and the occurrence and development of DN. In this study, we aimed to explore the potential association between RDW level and DN in 3,704 patients with T2DM.

MATERIALS AND METHODS

Enrollment of participants

The NHANES is a nationwide cross-sectional study aimed at assessing the health and nutritional status of both children and adults in the United States. This study has been conducted at regular intervals since the 1960s. Participants are selected using a complex, multistage, stratified sampling design, ensuring that the sample is representative of the national population. The data analyzed in this research were obtained from four NHANES cycles (2011 - 2012, 2013 - 2014, 2015 - 2016, and 2017 - 2018), because information regarding RDW and DN in patients with diabetes was available during these periods, and a total of 39,156 participants were initially included. Participants aged younger than 18 were excluded (n = 23,825). A total of 19,753 participants who had not been diagnosed with diabetes were excluded from the analysis (n = 4,072). The patients for whom there was no information regarding DN (n = 320) and RDW (n = 97) were also excluded. Six pregnant women were excluded. Finally, 3,704 patients with T2DM were involved in the final analysis (Figure 1). Participants were classified as having DN (n = 1,537) if UACR (urinary albumin-to-creatinine ratio) was at least 30 mg/g, or if eGFR (estimated glomerular filtration rate) fell below 60 mL/min/1.73 m² [13].

Data gathering

Professionals gathered fundamental demographic information and performed experimental assessments in accordance with the technical guidelines provided on the NHANES website. All data and experimental methodologies were accessible for download from the NHANES site. The laboratory analysis took place in Minnesota. Demographic information (such as gender, age, and race), examination data (including blood pressure and body mass index), and health-related behaviors (like smoking and alcohol consumption) were all collected. Laboratory information (fasting blood glucose, hemoglobin, glycated hemoglobin, albumin, hematocrit, mean corpuscular volume, RDW, total protein, alanine aminotransfease, gamma-glutamyltransferase, cholesterol, uric acid, triglyceride, high density lipoprotein cholesterol, etc.) were selected [14]. All measurements were then expressed using internationally recognized standard units.

Assessment criteria

Diagnosis of DN

Participants were categorized as having DN (n = 1,537) if UACR was at least 30 mg/g, or if eGFR fell below 60 mL/minute/1.73 m² [15].

Defining DM

The diagnostic criteria for diabetes were established based on international guidelines and previous research literature [16]. These criteria include individuals who have ever been diagnosed with diabetes, those with a fasting blood glucose level of ≥ 7.0 mmol/L, or those with a glycated hemoglobin level of ≥ 6.5 mmol/L.

Identification of hypertension

The diagnostic criteria for hypertension were defined as follows: individuals who have ever been informed that they have hypertension, or those with a systolic blood pressure (SBP) of ≥ 140 mmHg and/or a diastolic blood pressure (DBP) of ≥ 90 mmHg [17].

Assessment of body mass index (BMI)

Body mass index (BMI) is calculated by taking a person's weight in kilograms and dividing it by the square of their height in meters. The World Health Organization defines a normal BMI as being between 18.5 kg/m²

and 24.9 kg/m². A BMI ranging from 25.0 to 29.9 kg/m² is classified as overweight, while a BMI of 30.0 kg/m² or above is categorized as obese [15].

Evaluation of smoking and alcohol use

According to the analysis of the data and prior research, individuals who had smoked more than 100 cigarettes in their lifetime were classified as smokers, whereas those who had not exceeded this number were deemed non-smokers. Additionally, a non-drinker was defined as someone who consumed 12 or fewer alcoholic beverages over the course of a year, while individuals who surpassed this threshold were categorized as drinkers [18-20]. The atherogenic index of plasma (AIP) was computed using the formula: log10 (TG/HDL-C).

Covariable screening

Here, we screened the covariates based on the following criteria:

1) Demographic data
2) In light of our clinical experience
3) Factors that have been recognized as potential influences on diabetic nephropathy in previous research
4) The introduction of variability, which can lead to a shift in the regression coefficient of the base model exceeding 10%

Covariates that we collected included demographic data, laboratory data, examination data, and health-related behaviors.

Statistical analysis

The baseline characteristics of different RDW groups were examined using one-way ANOVA (assuming normal distribution), Kruskal-Wallis H (for skewed distribution), and chi-squared test (assuming categorical variables). The participants were categorized into two groups: individuals with DN (n = 1,537) and individuals without DN (n = 2,167). The statistical analysis in this study primarily involved three stages to evaluate the relationship between RDW and DN in the chosen participants. First, we used univariate and multivariate logistic regression to investigate the associations between RDW and DN. Second, the smooth curve fitting graph was made and fine-tuned based on the covariables in model 4. Following logical regression, a linear correlation between RDW and DN was identified. Third, subgroup analysis was conducted for all categories to evaluate the consistency of the findings. The analysis was carried out using R version 4.2.1 (http://www. Rproject.org; The R Foundation, Vienna, Austria) and Free Statistics software (version 1.9; Beijing FreeClinical Medical Technology Co., Ltd., Beijing, China). A two-tailed p-value < 0.05 was considered to be statistically significant.

RESULTS

Basic demographic information collected from each participant

This research included 39,156 participants from the NHANES dataset and took place over a span of eight years across four cycles. After applying the stringent screening criteria mentioned earlier, the final analysis comprised 3,704 diabetes mellitus patients, with a mean age of 60.8 ± 13.5 years. Among them, 1,537 had DN and 2,167 had no DN. The relevant clinical and laboratory data for the patients are presented in Table 1. RDW is evenly categorized into three levels, with low level T1 (11 - 13.3), middle level T2 (13.3 - 14.1), and high level T3 (14.1 - 29.8). Median of RDW was 13.7% for the patients in this study. The mean and standard deviation of RDW were 14.0% and 1.44, respectively.

Univariate analysis of factors associated with DN

The results of the univariate logistic regression analysis indicated that cholesterol, age, hemoglobin, hematocrit, MCV, RDW, GLU, Hba1c, ALT, ALB, UA, HDL, API, hypertension, and smoking were the related factors of DN. Age, MCV, RDW, GLU, Hba1c, UA, API, hypertension, and smoking demonstrated a positive correlation with the occurrence of diabetic nephropathy (DN), while cholesterol, hemoglobin, hematocrit, ALT, ALB, and HDL were negatively associated with it. In non-Hispanic Whites, RDW showed a positive correlation with DN when compared to Mexican Americans (Table 2).

Multivariate analysis of factors associated with RDW and diabetic nephropathy (DN)

After multiple imputation of the missing covariates, an analysis of logistic multiple factor regression was done. When RDW was evenly divided into three groups, four logistic regression models were created to analyze the relationship between RDW and DN. Table 3 provides a detailed analysis of the relationship between RDW and DN, with the effect value expressed as OR and 95% CI. The effect value can be explained as the proportional increase in the risk of diabetic nephropathy for each additional RDW unit. For example, in the unadjusted model 1, the effect size of 1.21 (1.18 - 1.25) can be interpreted as a 21% increase in the risk of DN for every additional unit of RDW. In the slightly adjusted model 2, the effect size of 1.17 (1.14 - 1.21) suggested a 17% rise in the risk of DN for each additional unit of RDW. In the further adjusted model 3, the effect size of 1.16 (1.12 - 1.19) indicated a 16% increase in the risk of DN for each additional RDW unit. In the fully adjusted model 4, the effect size was 1.16 (1.12 - 1.21), signifying a 16% rise in the risk of DN for each additional RDW unit. This finding was statistically significant (p-value < 0.001). In all models, as RDW increased, the diabetic nephropathy risk also increased, showing a consistent trend with a significant p-value of less than 0.001 (Table 3).

Table 1. Comparison of baseline data in individuals with T2DM based on RDW levels.

Variables	Total Subjects RDW (%)	RDW (%)			p
	(n = 3,704)	T1 (11 - 13.3) Q2 (13.3 - 14.1) Q3 (14.1 - 29.8)	T2 (13.3 - 14.1) Q2 (13.3 - 14.1) Q3 (14.1 - 29.8)	T3 (14.1 - 29.8) Q2 (13.3 - 14.1) Q3 (14.1 - 29.8)	
Gender, n (%)					
Male	1,953 (52.7)	651 (55.5)	656 (55.6)	646 (47.7)	< 0.001
Female	1,751 (47.3)	521 (44.5)	523 (44.4)	707 (52.3)	< 0.001
Age (years)	60.8 ± 13.5	58.1 ± 13.9	61.2 ± 12.8	62.7 ± 13.5	< 0.001
Race, n (%)					
Mexican American	627 (16.9)	236 (20.1)	207 (17.6)	184 (13.6)	< 0.001
Other Hispanic	422 (11.4)	147 (12.5)	170 (14.4)	105 (7.8)	< 0.001
Non-Hispanic White	1,146 (30.9)	368 (31.4)	370 (31.4)	408 (30.2)	< 0.001
Non-Hispanic Black	948 (25.6)	191 (16.3)	264 (22.4)	493 (36.4)	< 0.001
Other race	561 (15.1)	230 (19.6)	168 (14.2)	163 (12)	< 0.001
BMI (kg/m^2)	32.4 ± 7.6	30.9 ± 6.6	32.4 ± 7.2	33.8 ± 8.6	< 0.001
Hemoglobin (g/dL)	13.7 ± 1.6	14.2 ± 1.4	14.0 ± 1.4	13.0 ± 1.7	< 0.001
Hematocrit (%)	40.9 ± 4.5	41.8 ± 4.0	41.7 ± 4.1	39.5 ± 5.0	< 0.001
MCV (fL)	88.4 ± 6.2	90.5 ± 4.5	89.4 ± 4.8	85.8 ± 7.4	< 0.001
GLU (mmol/L)	7.7 (6.8, 9.7)	8.0 (7.0, 10.1)	7.7 (6.8, 9.8)	7.4 (6.4, 9.2)	< 0.001
Hba1c (%)	7.4 ± 1.8	7.7 ± 2.0	7.4 ± 1.7	7.2 ± 1.5	< 0.001
ALB (g/L)	41.0 ± 3.6	42.0 ± 3.4	41.4 ± 3.4	39.9 ± 3.7	< 0.001
TP (g/L)	71.5 ± 5.0	71.9 ± 4.7	71.5 ± 5.0	71.2 ± 5.2	0.003
Alcohol use, n (%)	1,589 (64.0)	553 (65.1)	496 (64.2)	540 (62.9)	0.656
Smoking, n (%)	1,778 (48.0)	562 (48)	553 (46.9)	663 (49)	0.563
Hypertension n (%)	2,643 (72.7)	732 (64.2)	851 (73.4)	1,060 (79.5)	< 0.001
Cholesterol (mmol/L)	4.6 (3.9, 5.4)	4.8 (4.0, 5.6)	4.6 (3.9, 5.4)	4.4 (3.8, 5.2)	< 0.001
ALT (U/L)	21.0 (16.0, 30.0)	23.0 (17.0, 32.0)	22.0 (17.0, 30.0)	19.0 (14.0, 27.0)	< 0.001
GGT (U/L)	25.0 (17.0, 38.0)	26.0 (18.0, 40.0)	24.0 (17.0, 38.0)	24.0 (17.0, 36.0)	0.006
UA (μmol/L)	333.1 (273.6, 398.5)	315.2 (267.7, 380.7)	339.0 (279.6, 398.5)	345.0 (285.5, 416.4)	< 0.001
HDL (mmol/L)	1.2 (1.0, 1.4)	1.2 (1.0, 1.4)	1.2 (1.0, 1.4)	1.2 (1.0, 1.4)	0.598

RDW red blood cell distribution width, BMI body mass index, MCV mean corpuscular volume, Hba1c glycated hemoglobin, ALB albumin, TP total protein, GLU glucose, HDL high density lipoprotein cholesterol, ALT alanine aminotransferase, GGT gamma-glutamyltransferase, UA uric acid.

Subgroup analysis and curve fitting

We explored whether there were differences in gender, race, BMI, alcohol use, smoking, and hypertension between RDW and diabetic nephropathy. The results indicated that the relationship between RDW and DN was stable in all subgroups (Figure 2); there was no interaction ($p > 0.05$). This suggests that the relationship between RDW and diabetic nephropathy was not influenced by clinical characteristics or demographic, such as gender, race, or BMI, alcohol use, smoking, and hypertension. These results support the notion that RDW might be a reliable biomarker for identifying individuals with diabetic nephropathy risk, irrespective of these factors. Moreover, in order to better elucidate the relationship between RDW and DN, a fitting curve of RDW and DN was plotted after adjustment according to model 4. The results indicate that there was a linear relationship between RDW and diabetic nephropathy (p for non-linearity = 0.658). RDW was positively correlated with diabetic nephropathy (Figure 3).

Table 2. Univariate analysis examining the association between factors related to T2DM and diabetic nephropathy.

Variable	DN	
	OR (95% CI)	p-value
Cholesterol (mmol/L)	0.92 (0.87 - 0.97)	0.003
Male	1	
Female	0.95 (0.84 - 1.09)	0.479
Age (years)	1.05 (1.04 - 1.05)	< 0.001
Mexican American	1	
Other Hispanic	0.98 (0.76 - 1.26)	0.868
Non-Hispanic White	1.71 (1.4 - 2.09)	< 0.001
Non-Hispanic Black	1.17 (0.95 - 1.44)	0.133
Other race	1.01 (0.8 - 1.28)	0.944
BMI, (kg/m^2)	1 (0.99 - 1.01)	0.868
Hemoglobin (g/dL)	0.8 (0.76 - 0.83)	< 0.001
Hematocrit (%)	0.92 (0.91 - 0.94)	< 0.001
MCV (fL)	1.02 (1.01 - 1.03)	< 0.001
RDW (%)	1.21 (1.16 - 1.27)	< 0.001
GLU (mmol/L)	1.05 (1.03 - 1.08)	< 0.001
Hba1c (%)	1.16 (1.11 - 1.2)	< 0.001
ALT (U/L)	0.99 (0.99 - 1)	0.006
ALB (g/L)	0.91 (0.89 - 0.93)	< 0.001
GGT (U/L)	1 (1 - 1)	0.349
TP (g/L)	0.99 (0.98 - 1.01)	0.305
UA (umol/L)	1.01 (1 - 1.01)	< 0.001
HDL (mmol/L)	0.83 (0.7 - 1)	0.045
Alcohol use	0.92 (0.78 - 1.09)	0.347
Smoking	1.23 (1.07 - 1.4)	0.002
Hypertension	2.69 (2.29 - 3.16)	< 0.001
API	1.63 (1.23 - 2.16)	0.001

BMI body mass index, MCV mean corpuscular volume, RDW red blood cell distribution width, GLU glucose, Hba1c glycated hemoglobin, ALT alanine aminotransferase, ALB albumin, GGT gamma-glutamyltransferase, TP total protein, UA uric acid, HDL high density lipoprotein cholesterol, AIP atherogenic index of plasma.

DISCUSSION

This large T2DM cross-sectional study used the NHANES 2011 - 2018 database to illustrate a correlation between RDW and diabetic nephropathy in the US population. To our knowledge, this was the first study to investigate the association between RDW and DN in the large, diverse population. We clearly exhibited that RDW, MCV, hemoglobin, and hematocrit were the related factors of DN, and RDW was independently associated with the risk of DN. There was a significant positive relationship between RDW and DN. No interactive role was identified in the relationship between RDW and DN, indicating that the abovementioned conclusions remained stable in the different subgroups. These results would have important implications for current DN administrative strategies of T2DM.

The CBC typically focuses on metrics such as hemoglobin, white blood cell count, and platelet count. However, the RDW is an important parameter that can provide valuable information about the size variability of circulating red blood cells. As a simple and inexpensive hematological parameter, RDW is commonly used as a laboratory index in the differential diagnosis of various anemias, particularly as an early warning indicator for iron deficiency anemia [21]. Furthermore, it is worth noting that RDW has been found to be influenced by various clinical conditions associated with inflammation, not limited to anemia [22,23]. Elevated RDW levels have been observed in patients with inflammatory

Table 3. Multivariate analysis of association between RDW and DN in individuals with T2DM.

Variable	Model 1		Model 2		Model 3		Model 4	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
RDW (%)	1.21 (1.18 - 1.25)	< 0.001	1.17 (1.14 - 1.21)	< 0.001	1.16 (1.12 - 1.19)	< 0.001	1.16 (1.12 - 1.21)	< 0.001
RDW group								
T1 (11 - 13.3)	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
T2 (13.3 - 14.1)	1.12 (1.01 - 1.23)	0.024	1.00 (0.90 - 1.10)	0.930	0.95 (0.86 - 1.05)	0.313	1.03 (0.92 - 1.16)	0.569
T3 (14.1 - 29.8)	1.85 (1.68 - 2.03)	< 0.001	1.59 (1.44 - 1.76)	< 0.001	1.48 (1.34 - 1.64)	< 0.001	1.58 (1.40 - 1.79)	< 0.001
p for trend		< 0.001		< 0.001		< 0.001		< 0.001

Model 1 non-adjusted, model 2 age, gender, race, model 3 model 2 + BMI, hypertension, alcohol use, smoking, model 4 model 3 + hematocrit, MCV, GLU, Hba1c, ALT, ALB, GGT, TP, HDL, UA, cholesterol, hemoglobin, API.

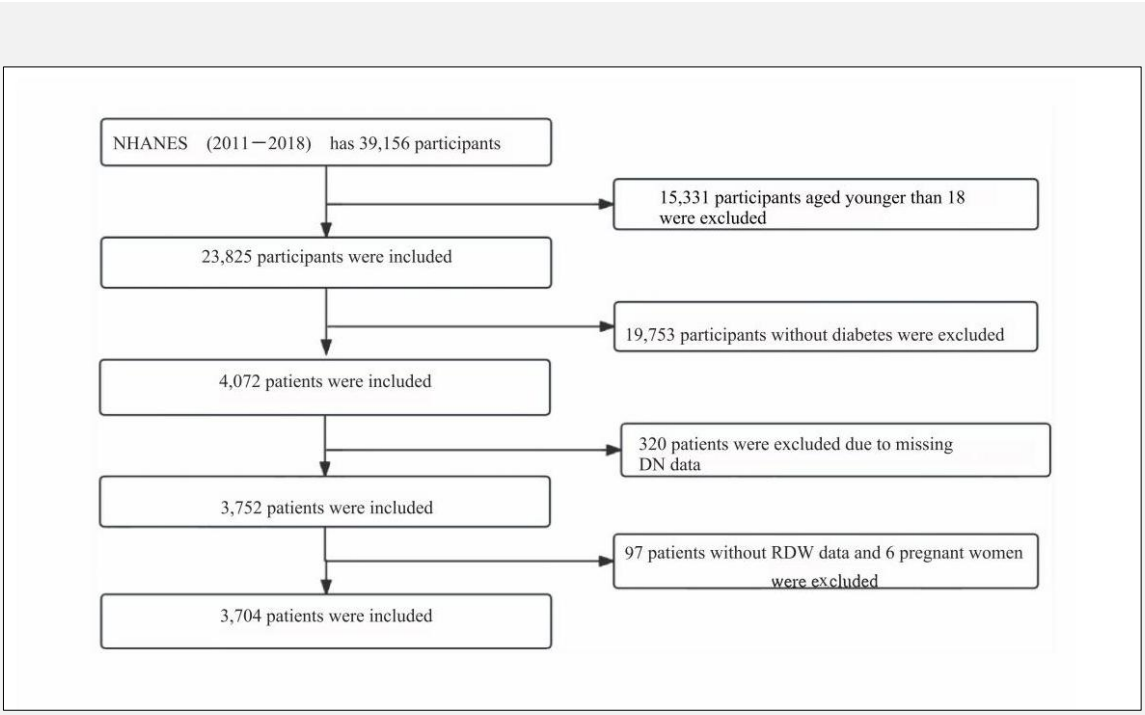

Figure 1. Flowchart of participant selection.

disorders such as systemic lupus erythematosus [24], rheumatoid arthritis [25], and cardiovascular disease. Additionally, Klisic et al. reported a negative correlation with RDW and body mass index in late adolescents [26], while Emamian et al. observed a reduction in RDW levels in the hypertensive group compared to the control group [27]. Besides that, previous studies have shown evidence suggesting that RDW could be a risk factor for cardiovascular disease morbidity and mortality in diverse populations. This finding underscored the potential clinical significance of monitoring RDW levels as an indicator of cardiovascular health and the need

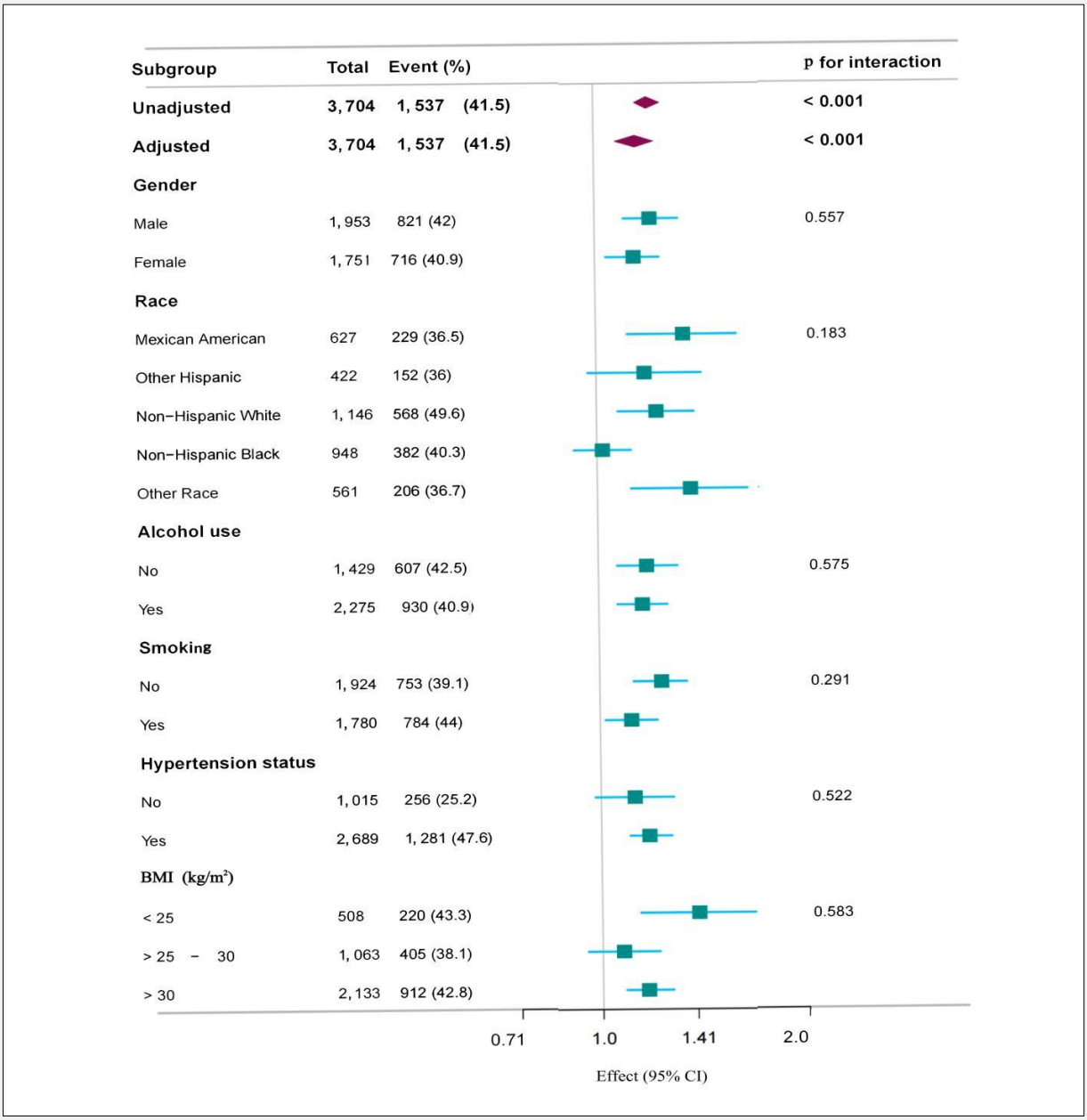

Figure 2. Forest plot of RDW and diabetic nephropathy.

for further research to better understand this association [28,29]. Although the specific mechanism underlying the positive correlation between RDW and DN still requires further investigation, our findings are bolstered by biological plausibility, as demonstrated by existing research. Chen et al. suggested that the molecular mechanism linking RDW to the incidence of glomerulonephritis might primarily be attributed to the function of RDW in patients with inflammatory conditions and its ability to accurately reflect rising levels of circulating cytokines [30]. Anemia and DN in individuals with T2DM are common disorders and often occur simultaneously. There is a strong link between DN and anemia. Anemia is now recognized as a frequent complication of DN, manifesting at an earlier stage than in non-diabetic renal disease and increasing the likelihood of cardiovas-

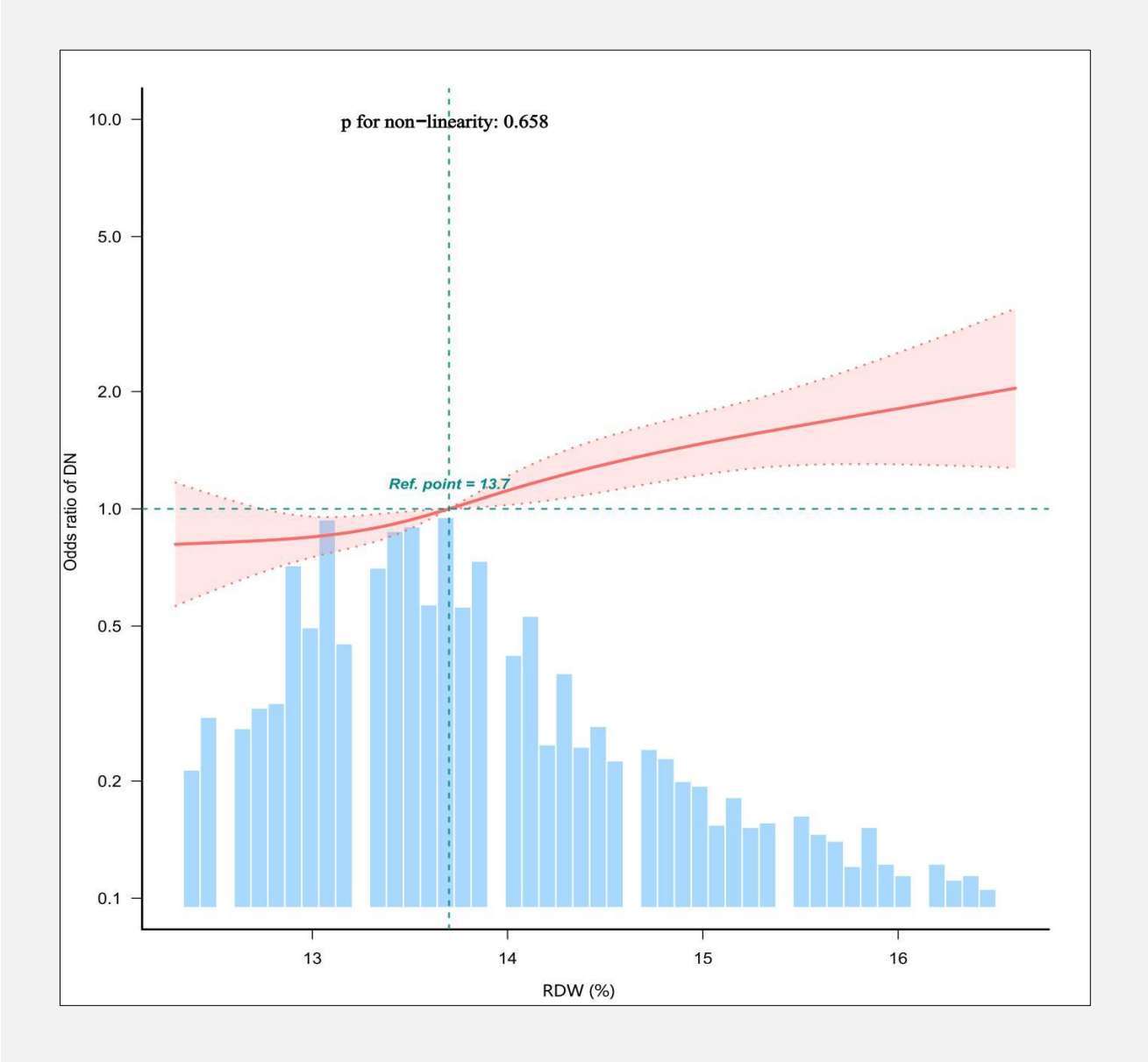

Figure 3. Fitting curve of RDW and diabetic nephropathy.

cular and microvascular complications. Several studies have suggested that correcting anemia may slow the progression of DN and reduce cardiovascular complications [31]. The main cause of anemia in DN is a decrease in erythropoietin levels, which is due to reduced production and, to a lesser extent, increased excretion of erythropoietin in the urine. The RDW, as a component of the CBC, has traditionally been utilized to categorize various forms of anemia. Therefore, it can be inferred that there is a relationship between RDW and DN. Some studies indicated that elevated RDW levels were linked to a decline in renal function [32,33]. This suggests a potential association between RDW and renal health, highlighting the importance of further investigation and monitoring of RDW levels in the clinical settings. Zhang reported on a study involving 175 patients with T2DM and DN at the West China Hospital of Sichuan University; this study demonstrated that elevated levels of RDW were significantly linked to a higher risk of progressing to end-stage renal disease in patients with DN, even though it was not identified as an independent predictor [31]. The aforementioned studies indicated a possible connection between RDW and DN in T2DM. It is noteworthy that the prior studies were constrained by small sample sizes and a narrow range of covariates, which hindered the capacity to draw overarching conclusions regarding the relationship between the variables studied. Future research should aim to ad-

dress these limitations by employing larger and more varied samples, in addition to taking into account a broader array of potential confounding factors. The NHANES offered us a unique opportunity to explore the possible relationship between RDW and DN as well as the comprehensive assessment of the risk-level relationship between RDW and DN fully adjusted for a wide array of covariates and conducted a variety of stratified analyses. The strength of the current study resides in its position as the first large-scale, ethnically diverse, population-based investigation that explores the relationship between RDW and diabetic nephropathy in adults with type 2 diabetes mellitus (T2DM) in the United States. Our findings have the potential to enrich the currently limited literature on the link between red cell distribution width (RDW) and diabetic nephropathy (DN).

The advantages of using RDW to detect the risk of diabetic nephropathy compared with creatinine, GFR, and urine albumin excretion (UAE) are quite evident. First, measuring RDW is a simple and straightforward procedure. It is a parameter that can be easily obtained through a routine complete blood count (CBC) test, which is widely accessible in most clinical laboratories and can be completed relatively fast. On the contrary, measuring creatinine, GFR, and UAE is far more complicated. Measuring creatinine calls for a specific laboratory assay. Calculating GFR involves complex equations that require taking into account multiple factors such as age, gender, race, and serum creatinine levels. And assessing UAE demands specialized techniques, like collecting a 24-hour urine sample or calculating the albumin-to-creatinine ratio in spot urine, which can be affected by patient compliance and other factors. Second, as RDW is routinely included in a standard complete blood count (CBC) test, its assessment incurs minimal additional expense. This affordability makes RDW an appealing option for implementing large-scale screening initiatives aimed at identifying individuals at risk of diabetic nephropathy (DN). In contrast, obtaining precise measurements of creatinine, estimating GFR, and quantifying urine albumin excretion (UAE) typically require more resource-intensive approaches. These methods rely on specialized laboratory reagents, advanced diagnostic equipment, and trained personnel, all of which contribute to higher operational costs. For healthcare providers operating under budgetary constraints, RDW emerges as a practical and economical choice for initial DN risk stratification. Finally, RDW offers distinct advantages over traditional markers like creatinine, GFR, and urine albumin excretion (UAE) by not only spotting early pathological changes in DN but also reliably predicting its progression in the early stages. While creatinine and GFR often remain normal until significant renal damage has occurred, and UAE may miss subtle early-stage damage, RDW reflects systemic inflammation and oxidative stress - key drivers of diabetic kidney injury. This makes RDW a more sensitive and proactive biomarker for early risk stratification, enabling timely interventions that could delay or prevent disease progression.

However, our findings had limitations; because the study relied on data from a cross-sectional survey, we were unable to determine a causal relationship between red cell distribution width (RDW) and diabetic neuropathy (DN). Therefore, further longitudinal studies or the inclusion of prospective data are required to confirm and validate our study. Moreover, the dependence on self-reported data may have resulted in recall bias and possible misclassification of diabetic neuropathy (DN). Additionally, a study that focused on a small cohort of U.S. adults meant that the findings might not be applicable to other populations. Finally, our study lacked information on certain potential confounding factors, such as medication use and dietary habits, which might have impacted the association between RDW and DN. Even considering these limitations, our findings provided worthy insights into the potential relationship between red cell distribution width (RDW) and diabetic neuropathy (DN) in T2DM individuals. Further studies should aim to overcome these constraints and explore this connection more thoroughly.

CONCLUSION

In summary, our findings indicate that elevated RDW levels are independently linked to the occurrence of DN in individuals with T2DM, suggesting RDW as a promising biomarker for the early identification, prevention, and strategic intervention of this severe complication. RDW could potentially be a predictor for the presence of DN in patients with T2DM.

Ethical Approval Statement:

The ethical considerations of the NHANES include obtaining informed consent from participants, ensuring the confidentiality of personal information, and adhering to ethical standards for data collection and usage. All procedures were approved by the appropriate institutional review boards.

Declaration of Interest:

The authors have no conflicts of interest to declare.

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