

## The relationship between red cell distribution width and the risk of Henoch–Schönlein purpura nephritis

X Zhu , M Zhang, F Lan, H Wei, Q He, S Li and X Qin

Department of Clinical Laboratory, Guangxi Medical University First Affiliated Hospital, Nanning, China

### ABSTRACT

**Introduction:** Red blood cell distribution width (RDW) is elevated in various inflammatory diseases, but its clinical significance in Henoch–Schönlein purpura nephritis (HSPN) is unknown. The aim of this study was to determine the value of RDW as a risk factor or marker for HSPN in children.

**Methods:** This was a case-control study of 105 Henoch–Schönlein purpura (HSP) patients, 120 HSPN patients and 192 healthy controls. The relationship between RDW-coefficient of variation (RDW-CV) and the clinical characteristics of HSPN patients was determined by a multiple logistic regression analysis (MVLRA). Receiver operating characteristic (ROC) curves were applied to compare the diagnostic potential of the RDW-CV, a panel of routine markers and combinations of these indices.

**Results:** The RDW-CV values were significantly higher in the HSPN group than the HSP group and controls ( $P < 0.001$ ). Significant correlations were found between RDW-CV and ESR ( $P = 0.001$ ). A combination of RDW-CV and ESR in a ROC curve showed 80% sensitivity and 84.9% specificity in the HSP patients, and 85.8% sensitivity and 93.8% specificity in the HSPN patients. The MVLRA revealed that RDW-CV (OR 1.69, 95% CI 1.16–2.48,  $P = 0.007$ ) was an independent predictor of HSPN.

**Conclusions:** The RDW levels were highest in the HSPN group, suggesting that RDW, especially the combination of RDW and ESR, may have value when assessing the risk of HSPN.

### ARTICLE HISTORY

Received 1 March 2017  
Accepted 1 August 2017

### KEYWORDS

Henoch–Schönlein purpura nephritis; anaphylactoid purpura; allergic purpura; children; red blood cell distribution width

### Introduction

Henoch–Schönlein purpura (HSP) is one of the most common types of hypersensitivity small-vessel vasculitis and is generally found in children. It is manifested by abdominal pain, haemorrhagic gastroenteritis, skin purpura, arthritis and kidney damage [1]. HSP is often self-limiting, and has a tendency to resolve spontaneously, usually within 6–8 weeks [2]. As an inflammatory disease, it is characterized by typical leukocytoclastic vasculitis and the deposition of circulatory immunoglobulin A1 (IgA1)-containing immune complexes [3,4]. Nephritis is a complication of HSP that may extend the course of the disease. Henoch–Schönlein purpura nephritis (HSPN) is a key factor in patients' prognosis as it accounts for approximately 79% of glomerular nephritis in children, and can result in chronic and even permanent organ injury [5,6]. The aetiologies and mechanisms of HSPN remain unclear although the disease is linked with both increased serum levels of IgA and elevated circulating immune complexes containing IgA [5]. Previous studies have suggested that the expression of aberrant pro-inflammatory cytokines, including interleukin (IL)-17,

IL-21, IL-6 and IL-1, may contribute to the pathogenesis of HSPN [3,7,8], providing reasonable grounds for the hypothesis that HSPN is an inflammatory disease mediated by autoimmune processes.

Red blood cell distribution width (RDW) is a widely used laboratory parameter that measures the heterogeneity of red blood cell dimensions, and is a recognised routine blood parameter commonly used in diverse diagnoses of anaemia [9]. However, RDW is increased in a variety of other conditions, including cardiovascular disease, diabetes mellitus, essential hypertension, colon cancer and celiac disease [10–14]. In addition, RDW levels are elevated in inflammatory conditions, including ankylosing spondylitis, inflammatory bowel disease, rheumatoid arthritis and other inflammatory disorders [9,15–17]. It has recently been shown that RDW is related to endothelial dysfunction independently of anaemia, as well as to increased inflammation in chronic kidney disease [18]. However, RDW has not yet been investigated as a predictive biomarker for the risk of HSPN. Taken together, we hypothesized that RDW levels are higher in HSPN patients and accordingly investigated whether they can be used to predict the risk for this disease.

**CONTACT** X Qin  [qinxue919@126.com](mailto:qinxue919@126.com)  Department of Clinical Laboratory, Guangxi Medical University First Affiliated Hospital, Nanning 530021, China.

Xuan Zhu and Meiyu Zhang should be considered co-first authors.

## Patients and methods

This was a prospective observational study conducted at the First Affiliated Hospital of Guangxi Medical University from January 2013 to December 2015. The University laboratory participated in the external quality assurance scheme organized by the National Centre for Clinical Laboratories in China, and the laboratory's external quality assurance results remained acceptable throughout the study. The study recruited 225 patients with HSP/HSPN from the Department of Paediatrics of Guangxi Medical University and 192 healthy controls from the Health Examination Centres of Guangxi Medical University. The study was approved by the ethics committee of the First Affiliated Hospital of Guangxi Medical University and complied with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

The diagnoses of all patients with HSPN were confirmed by percutaneous renal biopsy using inclusion criteria of the American College of Rheumatology (ACR): [19]. Inclusion criteria were age  $\leq 20$  years at disease onset, palpable purpura, gastrointestinal bleeding and biopsy showing granulocytes around arterioles or venules. Exclusion criteria were other autoimmune diseases, anaemia or another haematological disease, that they were on medications that commonly cause or treat anaemia or nephritis, liver disease, infectious diseases or malignancies, or other inflammatory diseases that could potentially influence the measurement of RDW. Both general information and laboratory results were gathered from the initial diagnoses of those patients who met these criteria.

We recorded RDW-CV, haemoglobin, white blood cell count, platelet count, erythrocyte sedimentation rate (ESR), serum creatinine, Ig A, IgG, IgM and 24-h urinary protein levels at presentation (LH750 Analyser, Beckman Coulter, Inc., Miami, FL). The results of biochemistry tests were analysed using an automatic biochemical analyser (Model 7600-120, Hitachi High-Technologies Corporation, Tokyo, Japan). ESR was measured using an

automated ESR analyser (Model Minitor-100, Electa Lab Srl, Forli, Italy). The range of the RDW-CV reference values 11–14%.

Continuous variables normally distributed are shown as mean with standard deviation (SD), and those non-normally distributed are shown as median with inter-quartile range (IQR). A one-way ANOVA compared normally distributed variables among all the groups, and multiple comparison tests were conducted on those features found to be significant. A Kruskal–Wallis test were used to compare the non-normally distributed variables. Categorical values were compared using the  $\chi^2$ -test. Correlations between the RDW-CV values and the continuous variables were sought using Spearman's method. To identify the independent factors associated with HSPN, a multi-variate logistic regression analysis (MVLRA) was performed, and the odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. In addition, to explore the performance of the variables, binary logistic regression analysis and receiver operating characteristic (ROC) curves were analysed using MedCalc version 9.2.0 for Windows (MedCalc Software, Ostend, Belgium). The remaining statistical analyses were performed using SPSS version 16.0 (SPSS, Inc., Chicago, IL, USA) and GraphPad Prism version 5.0 for Windows (GraphPad Software Inc., La Jolla, CA, USA). All the *P*-values given are two-tailed, and *P* < 0.05 was defined as indicating statistical significance.

## Results

Table 1 details the demographic and laboratory characteristics of the patients and controls who were matched for age, sex, haemoglobin and IgA. The white blood cell count, platelet count, ESR, IgG and IgM were all higher, and creatinine lower, in both patient groups than in the controls, with no difference between the patient groups. RDW-CV was higher in HSPN than in HSP, which was higher than in the controls. Urinary protein was higher in HSPN than in HSP. Parameters that showed significant differences between the three groups in the univariate

**Table 1.** Characteristics of participants.

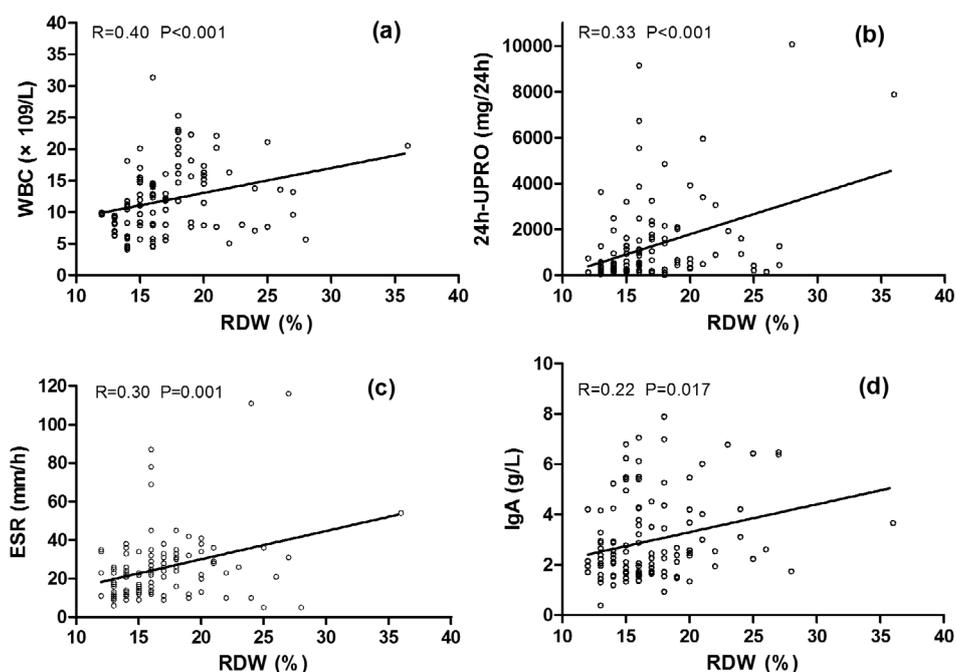
Parameters	HSPN patients (N = 120)	HSP patients (N = 105)	Healthy controls (N = 192)	<i>P</i> -values
Age (y)	8.5 $\pm$ 2.8	8.1 $\pm$ 2.8	8.8 $\pm$ 3.4	0.239
Sex (male/female)	85/35 (71%)	77/28 (58%)	146/46 (76%)	0.589
RDW (%)	16.9 $\pm$ 3.9	15.3 $\pm$ 2.7	13.4 $\pm$ 2.0	<0.001
Haemoglobin (g/L)	128 $\pm$ 15	130 $\pm$ 15	131 $\pm$ 8	0.061
WBC ( $10^9$ /L)	11.8 $\pm$ 5.2	11.6 $\pm$ 5.4	7.0 $\pm$ 1.5	<0.001
Platelets ( $10^9$ /L)	358 $\pm$ 109	342 $\pm$ 90	235 $\pm$ 57	<0.001
ESR (mm/h)	25 $\pm$ 2	24 $\pm$ 2	8 $\pm$ 4	<0.001
Creatinine (mmol/L)	42.1 $\pm$ 10.2	44.8 $\pm$ 14.6	78.2 $\pm$ 12.6	<0.001
IgG (g/L)	7.52 $\pm$ 3.02	9.16 $\pm$ 2.81	12.7 $\pm$ 0.77	<0.001
IgM (g/L)	1.27 $\pm$ 0.56	1.26 $\pm$ 0.47	1.14 $\pm$ 0.13	0.005
IgA (g/L)	2.37 (7.51)	2.40 (6.79)	2.24 (0.68)	0.257*
Urinary protein (mg/24 h)	1184.0 (110.3)	523.6 (1244.4)	–	<0.001*

Notes: Boldfaced values indicate a significant difference. Data were presented as mean  $\pm$  SD, or median (IQR) when appropriate. \**P* value calculated by Kruskal–Wallis; Remaining *P* values calculated by one-way ANOVA. HSP, Henoch–Schönlein purpura; HSPN, Henoch–Schönlein purpura nephritis; RDW, red blood cell distribution width; WBC, white blood cell count; ESR, erythrocyte sedimentation rate; Ig, immunoglobulin.

**Table 2.** Multivariate logistic regression analysis results.

Parameters	HSP patients (N = 105)		HSPN patients (N = 120)	
	OR (95% CI)	P-value	OR (95% CI)	P-value
ESR	1.61 (1.08–2.39)	<b>0.019</b>	1.62 (1.09–2.40)	<b>0.017</b>
RDW	1.50 (1.03–2.19)	<b>0.037</b>	1.69 (1.16–2.48)	<b>0.007</b>
WBC	3.03 (1.06–8.66)	<b>0.038</b>	3.07 (1.07–8.77)	<b>0.036</b>
Platelets	1.04 (1.00–1.07)	<b>0.033</b>	1.04 (1.00–1.07)	<b>0.029</b>
Creatinine	0.90 (0.83–0.97)	<b>0.004</b>	0.87 (0.81–0.95)	<b>0.001</b>
IgG	0.28 (0.09–0.87)	<b>0.028</b>	0.21 (0.07–0.67)	<b>0.008</b>
IgA	2.21 (0.43–11.34)	0.343	2.36 (0.46–12.16)	0.303
IgM	60.7 (0.48–7645.6)	0.096	78.5 (0.61–10087.3)	0.078

Notes: Boldfaced values indicate a significant difference. ORs are against the healthy controls as reference group. Abbreviations and units as Table 1. OR, odds ratio; CI, confidence interval.

**Figure 1.** Correlations coefficients between RDW and routine markers.

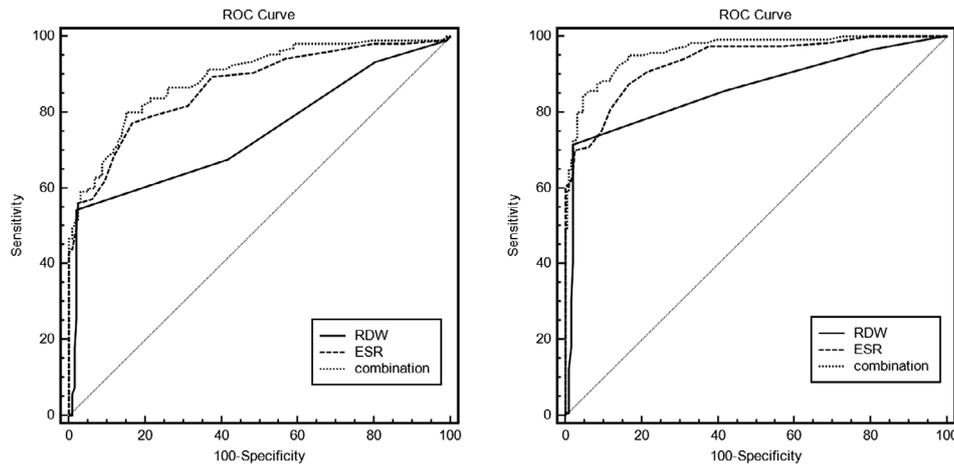
analysis were used in a MVLRA. ESR, RDW-CV, white blood cell count, platelet count, creatinine and IgG were independent predictors of the occurrence of HSP and HSPN (Table 2). Significant correlations were found between RDW-CV values and white blood cell count ( $r = 0.4$ ,  $P < 0.001$ ), ESR ( $r = 0.3$ ,  $P = 0.001$ ), IgA ( $r = 0.33$ ,  $P < 0.001$ ) and urinary protein ( $r = 0.22$ ,  $P = 0.017$ ) (Figure 1).

Binary logistic regression explored biomarker combinations, which showed that the optimal combination of markers was RDW-CV and ESR. Among the HSP patients, the ROC curves of the RDW-CV levels had a sensitivity of 54.3% and a specificity of 97.9%, with the optimal cut-off value of 14% (Area under the curve [AUC] 0.74, 95% CI 69.0–79.2%,  $P < 0.001$ ). At an ESR cut-off of 11%, the sensitivity was 77.1% and the specificity was 83.3% (AUC 0.87, 95% CI 82.4–90.5%,  $P < 0.001$ ). After adjusting by the regression coefficient of the binary logistic regression, the combination of RDW-CV and ESR had a sensitivity of 80% and a specificity of 84.9%, with the optimal cut-off values of 19.7% (AUC 0.89, 95% CI 85.1–92.5%,  $P < 0.001$ ; Figure 2). For the HSPN patients, at an RDW-CV cut-off of 14%, the sensitivity was 71.7% and

the specificity was 97.9% (AUC 0.86, 95% CI 81.8–89.7%,  $P < 0.001$ ). Whilst at an ESR cut-off of 11%, the sensitivity was 87.5% and the specificity was 83.3% (AUC 0.94, 95% CI 90.1–95.9%,  $P < 0.001$ ). For the combined RDW-CV and ESR cut-off value of 28.2%, the sensitivity and specificity were 85.8 and 93.8% (AUC 0.96, 95% CI 93.5–98.1%,  $P < 0.001$ ; Figure 2), respectively.

## Discussion

The extent of renal injury plays a vital role in early individualized HSPN therapy and prognostic assessment. Although a kidney biopsy is best practice for estimating renal disease, it is expensive, invasive, clinically risky and not easily tolerated by all patients. In contrast, RDW-CV is easily obtained as part of a routine blood examination and provides valuable information about HSPN without adding to the cost of diagnosis. RDW has been reported as an inflammatory biomarker with proven feasibility as a prognostic parameter in various diseases [20,21], whilst many studies have described inflammation as contributing to the mechanism of elevated RDW [22–24].



**Figure 2.** (a) The comparison of receiver operating characteristic (ROC) curves in Henoch–Schönlein purpura (HSP) patients. (b) The comparison of ROC curves in Henoch–Schönlein purpura nephritis (HSPN) patients.

In this case-controlled study, the baseline RDW-CV levels were remarkably elevated in the HSPN patients compared to the HSP patients and healthy controls, and correlated with ESR, IgA and urinary protein. The correlation between these biomarkers and RDW may provide valuable information. ESR is generally sensitive to anaemia, inflammatory conditions or other stress states, making it an appropriate indicator of the relationship between inflammation and RDW. No significant difference in haemoglobin between the groups excludes anaemia as a cause of raised ESR. Studies have suggested that in HSPN patients, the decreased activity of  $\beta$ 1,3-galactosyltransferase in peripheral B cells could result in a deficiency of terminal  $\beta$ 1,3-galactosyl residuals in the hinge region of IgA1. The combination of abnormal glycosylated IgA1 and IgG antibodies, the immune complexes deposits in the renal mesangium and activated mesangial cells could cause a proliferation of inflammatory cells and produce inflammatory cytokines, all ultimately leading to the renal injury [4,25]. The relationship between IgA and RDW levels suggests that the mechanism of HSPN is caused by inflammation activity mediated by immunity. Recently, Ye et al. [26] demonstrated that RDW values are positively correlated with 24-h UPRO in HSPN patients and that 24-h UPRO increased along with the pathological progression of HSPN. Our results indicated that increased RDW may be considered as part of the chronic inflammation process that is the pathogenetic basis of HSPN. In addition, to enhance the accuracy and the efficiency of diagnosis, RDW and ESR were applied as a combined biomarker were applied to plotting the ROC curve using binary logistic regression, which showed very good sensitivity and specificity compared to RDW or ESR alone. In addition, the combination achieved high predictive values for assessing HSPN. Furthermore, the multiple logistic regression analysis confirmed that RDW can more accurately predict the presence of HSPN than HSP, indicating that RDW may be an independent, reproducible predictor of HSPN (see Figure 2).

At present, the precise pathogenesis behind the relationship between RDW and HSPN is unknown. Some studies have shown that RDW may be influenced by inflammatory factors, including IL-6 and TNF- $\alpha$  [24]. Inflammatory cytokines may influence the function of bone marrow and suppress the maturation of erythrocytes, leading to increased RDW values [27]. Thus, higher RDW values could reflect an underlying inflammatory state caused by chronic inflammation that could in turn transform erythrocyte homeostasis and impair erythrocyte maturation [28]. The pathogenesis of HSPN may also be accounted for by inflammatory conditions. Chang et al. [29] has reported that the overexpression of IL-17, IL-4 and IFN- $\gamma$  contributes to the onset of HSP. Xu et al. [3] has also found that one single-nucleotide polymorphism of IL-17A gene is a risk factor for HSP and that IL-17A has an important function in the pathogenesis of HSP. Furthermore, Ding et al. [30] established that TNF- $\alpha$  (+308G/A) gene polymorphisms are associated with HSP in children. These findings indicate that inflammatory reactions contribute to the pathogenesis of HSPN. On the other hand, some reports have suggested that a decline in erythropoietin (EPO) contributes to the risk of renal injury [31,32]. EPO hyporesponsiveness could reduce the production of RBCs by promoting bone-marrow production and maturation and erythrocyte survival, hence elevating RDW [33,34]. Gurses et al. [35] have suggested that reduced erythrocyte deformability increases the risk of renal involvement. Patel et al. [36] have reported that elevated RDW is significantly correlated with decreased erythrocyte deformability. These data suggest that the robust relationship between RDW and a state of inflammatory conditions, a decline in EPO or erythrocyte deformability may explain why the RDW levels increased in the HSP and HSPN patients in this study.

Despite its convincing findings, the present study has some limitations. First, the sample size was modest. Second, other inflammatory indicators, such as C-reactive protein, IL-17 and IL-6, were not tested. Future

studies are required to classify patients with HSPN and define specific RDW values that could indicate specific risks for HSPN patients.

This work represents an advance in biomedical science because it shows that RDW levels are higher in HSP but more so in the HPSN, suggesting that RDW, and especially, the combination of RDW and ESR, is an inexpensive, convenient and promising test, and may have some potential values when assessing the risk of HSPN.

## Summary table

### What is known about this subject

- RDW is increased in a variety of inflammatory diseases.
- The relationship between RDW and HSPN has not yet been studied.
- Whether RDW have any potential value in assessing the risk of HSPN is unknown.

### What this study adds

- RDW and ESR values were increased in HSPN patients.
- The combination of RDW and ESR had higher sensitivity and specificity than RDW in HSPN patients.
- The combination of RDW and ESR as a biomarker may contribute some value to assess the risk of HSPN.

## Disclosure statement

No potential conflict of interest was reported by the authors.

## Funding

No funds to support this study.

## ORCID

X Zhu  <http://orcid.org/0000-0002-3501-7975>

## References

- [1] Calvino MC, Llorca J, Garcia-Porra C, et al. Henoch-Schonlein purpura in children from northwestern Spain: a 20-year epidemiologic and clinical study. *Medicine*. 2001;80:279–290.
- [2] Bluman J, Goldman RD. Henoch-Schonlein purpura in children: limited benefit of corticosteroids. *Can Fam Physician*. 2014;60:1007–1010.
- [3] Xu H, Pan Y, Li W, et al. Association between IL17A and IL17F polymorphisms and risk of Henoch-Schonlein purpura in Chinese children. *Rheumatol Int*. 2016;36:829–835.
- [4] Novak J, Moldoveanu Z, Renfrow MB, et al. IgA nephropathy and Henoch-Schoenlein purpura nephritis: aberrant glycosylation of IgA1, formation of IgA1-containing immune complexes, and activation of mesangial cells. *Contrib Nephrol*. 2007;157:134–138.
- [5] Davin JC. Henoch-Schonlein purpura nephritis: pathophysiology, treatment, and future strategy. *Clin J Am Soc Nephrol*. 2011;6:679–689.
- [6] Pohl M. Henoch-Schonlein purpura nephritis. *Pediatr Nephrol*. 2015;30:245–252.
- [7] Zhang Z, Zhao S, Zhang L et al. A higher frequency of CD4(+)CXCR5(+) T follicular helper cells in patients with newly diagnosed Henoch-Schonlein purpura nephritis. *Int Immunopharmacol*. 2016;32:8–15.
- [8] Chao TK, Rifai A, Ka SM, et al. The endogenous immune response modulates the course of IgA-immune complex mediated nephropathy. *Kidney Int*. 2006;70:283–297.
- [9] Rodriguez-Carrio J, Alperi-Lopez M, Lopez P, et al. Red cell distribution width is associated with cardiovascular risk and disease parameters in rheumatoid arthritis. *Rheumatology (Oxford)*. 2015;54:641–646.
- [10] Miyamoto K, Inai K, Takeuchi D, et al. Relationships among red cell distribution width, anemia, and interleukin-6 in adult congenital heart disease. *Circ J*. 2015;79:1100–1106.
- [11] Nada AM. Red cell distribution width in type 2 diabetic patients. *Diabetes Metab Syndr Obes*. 2015;8:525–533.
- [12] Chen L, Li Z, Li Y, et al. Red cell distribution width and inappropriateness of left ventricular mass in patients with untreated essential hypertension. *PLoS One*. 2015;10:e0120300.
- [13] Ay S, Eryilmaz MA, Aksoy N, et al. Is early detection of colon cancer possible with red blood cell distribution width? *Asian Pacific J Cancer Prevent*. 2015;16:753–756.
- [14] Kisaoglu A, Bayramoglu A, Ozogul B, et al. Sensitivity and specificity of red cell distribution width in diagnosing acute mesenteric ischemia in patients with abdominal pain. *World J Surg*. 2014;38:2770–2776.
- [15] Peng YF, Zhang Q, Cao L, et al. Red blood cell distribution width: a potential maker estimating disease activity of ankylosing spondylitis. *Int J Clin Exp Med*. 2014;7:5289–5295.
- [16] Song CS, Park DI, Yoon MY, et al. Association between red cell distribution width and disease activity in patients with inflammatory bowel disease. *Dig Dis Sci*. 2012;57:1033–1038.
- [17] Zhao Z, Liu T, Li J, et al. Elevated red cell distribution width level is associated with oxidative stress and inflammation in a canine model of rapid atrial pacing. *Int J Cardiol*. 2014;174:174–176.
- [18] Solak Y, Yilmaz A, Saglam S, et al. Red cell distribution width is independently related to endothelial dysfunction in patients with chronic kidney disease. *Am J Med Sci*. 2014;347:118–124.
- [19] Mills JA, Michel BA, Bloch DA, et al. The American College of Rheumatology 1990 criteria for the classification of Henoch-Schonlein purpura. *Arthritis Rheum*. 1990;33:1114–1121.
- [20] van Breda F, Emans ME, van der Putten K, et al. Relation between Red cell distribution width and fibroblast growth factor 23 cleaving in patients with chronic kidney disease and heart failure. *PLoS One*. 2015;10:e0128994.
- [21] Jo YH, Kim K, Lee JH, et al. Red cell distribution width is a prognostic factor in severe sepsis and septic shock. *Am J Emerg Med*. 2013;31:545–548.
- [22] Peng YF, Cao WY, Zhang Q, et al. Assessment of the relationship between red cell distribution width and multiple sclerosis. *Medicine (Baltimore)*. 2015;94:e1182.
- [23] Ozturk ZA, Unal A, Yigiter R, et al. Is increased red cell distribution width (RDW) indicating the inflammation in Alzheimer's disease (AD)? *Arch Gerontol Geriatr*. 2013;56:50–54.
- [24] Forhecz Z, Gombos T, Borgulya G, et al. Red cell distribution width in heart failure: prediction of clinical events and relationship with markers of ineffective erythropoiesis, inflammation, renal function, and nutritional state. *Am Heart J*. 2009;158:659–666.
- [25] Moura IC, Benhamou M, Launay P, et al. The glomerular response to IgA deposition in IgA nephropathy. *Semin Nephrol*. 2008;28:88–95.

- [26] Ye Q, Shang SQ, Liu AM, et al. 24 h urinary protein levels and urine protein/creatinine ratios could probably forecast the pathological classification of HSPN. *PLoS One*. 2015;10:e0127767.
- [27] Wang W, Liu J, Yang YH, et al. Red cell distribution width is increased in chronic thromboembolic pulmonary hypertension. *Clin Respir J*. 2016;10:54–60.
- [28] Afsar B, Saglam M, Yuceturk C, et al. The relationship between red cell distribution width with erythropoietin resistance in iron replete hemodialysis patients. *Eur J Intern Med*. 2013;24:e25–e29.
- [29] Chang H, Cao Y, Lin YI, et al. Association between toll-like receptor 6 expression and auxiliary T cells in the peripheral blood of pediatric patients with allergic purpura. *Exp Ther Med*. 2015;10:1536–1540.
- [30] Ding GX, Wang CH, Che RC, et al. Heat shock protein 70-2 and tumor necrosis factor-alpha gene polymorphisms in Chinese children with Henoch–Schonlein purpura. *World J Pediatr*. 2016;12:49–54.
- [31] Nand N, Savio D. Evaluation of protective effect of erythropoietin in patients at risk to develop acute kidney injury. *J Assoc Physicians India*. 2016;64:58.
- [32] Zhang Y, Chen W, Wu Y, et al. Renoprotection and mechanisms of erythropoietin and its derivatives Helix B surface peptide in kidney injuries. *Curr Protein Pept Sci*. 2017;18:1–8.
- [33] Kario K, Matsuo T, Nakao K, et al. The correlation between red cell distribution width and serum erythropoietin titres. *Clin Lab Haematol*. 1991;13:222–223.
- [34] Salvagno GL, Sanchis-Gomar F, Picanza A, et al. Red blood cell distribution width: a simple parameter with multiple clinical applications. *Crit Rev Clin Lab Sci*. 2015;52:86–105.
- [35] Gurses DM, Parlaz NM, Bor-Kucukatay MM-P, et al. Evaluation of oxidative stress and erythrocyte properties in children with henoch-shoenlein purpura. *Iran J Pediatr*. 2014;24:166–172.
- [36] Patel KV, Mohanty JG, Kanapuru B, et al. Association of the red cell distribution width with red blood cell deformability. *Adv Exp Med Biol*. 2013;765:211–216.