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Role of Hyperuricemiaand Red Cell Distributionwidth inAssessment of RenalMicrovascularDamage in Patients with Systemic Sclerosis

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Abstract

Objectives:*The aim of our study was noninvasive assessment of renal microvascular damage in patients with systemic sclerosis by studying correlation between serum uric acid / red cell distribution width and intrarenal arterial stiffness evaluated by Doppler ultrasound and relation between red cell distribution width and renal function.*

Method:*This is a cross sectional study that was carried out in Rheumatology and Rehabilitation department, Faculty of Medicine, Zagazig University Hospitals on 44 Systemic Sclerosis patients. These patients were subjected to detailed history, clinical and rheumatological examinations, lab investigations; complete blood picture, erythrocyte sedimentation rate, C reactive protein, antinuclear antibody, kidney functions, liver functions and serum uric acid and Doppler ultrasound of intrarenal arteries with evaluation of resistive index, pulsatile index and systolic / diastolic ratio.*

Result:*The serum uric acid showed significant positive correlation with Doppler indices, serum creatinine, creatinine clearance and blood urea nitrogen and negative correlation with chronic kidney disease epidemiology collaboration (CKD-EPI). Red cell distribution width showed significant positive correlation with Doppler indices, serum creatinine, creatinin clearance and blood urea nitrogen and negative correlation with CKD-EPI and mean corpuscular volume (MCV).*

Conclusion:*Uric acid and red cell distribution width are valuable markers in detection of renal microvascular damage in patients with Systemic Sclerosis. Also, kidney affection was more obvious in diffuse systemic sclerosis than limited.*

Keywords: *uric acid, Systemic sclerosis, renal Doppler ultrasound, red cell distribution width.*

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I. Introduction

Systemic sclerosis (SSc) leads to morbidity and mortality through a combination of inflammation, fibrosis, and vascular damage leading to internal organ complications affecting the heart, lung, bowel, and kidneys. Most often, SSc causes a range of renal manifestations, which occur in both subsets of the disease: limited cutaneous (lcSSc) and diffuse cutaneous (dcSSc) subsets [(1)].Most SSc-related deaths are attributable to heart, kidney and lung involvement. In the kidneys, renal ischemia and hypertension can result from the development of intimal hyperplasia of interlobular and arcuate arteries [(2)].

Scleroderma renal crisis is a life-threatening complication of scleroderma and presents with the abrupt onset of severe hypertension accompanied by rapidly progressive renal failure, hypertensive encephalopathy, congestive heart failure, and/or microangiopathic hemolytic anemia [(3)].

Microvascular changes, characterized by structural and functional abnormalitiesof the microcirculation, play a central role in the pathogenesis of systemic sclerosis [(4)]. Vascular abnormalities and dysfunction usually precede organ involvement by several years [(5)].

The most important renal complication in SSc is scleroderma renal crisis, but latent renal involvement is present such as isolated reduced glomerular filtration rate (GFR), microalbuminuria and increased intra renal arterial stiffness. A reduction of glomerular filtration rate (GFR) can be present in SSc patients with normal serum creatinine (sCr) [(6)]. In the course of SSc several manifestations of renal involvement are due to intrarenal vascular damage. In SSc patients without renal involvement, intrarenal arterial stiffness is increased and it correlates with digital microvascular damage [(7)], reduction of glomerular filtration rate (GFR) and autonomic dysfunction [(8)].

Uric acid (UA) is the final oxidation product of purine metabolism. Serum UA levels have been shown to be elevated in conditions of impaired oxidative metabolism [(9)]. Elevated serum uric acidhas been shown to be associated with impaired endothelium-mediated relaxation and vascular stiffness [(10)].

Red cell distribution width (RDW) is associated with endothelial dysfunction and inflammation. RDW increased with worsening kidney function[(11)]. There was an inverse, step wise association between RDW and kidney function [(12)]. Another cross sectional study revealed that elevated RDW was independently associated with a higher risk of microalbuminuria, which is a marker of renal injury [(13)].

The aim of our study was noninvasive assessment of renal microvascular damage in patients with systemic sclerosis by studying correlation between serum uric acid / red cell distribution width and intrarenal arterial stiffness evaluated by Doppler ultrasound and relation between red cell distribution width and renal function.

II. PATIENTS AND METHODS

Written informed consent was obtained from all participants, the study was approved by the research ethical committee (Institutional Review Board) of Faculty of Medicine, ZagazigUniversity. The study was done

according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Study design and subjects:

This is an observational cross sectional study that was carried out in Rheumatology and Rehabilitation department, Faculty of Medicine, ZagazigUniversity Hospitals. Forty four systemic sclerosis patients who fulfilled the classification criteria of American college of rheumatology/ European league against rheumatism (ACR/EULAR2013) of SSc were included in this study.

Clinical and Laboratory parameters of disease:

For all patients detailed history taking and clinical and rheumatological examinationswere performed. A blood sample was drawn from each patient to measure the complete blood count (CBC), erythrocyte sedimentation rate (ESR)(normal range for first hour: 2-7 mm and for second hour: 7-14 mm), C-reactive protein (CRP) (normal range: 1-5 mg/L), aspartate transaminase (AST) (normal range: up to 32 U/L), serum glutamic pyruvic transaminase (SGPT) (normal range: up to 33 U/L), serum albumin (normal range: 3.97-4.94), total bilirubin (normal range: up to 1.2 mg/dl), blood urea nitrogen (BUN) (normal range: 6-20 mg/dl), ,serum creatinine (normal range: 0.5-0.9 mg/dl), serum uric acid (normal range: 3.40–7.20 mg/dl), 24 hour protein in urine(normal range: up to 150mg/24hour), calculate the creatinineclearance (normal range: 78-110 ml/min) and complete urine analysis. GFR was calculated using the CKD-EPI equation, already validated inSSc patients **Giganteet al. [(14)],** expressed as a single equation: GFR = 141 × min (sCr/k, 1)α× max (sCr/k, 1)-1.209 × 0.993Age ×1.018 (if female) × 1.159 (if black), where k is 0.7 for females and 0.9 for males,α is−0.329 for females and 0.411 for males, min indicates the minimum of sCr/k or 1 and max indicates the maximum of sCr/k or 1. Doppler ultrasound for intra renal arteries with evaluation of resistive index, pulsatile index, and systolic / diastolic ratio was performed by expert radiologist.

Statistical Methods:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0**. (**Armonk, NY: IBM Corp**)** Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and inter quartile range (IQR). Significance of the obtained results was judged at the 5% level, Student t test was performed. Qualitative variables were compared using chi-square (X2) test.

III. RESULTS

***Demographic data, family history and disease duration of the studied cases*:**

Table (I) showed that 91% of cases were females and 9% males. Mean age was (44.50 ± 11.17) years with range of (25.0 – 66.0) years, family history was negative in 97.7% and positive in 2.3%, mean disease duration was (7.97 ± 4.39) year with range of (2.0 – 17.0) years

Different lab parameters of studied cases:

Table (II) showed that mean ESR of the studied cases was 41.97 ±20.85, mean CRP was 6.90 ± 6.84 and mean RDW was 14.30± 0.67 mean SGOT of the studied cases was 23.25 ± 8.20, mean SGPT was 19.64 ± 8.96, mean serum albumin was 4.09 ± 0.37 and mean total bilirubin was 0.54 ± 0.15. Mean BUN of the studied cases was 14.37 ± 4.51, mean serum creatinine was 0.75 ± 0.14 and mean serum uric acid was 4.38 ± 0.81, mean creatinine clearance of the studied cases was 102.95 ± 9.79 and mean 24 hour urine protein was 98.63 ± 29.07. Mean GFR of the studied cases was 97.73 ± 23.16. Mean hematuria of the studied cases was 1.70 ± 2.65 and mean pyuria was 4.30 ± 7.92.

Table (III) showed that mean Resistive index was 0.64 ± 0.06, mean Pulsatile index was 1.26 ± 0.30 and mean Systolic/diastolic ratio was 3.02 ± 0.83.

Table (IV) showed that there was high significant difference between low normal and high normal level of serum uric acid as regard resistive index, pulsatile index, systolic/diastolic ratio, serum creatinine, creatinine clearance and GFR, also there is significant difference between low normal and high normal uric acid level as regard BUN.Figure 1 showed the correlation between serum uric acid and pulsatile index.

Table (V) showed that there was high significant positive correlation between serum uric acid and resistive index, pulsatile index, Systolic/diastolic ratio and serum creatinine, creatinine clearance, BUN, also and there is high significant negative correlation between uric acid and GFR and between uric acid and MCV. There is high positive significant correlation between RDW and resistive index, pulsatile index, systolic/diastolic ratio, serum creatinine, creatinine clearance**,** BUN, There is high negative significant correlation between RDW and GFR and between RDW and MCV.Figure 2 showed the correlation between serum RDW and pulsatile index.

Table (VI) showed that there was high significant difference with higher levels in diffuse type than limited as regard resistive index, pulsatile index Systolic/diastolic ratio, sreumcreatinine, creatinine clearance and GFR and significant difference between limited and diffuse types as regard BUN.

Table (I): Demographic data, family history and disease duration of the studied cases: (n=44)

Demographic data	No.	%
Sex		
Female	40	91.0
Male	4	9.0
Age (years)		
Min. – Max.	25.0 – 66.0	

Mean ± SD.	44.50 ±11.17	
Family history	**No.**	**%**
Negative	43	97.7
Positive	1	2.3
Disease duration(years)	**No.**	**%**
<7	19	43.2
≥7	25	56.8
Min. – Max.	2.0 – 17.0	
Mean ± SD.	7.97 ±4.39	
Median (IQR)	7.0 (5.0–12.0)	

Table (II):Different lab parameters of the studied cases: (n=44)

	Min. – Max.	**Mean ± SD.**
ESR(mm/1st hour)	6.0 – 90.0	41.97 ±20.85
CRP(mg/l)	1.32 – 28.30	6.90 ±6.84
RDW (%)	13.30 – 15.50	14.30 ± 0.67
SGOT(U/L)	12.0 – 48.90	23.25 ±8.20
SGPT(U/L)	7.40 – 40.60	19.64 ±8.96
Serum albumin(g/dl)	3.32 – 5.05	4.09 ±0.37
Total bilirubin(mg/dl)	0.28 – 0.88	0.54 ±0.15
BUN(mg/dl)	7.0 – 22.0	14.37 ± 4.51

Serum creatinine(mg/dl)	0.52 – 1.03	0.75 ± 0.14
Serum uric acid(mg/dl)	3.19 – 6.0	4.38 ±0.81
Creatinine clearance(ml/min)	85.0 – 120.0	102.95 ± 9.79
24 hour Urine Protein Test(mg/24hour)	42.0 – 150.0	98.63 ± 29.07
GFR(mg/dl)	59.20 – 139.20	97.73 ±23.16
Hematuria(/HPF)	0.0 – 10.0	1.70 ±2.65
Pyuria(/HPF)	0.0 – 30.0	4.30 ±7.92

Table (III):Doppler findings of the studied cases: (n=44)

	Min. – Max.	**Mean ± SD.**	**Median (IQR)**
Resistive index	0.55 – 0.73	0.64 ±0.06	0.64(0.58–0.70)
Pulsatile index	0.86 – 1.71	1.26 ±0.30	1.21(1.01–1.63)
Systolic/diastolic ratio	1.59 – 4.45	3.02 ±0.83	2.83 (2.34–3.78)

Table (IV):Relation between serum uric acid and different parameters: (n= 44)

	Serum uric acid		**T**	**P**
	Low normal (n =22)	**High normal (n =22)**		
Serum creatinine				
Min. – Max.	0.52 – 0.80	0.68 – 1.03	7.203*	**<0.001***
Mean ± SD.	0.64 ± 0.09	0.85 ± 0.11		**(HS)**

Median	0.59	0.81		
GFR				
Min. – Max.	84.80 – 127.30	59.00 – 114.90	4.121*	**<0.001* (HS)**
Mean ± SD.	108.84 ± 12.77	87.01 ± 16.06		
Median	111.10	86.20		
Creatinine clearance				
Min. – Max	85.0 -115.0	88.0 - 120.0	4.36*	**<0.001* (HS)**
Mean ± SD	95.93±7.81	108.30±7.58		
Median	97.0	108.8		
BUN				
Min. – Max	7.0 - 22.0	9.5 - 22.0	3.0*	**0.006 (S)**
Mean ± SD	11.84±4.31	16.38±3.81		
Median	10.0	16.5		
Resistive index				
Min. – Max.	0.55 – 0.64	0.64 – 0.73	7.820*	**<0.001* (HS)**
Mean ± SD.	0.59 ± 0.03	0.69 ± 0.04		
Median	0.58	0.70		
Pulsatile index				
Min. – Max.	0.86 – 1.66	0.89 – 1.71	5.143*	**<0.001* (HS)**
Mean ± SD.	1.05 ± 0.20	1.47 ± 0.25		
Median	0.99	1.63		
Systolic/diastolic ratio				
Min. – Max.	1.59 – 3.70	2.03 – 4.45	5.174*	

Mean ± SD.	2.47 ± 0.49	3.61 ± 0.70		**<0.001*** **(HS)**
Median	2.58	3.85		

Table (V): Correlation between RDW and serum uric acid with different parameters: (n= 44)

	RDW		**Serum uric acid**	
	R	**P**	**R**	**P**
Serum creatinine	0.843	<0.001*	0.852	<0.001*
GFR	-0.748	<0.001*	-0.754	<0.001*
Creatinine clearance	0.652	<0.001*	0.613	<0.001*
BUN	0.573	<0.001*	0.553	<0.001*
Resistive index	0.882	<0.001*	0.879	<0.001*
Systolic/diastolic ratio	0.861	<0.001*	0.871	<0.001*
Pulsatile index	0.812	<0.001*	0.815	<0.001*
MCV	-0.987	<0.001*	-0.916	<0.001*

Table (VI): Comparison between limited and diffuse type as regard different parameters: (n= 44)

	Limited (n =30)	**Diffuse (n =14)**	**T**	**P**
S.CREAT Min. – Max.	0.52 – 0.78	0.68 – 1.03	4.81*	**<0.001***

Mean ± SD. Median	0.63 ± 0.12 0.57	0.86 ± 0.13 0.80		**(HS)**
GFR Min. – Max. Mean ± SD. Median	 59.00 – 127.30 108.91 ± 11.71 112.0	 0.72 – 113.10 87.0 ± 14.06 85.90	 4.52*	 **<0.001*** **(HS)**
Creatinine clearance Min. – Max Mean ± SD Median	 88.0 -115.0 95.71± 7.64 96.0	 87.0 - 120.0 108.54± 7.19 107.6	 4.41*	 **<0.001*** **(HS)**
BUN Min. – Max Mean ± SD Median	 7.0 - 21.0 11.63± 4.29 11.0	 9.5 - 22.0 16.41± 3.64 17.0	 3.01*	 **0.005** **(S)**
Resistive index Min. – Max. Mean ± SD. Median	 0.55 – 0.64 0.55 ± 0.04 0.56	 0.66 – 0.73 0.7 ± 0.03 0.71	 10.44*	 **<0.001*** **(HS)**
Pulsatile index Min. – Max. Mean ± SD. Median	 0.86 – 1.64 1.04 ± 0.21 0.97	 0.87 – 1.71 1.5 ± 0.24 1.62	 5.39*	 **<0.001*** **(HS)**
Systolic/diastolic ratio				

Min. – Max.	1.59 – 3.68	2.10 – 4.45		
Mean ± SD.	2.45 ± 0.5	3.64 ± 0.67	5.48*	**<0.001* (HS)**
Median	2.52	3.87		

Legends of figures:

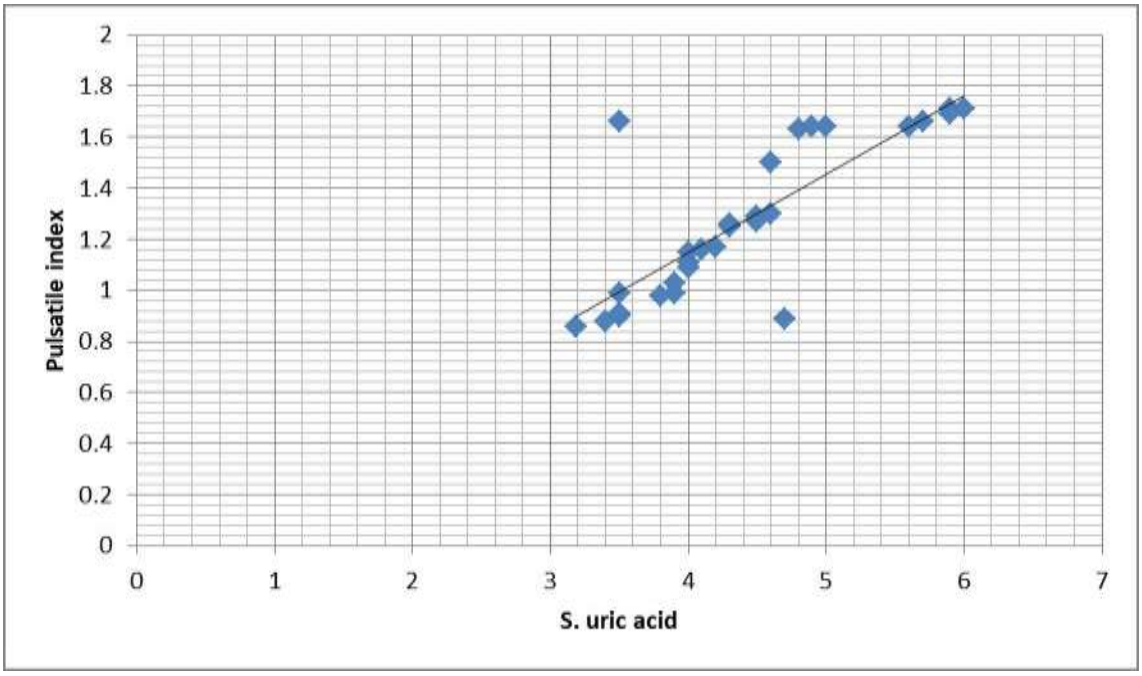

Fig (1): Correlation between serum uric acid and pulsatile index.

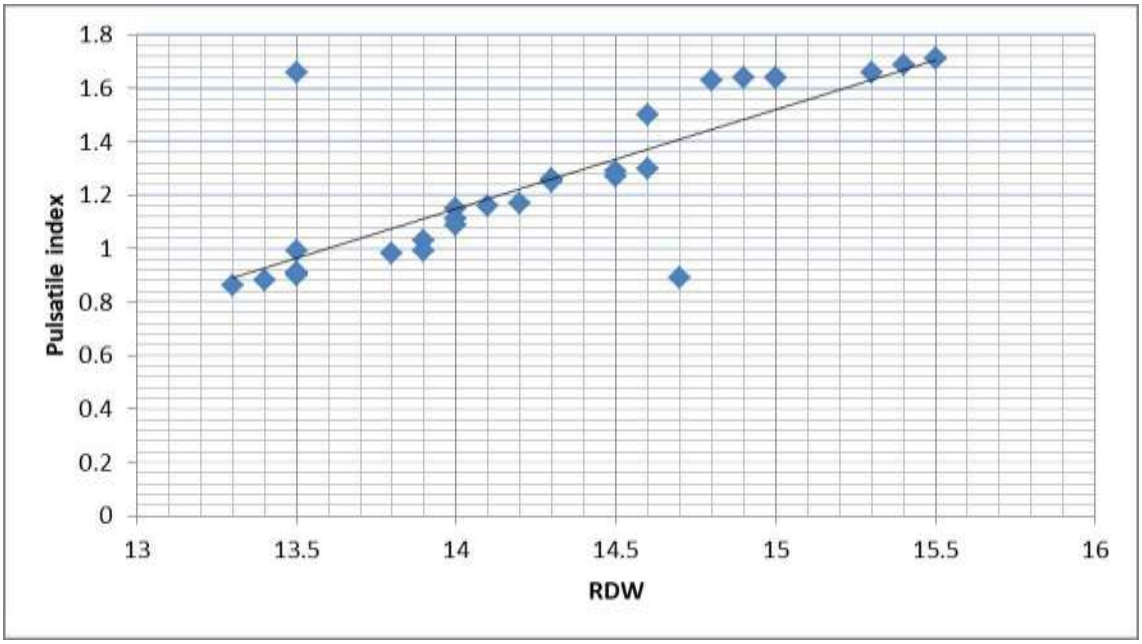

Fig (2): Correlation between RDW acid and pulsatile index.

IV. DISCUSSION

Systemic sclerosis (SSc) is a chronic, multisystem disease with distinctive pathogenetic features, comprising vascular derangement, immune system activation, tissue fibrosis and heterogeneous clinical profile [(15)].

Among kidney involvement in systemic sclerosis (SSc), scleroderma renal crisis (SRC) represents the principal manifestation of kidney damage [(16)]. Reflecting the vasculopathy that characterizes SSc, even in the absence of a renal crisis, chronic kidney diseases (CKDs) other than renal crisis may occur [(17)].

However, it has emerged that high serum uric acid level is a risk factor of cardiovascular disease [(18)]**.** The relation between uric acid and cardiovascular disease (CVD) is evident not only in the presence of overt hyperuricemia but also with serum uric acid levels considered in the normal to high range (5.2 to 5.5 mg/dL)[(19)]**.**

Red blood cell distribution width (RDW) is one of the RBC indices, which quantifies variation in circulating red blood cell size, pointing to the degree of anisocytosis in the complete blood count. It is an automated measure that is performed routinely as part of a complete blood cell count. In addition to iron deficiency anemia, thalassemia, and myelodysplastic syndrome, elevated RDW can be indicative of inflammation and nutritional deficiencies, pulmonary impairment [(20)]and renal failure [(21)]**.** Some previous studies have shown its usefulness as an adverse prognostic marker in patients with cardiovascular disease [(22)]**.**

In this study we verified that mean ESR of the studied cases was 41.97 ± 20.85, mean CRP was 6.90 ± 6while mean RDW was 14.30 ± 0.67. This was in agreement with **Farkas et al.,** [(23)] who reported the median RDW value of patients with SSc was 14.2%.

In our study we found that mean value of resistive index was 0.64 ± 0.06, pulsatile index was 1.26 ± 0.30 and systolic / diastolic ratio was 3.02 ± 0.83. There was high significant relation between uric acid level and Doppler indices of intrarenal arterial stiffness, we found that there is significant positive correlation between serum uric acid and resistive index (r= 0.879 / p < 0.001), pulsatile index (r= 0.815 / p < 0.001), systolic / diastolic ratio (r= 0.871 / p < 0.001). Moreover we found mean value of Doppler indices of intra renal arterial stiffness was high significantly different (p < 0.001) in SSc patients with low normal serum UA and high normal serum UA

Similar to the result of Giganteet al. [24]whoconducted their study in Rome, Italy over Forty-five SSc patients to evaluate the correlation between serum UA and intra renal arterial stiffness evaluated by Doppler ultrasound in SSc patients with normal renal function, the mean age of the studied population was 45 ± 13.8 years, 36 female and 9 male and their results reported that the mean value of resistive index was 0.64 ± 0.06, mean value of pulsatile index was 1.26 ± 0.29, systolic / diastolic rato was 3.02 ± 0.88 and reported that Doppler indices of intra renal stiffness are significantly different (p < 0.05) in SSc patients with low-normal serum UA or high-normal serum UA. Serum UA showed a significant positive correlation with intrarenal arterial stiffness.

Gigante et al., [25] reported that Doppler indices of intrarenal arterial stiffness increase and correlate with progression increase of capillaroscopic damage so he add in 2016 pulmonary function tests, nailfoldvideocapillerscopy and echocardiography to evaluate microvascular damage and found that serum uric acid concentration is higher in patients with high microvascular damage than in patients with low microvascular damage.

Rosato et al., [26]conducted study over 30 systemic sclerosis patients and 30 healthy controls to evaluate intrarenal arterial stiffness by Doppler ultrasound and examine the correlation between renal Doppler indices, glomerular filtration rate and digital microvascular damage in systemic sclerosis and reported that there was positive correlation between pulsatile index and creatinine clearance (p= 0.03) and demonstrated that intrarenal arterial stiffness is increased significantly in SSc patients than healthy control and correlate with capillaroscopic damage.

In our study we found that there was significant positive correlation between serum uric acid and serum creatinine (r= 0.852 / p < 0.001). There was significant negative correlation between serum uric acid and GFR (r = -0.754 / p < 0.001).This was in concordance with **Gigante et al.,** [24] who reported that there was significant positive correlation between serum uric acid and serum creatinine (r = 0.33, p < 0.0001) and negative correlation with CKD-EPI (r = − 0.35, p < 0.01).

RecentlyElera-Fitzcarrald et al., [27]studied serum uric acid association with damage in patients with systemic lupus erythromatosus concluded that in patients with SLE, serum uric acid has been recognized as a potential marker of endothelial dysfunction and renal disease, as an association has been found between active lupus nephritis and hyperuricemia.

In this study we reported that mean BUN of the studied cases was 15.98 ± 7.21, mean serum creatinine was 0.75 ± 0.21, mean serum uric acid was 4.38 ± 0.81, mean creatinine clearance was 102.95 ± 9.79 and mean GFR of the studied cases was 97.73 ± 23.16.This was in concordance with **Gigante et al.,** [24]who reported that the mean

serum creatinine was 0.75 ± 0.16 and mean serum uric acid was 4.24 ± 1.23, mean proteinuria was 0.13 ± 0.04, mean GFR was 101± 18.9.

In the present study we found that there was high positive significant correlation between RDW and resistive index, pulsatile index, Systolic/diastolic ratio,creatinine clearance**,** BUN, There was high negative significant correlation between RDW and GFR and between RDW and MCV.

Farkas et al., [(23)] who conducted a study in Budapest, Hungary over 62 with dcSSc and 106 with lcSSc reported that RDW value of patients with SSc was higher compared with group of primary Raynaud phenomenon and healthy volunteers and reported that RDW in SSc may represent an integrative measure of multiple pathological processes including extensive vasculopathy, fibrosis, or ongoing inflammation. An increase in RDW may indicate an impairment of cardiorespiratory function

Zhao et al., [(20)] studied red blood distribution width as a related factor of pulmonary arterial hypertention in patients with systemic sclerosis by diagnosis of PAH by echocardiography and was confirmed by right heart catheterization findings and concluded that high RDW was an independent predictor of PAH in patients with SSc so RDW may be a related factor for identifying the pulmonary arterial hypertension in SSc patients.

Solak et al., [(11)] who conducted a study in Turkey to assess the association of RDW with endothelial function (measured with flow-mediated dilatation and carotid intima media thickness (CIMT) reported that RDW levels were inversely and significantly correlated with eGFR, also they reported association of elevated RDW with low hemoglobin, moderately depressed mean corpuscular volume.

Also this was in agreement with **Ujszaszi et al., [(28)]** who conducted their study in to Toronto, Canada to examine the association between RDW and estimated glomerular filtration rate (eGFR) in a cohort of 723 prevalent kidney transplanted recipients who were not receiving erythropoietin-stimulating agents. Associations were examined in regression models adjusted for age, sex, comorbidity, blood haemoglobin, iron indices, markers of nutritional status and inflammation, markers of bone and mineral metabolism and the use of immune suppressants. Lower eGFR was significantly associated with higher RDW ($r = 0.382$, $P < 0001$). However, this was against with what stated by **Rosato et al., [(7)]** who illustrated that In SSc patients, renal function is normal despite the presence of increased intrarenal arterial stiffness. Renal function is preserved also in SSc patients with long disease duration.

Lippi et al., [(12)] have shown that there is an inverse graded association between RDW and kidney function tests in a large cohort of unselected adult population.

Yayla et al., [(29)]study association of simple hematological parameters with disease manifestations, activity, and severity in patients with systemic sclerosis and reported that RDW was higher in SSc patients with PAH and concluded that available and inexpensive hematological tests may be associated with vascular and cutaneous manifestations as well as disease activity and severity in SSc.

In this study that there was high significant difference between limited and diffuse types as regard Doppler parameters, serum creatinine, creatinine clearance and GFR. Also there was significant difference between limited and diffuse types as regard BUN. With higher levels in diffuse type as regard resistive index, pulsatile index

Systolic/diastolic ratio, creatinine clearance, BUN and serum creatinine and with lower level in diffuse type as regard GFR due to wide systemic affection in diffuse type more than limited type.

This was in the same direction with what stated by **Rosato et al., [7]** who conducted a study in Italy over 121 SSc patients to study prognostic factors of renal involvement in systemic sclerosis and in his observational study with Doppler ultrasound found that Doppler indices of intrarenal arterial stiffness increased with progression of capillarsocopic damage and with presence of digital ulcers and concluded that In SSc patients, renal function was normal for 4.1 years despite the presence of increased intrarenal arterial stiffness. SRC was observed in 4.9% of SSc patients. In SSc patients, a periodic follow-up based on clinical and laboratory evaluation, color Doppler ultrasound and, in some cases, renal biopsy is required to evaluate renal involvement.

From our study, there was positive correlation between serum uric acid / RDW and Doppler indices of intrarenal arteries so, follow up of the patients with SSc by serum uric acid and RDW is unexpensive and good predictive and preventive for complicated renal diseases in systemic sclerosis.

The main limitation of this study was represented by a limited number of patients, the absence of validation cohort.

V. conclusion

In conclusion, uric acid and Red Cell Distribution width are valuable markers in detection of renal microvascular damage in Patients with Systemic Sclerosis. Also, kidney affection was more obvious in diffuse systemic sclerosis than limited.

Conflict of interest: None to declare.

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