Research Article

Is Red Blood Cell Distribution Width (RDW) A Novel Renal Biomarker For Diabetic Complications ?

[1]T. Rajini Samuel*, [2]Manjula Devi, [3]Shanthi, [4]Balaji Rajagopalan

[1]Assistant Professor of Biochemistry, Shri Sathya Sai Medical College and Research Institute, Ammapettai, kancheepuram district, India.
[2]Professor & HOD of Biochemistry, Shree Balaji Medical College and Hospital, Chromepet, Chennai, Tamil Nadu, India.
[3]Professor of Biochemistry, Shree Balaji Medical College and Hospital, Chromepet, Chennai, Tamil Nadu, India.
[4]Professor & HOD of Biochemistry, Shri Sathya Sai Medical College and Research Institute, Ammapettai, kancheepuram district, India.
***Corresponding author's E-mail:** Samuel.biochemistry@gmail.com

Accepted on: 06-03-2016; **Finalized on:** 31-03-2016.

ABSTRACT

Diabetic nephropathy manifests as slowly progressive albuminuria with worsening hypertension and renal insufficiency. Diagnosis is based on history, physical examination, urine analysis and urine albumin/creatinine ratio. Sustained microalbuminuria is the earliest warning sign of asymptomatic diabetic nephropathy patients and is a potent risk factor for the development of progressive renal disease. Urine albumin creatinine ratio (ACR) is an accepted and useful screening test for microalbuminuria. Red blood cell distribution width (RDW) is a measurement of anisocytosis obtained in standard automated complete blood counts and is found to be an important clinical marker for diabetes complications independent of traditional risk factors and disease duration. The aim of the current study is to determine the relation between the albumin creatinine ratio level and the red blood cell distribution width. We have taken 49 diabetic nephropathy patients with 49 diabetic controls. We concluded our study by saying that RDW was found to be significantly associated with diabetic nephropathy patients and hence it may be a useful renal biomarker for diabetic complications.

Keywords: diabetic nephropathy, albumin creatinine ratio, red blood cell distribution width.

INTRODUCTION

Diabetic nephropathy (nephropatiadiabetica), also known as Kimmelstiel–Wilson syndrome, or nodular diabetic glomerulosclerosis and intercapillary glomerulonephritis, is a progressive kidney disease caused by angiopathy of capillaries in the kidney glomeruli.

Diabetic Nephropathy begins as glomerular hyperfiltration (increased GFR). GFR normalizes with early renal injury and mild hypertension, which worsens over time. Microalbuminuria, urinary excretion of albumin in a range of 30 to 300 mg albumin/day, then occurs.[1,2] Urinary albumin in these concentrations is called microalbuminuria because detection of proteinuria by dipstick on routine urinalysis usually requires > 300 mg albumin/day.[1-5]

Microalbuminuria progresses to macroalbuminuria (proteinuria > 300 mg/day at a variable course, usually over years.[6-9,14] Nephrotic syndrome (proteinuria ≥ 3 g/day) precedes end-stage renal disease, on average, by about 3 to 5 yr, but this timing is also highly variable.

Diagnosis is done by screening of all patients with diabetes with random urine albumin/creatinine ratio.[6,7,14] Red blood cell distribution width (RDW) is a measure of variability in size of circulating erythrocytes obtained in standard automated complete blood counts. RDW may represent an important clinical marker for diabetes complications independent of traditional risk factors and disease duration.[10-13]

MATERIALS AND METHODS

The study was conducted in a sample of 49 diabetic nephropathy patients and 49 diabetic control patients belonging to the age group between 40 and 80 attending diabetic and nephrology department. Exclusion criteria includes smokers, hypertension, alcoholics and chronic illness patients.

The blood samples were collected by venepuncture under aseptic precautions. Random urine sample was collected from the patients for the estimation of urine albumin creatinine ratio.[2-5]

Red blood cell distribution width (RDW)

RDW reflects the size distribution of the erythrocyte population. Most instruments (Coulter, Technicon, and Sysmex) calculate it as a coefficient of variation (CV) i.e., standard deviation of the distribution of RBC volumes divided by the MCV.[10-13] we used sysmex machine and RDW is a measurement of anisocytosis. Normal range: 11 % to 16 %.

ACR Estimation and Calculation

Both albumin and creatinine are measured in a random urine sample and an albumin/creatinine ratio **(ACR)** is calculated.

Calculation and expression of data

In our laboratory urinary albumin and creatinine concentrations are measured as (mg/dl). ACR is reported

© Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

in (mg/g). Albumin concentration in spot urine sample is reported as UAC (mg/L).

Albumin creatinine ratio (ACR)

It is the ratio of urinary albumin to urinary creatinine. It is usually expressed as milligram of albumin excreted per gram of urinary creatinine.[6,7]

ACR (mg/g) can be calculated by albumin (mg/dl) divided by creatinine (g/dl). Urinary albumin concentration (UAC): It is concentration of albumin present in one litre of urine or albumin excreted per litre of urine. It is expressed as (mg/L).

UAC (mg/L) = Albumin (mg/dl) x 10.

In our study urine albumin is expressed as (mg/L) and urine creatinine is expressed as (mg/dl). Here ACR is expressed as mg of albumin excreted per gram of creatinine.

Hence we divided the urine albumin mg/L by urine creatinine mg/dl and multiplied by 100.

(1 gram = 1000 mg; UAC (mg/L) = Albumin (mg/dl) x 10 ; 1000/10 =100 ; hence we multiplied by 100)

RESULTS AND DISCUSSION

Table 1: Data collection master chart (control)

S. No for Control	urine albumin mg/L / creatinine mg/dl	ratio mg of albumin / gram of creatinine	RDW-CV%
1	22/85.5	25.73	12.4
2	23/92.5	24.86	12.01
3	8.10/27.63	29.31	14.5
4	85.69/299.8	28.58	15.8
5	39/254	15.35	12.7
6	93.10/415	22.43	12
7	49.34/221.90	22.23	12.3
8	13/69.5	18.7	11.4
9	24/160	15	12.9
10	23.6/103.66	22.76	13
11	12.43/61.0	20.37	13.5
12	33.0/163.3	20.2	13.3
13	31.90/108	29.53	14.2
14	29.59/111.86	26.45	12.5
15	20/69.1	28.94	15.8
16	5/150	3.33	12.9
17	5/80	6.25	11.7
18	29/167	17.36	13
19	19.61/65.9	29.75	12.3
20	17.7/162.1	10.91	13.9
21	7/39.26	17.82	13.4
22	16.5/134.0	12.31	13
23	4.3/27.44	15.67	12.5
24	3.25/16.72	19.43	11.9
25	25.01/91.41	27.36	15.5
26	15.2/112	13.57	11.9

© Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

27	24.96/180.1	13.85	12.2
28	22/110.5	19.9	12.3
29	6/34.47	17.4	12.2
30	7.59/49.4	15.36	12.7
31	27.4/159.11	17.22	11.8
32	2.1/17.11	12.27	11.7
33	38.35/134.4	28.53	15
34	9.78/90.74	10.77	13.3
35	11.5/43.48	26.44	11.7
36	26.80/106.2	25.23	13.3
37	66.67/252.3	26.42	11.4
38	26.29/104.8	25.08	13.1
39	16.86/172.50	9.77	12.1
40	5.40/82.90	6.5	12.2
41	14.2/112.1	12.66	12.1
42	14.9/104.62	14.24	12.5
43	23.6/103.66	22.76	11.9
44	17.7/162.1	10.91	14.7
45	18.2/118	15.42	11.9
46	14/112	12.5	11.5
47	14.9/61.9	24.07	11
48	8.6/59.2	14.52	11.4
49	10/81.14	12.32	11.4

Table 2: Data collection master chart (cases)

S. No for Cases	urine albumin mg/L / creatinine mg/dl	ratio mg of albumin / gram of creatinine	RDW -CV %
1	81.46/71.7	113.61	22.8
2	41.59/39.5	105.29	22.4
3	79.22/144.0	55.01	19.9
4	80/228	35.09	17
5	78.39/116.2	67.46	20.1
6	33.18/66.7	49.74	19
7	38.0/77.19	49.22	19
8	41/19.6	209.18	23.7
9	31.07/91.86	33.82	17.5
10	84.38/231.9	36.38	18.2
11	11.6/21.35	54.33	19.7
12	37/15	246.66	24.5

© Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

13	11.5/20.84	55.18	19.5
14	23.8/24.9	95.58	21.2
15	48.03/29.0	165.62	23.1
16	11.6/27.1	42.8	18.4
17	37.62/30.0	125.4	23.7
18	32.1/60.8	52.79	19.4
19	417.8/226.6	184.37	24.5
20	38.25/84.01	45.53	18.6
21	32.99/75.30	43.81	18.6
22	71/60	118.33	22
23	69.48/126.7	54.83	19.3
24	55.37/46.0	120.36	23.3
25	17.7/5.5	321.81	26.7
26	58.9/61.7	95.46	21
27	29/10	290	26.1
28	51.07/106.8	47.81	19.1
29	131.6/154.7	85.06	20.9
30	93.35/50.20	185.95	24.8
31	52.6/130.75	40.22	18.2
32	42/102	41.17	18.9
33	34.2/32.33	105.78	21.3
34	44.87/31.0	144.74	24.4
35	68.10/45.4	150	23
36	58.78/47.0	125.06	24.3
37	161.6/41.1	39.31	18.2
38	58.54/73.70	79.43	20.7
39	114/250	45.6	18.9
40	44.70/15.6	286.53	24.5
41	93.57/114.6	81.64	20.9
42	40.53/88.10	46	18.7
43	30.0/42.70	70.25	20.7
44	48.3/38.3	126.1	24.4
45	26.85/56.3	47.69	18.8
46	56.10/75.7	74.11	20.5
47	57.65/72.6	79.41	20.7
48	67.44/125	53.95	19.5
49	34.43/89.0	38.68	18

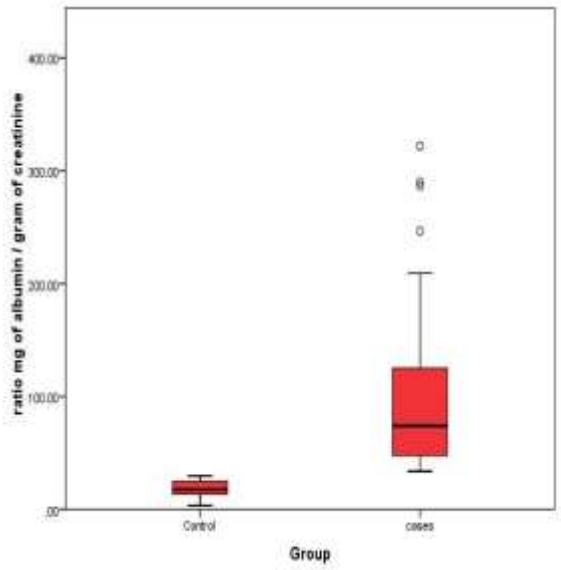
© Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

Table 3: Group Statistics

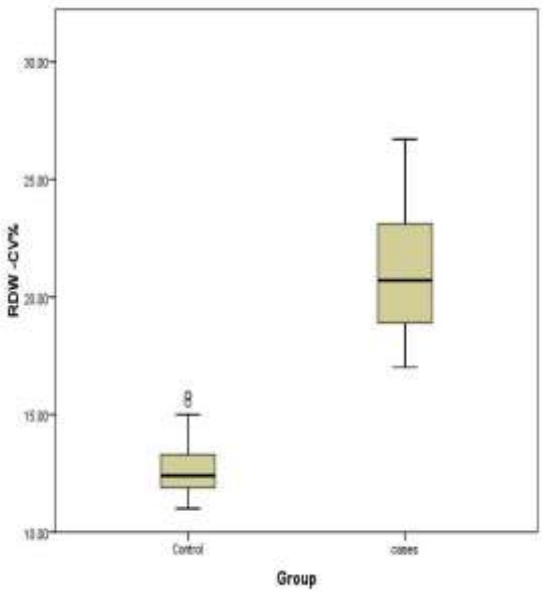
Group Statistics					
	Group	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**
Ratio mg of albumin / gram of creatinine	**Control**	49	18.7416	6.95669	.99381
	cases	49	99.2276	72.06525	10.29504
RDW -CV%	**Control**	49	12.7288	1.17744	.16821
	cases	49	20.9918	2.50880	.35840

The values are expressed in **Mean ± S.D**. The **ratio** of the mg of albumin per gram of creatinine among patients with diabetic nephropathy (**99.2276 ± 72.06525**) were significantly higher than controls (**18.7416 ± 6.95669**).

The **RDW** values among patients with diabetic nephropathy (**20.9918 ± 2.50880**) were significantly higher than controls (**12.7288 ± 1.17744**).



Graph 1: Both group 1 (control) and group 2 (cases) were compared with the ratio of mg of albumin per gram of creatinine on the bar diagram.



Graph 2: Both group 1 (control) and group 2 (cases) were compared with RDW values on the bar diagram.

DISCUSSION

DN is asymptomatic in early stages. Sustained microalbuminuria is the earliest warning sign. Hypertension and some measure of dependent oedema eventually develop in most untreated patients.[1-5]

In later stages, patients may develop symptoms and signs of uremia (eg, nausea, vomiting, anorexia) earlier (ie, with higher GFR) than do patients without DN, possibly because the combination of end-organ damage due to diabetes (eg, neuropathy) and renal failure worsens symptoms.[8,9]

Diagnosis is done by screening of all patients with diabetes with random urine albumin/creatinine ratio.[6,7] **Albumin creatinine ratio** is expressed as **mg** of albumin excreted **per gram** of creatinine or **µg (microgram)** of albumin excreted **per mg** of creatinine**.**

Method	**Normal Value**	**Micro Albuminuria**	**Macro Albuminuria**
Albumin creatinine ratio µg/mg	<30 µg/mg	30-300 µg/mg	>300 µg/mg

Red blood cell distribution width (RDW) is a measure of variability in size of circulating erythrocytes obtained in standard automated complete blood counts. RDW may represent an important clinical marker for diabetes complications independent of traditional risk factors and disease duration.[10-13] RDW was shown to be significantly associated with diabetic nephropathy in a type2 diabetic population.

Albumin creatinine ratio is estimated for diabetic and diabetic nephropathy patients that is shown in table 1 and table 2 respectively. In Graph 1 both group 1 (control) and group 2 (cases) were compared with the ratio of mg of albumin per gram of creatinine on the bar diagram. In Graph 2 both group 1 (control) and group 2 (cases) were compared with RDW values on the bar diagram.

The statistical analysis was done and the values are expressed in Mean ± S.D which is shown in table 3. The **ratio** of the mg of albumin per gram of creatinine among

© Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

patients with diabetic nephropathy (**99.2276 ± 72.06525**) were significantly higher than controls (**18.7416 ± 6.95669**). The **RDW** values among patients with diabetic nephropathy (**20.9918 ± 2.50880**) were significantly higher than controls (**12.7288 ± 1.17744**).

CONCLUSION

Microalbuminuria provides early warning of renal damage. Red blood cell distribution width (RDW) is a measurement of anisocytosis obtained in standard automated complete blood counts and is found to be an important clinical marker for diabetes complications independent of traditional risk factors and disease duration.

We conclude our study by saying that Sustained microalbuminuria is the earliest warning sign of asymptomatic diabetic nephropathy patients and is a potent risk factor for the development of progressive renal disease.

Urine albumin creatinine ratio (ACR) is an accepted and useful screening test for microalbuminuria. RDW was found to be significantly associated with diabetic nephropathy patients and hence it may be a useful renal biomarker for diabetic complications.

REFERENCES

1. Mogensen Ce, Vestbo E, PoulsenPl, Et Al. Microalbuminuria And Potential Confounders. A Review And Some Observations On Variability Of Urinary Albumin Excretion. Diabetes Care, 18, 1995, 572.
2. Schwab Sj, DunnFl, FeinglosMn. Screening For Microalbuminuria. A Comparison Of Single Sample Methods Of Collection And Techniques Of Albumin Analysis. Diabetes Care, 15, 1992, 1581.
3. Nathan Dm, Rosenbaum C, Protasowicki Vd. Single Void Urine Samples Can Be Used To Estimate Quantitative Microalbuminuria. Diabetes Care, 10, 1987, 414.
4. Ginsberg Jm, Chang Bs, Matarese Ra, Garella S. Use Of Single Voided Urine Samples To Estimate Quantitative Proteinuria.NEngl J Med, 309, 1983, 1543.
5. Witte Ec, LambersHeerspinkHj, De Zeeuw D. First Morning Voids Are More Reliable Than Spot Urine Samples To Assess Microalbuminuria. J Am SocNephrol, 20, 2009, 436.
6. Younes N, Cleary Pa, Steffes Mw, Comparison Of Urinary Albumin-Creatinine Ratio And Albumin Excretion Rate In The Diabetes Control And Complications Trial/Epidemiology Of Diabetes Interventions And Complications Study. Clin J Am Soc Nephrol, 5, 2010, 1235.
7. MattixHj, Hsu Cy, Shaykevich S, Curhan G. Use Of The Albumin/Creatinine Ratio To Detect Microalbuminuria: Implications Of Sex And Race. J Am SocNephrol, 13, 2002, 1034.
8. Mogensen Ce. Microalbuminuria Predicts Clinical Proteinuria And Early Mortality In Maturity-Onset Diabetes. N Engl J Med, 310, 1984, 356.
9. Glassock RJ. Prevention of Microalbuminuria in Type 2 Diabetes: Millimeters or Milligrams. J Am SocNephrol. 17, 2006, 3276–3278.
10. Hammarsten O, Jacobsson S, Fu M. The Red Cell Distribution Width In Chronic Heart Failure: A New Independent Marker For Its Prognosis? European Journal Of Heart Failure. 12, 2010, 213–14.
11. Association Between Red Blood Cell Distribution Width And Macrovascular And Microvascular Complications In Diabetes NMalandrino, Wc Wu, ThTaveira, HbWhitlatch - Diabetologia, 2012 – Springer.
12. Assessment Of Red Blood Cell Distribution Width(Rdw) As A Biomarker Of Diabetic Nephropathy InType2DiabetesMellitus Patients Reviewed At Kabwe General HospitalGNombwende - 2014 - Dspace.Unza.Zm
13. Red Blood Cell Distribution Width And Diabetes-Associated ComplicationsCjMagri, S Fava Diabetes& Metabolic Syndrome: Clinical Research & 2014 – Elsevier
14. Caramori ML, Fioreto P, Mauer M. The need for early predictors of diabetic nephropathy risk: Is albumin excretion rate sufficient? Diabetes. 49, 2000, 1399–1408.

Source of Support: Nil, **Conflict of Interest:** None.

© Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.