Original Article

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RDW as a Marker of Treatment Response in Primary Adult Nephrotic Syndrome

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Abstract

Background: Nephrotic syndrome has an incidence of three new cases per 100 000 each year in adults. Despite considerable advances in health care, glomerular disease constitutes one of the leading causes of renal failure resulting in considerable morbidity and mortality. In India, the histological type varies according to the demographic location, and treatment regime depends on the type of nephrotic syndrome. RDW is an inexpensive blood test and there are several studies that show a close relationship between RDW values and inflammatory activity. Our aim in this study is to test the predictive value of RDW in determining treatment response to therapy in adult nephrotic syndrome. **Subjects and Methods:** Newly diagnosed primary adult nephrotic syndrome patients admitted to Victoria hospital and hospitals attached to Bangalore Medical College and Research institute (BMCRI), between May 2018 to September 2020 were chosen for the study. The patients were recruited as per inclusion criteria and demographic profile, medical history, comorbidities, detailed physical examination and lab investigation such as serum creatinine, and 24 hour urine protein were recorded in the study performa . Patients who have nephrotic range proteinuria (> 3.5 gm/24 hrs) with sonographically normal sized kidneys were subjected to renal biopsy to identify the etiopathology. Following this appropriate treatment was iniated and the patients were followed up for the duration of the study. **Results:** Our study included 39 patients with nephrotic syndrome were treated in hospitals attached to BMCRI. Of these patients, males constituted 61.5% and females 38.5%. 53.8% of cases occurred in third decade of life. The commonest presenting symptom among these patients was pedal edema. MGN was the most common histological variant followed by IgA nephropathy and MCGN. Mean RDW values among those who were resistant to treatment was 18.58+/- 0.62 and 13.23+/- 0.74 among those who responded to treatment. Difference in RDW between the two groups was found to be statistically significant showing that high RDW values may be associated with poor treatment response. **Conclusion:** In our study high RDW values were found to be associated with high rates of treatment resistance. These findings suggest that RDW may be used as a useful biomarker to predict treatment response in nephrotic syndrome patients.

Keywords: adult nephrotic syndrome, red cell distribution width, kidney disease

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Introduction

Nephrotic syndrome is a clinical syndrome with a characteristic pentad. They are: (1) Proteinuria greater than 3-3.5 g/24 hour or spot urine protein: creatinine ratio of >300-350 mg/mmol (2) Serum albumin <2.5 g/dL (3) Clinical evidence of peripheral oedema (4) Severe hyperlipidaemia is often present (5) lipiduria.[1] These are associated with complications such as increased susceptibility to infections, thromboembolism, altered lipid and carbohydrate metabolism and losses in binding proteins in the urine.[2]

Nephrotic syndrome has an incidence of three new cases per 100 000 each year in adults.[3] Despite considerable advances in health care, glomerular disease constitutes one of the leading causes of renal failure resulting in considerable morbidity and mortality.[4] In India, the pattern varies according to the demographic location, Membraneous GN represents the most common cause of nephrotic syndrome from South India, whereas primary IgA nephropathy is more common in young adults from western India, and MCD dominates northern India.[5]

Renal biopsy is an invaluable tool in assessing the etiology in patients with suspected primary nephrotic syndrome and to plan the line of treatment as treatment varies according to the different histological types.[6]

RDW is a measure of the range of variation of red blood cell (RBC) volume that is reported as part of a standard complete blood count.[7] There are several studies that show a close relationship between RDW values and inflammatory activity. Our aim in this study is to test the predictive value of RDW in determining treatment response to therapy in adult nephrotic syndrome.

Subjects and Methods

Newly diagnosed primary adult nephrotic syndrome patients admitted to Victoria hospital and hospitals attached to Bangalore Medical College and Research institute (BMCRI), between May 2018 to September 2020 were chosen for the study. The patients were recruited as per inclusion criteria and demographic profile, medical history, comorbidities, detailed physical examination and lab investigation such as serum creatinine, and 24 hour urine protein were recorded in the study performa. Patients who have nephrotic range proteinuria (> 3.5 gm/24 hrs) with sonographically normal sized kidneys were subjected to renal biopsy to identify the etiopathology. Following this appropriate treatment was iniated and the patients were followed up for the duration of the study.

Objectives of the study

To assess the predictive value of RDW in determining treatment response to primary adult nephrotic syndrome.

Inclusion criteria

1. Patients willing to give written informed consent for the study.
2. Age >18 years of either gender
3. Proteinuria >3.5grams/day

Exclusion criteria

1. Coagulopathies
2. Contracted kidneys
3. Solitary kidney
4. Acute pyelonephritis
5. H/o vesico-ureter reflex
6. All long standing cases of diabetes mellitus
7. Patients who give negative consent for biopsy

Statistical Methods

Data was analyzed by descriptive statistics. The Statistical softwares used for data analysis were namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 and Microsoft word and Excel have been used to generate tables and graphs etc.

Results

Table 1: Distributionof- the Subjects Based on Age

Age (in years)	Frequency	Percent
30 and less	21	53.8
31 to 40	9	23.1
41 to 50	5	12.8
50 and above	4	10.3
Total	39	100.0

Table 2: Distribution of the Subjects Based on Gender

	Frequency	Percent
Females	15	38.5
Males	24	61.5
Total	39	100.0

Table 3: Distribution of the Subjects Based On Facial Puffiness

Facial puffiness	Frequency	Percent
Mild	25	64.1
Negative	14	35.9
Total	39	100.0

Table 4: Distributionof the Subjects Based on Pedal Edema

Pedal edema	Frequency	Percent
Mild	20	51.3
Moderate	14	35.9
Negative	5	12.8
Total	39	100.0

Out of 39 (100%) subjects, 21(53.8%) subjects were aged below or equal to 30 yrs followed by 9 (23.1%) subjects aged between 31 to 40 years, 5(12.8%) subjects aged between 41 to 50 yrs and 4 (10.3%0 subjects aged 50 years and above [Table 1].

1% subjects had facial puffiness whereas 14 (35 9% had no facial puffiness [Table 3]

Pedal edema was mild among 20 (51.3%) subjects, moderate among 14 (35.9%) subjects [Table 4].

Frothy Urine was seen (Mild) among 21 (53.8%) subjects whereas it was negative among the rest of the subjects- 18 (46.2%) [Table 5].

Table 5: Distributionof the Subjects Based on Frothy Urine

Frothy Urine	Frequency	Percent
Mild	21	53.8
Negative	18	46.2
Total	39	100.0

Table 6: Distribution of the Subjects Based on Histopathology

Histopathology	Frequency	Percent
C3 MEDIATED GLOMERULONEPHRITIS	1	2.6
FSGS	5	12.8
IgA NEPHROPATHY	8	20.5
LUPUS NEPHRITIS	1	2.6
MCGN	8	20.5
MPGN	1	2.6
PRIMARY MGN	15	38.5
Total	39	100.0

Table 7: Distributionof the Subjects Based on Treatment Response

Treatment response	Frequency	Percent
Not responded	4	10.3
Responded	35	89.7
Total	39	100.0

Table 8: Comparisonof the Demographic, Clinical and Lab Parameters Between the Groups (Based o n Treatment Response) Using Independent Sample T Test

Demographic and	Not responded		Responded		Mean diff	p value
	Mean	S.D	Mean	S.D		
AGE	35.50	14.82	32.31	12.35	3.19	.634
SBP	140.0	8.16	130.57	17.48	9.43	.298
DBP	87.50	5.00	81.31	12.76	6.19	.347
S creatinine	1.75	0.69	1.01	0.70	0.74	.054
24 hr urine protein (g/day)	5.93	2.19	6.59	2.09	-0.66	.553
TSH	7.20	3.18	5.10	2.08	2.10	.078
TC	256.00	47.42	309.91	92.83	-53.91	.264
LDL	131.25	22.23	160.86	48.30	-29.61	.238
RDW	18.58	0.62	13.23	0.74	5.35	.000*

*significant

Histopathology report showed that primary MGN was seen among 15 (38.5%) subjects followed by IgA nephropathy and MCGN among 8 (20.5%) subjects [Table 6].

Out of 39 (100%) subjects, 35 (89.7%) subjects responded to the treatment whereas 4(10.3%) subjects did not respond to the treatment [Table 7].

[Table 8] shows the comparison of the demographic, clinical and lab parameters between the groups (based on treatment response). Independent sample t test was applied to compare the parameters between the groups. Statistically significant difference was seen with respect to RDW (p=0.00) between the groups whereas there was no statistically significant difference

Table 9: Descriptive Analysis Using Chi-Square Test

			Treatment Response		Total	Chi-square	p value
			Not responded	Responded			
Age	30 and less	Count	2	19	21	1.53	0.67
		%	50.0%	54.3%	53.8%		
	31 to 40	Count	1	8	9		
		%	25.0%	22.9%	23.1%		
	41 to 50	Count	0	5	5		
		%	0.0%	14.3%	12.8%		
	50 and above	Count	1	3	4		
		%	25.0%	8.6%	10.3%		
Gender	Females	Count	2	13	15	0.25	0.61
		%	50.0%	37.1%	38.5%		
	Males	Count	2	22	24		
		%	50.0%	62.9%	61.5%		
Facial	Mild	Count	1	24	25	2.96	0.085
		%	25.0%	68.6%	64.1%		
	Negative	Count	3	11	14		
		%	75.0%	31.4%	35.9%		
Pedal	Mild	Count	2	18	20	0.66	0.71
		%	50.0%	51.4%	51.3%		
	Moderate	Count	1	13	14		
		%	25.0%	37.1%	35.9%		
	Negative	Count	1	4	5		
		%	25.0%	11.4%	12.8%		
Frothy	Mild	Count	2	19	21	0.027	0.87
		%	50.0%	54.3%	53.8%		
	Negative	Count	2	16	18		
		%	50.0%	45.7%	46.2%		
Histopathol	C3 mediated	Count	0	1	1	6.31	0.38
		%	0.0%	2.9%	2.6%		
	FSGS	Count	2	3	5		
		%	50.0%	8.6%	12.8%		
	IgA	Count	1	7	8		
		%	25.0%	20.0%	20.5%		
	lupus	Count	0	1	1		
		%	0.0%	2.9%	2.6%		
	MCGN	Count	0	8	8		
		%	0.0%	22.9%	20.5%		
	MPGN	Count	0	1	1		
		%	0.0%	2.9%	2.6%		
	primary	Count	1	14	15		
		%	25.0%	40.0%	38.5%		

seen with respect to age (p=0.63), SBP (p=0.298), DBP (p=0.347), Serum Creatinine (p=0.054), 24 hr urine protein (p=0.553), TSH (p=0.078), TC (p=0.264) and LDL (p=0.238).

Chi-square test was applied to associate the demographic characteristics, symptoms and histopathology with groups. Chi-square test showed no statistical significant association with respect to age (p=0.67), gender (p=0.61), facial puffiness (p=0.085), pedal edema (p=0.71), frothy urine (p=0.87) and histopathology (p=0.38) [Table 9].

Discussion

In our study clinical characteristics and biopsy findings of 39 patients were analysed. Males were 24 (61.5%) and females 15 (38.5%). Maximum number of cases occurred in the third decade among males and females. Membraneous nephropathy was found to be the most common occurring histopathological variant in our study. Out of the 39 patients in our study 10.25%(n=4) were found to be resistant to treatment, out of which 2 were males and 2 were females. Mean age among the patients who were resistant to treatment was 35.8+/- 14.2 years and among the responders was 32.31+/- 12.35 years.

In a similar study by Turgutalp et al in 176 patients, high RDW values were associated with higher rates of treatment resistance.[8] Yousefichaijan P et al also in their study found that high RDW values were associated with poor treatment response rates.[9] Hsieh et al in their study found that high RDW values were associated with increased risk of all cause mortality, cardiovascular disease and infection in CKD patients.[10]

There are other studies that show RDW to be a useful tool in determining treatment outcome in many other conditions. Balta et al in their study concluded that high RDW values may be a significant risk factor for in hospital mortality and decreased long term survival in post CABG patients.[11] Balta et al also in another study showed that increased RDW values had a strong positive correlation with 28 day mortality in sepsis patients.[12]

Tonelli et al in their population based cohort study concluded that high RDW values may be associated with adverse outcomes in people with chronic diseases.[13]

In our study too mean RDW values among those who were resistant to treatment was 18.58+/- 0.62 and 13.23+/- 0.74 among those who responded to treatment. Difference in RDW between the two groups was found to be statistically significant showing that high RDW values may be associated with poor treatment response.

Conclusion

In our study high RDW values were found to be associated with high rates of treatment resistance. These findings suggest that RDW may be used as a useful biomarker to predict treatment response in nephrotic syndrome patients.

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