Predicting the Renal Outcome and Correlation of Renal Parameters in IG-A Nephropathy using new Oxford-Mest Classification System

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ABSTRACT

Introduction: IgA nephropathy is the most common primary glomerulonephritis worldwide. It is defined as the glomerular disease with IgA-dominant or co-dominant mesangial immunoglobulin deposits, excluding lupus nephritis. Study aimed to assess the Prognosis of IgA Nephropathy by NEW OXFORD MEST scoring system and to assess the correlation of Mean Arterial Pressure, Serum Creatinine, Glomerular Filtration Rate and Proteinuria with MEST score

Material and Methods: Retrospective study reported which was conducted on IgAN patients using the Oxford-MEST classification system.

Results: Baseline Creatinine Clearance is a statistically significant individual predictor of disease Outcome. Mean total MEST score of Non Progressors and Progressors was 2.12 and 3.16 respectively. MEST score was higher in patients with Serum Creatinine >1.6 mg/dl in both Non-Progressor and Progressor group.

Conclusion: Tubular atrophy (T score in MEST) and Partial Crescents are individually predicting the Renal Survival. MEST score is not superior in predicting the Renal Outcome when compared to Creatinine Clearance and Nephrotic proteinuria.

Keywords: IgA Nephropathy, Classification, Proliferation, Tubular Atrophy, Interstitial Fibrosis, Glomerulosclerosis

INTRODUCTION

IgA nephropathy is the most common Glomerulonephritis in almost all parts of the world where the renal biopsy is widely practiced.[1,2] It is unique among Glomerular diseases is being defined by immunohistochemical findings of Mesangial deposition of IgA. Diseases associated with Glomerular IgA deposition can be divided into primary and secondary. Primary IgA nephropathy is an immune complex-mediated Glomerulonephritis. Diseases associated with primary causes are IgA nephropathy and Schonlein- Henoch Purpura.3 IgA nephropathy is a renal-limited disease, presented with the various histological presentation. Histologically IgA nephropathy varied from the Minimal lesion to Diffusive Proliferative Glomerulonephritis with Focal Mesangial proliferative Glomerulonephritis is the most common presentation. Schonlein- Henoch Purpura is distinguishable from primary IgA nephropathy from dominant systemic manifestation in a younger individual.[4,5] Dominant clinical features are the Leukocytoclastic vasculitic lesion in the lower limb, abdominal pain, arthritis and renal involvement in the form of Proteinuria and Renal failure. Diffuse and Focal Glomerulonephritis with Crescents are the dominant renal biopsy features.[6]

Secondary causes of IgA deposits in Mesangium are[7-10]

1. Diseases of the liver: alcoholic, primary biliary, or cryptogenic cirrhosis; hepatitis B (where endemic); chronic schistosomiasis
2. Diseases of the intestine: Celiac disease; Chronic ulcerative colitis; Crohn's disease
3. Diseases of the skin: Dermatitis herpetiformis; Psoriasis
4. Diseases of the bronchus or lung: Sarcoidosis, Idiopathic pulmonary hemosiderosis; Cystic fibrosis; Bronchiolitis obliterans
5. Neoplasia: Carcinoma of the lung, larynx, and pancreas; Mycosis fungoides
6. Infection: Human immunodeficiency virus; Leprosy
7. Other systemic or immunologic disorders: Systemic Lupus Erythematosus; Rheumatoid arthritis; Cryoimmunoglobulinemia;
8. Psoriatic arthritis; Ankylosing spondylitis; Sjögren's syndrome; Behçet's syndrome;
9. Reiter's syndrome; Familial immune Thrombocytopenia; Autoantibody-mediated (monoclonal IgA–mediated) Goodpasture's syndrome
10. Diseases coincident with IgA nephropathy: Anti Neutrophilic Cytoplasmic Antibody–associated vasculitis; Diabetic nephropathy; Membranous Nephropathy; Granulomatous polyangiitis

Study aimed to assess the Prognosis of IgA Nephropathy by NEW OXFORD MEST scoring system, to assess the correlation of Mean Arterial Pressure, Serum Creatinine, Glomerular Filtration Rate and Proteinuria with MEST score, to assess whether the MEST score is superior in predicting the Renal Outcome when compared to baseline Serum Creatinine, Creatinine Clearance, and Proteinuria and to assess the role

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of Clinical, Biochemical and Histopathological parameters other than MEST score (Crescents, Arteriolar Hyaline, and Blood Vessel Thickening) in predicting the Renal Outcome.

MATERIAL AND METHODS

This was a Retrospective cohort study, done in Kilpauk Medical College Nephrology department. This study protocol was approved by the Ethical committee for research studies of Government Kilpauk Medical College Hospital, Chennai. Case records of Patients with renal biopsy finding of IgA nephropathy were included in this study. Renal case records were thoroughly searched for clinical presentation (age, SHT, Diabetes mellitus, fever with throat pain, macroscopic hematuria, pedal edema, oliguria, loin pain, blood pressure and anthropometric measurements), urinalysis (urine protein, RBC's and RBC cast in urine, urine spot protein creatinine ratio(PCR), and urine culture and sensitivity, blood biochemistry (blood sugar, urea, serum creatinine, serum sodium, serum potassium, serum uric acid, total proteins, albumin, globulin and serum lipid profile) histopathological report of renal biopsy (both light microscopy and immunofluorescence microscopy results) and follow up investigations and treatment modalities. Creatinine clearance was calculated with Cockgrauft Gault Formula. The patients were divided into groups according to the serum creatinine at the time of presentation. The group of patients according to serum creatinine were; group I <1.0mg/dl, group II 1.1 to 1.5 mg/dl and group III >1.6 mg/dl. By applying the NEW OXFORD MEST scoring to each group (group divided according to the serum creatinine level) separately and the severity of renal lesion at the time presentation was analyzed. The contribution of the Mean Arterial Pressure, baseline Serum Creatinine, Creatinine Clearance, Proteinuria, Serum Uric Acid and serum Triglycerides in predicting the high Total MEST score (score of 3 and above) was analyzed. Clinical, Biochemical and Histopathological factors other than MEST score in predicting the progression of the disease was also analyzed. Follow up Serum creatinine, urine RBC and urine spot PCR was done to assess the latest renal status. Total patients were divided into two groups; i.e., Progressors and Non Progressors. Progressors were defined as those who had a doubling of serum creatinine, development of ESRD or initiation of Renal Replacement Therapy. Non Progressors had stable serum creatinine or had improvement in serum creatinine during the follow-up period. Apart from clinical, biochemical, MEST score and immunofluorescence findings, the associated renal biopsy findings including Cellular or Fibro cellular crescents, Arteriolar hyaline, Blood vessel thickening, mesangiolysis, Glomerular basement thickening and Capillary loop IgA deposit were also analyzed. The intensity of IgA deposits and codeposits like IgG, IgM, C3, and C1q in renal tissue was analyzed for its contribution in the progression of the disease.

RESULTS

245 Renal biopsies cases were analyzed. 48 patients with biopsy-proven IgA nephropathy were enrolled in the study. Among the 48 patients, 44 patients were followed in our hospital regularly or irregularly, Rest of the 4 patients lost for follow up. We excluded these 4 patients from our study because of incomplete case records. IgA nephropathy was found in 44 patients. The incidence of IgA nephropathy in our study was 16% (n=44). 25 patients were males (56.8%), and 19 patients were females (47.2%). Male: Female ratio was 1.3:1. Dominant age group of our patient was between 31 to 50yrs (52.7%) (n=23). 20 patients were in the age group of 15 to 30 yrs, 23 patients were in 31 to 50 yrs age group and one patient was in 51 to 65 yrs age group. Mean age group of the patient was 35.2 yrs. Mean period of follow up of the patients was 17.2 months. Follow up period varied from 4 months to 40 months. Non Progressors were followed for a mean period of 19.32 months, whereas Progressors were followed up for a mean period of 14.1 months. Time to Renal Replacement Therapy in Progressors was 5.2 months. Among 44 patients, 5 patients had history of Hypertension (11.3%) and on treatment for a period of 2 to 9yrs.Diabetes mellitus was found in 2 patients (4.5%). Duration of Diabetes Mellitus was 2 years in one patient and 6 years in another patient. 3 patients had the history of fever during the initial presentation (6.8%), none of the patients had throat pain. Except 2 patients all presented with pedal edema (n=42) (95.4%). In 25 out of 44 patients (56.8%)

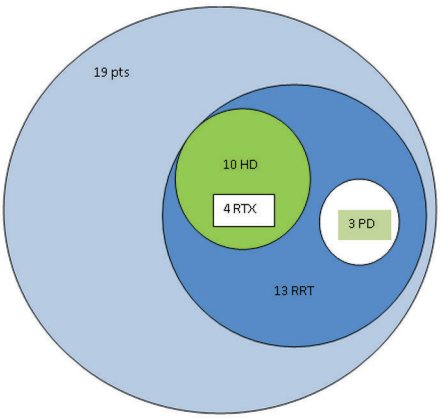

Figure-1: Renal Replacement Therapy modalities in Progressors

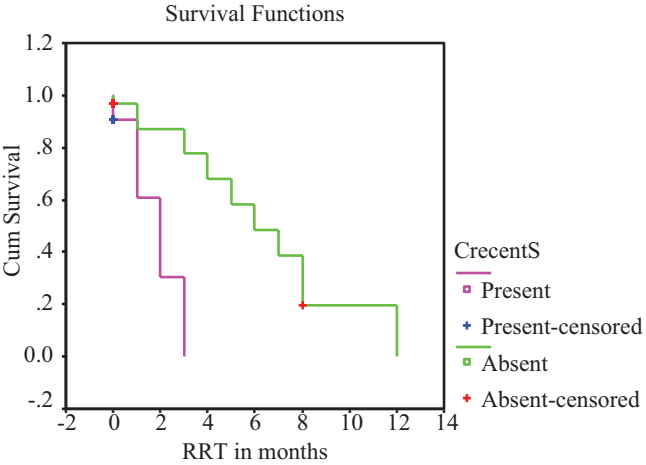

Figure-2: Kaplan meier analysis for crescents

Characteristics		Non Progressors	Progressors
Clinical Presentation	Macroscopic hematuria (n)	7	4
	Oliguria (n)	16	14
	Nephrotic proteinuria (n)	4	8
BMI		22.9	21.1
Urine Spot PCR		2.17gms	6.06 gms
Serum Creatinine	<1.0mg/dl (n)	7	0
	1.1 to 1.5 mg/dl (n)	8	2
	>1.6 mg/dl (n)	10	17
Serum Uric Acid		5.5 mg/dl	7.5 mg/dl
Serum TGL		176.24 mg/dl	179.42 mg/dl
Creatinine clearance		59.6 ml/min	28.63 ml/min
Intensity of IgA deposits	1+ (n)	0	0
	2+ (n)	1	1
	3+ (n)	6	11
	4+ (n)	12	13
Intensity of IgG	0 (n)	17	18
	1+ (n)	0	0
	2+ (n)	1	5
	3+ (n)	1	0
	4+ (n)	0	1
Intensity of C3	0 (n)	1	4
	1+ (n)	2	1
	2+ (n)	1	1
	3+ (n)	4	0
	4+ (n)	11	6
LM Findings	Crescents (n)	6	5
	Arteriolar hyaline (n)	3	0
	Blood vessel thickening mild (n)	2	6
	Blood vessel thickening moderate (n)	4	1
	Blood vessel thickening severe (n)	2	2

Table-1: Clinical presentation

MEST score	Non Progressors	Progressors
1	36%	0%
2	24%	15.80%
3	32%	57.80%
4	8%	21%
5	0%	5.30%

Table-2: MEST scoring

disease was stable, these patients were considered as Non-Progressors. Predominant age group of Non-Progressor was in 31 to 50 years of age (68%).In this group, Systemic Hypertension and Diabetes Mellitus was found in one patient respectively. The Disease progressed in 19 patients (43.1%). Progression of disease was defined as doubling of serum Creatinine, End Stage Renal Disease or initiation of Renal Replacement Therapy. In Progressors(n=19), history of Systemic Hypertension was found in 4 patients, and one patient had diabetes mellitus in addition to SHT. Disease progression was more in younger age group (15 to 30 years)(12 patients -63.15%) and Male patients (58%). 11 patients (22%) had macroscopic hematuria. Macroscopic hematuria was found in 7 (28%) and 4 patients (21%) of Non Progressors and Progressors respectively. Microscopic hematuria was found in all patients (100%). 4 patients (9.0%) presented with loin pain and 30 patients (68.1%) had Oliguria. Oliguria was a clinical feature in 16 (64%) and 14 patients (73.6%) of Non Progressors and Progressors respectively. Systemic hypertension was found in all patients at the time of presentation. The Mean Arterial Pressure of Non Progressors and Progressors were 109±37 mmHg and 110±51mm Hg respectively. Statistical correlation with Pearson product-moment coefficient was not a significant predictor of disease progression concerning mean arterial pressure (p=>0.05). Nephrotic Proteinuria was present in 12 patients (27.3%). Nephrotic Proteinuria in Non-Progressor and Progressor was in 4 (16%) and 8 (42.1%) patients respectively. Nephrotic Proteinuria and Oliguria were the dominant clinical features in Progressors, but macroscopic hematuria was the predominant feature found in Non-Progressors.

Average Body Mass Index of our patients was 22.21kg/m2; Body Mass Index varied from 16 to 30.1kg/m2. Average Body Mass Index of Non-Progressor group was 22.9 kg/m2, and Average Body Mass Index of Progressor group was 21.18 kg/m2. Body Mass Index of Non Progressors was found to be higher than Progressors (22.9±3.67 vs. 21.19±3.20kg/m2).

Among the 44 patients, 28 patients had frothy urine. Urine protein estimation varies from 2+ to 4+. Mean urine spot Protein Creatinine Ratio was 2.61gm/gm of creatinine. Urine Spot Protein Creatinine Ratio of Non-Progressor and

Data	Nonprogressor	Progressor	P value
Total no of patients	25	19	
Mean Age	37.12yrs	32.16 yrs	
Predominant Age group	31 -50 yrs	15-30 yrs	
Disease status	56.9%(M>F)	43.1%(M(58%)>F)	
MAP	109±37 mmHG	110±51mmHg	P=<0.05 NS
Nephrotic Proteinuria	16%	42.1%	
Macroscopic Hematuria	28%	21%	
Oliguria	64%	73.6%	
Microscopic Hematuria	100%	100%	
BMI	23±3.67	21.19±3.20.	P=>0.05 NS
Urine PCR	2.16±1.13	6.06±1.59	P=0.01
Serum Creatinine	1.4mg/dl	2.70mg/dl	P=>0.05 NS
Serum Uric acid	5.8±1.65 mg/dl	7.5±1.69 mg/dl	P=0.005
Serum TGL	176.24±48.68mg/dl	179.42±34.29mg/dl	P=>0.05 NS
Creatinine Clearance	59.60±27.86	29.29±13.60ml/min	P=0.005
Total MEST	2.12±1.01	3.16± 0.76	P=0.005
MEST and Creatinine<1.0	1.43±0.79		Invalid
MEST and Creat 1.1 to 1.5	2.00± 0.93	2.50± 0.71	P=>0.05 NS
MEST and Creatinine>1.5	2.70± 0.95	3.24±0.75	P=>0.05 NS
IgA intensity	3.48±0.59	3.53±0.80	P=>0.05 NS
Co deposits	C3 predominant	C3 predominant	
Cellular crescents	20%	31.5%	
Severe BV thickening	8%	10.5%	
Arteriolar hyaline	Nil	Yes	

Table-3: Summary of results: Univariate analysis: 'paired t' test

Data	Non progressor	Progressor
Map vs MEST score	p=<0.01 significant	P=>0.05 NS
TGL vs MEST score	P=<0.01 significant	P=>0.05 NS
PCR vs MEST score	P=>0.05 NS	P=<0.01 Significant
CR.CL vs MEST score	P=<0.01 significant	P=<0.01 Significant
Uric acid vs MEST score	P=>0.05 NS	P=>0.0 NS

Table-4: Summary of Pearson Product Moment Coefficient:

Progressor was 2.16±1.13 and 6.06±1.59 gm of protein per gm of Creatinine respectively. The Mean Urine Spot Protein Creatinine Ratio of Progressors was higher than Non-Progressors. Statistical analysis of Urine Spot Protein Creatinine Ratio by 'paired t' test was significant in predicting the progression of disease (p<0.01). Urine spot PCR had a statistically significant correlation with Total MEST score by Pearson product-moment coefficient (p<0.01).

Mean serum Creatinine of patients at the time of admission was 2.08mg/dl. Average serum Creatinine of Progressor (n=19) was 2.70 mg/dl. Among the 19 patients, 2 had Serum Creatinine of 1.1.to 1.5 mg/ dl and rest of them had Serum Creatinine of >1.6mgs/dl.

Among Non-Progressors (n=25), 7 patients had Serum Creatinine of <1.0 mg/dl, 8 patients had Serum Creatinine of 1.1 to 1.5 mg/dl and in rest of the patients (n=10) serum creatinine of >1.6mgs /dl was found at the time of presentation. Average Serum Creatinine of Non-Progressor was 1.4mg/dl.

Statistical analysis using 'paired t' test was not significant in predicting disease progression concerning Serum Creatinine (p=>0.05). Statistical analysis using 'paired t' test was not significant in predicting the high total MEST score concerning Serum Creatinine (p=>0.05).

Mean serum uric acid in the study population was 6.53 mg/dl. Serum uric acid of Non-Progressor was 5.8±1.65 mg/dl, and Progressor was 7.5±1.69 mg/dl.

Statistical analysis using 'paired t' test was significant in predicting disease progression concerning serum uric acid (p=0.005). In Pearson, the product-moment coefficient correlation between serum uric acid and total MEST score was not statistically significant (p=>0.05). Serum uric acid is an individual predictor of disease progression.

Mean serum Triglyceride 176.24mgs/dl. Average serum Triglyceride of Progressor 179.5 mg/dl (n=19). Average serum Triglyceride of Non-Progressor was 176.8mgs/dl (n=25). Statistical analysis using paired t-test was not significant in predicting disease progression concerning serum triglyceride (p=>0.05). Statistical analysis using Pearson product-moment coefficient correlation, serum Triglyceride was not significant in predicting high total MEST score (p=>0.05).

Mean Creatinine Clearance is 59.60 ml/min, with values varying from 14.3 ml/min to 113.5ml/min. Average Creatinine Clearance of Non Progressors and Progressors was 59.6ml/min and 28.63ml/min respectively.

Glomerular Filtration Rate <30 ml/min was a feature in 4 (9.0%) and 12 (27.5%) patients of Non-Progressor and

Progressor group respectively.

Statistically, analysis using 'paired t' test was significant in predicting the progression of disease concerning Creatinine Clearance (p=0.005). Creatinine Clearance had a statistically significant correlation with Total MEST score in Pearson product-moment coefficient correlation (p=0.01).

Average Creatinine Clearance of Progressors was 29.29 ml/min.

Baseline Creatinine Clearance is a statistically significant individual predictor of disease Outcome.

Total MEST score of cohort varied from 1 to 5, with the mean of 2.64. 36% (9 patients) of Non Progressors had total MEST score of one. Total MEST score of 3 and 4 was found in 32% and 8% of patients respectively in Non-Progressors. In Progressors, 57.8% (n=11) of patients had total MEST score of score 3 and score of 4 and 5 were found in 21% and 5.2% of patients respectively.

Mean total MEST score of Non Progressors and Progressors was 2.12 and 3.16 respectively. MEST score was higher in patients with Serum Creatinine >1.6 mg/dl in both Non-Progressor and Progressor group. High MEST score is a statistically significant individual predictor of Disease Outcome by paired t-test (p=0.005).

Total MEST score of patients with the serum creatinine of 1.1 to 1.5 mg/dl for Non-Progressor and Progressor was 2.00± 0.93 and 2.50± 0.71 respectively. Total MEST score of patients with the serum creatinine of >1.6 mg/dl for Non-Progressor and Progressor was 2.70± 0.95 and 3.24±0.75 respectively.

In Paired t-test analysis, no statistical significance was found between Total MEST score and serum creatinine in both non-Progressors and Progressors (p=>0.05).

Pearson product moment coefficient correlation analysis was done between Mean Arterial Pressure, Urine spot Protein Creatinine Ratio, creatinine clearance, Serum Triglyceride and Serum uric acid with Total MEST score of Progressors and Non-Progressor.

The significant statistical correlation was found between Urine spot PCR and creatinine clearance with Total MEST score of Progressors (p=0.01). In Non-Progressors, the statistically significant correlation was found between Mean Arterial Pressure, Serum Triglyceride and Creatinine Clearance with Total MEST score (p=0.01).

Hence high urine spot Protein Creatinine Ratio and low Creatinine Clearance at the time of presentation predicts severe histopathological lesion(high Total MEST score) and poor outcome.

The intensity of IgA deposits varies from 2+ to 4+ in IF microscopy. 4 + is the intensity of IgA found in both non-Progressors and Progressors. Statistical analysis using paired t-test was not significant in predicting the disease outcome concerning IgA intensity (p=>0.05).

Along with IgA, other immunoglobulins (IgG, IgM, C3, and C1Q) deposits were also found. Full house pattern (IgG, IgM, IgA) was found in 7 patients (6 – Non Progressors and 1 – Progressors), in all 7 patients C1q and ANA were negative.

Codeposits in immunofluorescence microscopy – Non Progressors

C3 in the intensity of 3 + (12 patients) was the predominant co deposit found in nonprogressor, and along with C3, IgG was also deposited in the intensity 2+in 5 patients.

Codeposits in immunofluorescence microscopy – Progressors

C3 in the intensity of 4 + was the predominant codeposit in immunofluorescence microscopy in Progressor (11 patients).

Cellular crescents, Arteriolar Hyaline and Blood Vessel Thickening, are the other Histopathological features found in light microscopy.

In Non-Progressor, 5 patients (20%) had partial Cellular Crescents. Blood Vessel Thickening was found in 9 patients (36%) with intensity varied from mild to severe. 2 patients (8%) had severe Blood Vessel thickening. None of the Non-Progressor had Arteriolar Hyaline.

In Progressor Partial Cellular crescents were found in 6 patients (31.5%). 8 patients (42.1%) had Blood Vessel Thickening, among them 2 (10.5%) had Severe Blood Vessel thickening. Arteriolar Hyaline was found in 3 patients (15.7%).

13 out of 19 patients on RRT (HD or PD), 4 patients received live related renal allograft. Mean period to initiation of RRT was 5.2 months after diagnosis.

Correlation between Clinical, Histopathological and Renal Survival (outcome) was done using three models of multivariate analysis. Ie, Logistic Regression Analysis, Cox Regression Analysis and Kaplan Meyer Series Analysis using SSPS 15 software. Age, Serum creatinine, Urine Spot Protein Creatinine Ratio, Creatinine Clearance, Individual and Total MEST score, Cellular Crescents, Arteriolar Hyaline, Blood Vessel Thickening and Time to Initiation of Renal Replacement Therapy was taken into account. The endpoint for analysis was fixed as ESRD or Initiation of Renal Replacement Therapy. In Kaplan Meyer series Correlation between T score and crescents with the outcome (ESRD or initiation of Renal Replacement Therapy) was analyzed.

Predictability of the test was 68.2% with 95% confident intervals (CI). Correlation between clinical variables and pathological lesion with outcome was not statistically significant in predicting the renal outcome.

Overall predictability of the test was 93.2% with 95% of Confident Interval (CI). Correlation between Clinical Variables and Pathological lesion (MEST) with Outcome was not statistically significant in predicting the renal outcome.

DISCUSSION

In our study, the incidence of IgA nephropathy is 16%. This result was comparable with a Retrospective study from Kerala, which showed an increasing trend of IgA nephropathy (15.52%) 18. We also compared our study results with the previous reports, an incidence of 4.2% was reported from Tamil Nadu11 in 1987, an incidence of 7.24% from New Delhi in 1992, and an incidence of 10.37% from the Union Territory of Chandigarh in 1995, and found an increasing trend of IgA nephropathy.[11-13]

Radford MG et al reported that Primary IgA nephropathy

occurs at any age, most commonly with clinical onset in the second and third decades of life. In discordant with this study report, our patients predominantly belonged to 4th and the 5th decade, and none of the patients had the age of fewer than 15 years.[14]

In similarity with the Ibels LS et al study, males were predominately presented in our cohort. Hogg et al (1994) observed 15 percent of the patients developed the end-stage renal disease in a mean follow up period of 4 yrs. In discordant with this study, 43.1% of our patients developed the end-stage renal disease in a mean follow up 17.2 months. The disease progressed more in the younger age group between 15 to 30 years of age.[15,16]

Mark Hass et al sub-classified IgAN into subclass I (Minimal or No Mesangial Hypercellularity) subclass II (Focal and Segmental Glomerular Sclerosis without Mesangial Cellularity) subclass III (Focal Proliferative Glomerulonephritis) subclass IV (Diffuse Proliferative Glomerulonephritis) and subclass V (>40% Global Glomerular Sclerosis and > 40% Tubular Atrophy).[17]

Mark's clinic pathological analysis revealed that prognosis was better in subclass I and II, the prognosis was intermediate in subclass III and prognosis was poor in subclass IV and V and additionally, the poor prognosis was found in the presence of Cellular Crescents, Fibro Cellular Crescents and Tubular Atrophy of > 20%. Clinical findings like high Serum Creatinine, Nephrotic Proteinuria and Hypertension were also markers of poor prognosis. Mark et al found that patients with Gross Hematuria had a good prognosis. Apart from proteinuria and hypertension all other variables were not statistically significant.[17]

In our study clinical factors like Proteinuria (Non Progressor and Progressor 2.16±1.13 and 6.06±1.59 p= 0.01), Serum Uric acid (Non Progressors and Progressor 5.8±1.65 mg/dl 7.5±1.69 mg/dl p= 0.005) and Creatinine Clearance (Non Progressors and Progressors 59.60±27.86 28.63±13.60 ml/min; p=0.005) were independent predictors of the outcome of the disease. When these findings were compared with the Clinicopathological correlation done by Hass, they were found to be concordant. Univariate Analysis with 'paired t' test confirms the statistical significance of these clinical variables.

In our study in addition to clinical factors, histological features like Cellular Crescents (20%vs 31.5%), Severe Blood Vessel Thickening (8% vs10.5%) and Arteriolar Hyaline were also associated with poor outcome (ESRD or initiation of RRT or doubling of serum creatinine).

In a large-scale cohort study by Masashi Goto et al., a scoring system was proposed to estimate the ESRD risk within 10 yrs of onset of disease, using eight variables; these variables were male sex, age less than 30 years, presence of family history of chronic renal failure and chronic glomerulonephritis, hypertension, proteinuria and Mild Hematuria, hypoalbuminemia, low GFR and high Histological grade. This prognostic score accurately classified the patients by ESRD risk. Patients with estimated scores of 0–4.9, 5.0–19.9, 20.0–49.9 and 50.0–100% had an observed incidence of 1.7, 8.3, 36.7 and 85.5%, of progression to ESRD respectively. This prognostic score quantitatively estimates the ESRD risk during 10 years follow up, and this serves as a useful prognostic tool in clinical practice.[18]

In our study male sex, age <30 years, Nephrotic range Proteinuria, low Creatinine Clearance and Histological severity in the form of Tubular atrophy, Crescents, Severe Blood Vessel thickening and Arteriolar Hyaline were the variables associated with poor outcome (ERSD, doubling of serum creatinine or initiation of Renal Replacement Therapy). These results were in concordance with the results of a large-scale cohort study by Masashi Goto et al.[18]

In a single-center study of 146 patients done by Michael Walsh et al., three Histopathological parameters 1.Fibrosis of Interstitial area >25%,2. Sclerosis of Glomerular area > 40% and 3.Prescence of Crescents were found to be independent predictors of the composite endpoint (doubling of serum creatinine, End Stage Renal Disease, and Death). Clinical variables like significant Proteinuria (80%), high Serum Creatinine (38%) and blood pressure of >130/90 mmHg (55%) were also predictors of poor prognosis.[19]

Similarly, in our study, patients with Nephrotic range Proteinuria had a statistically significant correlation with poor outcome. Also, low Creatinine Clearance and high Serum Uric acid levels were also independent predictors of poor outcome. In discordant to this single-center study by Michael Walsh et al, serum Creatinine was not a statistically significant predictor of disease outcome.[19]

Comparing the Histopathological variables in our study Tubular atrophy (T score >50%) and Cellular crescents were independent predictors of disease progression (Using Kaplan Meyer survival analysis). These results were similar to the study done by Michael Walsh el al.[19]

A Working Group of the International IgA Nephropathy Network and the Renal Pathology Society introduced the Oxford MEST scoring system by analysis of 265 Renal biopsy samples 60. This analysis consists of four variables, mesangial hypercellularity, segmental sclerosis, endocapillary proliferation and tubular atrophy/ interstitial fibrosis.

In their series, 15% of the patients were <18 yrs of age, Median follow up period was 5 yrs. A strong association was found between initial eGFR, MAP, proteinuria and poor renal outcome. Follow up MAP and proteinuria were also predictors of poor renal outcome. High MEST score was significantly associated with proteinuria. Segmental sclerosis, tubular atrophy, and arterial disease were strongly associated with low eGFR and initial high MAP. The poor Renal outcome was significantly associated with mesangial hypercellularity, segmental sclerosis, and tubular atrophy. These distinct pathological variables had prognostic value independent of all clinical and laboratory parameters. Endocapillary and extracapillary scores were not statistically significant in predicting the adverse renal outcome. Immunosuppressive drugs were prescribed according to endocapillary or extracapillary scores.

Oxford IgA Nephropathy classification was validated in

the North American cohort by Andrew M. Herzenberg et al, using an independent cohort of 187 adults and children. Their clinical characters were comparable in age, eGFR, proteinuria and mean arterial pressure at the time of biopsy with Oxford derivation cohort. Three of the four pathological variables as in Oxford cohort predicted the rapid decline in renal function. When compared to the Oxford cohort, North American cohort received more immunosuppressive drugs and antihypertensives.[20]

In similarity with OXFORD MEST scoring system and its North American cohort results, Clinical variables like Creatinine Clearance and Nephrotic range Proteinuria were concordant in predicting the renal outcome. (Univariate analysis -paired t-test) (p=0.005). Mean Arterial pressure was not a predictor of disease outcome in our study.

Correlation between Total MEST score and Renal outcome (ESRD/RRT) was statistically significant in univariate analysis (p=0.005). But Correlation between individual and total MEST score with renal outcome was not statistically significant in multivariate analysis (Logistic regression and Cox regression). T scores (Tubular) and crescents were found to be individual predictors of renal survival in Kaplan Meyer survival analysis. Results of this multivariate analysis were discordant with OXFORD MEST scoring system and its North American validation.

As there no strict immunosuppressive protocol followed in our study, our treatment protocols are not comparable with other studies. All the 44 patients received Angiotensin Converting Enzyme inhibitors and Statins. Inj Methyl Prednisolone and oral Prednisolone was prescribed for patients with crescents, but a standard immunosuppressive protocol was not followed.

CONCLUSION

In our study, High Total MEST score at the time of presentation is an individual predictor of Disease Outcome. Low baseline Creatinine clearance and Nephrotic Proteinuria are predictors of High MEST score. Low baseline Creatinine Clearance, Nephrotic proteinuria and Serum Uric acid are individual predictors of disease progression. Tubular atrophy (T score in MEST) and Partial Crescents are individually predicting the Renal Survival. MEST score is not superior in predicting the Renal Outcome when compared to Creatinine Clearance and Nephrotic proteinuria.

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