RETROSPECTIVE STUDY OF HISTOLOGICAL ANALYSIS AND ITS CORRELATION WITH CLINICAL PRESENTATION AND OUTCOME OF IGA NEPHROPATHY FROM A TERTIARY CENTRE OF GUWAHATI ASSAM.

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Abstract

Background: IgA nephropathy (IgAN) is one of the most common glomerular diseases with varied presentations. We aimed to study clinical presentation and outcome of IgAN and correlate with histopathology at the time of presentation.

Methods: This is a retrospective study in which we analyzed kidney biopsy data, clinical manifestations and outcome of 137 patients with a diagnosis of primary IgAN from 2012 to 2016. Kidney biopsies were reviewed as per Oxford classification assessing mesangial hypercellularity, endocapillary hypercellularity, segmental sclerosis/adhesion, tubular atrophy/interstitial fibrosis. Correlation analysis was done for biopsy findings and clinical presentation/outcome. P score less than 0.05 was taken as significant.

Results: Mean age for presentation was 27.35 years with 83 males and 54 females. Asymptomatic urinary abnormality was the most common clinical presentation (28.5%). Mean serum creatinine was 2.23 ± 2.06 mg/dl with mean proteinuria of 1.49 ± 1.43 g/day. Mesangial hypercellularity (M) and Endocapillary hypercellularity (E) lesions were significantly associated with proteinuria at the time of biopsy ($p=0.02$ & 0.04 respectively). Segmental glomerulosclerosis (S) and tubular atrophy (T) were significantly associated with eGFR and mean arterial pressure at the time of biopsy. Mean time of follow up was 1.6 years. M1, E0, S1, T0 were the most common lesions. M, S and T lesions in biopsy were significantly associated with decrease in GFR at the end of follow up.

Conclusion: In our study, most common presentation of IgAN was AUA with rarity of macroscopic hematuria. M, S and T lesions were associated with decreased GFR on follow up.

Key words: IgA Nephropathy, Nephrotic Syndrome, Oxford MEST classification,

Introduction:

IgA nephropathy (IgAN) or Bergers disease is one of the most common causes of primary

glomerulonephritis^[1]. It was first described by Berger et al in 1968 in around 300 kidney biopsies by applying fluorescein conjugated

antibodies against IgA, however, exact pathogenesis of the IgAN is still unknown^[2,3]. IgAN is defined histologically by the predominant glomerular deposition of IgA mainly in mesangium, which can be identified by immunofluorescence or immunohistochemistry^[4]. Around 5 -15% of normal population can have mesangial IgA deposits, with 1 in 50 patients with mesangial deposits developing clinical disease^[5]. Previously IgAN was presumed to be a benign disease with good renal outcome, however it has been seen to be associated with halving of glomerular filtration rate (GFR) or end stage renal disease (ESRD) in 27% at 10 years^[6]. IgAN has varied clinical presentation and course, with benign prognosis in the absence of adverse risk factors of proteinuria, hypertension, reduced GFR and obesity^[7].

Two most common presentation of IgAN are asymptomatic hematuria and progressive kidney disease. While progressive kidney disease has been seen in multiple cohorts asymptomatic hematuria is usually detected on screening programs^[8]. Other presentations can be synpharyngitic macroscopic hematuria, nephrotic syndrome and rapidly progressive glomerulonephritis. The Oxford Classification of IgAN was aimed to define reproducible biopsy based prognostic indicators^[9, 10]. On the basis of retrospective analysis of 265 IgAN patients, Oxford classification of IgAN was put forward to predict renal outcome based on MEST score (mesangial hypercellularity, segmental glomerulosclerosis, endocapillary hypercellularity, and tubular atrophy/interstitial fibrosis). Subsequently working group formed in 2014 added presence of crescents to this MEST score for prediction of renal outcome based on review of 3096 patients^[11]. There are several papers on large cohorts of IgAN^[12, 13] and validation studies^[14-16] based on Oxford classification. There are few studies from India with almost no data from our part of country regarding IgAN. In a study from our center of rapidly proliferative glomerulonephritis (RPGN), IgAN constituted 25% of cases^[17].

We present the retrospective data of biopsy proven IgAN from our centre with at least follow up of 1 year. The biopsies were classified as per Oxford classification. Clinical pathological correlation was evaluated and performance of prognostic factors of histopathology was evaluated on follow-up. The aim of this study was to study clinic pathological correlation in biopsy proven IgAN patients.

Materials and methods

Demographic data

In our study, all the native kidney biopsy (n=1253) done in last 6 years from 2012 to 2016 at the department of nephrology, Gauhati medical college and hospital were taken and retrospectively reviewed. A total of 154 cases of IGAN were registered. Data of the patients with biopsy proven IGAN was taken from hospital records. For definition of IGAN, we followed the recommendations of the International Consensus of IgAN study– the Oxford's classification of IgAN^[9, 10]. Demographic data included data on gender and age at the time of biopsy. Children were defined as less than 18 years and elderly patients as more than 65 years.

IgAN was diagnosed on biopsy by immunofluorescence (IF) microscopy depicting predominant IgA deposits in glomerular mesangium. All biopsy proven IgAN were included in the study and standard light microscopy (LM) and IF was performed in all biopsies. Patients having secondary causes of IgAN like Henoch–Schönlein purpura, Chronic liver disease, etc were excluded from the study. Patients having inadequate biopsies (<8 glomeruli), IgAN in combination with advanced diabetes mellitus, inadequate data or less than 1 year follow up were also excluded.

Pathology data

For LM, buffered formalin was used to fix the tissue which was processed into paraffin blocks; sections were stained with hematoxylin and eosin (H and E), periodic acid Schiff (PAS), and Jones' silver methanamine. Each biopsy was scored as per oxford classification^[9] MEST:

mesangial hypercellularity, M0/M1 (< or equivalent to >50% of glomeruli showing >4 mesangial cells in one area); endocapillary proliferation, E0/E1 (present/absent), segmental glomerulosclerosis/adhesion, S0/S1 (present/absent); tubular atrophy/interstitial fibrosis, T0/T1/T2. Glomerular membrane duplication, necrosis, cellular/fibrocellular crescent were categorized as present or absent. Crescent was not included in Oxford MEST as ours was a retrospective study and crescent was recently incorporated in the classification. For IF, frozen sections were labeled direct fluorescein isocyanate (FITC)-conjugated antibodies against IgG, IgA, IgM, C3, C1q, fibrinogen and kappa and lambda light chains of immunoglobulins. The intensity of IgA staining was more than trace, moderate or marked. Lupus nephritis was ruled out an intense positivity for all immunoglobulin antigens and complement fragments, especially C1q, IgG and IgM (DAKO).

Clinical data

Patients clinical data was collected at the time of biopsy and at the end of follow up documenting age at the time of biopsy, weight, height, body mass index (BMI), smoking history, presenting clinical syndrome at the time of biopsy, systolic and diastolic blood pressure (mmHg), serum creatinine (mg/dL), serum albumin (g/dL), serum cholesterol (mg/dL) and serum triglycerides levels (mg/dL), 24-h urine protein (g/24 hour), urinalysis, serology, virology at the time of biopsy. GFR was calculated by MDRD formula in adults and by Schwartz formula for children^[18], hematuria was defined by presence of more than three red blood cells (RBC) per high power field (HPF) in the urine sediment.

Based upon clinical presentation and laboratory data, patients were categorized into nephrotic syndrome, nephritic syndrome, RPGN, acute kidney injury (AKI), chronic renal failure and abnormal urine analysis. Patients clinical details were collected at the last follow up (FU). Decline in kidney function at follow up (FU) was expressed as slope of eGFR during the FU (delta GFR divided with the FU years) and delta

proteinuria divided by number of years of FU. Mean arterial pressure (MAP) was calculated by diastolic blood pressure (DBP) plus one third of pulse pressure. The renal function decline was correlated with the biopsy findings.

Statistical Analysis

All the clinical data of patients were collected in an Excel spreadsheet. Statistical analysis was performed using the SPSS v 20. To characterize the cohort, descriptive statistics was used. Qualitative data are presented as frequencies (percentage). Mean $\pm$ standard deviation (SD) is used for quantitative data. A P value of <0.05 was taken as statistically significant. Kidney function decline, expressed as slope of eGFR at the end of the FU, was shown as clinical outcome, and was analyzed.

Results

Out of 1253 biopsies analyzed, 154 fulfilled the criteria for primary IgAN. 17 patients had follow-up of less than 1 year and were excluded and rest of 137 were included in the study. Males were 61%, while as 39% were females. Clinical and demographic features are described in table 1. Mean age for presentation was 27.35 (10-51) years with mean age for men being 28 years and 26 for females; Figure 1 gives the distribution of the patients as per age groups. Mean BMI was 23.6 ± 3.7 and 38% of patients were smokers. Asymptomatic urinary abnormalities (AUA) in the form of microscopic hematuria or subnephrotic proteinuria or both was the most common clinical presentation (28.5%) followed by the nephrotic syndrome (23.3%). Unexplained renal failure was initial presentation in 19.7% patients, while as, RPGN was in 17.5% and AKI in 6.5%. Macroscopic hematuria was uncommon presentation. Hypertension defined by blood pressure more than 140/80 was seen in 38.6%. Mean serum creatinine was 2.23 ± 2.06 mg/dL with mean estimated GFR (eGFR) of 48.65 ± 35.5 mL/min/1.73m². Mean proteinuria was 1.49 ± 1.43 gram/day, which was more in males (1.50 ± 1.43 g/day) than females (1.48 ± 1.42 g/day); proteinuria more than 3 grams/day was seen in

38 patients, while as mild proteinuria (<1 gram/day) was seen in 60 patients.

Table 2 describes pathology finding of kidney biopsies on LM as per Oxford MEST classification, figure 2 shows the various co-deposition patterns on IF. M1, E0, S1, T0 were the most common lesions. Arteriosclerosis was present in 34 biopsies (24.8%), with 27% in male patients and 20% in female patients ($p = 0.4$). Thrombotic microangiopathy (TMA) was seen in 19 biopsies. Table 3 describes the correlation between clinical picture and histopathology at the time of biopsy. Mesangial hypercellularity (M) lesion was significantly associated with proteinuria ($p=0.02$) at the time of biopsy but was not significantly associated with eGFR and mean arterial pressure (MAP) at the time of biopsy. Endocapillary hypercellularity (E) lesion was not significantly associated with eGFR or MAP at the time of biopsy but was significantly associated with

proteinuria ($p=0.04$). Segmental glomerulosclerosis (S) and tubular atrophy (T) were significantly associated with eGFR and MAP at the time of biopsy.

Mean time of follow up was 1.6 (1-4.8) years with minimum follow up of 1 year. Table 4 describes the correlation of clinical features at the end of follow up with the biopsy findings. M lesion in biopsy was significantly associated with decrease in GFR ($p= 0.0001$) and increase in proteinuria ($p=0.0002$) at the end of follow up. E lesions in biopsy was significantly associated with increase in proteinuria ($p=0.01$), while as it was not significantly associated with decrease in GFR at the end of follow up. S and T lesions in biopsy was significantly associated with decrease in GFR ($p= 0.00001$ and 0.001 respectively) at the end of follow up but not with increase in proteinuria. Figure 3a to 3d shows graphically the GFR at the end of follow up with respect to biopsy lesions.

Table 1: Clinical features at the the time of kidney biopsy

Clinical features	All cases	male	Females
Gender, n (%)	137 (100)	83 (60.6)	54 (39.4)
Age, years, mean (range)	27.35 (10-51)	28 (10-51)	26 (16-45)
Macroscopic hematuria, no. (%)	6 (4.2)	4(2.9)	2 (1.4)
AUA, no. (%)	39(28.5)	27 (19.7)	12 (8.8)
Acute kidney injury, no. (%)	9 (6.5)	5 (3.65)	4 (2.9)
Nephrotic syndrome, no. (%)	32 (23.3)	18(13.1)	14(10.2)
RPGN, no. (%)	24 (17.5)	14 (10.2)	10 (7.3)
Unexplained renal failure	27 (19.7)	15(10.9)	12 (8.8)
CKD			
CKD G1	19%	18%	19%
CKD G2	20%	19%	21%
CKD G3	39%	38%	41%
CKD G4	12%	13%	11%
CKD G5	10%	12%	8%
HTN (140/80)	53	29	24
Creat, mg/dl, mean $\pm$ SD	2.23 $\pm$ 2.06	2.28 $\pm$ 2.17	2.15 $\pm$ 2.01
eGFR , ml/min/1.73m ² , mean $\pm$ SD	48.63 $\pm$ 35.5	49.38 $\pm$ 36.2	40.24 $\pm$ 35.9
Alb, gram/dl, mean $\pm$ SD	3.03 $\pm$ 0.61	2.99 $\pm$ 0.63	3.05 $\pm$ 0.62
Cholesterol, mg/dl, mean $\pm$ SD	205 $\pm$ 63.5	207 $\pm$ 73	202 $\pm$ 54
Triglycerides, mg/dl, mean $\pm$ SD	184 $\pm$ 57	184.6 $\pm$ 58	183 $\pm$ 54
Proteinuria g/day, mean $\pm$ SD	1.49 $\pm$ 1.43	1.50 $\pm$ 1.43	1.48 $\pm$ 1.42
Proteinuria			
<1 g/24 hrs	60	43	23
1-3.4 g/24 hrs	39	24	15
>3.5 g/24 hrs	38	22	16

Table 2: Distribution of histopathological changes in renal biopsies of patients with IgAN

Histopathology lesion	Frequency n, (%)
Mesangialhypercellularity	
M0	64 (46.7%)
M1	73 (53.7%)
EndocapillaryHypercellularity	
E0	89 (64.9%)
E1	48 (35.1%)
Segmental Glomerulosclerosis	
S0	66 (48.17%)
S1	71 (51.8%)
Tubular atrophy	
T0	85 (62.05%)
T1	39 (28.46%)
T2	13 (09.5%)

Table 3: Correlations between pathological and clinical features at the time of renal biopsy for the whole cohort

Histopathological lesion	GFR (mL/min/1.73 m ²)	p- Value	24h proteinuria (g/24h)	p- Value	MAP, mm Hg	p-Value
Mesangialhypercellularity						
M0						
M1	50.24 ± 34.6 45.36 ± 35.8	0.42	1.2 ± 0.7 1.6 ± 1.2	0.02	96.9 ± 10.2 99.8 ± 11.4	0.12
EndocapillaryHypercellularity						
E0						
E1	49.9 ± 35.2 42.8 ± 36.1	0.26	1.3 ± 1.1 1.7 ± 1.3	0.04	96.8 ± 9.8 99.2 ± 10	0.19
Segmental Glomerulosclerosis						
S0	55.63 ± 33.4	0.03	1.4 ± 0.9	0.56	95.5 ± 9.6	0.002
S1	42.56 ± 36.7		1.5 ± 1.1		101 ± 11.2	
Tubular atrophy						
T0	56.62 ± 34.6	0.01	1.4 ± 0.9	0.85	94.4 ± 9.2	0.001
T1	41.72 ± 35.3		1.5 ± 1.0		99.7 ± 9.9	
T2	29.82 ± 37.3		1.4 ± 1.1		103 ± 12	

Table 4: Correlation of biopsy findings to the clinical outcome atleast 1 year follow up.

Histopathological change	Change in GFR (mL/min/1.73m ² /year)	p- Value	Change in proteinuria (per year)	p- Value
Mesangialhypercellularity				
M0	2.64 ± 0.3	0.0001	0.1 ± 0.06	0.0002
M1	5.96 ± 0.5		0.3 ± 0.2	
EndocapillaryHypercellularity				
E0	3.20 ± 0.6	0.21	± 0.1	0.01
E1	3.24 ± 0.8		0.18 ± 0.1	
Segmental Glomerulosclerosis				
S0	1.69 ± 1.1	0.00001	0.08 ± 0.05	0.75
S1	5.74 ± 1.1		0.04 ± 0.03	
Tubular atrophy				
T0	2.46 ± 0.4	0.001	0.04 ± 0.02	0.91
T1	4.18 ± 1.1		0.02 ± 0.02	
T2	5.40 ± 1.5		0.10 ± 0.06

Figure 2: Immunofluorescence pattern of renal biopsy

Figure 3: Change in GFR at the end of end of follow up with respect to the biopsy lesions

Discussion

In our study, which was a retrospective study, 154 were IgAN out of 1253 biopsies with an incidence of 12.3%. In other studies from south India IgAN was reported in 5.02% [19], 9.13% [20]. In a study from east India IgAN was reported in 8.11% [21] cases, while as in another studies incidence of 7.5 and 7.8% has been seen [22,23]. Studies from other parts of Asia and Europe have shown higher prevalence of IgAN [24-26]. Prevalence of IgAN in our study was higher than other studies in India. This may be because of different racial stock of population.

Mean age presentation of IgAN in our study was 27.31 years with most patients presenting in 2nd

and 3rd decade with predominance of male. This was in accordance to the other studies with IgAN presenting in 2nd and 3rd decade [26, 27]. Most common presentation of IgAN in our study was asymptomatic urinary abnormality including microscopic hematuria and sub nephrotic proteinuria. Significant portion of our study population were having nephrotic syndrome and renal failure. RPGN was seen in 11.7 % of the patients; gross hematuria was very rare. In other studies of India, nephrotic syndrome and renal failure were the most common presentation of IgAN while as, in other studies from rest of the world, hematuria and subnephrotic proteinuria predominate [21-26, 27-29]. High occurrence of renal

failure and nephrotic syndrome in our part of the world can be attributed to late presentation of the patients and lack of screening programs especially school level. Also possibility of racial and genetic factors playing part can't be ruled out, need genetic studies to assess the genetic risk in our population. Arterial hypertension in IgAN occurs in 2.3% to 25.2% of cases and associated with higher risk of progression of renal failure, in our study arterial hypertension was more prevalent (37.9%) than literature [31, 32].

International IgA Nephropathy Work and Renal Society of Pathology work groups in 2009 proposed oxford classification, a new system of histological classification of IgAN [9, 10]. Based on the histological analysis of the mesangial hypercellularity, segmental glomerulosclerosis, endocapillary hypercellularity and tubular atrophy/ interstitial fibrosis, this classification graded histological changes with greater long term impact on the renal function of the patient. In our study, M1, E0, S1 and T0 were the most frequent histological lesions. In a study for histological pattern in kidney biopsy of IgAN, Riispere et al. found a distribution similar to ours [7]. In another studies by Kang et al. and Alamartine et al. found M0, E0, S1 and T0 lesions more common in their patients [33, 34]. On the other hand, M1, E1, S1 and T0 were more prevalent in the study by Shii, et al [35].

In our study, we observed M1 lesions were associated higher 24 hour proteinuria at the time of biopsy as compared to M0 lesions. M1 lesions were also significantly associated with increase in proteinuria at the end of follow up. Although at the time of biopsy, M1 lesions was not associated significantly decreased GFR, at the end of last follow up M1 lesion was significantly associated with decrease in GFR as compared to M0 lesion. Mesangial hypercellularity can be associated with poor prognosis of the renal function, since it shows the presence of an active renal lesion, which would need more powerful treatment when identified [33, 36 & 37]. M lesion at the time of biopsy was not associated with

higher arterial hypertension as compared to M0 lesions.

In our study, higher T lesions on biopsy were associated with decreased GFR and arterial hypertension. These findings have also been seen in previous studies [33-35]. Further at the end of follow up, higher T lesions were significantly associated with decreased GFR. Other studies also have shown poor prognosis with T lesions [31, 38 and 39]. T lesion is associated with chronic process of disease and will help in prognosticating the IgAN. In our study, E1 lesion was associated with proteinuria compared to E0 lesion on biopsy but not associated with decrease in GFR. This is in accordance with a study by Miranda et al. [32]; however, other studies show significant association with decrease in GFR with E lesion [33, 35]. The possibility of response to treatment by patients with E lesion may have decreased significance in the fall of GFR. In our study, S lesion was significantly associated with decrease in GFR at the time of biopsy and at the end of follow up. S lesion was also associated with arterial hypertension. This was also seen in other studies where S lesion was significantly associated with decrease in GFR [33, 35 & 40].

On immunofluorescence study of biopsy, IgAN is associated with dominant staining of IgA with variable co-staining by IgM, IgA and C3. In our study, co-deposition with of IgA and C3 was seen in around 97%. C3 staining in other studies is around 90% [41]. IgM staining was more frequent than IgG. Moriyama et al. in a study demonstrated that the concomitant deposition of IgG and IgM would be associated with glomerular sclerosis and with the adherence of capillary tufts, however pathogenesis and significance of this finding needs to be demonstrated [42].

This retrospective study characterizes the clinical spectrum of IgAN and histopathology profile of the disease. This is the first study from this part of India (North-east). There is a need of registry of glomerulonephritis for better characterization

of the glomerular diseases especially IgAN from North-east India.

Conclusion

In our study, most cases of IgAN were seen in second and third decade of life. Microscopic hematuria with subnephrotic proteinuria was the most common presentation, however significant number of patients presented late in the form of nephrotic syndrome and advanced renal failure. M1, E0, S1 and T0 were the common lesions seen on biopsy. M, S and T lesions were associated with decreased GFR on follow up. There is an urgent need of screening for earlier diagnosis and treatment if IgAN from our place.

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References

1. Donadio JV, Grande JP. IgA Nephropathy. N Engl J Med 2002;347:738-48.
2. Berger J, Hinglais N. Les. Depotsintercapillariesd'IgAlgG. J UrolNephrol; 74:694-5, 1968.
3. Rifai A, Dworkin LD. IgA nephropathy: markers of progression and clues to pathogenesis. Kidney Int 2008;73:1338-40.
4. Emancipator S. IgA nephropathy and Henoch-Schönlein Syndrome. Heptintall's Pathology of the Kidney, vol. I. 2007; p. 479-539.
5. Glasscock RJ. Concluding remarks. ContribNephrol 2007;157:169-73.
6. Barbour SJ, Espino-Hernandez G, Reich HN, et al; The MEST score provides earlier risk prediction in IgA nephropathy. Kidney Int 89: 167-175, 2016
7. Riispere Ž, Laurinavičius A, Kuudeberg A, et al. IgA nephropathy clinicopathologic study following the Oxford classification: Progression peculiarities and gender-related differences. Medicina (Kaunas). 2016;52(6):340-8.
8. Jennifer C. Rodrigues, Mark Haas, and Heather N. Reich. **IgA Nephropathy** Clin. J. Am. Soc. Nephrol. 2017: CJN.07420716v2-CJN.07420716.
9. Working Group of the International IgA Nephropathy Network and the Renal Pathology Society, Roberts IS, Cook HT, Troyanov S, et al. The Oxford classification of IgA nephropathy: pathology definitions, correlations, and reproducibility. Kidney Int 2009;76:546-56.
10. Working Group of the International IgA Nephropathy Network and the Renal Pathology Society, Cattran DC, Coppo R, Cook HT, et al. The Oxford classification of IgA nephropathy: rationale, clinicopathological correlations, and classification. Kidney Int 2009;76:534-45.
11. Haas M, Verhave JC, Liu ZH, et al. A multicenter study of the predictive value of crescents in IgA nephropathy [published online ahead of print September 9, 2016]. J Am SocNephrol
12. Maixnerova D, Bauerova L, Skibova J, et al. The retrospective analysis of 343 Czech patients with IgA nephropathy – one centre experience. Nephrol Dial Transplant 2011;27:1492-8.
13. Le W, Liang S, Hu Y, et al. Long-term renal survival and related risk factors in patients with IgA nephropathy: results from a cohort of 1155 cases in a Chinese adult population. Nephrol Dial Transplant 2011;27:1479-85
14. Tanaka S, Ninomiya T, Katafuchi R, et al. Development and validation of a prediction rule using the Oxford classification in IgA nephropathy. Clin J Am SocNephrol 2013;8:2082-90.
15. Coppo R, Troyanov S, Bellur S, et al; VALIGA study of the ERA-EDTA Immunonephrology Working Group: Validation of the Oxford classification of IgA nephropathy in cohorts with different presentations and treatments. Kidney Int 86: 828-836, 2014
16. Haas M, Rastaldi MP, Fervenza FC. Histologic classification of glomerular diseases: clinicopathologic correlations, limitations exposed by validation studies, and suggestions for modification. Kidney Int 2014;85:779-93

17. Sharma M, Bordoloi P, Das HJ, Barman AK. Histopathological Pattern in Patients Presenting with Rapidly Progressive Renal Failure: A Single Centre Study. *Int J Med Res Prof.* 2016, 2(2); 150-53
18. Schwartz GJ, Munoz A, Schneider MF, et al. New equations to estimate GFR in children with CKD. *J Am SocNephrol* 2009;20:629–37
19. Das U, Dakshinamurthy KV, Prayaga A. Pattern of biopsy-proven renal disease in a single center of south India: 19 years' experience. *Indian J Nephrol* 2011;21:250-7.
20. Balakrishnan N, John GT, Korula A. Spectrum of biopsy proven renal disease and changing trends at a tropical tertiary care centre 1990-2001. *Indian J Nephrol* 2003;13:29-35
21. Golay V, Trivedi M, Abraham A, Roychowdhary A, Pandey R. The spectrum of glomerular diseases in a single center: A clinicopathological correlation. *Indian J Nephrol* 2013;23:168-75.
22. Siddappa S, Kowsalya R, Mythri KM. IgA nephropathy in a tertiary care center from south India. *Indian J Nephrol* 2011;21:230-4.
23. Das U, Daskshinamurthy KV, Prayaga A, Uppin M. Spectrum of IgA nephropathy in a single center. *Saudi J Kidney Dis* 2015 ; 26:1057-63
24. Woo KT, Edmondson RP, Wu AY, Chiang GS Pwee HS, Lim CH. The natural history of IgA nephritis in Singapore. *ClinNephrol* 1986;25:15- 21.
25. Nicholls KM, Fairley KF, Dowling JP, Kincaid-Smith P. The clinical course of mesangial IgA associated nephropathy in adults. *Q J Med* 1984; 53:227-50.
26. Goto M, Wakai K, Kawamura T, Ando M, Endoh M, Tomino Y. A scoring system to predict renal outcome in IgA nephropathy: a nationwide 10-year prospective cohort study. *Nephrol Dial Transplant* 2009;24:3068-74.
27. Li PK, Ho KK, Szeto CC, Yu L, Lai FM. Prognostic indicators of IgA nephropathy in the Chinese – clinical and pathological perspectives. *Nephrol Dial Transplant* 2002;17:64-9.
28. Riansuwan T, Kanjanabuch T, Lewsuwan S, Eiam-Ong S. Clinical characteristics and histopathological findings in 120 IgA nephropathy patients in Thailand. *J Med Assoc Thai* 2006;89Suppl 2:S163-7.
29. Schena FP. Survey of the Italian registry of renal biopsies. Frequency of the renal diseases for 7 consecutive years. The Italian Group of Renal Immunopathology. *Nephrol Dial Transplant* 1997;12:418-26
30. Rivera F, López-Gómez JM, Pérez-García R. Clinicopathologic correlations of renal pathology in Spain. *Kidney International* 2004;66:898-904.
31. Ibels LS, Györy AZ. IgA nephropathy: analysis of the natural history, important factors in the progression of renal disease, and a review of the literature. *Medicine* 1994;73:79-102.
32. NevesPrecil Diego Miranda de Menezes, Machado Juliana Reis, Silva Marcos Vinícius da, et al . IgA nephropathy: histological analysis and clinicomorfolological correlation in patients from Minas Gerais State. *J. Bras. Nefrol.* 2012 June 34(2): 101-108.
33. Kang SH, Choi SR, Park HS, *et al.* The Oxford classification as a predictor of prognosis in patients with IgA nephropathy. *Nephrol Dial Transplant* 2012;27:252-8.
34. Alamartine E, Sauron C, Laurent B, Sury A, Seffert A, Mariat C. The use of the Oxford Classification of IgA nephropathy to predict renal survival. *Clin J Am SocNephrol* 2011;6:2384-8.
35. Shi SF, Wang SX, Jiang L, LV JC, Liu LJ, Chen YQ. Pathologic predictors of renal outcome and therapeutic efficacy in IgA nephropathy: validation of the Oxford classification. *Clin J Am SocNephrol* 2011;6:2175-84.
36. Roufosse CA, Cook HT. Pathologic predictors of prognosis in immu-noglobulinA nephropathy: a review. *CurrOpinNephrol Hypertension* 2009;18:212–9.
37. Lee HS, Lee MS, Lee SM, *et al.* Histological grading of IgA nephropathy predicting renal outcome: revisiting H.S. Lee's glomerular

- grading system. Nephrol Dial Transplant 2005;20:342-8.
- 38.** D'Amico G. Natural history of idiopathic IgA nephropathy: role of clinical and histological prognostic factors. Am J Kidney Dis 2000;36:227-37.
- 39.** Donadio JV, Bergstralh EJ, Offord KP, Holley KE, Spencer DC. Clinical and histopathologic associations with impaired renal function in IgA nephropathy. Mayo Nephrology Collaborative Group. ClinNephrol 1994;41:65-71.
- 40.** Halling SE, Söderberg MP, Berg UB. Predictors of outcome in paediatric IgA nephropathy with regard to clinical and histopathological variables (Oxford classification). Nephrol Dial Transplant 2012;27:715-22.
- 41.** Okada K, Funai M, Kawakami K, Kagami S, Yano I, Kuroda Y. IgA nephropathy in Japanese children and adults: a comparative study of clinicopathological features. Am J Nephrol 1990;10:191-7.
- 42.** Moriyama T, Shimizu A, Takei T, Uchida K, Honda K, Nitta K. Characteristics of immunoglobulin A nephropathy with mesangial immunoglobulin G and immunoglobulin M deposition. Nephrology 2010;15:747-54.