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CLINICAL PROFILE AND SHORT TERM OUT COMES IN PATIENTS OF IGA NEPHROPATHY

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ABSTARCT

T*he long-term outcome of patients with 'IgA' nephropathy needs to be studied including the clinical spectrum and outcome. We studied 50 patients with biopsy-proven 'IgA' nephropathy (IF 2+) who had urinary abnormalities at the time of presentation, we attempt to optimize the clinical spectrum of the patients with 'IgA' nephropathy and analyze the short term outcome of the patients including progression to 'ESRD'. The mean age of the patient was 45.63±3.56 years (IQR 32-48 years) odd ratio was 4.86 years. Majority of the patients were in third decade with male preponderance p=0.023 statistically significant with age group of the population. Renal biopsy showed focal and diffuse mesangio proliferative glomerulonephritis in (22%) and (8%) respectively. Chronic glomerulosclerosis was seen in (58%).Cresentric GN in (28%). IFTA >50% was seen in 44% of patients. 'IgAN' is a very common primary glomerulopathy conventionally described as a slowly progressive disease eventually leading to 'ESRD' in 30–40% patients. However, it manifests more aggressively in Indian patients with a 10-year renal survival of only 35%, which is lower than the other studies.*

KEYWORDS: *Iga Nephropathy, ESRD, CKD: Chronic Kidney Disease*

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INTRODUCTION

The long-term outcome of patients with 'IgA' nephropathy needs to be studies including the clinical spectrum and outcome [6,14,13]. We studied 50 patients with biopsy-proven IgA nephropathy (IF 2+) who had urinary abnormalities at the time of presentation [6.10]. The natural history of 'IgAN' can range from clinically silent urinary abnormalities and preserved renal function (RF) over many decades to ESRD [6,13,10,5]. Erstwhile, the progression of ESRD occurs in 10-50% of patients, usually developing slowly over 20 years [6]. The modern approach to such proteinuric patients emphasizes rigorous blood pressure (BP) control [5,3,4].

An increasingly vigorous Blood pressure (BP) control has been recommended in recent years for 'IgAN' supporting the additional benefit of an angiotensin-converting enzyme (ACE) inhibitor on progressive renal disease (RD)

to achieve additional reduction in proteinuria despite equivalent BP control [5,13].Hence, the literature cited about, the clinical profile and short term outcome and measures to prevent the decline in 'GFR' and reduce the morbidity and mortality rate [10,11]. Since its initial description in '1968' by Berger *et al*, 'IgA' nephropathy has become the most common cause of glomerulonephritis worldwide [9,13]. An 'IgAN' is characterized and defined by the presence of mesangial IgA dominant immune complex deposition in the diagnostic renal biopsy[13]. This disease characteristically affects men more often than women, and although its onset can occur at any age group it peaks in the second and third decade of life [9, 14]. The clinical phenotype of 'IgAN' is highly varied, ranging from asymptomatic hematuria, to slowly progressive chronic kidney disease (CKD) associated with proteinuria, to rapidly progressive renal failure [9,14]. In Indian scenario, IgAN is the most common cause of end-stage renal disease amongst those aged 1 - 45 years with median age --- [15]. Treatments for 'IgAN' range from fish oil and medications that block the rennin-angiotensin system (RAS), to the more toxic immunosuppressant agents such as prednisone and cyclophosphamide[7,8].IgA nephropathy remains one of, if not the, most common glomerular lesion of all of forms of glomerulonephritis [13,14]. Initially described in the late 1960s by Berget et *al*, the disorder is characterized by the deposition predominantly of 'IgA' (and, to a lesser extent, of other immunoglobulin) in the mesangium with mesangial proliferation and with clinical features that span the spectrum from asymptomatic hematuria to rapidly progressive glomerulonephritis[11,12]. Although, it was previously considered a benign disease, it is not clear that up to 40% of patients may geometrically progress to ESRD, Moreover, it has become recognized that, in addition to an 'idiopathic' form of the disorder, IgA nephropathy is also correlated with a variety of disease processes in Indian accord [12,14] and also the pauscity of literature with varietal set of diseases process we attempt to study the clinical spectrum of the patients with IgA nephropathy and analyze the short term outcome of the patients including progression to ESRD.

METHODOLOGY

A prospective study was conducted at Department of Nephrology, Institute of Nephro-Urology, Victoria Hospital Campus Bangalore, India between February 2016 - 2018. The study was conducted in 50 patients with biopsy proven 'IgA' nephropathy. A total 50 consecutive biopsy proven 'IgA' nephropathy patients was considered for the study. The Institutional ethical clearance was obtained as per the regularity ethical guidelines.Written consent was obtained from all the patients and care taker's.All recruited patients were met following inclusion and exclusion criteria. Inclusion criteria; All patients who are willing to undergo evaluation and renal biopsy.

Biopsy proven IgA nephropathy. Exclusion criteria: patients who are not willing for evaluation and renal biopsy. Demographic profile and history of the patients was collected from pretested questionnaires. One way ANOVA and paired t test was employed to test the hypothetical results.

RESULTS

A total fifty patients considered for the study intervention. Out of which male comprises 64% and female comprises 36% respectively. The mean age of the patient was 45.63±3.56 years (IQR 32-48 years) odd ratio was 4.86 years. Majority of the patients were in third decade with male preponderance p=0.023 statistically significant with age group of the population. Hypertension is the most common clinical feature seen in 43 patients 86% p=0.022 Confidence interval CI 95% is 0.85-0.96,Odd 8.63,p=0.0121. Hypertension is the most common clinical feature seen in 43 patients 86% p=0.0118. Proteinuria(>500mg/day) in 86%, nephrotic range proteinuria in 20% p=0.122, pedal edema in 44% p=0.003, microscopic hematuria in 40% hematuria and macroscopic hematuria in 8% p=0.185 was seen at the time of

presentation with mean protection level of eGFR was less than 15ml/min/1.73sq m showed in 38% of patients p=.

Table 1: Distribution of Clinical Presenting Features (N=50)

Sl	Presenting Feature	%	Weighted Odd Ratio	P-Value
01	Hypertension	86	11.25	0.001
02	Nephritic syndrome	24	2.45	0.108
03	Nephrotic range proteinuria	20	2.52	0.122
04	RPGN	28	3.02	0.142
05	microscopic hematuria	40	10.45	0.003
06	gross hematuria	08	1.10	0.185

***Significant at 51% Level p ≤0.01**

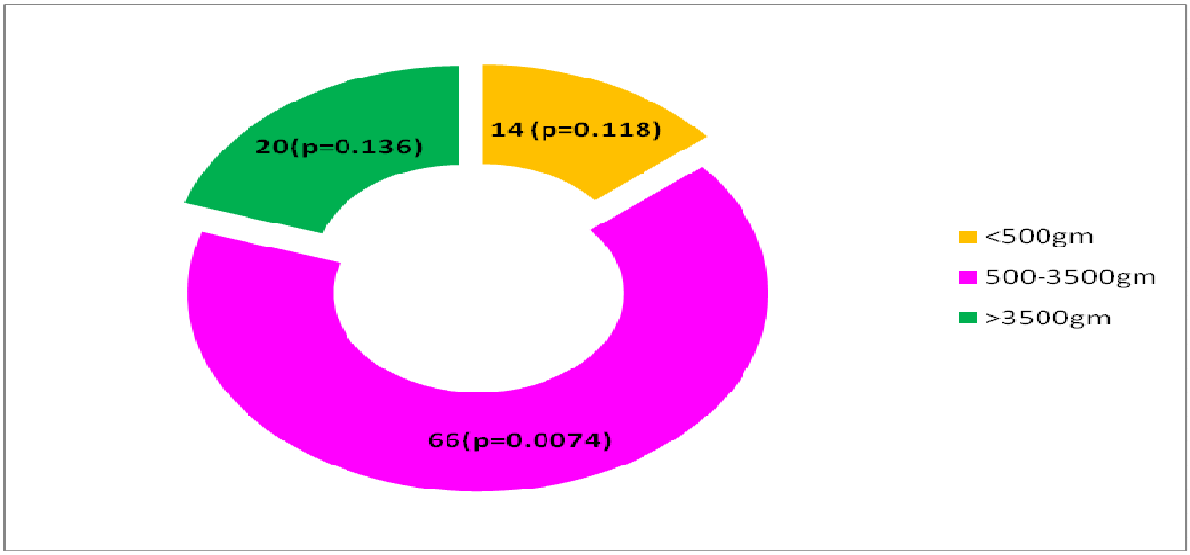

Figure 1: Distribution of Proteinuria among Recruited Patient's

Table 2: eGFR Presentation during the Study Period (N=50)

Egfr	Baseline	Maximum Likelihood	P-Value
>90	04(8%)	0.12	0.72
60-90	00(0%)	-	-
30-60	12(24%)	1.35	0.086
15-30	15(30%)	1.63	0.072
<15	19(38%)	1.79	0.042
Total	**50(100%)**		

Renal biopsy showed focal and diffuse mesangio proliferative glomerulonephritis in (22%) and (8%) respectively. Chronic glomerulosclerosis was seen in (58%).Cresentric GN in (28%). IFTA >50% was seen in 44% of patients presented in Table (2).

Table 3: Correlation of Histopathological Findings (N=50)

Sl	Histopathological Findings	No	Weighted Odd Ratio	P-Value
01	Normal Light microscopy	06	0.98	0.2869
02	Focalendocapillary proliferation	11	3.45	0.0211
03	Diffuse endocapillary proliferation	04	0.32	0.6323
04	Mesangial hypercellularity	18	4.02	0.0028
05	Chronicglomeruloscerosis	29	5.22	0.0001
06	Crescents	14	3.89	0.0189
07	IFTA >50%	22	4.89	0.0002

Table 3 showed that, the histopathological findings were correlated with nephropathic findings who showed elevated range of eFGR, asper the resulted findings the weighted odd ratio of normal light microscopy was found to uncorrelated (odd ratio 0.98 p>0.05) when compared Focalendocapillary proliferation (odd ratio 3.45 p=0.0211), Mesangial hypercellularity (odd ratio 4.02 p=0.0028), Chronicglomeruloscerosis (odd 5.22 p=0.0001), Crescents odd ratio (3.89 p=0.0189) and IFTA >50% (odd ratio 4.89 p=0.002)

Table 4: Distribution and Significance of 'IFTA' (N=50)

Ifta	Range				Total (N=50)	P-Value
	>90 (N=4)	30-60 (N=12)	15-30 (N=15)	<15 (N=19)		
Nil	3(75%)	4(33.3%)	1(6.7%)	0(0%)	8(16%)	<0.001**
<25	1(25%)	4(33.3%)	6(40%)	3(15.8%)	14(28%)	
25-40	0(0%)	0(0%)	4(26.7%)	2(10.5%)	6(12%)	
>40	0(0%)	4(33.3%)	4(26.7%)	14(73.7%)	22(44%)	

Table 4 revealed that the range of IFTA was analysed by using R statistical software, all collected data was edited and data transformation were done in Med calculator 2014 on line version. The Univariate analysis was employed to test the significance level with respect to 'eGFR', Asper the analysis the range was splitted >90,36-60,15-30 and <15 respectively. The 'IFTA' matched frequency was correlated the range value of 'eGFR'.The analysis showed 'no' IFTA was seen in 8 cases (16.0%), <25 IFTA was seen in 14(28%), between 25-40 was seen only in 06 (12%) cases and >40% IFTA was seen in 22 (44%) respectively. Moreover, the cumulative frequency is matched with range value eGFR,Many Indian literature cited IFTA was significantly p<0.01 associated with elevated 'eGFR' value and results were apparently statistically significant p=0.001 in relation to elevated range of 'eGFR' irrespective of gender categorical variable Table 4

DISCUSSIONS

'IgAN' is a very common primary glomerulopathy conventionally described as a slowly preogressive p<0.01 disease eventually leading to ESRD in 30-40% patients p<0.01. However, it manifests more aggressively in Indian patients with a 10 year renal survival of only 35%, which is lower than what is reported in other Asian and Caucasian populations reported by Schwartz G j e*t al*., Hematuria and subnephrotic proteinuria are more common presentations of 'IgA' nephropathy compared to NRP/NS. However, edema with NRP was the predominant presenting feature of patients in our study.This may be a selection bias as in the absence of a screening program in India, patients who were symptomatic due to significant proteinuria p<0.01 are more likely to come to the renal clinic and consent to a kidney biopsy compared to those who have isolated microscopic hematuria p<0.01, episodic gross hematuria p<0.01, or mild proteinuria. Typically, in developed countries which have screening strategies like Singapore and Japan have reported not only a very high incidence of 'IgAN' but also a very high proportion of patients with minimal or no symptoms.There was no significant difference p<0.01 in the clinical and 'MEST' chaaracteristics of the patients presenting with NRP compared to those who had sub-nephrotic proteinuria in our study except that the patients with NRP had better baseline renal function (eGFR). Our study shows a comparison of our cohort with other study populations conducted in Oxford. The findings was concealed a cohort 16 in terms of age (28.8 years vs. 30 years, respectively) and gender distribution (73.8% vs. 72% males, respectively). The mean proteinuria was higher p<0.01 in our study compared to the Oxford cohort (3.8 g vs.1.7 g/24 h, respectively) and other study populations Shima Y *et al*. reported that, an excluded patients with eGFR less than 30 mL/min, whre as in our study had 16.5% patients in this cartegory. Katafuchi R *et al*. reported had 13.6% eGFR, Katafuchi *et al* had reported 4% and the VALIGA cohort 22 had 9% patients with e GFR less than 30 mL/min respectively. Other studies had shown that a

large proportion of Indian patients with IgA nephropathy have significant renal p<0.01 dysfunction at the time of biopsy; however, renal failure has not been well defined in these studies reported by Katafuchi R et al. The distribution of histopathologic lesions in our study cohort was uniquely different from other aged populations p<0.01. The high proportion of patients with mesangial hypercellularity similar to the Oxford cohort but significantly higher p<0.01 than the VALIGA cohort 22 and the studies in Japanese and Chinese populations. Endocapillary hypercellularity, crescents and segmental glomerulosclerosis were less comon in our patients and proportion of tubulointerstitial lesions were similar compared to other studies from Asia. The other Indian study reported by Mittal *et a*l. he applied the Oxford criteria to kidney biopsies of 'IgAN' patients has also reported a similar proportion of mesangial hypercellularity and segmental glomerulosclerosis. However, we compared to our patient cohort, their study had higher proportion of endocapillary proliferation p<0.01 (9.7% vs.29.6%) and crescentic. (10.7% vx. 56.6%) p<0.01 lesions as well as very high percentage of tubular atrophy/interstitial fibrosis (39.8% vs. 74.2%) p<0.01. Lee MJ et al. reported that majority of their patients presented with renal failure (not defined) and NRP was less common, which could explain this difference in the satandard MEST score pattern. Walsh M et al. he analyzed 478 patients with IgAN and reported nephrotic syndrome in 55% their study also showed less crescentic lesions.

CONCLUSIONS

In summary, the present study showed that an increasing crescent proportion in IgAN was independently associated with unfavorable outcomes, even after adjusting for clinical factors and Oxford-MEST pathological parameters.IgAN is a very common primary glomerulopathy conventionally described as a slowly progressive disease eventually leading to ESRD in 30-40% patients, it manifests more aggressively in Indian population.However, the patients were expressed ESRD between 30-40% intact who referred to tertiary Government care centre at later stage,As it could be intrevened larger population study eventually correlate the accurate findings and research gap.

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