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Clinical Profile and Outcome in Patients with IgA Nephropathy

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Abstract: ***Aim: To evaluate clinical profile and outcome in a patients with IgA nephropathy. Methods: 989 patients with hematuria and proteinuria admitted in institute of kidney disease between jan 2002 to2004. Patients diagnosed to have IgA nephropathy included in study. The biopsy specimen examined for IF and histopathology. Patients were followed up for 6 to 15 month for outcome. Results: Maximum number of patients between 11 to 30years (28%). Male to female ratio is 2.1:1. Episodic hematuria (52%), edema (80%), and proteinuria (60%) are common presenting complains. Biopsy shows MPGN (38%) and Cresentric GN (24%) commonly. Hypertension is the most common complication (80%). Patients with cresentric glomerulonephritis deteriorated (24%). Conclusion: IgA is commonest primary glomerulonephritis. We can diagnose patients early by screening patients with hematuria and proteinuria. As there is no specific treatment available for IgA nephropathy meticulous control of blood pressure and judicious use of steroids and cytotoxic therapy may help to post pone dialysis and transplantation.***

Keywords: IgA Nephropathy, Primary Glomerulonephritis, Cresentric Nephropathy, hematuria, proteinuria

1. Introduction

Immunoglobulin A nephropathy is the most common primary glomerulonephritis on a worldwide basis. [(1)] It is characterized by glomerular deposits of IgA predominantly in the mesangial areas. [(2).] It was first reported by Berger et al at Third International congress of nephrology in Washington in 1966. IgA nephropathy has great degree of geographical variation in terms of incidence. It has been reported as low as 2% to as high as 52% in various part of the world [(3,4)]. It occurs in both primary (idiopathic) and secondary forms. Clinically, in most of the cases, it is presented as recurrent episodes of macroscopic hematuria, persistent microscopic hematuria with mild to moderate proteinuria.

2. Aim

To study clinical profile and outcome in patients with IgA nephropathy.

3. Material and Methods

This study is an evaluation of 989 patients admitted with hematuria and proteinuria in Institute of Kidney Diseases and Research Centre during the period of Jan. 2002 to Aug. 2004. Renal biopsies were done in all patients. Only those patients who were diagnosed to have predominantly IgA mesangial deposits on immunofluorescent microscopy were considered for the study. For study they were followed for evaluation of response to treatment. Patients were followed for a minimum of six months to more than 32 months when required in terms of improvement, stabilization or deterioration as per standard definitions. Complications and result of the treatment were recorded. Ultrasound guided, percutaneous renal biopsy was carried out in every patient .. The specimen was subjected to histopathological examination (H&E, PAS, silver and Gomori's trichrome staining) and Immunofluorescent study with anti-human IgG, IgM, IgA, C3, C1q. Patients were followed for a minimum period of 6 months to more than 15 months when required in terms of improvement, stabilization or deterioration as per standard definitions. Complications due to therapy were recorded. Detailed history, clinical examination, investigation, management and follow up were done according to proforma.

4. Results and Discussion

Out of these 989 renal biopsies 61 patients (6.2%) had IgA Nephropathy. This rate of prevalence correlate with Indian study by Bakshi et al(4.2%) Maximum patients between 21-30 years (36.7%) with male to female ratio 2.1:1. Time of presentation is maximum 5 years.(28%) after onset of symptoms.. In our study edema and hypertension share common presenting feature (80%).Oliguria (66%) . and altered creatinine (66%) are also common features . Hematuria was present in 26 patients (5%).

Table 1: Age Incidence in 50 Cases of IgA Nephropathy:

	Present study		Akio Koyama et al, Japan	
AGE	*No. of patients*	*%*	*No. of patients*	*%*
<10	2	4%	23	4.7%
11-20	14	28%	97	20%
21-30	14	28%	178	36.7%
31-40	12	24%	129	26%
41-50	6	12%	40	8.3%
51-60	2	4%	13	2.7%
61-70	0	0%	5	1%
TOTAL	**50**	**100%**	**485**	**100%**

Here 11 patients lost to follow up, so not included in present study.

In present study IgA Nephropathy affect almost all age group population, with minimum age at 6 years to maximum age at 54 yrs. Highest number of patients were observed in second and third decade (28%) and minimum incidence was found in age group of 51 to 60(4%), mean age was28.8yrs +/- 12.4 yrs. In the study from Japan by Akio Koyama et al, shows same age incidence as present study.

In the present study majority of the patients were male, and male: female ratio being 2.1:1 found. Similar result was

found in Christian et al study with male: female ratio is 2.8:1. [6]

Review of all 50 cases of IgA Nephropathy with adequate tissue revealed a wide spectrum of glomerular disease and findings are summarized in following table:

Table 2

Histology	*No of patients*	*%*
Minimal change disease	1	2
Focal- segmental glomerulosclerosis	4	8
Membranoproliferative glomerulonephritis	4	8
Endocapillary GN	1	2
Mesangio proliferative glomerulonephritis	19	38
Crescentic GN	12	24
Membranous nephropathy	2	2
CGN	7	14
Total	50	100

Histologically the patients revealed a wide spectrum of glomerular lesions ranging from minimal changes to crescentic glomerulonephritis. Overall the commonest glomerular pattern was of mesangioproliferative GN with 19(38%) cases. A significant high incidence of Crescentic GN was noted in 12 patients (24%). This may be because of the fact that our centre is referral centre for whole Gujarat for kidney diseases, so high risk renal patients reach to referral centre. Similarly in Bakshi et al, study mesangioproliferative GN was the commonest pattern. [8] MPGN was found in 4 patients (8%) along with IgA.

Table 3: Presenting features of IgA Nephropathy

Presenting features		*Present Study (N=50)*	*S. Muzaffer et al, Pakistan*
Hematuria	Microscopic	26(52%)	4(40%)
	Macroscopic	13(26%)	2(20%)
Proteinuria ≥ 3gm/d		9(18%)	2(20%)
Proteinuria ≤ 3gm/d		30(60%)	2(20%)
Edema		40(80%)	1(10%)
Oliguria		33(66%)	-
Hypertension		40(80%)	2(20%)
Abdominal pain		7 (14%)	1(10%)
Skin rash		3(6%)	1(10%)
Altered Renal function i.e S. cre.> 1.2mg/dl		30(60%)	3(30%)

Hematuria is the most common and consistent manifestation of IgA Nephropathy and was seen in 39 patients (78%). Episodic gross hematuria and persistent microscopic hematuria occurred in approximately 13(32.4%) and 26 patients (67.6%) respectively, in the present study. In Muzaffer et al study hematuria was found in 60% 0f the patients as a presenting feature [9].Oliguria was found in 33 patients (66%). 40 patients (80%) had hypertension and required one or more anti-hypertensive drugs. Non nephrotic range of proteinuria was found in 30 patients (60%). Out of them 10 patients (20%) had mild edema at presentation. In this study 9 patients (18%) presented with nephrotic syndrome, which was unusually seen in the patients with IgA nephropathy.

Altered renal function (s. creatinine > 1.2mg/dl) was found in 30 patients (60%)

Mesangioproliferative GN was the commonest histological finding and found in 19 patients (38%). An unusual feature was noted in present study, that is high incidence of severity of clinical presentation and high incidence of Crescentic GN, 12 cases (24%) were found on histology. FSGS with IgA deposits was noted in 4 patients (8%).

20 patients (40%) with normal renal function (s. creatinine < 1.2 mg/dl) and proteinuria of < 1gm/d were kept under observation and no specific treatment was given.

Anti-hypertensive therapy was required in 40 patients (80%). 21 patients (52.5%) had hypertension at the time of presentation but during follow up period another 19 patients (47.5%) developed hypertension. All patients with MPGN, 4 patients (8%) on histology were given antiplatelet agent (aspirin+ dipyridamole) in addition to antihypertensive agents. Infections, as and when occurred were treated with antibiotics during follow up.

9 patients (18%) with proteinuria > 3gm/d, mild glomerular changes and presented with normal renal function (S.cre ≤1.2mg/dl.) were treated with oral steroid. Out of them 8 remain stable during mean follow up period of 13 months (7—26months). One patient progressed to ESRD. 12 patients (24%) presenting with RPGN like features were treated with three doses of bolus steroid followed by oral steroid with oral cyclophosphamide. Out of them 2 patients improved and 2 remained stable (dialysis free). Eight patients did not improved and they required renal replacement therapy. However only five underwent renal transplantation after waiting period of 6 months and 3 remained on maintenance hemodialysis. 9 patients (18%) with progressive deterioration of renal function were treated with fish oil in addition to steroid, antiplatelet agents and anti-hypertensive drugs.

Table 4: Outcome of the patients with IgA Nephropathy:

	MCD	MePGN	MN	FSGS	MPGN	CRESCENT
Stable	1	12	2	0	2	0
Improved	0	7	0	3	0	4
Deteriorated	0	0	0	1	2	8
Total	1	19	2	4	4	12

Patients who had glomerular lesion like Mesangioproliferative GN, minimal change disease or membranous nephropathy, had normal renal function and remained stable during the follow up period. Twelve patients who had Crescentic GN were treated with prednisolone bolus with cyclophosphamide. All the patients with crescents required dialysis at the time of presentation. Out of 12 crescentic patients 4 became dialysis free after bolus treatment. 5 patients underwent renal transplantation, while three remained on maintenance hemodialysis. .

Total 18 patients (36%) progressed to ESRD and required renal replacement therapy.

Table 5: Demographic data for transplant patients:

		No.
Men/ Women		6/1
Duration of dialysis— Pre transplant		15.14m ±7.47
Mean age of Transplant		29.71±10.49
Kidney source	Cadaver	0
	Live related	6
	Live un related	1

Seven patients (M: F=6:1) underwent renal transplant had biopsy proven IgA Nephropathy . All patients with crescents with IgA were compelled to wait for 6 months before transplantation. Mean age at transplantation was 29.7 yrs. All the patients were transplanted with live donor. Six patients were transplanted with live related donor and one had live unrelated donor.. The majority of the patient received triple immunosuppressive therapy consisting CyA, steroid and MMF/ azathioprine

5. Summary

True prevalence of IgA nephropathy may be higher than reported incidence, because we are missing asymptomatic patients in general population. The commonest age of the patients with IgA Nephropathy was 21 to 40 years. with male to female ratio of 2.1: 1.Hematuria is the most common and consistent manifestation of IgA nephropathy.

There could be wide spectrum of histological findings in association with IgA nephropathy, though mesangioproliferative GN being the commonest Contrary to given impression that IgA nephropathy is slowly progressing and indolent illness our experience shows RPGN was also quite common .Early altered renal function is an important warning sign of renal progression..

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Abbreviations

ACE	Angiotensin converting enzyme
ARB	Angiotensin receptors blockers
CGN	Chronic glomerulonephritis
CRF	Chronic renal failure
CT	clotting time
ESR	Erythrocyte sedimentation rate
ESRD	End stage renal disease
FSGS	Focal segmental glomerulosclerosis
HIV	Human immuno deficiency virus
HPE	Histopathological examination
IF	Immunofluorescent
MCD	Minimal change disease
MePGN	Mesangioproliferative glomerulonephritis
MPGN	Membranoproliferative glomerulonephritis
PAS	Per-iodic acid Schiff
PT	Prothrombin time
RFT	Renal function test
RPGN	Rapidly progressive glomerulonephritis
SGPT/ALT	Serum alanine aminotransferase
URTI	Upper respiratory tract infection