



Clinico-Epidemiological Profile of Primary IgA Nephropathy – An Institutional Experience in South India

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Abstract

Background: *IgA nephropathy is the most common primary glomerulonephritis worldwide. Prognosis depends on the class of IgA nephropathy. There are only few studies to document the prevalence or clinicopathological spectrum of Primary IgA nephropathy in India.*

Objectives: *To study the clinic-epidemiological profile of primary IgA nephropathy.*

Methodology: *The study included renal biopsies diagnosed to have primary IgA nephropathy, received by the Department of Pathology, St. John's Medical College, Bangalore during a period of 10 years from January 2004 to December 2013. The study was both retrospective ((January 2004 to April 2012) and prospective (May 2012 to December 2013). The clinical data and laboratory findings were retrieved from the Medical Records Department of St. John's Medical College & Hospital, Bangalore in all cases. The histological sections were reviewed along with the immunofluorescence findings and the relevant clinical data was analysed*

Results: *Out of 123 cases studied, age group ranged from 4 years to 70 years with the largest incidence in the 20 – 30 years age group (35%) and an average age of 32.74 years, males predominated (70.7%) with a male: female ratio being 2.4:1. Hypertension was found in 48(39%) cases, hematuria in 53(43%) cases and proteinuria in 51(42%) cases.*

Summary and Conclusion: *The incidence of IgAN was 2.4 times more common in males than in females. Haas class IV was the most common class. Hematuria was the most common clinical presentation. This study necessitates for early intervention strategies as well as screening programmes, not only to identify and treat the patients, but also for a better understanding of the factors which lead to this rapid and early progression.*

Keywords: *IgA nephropathy, Haas classification, hematuria, proteinuria.*

Introduction

IgA nephropathy is the most common primary glomerulonephritis worldwide¹. It is defined as

IgA dominant or co-dominant mesangial deposits excluding lupus nephritis². Prognosis depends on the class of IgA nephropathy. The prevalence of

IgA nephropathy among glomerular diseases and its incidence in the general population show considerable variation among geographic regions. A higher incidence is noted in Asian countries including India. In Asia, Singapore³, Japan⁴ and China⁵ have a very high prevalence of IgA nephropathy. The prevalence of IgA nephropathy in India varies with geographical regions. IgA nephropathy has been reported in all age groups with a peak incidence in the second/third decade of life with a higher prevalence in males⁶

The exact pathogenesis of the disease is unknown. The current hypothesis is that mucosal antigenic exposure in genetically susceptible individual results in the generation of nephritogenic IgA antibodies that form complexes in the circulation and get deposited in the glomeruli leading to glomerular injury. The pathogenetic mechanism involved could be the production of an abnormal IgA1 with the subsequent generation of IgG and probably IgA1 antibodies directed against this. IgA-Immune complex formation may then occur either within the circulation or in situ within the glomerulus and results in mesangial cell activation and glomerular injury⁷.

IgA nephropathy can occur in individuals of virtually any age, from young children to the elderly but occurs most commonly between the ages of 10 and 40 years⁸. Most studies show a male predominance, with an overall average male: female ratio of approximately 2:1⁹. The two major clinical presentations of primary IgA nephropathy are asymptomatic urinary abnormalities and macroscopic hematuria, the former being more common in adults and the latter in children¹⁰. Hypertension is noted in approximately 25% of patients at presentation¹⁰.

Most patients with IgA nephropathy present with some degree of proteinuria. Proteinuria is often mild, and nephrotic range proteinuria is relatively uncommon. The frequency of renal insufficiency at the time of initial presentation or diagnosis likewise varies between different studies. Many clinical parameters and laboratory findings have been reported to correlate with clinical outcomes

in patients with IgA nephropathy. Reduced GFR (or elevated serum creatinine), severe proteinuria (defined in different studies as greater than 1 g/day, at least 2 g/day, at least 3 g/day, or nephrotic range), and hypertension were each found to be independent predictors of progression to end-stage renal disease (ESRD).

This study is being done to build up on the data on the clinico-epidemiological profile in Primary IgA nephropathy. There are only few studies to document the prevalence or clinicopathological spectrum of Primary IgA nephropathy in India.

Objectives

To study the clinic-epidemiological profile of primary IgA nephropathy.

Materials

This study included renal biopsies diagnosed to have primary IgA nephropathy, received by the Department of Pathology, St. John's Medical College, Bangalore during a period of 10 years from January 2004 to December 2013. The study was both retrospective ((January 2004 to April 2012) and prospective (May 2012 to December 2013). The clinical data and laboratory findings were retrieved from the Medical Records Department of St. John's Medical College & Hospital, Bangalore in all cases. The histological sections were reviewed along with the immunofluorescence findings and the relevant clinical data was analysed.

Methods

Selection of cases

Inclusion criteria

- 1) Confirmation by direct immunofluorescence of at least 2+ positivity with IgA antiserum, with IgA being the dominant or the co-dominant immunoglobulin deposited.
- 2) Availability of at least 5 glomeruli (light microscopy + immunofluorescence) for evaluation.

Exclusion Criteria

- 1) Exclusion of other systemic diseases which can affect/alter the morphology- for example, systemic lupus erythematosus, diabetes mellitus, etc
- 2) Exclusion of secondary causes of IgA nephropathy, such as Henoch Schonleinpurpura, liver diseases.

Clinical and laboratory data

The age, sex, clinical presentation (hypertension, hematuria & proteinuria) were collected/retrieved from the records and the data was tabulated.

Results

The study group included 123 cases that fulfilled the inclusion criteria

Age Distribution

The study group had a wide range of age, ranging from 4 years to 70 years with the largest incidence in the 20 – 30 years age group (35%) and an average age of 32.74 years. (Table 1, Table 2 & Fig 1)

Table 1: Age at presentation of the cases

	N	Minimum	Maximum	Mean	Median
Age (years)	123	4	70	32.74	36

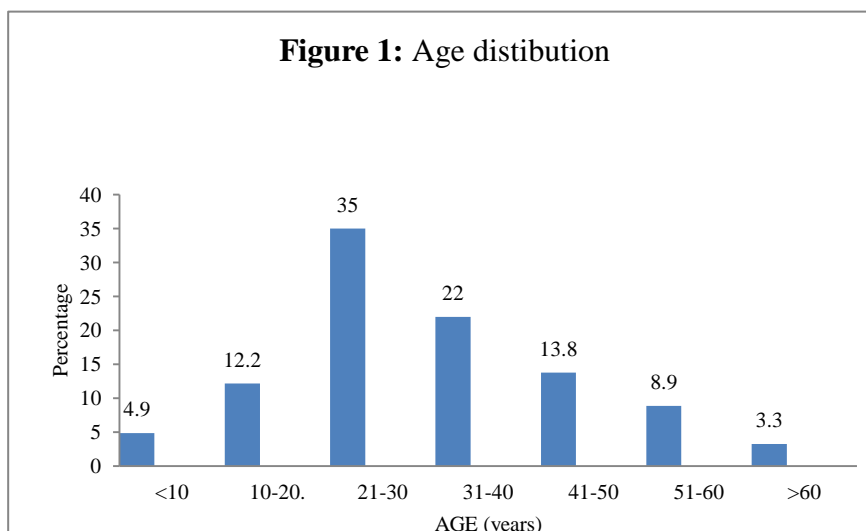
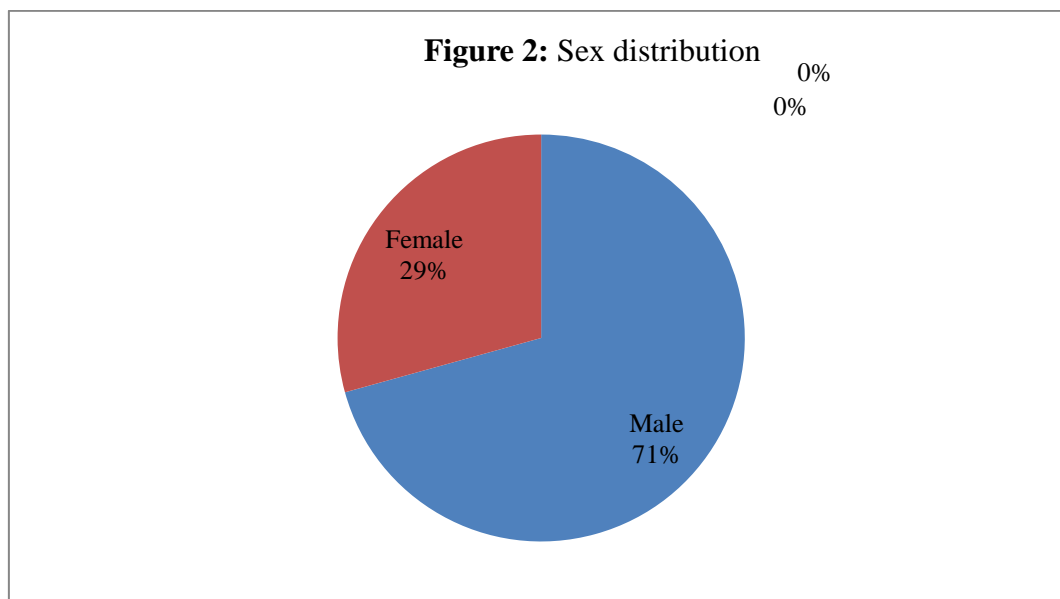


Table 2: Age distribution in various classes

HAAS CLASS	Age (in years)							Total
	<10	10-20	21-30	31-40	41-50	51-60	>60	
	4	4	13	4	4	3	2	34
II	0	0	1	0	0	1	0	2
II	0	0	4	4	1	2	0	11
I	2	10	11	13	9	1	2	48
V	0	1	14	6	3	4	0	28
Total	6	15	43	27	17	11	4	123

Sex Distribution

Out of the 123 cases studied, males predominated (70.7%, n=87) with a male: female ratio being 2.4:1 (fig 2)



Clinical and Laboratory Features

Among the three parameters (hypertension, hematuria and proteinuria) studied, hypertension was found in 48(39%) cases (Fig 3), hematuria in 53(43%) cases (Fig 5) and proteinuria in 51(42%) cases (Fig 7).Among the various classes of IgAN,

hypertension was commonly seen in Class V (82%) (Fig 4), hematuria was commonly seen in Class IV (62.5%) (Fig 6) and proteinuria was commonly seen in Class V (53.5%) (Fig 8). Combination of hematuria and proteinuria was the most combined clinical presentation (Fig 9).

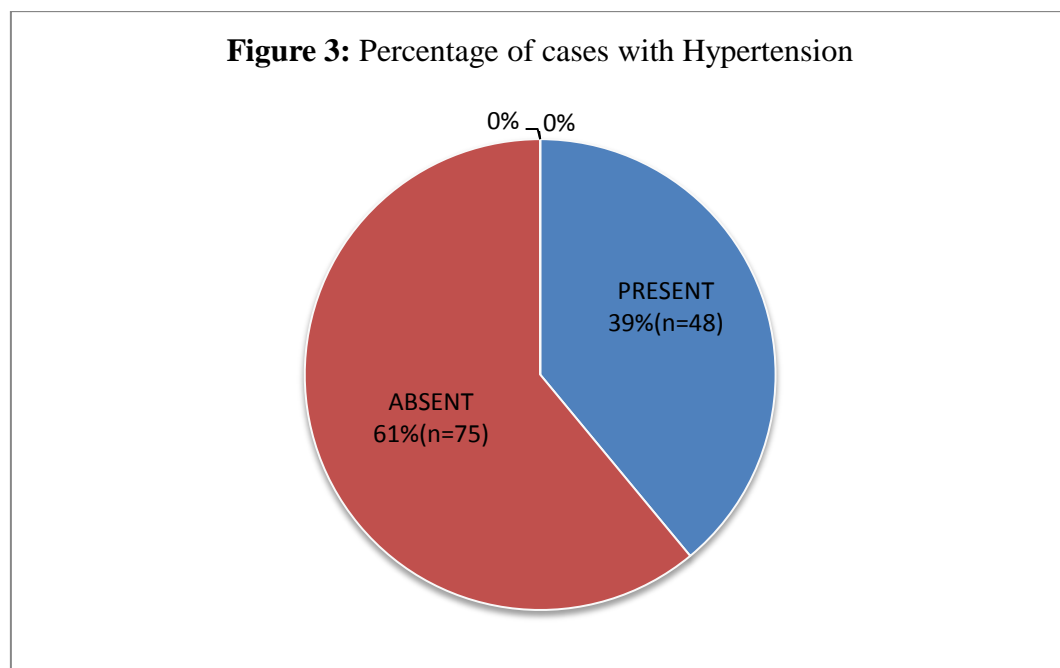


Figure 4: Hypertension among various classes of IgAN

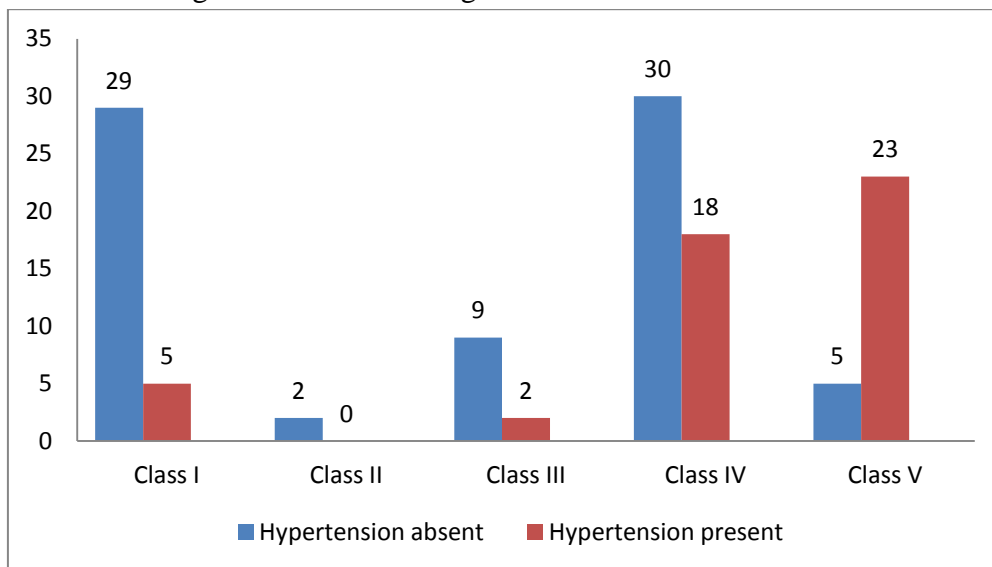


Figure 5: Percentage of cases with Hematuria

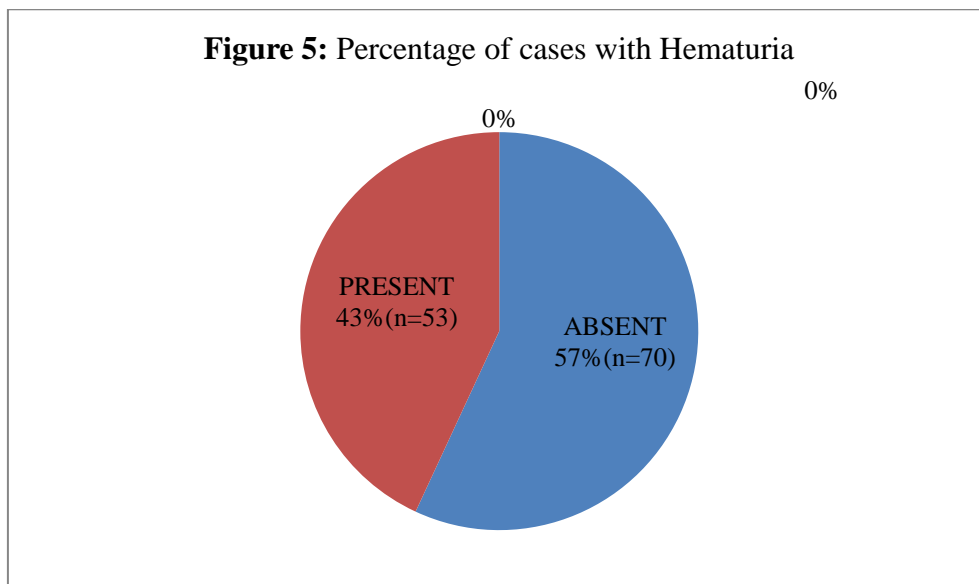
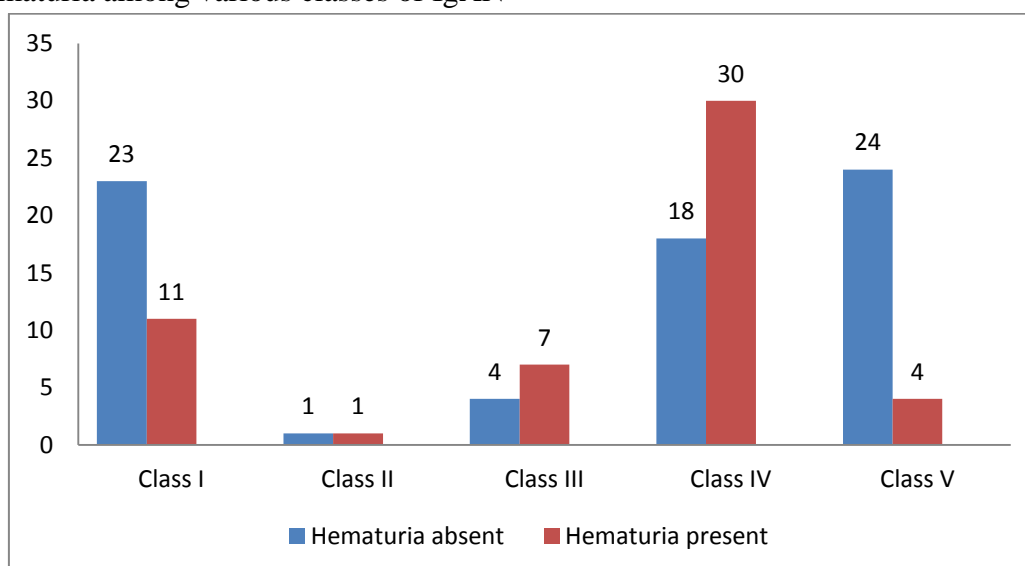


Figure 6: Hematuria among various classes of IgAN



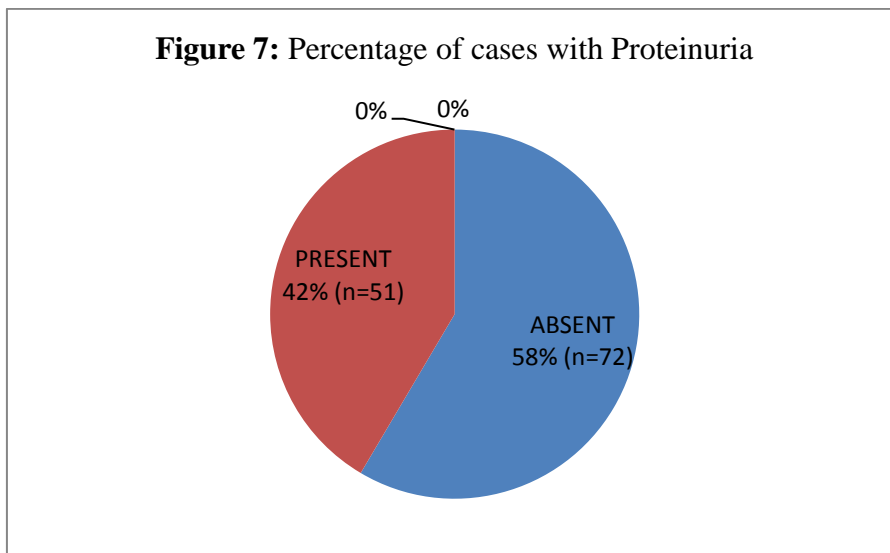


Figure 8: Proteinuria among various classes of IgAN

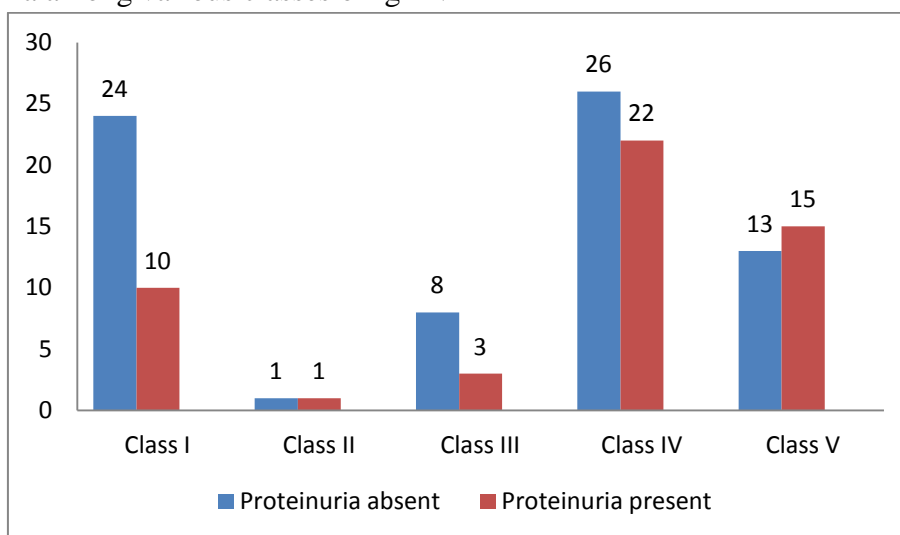
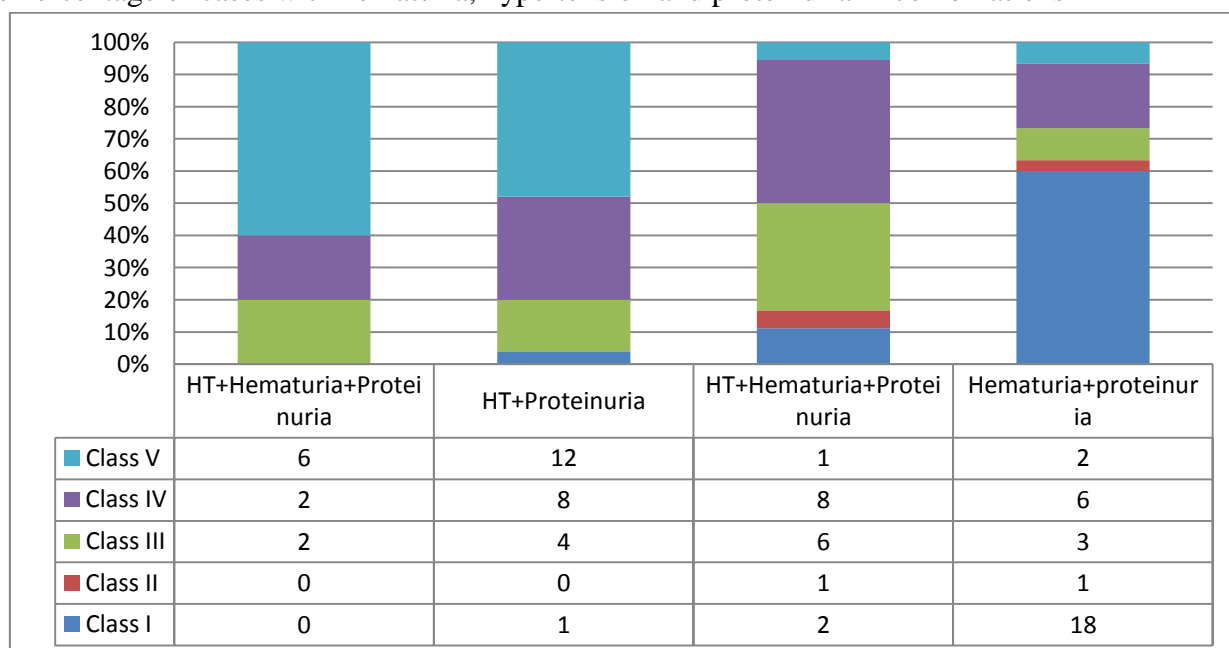


Fig 9: Percentage of cases with hematuria, hypertension and proteinuria in combinations



Discussion

123 cases of Primary IgAN have been studied during the 10 year period at St. John’s Medical College & Hospital, Bangalore. These cases were analysed with respect to their clinical presentation and immunological and morphological features based on Haas classification of IgAN.

Age: The study group had a wide range of age, ranging from 4 years to 70 years with the largest incidence in the 20 – 30 years age group (35%) and an average age of 32.74 years which is in concordance with other Indian studies^{11,12,13} which is atleast 5 to 6 years younger than the values quoted in the western literature.

Sex: Out of the 123 cases studied, males predominated (70.7%, n=87) with a male: female ratio being 2.4:1 which is in concordance with other Indian studies by Vanikar et al¹⁴, Chako et al¹³ and slightly higher male predominance was reported by Mittal et al¹³ and other western studies by Haas et al¹⁷.

Clinical and laboratory features: Among the three parameters (hypertension, hematuria and

proteinuria) studied, hypertension was found in 48(39%) cases, hematuria in 53(43%) cases and proteinuria in 51(42%) cases .Hypertension was found in 39% of cases which is in concordance with study by Meraet al¹⁵ (42%). A higher incidence of hypertension was reported by Chakoet al¹³ (58%), Mittal et al¹¹ (78.8%) and Haas et al¹⁷ (50%). Hematuria was found in 43% of cases which is in concordance with study by Chandrikaet al¹² and Koyama et al¹⁶ (49%). A higher incidence was found in studies by Chako et al¹³ (69%), Mittal et al¹¹ (81%) and Haas et al¹⁷ (100%). Proteinuria was found in 42% of cases which is in concordance Koyama et al¹⁶ (40.6%), Haas et al¹⁷ (36%) and Chandrika et al¹²(36.7%). A higher incidence of was found in study by Chakoet al¹³ (55%) and a lower incidence was found in studies by Mittal et al¹¹ (23.1%) and Koyama et al¹⁶ (11%).Among the various classes of IgAN, hypertension was commonly seen in Class V (82%) hematuria was commonly seen in Class IV (62.5%) and proteinuria was commonly seen in Class V (53.5%).

Table 3: Comparison of demographics, laboratory and histopathological findings with different Indian study groups

	Present study	Mittal et al ¹¹	Chako et al ¹³	Chandrika et al ¹²	Vanikar et al ¹⁴
Mean age (years)	32.74	29.9	32	3 rd decade	
Male: female ratio	2.4:1	4.4:1	1.85:1	1.5:1	2.6:1
Hypertension (%)	39	78.8	58	3.5	-
Haematuria (%)	43	81	69	49.3	100
Proteinuria (%)	42	23.1	55	36.7	-
Most frequent class	IV	V		II	II

Table 4: Comparison of demographics, laboratory and histopathological findings with different Western study groups

	Present study	Haas et al ¹⁷	Mera et al ¹⁵	Koyama et al ¹⁶
Mean age (years)	32.74	39.1	35.4	
Male: female ratio	2.4:1	5.6:1	0.86:1	1.23:1
Hypertension (%)	39	50	42	
Haematuria (%)	43	94	100	49.4
Proteinuria (%)	42	36	11	40.6
Most frequent class	IV	III		IV

Conclusions

To summarize IgA nephropathy is a disease of men in their mid 30s, which has a nephritic-nephrotic presentation and is morphologically a proliferative glomerulopathy, which is also the presentation in our study but with a higher incidence of advanced sclerosis. This is a finding of the utmost importance as a direct implication is that our patients are barely amenable to any form of therapy when they reach the hospital. This calls for early intervention strategies as well as screening programmes, not only to identify and treat the patients, but also for a better understanding of the factors which lead to this rapid and early progression. Geographical variation, genetic factors and biopsy practice also play an important role in the prevalence of IgA nephropathy. Various incidence of clinical presentation, laboratory features and histopathological findings as suggested by various studies depend on the geographical variation, genetics and biopsy practice.

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