Original Research Article

Journal of College of Medical Sciences-Nepal, Vol-20, No.4, Oct-Dec 2024

ISSN: 2091-0657 (Print); 2091-0673 (Online) Open Access

DOI: 10.3126/jcmsn.v20i4.72419

Clinicopathological Profile of Immunoglobulin a Nephropathy Patients

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ABSTRACT

Background

Immunoglobulin A nephropathy (IgAN) is the most prevalent glomerulonephritis (GN) in the world. It has variation in presentation among the patients. The aim of the research was to evaluate the clinical and histological characteristics of individuals identified by renal biopsy as having Immunoglobulin-A nephropathy (IgAN).

Methods

A retrospective cross sectional study was conducted in the department of Nephrology of College of Medical Science. Data was collected from medical records of patients with biopsy-proven IgAN between January 2021 to July 2024. Data was entered and analyzed in SPSS-17 using descriptive statistical tools

Results

Fifty two patients with primary IgAN fulfilled our requirements for inclusion. The prevalence of affected males was higher (61.5%). The average age was 35.26 ± 10.39 years. Of the patients, 84.5% had hypertension. At presentation, the estimated glomerular filtration rate (eGFR) was 15.8 mL/min/1.73 m2 and the median serum creatinine was 3.58 mg/dL. Mesangial hypercellularity (M1), endocapillary hypercellularity (E1), segmental glomerulosclerosis (S1), tubular atrophy/ interstitial fibrosis (T1/T2), and crescents (C1/C2) were present in 46.2%, 38.5%, 88.5%, 75% and 36.6% of patients respectively. 38.5% and 86.5% of patients, respectively, had hypertensive vasculopathy and thrombotic microangiopathy (TMA). Low eGFR at presentation was significantly correlated with tubular atrophy (T1/T2), hypertensive vasculopathy, and TMA on renal biopsy.

Conclusions

Since hypertension was the most frequent clinical manifestation of IgAN, we recommend that patients with hypertension be checked for microscopic dysmorphic hematuria and, if found, have a renal biopsy to confirm an early diagnosis of the condition. The presence of TMA on the renal biopsy and hypertensive vasculopathy along with tubular atrophy (T1/T2) were linked to low eGFR at presentation.

Keywords: clinical profile; histopathological profile; immunoglobulin-a nephropathy; kidney biopsy.

INTRODUCTION

After Hinglais and Berger first described IgA nephropathy (IgAN) in 1968 and named Berger disease, it has been established as the most common form of primary glomerular disease worldwide.[1-3] Despite its heterogeneity, it is increasingly recognized as a major cause of progressive renal dysfunction and failure, which occurs in 20%-50% of affected patients over 10 to 20 years.[2] Individuals with glomerular inflammation, interstitial fibrosis, increasing levels of proteinuria, and renal failure are at the most risk.[4] We attempted to retrospectively analyze the varying clinical presentation and histological characteristics of IgAN in our local community.

METHODS

A retrospective cross sectional study was conducted in the department of Nephrology of College of Medical Science, Chitwan, Nepal. In this study data where collected from medical records of all patients over the age of 18 years, diagnosed with kidney biopsy-proven primary IgAN, were retrospectively evaluated. Patients with secondary causes of IgAN

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were dropped. All kidney biopsies throughout the research period (January 2021–July 2024) were reported independently by renal pathologists. The obtained data comprised age, gender, clinical history, baseline biochemical, and urinary investigations (include urine protein/creatinine ratio or 24-hour proteinuria).[5] Estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI (2021) formula. MEST-C score was assigned as per the Oxford classification and presence or absence of crescents was noted.The MEST-C criteria comprised mesangial hypercellularity (with M0 and M1 corresponding to ≤50% and >50% of the glomeruli showing hypercellularity, respectively), endocapillary hypercellularity (defined as E0: absentor E1: present), segmental glomerulosclerosis (defined as S0: absent or S1: present), tubular atrophy/interstitial fibrosis (with T0, T1, and T2 corresponding to ≤25%, 26%–50%, and >50% of cortical area involvement, respectively), cellular/fibro cellular crescents (with C0, C1, and C2 corresponding to their absence, presencein ≥1 and <25% of glomeruli, and presence in ≥25% of the glomeruli, respectively).[5] The statistical analysis was done by using descriptive and inferential statistics, using Mann–Whitney U-test for continuous variables and Chi-square test for categorical variables. Software used in the analysis was StatisticalPackage for the Social Sciences (SPSS) 17 version (SPSS Inc., Chicago, Ill., USA). The study was approved by the Institutional Ethics Committee.

RESULTS

A total 280 kidney biopsies were performed during the study period. There were 48 patients who had primary IgAN and met our inclusion criteria. They were predominantly males (58.5%). The mean age at the time of kidney biopsy was 38.5 ± 10 years (Table 1).

Table 1. Clinical and laboratory profile of patients at the time of biopsy.

Age (years) (Mean±SD)	38.5±0.31
Gender (M:F) (n)	28:20:00
Hypertension (%)	38 (79.17)
Gross hematuria (%)	5 (10)
Serum creatinine (mg/dL) (median)	2.1
eGFR (mL/min/1.73 m^2) (median)	45.4

SD: Standard deviation, M:F: Male:female, SBP: Systolic blood pressure, eGFR: Estimated glomerular filtration rate.

Approximately 60% of patients had edema in their feet, 30% had renal failure discovered incidentally and 10% had extensive hematuria. Hypertension was detected in 79.17% of the individuals. At the time of presentation, 15% of patients required dialysis. Only five individuals (9.6%) had a history of prior upper respiratory tract infections. (Table 2). The most prevalent first syndromic diagnosis was nephritic syndrome (35%), followed by unexplained renal dysfunction (32%), acute kidney injury (24%), and rapidly progressing renal failure (15%). Five patients presented with pure nephrotic syndrome. In terms of complaints, hypertensive urgency symptoms were the first to appear in 16% of patients, while uremic symptoms (nausea, vomiting, and decreased appetite) occurred in 20% of patients.

The median blood creatinine level and eGFR at presentation were 2.1 mg/dL and 20.4 mL/min/1.73 m2, respectively. At presentation, 40 individuals had their urinary protein creatinine ratio (UPCR) tested. The average UPCR was 2.51 ± 2.05. The correlation of MEST –C scoring with serum creatinine and eGFR was assessed. The frequency of mesangial hypercellularity and endocapillary cellularity had no significant link with baseline serum creatinine and eGFR [serum creatinine (median in mg/dL)- M0: 1.75; M1: 2.3; P = 0.12, E0: 1.9; E1: 2.2; P = 0.15]. eGFR (median in mL/min/1.73 m2): M0: 48.75; M1: 42.55; P= 0.10, E0: 46.8; E1: 39.95; P = 0.12]. The median eGFR with segmental glomerulosclerosis (S1) was 19.55 mL/min/1.73 m2, compared to 48.45 mL/min/1.73 m2 with S0. There was no significant correlation between S1 and eGFR value at presentation. With tubular atrophy T1 and T2, median eGFR was 14.95 and 8.6 mL/min/1.73 m2, respectively. Median eGFR with T0 was 55.4 mL/min/1.73 m2, and eGFR showed a statistically significant decrease with increasing tubular atrophy. C1 and C2 had median eGFRs of 19.90 and 10.6 mL/min/1.73 m2, respectively, compared to C0's 24.30 mL/min/1.73 m2. The difference wasn't statistically significant (Table 3). TMA (thrombotic microangiopathy) was associated with significantly lower eGFR (8.65

mL/min/1.73 m2) (P <0.001). Similarly, the presence of hypertensive vasculopathy on renal biopsy was linked to considerably lower eGFR at presentation.

Table 2. Association of hypertensive vasculopathy and thrombotic microangiopathy with serum creatinine and estimated glomerular filtration rate at presentation.

Variables	Serum creatinine (mg/dL)		eGFR (mL/min/1.73 m^2)	
	Median	p-value	Median	p-value
No TMA	1.9	<0.001	40.5	<0.001
TMA	6.34		8.65	
Hypertensive vasculopathy	4.8	0.05	20.2	0.05
No hypertensive vasculopathy	1.035		68.15	

eGFR: Estimated glomerular filtration rate, TMA: Thrombotic microangiopathy.

In 50%, 40%, 78%, 68%, and 30% of patients, respectively, there was tubular atrophy/interstitial fibrosis (T1/T2), crescents (C1/C2), segmental glomerulosclerosis (S1), endocapillary hypercellularity (E1), and mesangial hypercellularity (M1). 25% and 60% of patients, respectively, had TMA and hypertensive vasculopathy. IgA deposition on immunofluorescence was predominantly mesangial in 44 patients (91.67%), but it was also detected in the mesangium and capillaries in 4 patients. In 16.67% and 73% of biopsies, respectively, IgG and C3 co-deposition was observed. 48 individuals underwent electron microscopy, of whom 28 had focal podocytopathy and 5 had widespread podocytopathy.

Table 3. Correlation of MEST-C scores with serum creatinine and estimated glomerular filtration rate.

Oxford Scores	Serum creatinine (mg/dL)		eGFR (mL/min/1.73 m^2)	
	Median	p-value	Median	p-value
M0	1.75	0.12	48.75	0.08
M1	2.3		42.55	
E0	1.9	0.17	46.8	0.1
E1	2.2		39.95	
S0	1.8	0.06	48.45	0.07
S1	3.42		19.55	
T0	1.31	<0.001	55.4	<0.001
T1	5.15		14.95	
T2	7.3		8.6	
C0	2.84	0.22	24.3	0.4
C1	3.31		19.9	
C2	6.8		10.6	

DISCUSSION

Of the data obtained from renal biopsies during the course of our investigation, 17.14% related to IgAN. Mean age at kidney biopsy was 38.5 ± 10 years, with men making up the majority of cases (58.5%). The traditional clinical first manifestation of IgAN, known as syndromic macroscopic hematuria, was reported to occur in 8%–10% of cases. A history of upper respiratory tract infections could only be elicited in 9.6% of patients in our study, which is comparable to other studies' findings that 10% of patients had gross hematuria as the initial presentation of IgA nephropathy.[6] Edema of foot were the most frequent presenting feature in our study (60%) as described in few Indian study.[7, 8] Renal biopsies were conducted for 32% of the patients due to incidentally discovered renal impairment (biochemical and/or urine abnormalities). Consequently, another study has noted that a prevalent characteristic of IgAN is progressive renal impairment.[9] Initial presentation of newly diagnosed hypertension was noticed in most of the patients (79.17%) and symptoms related to hypertensive urgency were presenting feature in 16% of patients. In order to check for microscopic hematuria and proteinuria, the authors recommend that all newly diagnosed hypertension have a urine microscopic examination. Whenever there are microscopic urine abnormalities that are asymptomatic, IgAN should be kept in mind when making a differential diagnosis of secondary causes of hypertension. The median eGFR (mL/min/1.73 m2) at presentation in our analysis was 45.4 mL/min/1.73 m2, which was higher compared to that reported by Balwani et al.[8] However similar Indian study had mean eGFR at presentation (mL/min/1.73 m^2) 76.0 ± 42.6.[7] This shows the more advanced and aggressive kidney disease at presentation in our patients. Our study population cohort's histopathologic lesions revealed advanced kidney disease. Comparing mesangial (50%) and endocapillary hypercellularity (40%) with segmental glomerulosclerosis (78%) and tubular atrophy/interstitial fibrosis (68%), we found a

higher percentage of patients with these conditions. These findings aligned with the research conducted by Balwani et al.[8] However, previous earlier Indian research included contrast observation, with the most typical findings being mesangial and endocapillary hypercellularity. This can be the result of differences in illness presentation between regions.[7, 10] Similar results of 36.6% were found in an Indian study that was comparable to ours, with crescents seen in 30% of patients.[8] In our research, we found that 25% of patients had TMA, while 60% of patients had hypertensive vasculopathy. It indicates the increased prevalence of hypertensive changes in our population. Increased blood creatinine levels were related to a significant drop in eGFR at presentation when hypertensive vasculopathy and TMA were found on kidney biopsy. The inclusion of TMA and hypertensive vasculopathy in the Oxford MEST-C scoring system, in our opinion, will improve the clinicopathological correlation of kidney biopsy results. In 91.67% of the patients in our investigation, the IgA deposition was primarily mesangial, although in four individuals, it was found in both the mesangium and the capillaries. In 3.8% and 80.8% of biopsies, respectively, IgG and C3 co-deposition was observed. These findings aligned with earlier research.[10,11] 10.41% of patients had diffuse podocytopathy, while 58.33% of patients had focal podocytopathy.At the time of biopsy, we tried to correlate the seven scores (TMA, hypertensive vasculopathy, and MEST–C) with serum creatinine and eGFR (Tables 3). Despite not being statistically significant, the median serum creatinine value with M0 and E0 was higher than that with M1 and E1. Although the S group's median serum creatinine level was greater in score 1 than in score 0, the difference was not statistically significant. On the other hand, the median serum creatinine level was significantly higher in the T1/TMA, hypertensive vasculopathy, and TMA groups than in the T0, without hypertensive vasculopathy, and without TMA, respectively.

CONCLUSIONS

We come to the conclusion that hypertension should be identified since it may be the only clinical characteristic of IgAN to be shown by the patient. A patient's blood pressure can be monitored to identify the disease in its early stages and urinary microscopic examination should be carried out in hypertensive individuals which would help to identify and retard the disease progression by early intervention. Among the patients low eGFR at presentation was significantly correlated with tubular atrophy (T1/T2), hypertensive vasculopathy, and TMA on renal biopsy however, no such correlation could be established with segmental glomerulosclerosis (S1), crescents (C1/C2), mesangial (M1), and endocapillary hypercellularity (E1).

Conflict of interest: None

Funding: None

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Citation: Sharma D, Bhusal P, Maharjan C, Ghimire M. Clinicopathological Profile of Immunoglobulin a Nephropathy Patients. JCMS Nepal. 2024; 20(4): 332-036.