

CLINICOPATHOLOGICAL PROFILE OF PATIENTS WITH INFECTION RELATED GLOMERULONEPHRITIS IN A TERTIARY CARE CENTRE

Elsa Thomas¹, Aneeb Raj V.P², Renny Issac³, Usha Nagadevi C S⁴

¹Senior Resident, Department of General Medicine, Government Medical College, Thrissur, Kerala, India.

²Assistant Professor, Department of Nephrology, Government Medical College, Thrissur, Kerala, India.

³Associate Professor, Department of Nephrology, Government Medical College, Thrissur, Kerala, India.

⁴Assistant Professor, Department of Medicine, Government Medical College, Thrissur, Kerala, India

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Corresponding Author:

Dr. Renny Issac,

Email:reniissac@gmail.com

ORCID: 0000-0002-1396-1594

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Abstract

Background: To study the clinic-epidemiological profile of IRGN. **Materials and Methods:** A prospective cross-sectional study was conducted among 79 patients, admitted with IRGN from 2019-2020. Clinical data including antecedent infection, comorbidities, symptomatology and investigations such as urinalysis, urine spot protein creatinine ratio, serum creatinine, complete blood count, serum ASO, serum C3 and microbiological cultures were analysed. **Result:** The mean age of the study population was 46.35 ± 13.9 years with majority belonging to the age group of 51 -60 years. 64.6% of population were females. Among the study population, 20 patients (25.3%) gave history of respiratory tract infection, 19 (24.1%) had skin and soft tissue infection and 12 had urinary tract infection. Regarding comorbidities, 32 patients (40.5%) had DM, 19 patients had SHTN, 19 patients had dyslipidemia and 12 patients had CAD. All patients had micro-hematuria and proteinuria, 85% had oedema, 82% had high blood pressure recording and 43% had macro-hematuria. Serum creatinine was elevated in 72 patients (91.1%). Nephrotic range proteinuria was observed in 34 patients (43%). Low serum C3 level was found in 71 patients (89.9%). Most common organism identified in culture was staphylococcus aureus (21.4%), followed by E coli (15.2%). Serum ASO titre was elevated in 29 patients (36.7%). During hospital stay, 17 patients developed hyperkalemia, 7 developed encephalopathy, 4 developed pulmonary oedema. Number of patients who developed complications were 24, constituting 30.4% of the study population. Among them 19 required hemodialysis (24.1%). **Conclusion:** This study demonstrates the shift in clinico-epidemiological profile with more incidence in elderly with comorbidities. Proteinuria, haematuria, oedema and high BP recording were the common presenting symptoms/signs. Along with respiratory tract infection, skin and soft tissue infection also contributes to disease burden with more cases being attributed to Staphylococcus aureus followed by E.coli. The disease has poor outcome with 30.3% developing uremic complications and 24% requiring hemodialysis.

INTRODUCTION

Postinfectious glomerulonephritis (PIGN) or Infection related glomerulonephritis (IRGN) is an immune mediated glomerulonephritis mediated by alternate complement pathway activation by several bacterial/viral/parasitic infections.^[1] In the past, majority of the cases were diagnosed in children and occurred one to two weeks after the Streptococcal

upper respiratory tract or 4-6 weeks after skin infections, and hence were called 'Post streptococcal Glomerulonephritis (PSGN)'. PSGN in children had good prognosis with recovery in 1-2 weeks. Over the last three decades, there has been a change with regards to its epidemiology, etiological agents, clinical presentation, histopathology, and immunofluorescence (IF) spectrum and its ultimate outcome.^[2]

There has been a decline in the global incidence of disease with more adults developing the disease, especially those with comorbidities such as diabetes; approximately one-third of adults with IRGN will have at least one comorbid factor such as diabetes mellitus, liver disease, malignancy and other immunocompromised conditions. They are more likely to have rapidly progressive renal failure, nephrotic range proteinuria, complications like pulmonary oedema and death.

Organisms causing IRGN are also changing, with fewer cases associated with streptococcus and more cases owing to staphylococcus followed by gram negative organisms.^[3] The sites of adult infection are more heterogeneous, including skin, upper respiratory tract, lung, heart, oral mucosa/teeth, and urinary tract, with few of them even harbouring infection at more than one site. And can have ongoing infection also, hence the term infection related glomerulonephritis. IRGN without an apparent infectious focus can be associated with occult visceral or deep seated abscess, making it imperative that there should be an extensive search for any occult primary source of infection.

The clinical spectrum may vary widely from asymptomatic microscopic haematuria incidentally detected on routine urinalysis to rapidly progressive glomerulonephritis requiring emergency dialysis.^[4] Symptomatic patients usually presents with acute nephritic syndrome with new onset haematuria and proteinuria, oedema, hypertension, and reduced renal function. Elderly individuals often develop uncontrolled hypertension. A quarter to a third of patients can develop full blown nephrotic syndrome. Almost all patients have microhaematuria, with or without red blood cell casts, and gross haematuria can also occur. Leucocytosis is frequent. Serum creatinine at presentation is elevated in a vast majority of patients, and it is higher in elderly patients than younger adults, and higher in those with underlying diabetic glomerulosclerosis. In contrast to children in whom the need for dialysis for severe acute renal failure is uncommon, close to a half of elderly patients require acute dialysis for uremic symptoms and/or fluid overload.^[2] Low c3 levels are seen in a majority.

The treatment of adult IRGN should include eradication of infection and management of complications of nephritis. Appropriate selection of antibiotics guided by culture and sensitivity and surgical intervention, if necessary, can reduce disease burden. Treatment of acute nephritic syndrome includes dietary salt restriction, diuretics, antihypertensives, adequate protein intake. For the treatment of persistent moderate or heavy proteinuria, renin-angiotensin system blockade is recommended to slow disease progression with monitoring of serum creatinine and potassium. If patient develops rapidly progressive renal renal failure, he/she may require renal replacement therapy to treat complications like hyperkalemia, pulmonary oedema and ureamic manifestations. In

contrast to children in whom complete remission occurs in the vast majority of patients, a significant proportion of adults do not recover renal function and may progress to ESRD, especially in diabetics. Till now, there has been no proven benefit with use of immunosuppressants in IRGN.^[5] Often the patients can have ongoing infections and may have diabetes, increasing the risk with use of immunosuppressants. It is important to be aware of these shifting features of IRGN, as the impacted patient population is at higher risk for poor renal outcome, so we decided to do a study on clinical profile of IRGN.

MATERIALS AND METHODS

A cross sectional study of patients aged 18-70 years, diagnosed as IRGN by clinical/ biochemical or histological methods or both, during 2019-2020 in our centre was included in the study. Clinical data including antecedent infection, comorbid illness, blood pressure, symptomatology and investigations such as urinalysis, urine spot protein creatinine ratio, serum creatinine, complete blood count, serum anti-streptolysin O (ASO) titer, complement (C3, C4), microbiological cultures were analysed. Patients with antinuclear antibody, hepatitis C, MPO ANCA, PR3 ANCA or double stranded DNA positivity at presentation and those with past history of CKD or other glomerulonephritis were excluded

Sample size calculation: According to 'Follow-up study of post infectious glomerulonephritis in adults: analysis of predictors of poor renal outcome',⁶ 56% had haematuria as clinical presentation, 74% had hypertension, 99% had oliguria, 99% had oedema (8). Let $p = 56$, then n will be calculated as $76 N = 76$

Convenient sampling technique was used. All cases satisfying inclusion and exclusion criteria was taken up for the study until sample size is met. Data was expressed as a mean standard deviation or where indicated, as median and ranges. Chi square test was used for categorical variables. $P < 0.05$ is considered statistically significant.

RESULTS

Our study included 79 patients among whom, 51 were females and 28 were males. Females constituted 64.6 % of the study population. The mean age of the study population was 46.35 ± 13.9 years, and among them males had higher mean age of 51.39 ± 16.1 years when compared to 43.6 ± 11.9 years for females. The age and gender distribution table demonstrated that the majority of the study population belonged to the age group of 51 to 60 years (63.2%).

Among the study population 20 patients gave history of recent respiratory tract infection (25.3%). There was evidence of skin and soft tissue infection in 19 patients (24.1%) and UTI in 12 patients.

Remaining 28 patients could not recollect any recent history of infection. While eliciting past history with respect to co-morbidities, 32 patients (40.5%) had diabetes mellitus, 19 patients had systemic hypertension, 19 patients had dyslipidemia and 12 patients had coronary artery disease. There were 20 patients who were smokers (25.3%) and 9 were alcoholics.

Among the study population, all had proteinuria and microscopic hematuria, 85% had oedema, 82% patients had high blood pressure recording and 43% had macro-hematuria at the time of presentation. Nephrotic range proteinuria was found in 34 patients (43%). Among them 34 patients developed oliguria. The serum creatinine showed elevated levels in 72

patients (91.1%). Elevated total WBC count over 11,000 in 36 patients (45.6%). Low C3 levels were seen in 71 patients (89.9%). In microbiological culture, most common organism identified were staphylococcus aureus (21.4%), followed by E coli in 12 patients (15.2%) Among the study population, 24 patients developed complications Serum Anti streptolysins O (ASO) titer was observed in 29 patients (36.7%).

Among the study population, 17 patients had hyperkalemia, 7 patients developed ureamic encephalopathy, 4 patients had acute pulmonary oedema (5.1%). Hemodialysis was required for 19 patients.

Table 1: Age and gender wise distribution of patients with IRGN (Male: n=28; Female: n=51nos.)

Age groups (years)	Male	Female
21-30 years	3(10.7%)	9(17.6%)
31-40 years	5(17.9%)	16(31.4%)
41-50 years	3(10.7%)	7(13.7%)
51-60 years	10(35.7%)	14(27.5%)
61-70 years	4(14.3%)	4(7.8%)
71-80 years	3(10.7%)	1(2%)

Table 2: Site of infection of patients with IRGN

Site of infection	Number
Respiratory tract infection	20(25.3%)
Skin and soft tissue infection	19(24.1%)
Urinary tract infection	12(15.2%)
No history of recent infection	28(35.4%)

Table 3: Comorbidities of patients with IRGN

Comorbidities	
DM	32(40.5%)
SHTN	19(24.1%)
DLP	19(24.1%)
CAD	12(15.2%)

Table 4: Microbiological culture organisms

Microbiological culture organisms	frequency
Staphylococcus Aureus	17(21.4%)
E.coli	12 (15.2%)
Klebsiella	8(10.1%)
Streptococcus Pneumonia	2 (2.5%)
Pseudomonas	2 (2.5%)

Table 5: Investigations

investigations		Frequency
hematuria	Microhematuria	79(100%)
	Macrohematuria	34(43%)
Urine spot protein creatinine ratio	Subnephrotic range proteinuria	34 (43%)
	Nephrotic range proteinuria	45 (57%)
Serum Creatinine	≤ 1.35mg/dl	7 (8.9%)
	> 1.35mg/dl	72 (91.1%)
Serum Albumin	< 3.4 g/dL	67 (84.8%)
	> 3.4 g/dL	12 (15.2%)
Total count	normal	43 (54.4%)
	elevated	36 (45.6%)
C3	elevated	71 (89.9%)
	normal	50 (63.3%)
ASO titre	normal	50 (63.3%)
	elevated	29 (36.7%)

DISCUSSION

In this cross-sectional study of patients with IRGN, 79 patients were included. Females (64.6%)

constituted the majority of study population. Mean age of the study population was 46.35 ± 13.9 years and majority belonged to the age group of 51 to 60 years (63.2%). Chiara Salviani et al,^[7] had forty-one

patients in their study with male: female ratio as 3:1 and mean age as 61 years. In the study, Sujatha Siddappa, et al,^[8] there were 32 males and 22 females and the mean age was 24.1 years. S. Arivazhagan, et al.^[9] observed that mean age of study population was 41.5 years (18- 70 years), with a female preponderance (1:1.25). According to the study by M. Trivedi, et al,^[10] the mean age of presentation was 22.7 ± 15.8 years with a slight male preponderance. In the study by Gopalakrishnan Natarajan et al,^[11] the mean age of the patients was 32.7 ± 15 years, with a male to female ratio of 1.2:1. Ramanathan Sakthirajan et al,^[12] had the mean age as 42 ± 13.5 years. In the study by Samih H Nasr et al, they reported 109 cases of IRGN in patients ≥ 65 years old diagnosed by renal biopsy and the male to female ratio was 2.8:1. The reviewed study observations were similar to the present study.

Among the study population, 20 patients (25.3%) had history of respiratory tract infection, 19 patients (24.1%) had skin and soft tissue infection and 12 patients had urinary tract infection. There was no history of any recent infection in 28 patients. In the current study the most common organisms identified were staphylococcus aureus (21.4%), followed by E coli in 12 patients (15.2%). Ramineni et al,^[14] observed that 63% had evidence of current/recent infection, Staphylococcus and Streptococcus being most common organism associated with IRGN (29.4%). In the study by S Arivazhagan, et al,^[9] only 53.3% of them had evidence of antecedent/ current infection, with skin/subcutaneous focus being the most common site. Chiara Salviani et al,^[7] staphylococci spp. accounted for 76.5% of positive cultures. According to Samih H Nasr et al,^[13] the most common causative agent was staphylococcus (46%) followed by streptococcus (16%) and unusual gram-negative organisms.

While eliciting past history with respect to comorbidities, 32 patients (40.5%) had diabetes mellitus, 19 patients had systemic hypertension, 19 patients had dyslipidemia and 12 patients had coronary artery disease. There were 20 patients who were smokers (25.3%) and 9 were alcoholics. Chiara Salviani et al,^[15] observed that smoking habit (47.2%), alcoholism (30.6%), and diabetes (27.5%) were the most common risk factors.

Among the study population, all had micro-haematuria and proteinuria, 85% had oedema, 82% patients had high blood pressure recording and 43% had macro-haematuria at the time of presentation. Among them 34 patients developed oliguria. In the study by S Arivazhagan, et al,^[9] the majority had oedema (100%), oliguria (84.4%), hypertension (80%) and haematuria (77.8%). Gopalakrishnan Natarajan et al,^[6] observed that, at presentation 99% of the patients had oedema and oliguria, 73% had hypertension, 55% had macrohaematuria and 60% had nephrotic range proteinuria.

In this study, serum creatinine was elevated in 72 patients (91.1%). Leukocytosis was seen in 36

patients (45.6%). Nephrotic range proteinuria was observed in 34 patients (43%) and remaining patients had sub-nephrotic range proteinuria (57%). Serum Anti-streptolysins O (ASO) titre was elevated in 29 patients (36.7%). Low C3 levels were observed in 71 patients (89.9%). In the study by Sujatha Siddappa, et al.⁸ hypocomplementemia was present in about 90% of the patients. As per, S Arivazhagan, et al,^[9] hypocomplementemia was present in 82.2% of patients. According to Gopalakrishnan Natarajan et al,^[6] sixty percent of the patients had serum creatinine >2 mg/dL at presentation, which was persistent in 30% at the end of one week and 68% had hypocomplementemia. In the study by Ramanathan Sakthirajan et al,^[12] hypocomplementemia was present in 100%. In the work by Samih H Nasr et al,^[13] hypocomplementemia was present in 72%. The mean peak serum creatinine was 5.1 mg/dl, and 46% of patients required emergency dialysis. The presence of diabetes, higher creatinine at biopsy, dialysis at presentation, the presence of diabetic glomerulosclerosis, and greater tubular atrophy and interstitial fibrosis predicted ESRD.

Among the study population, during in patient period, 17 patients developed hyperkalemia, 7 patients (8.9%) developed seizures/ encephalopathy, 4 patients developed acute pulmonary oedema (5.1%). Total number of patients developed complications were 24, constituting 30.4% of study population. Among them 19 patients required hemodialysis (24.1%). According to Chiara Salviani et al,^[7] Haemodialysis was required by 22.5% of patients at inception. Sujatha Sidappa et al.⁸ Twenty six percent of patients presented with acute renal failure and required dialysis support during the course of disease. In the study by S Arivazhagan, et al,^[9] 86.7% had renal insufficiency and 35.6% required dialysis. Ramanathan et al,^[16] described that Hemodialysis (HD) was required in 53.2% of patients and oral steroids were given in 78.7%.

CONCLUSION

In this study, majority of patients belonged to the age group 51-60 years. The mean age of the study population was 46.35 ± 13.9 years. Diabetes mellitus was the most common comorbidity. Haematuria, proteinuria, oedema and high blood pressure recording were the most common presenting symptoms/signs. No history of recent /ongoing infection was given by 35.4%. Among the study group, 25.3% had respiratory tract as source of infection, closely followed by skin and soft tissue site infection (24.1%). In the microbiological culture, most common organism identified was Staphylococcus aureus followed by E. coli Serum ASO titre was found to be elevated in 29 patients (36.7%) including those who cannot recollect history of respiratory tract infection. 30.3% of study population developed uremic complications and

24% required haemodialysis. Thus, we arrived at the conclusion that there has been a change in trends with regards to the epidemiology, clinical presentation, etiological agents and outcome in IRGN, demanding aggressive treatment of infection and management of co-morbidities for a better outcome.

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