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Original Research Article

Clinical, Microbiological, Histopathological Profile and Predictors of Adverse Renal Outcomes in Infection-Related Glomerulonephritis: A Prospective Observational Study

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Abstract

Background: Infection-related glomerulonephritis (IRGN) remains an important cause of acute renal dysfunction, particularly among adults with comorbid illnesses. Its clinical presentation, infectious triggers, histopathological spectrum, and outcomes are heterogeneous, and early identification of predictors of adverse renal outcomes is clinically important.

Objectives: To evaluate the clinical, laboratory, microbiological, histopathological, and outcome profile of patients with IRGN and to identify factors independently associated with adverse renal and patient outcomes.

Methods: This single-centre, hospital-based, prospective observational study included 160 patients with IRGN. Demographic characteristics, comorbidities, clinical presentation, infectious foci, microbiological findings, renal function parameters, complement levels, treatment, renal biopsy findings, and short-term outcomes were recorded. The composite adverse outcome comprised chronic kidney disease (CKD), end-stage kidney disease (ESKD), or death.

Results: The mean age was 45.4 ± 16.2 years and 63.1% were male. Acute kidney injury occurred in 72.5%, while 20.0% presented with rapidly progressive glomerulonephritis. An infectious focus was identified in 74.4%, most commonly involving skin and soft tissues. Renal replacement therapy was required in 23.8%. Among 100 biopsied patients, endocapillary proliferation and exudative inflammation were observed in 88.0% and 86.0%, respectively, with universal C3 positivity. Complete renal recovery at three months occurred in 66.9%, whereas the composite adverse outcome occurred in 27.5%. Age >50 years, baseline CKD, and requirement for renal replacement therapy independently predicted adverse outcomes. Interstitial fibrosis and tubular atrophy >10% and global glomerulosclerosis >20% were independent histopathological predictors.

Conclusion: IRGN was associated with substantial acute renal morbidity and clinically important adverse outcomes. Older age, pre-existing CKD, dialysis requirement, and chronic histopathological injury identified patients at increased risk and may aid early prognostic stratification.

Keywords: Infection-Related Glomerulonephritis, Acute Kidney Injury, Renal Biopsy, Complement C3, Chronic Kidney Disease, Renal Replacement Therapy.

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Introduction

Infection-related glomerulonephritis (IRGN) represents an immune-mediated glomerular injury occurring in association with an antecedent, concurrent, or occasionally occult infection. The terminology has evolved from "postinfectious glomerulonephritis" because, particularly in adults, the responsible infection may remain active when glomerular disease becomes clinically apparent, and infectious sources now extend beyond classical streptococcal pharyngitis and impetigo to skin and soft-tissue infections, pneumonia, endocarditis, urinary tract infections, osteomyelitis, and other systemic infections. Nasr et al. emphasized this epidemiological transition and the increasing involvement of older and immunocompromised adults. [1] Adult IRGN may cause substantial renal

morbidity. In a biopsy-based study of 86 adults reported by Nasr et al., the mean age was 56 years, 38.4% had an immunocompromised background, and the predominant infections involved the upper respiratory tract (23.3%), skin (17.4%), lungs (17.4%), and endocardium (11.6%); Streptococcus and Staphylococcus accounted for 27.9% and 24.4% of identified organisms, respectively. Hypocomplementemia occurred in 73.9% of patients, demonstrating the prominent role of complement activation in the disease phenotype.[1]

Disease severity becomes particularly evident in older patients. Nasr et al. evaluated 109 biopsy-proven cases in patients aged ≥65 years and found an immunocompromised state in 61%, Staphylococcus infection in 46%, hypocomplementemia in 72%, and a mean peak serum creatinine of 5.1 mg/dL; 46% required acute dialysis.[1] Among patients with adequate follow-up, only 22% achieved complete renal recovery, whereas 33% progressed to end-stage renal disease, highlighting the adverse prognostic influence of advanced age, comorbidity, severe renal dysfunction, and chronic histological injury. Histopathologically, IRGN most characteristically demonstrates endocapillary hypercellularity with prominent neutrophilic infiltration, while immunofluorescence typically shows strong C3 deposition with or without accompanying immunoglobulins. Khalighi and Chang described subepithelial "hump"-shaped electron-dense deposits as the characteristic ultrastructural finding, although similar deposits may also occur in C3 glomerulopathy. [2] The distinction between IRGN and C3 glomerulopathy is clinically important because both may demonstrate hypocomplementemia, C3-dominant glomerular staining, and overlapping proliferative patterns. Sethi and colleagues' subsequent conceptual framework has been expanded by recent analyses showing that persistent complement abnormalities may indicate sustained alternative-pathway dysregulation rather than uncomplicated resolving IRGN. [3]

Consequently, evaluation of IRGN requires integration of clinical presentation, infectious etiology, renal functional impairment, complement abnormalities, and histopathological features to identify patients at greatest risk of persistent kidney dysfunction and adverse renal outcomes. Against this background, the present study aimed to evaluate the clinical profile, histopathological findings, and outcomes of patients with infection-related glomerulonephritis. The study further aimed to assess the spectrum of underlying infectious foci and microbiological aetiologies, characterize the renal biopsy findings on light microscopy and immunofluorescence, and determine the renal and patient outcomes during follow-up. In addition, the study aimed to identify clinical, laboratory, and histopathological factors associated with adverse renal outcomes, including progression to chronic kidney disease and end-stage renal disease, as well as mortality.

Materials and Methods

This was a single-centre, hospital-based, prospective observational study conducted in the Departments of General Medicine, Pathology and Radiodiagnosis of a tertiary teaching healthcare facility in South India over a period of two years (January 2024–December 2025). The study was approved by the Institutional Human Ethics Committee (IHEC). Each participant was provided with a Participant Information Sheet (PIS) translated into their local language. The information was also explained verbally to ensure clear understanding and voluntary agreement. Patients who were diagnosed with IRGN during the study period and who fulfilled the predefined clinical, laboratory, and, where indicated, histopathological criteria for IRGN were included in the study.

Patients who provided written informed consent and were willing to participate in the required clinical and laboratory evaluation and follow-up were eligible for inclusion. Patients who had an alternative established diagnosis of glomerulonephritis, including lupus nephritis or C3 glomerulopathy, were excluded. Patients in whom the available clinical, laboratory, and histopathological findings were insufficient to establish a diagnosis of IRGN were also excluded. Participants who were unwilling to provide informed consent or who did not have the minimum required follow-up for assessment of study outcomes were excluded from the analysis.

The sample size for the present study was calculated using the single-proportion estimation formula, $n = Z^2pq/d^2$. The anticipated proportion was taken as 24%, based on the proportion of patients with IRGN who required renal replacement therapy in the study by Sanathkumar et al.[4] In that prospective observational study, 30 of 125 patients (24%) required renal replacement therapy. Accordingly, assuming an expected proportion (p) of 0.24, $q = 1 - p = 0.76$, a 95% confidence level ($Z = 1.96$), and an absolute precision (d) of approximately 6.6%, the calculated minimum sample size was 160 participants; enrolled using nonprobability sampling technique – convenience sampling/complete enumeration. At enrolment, demographic characteristics, including age, sex, and relevant sociodemographic details, were recorded. A detailed clinical history was obtained regarding the duration and nature of presenting symptoms, including facial or peripheral edema, oliguria, gross or microscopic hematuria, dyspnea,

fever, and symptoms suggestive of an antecedent or concurrent infection. A detailed history of recent infections, including skin and soft-tissue infection, pharyngitis or tonsillitis, respiratory infection, urinary tract infection, dental infection, ear infection, ocular infection, osteomyelitis, and other clinically relevant infectious illnesses, was documented, together with recent antimicrobial treatment where applicable. Relevant comorbidities, including diabetes mellitus, hypertension, pre-existing CKD, cardiovascular disease, chronic liver disease, and other major systemic illnesses, were recorded. On clinical examination, blood pressure, pulse rate, temperature, respiratory status, urine output, presence and severity of edema, volume status, and other relevant systemic findings were documented. The clinical syndrome at presentation was categorized as acute nephritic syndrome, nephrotic syndrome, RPGN, or RPGN occurring on a background of CKD.

Baseline laboratory investigations included complete blood count, serum urea, serum creatinine, serum electrolytes, serum albumin, total protein, liver function tests, and blood glucose, with glycated hemoglobin assessed where clinically indicated. Renal involvement was evaluated by urine routine and microscopy, including assessment for hematuria, proteinuria, leukocyturia, and red-cell casts. Quantitative urinary protein excretion was recorded using 24-hour urinary protein estimation or urine protein-to-creatinine ratio; urine albumin-to-creatinine ratio was additionally recorded where available. Estimated glomerular filtration rate (eGFR) was calculated using the validated creatinine-based equation appropriate for the participant's age group, without use of a race coefficient, in keeping with current KDIGO recommendations. Serum complement levels, including C3 and C4, were measured at presentation and during follow-up where indicated. The presence and subsequent normalization or persistence of hypocomplementemia were documented. Serological investigations, including antinuclear antibody and ANCA testing, were performed when clinically indicated to evaluate differential diagnoses of glomerulonephritis. Additional investigations, including antistreptolysin-O and/or anti-DNase B titres were performed. Evaluation for occult infectious foci included detailed examination of the skin and soft tissues, ENT and dental assessment, chest imaging, abdominal ultrasonography, echocardiographic assessment when infective endocarditis was suspected, and other site-specific imaging or microbiological investigations according to clinical findings.

Patients with atypical clinical or laboratory findings underwent renal biopsy according to predefined indications, including RPGN, absence of an identifiable infectious focus, normal serum complement or low C4 levels, failure of serum creatinine to trend toward baseline, nephrotic-range proteinuria, or persistent depression of serum C3 during follow-up. For patients undergoing renal biopsy, histopathological data were obtained: number of glomeruli examined, light-microscopic pattern of glomerular injury, endocapillary and mesangial proliferation, exudative/neutrophilic infiltration, capillary-loop obliteration, lobular accentuation, crescent formation and percentage of glomeruli with crescents, necrotizing lesions, interstitial inflammation and edema, acute tubular injury, global glomerulosclerosis, and interstitial fibrosis and tubular atrophy (IFTA). Immunofluorescence findings were recorded for IgG, IgA, IgM, C3, C1q, and kappa and lambda light chains, including the intensity and pattern of staining and the presence of C3 dominance or IgA-dominant IRGN.

Electron microscopy findings, including the presence and distribution of electron-dense deposits and subepithelial humps, were recorded when performed. Treatment variables were also documented: identification and treatment of the underlying infection, antibiotic therapy, diuretic and antihypertensive treatment, renin-angiotensin system blockade where indicated, corticosteroid therapy where administered, intensive-care admission, ventilatory support, and renal replacement therapy. The indication, modality, and duration of dialysis or other renal replacement therapy were recorded. Patients were followed prospectively after the index presentation, with serial assessment of symptoms, blood pressure, urine output, serum creatinine, eGFR, urinary protein excretion, serum albumin, and serum complement levels, as appropriate. The occurrence of acute complications, requirement for RRT, persistence or resolution of renal dysfunction and proteinuria, and subsequent renal recovery were documented. The outcomes included progression to CKD, progression of pre-existing CKD, development of ESKD, continued requirement for dialysis, and death. CKD progression was assessed using persistent reduction in eGFR and/or persistent proteinuria after the predefined follow-up period; for participants with pre-existing CKD, progression to a more advanced CKD stage or ESKD was recorded.

Statistical analysis: Statistical analysis was performed using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using the independent-samples Student’s

t-test for continuous variables and the Chi-square test or Fisher's exact test, as appropriate, for categorical variables. Variables showing significant associations with adverse renal outcomes on univariate analysis were entered into a multivariable binary logistic regression model to identify independent predictors, with results expressed as odds ratios (ORs) with 95% confidence intervals (CIs). A two-tailed p value <0.05 was considered statistically significant.

Results

The study included 160 patients with a mean age of 45.4 ± 16.2 years, of whom 63.1% were male and 35.6% were aged >50 years. Diabetes mellitus, pre-existing hypertension, and baseline chronic kidney disease were present in 15.6%, 27.5%, and 10.0% of patients, respectively. Edema was the most frequent clinical manifestation (91.2%), followed by hypertension at presentation (64.4%), oliguria (48.1%), and dyspnea (33.1%); acute kidney injury was documented in 72.5% of the cohort. Acute nephritic syndrome was the predominant clinical presentation (55.6%), while 20.0% presented with RPGN. An identifiable infectious focus was found in 74.4% of patients, most commonly involving the skin and soft tissues (21.2%) and pharynx/tonsils (14.4%), whereas microbiological confirmation was obtained in 47.5%, with Streptococcus spp. and Staphylococcus spp. accounting for 19.4% and 16.2%, respectively. The median serum creatinine at presentation was 3.0 mg/dL (IQR 2.2–4.6), with a median estimated glomerular filtration rate of 30.0 mL/min/1.73 m² (IQR 21.1–39.8); low serum C3 was observed in 70.6% and nephrotic-range proteinuria in 27.5%. Renal biopsy was performed in 100 patients (62.5%), among whom endocapillary proliferative glomerulonephritis (88.0%) and exudative/neutrophilic infiltration (86.0%) were the predominant light-microscopic findings. Crescents involving >20% of glomeruli were present in 18.0%, acute tubular injury in 56.0%, and interstitial fibrosis and tubular atrophy >10% in 22.0%. C3 positivity was universal on immunofluorescence, with C3 dominance by ≥2 intensity grades in 58.0%, while IgA-dominant IRGN was identified in 7.0%. Electron microscopy was performed in 16 biopsy specimens, of which 75.0% demonstrated characteristic subepithelial humps.

Among the 160 patients, 64.4% received antibiotic therapy for documented or suspected active infection, while 23.8% required RRT during the acute illness and 15.6% required intensive care admission. Among patients with initially low serum C3, normalization by 8 weeks occurred in 89.4%, whereas persistent hypocomplementemia was observed in 10.6%. At 3 months, complete renal recovery was achieved in 66.9% of patients, while 17.5% developed CKD, 6.9% progressed to end-stage kidney disease, and 3.1% died; the composite adverse renal/patient outcome occurred in 27.5%.

Patients with an adverse outcome were significantly older than those without an adverse outcome (53.8 ± 14.1 vs. 42.2 ± 15.9 years; p<0.001) and more frequently had baseline CKD (27.3% vs. 3.4%; p<0.001), RPGN presentation (47.7% vs. 18.1%; p<0.001), and requirement for RRT (50.0% vs. 13.8%; p<0.001). They also had higher serum creatinine and lower estimated GFR at presentation. Within the biopsy subgroup, IFTA >10% and global glomerulosclerosis >20% were significantly more frequent among patients with adverse outcomes. On multivariable analysis, age >50 years (adjusted OR 3.76; 95% CI 1.67–8.47; p=0.001), baseline CKD (adjusted OR 4.14; 95% CI 1.11–15.46; p=0.034), and requirement for RRT (adjusted OR 4.02; 95% CI 1.67–9.70; p=0.002) independently predicted the composite adverse outcome in the clinical model. In the histopathology model, IFTA >10% (adjusted OR 5.88; 95% CI 1.92–18.04; p=0.002) and global glomerulosclerosis >20% (adjusted OR 7.85; 95% CI 1.48–41.79; p=0.016) were independently associated with adverse outcomes.

Table 1: Demographic, comorbidity, and clinical profile of the study cohort (N = 160)

	Value
Age, years	45.4 (16.2)
Age >50 years	57 (35.6%)
Male sex	101 (63.1%)
Diabetes mellitus	25 (15.6%)
Pre-existing hypertension	44 (27.5%)
Baseline chronic kidney disease	16 (10.0%)
Cardiovascular disease	9 (5.6%)
Chronic liver disease	6 (3.8%)
Edema	146 (91.2%)
Oliguria	77 (48.1%)
Gross hematuria	45 (28.1%)
Dyspnea	53 (33.1%)
Hypertension at presentation	103 (64.4%)

Acute kidney injury	116 (72.5%)
Acute nephritic syndrome	89 (55.6%)
Nephrotic syndrome	29 (18.1%)
Rapidly progressive glomerulonephritis (RPGN)	32 (20.0%)
RPGN on background CKD	10 (6.2%)

Table 2: Infectious, microbiological, and laboratory profile at presentation (N = 160)

		Value
Identifiable infectious focus		119 (74.4%)
	Skin/soft tissue	34 (21.2%)
	Pharyngitis/tonsillitis	23 (14.4%)
	Urinary tract	17 (10.6%)
	Lower respiratory tract	17 (10.6%)
	Dental/ENT	10 (6.2%)
	Other	18 (11.2%)
	No identifiable focus	41 (25.6%)
Microbiological confirmation		76 (47.5%)
	Streptococcus spp.	31 (19.4%)
	Staphylococcus spp.	26 (16.2%)
	Gram-negative bacilli	9 (5.6%)
	Other	10 (6.2%)
	No organism isolated	84 (52.5%)
Hemoglobin, g/dL		11.3 (1.4)
Total leukocyte count, $x10^3$/uL		12.9 (4.3)
Serum urea, mg/dL		84.7 (42.0)
Serum creatinine, mg/dL		3.0 (2.2-4.6)
Estimated GFR, mL/min/1.73 m^2		30.0 (21.1-39.8)
Serum albumin, g/dL		3.07 (0.47)
Urinary protein excretion, g/day		1.94 (1.43-2.89)
Nephrotic-range proteinuria		44 (27.5%)
Microscopic hematuria with RBC casts		48 (30.0%)
Leukocyturia		54 (33.8%)
Low serum C3		113 (70.6%)
Low serum C4		20 (12.5%)
Serum C3, mg/dL		71.0 (27.9)
Serum C4, mg/dL		24.4 (7.6)
Elevated antistreptolysin-O titre		48 (30.0%)

Table 3: Renal biopsy, light-microscopy, immunofluorescence, and electron-microscopy findings (biopsy subgroup, n = 100)

	Value
Patients undergoing renal biopsy	100 (62.5%)
Endocapillary proliferative pattern	88 (88.0%)
Exudative/neutrophilic infiltration	86 (86.0%)
Mesangial proliferation	33 (33.0%)
Any cellular/fibrocellular crescents	38 (38.0%)
Crescents in >20% of glomeruli	18 (18.0%)
Crescents in >50% of glomeruli	5 (5.0%)
Acute tubular injury	56 (56.0%)
IFTA >10%	22 (22.0%)
Global glomerulosclerosis >20%	12 (12.0%)
C3 positivity on immunofluorescence	100 (100.0%)
C3-only staining	22 (22.0%)
C3 dominance by >=2 intensity grades	58 (58.0%)
IgG deposition	72 (72.0%)
IgM deposition	12 (12.0%)
IgA deposition	10 (10.0%)
IgA-dominant IRGN	7 (7.0%)

C1q deposition	19 (19.0%)
Electron microscopy performed	16 (16.0%)
Subepithelial humps among EM specimens	12 (75.0%)

Table 4: Treatment and short-term renal and patient outcomes (N = 160)

	Value
Antibiotic therapy for documented/suspected active infection	103 (64.4%)
Diuretic/antihypertensive therapy	103 (64.4%)
Renin-angiotensin system blockade during follow-up	43 (26.9%)
Corticosteroid therapy	13 (8.1%)
Intensive care admission	25 (15.6%)
Mechanical ventilatory support	16 (10.0%)
Renal replacement therapy during acute illness	38 (23.8%)
Normalization of initially low C3 by 8 weeks	101/113 (89.4%)
Persistent low C3 at 8 weeks	12/113 (10.6%)
Complete renal recovery at 3 months	107 (66.9%)
Persistent urinary abnormality with preserved renal function	9 (5.6%)
Chronic kidney disease at 3 months	28 (17.5%)
End-stage kidney disease	11 (6.9%)
Death	5 (3.1%)
Composite adverse renal/patient outcome (CKD, ESKD, or death)	44 (27.5%)

Table 5: Factors associated with the composite adverse outcome

	No adverse outcome (n = 116)	Adverse outcome (n = 44)	P value
Age, years	42.2 (15.9)	53.8 (14.1)	<0.001*
Age >50 years	29 (25.0%)	28 (63.6%)	<0.001*
Diabetes mellitus	12 (10.3%)	13 (29.5%)	0.003*
Pre-existing hypertension	24 (20.7%)	20 (45.5%)	0.002*
Baseline CKD	4 (3.4%)	12 (27.3%)	<0.001*
RPGN presentation	21 (18.1%)	21 (47.7%)	<0.001*
Nephrotic-range proteinuria	25 (21.6%)	19 (43.2%)	0.006*
Requirement for RRT	16 (13.8%)	22 (50.0%)	<0.001*
Low serum C3	81 (69.8%)	32 (72.7%)	0.719
Serum creatinine, mg/dL	2.7 (2.0-3.8)	3.8 (2.8-5.9)	<0.001*
Urinary protein excretion, g/day	1.78 (1.36-2.50)	2.73 (1.57-4.27)	0.004*
Estimated GFR, mL/min/1.73 m²	32.9 (24.5-42.6)	24.8 (16.9-31.8)	<0.001*
Any crescents	19 (29.7%)	19 (52.8%)	0.022*
IFTA >10%	6 (9.4%)	16 (44.4%)	<0.001*
Global glomerulosclerosis >20%	2 (3.1%)	10 (27.8%)	<0.001*
C3 dominance	34 (53.1%)	24 (66.7%)	0.188
IgA-dominant IRGN	2 (3.1%)	5 (13.9%)	0.095

Table 6: Multivariable logistic regression for predictors of the composite adverse outcome

Model	Predictor	Adjusted OR	95% CI	P value
Clinical model (N=160)	Age >50 years	3.76	1.67-8.47	0.001*
Clinical model (N=160)	Baseline CKD	4.14	1.11-15.46	0.034*
Clinical model (N=160)	Requirement for RRT	4.02	1.67-9.70	0.002*
Histopathology model (n=100)	IFTA >10%	5.88	1.92-18.04	0.002*
Histopathology model (n=100)	Global glomerulosclerosis >20%	7.85	1.48-41.79	0.016*

Discussion

The present study characterized the clinical, microbiological, histopathological, and short-term outcome spectrum of IRGN in 160 patients.

The mean age was 45.4 ± 16.2 years, 63.1% were male, and more than one-third were aged >50 years, illustrating the substantial burden of IRGN among middle-aged and older adults. The demographic profile differed from the Indian cohort of Sanathkumar et al., in which the mean age was 37 ± 17.6 years and females constituted 59%, but was directionally closer to the adult phenotype described in staphylococcal infection-associated GN.[4] In a pooled analysis of 83 patients with staphylococcal-associated GN, Wang

et al. reported a mean age of 58 ± 17 years and a marked male predominance, with 64 of 83 patients being men.[5] These differences emphasize the heterogeneity of IRGN according to age distribution, infecting organism, underlying comorbidities, and referral patterns. Diabetes mellitus, pre-existing hypertension, and baseline CKD were present in 15.6%, 27.5%, and 10.0% of the present cohort, respectively. Sanathkumar et al. similarly reported diabetes in 18%, hypertension in 16%, and baseline CKD in 13% of 125 patients.[4] Clinically, edema was observed in 91.2%, oliguria in 48.1%, and AKI in 72.5% of the present study; in corroboration with Sanathkumar et al.[4] Acute nephritic syndrome remained the predominant presentation in the present study (55.6%), whereas 20.0% presented with RPGN. In the Sanathkumar et al., 59% presented with acute nephritis, while RPGN occurred in 30% and an additional 6% had RPGN superimposed on CKD.[4] Thus, the present findings reinforce that although acute nephritic syndrome remains the classical phenotype, a substantial subgroup of adults presents with severe rapidly progressive renal dysfunction.

An infectious focus was identified in 74.4% of patients, with skin and soft-tissue infection being the most frequent source (21.2%), followed by pharyngitis/tonsillitis (14.4%). This pattern was consistent with Sanathkumar et al., who identified an infectious source in 72% of patients, with skin and soft-tissue infection accounting for 31% and pharyngitis/tonsillitis for 20%.[4] Trivedi et al. documented clinical or microbiological evidence of preceding infection in 78.1% of 137 patients, although a specific microbiological agent could be established in only 8%. [6] In contrast, microbiological confirmation in the present study was achieved in 47.5%, with Streptococcus spp. identified in 19.4% and Staphylococcus spp. in 16.2%. The coexistence of streptococcal and staphylococcal disease reflects the changing spectrum of IRGN, in which the traditional post-streptococcal phenotype coexists with infection-associated GN occurring during active bacterial infections, particularly in adults with comorbid disease. [7-9]

Renal dysfunction at presentation was substantial, with a median serum creatinine of 3.0 mg/dL and median eGFR of 30.0 mL/min/1.73 m². Trivedi et al. reported a mean creatinine of 2.37 ± 1.87 mg/dL and mean eGFR of 39.36 ± 22.83 mL/min/1.73 m², whereas Sanathkumar et al. reported a mean peak serum creatinine of approximately 3.6 mg/dL. [4] Nephrotic-range proteinuria was present in 27.5% of the present cohort, compared with 13.8% in Trivedi et al. and approximately one-third in the Sanathkumar cohort. [4,6] Low serum C3 was detected in 70.6% and normalized by 8 weeks in 89.4% of initially hypocomplementemic patients. Transient C3 consumption is compatible with complement activation in IRGN, whereas persistent hypocomplementemia requires consideration of continuing complement dysregulation and alternative diagnoses such as C3 glomerulopathy. [3,10,11] Renal biopsy demonstrated the characteristic pathological spectrum of IRGN. Endocapillary proliferation occurred in 88.0% and exudative neutrophilic infiltration in 86.0%, closely paralleling the 91% endocapillary proliferative pattern and 80% exudative pattern reported by Sanathkumar et al.(4) Crescents involving >20% of glomeruli were present in 18.0%, identical to the 18% reported by Trivedi et al. and comparable with 14% in the Sanathkumar cohort. [4, 6] Acute tubular injury occurred in 56.0%, while IFTA >10% was present in 22.0%, almost identical to the 59% and 20%, respectively, reported by Sanathkumar et al.[4] These chronic tubulointerstitial changes are particularly relevant because they represent reduced residual nephron reserve rather than merely acute inflammatory activity.[12]

C3 deposition was universal on immunofluorescence in the present study and C3 dominance by ≥2 intensity grades occurred in 58.0%. Sanathkumar et al. similarly demonstrated C3 staining in 100% of 86 biopsies and C3 dominance in 57%, supporting complement activation as a central pathological feature of IRGN.[4] IgA-dominant IRGN constituted 7.0% of biopsies. Dhanapriya et al. identified IgA-dominant disease in 12 of 230 IRGN cases (5%); their patients had a mean age of 52.4 ± 21 years, 92% had low C3, 92% had nephrotic-range proteinuria, and 58% showed crescentic GN, illustrating the particularly aggressive phenotype that may accompany IgA-dominant IRGN.[13] Electron microscopy demonstrated subepithelial humps in 75% of specimens examined in the present study, a classical supportive feature incorporated into established clinicopathological diagnostic criteria for IRGN. [14]

Nearly one-quarter of patients (23.8%) required RRT during the acute illness, similar to the 24% reported by Sanathkumar et al. and somewhat higher than the 17.5% reported by Trivedi et al. [4,6] The higher dialysis requirement relative to the latter study may partly reflect the older age and greater severity of renal dysfunction in the present cohort. Corticosteroids were administered to only 8.1%, which is consistent with the cautious approach required in active infection. Arivazhagan et al., in a randomized trial of 52 patients with biopsy-proven IRGN, found complete renal recovery at 6 months in 65.4% receiving corticosteroids plus supportive care versus 53.8% receiving supportive care alone (p=0.397), while adverse events occurred significantly more often

with corticosteroids (46.2% vs. 7.7%; p=0.002).[15] These findings support prioritization of infection eradication and supportive renal care, with immunosuppression reserved for carefully selected situations. Complete renal recovery at 3 months occurred in 66.9% of the present cohort, while 17.5% developed CKD, 6.9% progressed to ESKD, and 3.1% died. Trivedi et al. reported a more favourable 83.2% complete recovery rate and CKD progression in 8.09%,[6] whereas Sanathkumar et al. observed CKD progression in 33%, ESKD in 12%, and mortality in 10%.[4] These differences likely reflect differences in age distribution, baseline CKD, proportion of RPGN, case-selection criteria, and duration of follow-up. Importantly, the present study identified a distinct high-risk subgroup: age >50 years independently increased the odds of the composite adverse outcome 3.76-fold, baseline CKD 4.14-fold, and acute RRT requirement 4.02-fold. Sanathkumar et al. similarly identified age >50 years, RPGN presentation, and baseline CKD as independent predictors of CKD progression, while dialysis requirement was strongly related to adverse outcomes.[4] Increasing age has also been identified as an independent adverse prognostic factor in pooled analyses of staphylococcal-associated GN.

The histopathological predictors further strengthened the prognostic significance of chronic structural damage. IFTA >10% independently predicted the composite adverse outcome with an adjusted OR of 5.88, while global glomerulosclerosis >20% carried an adjusted OR of 7.85. Sanathkumar et al. likewise found global glomerulosclerosis >20%, IFTA >10%, and extensive crescents to be associated with ESKD on univariate analysis, with IFTA >10% emerging as an independent predictor of ESKD with an OR of 30.9. [4] In contrast, low serum C3 and C3 dominance were not significantly associated with the composite outcome in the present study, suggesting that acute complement activation itself may be less prognostically informative than baseline renal reserve, dialysis-requiring disease severity, and established chronic histological injury. Collectively, these findings support combining clinical severity indicators with biopsy markers of chronicity for meaningful risk stratification in adults with IRGN.

The present study had several limitations. First, it was a single-centre study conducted at a tertiary teaching healthcare facility, which may have introduced referral bias and limited the generalizability of the findings to other healthcare settings and populations. Second, although the study prospectively evaluated clinical, laboratory, microbiological, radiological, and histopathological characteristics, renal biopsy was performed only in selected patients with atypical or severe presentations; therefore, histopathological analyses were restricted to a subgroup and may not represent the entire spectrum of infection-related glomerulonephritis. Third, microbiological confirmation of the underlying infection could not be obtained in all patients.

Fourth, the relatively short follow-up period limited assessment of long-term renal recovery, late progression of chronic kidney disease, recurrence, and long-term mortality. Finally, residual confounding from unmeasured clinical factors, variations in infection severity, timing of antimicrobial therapy, and treatment decisions could not be completely excluded despite multivariable adjustment.

Conclusion

The present study demonstrated that IRGN continues to be an important cause of acute and progressive renal dysfunction, with a broad spectrum of clinical, microbiological, and histopathological manifestations. Acute nephritic syndrome was the predominant presentation, while a substantial proportion of patients developed RPGN, required RRT, or had adverse renal outcomes. Skin and soft-tissue infections were the most frequently identified infectious source, and Streptococcus and Staphylococcus species were the predominant microbiological isolates.

Renal biopsy most commonly showed endocapillary proliferative and exudative glomerulonephritis with universal C3 deposition. Although complete renal recovery occurred in the majority of patients, chronic kidney disease, end-stage kidney disease, and mortality were observed in a clinically important subset. Older age, pre-existing chronic kidney disease, and the requirement for renal replacement therapy independently predicted adverse outcomes, while interstitial fibrosis and tubular atrophy and global glomerulosclerosis were important histopathological predictors. These findings emphasize the importance of early recognition of severe disease, prompt identification and treatment of the underlying infection, careful assessment of baseline renal reserve, and appropriate use of renal biopsy for prognostication and risk stratification.

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