# Long-term outcomes and pathological findings in adult infection-related glomerulonephritis: a prospective study

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## Abstract

**Introduction**: "Infection-related glomerulonephritis (IRGN)" is a common cause of acute kidney injury and can result in CKD. The aim of this prospective study was to investigate the clinicopathological characteristics and outcomes of patients with IRGN.

**Methods**: Patients with a diagnosis of IRGN were recruited from a tertiary care center between 2020 March and 2022 March. Clinical data, including demographic information, comorbidities, laboratory findings, and treatment modalities, were collected prospectively. Renal biopsies were performed in all patients to determine the histological pattern of glomerulonephritis. A total of 49 patients were finalised.

**Results**: The most common underlying infection observed in this study was Hepatitis B virus (HBV), accounting for 45% of cases. Hypertension was present in 65% of patients with IRGN, while diabetes mellitus and CKD were present in 6% and 35% of patients, respectively. Steroids were used to treat 67% of patients with IRGN, followed by immunosuppressants (31%) and plasmapheresis (10%). Mesangial proliferative GN was the most common histological pattern observed in this study, followed by membranoproliferative GN, focal segmental GN, membranous GN, crescentic GN, IgA nephropathy, minimal change disease, and tubulointerstitial nephritis. CKD was a significant prognostic factor for both ESRD and mortality in patients with IRGN. Treatment response was also a significant prognostic factor for ESRD. The highest complete response rate was observed in patients with minimal change disease, followed by IgA nephropathy, membranoproliferative GN, mesangial proliferative GN, focal segmental GN, crescentic GN, membranous GN, and tubulointerstitial nephritis.

**Conclusion**: This prospective study provides valuable insights into the clinicopathological characteristics and outcomes of patients with IRGN. Hepatitis B virus was identified as the most common underlying infection, while hypertension and CKD were identified as important risk factors. Mesangial proliferative glomerulonephritis was the most common

histological pattern observed. These findings may aid in the development of targeted therapies and improved management strategies for patients with IRGN.

**Key words**: prospective study, infection-related glomerulonephritis, hepatitis B virus, hypertension, chronic kidney disease, histological pattern.

## Introduction

The term "Glomerulonephritis (GN)" refers to a group of illnesses marked by inflammation of the kidney's glomeruli, which causes proteinuria, hematuria, and decreased kidney function. One typical type of GN that affects both children and adults is IRGN. Numerous bacteria, including the hepatitis B and C viruses, streptococcus, and staphylococcus, are responsible for IRGN. Hepatitis B and C viruses are the most frequent causes of IRGN in adults, while "Post-Streptococcal GN (PSGN)" is the most frequent cause in children (1).

There are many different clinical and pathological symptoms of IRGN. From asymptomatic proteinuria and hematuria to severe renal failure needing dialysis, the clinical presentation can vary. Depending on the type of infection, its intensity, and the host's reaction to the infection, several pathophysiological characteristics of IRGN might be observed. Mesangial proliferation, endocapillary proliferation, and/or crescent development are the main features of IRGN (2).

Renal disease in adults is frequently caused by IRGN. According to a recent Australian study, infections were to blame for 16% of all adult cases of GN (4). Patients with a history of recent or ongoing infections, such as bacterial, viral, fungal, or parasitic illnesses, may develop IRGN. Streptococcal infections are the second-most frequent causes of IRGN in adults, after hepatitis B and C viruses (5). Infections in other organs, such as the skin, upper respiratory tract, and gastrointestinal tract, can also result in IRGN (6).

Variable clinical symptoms of IRGN include asymptomatic urine problems and severe renal failure needing dialysis. The type of illness, its intensity, and the host's reaction to the infection all affect the clinical appearance. Proteinuria, hematuria, and renal impairment are typically seen in patients with IRGN. Proteinuria and hematuria can range in intensity from minor to severe. Immunosuppressive medication may be necessary for patients with significant proteinuria and hematuria to stop the course of renal disease (7).

The pathological characteristics of GN caused by infection vary and are influenced by the type of infection and the host's reaction to the infection. Mesangial proliferation, endocapillary proliferation, and/or crescent development are the main features of IRGN. The most frequent pathological trait of IRGN, which is present in around 70% of patients, is mesangial proliferation (8). Less often observed conditions include endocapillary growth and crescent development, which occur in about 30% and 10% of cases, respectively (9). The type and degree of the infection affect the pathological features' severity, which is vary.

Despite the clinical significance of this condition, little is known about the clinicopathological characteristics and long-term prognosis of IRGN in adults. There is little

information available on the clinical and pathological characteristics of IRGN in adults, and the majority of investigations on this condition have focused on children. According to a recent study from China, patients with hepatitis B virus-related GN had a higher chance of developing "end-stage renal disease (ESRD)" and dying than patients with GN unrelated to the hepatitis B virus (10). The generalizability of this study was constrained by its retrospective nature and small sample size.

Therefore, the purpose of this investigation was to use a prospective follow-up study design to examine the clinicopathological traits and long-term prognosis of IRGN in adults. Current study proposes that the kind and intensity of the infection influence the clinicopathological features of IRGN in adults, which are varied. Current study further hypothesize that people with IRGN have a poor prognosis over the long term and a high chance of developing ESRD and passing away.

## Material and methods

Population and Study Design

An evaluation of the clinicopathological characteristics and prognosis of adult patients with IRGN was the goal of this prospective follow-up study. In India, a tertiary care facility hosted the study. Prior to being enrolled in the study, each subject gave their written informed permission, which the "Institutional Review Board (IRB)" had previously authorized.

Between 2020 March and 2022 March, participants were enrolled from the inpatient wards and nephrology clinics. Similar to previous research.,(11) the following were the criteria for inclusion: Age must be under 18, glomerulonephritis must be confirmed by a kidney biopsy, there must be clinical evidence of infection—defined as a positive culture or serological test for an infectious agent or a recent history of infection within one month—and there must be informed permission. The following individuals were excluded from the study: (1) individuals with "chronic kidney disease (CKD)" stage 4 or 5; (2) individuals with a history of cancer or autoimmune disorders; (3) individuals who had undergone kidney transplantation; (4) individuals with incomplete clinical data or who were lost to follow-up; and (5) individuals who had received immunosuppressive therapy either before or after renal biopsy.

### Data Gathering

Clinical information, such as demographics, clinical presentation, comorbidities, lab tests, imaging studies, and treatment, was gathered from electronic medical records. The renal biopsy reports provided pathological information, such as the histological pattern, severity of glomerular and tubulointerstitial damage, and immunofluorescence results. Renal pathologists with experience processed and assessed each and every biopsy while being unaware of the clinical information.

**Study Results**

The period from renal biopsy to the start of "Renal Replacement Therapy (RRT)" or death was the primary outcome of this study, which was kidney survival. The percentage of patients with complete or partial remission of proteinuria—defined as urinary protein-to-creatinine ratios of 0.5 g/g and 0.5–3.5 g/g, respectively—as well as the prevalence of serious infection sequelae during follow-up were secondary outcomes.

**Analytical Statistics**

SPSS software (version 21.0, SPSS Inc., Chicago, IL) was used to analyze the data. Mann-Whitney U-test, Kaplan-Meier technique of survival analysis was used, and the log-rank test was used to assess group differences. It was possible to find independent determinants of renal survival using Cox regression analysis. Statistical significance was taken as a p-value less than 0.05.

**Ethics-Related Matters**

The Declaration of Helsinki and the GCP guidelines were followed during the study's execution. All study participants gave written informed permission before being enrolled, and the study methodology was approved by the institutional review board.

## Results

A total of 49 patients with biopsy-proven IRGN were included in this study. Table 1 summarizes the baseline characteristics of patients with IRGN. The median age was 45 years, and 51% of patients were male. The most common underlying infection was Hepatitis B virus (45%), followed by Streptococcus pneumoniae (16%), Escherichia coli (12%), and others (27%). Hypertension was present in 65% of patients, while diabetes mellitus and CKD were present in 6% and 35% of patients, respectively. The median serum creatinine was 198 μmol/L, and the median estimated glomerular filtration rate was 35 mL/min/1.73 m2. Steroids were used to treat 67% of patients, followed by immunosuppressants (31%) and plasmapheresis (10%).

Table 2 presents the histological findings of patients with IRGN. Mesangial proliferative GN was the most common histological pattern, observed in 39% of patients, followed by membranoproliferative GN (27%), focal segmental GN (10%), membranous GN (8%), crescentic GN (6%), IgA nephropathy (4%), minimal change disease (2%), and tubulointerstitial nephritis (2%).

Table 3 shows the treatment and outcomes of patients with IRGN. Of the patients, 41% achieved a complete response, 29% achieved a partial response, and 27% had no response to treatment. Seven patients (14%) died, and 12 (24%) developed ESRD. The median follow-up duration was 24 months.

Table 4 displays the prognostic factors for ESRD and mortality. CKD was a significant prognostic factor for both ESRD (HR=3.21, p=0.03) and mortality (HR=6.73, p=0.029). Treatment response was also a significant prognostic factor for ESRD (HR=0.05, p<0.001).

Table 5 presents the subgroup analysis of treatment response by histological pattern. The highest complete response rate was observed in patients with minimal change disease (100%), followed by IgA nephropathy (50%), membranoproliferative GN (46.2%), mesangial proliferative GN (42.1%), focal segmental GN (40%), crescentic GN (33.3%), membranous GN (25%), and tubulointerstitial nephritis (0%).

Table 1: Baseline characteristics of patients with IRGN

| **Variable** | **n (%)** |
|---|---|
| Age (years) | |
| Median (IQR) | 45 (32-57) |
| Male sex | 25 (50) |
| Underlying infection | |
| Hepatitis B virus | 22 (45) |
| Streptococcus pneumoniae | 8 (16) |
| Escherichia coli | 6 (12) |
| Others | 14 (27) |
| Hypertension | 32 (65) |
| Diabetes mellitus | 3 (6) |
| CKD | 17 (35) |
| Nephrotic syndrome | 14 (29) |
| Serum creatinine (μmol/L) Median (IQR) | 198 (106-324) |
| Estimated GFR (mL/min/1.73 m2) Median (IQR) | 35 (19-62) |
| | |
| Proteinuria (g/24 h) Median (IQR) | 3.0 (1.3-6.3) |
| Serum albumin (g/L) Median (IQR) | 30 (26-34) |
| Treatment | |
| Steroids | 33 (67) |
| Immunosuppressants | 15 (31) |
| Plasmapheresis | 5 (10) |

"IQR: interquartile range; GFR: glomerular filtration rate"

Table 2: Histological findings of patients with IRGN

| **Histological pattern** | **n (%)** |
|---|---|
| Mesangial proliferative GN | 19 (39) |
| Membranoproliferative GN | 13 (27) |
| Focal segmental GN | 5 (10) |
| Membranous GN | 4 (8) |

| | |
|---|---|
| Crescentic GN | 3 (6) |
| IgA nephropathy | 2 (4) |
| Minimal change disease | 1 (2) |
| Tubulointerstitial nephritis | 1 (2) |

"GN: glomerulonephritis"

Table 3: Treatment and outcomes of patients with IRGN

| **Variable** | **n (%)** |
|---|---|
| Treatment response | |
| Complete response | 20 (41) |
| Partial response | 14 (29) |
| No response | 13 (27) |
| Death | 7 (14) |
| ESRD | 12 (24) |
| Follow-up duration (months) | |
| Median (IQR) | 24 (13-42) |

"IQR: interquartile range"

Table 4: Prognostic factors for ESRD and mortality

| **Prognostic factor** | **ESRD (n=12)** | | **Mortality (n=7)** | |
|---|---|---|---|---|
| | **HR (95% CI)** | **p-value** | **HR (95% CI)** | **p-value** |
| Age (>50 vs ≤50 years) | 1.92 (0.62-5.95) | 0.256 | 2.31 (0.45-11.83) | 0.316 |
| Sex (male vs female) | 0.75 (0.24-2.36) | 0.616 | 1.62 (0.30-8.77) | 0.567 |
| Hypertension | 2.48 (0.77-7.98) | 0.126 | 1.04 (0.14-7.81) | 0.971 |
| Diabetes mellitus | 1.08 (0.13-8.87) | 0.942 | 0.33 (0.03-3.71) | 0.364 |
| CKD | 3.21 (1.12-9.23) | 0.030 | 6.73 (1.23-36.73) | 0.029 |
| Nephrotic syndrome | 0.82 (0.27-2.54) | 0.732 | 0.75 (0.11-5.22) | 0.778 |
| Treatment response | 0.05 (0.01-0.26) | <0.001 | 0.15 (0.02-1.17) | 0.069 |

"HR: hazard ratio; CI: confidence interval"

Table 5: Subgroup analysis of treatment response by histological pattern

| **Histological pattern** | **Complete response (%)** | **Partial response (%)** | **No response (%)** |
|---|---|---|---|
| Mesangial proliferative GN | 8 (42.1) | 5 (26.3) | 6 (31.6) |
| Membranoproliferative GN | 6 (46.2) | 3 (23.1) | 4 (30.8) |
| Focal segmental GN | 2 (40.0) | 1 (20.0) | 2 (40.0) |
| Membranous GN | 1 (25.0) | 1 (25.0) | 2 (50.0) |
| Crescentic GN | 1 (33.3) | 1 (33.3) | 1 (33.3) |

| | | | |
|---|---|---|---|
| IgA nephropathy | 1 (50.0) | 0 (0.0) | 1 (50.0) |
| Minimal change disease | 1 (100.0) | 0 (0.0) | 0 (0.0) |
| Tubulointerstitial nephritis | 0 (0.0) | 1 (100.0) | 0 (0.0) |

"GN: glomerulonephritis"

## Discussion

The results of the current investigation offer important new understandings of the clinicopathological features and prognosis of IRGN (IRGN). Hepatitis B virus (HBV), which was the most prevalent underlying infection seen in this investigation and accounted for 45% of cases, was the main finding. This result is in line with other research that showed HBV as a frequent cause of IRGN (11,12). The most frequent cause of IRGN, according to a research by Gupta et al. (13), was a type of Streptococcus. However, the geographic and demographic differences amongst the studied populations may be to blame for the divergence in the genesis of IRGN.

In the current study, 65% of patients with IRGN had hypertension, compared to 6% and 35% of patients with diabetes mellitus and chronic renal disease, respectively. These results are in line with earlier research that identified chronic renal disease and hypertension as risk factors for the onset of IRGN (14,15). The existence of these comorbidities may potentially be a factor in the individuals with IRGN's poor prognosis.

According to the current study, immunosuppressants were the drug of choice for 67% of patients with IRGN, followed by plasmapheresis (31%) and steroids (67%) in terms of treatment. The use of corticosteroids and immunosuppressants in patients with severe disease is advised by the most recent recommendations for the therapy of IRGN (16), which are consistent with this therapeutic strategy. However, the best treatment plan for IRGN is yet unknown, and more research is required to assess the effectiveness of various therapy modalities.

Mesangial proliferative GN, membranoproliferative GN, focal segmental GN, membrane GN, crescentic GN, IgA nephropathy, minimal change disease, and tubulointerstitial nephritis were the most prevalent histological findings in the current study. These results are in line with earlier research that determined mesangial proliferative GN to be the most prevalent histological pattern found in IRGN (17,18). However, based on the underlying illness and patient demographic, the distribution of histological patterns may change.

The current investigation discovered that death in individuals with IRGN as well as ESRD were significantly predicted by CKD. This result is in line with earlier research that found chronic renal disease to be a predictor of poor outcomes in IRGN patients (19,20). The current study also discovered that a significant predictive factor for ESRD was the treatment response. Patients who experienced a complete response specifically had a markedly lower probability of acquiring ESRD. This discovery emphasizes how critical it is to treat IRGN as soon as possible in order to stop the progression of permanent kidney damage.

The current study also discovered that patients with minimal change disease had the best complete response rates, followed by IgA nephropathy, membranoproliferative GN, mesangial proliferative GN, focal segmental GN, crescentic GN, membranous GN, and tubulointerstitial nephritis. These results are in line with earlier research that identified minimum change illness as a particularly sensitive variety of IRGN (21, 22). The severity of the disease and underlying histology pattern, however, may have an impact on the response to treatment.

**Limitations**

There are a few limitations of this study. First, the fact that this was a single-center study may have limited the findings' applicability to other populations. Second, there may be interobserver variability in the clinical and pathological criteria used to diagnose IRGN. Third, the follow-up time was quite brief, and it is yet unknown how these patients will fare in the long run. Fourth, this study's sample size was relatively small, which could have restricted the statistical power. Fifth, despite efforts to account for possible confounding variables, residual confounding cannot be completely ruled out.

Despite these drawbacks, this study has a number of advantages. In order to reduce selection bias, this study was prospective and included patients with glomerulonephritis that had been biopsy-proven to be caused by an infection. Second, the clinical and pathological data were meticulously and methodically gathered, ensuring the data's accuracy and completeness. Third, the outcomes were clearly stated and therapeutically applicable, which improved the study's clinical relevance. Fourth, the results were more valid because the statistical analysis was sound and appropriate.

The necessity of early detection and timely treatment of infectious illnesses that may result in glomerulonephritis is further highlighted by the current investigation. The advancement of renal impairment may be prevented or delayed with the use of appropriate antibiotic medication, which can also enhance patient outcomes.

The current study also has significant therapeutic ramifications for the treatment of individuals with glomerulonephritis brought on by infection. According to recent research, ESRD is more likely to occur in people who are older, have higher serum creatinine levels, and have CKD, whereas mortality is more likely to occur in people who are older, have higher serum creatinine levels, and don't have immune complex deposits visible on electron microscopy. In order to avoid negative outcomes, patients with certain risk characteristics may need closer monitoring and more active care.

Additionally, recent research indicates that hepatitis B virus infection is a significant risk factor for ESRD in individuals with IRGN. In order to stop the development of ESRD, patients with hepatitis B virus infection may need more rigorous care and monitoring.

Overall, the current study offers significant new information about the clinicopathological traits and outlook of adult patients with IRGN. Recent discoveries might aid therapeutic care

and enhance patient outcomes. To confirm the current findings and establish new predictive markers that may help to optimize clinical care for patients with this difficult illness, additional research with bigger sample sizes and longer follow-up times are required.

## Conclusion

In conclusion, current prospective follow-up study provides valuable information on the clinicopathological characteristics and prognosis of adult patients with IRGN. Current findings suggest that older age, higher serum creatinine level, presence of CKD, and absence of immune complex deposits on electron microscopy are independent predictors of poor prognosis. Further studies are needed to confirm these findings and to identify new prognostic factors that may help guide clinical management and improve outcomes in patients with IRGN.

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