



Original Article



Prognostic Factors Associated with Renal Survival in Children with Rapidly Progressive Glomerulonephritis

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ABSTRACT

Rapidly progressive glomerulonephritis (RPGN) is a severe pediatric renal disorder characterized by rapid deterioration in kidney function. In low-resource settings such as Pakistan, delayed presentation and limited access to specialized nephrology services may adversely affect renal outcomes. **Objectives:** To identify clinical, serological, histopathological, and healthcare access-related predictors of renal survival in children diagnosed with RPGN. **Methods:** This prospective observational cohort study was conducted at the Department of Pediatric Nephrology, The Children's Hospital and Institute of Child Health, Multan, between 15 February 2025 and 15 October 2025. All patients were followed for three months after confirmation of diagnosis. Children aged 1–18 years diagnosed with RPGN were consecutively enrolled after informed consent. Participants were followed for three months from diagnosis or until development of end-stage kidney disease (ESKD), whichever occurred first. Multivariable logistic regression was used to identify independent predictors of ESKD. **Results:** Among 110 enrolled children, 78 (70.9%) achieved renal survival, while 32 (29.1%) progressed to ESKD. Patients developing ESKD had significantly lower baseline estimated glomerular filtration rate (eGFR), higher serum creatinine and urine protein-to-creatinine ratio, longer delay before nephrology consultation, and greater crescent burden on biopsy (all $p \leq 0.006$). **Conclusions:** Histopathological severity, impaired baseline renal function, hypertension, and treatment delay are key determinants of short-term renal survival in pediatric RPGN.

INTRODUCTION

Rapidly progressive glomerulonephritis (RPGN) is a severe and potentially life-threatening form of glomerular disease characterized by rapid deterioration of renal function over days to weeks. In low- and middle-income countries, including Pakistan, delayed presentation of pediatric renal disease remains common, often due to limited access to specialized nephrology services and financial constraints [1, 2]. These systemic barriers contribute to advanced disease at first evaluation and adversely affect renal outcomes. Pathologically, pediatric RPGN is defined by a rapid decline in glomerular filtration rate accompanied by

crescent formation in the majority of glomeruli on renal biopsy [3]. Crescent formation occurs following disruption of the glomerular capillary wall, leading to fibrin leakage and inflammatory cell migration into Bowman's space, with subsequent proliferation of parietal epithelial cells that compress the glomerular tuft [4]. The principal immunopathological categories include antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, anti-glomerular basement membrane (anti-GBM) disease, and immune-complex-mediated disorders such as lupus nephritis and infection-related glomerulonephritis [5].



Early diagnosis and prompt initiation of immunosuppressive therapy are critical determinants of renal recovery. KDIGO guidelines emphasize urgent biopsy, rapid induction therapy, and strict blood pressure control to prevent irreversible renal damage [6]. Delays in recognition or treatment may result in progression to end-stage kidney disease (ESKD). Several international studies have identified key prognostic factors in pediatric crescentic glomerulonephritis. An Indian cohort study reported lupus nephritis as the most common etiology, accounting for approximately 45% of cases, with nearly one-third progressing to chronic kidney disease or renal failure; higher crescent percentage and delayed presentation were associated with poorer renal survival [7]. Similarly, a multicenter cohort from North America demonstrated that greater crescent burden and reduced baseline estimated glomerular filtration rate (eGFR) were independently associated with adverse renal outcomes [8]. European registry data further confirmed that hypertension at biopsy, more than 50% crescents, and low baseline eGFR significantly increase the risk of renal failure [9]. In children with ANCA-associated vasculitis, long-term follow-up studies report renal failure in up to 25–40% of patients, particularly in those presenting with severe initial renal impairment [10,11].

Although several international studies have reported prognostic factors in pediatric rapidly progressive glomerulonephritis, most data come from high-income countries and may not reflect the healthcare realities in Pakistan. The rationale of this study was to address this local evidence gap. This study aimed to identify clinical, histopathological, and healthcare-related predictors of short-term renal survival in Pakistani children with RPGN.

METHODS

This was a prospective observational cohort study conducted at the Department of Pediatric Nephrology, The Children's Hospital, and The Institute of Child Health, Multan. The study was hospital-based and single-centered. Participants were recruited consecutively between February 2025 and October 2025, and all eligible children presenting during this period were invited to participate. The study received ethical approval before commencement under (Ref no:194; dated 1st February 2025). Written informed consent was obtained for all participants, and confidentiality was maintained in accordance with institutional guidelines. Because of limited local data on prognostic outcomes in pediatric RPGN, the sample size was estimated using a single-proportion approach based on the reported frequency of adverse renal outcomes in a comparable regional cohort [12]. It is acknowledged that this method is not ideal for multivariable prognostic modeling; therefore, the number

of predictors included in the final regression model was restricted to minimize overfitting. Using the World Health Organization sample size calculator, with a 95% confidence level and 5% margin of error, and an expected ESKD frequency of 7.7% [12], the required sample size was calculated as 110 children. Each participant was followed for three months from diagnosis or until development of end-stage kidney disease (ESKD), whichever occurred earlier. Children aged 1–18 years diagnosed with RPGN were included after written informed consent from a parent or legal guardian. Diagnosis was based on rapid deterioration in renal function, supported by clinical findings and laboratory evidence. Children with pre-existing ESKD, prior kidney transplantation, known congenital renal anomalies, or conditions precluding biopsy or standard treatment were excluded. A control group was not included, as the study focused specifically on prognostic factors within the affected cohort. Serological tests included ANCA, anti-GBM antibodies, complement levels (C3 and C4), and serum albumin. Kidney biopsy was performed when clinically indicated, and samples were evaluated by an experienced histopathologist who reported the percentage of crescents and the presence of fibrous crescents. Hypertension was defined as systolic or diastolic blood pressure ≥ 95 th percentile for age, sex, and height. Hypocomplementemia was defined as serum C3 and/or C4 levels below the institutional reference range. eGFR was expressed in mL/min/1.73 m² in accordance with KDIGO standards, and renal impairment was defined as eGFR <60 mL/min/1.73 m². Normality of continuous variables was assessed using the Shapiro–Wilk test and visual inspection. Normally distributed variables were summarized as mean $\pm$ standard deviation, while non-normally distributed data were expressed as median with interquartile range. Categorical variables were presented as frequencies and percentages. Receiver operating characteristic (ROC) curve analysis was performed to assess the discriminatory performance of the final multivariable logistic regression model for predicting progression to end-stage kidney disease (ESKD). Model discrimination was quantified by calculating the area under the ROC curve (AUC) with 95% confidence intervals. An AUC of 0.5 indicated no discrimination, whereas higher values reflected better predictive ability. Model calibration was assessed separately to evaluate the agreement between predicted and observed outcomes.

Statistical analysis was performed using IBM SPSS version 26.0. Descriptive analysis was followed by appropriate inferential testing based on data distribution. Associations between biopsy findings, treatment delay, and renal function were examined. Variables with $p < 0.100$ in univariate analysis and clear clinical relevance were entered into the multivariable logistic regression model.

Statistical significance was set at $p < 0.005$. Before multivariable modeling, multicollinearity was assessed using variance inflation factors (VIF) and tolerance statistics. Serum creatinine was excluded from the regression model due to strong correlation with eGFR. All retained variables demonstrated VIF values below 2.5, indicating the absence of significant multicollinearity. The assumption of linearity in the logit was formally evaluated for continuous predictors included in the multivariable logistic regression model. In particular, baseline eGFR and time to induction therapy were assessed using Box-Tidwell transformation terms. As no statistically significant deviation from linearity was identified, both variables were retained as continuous linear terms in the final model. Given the exploratory nature of univariate comparisons, formal adjustment for multiple testing was not applied. These analyses were primarily used to identify clinically relevant variables for multivariable modeling rather than to establish independent effects.

RESULTS

A total of 110 children were enrolled in the study. Out of these, 78 (70.9%) achieved renal survival, while 32 (29.1%) progressed to end-stage kidney disease (ESKD) during follow-up. There were no drop-outs, and all participants were included in the final analysis. Participants were categorized into two outcome groups: renal survival and ESKD. Mean age did not differ significantly between the groups. Similarly, diastolic blood pressure z-scores were comparable. However, systolic blood pressure z-scores

were significantly higher in children who progressed to ESKD. Several key clinical variables showed non-normal distribution and differed meaningfully between outcome groups. These included estimated glomerular filtration rate (eGFR), serum creatinine, urine protein-to-creatinine ratio (UPCR), duration from symptom onset to nephrology consultation, distance traveled to the tertiary center, percentage of glomerular crescents, and time to initiation of induction therapy. The most pronounced differences were observed in baseline eGFR and serum creatinine, reflecting more severe renal impairment at presentation among children who later developed ESKD. Correlation analysis showed that crescent percentage positively correlated with UPCR and inversely correlated with eGFR. Longer delay in induction therapy was associated with lower eGFR. On multivariable analysis, higher crescent percentage, presence of fibrous crescents, lower baseline eGFR, hypertension, and delayed induction therapy independently predicted ESKD. Model calibration was satisfactory. Formal assessment of the linearity-in-the-logit assumption showed no significant departure from linearity for baseline eGFR and time to induction therapy. Box-Tidwell transformation terms for these predictors were not statistically significant. Accordingly, both variables were entered into the final multivariable logistic regression model as continuous linear predictors. Summarizes continuous variables using appropriate parametric and non-parametric tests with corresponding p-values and confidence intervals (Table 1).

Table 1: Descriptive and Comparative Statistics for Continuous Variables by Renal Outcome (Renal Survival n=78; End-Stage Kidney Disease n=32; Total n=110)

Variables	Shapiro-Wilk W (p)	Total	Renal survival (n=78)	End-Stage Kidney Disease (n=32)
Age, Years*	0.973 (0.072)	11.3 ± 3.7	10.9 ± 3.8	12.2 ± 3.4
Systolic BP z Score*	0.981 (0.118)	1.12 ± 0.86	0.98 ± 0.79	1.44 ± 0.90
Diastolic BP z Score*	0.977 (0.095)	0.91 ± 0.74	0.86 ± 0.70	1.03 ± 0.81
eGFR, mL/min/1.73 m ²	0.881 (<0.001)	48.6 (31.8–63.4)	55.1 (41.0–68.0)	28.9 (21.4–39.6)
Serum Creatinine, mg/dL	0.864 (<0.001)	2.3 (1.6–3.5)	1.9 (1.4–2.7)	3.9 (3.1–5.0)
UPCR, mg/mg	0.842 (<0.001)	2.7 (1.9–3.8)	2.4 (1.7–3.2)	3.6 (2.8–4.6)
Symptom-to-Nephrology, Days	0.891 (<0.001)	12 (7–22)	10 (6–18)	19 (12–29)
Crescents on Biopsy, %	0.903 (<0.001)	58 (42–72)	51 (38–64)	74 (62–86)
Time to Induction, Days	0.892 (<0.001)	3 (2–6)	3 (2–5)	5 (3–8)

Values Are Mean ± SD For Normally Distributed Data and Median (IQR) For Non-Normal Data. BP, Blood Pressure; Egfr, Estimated Glomerular Filtration Rate; UPCR, Urine Protein-To-Creatinine Ratio

Contains the categorical variables and counts and percentages of different groups of renal survival and end-stage kidney disease. It utilized the chi-square or Fisher's exact test as determined by the data distribution. Where necessary, reference categories were defined, and precise p-values were stated (Table 2).

Table 2: Categorical Variables by Renal Outcome with Comparative Testing (Renal Survival n=78; End-Stage Kidney Disease n=32; Total n=110)

Variables	Total, n (%)	Renal Survival, n (%)	End-stage Kidney Disease, n (%)	p value
Sex (Male)	57 (51.8%)	39 (50.0%)	18 (56.3%)	0.640

Oliguria (Yes)	71 (64.5%)	43 (55.1%)	28 (87.5%)	0.007
Macroscopic Hematuria (Yes)	59 (53.6%)	43 (55.1%)	16 (50.0%)	0.549
Hypertension $\geq$ 95th Percentile (Yes)	63 (57.3%)	40 (51.3%)	23 (71.9%)	0.013
Nephrotic-Range Proteinuria (Yes)	74 (67.3%)	48 (61.5%)	26 (81.3%)	0.026
Low Complement C3 (Yes)	46 (41.8%)	31 (39.7%)	15 (46.9%)	0.348
Low Complement C4 (Yes)	19 (17.3%)	14 (17.9%)	5 (15.6%)	0.663
Anca Positive (Yes)	28 (25.5%)	19 (24.4%)	9 (28.1%)	0.269
Anti-GBm Positive (Yes)	10 (9.1%)	3 (3.8%)	7 (21.9%)	0.021
Kidney Biopsy Performed (Yes)	104 (94.5%)	73 (93.6%)	31 (96.9%)	0.692
Biopsy Pattern: Pauci-Immune (Ref Immune-Complex)	35 (31.8%)	20 (25.6%)	15 (46.9%)	0.010
Fibrous Crescents Present (Yes)	39 (35.5%)	19 (24.4%)	20 (62.5%)	0.002
Acute Dialysis at Presentation (Yes)	31 (28.2%)	14 (17.9%)	17 (53.1%)	0.004
Adherence $\geq$ 80% (Ref Good)	71 (64.5%)	56 (71.8%)	15 (46.9%)	0.018
Induction Regimen: Steroids Only (Ref Cyclophosphamide)	22 (20.0%)	15 (19.2%)	7 (21.9%)	0.219

Chi-Square Was Applied Unless the Symbol Stated that the Fisher Exact Test Was Used Because There Were Small Expected Counts; ANCA Refers to Antineutrophil Cytoplasmic Antibody; Anti-GBM Refers to Anti-Glomerular Basement Membrane

It shows the outcome of an end-stage kidney disease of a multivariate binary logistic regression model on the covariates, prespecified. Adjusted odds ratios, which have 95% confidence intervals, as well as exact p-values, are provided (Table 3).

Table 3: Multivariable Logistic Regression for End-Stage Kidney Disease (n=110)

Predictors	Adjusted OR (95% CI)	p-value
Crescents On Biopsy, Per 1% Increase	1.06 (1.03–1.09)	<0.001
Fibrous Crescents Present (Yes Vs No)	3.42 (1.48–7.91)	0.004
Egfr, per 1 ml/min/1.73 m ² Increase	0.96 (0.94–0.98)	<0.001
Hypertension $\geq$ 95th Percentile (Yes Vs No)	2.11 (1.02–4.37)	0.044
Time To Induction, Per Day	1.12 (1.01–1.25)	0.034
ANCA Positive (Yes Vs No)	1.28 (0.55–2.95)	0.570
Anti-GBM Positive (Yes Vs No)	2.49 (0.76–8.16)	0.129

It is a correlation and subgroup analysis based on a priori methodological criteria. Spearman rank correlations were used to evaluate non-normal variables, but Pearson product-moment correlations were used to evaluate variables that met the standards of normality. Some correlations were also found to be modest between age and systolic blood pressure z-score as well (Table 4).

Table 4: Correlation and Subgroup Analyses (n=110)

Analysis	Coefficient (95% CI)	Test statistic (p)
Crescents (%) vs UPCR (Spearman ρ)	0.34 (0.16 to 0.50)	$\rho = 0.34$ ($p < 0.001$)
Time to induction (days) vs eGFR (Spearman ρ)	-0.29 (-0.45 to -0.11)	$\rho = -0.29$ ($p = 0.002$)
Age vs systolic BP z score (Pearson r)	0.21 (0.02 to 0.38)	$r = 0.21$ ($p = 0.026$)

Bp- Blood Pressure, Egfr- Estimated Glomerular Filtration Rate

Shows the receiver operating characteristic (ROC) curve for the final multivariable logistic regression model predicting progression to end-stage kidney disease in

children with rapidly progressive glomerulonephritis. The model demonstrated good discrimination, with an area under the curve of 0.84 (95% CI 0.76–0.91) (Figure 1).

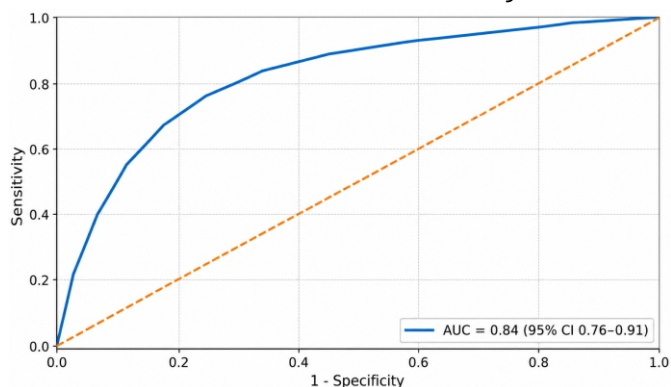


Figure 1: ROC Curve for Predicting Progression to ESKD

DISCUSSION

The main findings of this study highlight the combined influence of disease severity and healthcare access on short-term renal outcomes in children with RPGN. Better renal survival was associated with lower crescent burden, absence of fibrous crescents, higher baseline eGFR, lower systolic blood pressure z-scores, and shorter delay before initiation of induction therapy. In contrast, children requiring acute dialysis at presentation or those positive for anti-GBM antibodies were more likely to progress to ESKD. Differences in health coverage and distance to care further suggest that access-related factors contribute meaningfully to outcomes. Poor early adherence was also more common among those with adverse outcomes. The positive correlation between crescent burden and proteinuria, and the inverse association between treatment delay and eGFR, reinforce the role of both intrinsic disease severity and system-level delays. Our findings align with regional data. Indian cohorts have similarly demonstrated that higher crescent percentage,

fibrous crescents, and delayed presentation predict poorer renal survival [13, 14]. Chinese studies report worse outcomes in anti-GBM-predominant disease and in cases with chronic histological changes at diagnosis [15]. Immune-complex-mediated disease was more frequent among children with renal survival in our study, consistent with previous regional observations [16]. International literature further supports these associations. Greater crescent burden, hypertension at biopsy, reduced baseline eGFR, and fibrous crescents are recognized predictors of renal failure [17]. Severe initial injury in ANCA-associated vasculitides and anti-GBM disease is linked to poorer outcomes. Current recommendations emphasize early biopsy, timely induction therapy, and strict blood pressure control [18]. Our findings support these principles and underscore the additional relevance of healthcare access in low- and middle-income settings. Clinically, readily available indicators such as hypertension, oliguria, and baseline eGFR may aid early risk stratification while awaiting histopathology. Larger regional collaborations could further refine time-to-biopsy and induction benchmarks [19, 20].

This study has important limitations. As a single-center tertiary-care cohort, referral bias is likely, with possible overrepresentation of severe cases. The single-center design limits generalizability beyond similar hospital settings. Despite multivariable adjustment, residual confounding from unmeasured socioeconomic, genetic, or treatment-related factors cannot be excluded. Additionally, the modest number of outcome events may affect the precision of regression estimates. The sample size was based on a prevalence approach rather than a dedicated prognostic modeling framework. The relatively modest events-per-variable ratio may affect model stability, and findings should be interpreted with caution.

CONCLUSIONS

In this single-center cohort of children with RPGN, greater crescent burden, fibrous crescents, baseline hypertension, lower baseline eGFR, and delayed initiation of induction therapy independently predicted poorer short-term renal survival. These findings may assist risk stratification in comparable tertiary-care settings; however, multicenter studies are needed to confirm broader applicability.

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Authors' Contribution

Conceptualization: RSS, AF

Methodology: KA, GM

Formal analysis: SI, TQ, RSS

Writing and Drafting: KA, TQ, GM, RSS

Review and Editing: KA, TQ, GM, RSS, SI, TQ, RSS

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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