

Association of Laboratory Parameters with Glomerular Crescent Formation in Pediatric Rapidly Progressive Glomerulonephritis

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Abstract

Introduction: Glomerular crescents are a histopathological hallmark of rapidly progressive glomerulonephritis (RPGN), reflecting severe kidney injury and inflammation. This study investigates the association between various laboratory parameters and the formation of glomerular crescents in pediatric patients with rapidly progressive glomerulonephritis (RPGN). **Methods:** This prospective observational study was conducted at the Department of Paediatric Nephrology, Bangladesh Institute of Child Health (BICH) & Dhaka Shishu (Children) Hospital, Bangladesh, from July 2018 to June 2020, with a sample size of 28. A non-probability sampling technique was employed, and data were collected through interviews and then analyzed using the SPSS version 20.0 program. **Result:** In patients with >50% crescentic group, the mean hemoglobin percentage was 9.2 ± 1.07 (gm/dl), while in those with <50% crescentic group, it was 9.94 ± 0.98 (gm/dl), showing a statistically significant difference ($p=0.045$). Other laboratory parameters did not exhibit significant differences between the two groups. The percentage of crescent and serum creatinine showed a weak correlation, but it was not statistically significant (r value=0.277; p value=0.154). Low serum C3 levels were observed in patients with <50% crescentic group. None of the patients in the >50% crescentic group tested positive for ANA and anti-ds DNA. Overall, no significant differences were found between the groups. **Conclusion:** Concluding from the findings, patients with >50% glomerular crescent formation exhibit a statistically significant lower mean hemoglobin percentage. Although there is a weak correlation between the percentage of crescent and serum creatinine, no statistical significance was observed.

Keywords: Glomerulonephritis, Hemoglobin, Serum creatinine, Kidney, RPGN

I. INTRODUCTION

Glomerulonephritis (GN) refers to a group of glomerular diseases marked by inflammation-associated glomerular injury.¹ The diseases causing GN are typically categorized as primary, where the kidney is the primary affected organ, or secondary, involving systemic disorders affecting multiple organs like systemic lupus erythematosus (SLE).² IgA nephropathy (IgAN) stands out as one of the most common primary glomerulonephritis in children and adolescents worldwide, with approximately 20% of children progressing to end-stage kidney disease (ESKD) within two decades of diagnosis.³ Rapidly progressive glomerulonephritis represents a form of GN characterized by an abrupt nephritic illness, leading to swift renal function loss over days to weeks, accompanied by histological evidence of crescent formation. Crescentic GN is identified by the presence of large epithelial crescents in Bowman's space, involving 50 percent or more glomeruli. The terms RPGN (Rapidly Progressive Glomerulonephritis) and crescentic GN are frequently used interchangeably.⁴ This condition can co-occur with most primary forms of glomerulonephritis, and it is also linked to various systemic diseases. The pathology and immunopathology of crescentic glomerulonephritis encompass three main categories: (i) anti-GBM crescentic glomerulonephritis, (ii) immune-complex crescentic glomerulonephritis, and (iii) pauci-immune crescentic glomerulonephritis.⁵ In contrast to immune complex glomerulonephritis and anti-GBM glomerulonephritis, pauci-immune crescentic glomerulonephritis is characterized by an absence or scarcity of glomerular staining for immunoglobulin.⁶ The severity of the disease is, to some extent, linked to the extent of crescent formation. Patients with crescents in more than 80% of glomeruli often present with advanced renal failure that may not respond well to therapy. Conversely, patients with less than 50% of crescents typically experience a more gradual progression of the disease.⁷ Crescents are classified as cellular, fibro cellular, or fibrous based on the following definitions modified from the World Health Organization classification of renal disease.⁸ Crescentic glomerulonephritis (GN) encompasses three major categories in its pathology and immunopathology: anti-GBM crescentic GN, immune-complex crescentic GN, and pauci-immune crescentic GN. While anti-GBM

and immune-complex forms involve distinct immunoglobulin patterns, pauci-immune GN is characterized by an absence or scarcity of glomerular immunoglobulin staining.⁹ The severity of the disease is linked to the degree of crescent formation, with patients exhibiting more than 80% crescents often experiencing advanced renal failure. Timely and precise diagnosis is crucial for initiating appropriate treatment quickly. Patients suspected of rapidly progressive GN should undergo comprehensive investigations, including serology and urgent biopsy, with elevated plasma creatinine commonly observed at diagnosis.¹⁰ This study aims to assess the association between laboratory parameters and histology in pediatric cases of rapidly progressive glomerulonephritis.

II. OBJECTIVE

General Objective

- To analyze the association of laboratory parameters with glomerular crescent formation in pediatric RPGN.

Specific Objectives

- To know the age and gender distribution of the study population.
- To assess the correlation of the percentage of crescent with serum creatinine.
- To see the correlation of days of follow-up with eGFR.

III. METHODS

This observational study was conducted at the Department of Paediatric Nephrology, Bangladesh Institute of Child Health (BICH) & Dhaka Shishu (Children) Hospital, Bangladesh. The research spanned from July 2018 to June 2020 and included a total of 28 pediatric cases exhibiting features of rapidly progressive glomerulonephritis as the study subjects. Ethical approval was obtained from the Bangladesh Institute of Child Health (BICH) ethical committee at the commencement of the study.

Inclusion Criteria

- Patients of 2 to 18 years of age.
- Patients who presented with glomerulonephritis with features of RPGN with rapidly rising serum creatinine concentration than the upper limit of the age-matched normal range.

Exclusion Criteria

- Pre-renal and post-renal AKI.
- Patients who already have treatment with methylprednisolone.
- Patients who have already developed CKD

In this study, a non-probability sampling technique was utilized to enrol participants. Data collection was done from parents or legal guardians, employing a structured questionnaire covering all relevant variables. Ethical approval was obtained from the institutional review committee (IRC), and informed written consent was secured from parents or legal guardians before initiating data collection. The process encompassed detailed history-taking, clinical examinations, laboratory investigations, and renal biopsy. Subsequently, all collected data were entered into a computer and analyzed using Statistical Package for Social Science (SPSS) version 20.0. Quantitative observations were presented as frequencies and percentages. Associations between variables were evaluated using Fisher's exact test for categorical variables and a one-sample t-test for continuous variables, with a P value of <0.05 considered statistically significant.

IV. RESULTS

This prospective observational study was carried out at the Department of Paediatric Nephrology, Bangladesh Institute of Child Health (BICH) & Dhaka Shishu (Children) Hospital, Bangladesh, spanning from July 2018 to June 2020. The study included a total of 28 pediatric cases displaying features of rapidly progressive glomerulonephritis as the study subjects. The majority of patients in this study were male (61%) and younger than 10 years (75%). Additionally, a significant proportion of them hailed from rural areas, constituting 82% of the study population. The mean hemoglobin percentage was 9.2 ± 1.07 in the >50% crescentic group and 9.94 ± 0.98 in the <50% crescentic group, showing a statistically significant difference ($p=0.045$). Other laboratory parameters did not exhibit significant differences between the two groups. The percentage of crescent and serum creatinine showed a weak correlation with an R-value of 0.277, but the association was not statistically significant (p -value=0.154). The analysis of the improvement of estimated GFR in relation to the duration of follow-up revealed a positive and significant relationship between the two parameters, with an R-value of 0.678 and a p -value of less than 0.001. The analysis of the serological parameters in the studied patient population revealed a low serum C3 level in the <50% crescentic group. None of the patients in the >50% crescentic group tested positive for ANA and anti-ds DNA. However, no significant difference was found between the two groups in this regard.

Table 1: Demography of study subjects (N=28)

Variables	N	%
Age (years)		
2-10	21	75
11-18	07	25
Gender		
Male	17	61
Female	11	39
Residence		
Urban	05	18
Rural	25	82

Table 2: Association of lab parameters of RPGN with >50% crescent and <50% crescent (N=28)

Variables	With >50% crescent	With <50% crescent	P-value
	(Mean \pm SD)	(Mean \pm SD)	
Hb% (gm/dl)	9.20 \pm 1.07	9.94 \pm 0.98	0.045*
S. creatinine at entry (mg/dl)	3.0 \pm 1.7	2.1 \pm 1.0	0.162
Peak s. creatinine (mg/dl)	6.98 \pm 4.49	5.6 \pm 2.59	0.157
Peak blood Urea (mmol/L)	37.46 \pm 10.7	35.18 \pm 12.38	0.41
pH	7.23 \pm 0.09	7.23 \pm 0.07	0.5
-HCO ₃ (mmol/L)	10.16 \pm 3.72	11.67 \pm 4.94	0.222
S. Sodium (mmol/L)	136 \pm 8.96	138 \pm 5.3	0.234
S. Potassium (mmol/L)	4.8 \pm 1.09	4.7 \pm 0.64	0.381
S. Calcium (mmol/L)	1.87 \pm 0.22	1.93 \pm 0.15	0.205
S. Albumin (gm/L)	23.68 \pm 8.07	26.0 \pm 4.89	0.442
S. Cholesterol (mmol/L)	5.3 \pm 2.2	4.26 \pm 2.07	0.124
eGFR (ml/min/1.73 m ²) on admission	18.2 \pm 13.6	26.14 \pm 10.16	0.101

P-value <0.05=significant, * p-value reached from one sample t-test

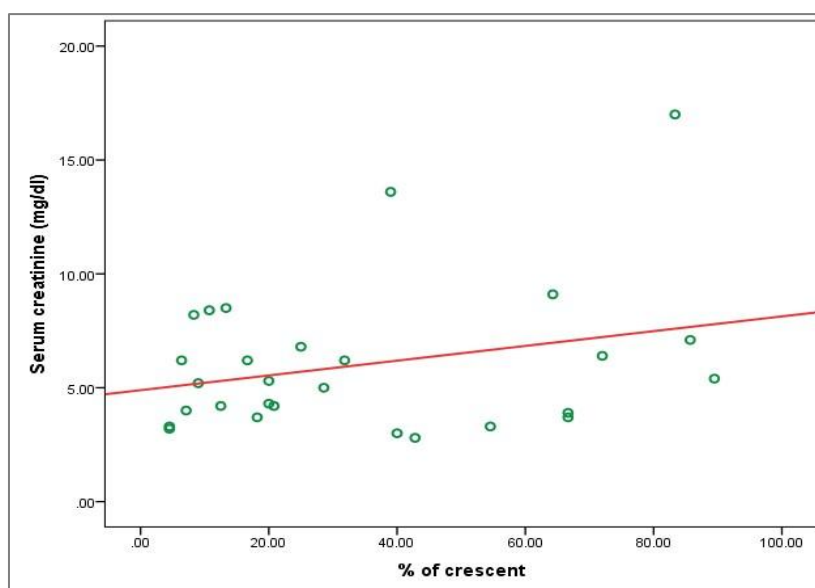


Figure 1: Correlation of % of crescent with serum creatinine (N=28)

Pearson correlation was done. r value (0.7-1.0) = strong correlation, (0.4-0.7) = moderate, (0.2-0.4)=weak, (0.01-0.2)= negligible correlation. p-value <0.05 =significant

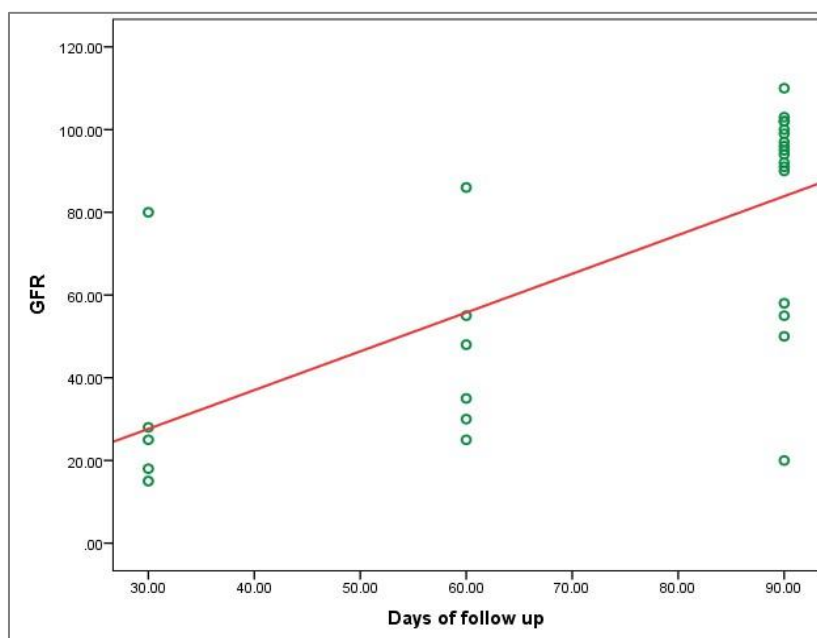


Figure 2: Correlation of days of follow-up with eGFR (N=28)

Table 3: Association of serological parameters of RPGN with >50% and <50% crescent (N=28)

Variables	With >50% crescent	With <50% crescent	P-value
	(n=8)	(n=20)	
	n (%)	n (%)	
Low S. C3 level	5(62)	16(80)	0.334
Low S. C4 level	4(50)	11(55)	0.811
ANA positive	0(00)	3(15)	0.246
Anti-ds DNA positive	0(00)	3(15)	0.246

P-value <0.05=significant, * p-value reached from Fisher's exact test

V. DISCUSSION

The histological features of various forms of crescentic glomerulonephritis (GN) share similarities, mainly characterized by crescents, defined as an accumulation of two or more layers of cells partially or entirely filling the Bowman space.¹¹ These crescents may be entirely cellular or exhibit varying degrees of scarring and fibrosis. Cellular crescents indicate the proliferation of neutrophils, macrophages, and epithelial cells, while fibrous crescents are characterized by the replacement of cells with collagen.¹² Fibro cellular crescents demonstrate features of both cellular and fibrous types. Determining the cause of crescentic GN involves assessing the presence, location, and nature of immune deposits. Different types of GN are associated with distinct patterns of immune deposits, such as IgA deposits in IgA nephropathy and HSP, granular subepithelial deposits of IgG and C3 in post-infectious GN, and mesangial, subendothelial, and intramembranous deposits of IgG and C3 in MPGN.¹³ Vasculitis patients, with or without ANCA positivity, typically exhibit few or no immune deposits in the glomeruli, while anti-GBM disease is characterized by linear staining of the GBM with IgG (occasionally IgM and IgA) and C3. In this study, the onset of the disease ranged from 2 to 18 years, with a mean age of 8.8 ± 2.1 years. The majority of patients were male (61%), with 75% of children being younger than 10 years and 82% residing in rural areas. These demographic characteristics align with the findings of Dewan et al. (2008).⁴ The study observed significantly reduced levels of hemoglobin (Hb%) in the >50% crescentic GN group. While the mean peak serum creatinine was higher in both groups, there was no significant difference between them (6.9 ± 4.9 versus 5.6 ± 2.5 mg/dl). A lower glomerular filtration rate (GFR) was found in >50% crescentic GN compared to <50% crescentic GN (18.2 ± 12.6 ml/min and 26.14 ± 10.16 ml/min, respectively), indicating severe renal failure in the studied children. Other laboratory parameters, including serum electrolytes, blood pH, bicarbonate, and immunological parameters, showed no significant differences between the two groups, consistent with the findings of Dewan D et al.⁴ Karakaya et al. reported significantly low levels of complement factor 3 and albumin in patients with RPGN ($P = 0.019$). Inflammatory parameters, including C-reactive protein (CRP), platelet-to-lymphocyte ratio, CRP/albumin ratio, and erythrocyte sedimentation rate at presentation, were significantly higher in RPGN patients ($P < 0.05$).¹⁴ Another study found that most patients with RPGN had elevated serum creatinine

levels, with creatinine clearance usually less than 10% of normal. Normochromic, normocytic anemia was prevalent, with hemoglobin ranging from 5.2 to 10.9 gm.%. Platelet counts were normal, and ESR was raised in all subjects. Zent R et al. reported low total complement levels and C3 levels in RPGN patients, while C4 levels were low in some cases.¹⁵ In terms of statistical significance, the mean hemoglobin percentage was 9.20 ± 1.07 in the >50% crescentic group and 9.94 ± 0.98 in the <50% crescentic group, showing statistical significance ($p=0.045$).

Limitations of the study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

VI. CONCLUSION & RECOMMENDATION

In conclusion, the study indicates that patients with more than 50% glomerular crescent formation tend to have a significantly lower mean hemoglobin percentage. While there is a weak correlation between the percentage of crescents and serum creatinine levels, the observed association did not reach statistical significance. Additional multicenter research, encompassing a substantial sample size and long-term follow-up, is imperative. Collaboration with pediatric nephrologists is essential to formulate comprehensive guidelines for therapeutic approaches. This collaborative effort aims to enhance renal and patient survival over the long term.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethical committee

REFERENCES

- [1]. Chadban SJ, Atkins RC. Glomerulonephritis. The Lancet. 2005 May 21;365(9473):1797-806.
- [2]. Srivastava R N. and Bagga A.(eds.), 2016, Pediatric nephrology, 6th ed, Jypee the health sciences publisher, New Delhi, India.
- [3]. Cambier A, Boyer O, Deschenes G, Gleeson J, Couderc A, Hogan J, Robert T. Steroid therapy in children with IgA nephropathy. Pediatric nephrology. 2020 Mar; 35:359-66.
- [4]. Dewan D., Gulati S., Sharma R K., Prasad N., Jain M., Gupta A. et al., 2008, 'Clinical spectrum and outcome of crescentic glomerulonephritis in children in developing countries', Pediatric Nephrology, vol. 23, pp. 389-94.
- [5]. Al Mushafi A, Ooi JD, Odobasic D. Crescentic Glomerulonephritis: Pathogenesis and Therapeutic Potential of Human Amniotic Stem Cells. Frontiers in Physiology. 2021 Oct 15; 12:724186.
- [6]. Jennette J C., 2003, Rapidly progressive crescentic glomerulonephritis, Kidney International, vol. 63, pp. 1164-177.
- [7]. El-Husseini A A., Sheashaa H A., Sabry A A., Moustafa F., Sobh M A., 2005, 'Acute postinfectious crescentic glomerulonephritis: Clinicopathologic presentation and risk factors', International Urology and Nephrology, vol.37, pp. 603-09.
- [8]. Shlipak MG, Tummalapalli SL, Boulware LE, Grams ME, Ix JH, Jha V, Kengne AP, Madero M, Mihaylova B, Tangri N, Cheung M. The case for early identification and intervention of chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney international. 2021 Jan 1;99(1):34-47.
- [9]. Morita T, Suzuki Y, Churg J. Structure and development of the glomerular crescent. The American Journal of Pathology. 1973 Sep;72(3):349.
- [10]. Moorani KN, Aziz M, Amanullah F. Rapidly progressive glomerulonephritis in children. Pakistan Journal of Medical Sciences. 2022 Jan;38(2):417.
- [11]. Davin JC, Coppo R. Henoch-Schönlein purpura nephritis in children. Nature Reviews Nephrology. 2014 Oct;10(10):563-73.
- [12]. Jardim HM, Leake J, Risdon RA, Barratt TM, Dillon MJ. Crescentic glomerulonephritis in children. Pediatric Nephrology. 1992 May; 6:231-5.
- [13]. Bagga A, Menon S. Rapidly progressive glomerulonephritis. Pediatric Kidney Disease. 2016:567-80.
- [14]. Karakaya D, Güngör T, Çakıcı EK, Yazılıtaş F, Çelikkaya E, Yücebaş SC, Bülbül M. Predictors of rapidly progressive glomerulonephritis in acute poststreptococcal glomerulonephritis. Pediatric Nephrology. 2023 Mar 16:1-7.
- [15]. Zent R. Rapidly progressive glomerulonephritis at Groote Schuur hospital (Master's thesis, University of Cape Town).