e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2023; 15(10); 385-389

Original Research Article

A Hospital-Based Assessment of the Spectrum and Outcomes of Crescentic Glomerulonephritis: An Observational Study

Gopal Prasad[1], Saurav Suman[2]

[1]Associate Professor, Department of Nephrology, Patna Medical College and Hospital, Patna, Bihar, India

[2]Junior Resident, Department of Pediatrics, Patna Medical College and Hospital, Patna, Bihar, India

Received: 04-01-2023 / Revised: 18-04-2023 / Accepted: 21-05-2023

Corresponding Author: Dr. Gopal Prasad

Conflict of interest: Nil

Abstract:

Aim: The aim of the present study was to identify the etiology, assess and compare the clinical features, histomorphological parameters and outcomes of patients with Crescentic glomerulonephritis (CrGN).

Methods: This observational study was conducted in the Department of Nephrology, Patna Medical College and Hospital, Patna, Bihar, India for a period of 2 years. Fifty biopsy proven crescentic glomerulonephritis patients with variable presentation were analysed in this study. Crescentic glomerulonephritis was defined by crescent formation over 50% sampled glomeruli in biopsy specimen.

Results: Immune-complex glomerulonephritis (ICGN) was the most common etiology (n = 40; 80%) followed by pauci-immune glomerulonephritis (PauciGN; n = 8; 16%) and anti-glomerular basement membrane disease (n = 2; 4%). The most common etiology of ICGN was IgA nephropathy (n = 13; 26%) followed by lupus nephritis (n = 10; 20%) and post-infectious glomerulonephritis (PIGN) (n = 10; 20%).There was no difference in the clinical, biochemical and histopathological parameters between these categories.

Conclusion: Immune-complex glomerulonephritis is the most common cause of CrGN in this part of the country with IgA nephropathy being the predominant disease. The clinical presentation is marked by severe renal failure at presentation and comparatively lesser response rates, higher mortality and progression to ESRD in spite of strict adherence to standard immunosuppressive therapy.

Keywords: Crescentic glomerulonephritis, immune-complex glomerulonephritis, pauci-immume glomerulonephritis.

Introduction

Crescentic glomerulonephritis (CrGN) is an uncommon entity in children. [1] Histopathologically, it is characterized by crescents in 50% or more of the glomeruli and clinically by sudden and progressive decline in renal function. It can accompany most forms of primary glomerulonephritis but may be associated with various systemic diseases. An early diagnosis and prompt therapy is the key to the management of this entity. Over the years, there have been significant advancements in supportive as well as specific therapy.

Disruption of glomerular basement membrane (GBM) due to the antibody or immune-complex-mediated injury leads to the accumulation of circulating leukocytes, inflammatory mediators, and coagulation factors in the Bowman's space. Fibrin exudation and proliferation of parietal epithelial cells, macrophages, and interstitial fibroblasts result in the obliteration of Bowman's space and crescent formation. [2] The extent of crescent formation correlates with the severity of glomerular damage. [3] Crescents with predominant cellular components represent acute glomerular injury which can resolve with timely immunosuppressive treatment, whereas fibrous crescents, interstitial fibrosis, or tubular atrophy have irreversible renal outcomes. [4]

The WHO definition for glomerular crescents is "two or more layers of proliferating cells between the visceral and parietal epithelial cells that are partially or completely filling the Bowman's space". While occasional crescents may be seen in various renal diseases, the presence of crescents in more than 50% of the glomeruli defines "Crescentic glomerulonephritis" as per WHO definition. [5,6] Active crescents tend to be cellular and consist of a mixture of inflammatory cells (leukocyte), intrinsic epithelial cells of the Bowman's capsule, extracellular matrix, and few fibroblasts. Over time, the cellular crescents develop into fibro cellular and fibrous crescents.

The initiating event is the development of physical gaps (also called rents or holes) in the glomerular basement membrane and Bowman's capsule. Clinical hallmark of CrGN is rapidly progressive glomerulonephritis (RPGN). RPGN refer to clinical syndrome characterised by rapid and progressive loss of renal function over hours and days, often accompanied by oliguria or anuria and features of acute glomerulonephritis including dysmorphic erythrocyturia, and glomerular proteinuria.5 Crescentic Glomerulonephritis (CrGN) is most aggressive structural phenotype and accounts for 2%-7% of renal biopsy in most series and a smaller proportion of all patients with end stage renal disease. [7-9]There is significant heterogeneity in the aetiology and outcome of CrGN, [10] with limited data from India. [11,12]

The aim of the present study was to identify the etiology, assess and compare the clinical features, histomorphological parameters and outcomes of patients with Crescentic glomerulonephritis.

Materials and Methods

This observational study was conducted in the Department of Nephrology, Patna Medical College and Hospital,Patna, Bihar, India for a period of 2 years. Fifty biopsy proven crescentic glomerulonephritis patients with variable presentation were analysed in this study. Crescentic glomerulonephritis was defined by crescent formation over 50% sampled glomeruli in biopsy specimen.

The patient's detailed clinical history and physical examination record were retrieved and analysed. The laboratory investigations including complete Haemogram, ESR, Renal function test, Liver function test, Lipid profile and immunological assay (RA factor, C3, C4, ANA, Anti ds DNA antibody, PR3 ANCA, MPO ANCA and Anti GBM Ab) were recorded. The result of urinalysis was noted if available. Renal biopsy sample was preserved in 10% buffered aqueous formaldehyde solution for light microscopy. Sample were studied under light microscopy using Haematoxylin and eosin stain, Periodic acid-Schiff stain, Acid fuchsine Orange G and Periodic acid Silver Methenamine stain. Electron microscopy were not done due to lack facility at our centre and high cost in sending the samples at outside centre. Immuno-fluorescence test was done in each sample and samples were sent in Michelle's stain. Renal biopsy were examined in detail for total number of glomeruli, number of sclerosed glomeruli - segmental or global, percentage of glomeruli with crescent formation type of crescent-cellular, fibro-cellular or fibrous, features of vasculitis, and extent of interstitial fibrosis and tubular atrophy. Crescentic glomerulonephritis are classified based on light microscopy and immunohistological features into following five group type I, II, III, IV, and type V[11] . Records of treatment and immuno suppressants used were collected. Total numbers of patients requiring haemodialysis at the time of hospitalisation were noted. Renal function test, urine microscopy, Complete Blood Count and requirement of haemodialysis assessment were done monthly, till their last follow up. Outcome assessment at three month were carried using improvement in renal function or progression to end stage renal disease (ESRD).

The baseline clinical, biochemical and histopathological parameters and primary outcomes were compared between immune-complex glomerulonephritis (ICGN) and pauci-immune glomerulonephritis (PauciGN). All categorical and ordinal variables were expressed as frequencies and percentages and compared by Chi-square test or Fisher's exact test. Continuous variables were expressed as mean with standard deviation or median with range and compared by independent Student's t-test or Mann–Whitney U-test. Relative risk (RR) along with confidence intervals (CIs) was estimated to assess the risk for the primary outcome. Survival times were compared by log-rank test. A logistic regression analysis was done to assess the predictors of adverse outcomes (death + end-stage renal disease [ESRD]) at 3 months. All the statistical analyses were carried out at 5% level of significance, and $P < 0.05$ was considered as statistically significant. Data were analyzed using SPSS version 19.0 (IBM Corporation, US).

Results

Table 1: Etiology of crescentic glomerulonephritis

Etiology	N%
ICGN	40 (80)
IgA Nephropathy	13 (26)
Lupus Nephritis	10 (20)
Post infectious GN	10 (20)
Membranoproliferative GN	3 (6)
Unclassified	4 (8)
Pauci Immune GN	8 (16)
Anti-GBM disease	2 (4)

Immune-complex glomerulonephritis (ICGN) was the most common etiology (n = 40; 80%) followed by pauci-immune glomerulonephritis (PauciGN; n = 8; 16%) and anti-glomerular basement membrane disease (n = 2;

4%). The most common etiology of ICGN was IgA nephropathy (n = 13; 26%) followed by lupus nephritis (n = 10; 20%) and post-infectious glomerulonephritis (PIGN) (n = 10; 20%).

Table 2: Clinical parameters at baseline age distribution -

Parameters	Total n=50	ICGN N=40	Pauci GN N=8
Hypertension	42 (84)	32 (80)	8 (100)
Edema	25 (50)	20 (50)	5 (62.5)
Breathlessness	16 (32)	12 (30)	3 (37.5)
Gross hematuria	10 (20)	8 (20)	2 (25)
Anuria	5 (10)	2 (5)	3 (37.5)
Need for RRT	36 (72)	26 (65)	7 (87.5)
Urine output Mean±SD	850±650.5	936±656.4	582±802
Duration of symptoms Mean±SD	28.2±25.5	26.4±22.8	35.5±32.8

There was no difference in the clinical parameters between two categories.

Table 3: Biochemical parameters

Parameters	Total n=50	ICGN N=40	Pauci GN N=8	P Value
24 hr urine output (g/day)	1.64±1.2	1.55±1.8	1.54±1.4	0.6
Creatinine (mg/dl)	7.32±3.2	6.4±2.5	9.2±5.6	0.08
eGFR (ml/min/1,73 $m^{2)}$	12.8±10.5	13.7±11.2	9.1±9.1	0.02
Serum albumin (mg/dl)	2.8±0.6	2.5±0.2	2.7±0.1	0.30

There was no difference in the biochemical parameters between two categories.

Table 4: Histopathological parameters

Parameters	Total n=50	ICGN N=40	Pauci GN N=8	P Value
Number of glomeruli	12 (7.5-15)	12 (9-15)	8.5 (5.5-13.5)	0.2
Number of sclerosed glomeruli	2 (0-3)	2 (1-3)	0 (0-1.5)	0.001
Crescents	72.5±78.2	74.4±16.4	76.4 (40.25)	0.5
Cellular crescents	54.6±25.5	54.6±26.4	56.4±32	0.6
Fibrocellular crescents	18±48.2	18.2±16.4	18.4±12.6	0.8
100% crescents	10 (20)	8 (20)	2 (25)	0.6
Interstitial inflammation	18 (10-30)	25 (20-30)	10 (10-35)	0.16
Tubular atrophy	17 (10-30)	20 (10-30)	10 (6.2-13.7)	0.18
Interstitial fibrosis	10 (5-13.7)	10 (5-20)	5 (5-10)	0.2
Acute tubular necrosis	5 (0-10)	5 (0-10)	7.5 (5-17.5)	0.1

There was no difference in the histopathological parameters between two categories.

Discussion

Crescentic glomerulonephritis (CrGN) is a disease with serious prognosis. Retrospective biopsy based series has reported a prevalence varying from 2.1% to 4.2%. [13,14] The etiology and outcomes of the CrGN are heterogeneous. [6,10] CrGN is classified based on the immunofluorescence (IIF) pattern into anti-GBM disease, immune-complex-mediated glomerulonephritis, and pauci-immune glomerulonephritis. [6] Pauci-immune glomerulonephritis represents the majority of cases in the adult population, especially amongst white males and people aged more than 65 years [6,15], whereas CrGN in children is more commonly immune-complex-mediated. [16] The clinical course of CrGN depends both on the percentage of glomeruli with crescents and the underlying disease. [17,18] The renal outcome is also determined by the severity of renal insufficiency at the time of presentation. [19,20] Crescentic glomerulonephritis (CGN) is an important pathologic correlate of rapidly progressive renal failure and it is most aggressive structural phenotype and accounts for 2%-7% of renal biopsy in various reported series and accounts for a smaller proportion of all patients with end stage renal disease (ESRD). [7-9]

Immune-complex glomerulonephritis (ICGN) was the most common etiology (n = 40; 80%) followed by pauci-immune glomerulonephritis (PauciGN; n = 8; 16%) and anti-glomerular basement membrane disease (n = 2; 4%). The most common etiology of ICGN was IgA nephropathy (n = 13; 26%) followed by lupus nephritis (n = 10; 20%) and post-infectious glomerulonephritis (PIGN) (n = 10; 20%).A few studies from Asia have reported ICGN as the predominant etiology in adults. [21,22] This observation is not surprising considering the high prevalence of IgA nephropathy in Asian countries. [23,24] Another interesting observation is the higher proportion of patients with PIGN, a disease that is considered to be common in the pediatric population. The histological parameters were comparable in the two groups except for the higher proportion of sclerosed glomeruli in ICGN. This

might be secondary to the high proportion of patients with IgA nephropathy and lupus nephritis, which follows a more indolent course. [22,25]The probable reasons for higher rate of progression to CKD and ESRD might be secondary to a high proportion of IgA nephropathy and lupus which are well-known to be associated with inferior survival. We found that hypertension, need for renal replacement therapy, serum creatinine at presentation and hence, eGFR and percentage of fibrocellular crescents were predictive of adverse outcomes. [26,27] We did not find any association with arterial fibrinoid necrosis, proportion of cellular crescents and tubulointerstitial inflammation as described in other studies. [27]

Conclusion

Immune-complex glomerulonephritis is the most common cause of CrGN in this part of the country with IgA nephropathy being the predominant disease. The clinical presentation is marked by severe renal failure at presentation and comparatively lesser response rates, higher mortality and progression to ESRD in spite of strict adherence to standard immunosuppressive therapy. Further research is needed to formulate more aggressive treatment policies to ensure renal as well as patient survival in long-term.

References

1. Bidani AK, Lewis EJ. Idiopathic rapidly progressive glomerulonephritis and Goodpasture's syndrome. Pediatric kidney disease, 2nd edn. Little, Brown & Company, New York. 1992: 1223-45.
2. Tipping PG, Kitching AR, Cunningham MA, Holdsworth SR. Immunopathogenesis of crescentic glomerulonephritis. Curr Opin Nephrol Hhypertens. 1999;8(3):281–6.
3. Couser WG. Rapidly progressive glomerulonephritis: Classification, pathogenetic mechanisms, and therapy. Am JKidney Dis. 1988; 11(6):449–64.
4. Sasatomi Y, Kiyoshi Y, Takabeyashi S. A clinical and pathological study on the characteristics and factors influencing the prognosis of crescentic glomerulonephritis using a cluster analysis. Pathol Int. 1999;49(9):781–5.
5. Churg J and Sobin L. Classification of glomerulonephritis. In Renal disease Classification and Atlas of Glomerular Diseases. Churg J, Bernstein J, Glassock R (eds). Igaku-Shoin: Tokyo, 1995; 3-19.
6. Jennete JC. Rapidly progressive crescentric glomerulonephritis. Kidney Int 2003; 63:1164-77.
7. Whitworth J, Morel-Maroger L, Mignon F, et al: The significance of extra capillary proliferation: Clinicopathological review of 60 patients. Nephron 1976; 16:1-19.
8. Beirne G, Wagnild J, Zimmerman S, et al: Idiopathic crescentric glomerulonephritis. Medicine 1977; 56:349-381.
9. Bolton WK: The role of corticosteroids in nephritic syndromes: The case for aggressive use, in Narins RG(ed): Controversies in Nephrology and Hypertension. New York, Churchill Livingstone, 1984; 421-459.
10. Oudah N, Al Duhailib Z, Alsaad K, Qurashi S, Ghamdi G, Flaiw A, et al. Glomerulonephritis with crescent among adult Saudi patients outcome and its predictors. Clin Exp Med 2012; 12:121-5.
11. Choudhury TA, Singh RG, Usha, Singh S, Singh TB, Rathore SS, et al. Clinicopathological spectrum of crescentric glomerulonephritis: A hospital-based study. Saudi J Kidney Dis Transpl 2014; 25:689-96.
12. Gupta R, Singh L, Sharma A, Bagga A, Agarwal SK, Dinda AK, et al. Crescentic glomerulonephritis: A clinical and histomorphological analysis of 46 cases. Indian J Pathol Microbiol. 2011; 54:497-500.
13. Habib MA, Badruddoza SM. Pattern of glomerular diseases among adults in Rajshahi, the Northern Region of Bangladesh. Saudi J Kidney Dis Transpl. 2012 Jul;23(4):876-80.
14. Panichi V, Pasquariello A, Innocenti M, Meola M, Mantuano E, Beati S, Paoletti S, Consani C, Puccini R, Casarosa L, Gattai V, Filippi C, Moriconi L, Barsotti G, RindiP, Palla R. The Pisa experience of renal biopsies, 1977-2005. J Nephrol. 2007 May-Jun;20(3):329-35.
15. Falk RJ. ANCA-associated renal disease. Kidney Int.1990;38(5):998–1010.
16. Dewan D, Gulati S, Sharma RK, Prasad N, Jain M, Gupta A, Kumar A. Clinical spectrum and outcome of crescentic glomerulonephritis in children in developing countries. Pediatric Nephrology. 2008 Mar; 23:389-94.
17. Baldwin DS, Neugarten J, Feiner HD, Gluck M, Spinowitz B. The existence of a protracted course in crescentic glomerulonephritis. Kidney Int. 1987;31(3):790–4.
18. Jennette JC, Thomas DB. Crescentic glomerulonephritis. Nephrol Dial Transplant. 2001; 16(suppl_6):80–2.
19. Levy JB, Turner AN, Rees AJ, Pusey CD. Long-term outcome of anti–glomerular basement membrane antibody disease treated with plasma exchange and immunosuppression. Ann Int Med. 2001;134(11):1033–42.
20. Hogan SL, Nachman PH, Wilkman AS, Jennette JC, Falk RJ.Prognostic markers in patients with antineutrophil cytoplasmic autoantibody-associated microscopic polyangiitis and glomerulonephritis. J Am Soc Nephrol. 1996; 7 (1):23–32.
21. Lin W, Chen M, Cui Z, Zhao MH. The immunopathological spectrum of crescentic glo-

merulonephritis: a survey of 106 patients in a single Chinese center. Nephron Clin Pract. 20 10;116(1):c65-74.
22. Tang Z, Wu Y, Wang Q, Zeng C, Yao X, Hu W, Chen H, Liu Z, Li L. Clinical spectrum of diffuse crescentic glomerulonephritis in Chinese patients. Chin Med J (Engl). 2003 Nov; 116(11):1737-40.
23. Siddappa S, Kowsalya R, Mythri KM. IgA nephropathy in a tertiary care center from south India. Indian J Nephrol. 2011 Oct;21 (4): 230-4.
24. Vanikar AV, Kanodia KV, Patel RD, Trivedi HL. Primary immunoglobulin A (IgA) nephropathy in western India. Indian J Nephrol. 2005 Oct 1;15(4):227-31.
25. Yu F, Tan Y, Liu G, Wang SX, Zou WZ, Zhao MH. Clinicopathological characteristics and outcomes of patients with crescentic lupus nephritis. Kidney Int. 2009 Aug;76(3):307-17.
26. Chen S, Chen H, Liu Z, Zhang H, Hu W, Tang Z, Liu Z. Pathological spectrums and renal prognosis of severe lupus patients with rapidly progressive glomerulonephritis. Rheumatol Int. 2015 Apr;35(4):709-17.
27. Gigante A, Salviani C, Giannakakis K, Rosato E, Barbano B, Moroso A, Gasperini ML, Nofroni I, Salsano F, Cianci R, Pugliese F. Clinical and histological outcome predictors in renal limited pauci-immune crescentic glomerulonephritis: a single centre experience. Int J Immunopathol Pharmacol. 2012 Jan-Mar;25 (1):287-92.