

# HISTOPATHOLOGICAL PATTERN IN PATIENTS WITH CLINICALLY SUSPECTED RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

Muhammad Ikram<sup>1</sup>, Shad Muhammad<sup>1</sup>, Amer Azhar<sup>2</sup>, Akhtar Ali<sup>1</sup>, Sartaj Alam<sup>1</sup>, Khan Bahadar<sup>1</sup>

<sup>1</sup>Department of Nephrology, MTI, Lady Reading Hospital, Peshawar - Pakistan

<sup>2</sup>Department of Nephrology, MTI, Khyber Teaching Hospital, Peshawar - Pakistan

## ABSTRACT

**Objective:** To analyze the histopathological patterns of renal diseases in patients who presented with clinically suspected rapidly progressive glomerulonephritis (RPGN).

**Material and Methods:** This is a descriptive review of data of renal biopsies in patients with clinically suspected RPGN, who underwent renal biopsy at Nephrology unit Lady Reading Hospital, Peshawar, Pakistan from July 2010 to July 2016. All patients admitted to Nephrology unit with a clinical suspicion of RPGN and had renal biopsies done for histological diagnosis.

**Results:** Tubulo-interstitial Nephritis (TIN) 38(39.5%) was the most common histopathological diagnosis in our study followed by Crescentic GN (CSGN) 16(16.6%) and Mesangiocapillary GN (MPGN) 12(12.5%). Pauci-immune GN (PI) was the most common cause of Crescentic GN; 7/16(43.75%), followed by Immune mediated GN; 2/16(12.5%).

**Conclusion:** Histopathological patterns of patients with clinically suspected RPGN is an integral part of investigation of such patients both for diagnostic and prognostic purpose. Tubulo interstitial Nephritis turns out to be the most common histopathological diagnosis in patients with clinical RPGN. As opposed to Crescentic GN in most studies.

**Key Words:** Kidney, Glomerulonephritis, Crescentic GN.

---

**This article may be cited as:** Ikram M, Muhammad S, Azhar A, Ali A, Alam S, Bahadar K. Histopathological pattern in patients with clinically suspected Rapidly Progressive Glomerulonephritis. *J Med Sci* 2017; 25: (4) 442-445.

---

## INTRODUCTION

Rapidly Progressive Glomerulonephritis (RPGN) is a clinic-pathologic entity characterized by extensive crescent formation and rapid deterioration of renal function within weeks to months<sup>1</sup>, manifested by features of glomerular disease in the urine and it is characterized morphologically by extensive crescent formation.<sup>2,3</sup> The severity of the RPGN is in part related to the degree of crescent formation. Patients with circumferential crescents in >80% of the glomeruli tend to present with advanced renal failure.

By comparison, patients with crescents in <50% of the glomeruli, particularly if the crescents are non-circumferential, typically follow a more indolent course<sup>4</sup>. It has been reported that Crescentic Glomerulonephritis (CSGN) comprises 2.1-4.5% of the total number of kidney biopsies<sup>5</sup>.

The correlation between RPGN and CSGN has been a topic of interest since long. Volhard and Fahr<sup>6</sup> reported this correlation between clinically severe renal disease and glomerular crescents in 1914. They called the clinical expression "subacute nephritis" and the renal lesion as 'extra-capillary nephritis'. In 1942, Ellis<sup>7</sup> referred to this aggressive category of glomerulonephritis as "rapidly progressive type I nephritis".

CSGN, an uncommon rapidly progressive disease, is characterized by severe glomerular inflammation. The lack of specific CSGN biomarkers delays diagnosis and threatens life. Urinary thrombin is considered a specific CSGN biomarker; supported by studies and led to propose the application of urinary thrombin activity to CSGN diagnosis and screening<sup>8,9</sup>. Above all,

---

**Dr. Shad Muhammad** (Corresponding Author)

Assistant Professor

Department of Nephrology, MTI, Lady Reading Hospital,  
Peshawar - Pakistan

Cell: +92-333-9354462

E-mail: dr.shadmuhammad@yahoo.com

**Date Received:** June 16, 2017

**Date Revised:** September 23, 2017

**Date Accepted:** November 20, 2017

## Histopathological pattern in patients with clinically suspected Rapidly.....

kidney biopsy is considered as the best method for diagnosing renal parenchymal disease and crescents formations<sup>10</sup>. Renal biopsy is of critical importance and the gold standard for establishing the diagnosis of RPGN<sup>11</sup> and is associated with a higher diagnostic yield and lower procedural risk<sup>12</sup>.

Limited number of studies are available on this topic. This study will highlight the histological pattern of renal diseases in patients who are labeled as RPGN on clinical basis in our population. It will give us a hope to predict the early diagnosis and if needed to start the patient on immunosuppressive therapy.

### MATERIAL AND METHODS

This is a descriptive review of data of renal biopsies in patients with clinical suspicion of RPGN, performed at Nephrology unit, Lady Reading Hospital, Peshawar, Pakistan from July 2010 to July 2016. Patients were selected through consecutive non-probability sampling. All patients admitted to nephrology unit with a clinical suspicion of RPGN and underwent a renal biopsy procedure for confirmation of histological diagnosis were enrolled. While patients with solitary kidney, uncontrolled blood pressure and deranged coagulation profile were excluded from this study.

Data of the patients underwent renal biopsies for the diagnosis of RPGN during these seven years was collected on a printed proforma highlighting age, gender, diagnosis of RPGN and biopsy findings. Further investigations and the etiologies of RPGN based on the histopathological findings were also recorded. Furthermore, the proliferative (active) diseases as a cause of RPGN were noted and common causes of CSGN were also looked at.

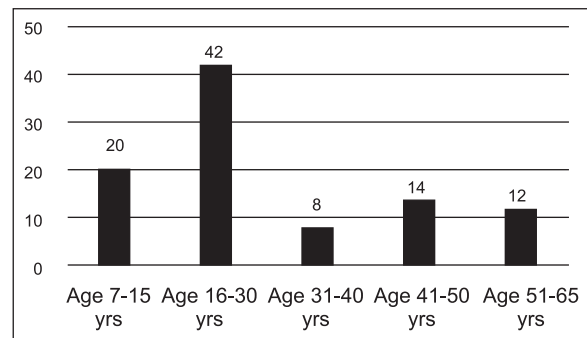
### RESULTS

A total of 96 patients were studied. Out of which 62(64.58%) were male and 34(35.41%) were female. Mean age was  $28.92 \pm 14.77$  years, with minimum of 7 years and maximum 65 years. Male to female ratio was 1.8:1.as shown in Fig 1. The distribution of different histopathological diagnosis, among which Tubulo-interstitial Nephritis 38(39.5%) was the most common followed by Crescentic GN 16(16.6%) and Mesangiocapillary GN 12(12.5%) is shown in Table 1.

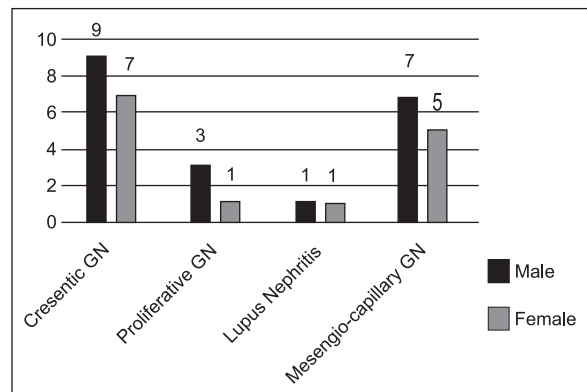
The percentage of histological diagnosis of active (proliferative) diseases is shown in Figure 2. The most common is Crescentic GN 16(16.6%), followed by Mesangiocapillary GN 12(12.5%). The most frequent causes of Crescentic GN are highlighted in Figure 3. Pauci-immune GN; 7/16(43.75%) was found to be the most frequent cause followed by Immune mediated GN; 2/16(12.5%), Lupus Nephritis; 2/16(12.5%),

**Table 1: Histological Diagnosis of clinically suspected RPGN**

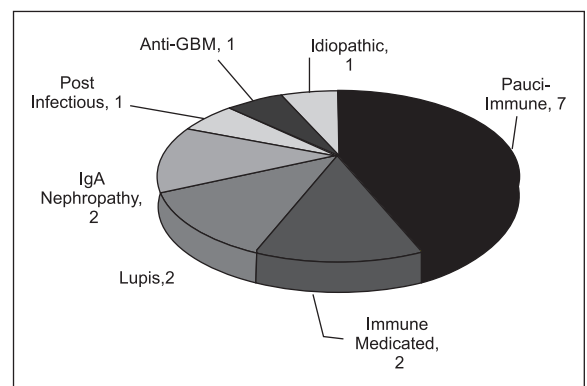
S. No.	Histological diagnosis	No.
1.	TIN	38
2.	Crescentic GN	16
3.	Others	13
4.	Mesengio-capillary GN	12
5.	FSGS	5
6.	Proliferative GN	4
7.	ATN	3
8.	IgA Nephropathy	3
9.	Lupus Nephritis	2



**Fig 1: Age wise distribution of patients (n=96)**



**Fig 2: Histologic Diagnosis of Active Cellular Proliferative Diseases**



**Figure 3: Causes of crescentic GN (n=16)**

IgA Nephropathy; 2/16(12.5%), Post infectious GN; 1/16(6.25%), Anti GBM; 1/16(6.25%) and Idiopathic: 1/16(6.25%). Average serum creatinine on presentation was  $6.15 \pm 3.73$  mg/dl, with a minimum of 0.8mg/dl and maximum 17 mg/dl.

### DISCUSSION

RPGN is a useful initial clinical suspicion for patients who present with progressive renal impairment of short duration. It is not the final definitive diagnosis and needs prompt evaluation including good history, physical examination and appropriate investigations. Our attempt to take the clinically suspected RPGN and look into its histological diagnosis; turned out to be a very interesting topic.

As RPGN is a clinico-pathologic entity characterized by extensive crescent formation. Looking into the incidence of CSGN, it varies with geographic location and policies of kidney biopsies. The incidence of CSGN was 1.75% in a study from China<sup>13</sup>. However, studies from Western Europe, North America (2-10%), South Africa (3.8%) and India (5.8%) showed a near-similar incidence<sup>14,15</sup>. Gupta et al<sup>16</sup> found an incidence of 2.65% of kidney biopsies, but the study included both pediatric and adult patients. The difference with the present study is due to the differing patient cohorts as we had selected patients who have presented with clinical RPGN. That is why prevalence of CSGN is higher in our study.

In stark contrast to the above mentioned studies and to our study as well; is, the clinical and histological features of 43 patients with RPGN in a study. All had extensive crescent formation in more than 50% of glomeruli<sup>17</sup>. Our study looked into those patients who were labelled clinically as RPGN as per data available and may not have fully filled a very strict criterion during labelling RPGN. That is why the prevalence of CSGN was less in our study as compared to the study mentioned in this para while prevalence of other diseases as a cause of renal failure is high in our study.

While considering the etiology of CSGN, the idiopathic (44.1%) is the most common variety, followed by ANCA-associated (23.5%) and lupus nephritis (11.7%)<sup>18</sup>. Vasculitis is the most common form in western countries<sup>19</sup>. Data from a study in China demonstrated that lupus nephritis was the most common etiology, followed by IgA nephropathy and vasculitis<sup>13</sup>. In Saudi Arabia, 34 cases of CSGN, accounting for an incidence of 5.5% among kidney biopsies. The immunological profile of CSGN showed vasculitis (33.2%), anti-GBM antibody (14.7%) and lupus nephritis in (17.6%) patients<sup>18</sup>. In India, among a total of 46 cases of CSGN; 71.7% were pauci-immune (PI) while 28.3% were immune complex-mediated<sup>15,16</sup>. Pauci-immune was the most common cause of CSGN in another study from India as

well<sup>20</sup>. Pauci-immune GN (43.75%) was the most common cause of CSGN in our study as evident from other international studies. In stark contrast; of 528 cases of CSGN, Lupus nephritis was the most common type of crescentic GN in China, followed by pauci-immune crescentic GN and IgA nephropathy<sup>21</sup>.

Looking into etiology of Immune complex GN in 46 patients; it was secondary to SLE in 4 patients, and IgA nephropathy, Henoch Schonlein purpura and membranoproliferative GN type II in two cases each; GN was post infectious in 3 cases and idiopathic in 05 patients<sup>22</sup>. While our study showed Lupus Nephritis (12.5%), IgA (12.5%), Post infectious (6.25%), Anti GBM (6.25%) and Idiopathic (6.25%) which is in comparison with most of the international studies.

The best predictor of renal outcomes is the initial serum creatinine, as well as the extent of renal injury and fibrosis on biopsy<sup>23</sup>. In our study the percentage of patients presented with higher creatinine (>3.1 mg/dl) was much higher 78.12% as compared to low creatinine values (< 3.0 mg/dl), which was 21.87%. We did not follow the patient's prognosis and outcome in regard to serum creatinine concentration and the type of treatment given. Which needs long term follow up studies.

### CONCLUSION

Histopathological patterns of patients with clinically suspected RPGN is an integral part of investigation of such patients both for diagnostic and prognostic purpose. Tubulo-interstitial Nephritis turns out to be the most common histopathological diagnosis in patients with clinical RPGN in our population, as opposed to Crescentic GN in most of the studies.

### REFERENCES

1. Cho HY, Chung DL, Kang JH, Ha IS, Cheong HI, Choi Y. A Clinico-pathological Study of Rapidly Progressive Glomerulonephritis in Children. *Journal of the Korean Society of Pediatric Nephrology* 2004; 8(2): 176-85.
2. George HB, Greenhall, Alan D, Salam. What is new in the management of rapidly progressive glomerulonephritis? *Clin Kidney J* 2015;8 (2): 143-50.
3. Moroni G, Ponticelli C. Rapidly progressive crescentic glomerulonephritis: Early treatment is a must. *Autoimmun Rev* 2014;13(7):723-29.
4. David S, Baldwin DS, Neugarten J, Gluck M, Spinowitz B, Feiner HD. The existence of a protracted course in crescentic glomerulonephritis. *Kidney Int* 1987; 31:790.
5. Habib MA, Badruddoza SM. Pattern of glomerular diseases among adults in Rajshahi, the Northern Region of Bangladesh. *Saudi J Kidney Dis Transpl.* 2012; 23:876-80.

## Histopathological pattern in patients with clinically suspected Rapidly.....

6. Volhard F, Fahr T. Die bright schenierenkrankheit: klink, pathologic und atlas. Berlin, Springer, 1914:300-02.
7. Ellis A. Natural history of Bright's disease: Clinical, histological and experimental observations. Lancet 1942; 1:1-7.
8. Kitamoto Y, Arizono K, Fukui H, Tomita K, Kitamura H. Urinary thrombin: a novel marker of glomerular inflammation for the diagnosis of crescentic glomerulonephritis. PLoS One. 2015; 5;10(3). 87-90.
9. Kitamoto Y, Tomita K, Imamura T. Assessment of thrombin in the urine of glomerulonephritic patients by enzyme-linked immunosorbent assay. Ann Clin-Biochem 2004; 41:133-37.
10. Philipponnet C, Guérin C, Canet E, Robert R, Mariat C, Dijoud F, et al. Kidney biopsy in the critically ill patient, results of a multi-center retrospective case series. Heng Minerva Anestesiologica. January 2013;79(1): 53-60.
11. Annelies E. Berden, Franco Ferrario. Histopathologic Classification of ANCA-Associated Glomerulonephritis. J Am SocNephrol 2010; 21:1628-36.
12. N. Kambham. Crescentic glomerulonephritis: an update on pauci-immune and anti-GBM diseases. Advances in Anatomic Pathology 2012;(19) 2:111-24.
13. Tang Z, Wu Y, Wang Q, Zeng C, Yao X, Hu W, et al. Clinical spectrum of diffuse crescentic glomerulonephritis in Chinese patients. Chin Med J 2003;116: 1737-40.
14. Peteersson EE, Saunedlin B, Heigl Z. Incidence and outcome of pauci-immune necrotizing and crescentic glomerulonephritis in adults. ClinNephrol 1995; 43:141-49.
15. Rampelli K, Rajesh NG, Srinivas BH, K.T. Harichandra Kumar K.T, Swaminathan R.P, and Priyamvada P.S. Clinical spectrum and outcomes of crescentic glomerulonephritis: A single center experience. Indian J Nephrol. 2016; 26(4):252-56.
16. Gupta R, Singh L, Sharma A, Bagga A, Agarwal SK, Dinda AK. Crescentic glomerulonephritis: A clinical and histomorphological analysis of 46 cases. Indian J PatholMicrobiol 2011; 54:495-500.
17. McLeish KR, Yum MN, Luft FC. Rapidly progressive glomerulonephritis in adults: clinical and histologic correlations. Clinical Nephrology 1978, 10(2):43-50.
18. Tauhidul AC, Rana GS, Usha, Shivendra Singh, Takhellambam B.S,Surendra S.R. Clinicopathologic Spectrum of Crescentic Glomerulonephritis: A Hospital-based Study. Saudi J Kidney Dis Transpl 2014;25(3):689-96.
19. Andrassy K, Kuster S, Waldherr R, Ritz E. Rapidly progressive glomerulonephritis, analysis of prevalence and clinical course. Nephron 1991; 59:206-12.
20. Ranjana W Minz, Seema Chhabra, Kusum Joshi. Renal histology in pauci-immune rapidly progressive glomerulonephritis: 8-year retrospective study. Indian Journal of pathology and microbiology 2012;55:1:28-32.
21. Chen S, Tang Z, Xiang H, Li X, Chen H, Zhang H, et al. Etiology and Outcome of Crescentic Glomerulonephritis. From a Single Center in China: A 10-year Review. Am J Kidney Dis. 2016; 67(3):376-83.
22. Aditi Sinha, Kriti Puri, Pankaj Hari, Amit Kumar Dinda, Arvind Bagga. Etiology and Outcome of Crescentic Glomerulonephritis. Indian Pediatr 2013;50:283-88.
23. Gigante A, Salviani C, Giannakakis K, Rosato E. Clinical and histological outcome predictors in renal limited pauci-immune crescentic glomerulonephritis: a single center experience. Int J ImmunopatholPharmacol. 2012;25(1):287-92.

**CONFLICT OF INTEREST:** Authors declare no conflict of interest

**GRANT SUPPORT AND FINANCIAL DISCLOSURE NIL**

### AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

- Ikram M:** Idea and writing of the manuscript.  
**Muhammad S:** Data collection.  
**Azhar A:** Data and statistical analysis.  
**Ali A:** Overall supervision of the study during collection of data and compiling, corrections and re-writing.  
**Alam S:** Assistance in writing manuscript.  
**Muhammad N:** Bibliography.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.