

## Histopathological Pattern and Outcome of Patients Presenting With Rapidly Progressive Renal Failure: A Single Centre Experience.

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### Abstract:

**Back Ground:** Rapidly Progressive Renal Failure (RPRF) is a clinical syndrome characterized by rapid deterioration of renal function, over a period of few weeks. The present study was conducted to evaluate the pattern of histopathology in patients presenting with RPRF and to correlate the outcome of the patients with reference to the histological pattern.

**Materials and Methods:** A prospective observational study was conducted in the department of nephrology, Andhra Medical College and King George Hospital, Visakhapatnam over a period of 2 years between 2017 January to December 2018 with 3 months of follow-up. 66 patients who presented with RPRF were included in the study.

**Results:** There was male preponderance with male to female ratio of 1.27: 1, mean age was  $38 \pm 8$  years. All the 66 patients underwent renal biopsy and crescenticGN was seen in 51 patients (77%). Out of the 66 patients the most common histological diagnosis was PIGN (21.2%) followed by Lupus Nephritis 9(13.6%), C3 glomerulopathy (12.1%), ATN/ATIN (12.1%) and IgA Nephropathy (10.6%).

**Conclusions:** Rapidly Progressive Renal Failure is a useful initial clinical diagnosis for patients who present with progressive renal impairment of short duration. It is not the final definitive diagnosis and needs proper work up, a prompt diagnosis and appropriate treatment is most essential to prevent progression to ESRD.

**Key words:** Rapidly Progressive Renal Failure, histological diagnosis, ESRD, Andhra Medical College.

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### I. Introduction

In clinical medicine physicians encounter patients who present with progressive renal impairment of seemingly unknown etiology. The duration of disease is brief or may even be undefined. These patients are neither Acute Kidney Injury (previously called acute renal failure) nor Chronic Kidney Disease (previously called chronic renal failure). The initial clinical diagnosis of these cases may be called Rapidly Progressive Renal Failure (RPRF), which may be defined as progressive renal impairment over a period of few weeks.<sup>1</sup> On ultrasonography of the kidneys, patients with RPRF have normal sized kidneys, while the presence of small contracted echogenic kidneys establishes the diagnosis of CKD. <sup>2</sup>RPRF encompasses a heterogeneous group of clinical syndromes. <sup>3</sup> Since a wide variety of different diseases may present with a similar clinical picture, it is essential to properly work-up cases of RPRF so that the exact diagnosis is established. Time is a valuable factor since if the appropriate treatment is not initiated, then the patient may progress to irreversible end-stage renal disease (ESRD) needing life-long renal replacement therapy. RPRF may in fact be considered as 'Renal Emergency.'<sup>2</sup>

The renal histopathology shows lesions affecting any or a combination of the three traditional renal compartments: glomerular, tubulointerstitial or vascular. Good history taking, clinical examination and relevant investigations including serology and ultimately kidney biopsy are helpful in clinching the diagnosis. Early definitive diagnosis of RPRF is essential to reverse the otherwise relentless progression to end-stage kidney disease.

## II. Aim

The aim of the study is to know the histopathological pattern and outcome of rapidly progressive renal failure patients who presented to a tertiary care hospital in Visakhapatnam, Andhra Pradesh.

## III. Materials And Methods

The study was conducted in the department of nephrology, Andhra Medical College / King George Hospital, Visakhapatnam. It is a prospective observational study over a period of 2 years between 2017 January to December 2018 with 3 months of follow-up. 66 patients who presented with RPRF were included in the study.

Diagnosis was suggested by presence of proteinuria, active sediments in urine, deranged renal function, some special serological investigations like ANA (antinuclear antibody), dsDNA (anti double stranded DNA), ANCA (anti neutrophilic cytoplasmic antibody), Complement level, ASO (anti streptolysin O) titre, serum electrophoresis and ultrasonography. Renal biopsy was performed in all the cases

**Inclusion Criteria:** Patients of any age and gender presenting with features of RPRF.

**Exclusion Criteria:** Known patients of hypertension, diabetes mellitus or significant past history of renal diseases.

**Statistical analysis:** Data was entered in the Microsoft excel spread sheet ver 2016. Later exported to SPSS (Statistical package for social science) version 16. Quantitative variables were described in the forms of mean and standard deviation. Qualitative variables were described in the form of frequency and percentages. Statistical tests like ANOVA and Fischer's exact was applied. A p value of 0.05 or less was considered as statistically significant.

## IV. Results

**Table 1: Gender Distribution**

	Frequency	Percent
Male	37	56.1
Female	29	43.9
Total	66	100

A total of 66 patients were included in the study among them 6 patients lost followup. Male to female ratio was 1.27:1. Mean age was  $38 \pm 8$  years.

**Table 2: Systolic and Diastolic BP readings**

Systolic BP	FREQUENCY	PERCENT
<140	20	30.3
>140	46	69.6
Diastolic BP		
<90	17	25.75
>90	49	74.24

Systolic BP in hypertensive range was in 69.6% cases. Mean systolic BP was  $150 \pm 20$  mm of Hg. Mean diastolic BP was  $96 \pm 15$  mm of Hg.

**Table 3: Table showing various clinical and lab parameters**

	Minimum	Maximum	Mean
Age	10	67	37.92
Systolic	100	180	149.24
Diastolic	70	120	96.36
S.Creatinine	2	18	6.209
Urea	9	260	102.88
T.Protein	3	10.2	5.6091
S.Albumin	2	5	3.102
S.Cholesterol	73	360	184.42
Hb	6	13	9.256
TLC	4400	16000	8877.12
24 hr Protein	0.1	6	2.594

**Table 4: Showing Various Histopathological patterns in RPRF**

REPORT	FREQUENCY	PERCENT
PIGN	14	21.2
SLE	9	13.6
ATN/ATIN	8	12.1
C3 Glomerulopathy	8	12.1
IgA Nephropathy	7	10.6
MPGN Pattern	6	9.1

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CIq Nephropathy	4	6.1
HTN Nephrosclerosis	3	4.5
PAUCIIMMUNE GN	3	4.5
LCN	2	3
ANTI GBM	1	1.5
Post Partum TMA	1	1.5

\* LCN= Light Chain Cast nephropathy ,ATN= Acute Tubular necrosis  
 PIGN= Post infective GN , GBM = Glomerular basement membrane ,TMA = Thrombotic Micro Angiopathy  
 Patient underwent renal biopsy and they showed Crescentic pattern in 51 of 66 patients(77%). Most common lesion are PIGN (21.2%) followed by Lupus Nephritis 9(13.6%) , C3 glomerulopathy,ATN/ATIN and IgA Nephropathy.

**Table 5 :** Table showing outcome of the study group during follow up period.

OUTCOME	FREQUENCY	PERCENT
Death	11	16.7
Dialysis Dependent	20	30.3
Recovery Partial/Complete	29	43.9
Lost Followup	6	9.1

Out of 66 patients 6 people lost to followup. In the remaining 60 patients, death occurred in 17% and 30% of patients became dialysis dependent. Out of 66 patients 4 were found to be HbsAg positive. Most common histopathological pattern in these patients is MPGN followed by C3 glomerulopathy and DPGN.

Statistical test ANOVA is applied to see whether a significant difference in the means of lab parameters in relation to the three outcome groups exists. There is significant difference in the mean values of diastolic BP, blood urea and haemoglobin between the groups (Death, Dialysis Dependence And Recovery)

**Table 6:** Gender Vs Outcome

Gender	Death	Nonrecovery	Recovery
Females	4	10	13
Males	7	10	16

**Table 7:** Histopathological pattern in relation to outcome

Histopathological Pattern	Total(n)	Death	Recovery	Nonrecovery	P value
PauciimmuneGN	3	3	0	0	0.013*
SLE	9	3	6	0	
C3 glomerulopathy	8	2	2	4	
ATN	8	0	8	0	

\* Fischer's exact

Fischer's exact test was applied (after clubbing the recovery and Nonrecovery group) to correlate the outcome (Death or Survival) of the patients with reference to the histological pattern, which was found to be statistically significant.

Common histopathological lesions associated with death are pauci-immune GN followed by SLE, C3 glomerulopathy and MPGN pattern. Most common histopathological pattern associated with non recovery /dialysis dependency are Immune complex GN followed by C3 glomerulopathy and MPGN.

Among various lesions, ATN/ATIN has the best prognosis for outcome, out of 8 patients who were found to have ATN/ATIN all showed either complete or partial recovery. Patients with pauciimmune pattern has worst prognosis of all lesions with 100% mortality. Common histopathological lesion in patients with HbsAg positivity is MPGN pattern.

## V. Discussion

The prevalence of biopsy proven glomerulonephritis varies according to the geographic area, socioeconomic condition, race, age, demography and indication of biopsy. In a study of biopsy proven renal disease over 19 years, RPRF was seen in 12% of the patients.<sup>4</sup> A recent retrospective study from the Spanish Registry of patients with RPRF, in whom kidney biopsy was done, has shown that crescentic glomerulonephritis accounted for 33% cases, AIN 11%, IgA 9%, ATN 5%, and lupus nephritis, PIGN, myeloma kidney and TMA approx 3% each.<sup>5</sup> In another similar study in elderly patients with RPRF, crescentic GN accounted for 71% cases of RPRF, and AIN 17%. In an Indian study of 46 cases of crescentic glomerulonephritis, 71.7% were pauci immune and 28.3% immune complex mediated.<sup>6</sup> In a recent Indian study of children with crescentic glomerulonephritis, out of 36 children, 17 had immune complex GN and 19 had pauci immune GN. The etiologies of the former were LN (4), PIGN (3) and IgAN, HSP and MPGN type II. RPGN was present in 33 patients.<sup>7</sup>

In the study conducted by Sharma M et al, most of the patients were found to be LN followed by IgAN. This may be because majority patients were in the younger age group.<sup>1</sup>

Approximately 20% myeloma patients develop progressive renal failure during course of disease.<sup>8,9</sup> In the study by Prakash J et al. with multiple myeloma, oliguric ARF was seen in 73% patients.<sup>10</sup> In the present study cast nephropathy was seen in 2 patients, in a study done by Sharma M et al out of 6 patients out of 6 patients of multiple myeloma, 5 had cast nephropathy and 1 had amyloidosis.<sup>1</sup>

**Table 8:** Comparison between different studies on RPRF

Etiology of RPRF	Present study (%)	Spanish registry study (%)	Uezono S et al (%)	Sharma M et al (%)
CrescenticGN	77	33.4	71	----
ANTI GBM	1.5	2.0	----	----
ATN/ATIN	12.1	16.3	17	5
C1q Nephropathy	6.1	---	----	----
C3 Glomerulopathy	12.1	---	----	----
PIGN	21.2	2.5	4	8.75
IgA Nephropathy	10.6	8.8	33	25
LCN	3	0.7	---	6.25
HTN Nephrosclerosis	4.5	3.8	---	----
MPGN TYPE I	9.1	2.7	---	5
PauciimmuneGN	4.5	----	43	10
TMA	1.5	2.8	---	----
SLE	9.1	3.3	---	37.5

## VI. Conclusions

The present study provides comprehensive information about the pattern of kidney diseases in patients presenting as RPRF. Most common histological pattern in patients presenting with RPRF is immune complex GN. There is significant difference in the mean values of diastolic BP, blood urea and haemoglobin between different outcome groups. The common histopathological pattern associated with high mortality is pauciimmune GN. The histopathological pattern associated with good prognosis is ATN/ATIN. Renal biopsy is very essential for determining the underlying pathology which has important implications for therapy and outcome later on. A prompt proper diagnosis of RPRF and appropriate treatment is most essential to decrease the morbidity and mortality of the patients and also prevent progression to ESRD.

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