Research Article

Renal Biopsy Findings in Patients with Rapidly Progressive Glomerulonephritis and its Prediction on Treatment Outcome

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Abstract
RPGN, a type of nephritic syndrome, accompanied by extensive glomerular crescent formation that, if untreated, progresses to end-stage renal disease over weeks to months. Our study aims to study the renal biopsy findings in patients with rapidly progressive glomerulonephritis and its impact on remission outcome.

Materials and Methods: A hospital based retrospective study conducted for a period of one year after obtaining ethical clearance. Adults with rapidly progressive glomerulonephritis on the basis of renal biopsy were included. Light microscopy renal biopsy findings at the baseline were obtained and treatment outcome was analyzed as per the biopsy finding. Treatment outcome identified the remission of the patient with 24-hour urine protein <500 mg/day and serum creatinine <1.4 mg/dl. Quantitative variables were compared using Mann-Whitney Test and qualitative variables were correlated using Chi-Square test/Fisher’s exact test. A p value of <0.05 was considered statistically significant.

Results: In our study, about two-third of patients (63.64%) had showed no response. About one-fourth (25.45%) of patients showed partial remission and 10.91% had complete remission. Three-fourth of patients who achieved remission in study had sclerosis in < 35% of their glomeruli, and between 50-75% of crescents in their glomeruli, suggesting to be a predictor of response, p<0.05

Conclusion: RPGN is an important cause of renal failure. Renal biopsy findings can correlate with the prognosis of the disease and the treatment outcome. An early referral to nephrologist for early diagnosis and treatment is stressed.

Keywords: glomerulonephritis, RPGN, nephritic syndrome, renal biopsy.

Introduction
RPGN, is a pathologic diagnosis accompanied by extensive glomerular crescent formation (i.e., > 50% of sampled glomeruli contain crescents which can be seen in a biopsy specimen). It is relatively uncommon, affecting 10 to 15% of patients with glomerulonephritis (GN), and occurs predominantly in patients 20 to 50 years.[1-3]
may arise when respiratory exposures (eg, cigarette smoke, viral URI) or some other stimulus exposes alveolar capillary collagen, triggering formation of anticollagen antibodies. The term Goodpasture syndrome refers to a combination of GN and alveolar hemorrhage in the presence of anti-GBM antibodies. GN without alveolar hemorrhage in the presence of anti-GBM antibodies is called anti-GBM glomerulonephritis.

**Immunofluorescent** staining of renal biopsy tissue demonstrates linear IgG deposits.[4-7]

**Immune complex RPGN**

Immune complex RPGN (type 2 RPGN) complicates numerous infectious and connective tissue disorders and also occurs with other primary glomerulopathies. Immunofluorescent staining demonstrates nonspecific granular immune deposits. The condition accounts for up to 40% of RPGN cases. Pathogenesis is usually unknown.[8-11]

**Pauci-immune RPGN**

Pauci-immune RPGN (type 3 RPGN) is distinguished by the absence of immune complex or complement deposition on immunofluorescent staining. It constitutes up to 50% of all RPGN cases. Almost all patients have elevated antineutrophil cytoplasmic antibodies (ANCAs, usually antiproteinase 3-ANCA or myeloperoxidase-ANCA) and systemic vasculitis.[12-15]

Early renal biopsy is essential. The feature common to all types of RPGN is focal proliferation of glomerular epithelial cells, sometimes interspersed with numerous neutrophils, that forms a crescentic cellular mass (crescents) and that fills Bowman space in >50% of glomeruli.[16-18]

**Immunofluorescence microscopy** findings differ for each type:

- In anti-GBM antibody disease (type 1), linear or ribbon-like deposition of IgG along the GBM is most prominent and is often accompanied by linear and sometimes granular deposition of C3.
- In immune complex RPGN (type 2), immunofluorescence reveals diffuse, irregular mesangial IgG and C3 deposits.
- In pauci-immune RPGN (type 3), immune staining and deposits are not detected. However, fibrin occurs within the crescents, regardless of the fluorescence pattern.[19]

**Prognosis:** Spontaneous remission is rare, and 80 to 90% of untreated patients progress to end-stage renal disease within 6 months. Prognosis improves with early treatment. Death is usually due to infectious or cardiac causes, providing that a uremic death is prevented by dialysis.

**Treatment**

Treatment varies by disease type. Corticosteroids and cyclophosphamide are usually given.

**Methodology**

A retrospective study was conducted in a tertiary centre for a period of one year, November 1st 2017 to 31st October 2018. The diagnosis of rapidly progressive glomerulonephritis was based on renal histology showing crescents in >50% of glomeruli. Any other cause of rapidly progressive renal failure with <50% crescents was excluded. Kidney biopsy (light microscopy) was studied. Treatment outcomes were labelled as complete, partial or no remission. Complete remission defined as 24-hour urine Protein <500 mg/day and serum creatinine <1.4 mg/dl. Partial remission as dialysis independence and serum creatinine <5.8mg/dl. No response as dialysis dependency and serum creatinine > 5.8 mg/dl.

**Statistical Analysis**

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and median. Quantitative variables were compared using Mann-Whitney Test between male and female. Qualitative variables were correlated using Chi-Square
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Fisher’s exact test. A p value of <0.05 was considered statistically significant.

**Results**

Fifty-five patients of rapidly progressive glomerulonephritis were included. The mean age of patients was 46.27 ± 16.6 years, with a range of 20 to 75 years. Only one patient was less than 20 years. (Figure 1)

There were 23 females (41.82%) and 32 males (58.18%), thus giving a male to female ratio of 1.38:1. (Table 1)

The mean number of sclerotic glomeruli observed in our study was 19.82% ± 16.54%, suggesting an advanced stage of disease. Four-fifth (80%) of patients had <35% sclerosed glomeruli, however one-fifth (20%) of them had between 36-65%. (Table 2)

Diagnosis of RPGN is based on >50% glomeruli showing crescents. The mean value of crescents in our study was 70.78 ± 16.24%. More than half (58.18%) of the patients had 50 – 70% glomeruli with crescents however, in nine (16.36%) patients > 90% glomeruli were found crescentic. (Table 3) About two-third of patients (63.64%) had showed no response. One third of patients (36.36%) responded to treatment and had remission. About one-fourth (25.45%) of patients showed partial remission and 10.91% had complete remission. (Figure 2)

While 71% of patients who achieved remission in study had sclerosis in < 35% of their glomeruli, one-third (32%) of non-responders show sclerosis in > 35% of their glomeruli, suggesting on marker of advance disease. (p< 0.05). (Figure 3)

Similarly, three-fourth of patients who achieved remission had between 50-75% of crescents in their glomeruli on the contrary, about half of non-responders had > 70% crescents in their glomeruli, suggesting to be a predictor of poor response. p<0.05. (Figure 4)

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**Figure 1** Age Distribution of the Patients

![Age Distribution of the Patients](image)

**Table 1** Gender Distribution of the Patients

<table>
<thead>
<tr>
<th>Gender</th>
<th>No.</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>23</td>
<td>41.82</td>
</tr>
<tr>
<td>Male</td>
<td>32</td>
<td>58.18</td>
</tr>
<tr>
<td>Total</td>
<td>55</td>
<td>100</td>
</tr>
</tbody>
</table>
Table 2 Distribution of Sclerosed Glomeruli

<table>
<thead>
<tr>
<th>% Sclerosed Group</th>
<th>No.</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 35.0</td>
<td>44</td>
<td>80.0%</td>
</tr>
<tr>
<td>36 – 65.0</td>
<td>11</td>
<td>20.0%</td>
</tr>
<tr>
<td>&gt;65</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Total</td>
<td>55</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Mean = 19.82  SD = 6.54

Table 3 Distribution of Crescentic Glomeruli

<table>
<thead>
<tr>
<th>% Crescents</th>
<th>No.</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 – 70.0</td>
<td>32</td>
<td>58.18%</td>
</tr>
<tr>
<td>70 – 90.0</td>
<td>14</td>
<td>25.45%</td>
</tr>
<tr>
<td>&gt;90</td>
<td>9</td>
<td>16.36%</td>
</tr>
<tr>
<td>Total</td>
<td>55</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Mean = 70.78  SD = 16.24

Figure 2 Treatment Outcomes

![Primary outcome](Image)

Figure 3 Association of Sclerosed Glomeruli with Treatment Outcome

![Percentage](Image)
Discussion
The mean age of patients was 46.27 ± 16.6 years, with a range of 20 to 75 years. Only one patient was less than 20 years. The mean age of females was 48.44 ± 16.27 years and for males it was 44.72 ± 16.92 years. There was a slight male preponderance. Age difference both the groups was not statistically significantly (P = 0.699). Similar observation have been reported by others. Naidu et al., from North India in their study of forty-three patients with pauci-immune glomerulonephritis reported the age range of 40 to 70 years with a mean of 41.1 [20].

In our study, about two-third of patients (63.64%) had showed no response. One third of patients (36.36%) responded to treatment and had remission. About one-fourth (25.45%) of patients showed partial remission and 10.91% had complete remission.

Tang et al., in their study from China enrolled 94 patients with lupus nephritis with diffuse crescentic glomerulonephritis. All the patients were under more than 6 months follow up. At the end of follow up, 12.8% were in clinical remission and 29.8% were in partial remission. [21]

The mean number of sclerotic glomeruli observed in our study was 19.82% ± 16.54%, suggesting an advanced stage of disease. Four fifth (80%) of patients had <35% sclerosed glomeruli, however one-fifth (20%) of them had between 36-65%. The mean value of crescents in our study was 70.78 ± 16.24%. More than half (58.18%) of the patients had 50 – 70% glomeruli with crescents however, in nine (16.36%) patients > 90% glomeruli were found crescentic.

While 71% of patients who achieved remission in study had sclerosis in < 35% of their glomeruli, one-third (32%) of non-responders show sclerosis in > 35% of their glomeruli, suggesting on marker of advance disease. (p< 0.05).

Similarily, three-fourth of patients who achieved remission had between 50-75% of crescents in their glomeruli on the contrary, about half of non-responders had > 70% crescents in their glomeruli, suggesting to be a predictor of poor response. p<0.05.

Marta et al., in their retrospective study conducted over a period of six years observed that the sclerotic group (HR 3.679, 95% CI, 1.164–11.628, p< 0.05) and baseline eGFR of <15
mL/min (HR 4.832, 95% CI, 1.55–15.08, p< 0.01) had an unfavourable effect for renal survival.\(^{(17)}\)

Similarly, El Husseini \textit{et al.}, concluded that the serum creatinine at presentation, nephrotic range proteinuria during the follow-up period, percentage of glomeruli affected by crescents, percentage of fibrous crescents and absence of cellular infiltration were significant risk factors affecting the kidney function.\(^{(22)}\)

\textbf{Conclusion}

Patients with extent sclerosis and crescents in their renal biopsy specimens have a higher risk of developing end stage renal disease. This negative outcome is present despite treatment with aggressive immunosuppression. Of course, further clinical studies are needed to confirm our results and to move histopathological classification into daily protocols.

RPGN is an important cause of renal failure. An early referral to nephrologist for early diagnosis and treatment is stressed.

\textbf{References}


