**INTRODUCTION:**

Crescentic glomerulonephritis is categorized by immunohistology into anti GBM crescentic glomerulonephritis with linear GBM staining for immunoglobulins, immune complex crescentic glomerulonephritis with granular staining of glomeruli for immunoglobulin’s and or complement, and pauci-immune GN with little or no glomerular staining for immunoglobulin’s and or complement.2

The aim of this study is to study the clinical presentation, the histologic features and immunofluoresence patterns of extracapillary proliferative glomerulonephritis and to correlate the pathologic features with clinical outcome.

To acheive this, we have retrospectively and prospectively analysed the renal biopsies, light microscopy and immunofluorescence with serological markers.

Most of the renal diseases are diagnosed by histology, immunofluoresence and electron microscopic examination. RPGN is a renal disease which can be diagnosed by immunohistology alone. Hence with in our hospital set up a definitive early diagnosis of crescentic glomerulonephritis could be reached with histology and immunofluorescence alone with the support of serologist markers, without electronmicroscopy study for early management of the disease as it presents as a medical emergency. Microscopy becomes essential only for the categoization especially for the immune complex mediated disorders.

**MATERIALS AND METHODS:**

**CLINICAL DATA**

Patients diagnosed as extracapillary crescentic glomerulonephritis on kidney biopsies in Apollo hospital, Chennai from 1996 to 2010. The hospital receives renal biopsies from various private and public hospitals not only from city of Chennai but from other centers in tamilnadu, the average number being 20,000 biopsies per year.

The biopsies were on both out patients and inpatients received from various government and private hospitals. The age at presentation varied from 6 yrs to 74 yrs. There were 19 males and 21 females. The mode of presentation, relevant clinical data and laboratory data were obtained from the medical records.

**HISTOLOGICAL DATA**

In the retrospective study, fresh sections were cut from the paraffin blocks retrieved from the archives of the pathology department, Apollo hospitals Chennai. Prospective cases were those that which were diagnosed in the year 2019-12. For all the cases,histological sections were cut from Bouin’s fixed paraffin embedded renal tissue at 3 micron section thickness. Sections were stained with Hematoxylin & Eosin (H&E), periodic Acid schiff (PAS), periodic acid-silver methanamine (PASM), Masson’s Trichrome and maritus scarlet blue (MSB) Staining Methods. The Slides Were studied.

Under the following headings

1. **Number of glomeruli** No of viable glomeruli

 No of Sclerosed glomeruli

1. **Cellularity**

 a. Grading

 Mild/Moderate/severe

Mesangial

 b. Types of cells Endothelial

 Epithelial

 Focal/Diffuse

 c. Distribution of cells Segmental/Global

1. **Glomerular tuft**
2. Glomerulitis

Present : Neutrophils/Monocytes absent

1. Glomerular tuft necrosis

Present / Absent

1. Bowmans capsule disruption

Present / Absent

1. Periglomerular inflammation

Present / Absent

1. **Glomerular crescents**
2. Percentage of glomerular crescents

 Cellular

1. Type of crescents Filbrocellular

Fibrous

1. **Membrane thickening** Mild

 Present Moderate

Severe

 On PASM stain vacuolation

 Silver positive Spikes

 Tram track appearance

 Expansion of basement membrane with silver

 negative deposits

 **6. Tubulointerstitial changes were graded from 0 to 4.**

Grade 0 : Normal

 Grade 1 : Focal tubular atrophy

 Grade 2 : multifocal tubular atrophy

 Grade 3 : Patchy tubular atrophy

 Grade 4 : Extensive tubular atrophy

1. **Interstitial inflammation :**

Grade I : Mild

Grade II : Moderate

 Grade III : Severe

 Granulomatous Nonnecrotizing

 Necrotizing

Composition Neutrophils Lymphocytes Eosinophils plasma cells histiocytes

 Non Granulomatous

1. **Interstitial Fibrosis**

Grade 0 : Nil

Grade 1 : Focal

Grade 2 : Multifocal

Grade 3 : Patchy

Grade 4 : Extensive

1. **Vascular changes:**

Vessel wall thickness of small and medium size were graded from 0 to 3

Grade 0 : Normal

Grade 1 : Mild thickness of wall equal to the luminal diameter

Grade 2 : Moderate thickness of wall greater than luminal diameter

Grade 3 : Marked thickness of wall with severe luminal narrowing

or occlusion

1. **Vasclitis:**

**a**. Necrosis : Present / Absent

 Lymphocyte

b. Inflammation Neutrophil

 Eosinophil

**IMMUNOFLUORESCENCE**

The immunofluorescence data was collected from the old reports for the retrospective cases. immunofluorescence was done for all the prospective cases, and were reported as per the standard practice. The technique used was as follows.

 A fresh core of renal tissue was obtained by the percutaneous needle biopsy and was placed on a gauze wetted in cold normal saline kept on a bed of ice in a petri dish.

 The sample was frozen immediately in a cryostat cooled to – 200C Approximately 3 micron thick sections were obtained on five slides (with 1 section per slide) and was washed with PBS and stained with fluorescein conjugated monoclonal antibodies IgG, IgM, IgA, C3c and C1q.

Immunofluorescence microscopy on Renal Biopsy

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **G** | **M** | **A** | **C3c** | **C1q** |
| I Glomeruli localization pattern scoreII Arteries patternIII tubules pattern |  |  |  |  |  |

M- Mesangium; P-Peripheral; C-Capsular

S-Segmental; G-Global; F-Focal; D-Diffuse

GrF: Granular fine; GrC : Granular Coarse

Lc:Linear Continuous; Li:Linear interrupted

B’Cap : Bowman’s Capsule

1. Glomeruli

 localization : Mesangial / Peripheral

 Pattern : Focal/ Diffuse/ Segmental / Global

 Type : Granular fine / Granular coarse/ linear continuous / Linear

Interrupted

 Score : 1 + to 4+

2. Arteries

 SCORE : 1+ to 4+

3. Tubules

 Score : 1 + to 4+

 Type : Granular / Linear smooth

The immunofluoresence and morphological findings were correlated.

**RESULTS AND OBSERVATIONS**

 This study composed of 40 cases diagnosed as Extra capillary proliferative glomerulonephritis, on percutaneous needle biopsy, of which 6 cases were followed up retrospectively and 34 cases were studied prospectively from the data available in the medical records. Of the 40 cases diagnosed as extracapillary proliferative GN, 4 cases were categorized as anti-GBM crescentic GN, 13 cases as pauci-immune crescentic GN and 23 cases as immune-complex crescentic GN.

 Among 40 cases, anti-GBM patients were in a younger age group i.e,20-45 years with a minimum of 22 years and maximum age of 43 years.

 Pauci-immune crescentic GN were of older age group i.e, 40-60 years, with a minimum of 18 years and maximum 50 years.

 In Immune complex crescentic GN majority were children and of younger age group i.e, 20-40 years, with a minimum of 16 years to maximum of 57 years.

 The age distribution graph represented in fig.1.

**SEX**

19/40 cases (47%) were males and 21/40 cases (53%) were females. Thus the sex incidence in this study is 1:1.1 with mild predominance of female sex. On comparison with clinical outcome, no significant difference was noticed, as represented in fig.2 and table 1.

**Clinical features**

The most common clinical presentation is protenuria 34/30 cases (85%). The other clinical features present at the onset are Edema 75%, hematuria 60%, Oliguria 18% Hypertension 40%. Among these various clinical features, patients with Hypertension 10/16 (62%), Oliguria 11/19 (58%) and hematuria 14/24 (58%) cases exhibited worse clinical outcome. The clinical feature with respect to clinical outcome is represented in fig.3 and table2.

**Albuminuria**

Patients presented with various grades of albuminuria. Majority of the patients 21/40 cases (52%) presented with 3+ albuminuria. Worse clinical outcome was seen in patients with 3+ albuminuria.

The clinical outcome of patients as shown in fig.4 and table3.

**Hematuria**

30/40 cases (75%) had microscopic hematuria, out of which 50% had bad prognosis, which is represented in fig.5 and table-4.

**SERUM CREATININE**

37/40 cases (92%) had serum creatinine ranging from a minimum of 1 mg/dl to a maximum of 17.2 mg/dl . The highest serum creatinine level is seen in anti-GBM category with 17.2 and all patients in this group had a worse clinical outcome.

 Patients who had good outcome had a serum creatinine of < 3.1 mg/dl, compared to patients with a serum creatinine of > 8.4 mg/dl who had a worse clinical outcome as shown in fig.6 and table 5.

**Immune complex mediated GN**

The following histologic parameters were assessed in each case on light microscopy

1. Glomeruli: number of glomeruli/percentage of crescents/type of crescents
2. Glomerular tuft inflammation / glomerulitis
3. Glomerular tuftnecrosis
4. Interstitial inflammation
5. Vascular changes

**Number of glomeruli**

Average (mean) of 10.5 glomeruli per biopsy specimen were examined ranging from a minimum of 4 glomeruli per biopsy to a maximum of 20 glomeruli per biopsy specimen.

**Percentage of glomeruli crescents**

Out of 40 cases, majority 38% of cases exhibited 90-100% glomerular crescents, 32% cases exhibited 50-70% glomerular crescents and 30% with 70-90% as represented in fig.7 and percentage of glomerular crescents with respect to clinical outcome as represented in table 7.

 Out of 15/40 cases(38%) which exhibited 90-100% glomerular crescents 53% had a worse clinical outcome.

 Out of 13/40 cases (32%) which exhibited 50-70% glomerular crescents, only 23% had a worse clinical outcome and 54% had a good outcome,

Out of 4/40 cases of anti-GBM,2/4 cases (50%) showed 100% glomerular crescents, all had a worse clinical outcome and 2/4 cases (50%) showed 70-90% crescents of which 1 has a good outcome and I had lost to follow up. This is shown in fig 8 and table 8.

**Pauci-immune glomerilonephritis ( Group-B)**

Out of 13/40 cases, 3/13 cases presented with 50-70% glomerular crescents and had a good clinical outcome except for 1 case which was lost to follow up. 5/13 cases (38%) presented with 70-90% glomerular crescents out of which 2 (40%) had bad outcome, 1 lost to follow up and 5/13 cases (38%) exhibited 90-100% glomerular crescents of which 2 cases (40%) had a worse clinical outcome, represented in the fig9 and table 9.

**Immune-complex GN (GROUP-C)**

Out of 23 cases, majority of cases 10/23 cases (43%) exhibited 50-70% glomerular crescents of which only 3 cases (30%) had a bad outcome as compared to 8/23 cases (35%) exhibited 90-100% glomerular crescents of which 50% had a bad clinical outcome represented in the fig 10 and table 10.

All 3 cases (100%) of ANCA – negative pauci-immune crescentic GN exhibited 100% cellular crescents and all patients had a bad clinical outcome.

**Glomerular tuft inflammation/ glomerulitis**

 18/40 (45%) exhibited glomerular tuft inflammation of which only 7/18 cases had worse clinical outcome and 22/40 cases were negative for glomerular tuft inflammation, of which 45% had a bad clinical outcome which is represented in fig11 and table11.

**Glomerular tuft necrosis**

7/40 (17%)exhibited glomerular tuft necrosis, of which 43% had a bad clinical outcome and 33/40 cases (83%) did not exhibit glomerular tuft necrosis of which 42% had a bad clinical outcome which is represented in a fig 12 and table 12.

**Interstitial inflammation**

33/40 cases exhibited interstitial inflammation of variable intensity. Majority of the patients belong to grade 2 (45%), and grade-3 (28%). Among these 64% and 50% cases belonging to grade 3 and 2 grade respectively had a worse clinical outcome as shown in fig 13 and table 13.

**Vascular changes**

2 cases (70%) exhibited various grads of vascular changes. Among these 48% belong to grade-1,22% belong to grade -2, among these 37% grade-1 had bad outcome as to 56% grade-2 had worse outcome, 11% had good outcome and 33% had lost to follow up.

1 case had fibrinoid necrosis of vessel wall in ANCA-negative pauci-immune crescentic GN had a bad clinical outcome as represented in fig 14 and table 14.

**Immunofluoresence**

 Immunofluoresence was done on all 40 cases, showed various degrees of positivity and those cases with 2+or greater staining for immunoglobulin were taken as positive, Immunofluoresence was done for the following groups of immunoglobulin IgG,IgM,IgA,C3c and C1q.

 Anti-GBM cases exhibited 2+ to 4+ linear smooth staining of glomerular basement membrance with IgG and C3c.

 Pacui-immune mediated crescentic GN exhibited minimal granular staining for C3C in 54%, IgM & C3c in 16%, IgM in7%,IgG,IgM, C3c in 7% and no staining 16% of cases.

 IgA crescentic GN exhibited 3+ to 4+ coarse granular mesangial staining for IgA and C3c. Mesangial deposits of IgM of low intensity also seen in few cases.

 Lupus nephritis exhibited 3+ to 4+ coarse granular staining in all classes of immunoglobulins and complement component, had a “full house” pattern positive with IgG,IgM,IgA,C3c and C1q.

 Membranoproliferative GN exhibited strong positivity 3+ to 4+ staining for C3c in a coarse granular pattern along the glomerular capillaries. Deposits of IgG and C1q of low intensity was also seen in few cases.

**MODE OF TREATMENT**

All the patients were treated with either of the following regimes.

A Prednisolone

B Prednisolone + Cyclophoshamide

C Prednisolone + Cyclophoshamide + Hemodialysis

D Prednisolone + Fresh frozen plasma + Hemodialysis

Out of 40% cases, 5% of patients treated with regime “A”,25% with regime “B” 45% with regime “C”, 7.5% with regime “D” and 17.5% were lost to follow up.

30% of patients treated with regime “A” and “B” had favorable outcome.

52.5% patients treated with regime “C” and “D” had worse clinical outcome.

Out of 40 cases, ¾ cases (75%) of anti – GBM had worse clinical outcome.

6/13 cases (46%) of pauci-immune had good outcome a against 4/13 (31%) with bad outcome.

8/23 cases (35%) of immune – complex had good clinical outcome, as against 10/23 (43%) with worse clinical oucome.

Hence in the overall oucome of patients in extracapillary crescentic GN anti-GBM crescentic GN had a worse outcome compared to pauci-immune crescentic GN and immunecomplex GN. A favorable outcome is seen in immune complex crescentic GN. This is shown in fig.15 and table-16.

Test, ANOVA was used to derive the univariate statistical analysis with respect to clinical outcome.

**Statistical analysis**

Statistical software used:SPSS V.10.0

 Statistical tools used: Mc Nemar’s Chi square test, ANOVA

|  |  |  |
| --- | --- | --- |
| Parameter | P-value | Result  |
| Hypertension | 0.21 | Not significant  |
| Proteinuria  | <0.001 | Highly significant |
| Oliguria  | 0.108 | Not significant |
| Serum creatinine  | <0.001  | Highly significant |
| Albumin | <0.001  | Highly significant |
| Hematuria  | <0.001 | Highly significant |
| % of glomerular crescents | 0.093 | Not significant |
| Glomerular tuft inflammation | 0.129 | Not significant |
| Interstitial inflammation  | 0.031 | significant |
| Tubular atrophy | 0.778 | Not significant |

**DISCUSSION:**

This study comprising 40 cases diagnosed as Extra capillary proliferative Glomerulonephritis (crescentic GN) were observed and the course analysed. This study was partly retrospective and partly prospective.

 The age range at diagnosis of anti-GBM disease varied from 20-45 years with a mean of 32.5 years and this was the most uncommon category of extracapillary proliferative GN, as it has been observed in the literature. Anti-GBM is uncommon at any age, which is well illustrated in this study.

 Pauci-immune crescentic GN presented at an age range of 40-60 years at an older age group which correlates with the literature study.1

Immune complex crescentic GN presented at an younger age group, 20-40 years with a minimum age of 16 years at presentation.1

 This study did not show any significant correlation between age and progression to ESRD.

 In this study the most common category was immune-complex mediated Glomerulonephritis, affecting young children and young adults. The categories included are IgA nephropathy, post infective Glomerulonephritis, membranoproliferative Glomerulonephritis, Lupus nephritis and Henoch-schonlein purpura.

 In the elderly age group, renal limited vasculitis was the most likely diagnosis, out of which 30% were ANCA – negative.

The overall presentation of number of males affected to female ratio is 1:1.1. The reported incidence in other studies ranged from 1:0.9 to 1.6.1 the clinical income in 53% females and 47% males showed no significant difference.

The most common clinical presentation is protenuria. The other clinical features present at the onset are edema, hematuria, oliguria, hypertension and high serum creatinine level.

 46% of patients predominantly of pauci-immune GN, presented with a preceding history of fever, flu like illness, which has been described in the literature. Approximately 90% of the patients report a flu-like illness before the onset of signs and symptoms of small vessel vasculitis. 4,25

3 cases of ANCA-negative pauci-immune crescentic GN presented with short duration of history of symptoms of edema,hematuria without much systemic involvement, had a very bad outcome. Out of the 3 cases, 1 patient expired within 5 months of diagnosis, 1 patient went on to ESRD gradually, 1 patient underwent transplant after reaching ESRD.

 This has been shown in literature that poor prognosis associated with ANCA negativity was due to delay in diagnosis since these patients frequently lacked systemic involvement.3

 Of the 2 cases (15.3%) of pauci-immune GN which were cases of Wegeners granulomatosis, one case was biopsy proven with bronchial granulomas and other case had respiratory symptom, but no biopsy was done. Both cases had skin biopsy proven vasculitis with pauci-immune GN as shown by renal histology and immunofluourescence. Both these cases had a serum creatinine level of 2mg/dl and 2.4mg/dl at the time of diagnosis and had a good clinical outcome. 25

 Both cases of Wegeners granulomatosis with pulmonary involvement had c-ANCA positivity, this fact was well noted on a study by Ronald J falk that showed diseases limited to the kidneys have a higher frequency of P-ANCA reacting with MPO, whereas patients with pulmonary and sinus disease have a higher incidence of C-ANCA reacting with PR-3.25

 2 cases of post-infectious GN presented with a preceeding symptom of fever before the onset of Glomerulonephritis.

 1 case of Henoch-schonlein purpura, immune-complex mediated crescentic GN presented with arthritis and skin rashes. Biopsy of the skin showed small vessel vasculitis with significant IgA deposits in the papillary dermal vessels on immunofluoresence.

**URINE ALBUMIN AND RBC**

 In this study out of 21 patients with 3+ albuminuria, 12 cases (57%) had a worse clinical outcome and 1 out of 2 patients with 4+ albuminuria had severe renal failure. Albuminuria (p<0.001) seems to be a significant prognostic indicator of disease progression.

 Out of 40 cases, 30(75%) had microscopic hematuria, of which 15(50%) had worse clinical outcome. Thus microscopic hematuria seems to be a significant prognostic indicator.

**SERUM CREATININE**

The serum creatinine range at diagnosis of extra capillary proliferative GN ranged from 1mg/dl to 17.2mg/dl.

All 4 cases of anti-GBM presented with a serum creatinine of >8.7mg/dl and with a highest serum creatinine level of 17.2mg/dl. All these patients required immediate dialysis and remained dialysis dependent.

The lowest serum creatinine level was in the immune-complex mediated GN, which had a fairly good clinical outcome.

Several studies have reported that the serum creatinine level at the time of presentation of the renal biopsy has a strong influence on the further course of the disease and outcome. In this study we found that, patients who had mean serum creatinine level of <3.1mg/dl had a good outcome as compared to patients who had a mean serum creatinine level of >8.4mg/dl who had worse clinical outcome.1,27,30

Using univariable analysis, serum creatinine level at biopsy and all histologic variables examined significantly correlated with severe renal impairment and progression early to ESRD. Serum creatinine level at the time of renal biopsy may reflect the extent of active glomerular lesions.28

 Patients who had a serum creatinine of <3.1mg/dl recovered with immunosupession therapy alone as compared to patients with high serum creatinine of >=8.4mg/dl reached end stage very rapidly. Thus serum creatinine seems to be a definite prognostic indicator (p<0.001) of disease progression.

 Serological markers such as ANA,p-ANCA,c-ANCA,ANTI-dS DNA, ANTI-GBM were done in all the cases and were positive in respective categories, which supported the diagnosis of different immunopathologic categories of extra capillary proliferative crescentic GN along with histology and immunfluorescent microscopy.

Cases of post infections crescentic GN had reduced serum complement levels and had a high ASO titres.

2 cases of Lupus nephritis exhibited ANA positivity.

 Numerous studies have proposed that certain histologic parameters had a bearing on the prognosis. In the study, we selected a few histologic parameters and graded them and tried to correlate with the clinical outcome.

The parameters assessed are,

1. Percentage of glomeruli with crescents
2. Type of crescents
3. Glomerular tuft inflammation/glomerulitis
4. Glomerular tuft necrosis
5. Interstitial inflammation – graded
6. Vascular changes – graded

Percentage of glomerular crescents had an effect on clinical outcome. Patients with glomerular crescents of 70-90%, of which 50% had a bad outcome, as compared to patients with 90-100% of which 53% had a bad prognosis. Hence as the percentage of glomerular crescent increased increased the percentage of patients with bad outcome increased. Thus glomeruli with crescents seems to be a prognostic factor. 1,27,28,29,30

In anti-GBM disease out of the 4 cases,3 cases (75%) had 100% glomerular crescents, 1 case had 60% glomerular crescent. All patients went to end stage renal disease rapidly.

In contrast immune-complex GN such as IgA nephropathy,Lupus nephritis, MPGN, post infectious GN, had a lower average number of crescent formation and better outcome. These findings are compatible with the study from the united states by Jennette.1

In immune-complex glomeulonephritis out of 10 cases (43%) with crescents, 3(30%) had relatively bad prognosis who had crescents of 70%.

In this study no significant correlation is seen between the number of the sclerosed glomeruli and the clinical outcome of the patient.

Glomerular tuft inflammation was predominantly seen in ANCA-associated pauci-immune GN, as compared to anti-GBM, and immune complex GN. No significant correlation was seen between glomerular tuft inflammation and clinical out-come.

This study had 40 cases exhibiting different grades of tubular atrophy and interstitial fibrosis. Both tubular atrophy and interstitial fibrosis are signs of chronicity and were independent predictors of clinical outcome. Extra capillary proliferative GN is an acute disease process hence in this study, the effect of tubular atrophy and interstitial fibrosis on clinical outcome of the patient could not be defined as the period of follow up after the observation was short to make a definite conclusion.

Interstitial inflammation had a significant effect on disease course and outcome (p<0.031). This study had 40 cases exhibiting various grades of interstitial inflammatory changes. About 50% grade 2 patients and 64% of grade 3 patients had severe renal impairment, and this fact is very well supported by the literature.13

In this study ANCA negative cases were of older age group, presented with higher serum creatinine level as compared to ANCA positive cases. Extensive crescent formation of 100% glomerular crescents was seen, in comparison with ANCA positive pauci-immune crescentic GN which had variable number of percentage of glomerular crescents.3 All ANCA negative patients had a poor prognosis and became dialysis dependent, while majority of ANCA positive patients though initially were dialysis dependent, later on recovered partially or fully.3

50% of pauci-immune glomerulonephritis exhibited grade 1 and 30% were grade 0, had good outcome. 1 case exhibited fibrinoid necrosis of the vessel wall with granuloma, had a worse outcome and patient expired within 5 months of diagnosis.

Endothelial cell proliferation and mesangial cell proliferation was predominantly seen in immune-complex GN. However tuft celluarity did not have an effect on the clinical outcome.

Immunofluoresence is absolutely necessary for the conformation of the diagnosis of different immnuopathologic groups of crescentic GN. A staining of 2+ or more for any immunoglobulins were taken as positive for respective categories.

Clinical features that predicated the outcome of crescentic GN patient are

1. Albuminuria
2. Hematuria
3. Serum creatinine level at biopsy

Patients with 3+ and above albuminuria, had a worse clinical outcome. Albuminuria (p<0.001) seems to be a significant prognostic factor.

30/40 cases exhibited microscopic hematuria and 50% of these cases had a bad prognosis. Hence patients with microscopic hematuria had a bad clinical outcome as compared to cases without hematuria. Thus microscopic hematuria is a significant prognostic indicator.

All 4 cases of anti-GBM presented with a serum creatinine of >8.7mg/dl and with a highest serum creatinine level of 17.2mg/dl. All these patients required immediate dialysis and remained dialysis dependent. The lowest serum creatinine level was in the immune-complex mediated GN, which had a fairly good clinical outcome.

 In this study we found that, patients who had mean serum creatinine level of < 3.1mg/dl had a good outcome as compared to patients who had a mean serum creatinine level of >8.4mg/dl who had worse clinical oucome.1,27,30  Serum creatinine level at biopsy and all histologic variables examined significantly correlated with ESRD. Serum creatinine level at the time of renal biopsy may reflect the extent of active glomerular lesions.28

Patients who had a serum creatinine of <3.1mg/dl recovered with immunosupression therapy alone as compared to patients with high serum creatinine of >8.4mg/dl reached end stage very rapidly. Thus serum creatinine is s definite prognosic indicator (p<0.001) of disease progression.

 Histological parameters that predicted the outcome are

1. Interstitial inflammation
2. Vascular changes

d)Interstitial inflammation had a significant effect on disease course and outcome (p<0.031). Various grades of interstitial inflammatory changes were exhibited. Grade 2 patients and grade 3 patients had severe renal impairment, and this fact is very well supported by the literature.13

e)Vascular changes exhibited various grades. Blood vessels with thickening of grade 0 and grade 1 case had a good clinical outcome as compared to patients with grade 2 changes and 5/9 cases had a bad clinical outcome.

One patient exhibited fibrinoid necrosis of the vessel wall with granuloma, had a worse outcome and patient expired. Hence vascular changes is one of the prognostic indicator of clinical outcome.

1. Initial treatment received by the patient.

Majority of the patients who were dialysis dependent at the time of presentation and diagnosis, usually remained dialysis dependent in most of the case. Hence in the overall outcome of patients in crescentic GN, anti-GBM crescenric GN has a worse outcome compared to pauci-immune crescentic GN and immunecomplex GN. A favorable outcome is seen in immune complex crescentic GN.

 **CONCLUSION:**

 Of 40 cases of extra capillary proliferative GN, 21 were females and 19 were males.

Most common clinical presentation was edema, protenuria, hematuria. Co-morbidities included systemic hypertension, type 2 diabetes mellitus, respiratory diseases like tuberculosis.

On biopsy of 40 cases, 23 cases were immune-complex mediated GN, 13 cases were pauciimmune GN,4 cases were antiGBM GN.

The common aetiology of immune complex GN were IgA nephropathy followed by systemic lupus erythematosus, postinfectious and membranoproliferative GN.

Immune complex mediated GN was commoner in younger age group, pauci-immune in the elderly age. Anti-GBM being very rare could not be analyzed.

Patients with a serum creatinine level of <3.1mg/dl had a good outcome as compared to patients who had a mean serum creatinine level of >8.4mg/dl who had worse clinical outcome.

Anti-GBM is the most aggressive form of glomerulonephritis with the highest frequency of renal insufficiency and the highest frequency of crescent formation at the time of diagnosis as compared to pauci-immune and immune complex crescentic-GN.

Immune complex GN have a much lower frequency of crescent formation and, when crescents are present, they rarely affect 50% or more of glomeruli.

ANCA negative pauci-immune GN has a more aggressive clinical course as compared to ANCA positive pauci-immune GN.

Hence within our hospital set up a definitive early diagnosis of crescentic glomerulonephritis could be reached with histology and immnuofluorescence alone without electron microscopy study for early management of the disease as it presents as a medical emergency. Several days delay in diagnosis and treatment can have a major negative impact on outcome because of the rapidly progressive loss of renal function.

Thus this study has clearly shown that even in the absence of electron microscopy a definite aetiological diagnosis can be made in cases of extra capillary proliferative GN presenting as a medical emergency with sudden onset of acute renal failure (RPGN) and helps the clinician in the successful management of the patient.

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**FIGURE WITH LEGENDS AND TABLES :**

**Fig1-Histogram showing Age distribution of various groups (total no of cases 40)**

 Group A – Anti-GBM Group B- Pauci-Immune Glomerolonephritis Group C – Complex Glomerolonephritis

 **Fig-2 Histogram showing sex distribution**

**Fig.3 Histogram showing clinical symptoms with respect to clinical outcome**

**Fig-4 Histogram showing urine Albumin**

**Fig-5 Histogram showing urine RBC and Outcome**

**Fig6- Diagram showing serum creatinine with outcome**

**Fig-7 Diagram showing percentage of glomerular crescents**

**Fig-8 Histogram showing percentage of glomerular crescents with respect to clinical outcome in anti -GBM**

**Fig-9 Histogram showing percentage of glomerular crescents with respect to clinical outcome in Pauci-immune Glomerulonephritis**

**Fig-10 Histogram showing percentage of glomerular crescents with respect to clinical outcome in immune-complex glomerulonephritis**

**Fig-11 Histogram showing glomerular Tuft inflammation with respect to clinical outcome**

**Fig-12 Histogram showing Glomerular Tuft Necrosis with respect to clinical outcome**

**Fig-13 Histogram showing Interstitial Inflammation with respect to clinical outcome**

**Fig-14 Histogram showing Vascular changes with respect to clinical outcome**

**Fig-15 Histogram showing clinical outcome patients**

**Table -1 Sex with respect to clinical outcome**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **No.of.patients** | **%** | **Outcome**  |
| **Good** | **Bad** | **No follow-up** |
| **Female** | **21** | **53%** | **6(29%)** | **9(42%)** | **6(29%)** |
| **Male** | **19** | **47%** | **8(42%)** | **8(42%)** | **3(16%)** |

**Table -2 clinical features with respect to clinical outcome**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **No.of.patients** | **%** | **Good Outcome** | **Bad Outcome** | **No follow-up** |
| Hypertension | **16** | **40%** | **6(38%)** | 10(62%) | 0(0%) |
| Oliguria | 19 | 48**%** | 6(32%) | 11(58%) | 2(10%) |
| Edema | 30 | 75**%** | 12(40%) | 12(40%) | 6(20%) |
| protenuria | 34 | 85**%** | 13(38%) | 15(44%) | 6(18%) |
| Hematuria  | 24 | 60**%** | 8(34%) | 14(58%) | 2(8%) |
|  |  |  |  |  |  |

**Table 3. Albuminuria with respect to clinical outcome**

|  |  |  |
| --- | --- | --- |
| Albumin  | No.of.patients | Outcome  |
| Good | Bad | No follow-up |
| 1+ | 5 | 2(40%) | 1(20%) | 2(40%) |
| 2+ | 7 | 4(57%) | 2(29%) | 1(14%) |
| 3+ | 21 | 7(33%) | 12(57%) | 2(10%) |
| 4+ | 2 | 0(0%) | 1(50%) | 1(50%) |
| N | 1 | 1(100%) | 0(0%) | 0(0%) |
| ND | 2 | 0(0%) | 0(0%) | 2(100%) |
| NH | 2 | 0(0%) | 1(50%) | 1(50%) |
|  |  |  |  |  |

**Table 4. Hematuria with respect to clinical outcome**

|  |  |  |
| --- | --- | --- |
| **RBC** | **No.of.patients** | **Outcome**  |
| **Good** | **Bad** | **No follow-up** |
| N | 8 | 2(25%) | 2(25%) | 4(50%) |
| ND | 1 | 0(0%) | 0(0%) | 1(100%) |
| NH | 1 | 0(0%) | 0(0%) | 1(100%) |
| P | 30 | 12(40%) | 15(50%) | 3(10%) |

**Table-5. Serum creatinine with respect to clinical outcome**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **N** | Mean | SD | Minimum | Maximum | P Value  | Result  |
| Good outcome | 14 | 3.187 | 2.23 | 1 | 9.5 | P<0.001 | Highly significant  |
| Bad outcome  | 17 | 8.441 | 2.577 | 4.7 | 13 |
| No followup | 6 | 7.567 | 5.321 | 2.4 | 17.2 |
| Total  | 37 | 6.311 | 3.857 | 1 | 17.2 |

**Table-6. Features of different types of Crescentic GN in comparisom with North Carolina Nephrology Laboratory**

|  |  |  |
| --- | --- | --- |
| **Group** | **Present study** | **Nephrology forum** |
| **Mean Age** | **Male: female** | **Creatinine** | **Mean Age** | **Male female** | **Creatinine**  |
| A | 33.25+9.91 (22-43)N=4 | 1:1, 2:2 N=4 | 12.5+3.5 (8.7-17.2)N=4 | 52+21(14-84)N=92 | 1:1 45:47 N=92 | 9.7+7.2 (0.8-50) N=86 |
| B | 45+17.63(18-70)N=13 | 1.6:1,8:5 N=13 | 5.2+3.9 (1.4-13)N=11 | 56+20(2-92) N=377 | 1:0.9,202:177 N=379 | 6.5+4 (0.8-22.1) N=338 |
| C | 36.83+17(6-74) N=23 | 1:1, 11:12 N=23 | 5.8+2.9 (1-10) N=22 | 33+17(4-77)N=154 | 1:1.6, 61:95 N=156 | 4.9+3.8 (0.8-21.7) N=145 |

**GroupA-antiGBMcrescenticGN,GroupB-Pauci-immunecrescenticGN,GroupC-Immune complex mediated GN**

**Table-7 % of Glomerular crescents with respect to clinical outcome**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **No.of.patients** | **%** | **Outcome** |
| **Good** | **Bad** | **No follow-up** |
| 50-70 | 13 | 32**%** | 7(54%) | 3(23%) | 3(23%) |
| 70-90 | 12 | 30**%** | 5(33%) | 6(50%) | 2(17%) |
| 90-100 | 15 | 38**%** | 3(20%) | 8(53%) | 4(27%) |

**Glomerular crescents with respect to clinical outcome in various groups :**

**Table – 8 ANTI -GBM (Group A) Disease**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **No.of.patients** | **%** | **Outcome**  |
| **Bad** | **No follow-up** |
| 70-90 | 2 | 50**%** | 1(50%) | 1(50%) |
| 90-100 | 2 | 50**%** | 2(100%) | 0(0%) |

 **Table-9 . % of glomerular crescents with respect to clinical outcome in Pauci-immune crescentic GN - GROUP -B**

|  |  |  |  |
| --- | --- | --- | --- |
| **Pauci-Immune** | **No.of.patients** | **%** | **Outcome** |
| **Good** | **Bad** | **No follow-up** |
| 50-70 | 3 | 24**%** | 2(67%) | 0(0%) | 1(33%) |
| 70-90 | 5 | 38**%** | 2(40%) | 2(40%) | 1(20%) |
| 90-100 | 5 | 38**%** | 2(40%) | 2(40%) | 1(20)% |

**Table 10. Immune-complex crescentic GN –GROUP C**

|  |  |  |  |
| --- | --- | --- | --- |
| **IMMUNE COMPLEX** | **No.of.patients** | **%** | **Outcome** |
| **Good** | **Bad** | **No follow-up** |
| 50-70 | 10 | 43**%** | 5(50%) | 3(30%) | 2(20%) |
| 70-90 | 5 | 22**%** | 2(40%) | 3(60%) | 0(0%) |
| 90-100 | 8 | 35**%** | 1(13%) | 4(50%) | 3(37%) |

**Table- 11 Glomerular tuft inflammation with respect to clinical outcome**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **No.of.patients** | **%** | **Outcome** |
| **Good** | **Bad** | **No follow-up** |
| N | 22 | 55**%** | 5(23%) | 10(45%) | 7(32%) |
| P | 18 | 45**%** | 9(50%) | 7(39%) | 2(11%) |

**Table-12 glomerular tuft necrosis with respect to clinical outcome.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **No.of.patients** | **%** | **Outcome** |
| **Good** | **Bad** | **No follow-up** |
| N | 33 | 83**%** | 10(30%) | 14(42%) | 9(27%) |
| P | 7 | 17**%** | 4(57%) | 3(43%) | 0(0%) |

**Table-13 Interstitial inflammation with respect to clinical outcome**

|  |  |  |  |
| --- | --- | --- | --- |
| **INFL** | **No.of.patients** | **%** | **Outcome** |
| **Good** | **Bad** | **No follow-up** |
| 0 | 7 | 18**%** | 2(29%) | 1(14%) | 4(57%) |
| 1 | 3 | 7**%** | 3(100%) | 0(0%) | 0(0%) |
| 2 | 18 | 45**%** | 6 (33%) | 9(50%) | 3(17%) |
| 3 | 11 | 28**%** | 3(27%) | 7(64%) | 1(9%) |
| 4 | 1 | 2**%** | 0(0%) | 0(0%) | 1(100%) |

**Table-14 vascular changes with respect to clinical outcome**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **No.of.patients** | **%** | **Outcome** |
| **Good** | **Bad** | **No follow-up** |
| 1 | 19 | 48 % | 9(47%) | 7(37%) | 3(16%) |
| 2 | 9 | 22 % | 1(11%) | 5(56%) | 3(33%) |
| FN,GR | 1 | 2 % | 0 (0%) | 1(100%) | 0(0%) |
| N | 11 | 28 % | 4(36%) | 4(36%) | 3(28%) |

**Table-15 Serum creatinine levels before and after treatment**

|  |
| --- |
|  **Mean N SD Pvalue Result** |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| SR.CREATININE BEFORE  | 5.463 | 24 | 5.433 | 0.000 | Significant  |
| SR.CREATININE AFTER | 4.16 | 24 | 3.41 |  |

 **Table-16 Clinical Outcome in Different Groups**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **No.of.patients** | **%** | **Outcome** |
| **Good** | **Bad** | **No follow-up** |
| Group A | 4 | 10 % | 0(0%) | 3(75%) | 1(25%) |
| Group B | 13 | 33 % | 6(46%) | 4(31%) | 3(23%) |
| Group C | 23 | 57% | 8(35%) | 10(43%) | 5(22%) |

**Glossary**

 ODM - Edema

 PRU - Protenuria

 HM - Hematuria

 DRN - Duration

 PRE - Preceding Events

 ANTS - Antecedent Events

 FEV - Fever

 JTP - Joint Pain

 GDT - Gastroduodenitis

 ULC - Ulcer

 BNS - Burns

 SA - Serum Albumin

 MHM - Microscopic Hematuria

 24UP - 24 hours urinary Protein

 UCS - Urinary Casts

 SC - Serum Creatinine

 CMP - Complement

 RED - Reduced

 TG - Total Number of Glomeruli

 NG - Normal Glomeruli

 SC - Sclerosed Glomeruli

%GC - percentage of Glomerular crescents

%CL - Percentage of Cellular crescents

%FR - Percentage of Fibrous crescents

%FC - Percentage of Fibrocellular Crescents

GIF - Glomerular Tuft Inflammation

GTN - Glomerular Tuft Necrosis

BCD - Bowmans Capsule Disruption

PGI - Periglomerular Inflammation

L - Lymphocyte

PL - Polymorphonuclear Leukocytes

GR - Granuloma

MGC - Multinucleated Giant Cells

EP - Epithelioid Cells

HST - Histiocytes

FN - Fibrinoid Necrosis

CBT - Capillary Basement Membrance Thickening

EPR - Endothelial Cell Proliferation

MPR - Mesangial Cell Proliferation

TA - Tubular Atrophy

IFL - Interstitial Inflammation

TRP - Transplant

RST - Response to Therapy

RF - Renal Failure

ESRD - End stage Renal Disease

RCV - Recovered

EXP - Expired

LFUP - Lost Follow Up

FD - Final Diagnosis

AGCGN - Anti – Glomerular Basement Membrane Crescentic Glomerulonephritis

PAPCGN - P-ANCA Positive Pauci-Immune Crescentic Glomerulonephritis

CAPCGN - C-ANCA Positive Pauci-Immune Crescentic Glomerulonephritis

ANPGN - ANCA Negative Pauci-Immune Crescentic Glomerulonephritis

WG - Wegeners Granulomatosis

HSP - Henoch Schonlein Purpura

LPN - Lupus Nephritis

PINCGN - Post Infectious Glomerulonephritis

DPGN - Diffuse Proliferative Glomerulonephritis

CSPGN - Chronic Sclerosing proliferative glomerulonephritis