Original Article

DOI: 10.21276/AABS.1857

Crescentic Glomerulonephritis: Morphological Study and Its Clinicopathological Correiation

Sridevi Bezwada*, Tabassum Anjum, Rama Mani, Ashok Parameshwaran and Mitra Gosh

Dept of Histopathology,Apollo Hospital, Chennai, India

ABSTRACT

Background: Extracapillary Proliferative Glomerulonephritis(Crescentic glomerulonephritis), is usually a clinical emergency, with men being affected twice than women and consists of three main categories based on immunofluoresence and serology. Overall incidence regardless of country of origin is 2 – 5%.

1. Anti – glomerular basement membrane crescentic glomerulonephritis
2. Immune complex mediated crescentic glomerulonephritis
3. Pauci-immune crescentic glomerulonephritis

Methods: Patients diagnosed as Crescentic glomerulonephritis on percutaneous needle biopsies of kidney in Apollo hospital, Chennai from 1996 to 2010, age group from 6 to 74 yrs, with 19 males and 21 females. The mode of presentation, relevant clinical data, laboratory data, histologic features and immunofluorescence patterns are studied and pathological features are correlated with clinical outcome.

Result: Out of 40 cases diagnosed as crescentic glomerulonephritis, 6 were followed up retrospectively and 34 prospectively. 4 were categorized as anti-Glomerular basement membrane , 13 as pauci-immune,, and 23 as immune-complex.

Conclusion: Anti-GBM is the most aggressive form of glomerulonephritis with the highest frequency of renal insufficiency and 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.

Thus this study has clearly shown that even in the absence of electron microscopy a definite aetiological diagnosis can be made with histology and immunoflourescence alone 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.

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.

Materials And Methods

Clinical data: Patients, both inpatients and outpatients diagnosed as extracapillary crescentic glomerulonephritis on kidney biopsies in Apollo hospital, Chennai from 1996 to 2010. The age at presentation varied from 6 yrs to 74 yrs, with 19 males and 21 females. The mode of presentation, relevant clinical 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 were diagnosed in the year 2009-10. 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 Martius scarlet blue (MSB) Staining Methods and studied.

Immunofluorescence: Data was collected from the old reports for the retrospective cases and was done for all the prospective cases, and reported as per standard practice by the technique used 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.

Statistical analysis: Statistical software used:SPSS V.10.0. Statistical tools used: Mc Nemar's Chi square test, ANOVA

Results

This study composed of 40 cases diagnosed as Extra capillary proliferative glomerulonephritis, on percutaneous needle biopsy, 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.

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.

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.

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.

Out of 40, 30 cases (75%) had microscopic hematuria, out of which 50% had bad prognosis.

Out of 40, 37 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 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.

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.

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,as shown in Table2.

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 1had lost to follow up.

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.

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.

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

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.

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 had a "full house" pattern positive with IgG,IgM,IgA,C3c and C1q.

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. This is shown in table-6. Test, ANOVA was used to derive the univariate statistical analysis with respect to clinical outcome.

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

Table 1: 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

Group A- antiGBM crescentic GN, Group B-Pauci-immunecrescentic GN, Group C- Immune complex mediated GN.

Table-2.% 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%)

Table 3: 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 4; 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 5: 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 6: 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%)

Discussion

Fourty cases diagnosed as Extra capillary proliferative Glomerulonephritis (crescentic GN) were observed and the course analysed. 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, as shown in Table1.

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 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.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 , both had skin biopsy proven vasculitis. Both 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-3.2

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.

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 Serum creatinine level at the time of renal biopsy may reflect the extent of active glomerular lesions.28

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.

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 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 crescents. 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 our 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. Both tubular atrophy and interstitial fibrosis are signs of chronicity and were independent predictors of clinical outcome,they 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 ($p<0.031$). 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

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- Albuminuria, Hematuria & Serum creatinine level at biopsy. Patients with 3+ and above albuminuria, had a worse clinical outcome. Albuminuria ($p<0.001$) and microscopic haematuria seems to be a significant prognostic factor.

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: Interstitial inflammation, Vascular changes.

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 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.

Conclusion

Of 40 cases of extra capillary proliferative GN, 21 were females and 19 were males, 23 cases were immune-complex mediated GN, 13 were pauciimmune GN,4 were antiGBM GN with Anti-GBM being 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.

Hence within our hospital set up this study has clearly shown that 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, with sudden onset of acute renal failure.

Acknowledgements

Residents, Registrars, Technical staff, Medical records staff, colleagues, Head of the departments, Chief of lab services

References

1. J.Charles Jennette. Rapidly progressive crescentic glomerulonephritis. Kidney international : 2003; 63:1164-1177.
2. Cees G.M.Kallenberg, Elisabeth Brouwer, Jan J. Weening, et al. Anti-neutrophil cytoplasmic antibodies: current diagnostic and pathophysiological potential. Kidney international ; 1994;46:1-15.
3. Peir-Haur-Hung, Yen-Ling Chiu, Wei-Chou Lin, et al. Poor Renal Outcome of Antineutrophil Cytoplasmic Antibody Negative Pauci-Immune Glomerulonephritis in Taiwanese. J Formos Med Assoc: 2006: 105(10): 804-812.
4. Jeremy Levy and Charles D. Pusey. Crescentic glomerulonephritis; Oxford text book of clinical nephrology : Oxford university press 2005; 3rd Edition, chapter 3.10; vol 1 : 559-577.
5. Herbert A hauer, ingeborg M.Bajema, Hans C. van Houwelingen, et al. Renal histology in ANCA – associated vasculitis: difference between diagnostic and serologic subgroups. Kidney International; 2002;61:80-89.
6. J . Charles Jennette and Volker Nickeleit. Anto-glomerular basemant membrance glomerulonephritis and goodpasture's syndrome; Hepinstall's pathology of the kidney; Lippincott Williams & Wikins publishers, Philadelphia 2007; 6th edition chapter 13; 1:613-641.
7. Malcolm A.Cunningham, Xiao Ru Huang, John P. Dowling, et al. prominence of cell-Mediated immunity effectors on pauci-immune glomerulonephritis J AmSoc Nephrol; 1999:10:499-506.
8. RC Atkins, DJ Nikolic – Paterson, q song, et al. Modulators of crescentic glomerulonephritis JourNal of the amercian socity of nephrology; 1996: 7:2271-2278.
9. Ayman M.karkar, Jennifer Smith, Charles D. Puesy. Prevention and treatment of experimental crescentic glomerulonephritis by blocking tumour necrosis factor –a Nephrol Dial Transplant; 2001; 16:518-524.
10. Jeremy B. Levy, A.Neil Turner, Andrew J.Rees, et al. long-term outcome of Anti- Glomerular basement membrane antibody disese treated with plasma exchange and immunosuppression. Ann Intern Med; 2001;134: 1033-1042.
11. J.Charles Jennette and David B. Thomas. Pauci-Immune and antineutrophil Cytoplasmic autoantibody mediated crescentic glomerulonephritis and vasculitis; Hepinstall's pathology of the Kidney; Lippincott Williams & wlkins publishers, Philadelphria . 2007: 6th edition , chapter 14; vol 1:643-673.
12. Brian h. Ewert J Charles Jennette and Ronald J.Falk. Anti-myeloperxidase antibodies stimulate neutrophils to damage human endothelial cells. Kidney international ; 1992;41:375-383.
13. Ute Eisenberger, Fadi Fakhouri, Philippe, et al. ANCA-negative pauci-immune renal vasculitis: histology and outcome. Nephrol dial transplant ; 2005; 20:1392-1399.
14. Langford, Carol A, Balow, et al. New insights into the immunopathogenesis and treatment of the kidney. Current opinion in nephrology and Hypertension; may 2003; vol 12(3) :267-272.
15. Judy Savige, David Davies, Ronald J Falk er al. Antineutrophil cytoplasmic antibodies and associated diseases: A review of the clinical and laboratory features. Kidney international; 2000; 57:846-862.
16. Ingeborg M.Bajema, E.Christian hagen, Email de heer, et al. colocatization of ANCA- antigens and fibrinoid necrosis in ANCA – associated vasculitis. Kidney international; 2001;60:2025-2030.
17. Abraham Rutgers, Marjan Slot Pieter Van Paassen, et al. Coexistence of anti-glomerular basement membrance antibodies and myeloperxidase- AQNCAs in crescentic glomerulonephritis. American journal of kidney diseases; august 2005; vol 46, no 2:253-262.
18. Xavier Bosch, Eduard Mirapeix, Josep Font, et al. Anti-myeloperoxidase autoantibosies in patients with necrotizing glomerular and alveolar capillaritis. American journal of kidney disease; September 1992; vol 20, issue 3:231-293.
19. Tabor Nadasdy and Fred G. Sliva. Acute postinfectious Glomerulonephritis and Glomerulonephritis caused by persistent bacterial infection; Hepinstall's pathology of the kidney, Lippincott Williams & wilkins publishers, phildelphia. 2007; 6th edition ; chapter 8; vol.1.: 322-396.
20. Vincent Audard, Thomas Hellmark, Khalil El Karoui, et al. A 59-kd renal antigen as a new target for rapidly progressive Glomerulonephritis. Amercian journal of kidney diseases; may 2007; vol 49 no 5: 710-716.
21. David R.W. Jayne, Philip D.Marshall, Sally J.Jones et al. Autoantibodies to GBM and neutrophil cytoplasm in rapidly progressive Glomerulonephritis, Kidney international; 1990; 37,965-970.
22. Casper F.M Franssen, Coen A.Stegeman , Cess G.M.Kallenberg, et al. Antiproteninase 3 and Antimyeloperxidase-associated vasculitis. Kidney international; 2000; 57:2195-2206.
23. Kallenberg, Cees G.M, Cohen Tervant et al. Whats new with anti-neutrophil cytoplasmic antibodies: and therapeutic implications. Current opinion in nephrology and Hypertension; May 1999; vol 8 (3): 307-315.
24. E.christiaan hagen, mohanmed r. daha, jo hermans , et al. diagnosis value of standardized assays for anti-neutrophil cytoplasmic antibodies in idiopathic systemic vasculits. Kidney international; 1998;53: 743-753.

25. Ronald J Falk. ANCA-associated renal disease. Kidney international; 1990; 38: 998-1010.

26. H.G.Sieberth and N.Maurin. The therapy of rapidly progressive Glomerulonephritis. Kin Wochenschr; 1983 ; 61: 1001-1010.

27. Joshus F.Zeidner, Edwin J.Ostrin, Emily Sydnor, et al. the tissue's the issue. The American journal of medicine; may 2010; vol 123, no 5 : 420-422.

28. Penelope P. Kapitsinou. John P.A.Loannidis, John N.Boletis, et al. Clinicopqthologic predicator of death and ESRD in patients with pauci-immune necrotizing Glomerulonephritis. American journal of kidney diseases; January 2003; vol 41,1 : 29-37.

29. Herbert A.Hauer, Ingeborg M.Bajema, Hans C. Van Houwelingen, et al.Determinants of outcome in ANCA-associated Glomerulonephritis: A prospective clinic-histopathological analysis of 96 patients. Kidney international; 2002 ; 63: 1732-1742

30. Clara J Day, Alec J Howie, Peter Nightingle, et al. Predication of ESRD in pauci-immune necrotizing Glomerulonephritis: Quantitative histomorphometric assessment and serum creatinine. American journal of kidney diseases; February 2010; vol 55, no 2:250-258.

***Corresponding author:**
Dr. Sridevi Bezwada, C1 – 302, Belvedere, Akshaya Apts, Nandivaram, Guduvanchery , Kancheepuram -603202 India
Phone: +91 08838213319
Email: sridevibez@gmail.com

Financial or other Competing Interests: None.