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Original Research Article

A study of clinicopathological features and outcomes of crescentic glomerulonephritis

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ABSTRACT

Background: Crescentic Glomerulonephritis (CrGN) is characterized by rapidly progressive renal failure. Most of the literatures have defined >50% crescents in biopsy as CrGN. Only very few studies have included the presence of <50% crescents as CrGN.
Methods: To assess the clinico-pathological features and outcome of CrGN with >10% crescents on renal biopsy and comparing them splitting our diagnosis into Immune Complex Mediated CrGN (ICCGN) and non-immune complex mediated CrGN (NICCGN) groups.
Results: ICCGN was the commonest group. When compared to ICCGN group, NICCGN patients were older, anuric, had more glomerular necrosis and severe IFTA in biopsy at presentation, more became dialysis dependent at index visit discharge. When patients with >50% crescents in both the groups were compared similar results were seen except that infective complications and proliferative lesions were more in ICCGN. When patients with <50% crescents in both the groups were compared similar findings were seen except that no difference was seen in clinical features and dialysis dependency between them.
Conclusions: Oliguria at presentation, Hb <9 g/dl, index visit eGFR<15 ml/min, crescents >60%, moderate to severe IFTA are the independent risk factors for dialysis dependency at index visit discharge.

Keywords: Crescentic glomerulonephritis, Immune complex mediated crescentic glomerulonephritis, Non-immune complex mediated crescentic glomerulonephritis

INTRODUCTION

Crescentic Glomerulonephritis (CrGN) is a renal pathological entity manifested clinically as rapidly progressive glomerulonephritis (RPGN) in majority of the patients.[1] CrGN is defined as any glomerular disease characterized by extensive crescents involving >50% of the glomeruli with a rapid loss of renal function (at least 50% decline in the Glomerular Filtration Rate (GFR) within 3 months).[2] It occurs in a wide variety of primary glomerular and systemic diseases secondary to immune or non-immune etiologies. NICCGN group includes Anti GBM disease, ANCA Associated Vasculitis (AAV), Pauci immune CrGN and dual positive CrGN. Rest of the diagnosis which showed immune complex deposition on immune fluorescence were considered as ICCGN.[3] The percentage of crescents in renal biopsy can vary with the timing of biopsy and the plane of cut during processing of the specimen. So, considering the presence of >50% crescents alone as CrGN may underestimate the disease burden, treatment requirement and hence the outcome.[4] Most of the literatures have defined >50% crescents in biopsy as CrGN. Only very few studies have included the presence of <50% crescents as CrGN.[5] This study aims to assess clinicopathological features and outcome of CrGN with >10% crescents on biopsy splitting our diagnosis into ICCGN and NICCGN groups at a tertiary care center in South India.

METHODS

This is an observational retrospective cohort study done at a tertiary care centre in South India.

This study aims to assess the clinico-pathological features and outcome of CrGN with >10% crescents on renal biopsy and comparing them splitting our diagnosis into ICCGN and NICCGN groups.

Inclusion criteria

- Patients admitted in our hospital from December 2014 to December 2018 with biopsy proven CrGN with >10% crescents.

Exclusion criteria

- Age <18 years
- Renal allograft biopsy with crescents.

Data regarding their clinico-demographic profile, histopathological reports, treatment started at index visit and their state of dialysis dependency at index visit and discharge were retrieved from clinical workstation and patients' records maintained in hospital. Pathological findings are collected from biopsy registry maintained in our department. Follow up data regarding their dialysis requirement and complications if any were collected till March 2019 at various intervals including last visit.

Data was analyzed using SPSS software 16.0. Data was analyzed for whole cohort and compared separately after dividing the diagnosis into ICCGN and NICCGN groups. Subgroup analysis was done for those having >50% crescents and <50% crescents.

RESULTS

A total of 265 patients between December 2014 to December 2018 whose renal biopsy was reported as having >10% crescents were included in this study. The mean age of patients was 40.14±14.34 years with median follow up period of 3 (1-83) months. As show in table 1 the commonest cause of CrGN in this study was Lupus nephritis (26%), then pauci-immune ANCA negative GN (18.9%).

Data was analyzed after splitting our diagnosis into ICCGN and NICCGN.

Table 2 shows females outnumbered the males in both groups (p=0.176). Most common disease among NICCGN group was ANCA negative pauci-immune CrGN (44.2%). In ICCGN group, most common disease was lupus nephritis (45.4%). Mean age of patient in NICCGN group was 43.85±14.3 and in ICCGN group it was 37.3±13.6. Median time of follow up in NICCGN group was 3(1-83) months and in ICCGN group it was 4(1-78) months.

Table 1: Different causes of CrGN in this study.

Types of CrGN		Frequency (n=)	%
1	Anti-GBM disease	16	6.0
2	AAV	41	15.5
3	PAUCI-immune ANCA negative	50	18.9
4	Lupus nephritis	69	26.0
5	IgA nephropathy	31	11.7
6	HSP	6	2.3
7	PIGN	36	17.2
8	MPGN	3	1.1
9	Diabetic sclerosis	2	0.8
10	Dual positive	6	2.3
11	FSGS with crescent	1	0.4
12	C1q nephropathy	4	1.5
	Total	265	100.0

Table 2: Male and female distribution among the groups.

Type of CrGN		Frequency	Percent
NICCGN	Female	59	52.2
	Male	54	47.8
	Total	113	100
ICCGN	Female	92	60.5
	Male	60	39.5
	Total	152	100

Table 3: Various symptoms at the time of admission.

Presenting symptoms	Nonimmune complex	Immune complex	p value
Oedema	66.4%	75%	0.125
Hypertension	54%	52%	0.641
Oliguria	45.1%	38.8%	0.302
Fever	30.1%	32.2%	0.709
Arthralgia	19.5%	21.1%	0.752
Uremic symptoms	35.4%	19.1%	0.003
Skin lesions	12.4%	20.4%	0.086
Gross haematuria	14.2%	8.6%	0.148
Anuria	15%	3.3%	0.001
Haemoptysis	10.6%	0.7%	0.00
Frothy urine	1.8%	0.7%	0.577
Photosensitivity	1.8%	7.9%	0.028

Table 3 illustrated that the Anuria, hemoptysis and uremic symptoms were more common in NICCGN group which is statistically significant (p<0.05). Photosensitivity was more common in ICCGN group (p=0.028). Patient with NICCGN presented with higher creatinine with lower hemoglobin and higher titers of ANCA. Patient with ICCGN presented with higher proteinuria with lesser serum albumin, higher cholesterol, triglycerides, and LDL than non-immune group.

Statistically significant number of patients received Immunosuppressants (IMS) before biopsy in both the groups. 15.9% of NICCGN and 32.3% ICCGN group patients received IMS before biopsy.

Table 4 shows NICCGN group had higher percentage of sclerosed glomeruli, higher number of crescents and higher percentage of crescents in renal biopsy compared to ICCGN, which was statistically significant.

Table 4: Renal biopsy findings of the two groups.

Biopsy findings	NICCGN	ICCGN	p value
Total glomeruli	9.9±5.13	10.48±5.27	0.466
Sclerosed glomeruli	2.54	1.61	0.039
Total no of crescents	5.08±3.53	3.7±2.71	0.001
Crescentic percentage	60.08±29.5	44.01±27.79	0.000

Statistically significant number of patients in NICCGN group had >50% crescents (p=0.001). In NICCGN group 67.3% of renal biopsy showed >50% crescents with predominant fibro-cellular (45.1%) and in ICCGN group out of 44.75% of renal biopsy showed >50% crescents with 45.4% were predominantly fibro-cellular (Table 5).

Table 5: Percentage of crescents among the two groups.

Percentage of crescents		Frequency	Percent
Non-immune complex	<=10	1	0.9
Immune complex	>=50%	76	67.3
	26-49%	17	15
	11-25	19	16.8
	Total	113	100
	<=10	10	6.6
	>=50%	68	44.7
	26-49%	25	16.4
	11-25	49	32.2
	Total	152	100

Table 6 shown patients with NICCGN group presented with significant glomerular necrosis and severe IFTA than ICCGN. Neutrophilic infiltration, mesangial proliferation, endocapillary proliferation were significantly seen in ICCGN than in NICCGN groups.

Table 7 illustrated that therapeutic Plasma Exchange (TPE) was given for renal indications like Anti-GBM disease, ANCA associated CrGN on dialysis, HUS and non-renal indications like pulmonary hemorrhage. Totally six patients died (NICCGN=2, ICCGN=4) at index visit, sepsis being the most common cause of mortality. NICCGN patients were more commonly received TPE, dialysis during index visit and they were more commonly dialysis dependent at discharge than ICCGN group. Significantly a greater number of patients in NICCGN were started on steroid alone. 4.7% patient in Non-dialysis dependent group and 14.7% of patient in dialysis dependent group received plasma exchange which was statistically significant (p=0.006).

Table 6: Other renal biopsy findings in both the groups.

Renal biopsy findings	NICCGN	ICCGN	p value
Mesangial hypercellularity	42.5%	62.5%	0.001
Endocapillary proliferation	76.1%	90.8%	0.001
Glomerular tuft necrosis	31%	14.5%	0.001
Neutrophilic glomerular infiltrates	37.2%	57.2%	0.001
Vascular arterio and arteriolar sclerosis	60.2%	65.2%	0.348
Vascular necrosis	1.8%	2%	0.904
Moderate and Severe IFTA	40.7%	25.7%	0.009

Table 7: Various treatment modalities given.

Treatment modality	NICCGN	ICCGN	p value
Received TPE	16.8%(n=19)	0.7%(n=1)	0.000
Received HD at index visit	54%	22.4%	0.000
Started on steroids alone after biopsy	15.9%	36.2%	0.000
No IMS	12.4%	7.2%	0.156
Dialysis dependent at index visit	42.5%(n=48)	17.8%(n=27)	0.000

During index visit discharge 2/3 of patient in NICCGN were in CKD stage 5/DD, but in ICCGN group only 35.5% were in CKD stage 5/DD which was statistically significant (p=0.000),54 patients in NICCGN and 79 patients in ICCGN group came for at least one revisit follow up at or after 3 months (Table 8).

NICCGN patients were presented with severe renal failure at index visit when compared to ICCGN group. For third month and at one year follow up NICCGN patients had lesser eGFR than in ICCGN. There was no significant difference in eGFR between groups at third year, probably due to lesser number of patients at this period of follow up. During last follow up, statistically significant number of patients in ICCGN group had eGFR >60 ml/min when compared to NICCGN group (Table 9).

Table 8: Index visit CKD stages of patient.

Index visit eGFR		Frequency	Percent
Non-Immune complex	eGFR >60 ml/min	6	5.3
	eGFR <60 ml/min	107	94.7
	Total	113	100
Immune complex	eGFR >60 ml/min	28	18.4
	eGFR <60 ml/min	124	81.6
	Total	152	100

Table 9: Follow up of patients.

Visit	NICCGN	ICCGN	p value
Mean GFR at index GFR (ml/min/1.73m^2)	17.12±21	34.39±32	0.000
Mean GFR at 3rd month GFR (ml/min/1.73m^2)	40.18±27.93	64.62±34.3	0.000
Mean GFR at 1year GFR (ml/min/1.73m^2)	50.19±26.73	70.07±32.63	0.009

Table 10 shows that infectious complications are more common in ICCGN group than in NICCGN group.

Table 10: Infectious complications in both the groups.

Group	Complication	Frequency
Non-Immune Complex	Non-infection/Nil	92.9%
	Infection	7.1%
Immune Complex	Non-infection/Nil	92.1%
	Infection	7.9%

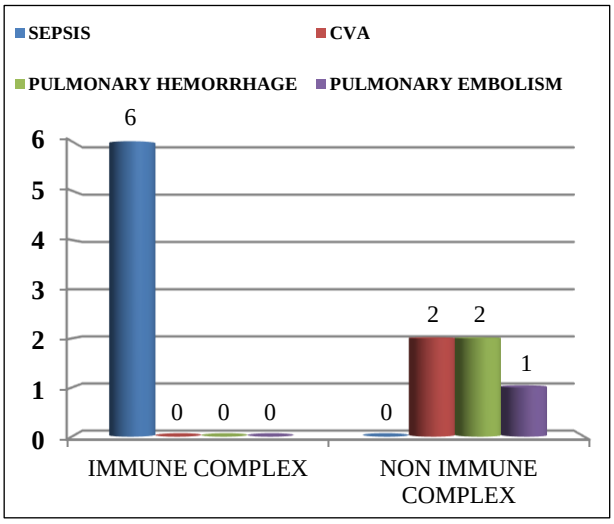

Figure 1: Causes of death were mentioned below.

Total eleven patients died during study period. Sepsis being the most common cause of death in ICCGN group, other causes like CVA, pulmonary haemorrhage and embolism in NICCGN group.

Logistic regression analysis for predictors of dialysis dependency at discharge was evaluated and its results are shown below. The univariant analysis showed that patient with Hb <9 g/dl, eGFR <15 ml/min at presentation, >60% crescents, vascular necrosis, moderate to severe IFTA in renal biopsy were significant risk factors for dialysis dependency at discharge (Table 11).

Table 11: Predictors of dialysis dependency at discharge.

Variable at index visit	p value	Odds ratio
Oliguria	0.005	3.289(1.432-7.555)
Hb <9 g/dl	0.023	2.533(1.139-5.634)
Index visit eGFR <15 ml/min	0.000	28.328(6.286-127.6)
Crescent >60%	0.002	3.479(1.592-7.605)
Vascular necrosis	0.261	4.033(0.354-45.932)
Moderate to severe IFTA	0.021	2.499(1.151-5.426)
IF type	0.186	0.581(0.26-1.298)

DISCUSSION

The commonest cause of CrGN in this study was Lupus nephritis which accounts for 26% of patients followed by pauci-immune ANCA negative GN accounting for 18.9% of patients. It differs from study by Jennette et al, from USA and Gupta et al, from India which showed pauci immune CrGN predominance.[4,6] Men were commonly affected than women in most of the studies but in the study females outnumbered males not only in ICCGN but also in NICCGN and in whole cohort which suggested female predominance was not because of lupus dominance alone.[6,7] Most common IF finding was presence of immune complexes (N=152), followed by pauci immune and then linear deposits disease. Among the ICCGN group, most common disease was lupus nephritis (n=69). Study from china by Tang et al, also showed predominant ICCGN type of CrGN with lupus predominance.[7] Gupta et al, reported no case of Anti GBM disease in their study cohort, but in this study 16 cases of Anti-GBM disease and 6 cases of dual positive disease (Anti-GBM with ANCA positive) were documented which showed this is not an uncommon entity, consistent with study by Sharma et al from SGPGI Lucknow, documented 18 cases of Anti-GBM disease over a period of 2 years.[6]

Mean age of patients in the study was 40.14±14.34 years, which is lesser than study by Jennette et al4 (47±19.3 years). Edema was the commonest presenting symptom in this study. Hypertension was present in 53% of

patients at presentation. Microscopic hematuria (87.4%) and proteinuria (98.1%) were common abnormalities noted. Study by Tang et al, showed 45.3% patient presented with nephrotic syndrome.[7] Nephrotic range of proteinuria was present in 52.5% of patients. ANA was nonspecifically positive in patients (n=16) other than lupus nephritis in the study. Pan et al, reported ANCA positivity in a lupus patient.[8] In this study lupus patient with ANCA positivity (n=4) has been documented.

Predominant type of crescent in this study was fibro cellular crescent (45.3%), could be due to late presentation. Half of the patient had only focal interstitial fibrosis and one fourth had severe IFTA consistent with Saudi study.[9]

Among the total patients of Anti-GBM disease (n=22) only 8 patients received TPE, rest of them did not receive because of late presentation. Patient with vasculitis also received TPE (n=11) for renal indications (n=9) and for diffuse alveolar hemorrhage (n=2). Mean creatinine at presentation was 5.15±4.04 mg% with median eGFR of 27.02(2-127), 48.3% of the study cohort presented with eGFR <15 ml/min which showed severe renal disease at presentation, 28% (n=75) cohort were dialysis dependent at index visit. During follow up at last visit (n=133) when compared to index visit eGFR, 88 (66.16%) patients showed improvement in GFR. Mean proteinuria at presentation was 4.14±3.39 grams per day. In Jennette study mean proteinuria was 2.65 grams which was lesser than this study cohort.[4] Totally proteinuria data was available at last visit in 116 patients. Among these 44.8% of patients had complete remission, 24.1% of patients had partial remission and 28.3% of patients had worsening proteinuria.

Totally 51 events of complications occurred during the course. Most common complication was neutropenia (n=14) followed by infection (n=13). Totally eleven ‘in hospital death' were documented (6 at index visit, 5 during follow up). Most common cause of documented death was sepsis (54.5%).

ICCGN patients were younger than NICCGN group (p=<0.05). Study by Jennette et al, also showed ICCGN were younger than NICCGN.[4] Anuria, hemoptysis and uremic symptoms were more common in NICCGN group than ICCGN group. NICCGN had less extra renal manifestations except hemoptysis (p<0.005). Tang et al, also showed lesser uremia in ICCGN than NICCGN. NICCGN type received empirical steroids before biopsy less likely than ICCGN type.[7]

Even though ANCA was positive in ICCGN group (5.8%) their titers were significantly lower than NICCGN group and most of them had p-ANCA which could be nonspecific. NICCGN group presented with greater degrees of renal failure with significantly lesser eGFR at presentation and a greater number of patients required dialysis before biopsy than ICCGN. Patient with ICCGN presented with higher proteinuria than NICGN (p=0.001). Jennette et al, also noted in their study that ICCGN patient presented with more proteinuria and lesser degrees of renal failure than NICCGN. Hemoglobin was lower in NICCGN group probably because of associated hemoptysis.[4]

In renal biopsy total number of crescents, total percentage of crescents and number of sclerosed glomeruli were significantly more in NICCGN consistent with study by Jennette et al and Shasha chen et al.[4,10] In histology mesangial proliferation, endocapillary proliferation, neutrophilic infiltration, hyaline thrombi were significantly more in ICCGN than NICCGN (p=<0.05). Glomerular necrosis and severe interstitial fibrosis were common in NICCGN type than ICCGN (p<0.05).

At index visit discharge significantly more patients in NICCGN group were dialysis dependent (p=0.00). All except one with Anti-GBM disease were dialysis dependent at discharge. During index visit, follow up at 3 months, one year and at last follow up eGFR were significantly lower in NICCGN than ICCGN. Among the documented in hospital deaths (n=11) six were due to sepsis and were from ICCGN type.

Subgroup analysis

Subgroup with >50% crescents

Among 76 patients in NICCGN and 68 patients in ICCGN (Total=144) had >50% crescents. In both groups’ females outnumbered males. Mean age of patients in NICCGN group was 41.67±14.57 and in ICCGN group was 36.8±13.5 years which didn’t show statistically significant difference (p=0.051). Anuria and hemoptysis were common in NICCGN than ICCGN group with >50% crescents. Patient with NICCGN with >50% crescents presented with higher creatinine with low eGFR, lower hemoglobin than ICCGN group at presentation. Patient with ICCGN with >50% crescents presented with higher proteinuria with lesser serum albumin and higher triglycerides than NICCGN with >50% crescents.

Crescentic percentages were higher and glomerular tuft necrosis was common in NICCGN with >50% crescents than ICCGN >50% crescents. Proliferative lesions and neutrophilic infiltrations were common in ICCGN than NICCGN with >50% crescents. Vascular lesions and severe interstitial fibrosis were not significantly different between two groups. Significantly higher percentage of patient in NICCGN group >50% crescents received plasma exchange and dialysis during index visit. More of the NICCGN group patients were dialysis dependent at discharge during index visit. Steroid alone was started in ICCGN with >50% crescents group in significant number of patient than NICCGN with >50% crescents. Mean GFR at index visit and at third month were lower in NICCGN group compared to ICCGN group with >50% crescents. But this was not different for first year, third year and at last visit. During follow up 26.3% of patients in NICCGN group with >50% crescents and 16% of patients in ICCGN group with >50% crescents attained proteinuric remission, but which was not

statistically significant between groups. During follow up, patients of ICCGN group with >50% crescents had significantly (p=0.044) higher episodes of infection related complications (13.2%) than NICCGN group with >50% crescents (3.9%), although significant number of patients received steroid alone in ICCGN group with >50% crescents.

Subgroup analysis in patient with <50% crescents

Among NICCGN and ICCGN groups with <50% crescents, except age no clinical features at presentation were significantly different between the groups. As in patient with more than 50% crescents, patients with less than 50% crescents also showed significant serological difference in complement levels and autoantibody titers between groups as expected. There was no significant difference in renal biopsy finding between groups except glomerular necrosis which was common in NICCGN group with <50% crescents. As in patient with >50% crescents, NICCGN with <50% crescents also showed lower eGFR than ICCGN at index visit, at third month and at last visit. Dialysis requirement and dialysis dependency at index visit were not different between groups with <50% crescents. As in patient with >50% crescents, ICCGN with <50% crescents also showed higher proteinuria at index visit than NICCGN.

Logistic regression analysis for predictors of dialysis dependency at discharge showed oliguria at presentation, Hb <9 g/dl with hemoptysis, index visit eGFR<15 ml/min, crescents >60%, moderate to severe IFTA in renal biopsy as the independent risk factors for dialysis dependency at index visit discharge.

CONCLUSION

ICCGN was the commonest type with lupus nephritis being the commonest cause of CrGN. At presentation nephrotic range of proteinuria and severe renal failure were seen in half of the patients. Anti-GBM disease patients were mostly dialysis dependent at discharge. Neutropenia was the commonest complication. Sepsis was the commonest cause of mortality.

When compared to ICCGN patients, NICCGN patients were older, anuric and had less extra renal manifestation except hemoptysis, lesser proteinuria, severe renal failure and more glomerular necrosis and severe IFTA in biopsy at presentation. More NICCGN patients became dialysis dependent at index visit.

When patients with >50% crescents in ICCGN and NICCGN groups were compared similar results were seen except that infective complications and proliferative lesions were more in ICCGN. When patients with <50% crescents in ICCGN and NICCGN were compared similar findings were seen except that no difference was seen in clinical features and dialysis dependency between them. Oliguria at presentation, Hb <9 g/dl with hemoptysis, index visit eGFR <15 ml/min, crescents >60%, moderate to severe IFTA in renal biopsy were independent risk factors for dialysis dependency at index visit discharge.

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REFERENCES

1. Nagaraju SP, Laxminarayana SL, Kosuru S, Parthasarathy R, Attur RP, Rangaswamy D, et al. Clinicopathological characteristics and outcomes of diffuse crescentic glomerulonephritis-A single center experience from Southern India. J Clini Diagnostic Res: JCDR. 2017;11(9):OC21-OC24.
2. Hedger N, Stevens J, Drey N, Walker S, Roderick P. Incidence and outcome of pauci-immune rapidly progressive glomerulonephritis in Wessex, UK: a 10-year retrospective study. Nephrol Daily Transplant. 2000 Oct 1;15(10):1593-9.
3. Abraham A, Golay V, Pandey R, Roychowdhary A, Trivedi M. The spectrum of glomerular disease in single centre: A clinicopathological correlation. Indian J Nephrol. 2013;May-June:23(3);168-75.
4. Jennette C. Rapidly progressive glomerulonephritis. Kidney Inter. 2003;63:1164-77.
5. Tumlin JA, Hennigar RA. Clinical presentation, natural history, and treatment of crescentic proliferative IgA nephropathy. Semina Nephrol. 2004 May 1;24(3):256-68.
6. Gupta R, Singh L, Sharma A, Bagga A, Agarwal SK, Dinda AK. Crescentic glomerulonephritis: A clinical and histomorphological analysis of 46 cases. Ind J Pathol Microbiol. 2011;54(3):497-500.
7. Tang Z, Wu Y, Wang Q, Zeng C, Yao X, Hu W, et al. Clinical spectrum of diffuse crescentic glomerulonephritis in Chinese patients. Chinese Medica J. 2003 Nov;116(11):1737-40.
8. Pan HF, Fang XH, Wu GC, Li WX, Zhao XF, Li XP, et al. Anti-neutrophil cytoplasmic antibodies in new-onset systemic lupus erythematosus and lupus nephritis. Inflammation. 2008 Aug;31(4):260-5.
9. Oudah N, Al Duhailib Z, Alsaad K, Qurashi S, Ghamdi G, Flaiw A, et al. Glomerulonephritis with crescents among adult Saudi patients outcome and its predictors. Clini Experimental Med. 2012 Jun 1;12(2):121-5.
10. Chen S, Tang Z, Zhang Y, Liu Z, Zhang H, Hu W, Liu Z. Significance of histological crescent formation in patients with diffuse proliferative lupus nephritis. Am J Nephrol. 2013;38(6):445-52.

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