RESULTS

This study was planned to identify the clinical, laboratory and histopathologic characteristic of severe proliferative lupus nephropathy, which may predict the indices for using intravenous cyclophosphamide(IV-cy), therapy in patients with proliferative lupus nephritis types (class lll and class lV) according to WHO classification and may discriminate those who may and those who may not respond to I.V-cy. therapy over 12 months follow up.

In this study 75 eligible patients were subjected to regular I.V-cy. pulses which were given monthly for at least 12 month with initial dosage 0.5-1.0 gm/m^2 of body surface area over 60 minutes with vigorous hydration prior, during, and after each pulse therapy. The duration of pulses was in average (19.9) months, during which patients recieved in average (11.4) pulses. The discrepancy between number of pulses and the extrapliotic visit schedule were primary due to the fact that we could not give pulses at schedule time because of infection or Leucopenia, during the course of treatment (87%) of patients completed 12 pulses of I.V-cy therapy.

Eleven cases (14.7%) which didn't compliance to that therapy was dropped out, mortality was responsible for 4 cases (5.3 %) and failure to show any response in the early months of therapy was responsible for (9.3%) of cases.

Systematic information concerning clinical and Laboratory data was obtained at the termination of the study after 12 month I.V-cy. therapy.

Characteristics of patients at commencement of the study
Table (1)

- **Demographic and clinical data: (n:75)**

Variable		value
- Sex	[M-F]	12 - 63
- Age	[Mean ± SD / years]	23.6 ± 8.7
- Duration of SLE	[mean ± SD / month]	8.4 ± 11.4
- Skin Lesion	[frequency +ve (%)]	69 (92 %)
- Heart involvement	[frequency +ve (%)]	30 (40 %)
- Lung involvement	[frequency +ve (%)]	16 (21.3 %)
- Pleura involvement	[frequency +ve (%)]	40 (53 %)
- Arthritis	[frequency +ve (%)]	35 (64.7%)
- CNS involvement	[frequency +ve (%)]	21 (28 %)
- Oedema	[frequency +ve (%)]	69 (92 %)
- Hypertension (total)	[frequency +ve (%)]	55 (73.3%)
- mild	[frequency +ve (%)]	10 (13.3 %)
- moderate	[frequency +ve (%)]	31 (41.3 %)
- Sever	[frequency +ve (%)]	14 (18.7 %)

- **Demographic and clinical data at commencement of the study- Table (1):**

- This table shows that male- Female ratio was encountered one- five most of them was middle age ranged from 10 to 40 years, the severity of the disease was evidenced clinically through severe serositis where pleuritis or pleural effusion was in average (53%) of patients, pleuro-peri-carditis and pericardial effusion was encountered in around (40%) of patients, neurological disorder (seizures or psychosis) was encountered in (28%), In parallel, the oedema and hypertension were encountered high in our patients(92%&74% respectively).

Table (2)

• **Laboratory data at commencement of the study (n:75)**

Variable		Value
(1) Hematological disorder:		
• Leukopenia (< 4000 /cmm)	[frequency +ve (%)]	18 (2.8 %)
• Anaemia (gm/dl)	[frequency +ve (%)]	70 (93 %)
• Thrombocytopenia (< 100,000 /cmm)	[frequency +ve (%)]	53 (70 %)
• Lymphopenia (< 1500 / cmm)	[frequency +ve (%)]	45 (60 %)
(2) Immunological disorder:		
• ESR (mm)	[mean ± SD]	106 ± 16
• Anti -ds DNA - Ab	[frequency +ve (%)]	64 (85%)
• Anti -ds DNA - Ab titre	[mean ± SD]	111 ±29
• C_3 mg /dl	[mean ± SD]	49.6 ± 19.5
• C_4 mg /dl	[mean ± SD]	21.2 ±15.3
(3) Renal disorder:		
• Serum Creatinine (mg %)	[mean ± SD]	3.1 ± 1.3
• Creatinine clearance (ml/ minute)	[mean ± SD]	28.3 ± 22.2
• Protein 24h (gm / day)	[mean ± SD]	3.1+2.2
• Hematuria		
1 - 5 cell / cmm	[frequency +ve (%)]	1 (1.3 %)
5 - 15 cell / cmm	[frequency +ve (%)]	7 (9.3 %)
15 - 30 cell / cmm	[frequency +ve (%)]	27 (36 %)
> 30 cell / cmm	[frequency +ve (%)]	40 (53 %)
• Serum albumin (gm)	[mean ± SD]	2.1 ± 0.6

- Laboratory data at commencement of the study-Table (2):-

- Laboratory features indicates at commencement of the study, majority of the patients had an active disease which reflected in anaemia was encountered in (93%), lymphopenia was encountered in (60%), thrombocytopenia was encountered in (70%), ESR was in average more than (100), anti-ds DNA-Ab was encountered in (85%) and the titer also was relatively high more than (100), C_3 and C_4 was also depressed in average (49 mg/dl & 21 mg/dl respectively) . In parallel to that the evidence of active lupus nephritis reflected in serum creatinine was in average > 3 mg%, proteinuria was in average > 3 gm/day and nephrotic range proteinuria was encountered in (50%) of patients, most of patients also have haematuria which was encountered in (98%) of patients.

Table (3)

- **Biopsy data at commencement of the study (n:75)**

Variable	Value
• **WHO Type**	
• Class III	24 (32%)
• Class IV	51 (68 %)
• **Proliferation:**	
• < 25 % of glomeruli affected	18 (24 %)
• 25 - 50 % of glomeruli affected	32(42.7 %)
• > 50 % of glomeruli affected	25 (33.3 %)
• **Cellular Crescent**	
• No cellular crescent	22 (29.3%)
• <25 % of glomeruli affected	30 (40.3%)
• 25 - 50 % of glomeruli affected	17(22.7%)
• > 50 % of glomeruli affected	6 (8%)
• **Fibriniod necrosis or koryorrhexis**	
• No	41 (54.7%)
• < 25 % of glomeruli affected	31 (41.3%)
• 25 - 50 % of glomeruli affected	2 (2.7%)
• > 50 %of glomeruli affected	1 (1.3%)
• **Hyaline deposit (thrombi & wire loop)**	
• No	37 (49.3%)
• <25 % of glomeruli affected	26 (34.7%)
•25 - 50 % of glomeruli affected	12 (16%)
• > 50 % of glomeruli affected	0

Table (3). Cont.

Variable	value
• **Neutrophil infiltration**	
• No	34 (45.3%)
• + 2/ glomerulous	24 (32%)
• + 3 / glomerulous	9 (12%)
• > 4 / glomerulous	8 (10.7%)
• **Interstitial inflammation**	
• No	10 (13.3%)
• < 20 % of interstitial affected	42 (56%)
• 20 -40 % of interstitial affected	19 (25.3%)
• > 40 % of interstitial affected	4 (5.3%)
• **Glomerular sclerosis**	
• No	32 (42.7%)
• < 20 % of glomeruli affected	34 (45.3%)
• 20 - 40 % of glomeruli affected	9 (12%)
• 40 % of glomeruli affected	0
• **Fibrous Crescent**	
• No	54 (72%)
• < 20 % of glomeruli affected	15 (20%)
• 20-40 % of glomeruli affected	6 (8%)
• > 40 % of glomeruli affected	0
• **Interstitial fibrosis**	
• No	16 (21.3%)
• < 20 % of interstitial affected	45 (60%)
• 20 - 40 % of interstitial affected	13 (17.3%)
• > 40 % of interstitial affected	1 (1.3 %)

Table (3). Cont.

Variable	Value
• **Tubular atrophy**	
• no	17 (22.7%)
• < 20 % of cortical affected	49 (65.3%)
• 20 - 40 % of cortical affected	9 (12.0%)
• > 40 % of cortical affected	0
• **Immunofluorescence**	
• IGG deposit	54 (74%)
• IGA deposit	44 (60.3%)
• IGM deposit	62 (84.9)
• C1q deposit	65 (89%)
• C_3 deposit	60 (82.2%)
• C4 deposit	26 (35.6%)
• Fibrin deposit	44 (61.1%)
• **Activity index (Mean ± SD)**	8.2 ± 3.6
•**Chronicity index (Mean ± SD)**	3 ± 1.9

- Biopsy data at commencement of the study Table (3):-

Patients with focal and diffuse proliferative types were included in this study, most of them had marked signs of activity a cellular crescent involve (> 25%) of glomeruli were encountered in (30 %) of patients, and fibriniod necrosis was encountered in different severity was encountered in (45 %) of patients, also glomerulitis or neutrophils infiltration was encountered in (54%) of patients, and interstitial inflammation was prominent in about (30.6%) of patients, on the other hand apparently concomitant signs of chronicity insignificant proportional, patients showing tendency to chronicity, glomerular sclerosis was encountered in (57.3%) of patients, fibrous crescent was observed in about 28% of patients, interstitial fibrosis which considered an important factor of prognosis other than lupus, were observed early in majority of our patients, about (18.6%) with significant interstitial fibrosis. Immunofuorescance study show deposit of immunoglobulins, and component of complement, all of them was in higher than (60%) of patients, Interestingly fibrin deposits were also significant about (61%) which are not common in other renal disease, collectively, our patients, in general had scores of (AI+CI) Slightly higher (AI : 8.2 ± 3.6 & CI: 3 ± 1.9).

Table (4)

- **Complications and causes of death in patients treated with I.V cy. therapy during 12 month fallow up period(n:75 case)**

Side effects	value
- Nausea & Vomiting	12 (16%)
- Leukopenia	15 (20%)
- Pancytopenia	10 (13.3%)
- Septicemia	7 (9.3%)
- Pulmonary infection	13 (17.3%)
- Herpes Zoster infection	15 (20%)
- Amenorrhea	2 (2.6%)
- Alopecia	3 (4%)
- hemorrhagic cystitis	0
- Malignancy	0
- Failure of endoxan therapy	7 (9.3%)
- Causes of death:	
- septicemia	2 (2.6%)
- Encephalitis	1 (1.3%)
- gastro- intestinal bleeding	1 (1.3%)

- **Complications and causes of death in patients treated with I.V-cy. therapy (Table 4):-**

Complications encountered during follow up phase of this study which may inpart reflect complications of immunosuppression or inpart reflect complications of the diseases septicemia was encountered in (9.3%) of cases. Pulmonary infection was recorded in (17.3%) of cases. Herpes Zoster infection was noted in about (20%) of cases, Leukopnia and pancytopenia at a one time point or more during follow up period was encountered in average (20%& 13.3% respectively) of cases. Alopecia occurred infrequently and was observed in (4%) of cases.

Nausea and vomiting were transient problems in about (16%) of patients despite treatment with metoclopramide. Amenorrhea was noted transiently in about (2.6%) of the menstruating female. No patients in our study had clinical hemorrhagic cystitis or evidence of malignancy up to12 month follow up.

Failure to endoxan therapy was encountered in (9.3%) of patients, during the course of the study, 4 patients died, 2 of them (2.6%) died with septicemia, gastro-intestinal bleeding and encephalitis was single mortality each.

Table (5)

- **Comparison of clinical data at commencement of study and after 6 months in patients treated with I.V-cy. therapy (n:75 case)**

Variable	At commencement of the study	After 6 months	P
• Skin lesion	69 (92%)	15 (20%)	< .001
• Heart involvement	30 (40%)	6 (8%)	<.001
• Lung involvement	16 (21.3%)	11 (14.7%)	0.03
• Pleura involvement	40 (53%)	5 (6.7%)	<.001
• Arthritis	35 (46.7%)	17 (22.7%)	0.05
• CNS involvement	21 (28%)	12 (16%)	0.065
• Oedema	69 (92%)	53 (70.7%)	0.006
• Hypertension	55 (73.3%)	30 (40%)	0.036

Table (6)

- **Comparison of clinical data at commencement of the study and at 12 month in patients treated with I.V-cy. therapy (n:75 case)**

Variable	At commencement of the study	After 12 month	P
• Skin lesions	69 (92%)	4 (5.3%)	< .001
• Heart involvement	30 (40%)	2 (2.7%)	<.001
• Lung involvement	16 (21.3%)	5 (6.8%)	<.001
• Pleura involvement	40 (53%)	2 (2.7%)	<.001
• Arthritis	35 (46.7%)	4 (5.3%)	0.001
• CNS involvement	21 (28%)	7 (9.3%)	0.001
• Oedema	69 (92%)	5 (6.8%)	0.001
• Hypertension	55 (73.3%)	15 (20%)	0.001

Table (7)

- **comparison of laboratory data at commencement of the study and after 6 months in patients treated with I.V-cy therapy (n: 75)**

Variable		At commencement of the study	After 6 months	P
•Hematologic disorder				
• WBC (cmm)	[Mean ± SD]	6.1 ± 2.7	7.8 ± 2.9	< .001
• HB (gm/dl)	[Mean ± SD]	7.8 ± 1.8	9.7 ± 1.7	<.001
• Platelet (cmm)	[Mean ± SD]	133.5 ± 74	185 ± 89	<.001
• Lymphocyte (cmm)	[Mean ± SD]	1± 0.4	1.4 ± 0.46	<.001
•Immunological disorder				
• Anti-dsDNA-Ab	[Frequency ve+ %]	64 (85%)	20 (27%)	<.002
• Anti-ds DNA - titer	[Mean ± SD]	106 ± 101	41.9 ± 41.4	<.001
• ESR (mm)	[Mean ± SD]	111 ± 29	42 ± 2.3	<.001
• C_3 (mg / dl)	[Mean ± SD]	49.6 ± 19.5	75.7 ± 32	<.001
• C_4 (mg / dl)	[Mean ± SD]	21 ± 5.4	26 ± 20.7	0.005
• Renal disorder				
• Serum creatinine	[mg %]	3.2 ± 2.2	1.2 ± 0.6	0.016
• Creatinine clearance	[ml/ min]	28.8 ± 22	55 ± 26	<.001
• protein 24h	[gm / day]	3 ± 1.3	1.8 ± 1	<.001
• Hematuria	[cell / cmm]	3.4 ± 0.7	2.3 ± 0.9	<.001
• Serum albumin	[gm/dl]	2.1 ± 0.6	2.8 ± 0.5	<.001

Table (8)

- **Comparison of laboratory data at commencement of the study and after 12 month in patients treated with I.V-cy.therapy (n:75).**

Variable		At commencement of the study	After 12 month	P
• Hematological disorder				
• WBC count (cmm)	[mean ± SD]	6.1 ± 2.7	10± 15	<.001
• HB conc (gm/dl)	[mean ± SD]	7.8 ± 1.8	11.6 ± 1.8	<.001
• Platelet count (cmm)	[mean ± SD]	133.5 ± 74	215 ± 19	<.001
• Lymphocyte (cmm)	[mean ± SD]	1± 0.4	1.7 ± 0.5	<.001
•Immunological disorder				
• ESR (mm)	[mean ± SD]	111 ± 29	41 ± 18	<.001
• Anti-ds DNA-Ab	(frequency ve+ %)	64 (85%)	10 (13.3%)	<.001
• Anti-ds DNA - Ab titer	[mean ± SD]	106 ± 101	15.4 ± 23	<.001
• C_3 (mg / dl)	[mean ± SD]	49.6 ± 19.5	106.9± 122	<.001
• C_4 (mg / dl)	[mean ± SD]	21 ± 15.4	29 ± 22	0.001
• Renal disorder				
• Serum creatinine (mg %)	[mean ± SD]	3.1± 2.2	1.1 ± 0.6	<.001
•Creatinine clearance (ml/ min)	[mean ± SD]	28.8 ± 22	74 ± 32	0.001
• protein 24h (gm / day)	[mean ± SD]	3 ± 1.3	0.9 ± 0.8	<.001
• Hematuria (cell / cmm)	[mean ± SD]	3.4 ± 0.7	1.4 ± 0.7	<.001
• Serum albumin (gm/dl)	[mean ± SD]	2.1 ± 0.6	3.2 ± 0.6	<.001

- **Comparison of clinical and laboratory data at 3 time points (0,6,12 month) in patients treated with I.V-Cy.therapy(n:75)- Table (5,6,7,8)**

When analyzed on univariate basis at 3 time point 0,6,12 month, there is marked statistically significant improvement in several studied variables.

At 6 months follow up period, there is highly significant improvement of all variables (Clinical and Laboratory data) and this remission was sustained without relapsed cases up to 12 month follow period.

Table (9)

- **Comparison of demographic and clinical data between patient with improved serum creatinine and patients without improvement after 6 months (no:75 case)**

Variable	Improved group	Not improved group	P
• **Age**	33.2±9	25.7±6.8	0.25
• **Sex** - female	56 (88.9 %)	7 (11.1%)	0.15
- male	8 (66.7 %)	4 (33.3 %)	
• **Duration of SLE**	8.2 ± 10.8	8.4 ± 10.6	0.8
• **Skin Lesions**			
- positive	12 (80 %)	3 (20 %)	0.5
- negative	52 (86.7 %)	8 (13.3 %)	
• **Heart - involvement**			
- positive	3 (50 %)	3 (50 %)	0.011
- negative	61 (88.4 %)	8 (11.6 %)	
• **Lung - involvement**			
- positive	8 (72.7 %)	3 (27.3 %)	0.2
- negative	56 (87.5 %)	8 (12.5 %)	
•**Pleura - involvement**			
- positive	3 (60 %)	2 (40 %)	0.049
- negative	61 (87.1 %)	9 (12.9 %)	

Table (9). Cont.

Variable	Improved group	Not improved group	P
•Arthritis			
- positive	10 (58.8 %)	7 (41.2 %)	<.001
- negative	54 (93.1 %)	4 (6.9 %)	
•CNS -involvement			
- positive	6 (50 %)	6 (50 %)	< .001
- negative	58 (92 %)	5 (8 %)	
• Oedema			
- positive	42 (79.2 %)	11 (20.8 %)	0.02
- negative	22 (100 %)	.0	
• Hypertension			
- positive	25 (53.3%)	5 (16.7%)	0.049
- negative	39 (86.7%)	6 (13.3%)	

Table (10)

- **Comparison of Laboratory data between patients with improved serum creatinine and patients without improvement after 6 months (no : 75 case)**

Variable		Improved group	Not improved group	P
• Haematologic disorder				
- WBC count (cmm)	[mean ± SD]	7.9 ± 2.7	7.2 ± 3.9	0.2
- HB conc (gm/dl)	[mean ± SD]	9.8 ± 1.7	9.3 ± 1.9	0.02
- Platelet count (cmm)	[mean ± SD]	192 ± 92	138 ±51	0.07
- Lymphocyte count (cmm)	[mean ± SD]	1.34 ± 0.46	1.2 ± 0.5	0.8
• Immunologic disorder				
- Anti -ds DNA-ab				
- positive	[frequency +ve%]	53 (82.8 %)	11 (17.2 %)	0.2
- negative	[frequency +ve%]	11(100%)	0	
- Anti -ds DNA-Ab titer	[mean ± SD]	42.5 ± 43.8	37.8 ± 26.8	0.8
- ESR (mm)	[mean ± SD]	43.1 ± 24	36.9 ± 15.9	0.7
- C3 (mg/dl)	[mean ± SD]	77.9 ±32	61.7 ± 31.8	0.09
- C4 (mg/dl)	[mean ± SD]	25.7 ±20	31.1 ± 25.7	0.5
• Renal disorder				
- S.cr (mg %)	[mean ± SD]	1.1 ± 0.4	2.3 ± 0.7	<.001
- Cr.cl (ml/min)	[mean ± SD]	29.6 ± 25.6	27.4 ± 10.2	< .001
- protein 24 h (gm/day)	[mean ± SD]	1.7 ±1	2.4 ± 1.1	0.04
-Haematuria (cell/cmm)	[mean ± SD]	2.2 ± 0.8	2.9 ± 0.9	0.02
- Serum albumin (gm)	[mean ± SD]	2.8 ± 0.5	2.8 ± 0.4	0.9

Table (11)

•Comparison of biopsy data between the patients with improved serum creatinine and patients without improvement after 6 months (n:75)

Variable	Improved group	Not improved group	P
• WHO type III	23 (95.8 %)	1 (4.2 %)	0.1
I V	42 (82.4 %)	9 (17.6 %)	
• Proliferation			
- No	0	1 (100 %)	0.005
- < 25 % of glomeruli affected	16 (94.1 %)	1 (5.9 %)	
-25- 50 % of glomeruli affected	28 (87.5 %)	4 (12.5 %)	
- > 50 % of glomeruli affected	21 (84 %)	4 (10 %)	
• Cellular crescent			
- No	22 (100 %)	0	0.01
- < 25 % of glomeruli affected	26 (86.7 %)	4 (13.3 %)	
- 25- 50 % of glomeruli affected	11 (64.7 %)	6 (35.3 %)	
- > 50 % of glomeruli affected	6 (100 %)	0	
• Fibriniod necrosis			
- No	37 (90.2 %)	4 (9.8 5)	0.5
- < 25 % of glomeruli affected	25 (80.6 %)	6 (19.4 %)	
- 25- 50 % of glomeruli affected	2 (100 %)	0	
- > 50 % of glomeruli affected	1 (100 %)	0	

Table (11). Cont.

Variable	Improved group	Not improved group	P
• **Hyaline deposit**			
- No	20 (80 %)	5 (20 %)	0.6
- < 25 % of glomeruli affected	24 (92.3 %)	2 (7.7 %)	
- 25- 50 % of glomeruli affected	10 (83.3 %)	2 (16.7 %)	
- > 50 % of glomeruli affected	11 991.7 %)	1 (8.3 %)	
• **Neutrophils infiltration**			
- No	31 (91.2 %)	3 (8.8 %)	0.2
- +2 / glomerulous	18 (75 %)	6 (25 %)	
- + 3 / glomerulous	8 (88.9 %)	1 (11.1 5)	
- + 4 / glomerulous	8 (100 %)	0	
• **Interstitial inflammation**			
- No	10 (100 %)	0	0.4
- < 20 % of interstitum affected	35 (83.3 %)	7 (16.7 %)	
- 20- 40 % of interstitum affected	16 (84.2 %)	3 (15.8 %)	
- > 40 % of interstitum affected	4 (100 %)	0	
• **Glomerular Sclerosis**			
- No	29 (90.6 %)	3 (9.4 %)	0.02
- < 20 % of glomeruli affected	30 (88.2 %)	4 (11.8 %)	
- 20- 40 % of glomeruli affected	6 (66.7 %)	3 (33.3 %)	
- > 40 % of glomeruli affected	0	0	
• **Fibrous crescent**			
- No	47 (87 %)	7 (13 %)	0.017
- < 20 % of glomeruli affected	14 (93.3 %)	1 (6.7 %0	
- 20- 40 % of glomeruli affected	4 9 (66.7 %)	2 (33.3 %)	
- > 40 % of glomeruli affected	0	0	

Table (11). Cont.

Variable	Improved group	Not improved group	P
• **Interstitial fibrosis**			
- No	16 (100 %)	0	0.005
- < 20 % of interstitum affected	36 (80 %)	9 (20 %)	
- 20- 40 % of interstitum affected	13 (100 %)	0	
- > 40 % of interstitum affected	0	1 (100 %)	
• **Tubular atrophy**			
- No	16 (94.1 %)	2 (5.9 %)	0.2
- < 20 % of cortical affected	40 (81.6 %)	8 (18.4 %)	
- 20- 40 % of cortical affected	9 (100 %)	0	
- > 40 % of cortical affected	0	0	
• **Immunofluorescence**			
- IGG deposit			
- positive	47 (87 %)	7 (13 %)	0.7
- negative	17 (89.5 %)	2 (10.5 %)	
- IgA deposit			
- positive	36 (81.8 %)	8 (18.2 %)	0.06
- negative	28 (96.6 %)	1 (3.4 %)	
• IgM deposit			
- positive	54 (87.1 %)	8 (12.9 %)	0.7
- negative	10 (90.9 %)	1(9.1 %)	
• C_1q deposit			
- positive	58 (89.2 %)	7 (10.8 %)	0.2
- negative	6 (75 %)	2 (25 %)	

Table (11). Cont.

Variable	Improved group	Not improved group	P
• C_3 deposit			0.7
- positive	53 (88.3 %)	7 (11.7 %)	
- negative	11 (84.6 %)	2 (15.4 %)	
• C_4 deposit			0.2
- positive	21 (80.8 %)	5 (19.2 %)	
- negative	43 (91.5 %)	4 (8.4 %)	
• Fibrin deposit			0.007
- positive	36 (81.8 %)	8 (18.2 %)	
- negative	27 (96.4 %)	1 (3.6 %)	
• **Activity Index**	8.1 ± 3.8	9 ± 1.9	0.24
• **chronicity Index**	2.9 ± 2	3.6 ± 1.3	0.12

- **Comparison of demographic, clinical, laboratory, biopsy data, between patients with improved serum creatinine (50 % of basal or < 1.4 mg %) and patients without improvement after 6 months in patients treated with I.V-cy. therapy (n:75 case)-table (9,10,11):-**

When change in serum creatinine was considered to classify the patients who had improved and those who didn't improved during 6 months follow up period, it was evident that improvement in serum creatinine was associated with significant improvement of arthritis (P<.001), oedema (p = 0.02) and CNS (P<.001), while other demographic and clinical data didn't contribute this discrimination to identify who had significant improvement at 6 months.

In parallel to that the significant improvement in serum creatinine (1.1±0.4) was also associated with significant improvement of 24-hours protein excretion level (1.7±1) and microscopic Haematuria (2.2±0.8) after 6 months, while other laboratory features didn't contribute this discrimination between who had improved and those who didn't improved after 6 months.

In contrast, patients who had evident of cellular crescent (p = 0.01) proliferation (p= 0.005), fibrous crescent (p= 0.017) and interstitial fibrosis (P = .005)did show significant improvement of serum creatinine, while the improvement of kidney function was not dependant on other features in kidney biopsy at 6 months follow up period.

Interestingly, the improvement was not dependant on activity index or chronicity index scores (P: 0.24 & 0.12 respectively) in renal biopsy at 6 months follow up period.

Table (12)

- **Comparison of demographic and clinical data between patients with improved serum creatinine and patients without improvement after 12 month (n:75 case).**

Variable		Improved group	Not improved group	P
- Age	(mean ± SD / year)	24.2 ± 8.9	19.8 ± 6.2	0.2
- Sex-female	[frequency +ve%]	56 (88,99)	7 (11.7%)	0.46
- male	[frequency +ve%]	8 (66.7%)	4 (33.3%)	
- Duration of SLE	[Mean ± SD /month]...	8.2 ±10.8	8.4 ±11.6	0.8
- Skin lesion				
- positive	[frequency +ve%]	2 (50%)	2 (50%)	0.5
- negative	[frequency +ve%]	61 (83.6%)	8 (16.4%)	
- Heart involvement				
- positive	[frequency +ve%]	1 (50%)	1 (50%)	0.03
- negative	[frequency +ve%]	62 (87.8%)	9 (12.7%)	
- Lung involvement				
-positive	[frequency +ve%]	3 (60%)	2 (40%)	0.2
- negative	[frequency +ve%]	60 (88.2%)	8 (11.8%)	
- pleura involvement				
-positive	[frequency +ve%]	1 (50%)	1 (50%)	0.01
- negative	[frequency +ve%]	62 (87.3%)	9 (12.7%)	
- Arthritis				
- positive	[frequency +ve%]	2 (50%)	2 (50%)	0.04
- negative	[frequency +ve%]	61 (83.6%)	8 (16.4%)	

Table (12): Cont.

Variable		Improved group	Not improved group	P
- CNS involvement				
-positive	[frequency +ve%]	3 (42.9%)	4 (57.1%)	0.002
- negative	[frequency +ve%]	61 (92.4%)	5 (7.6%)	
- Oedema				
-positive	[frequency +ve%]	1 (20%)	4 (80%)	0.001
- negative	[frequency +ve%]	62 (91.2%)	6 (8.8%)	
- Hypertension				
-positive	[frequency +ve%]	11 (73.3%)	4 (26.7%)	0.001
- negative	[frequency +ve%]	54 (91.5%)	5 (8.5%)	

Table (13)

•Comparison of Laboratory data between patients with improved serum creatinine and patients without improvement after 12 month (n:75 case)

Variable		Improved group	Not improved group	P
• **Haematologic disorder**				
- WBC count (cmm)	[mean ± SD]	9.5±15	13.7+16	0.14
- HB conc (gm/dl)	[mean ± SD]	11.9±1.3	9.3+2.4	0.002
- Platelet count (cmm)	[mean ± SD]	413±230	135.5+66	0.001
- Lymphocyte count (cmm)	[mean ± SD]	1.71±0.63	1.5+0.46	0.5
• **Immunological disorder**				
- Anti- ds DNA Ab	[frequency +ve %]	25 (80.6%)	6 (19.4%)	0.2
- positive	[frequency +ve %]	39 (90.7%)	4 (9.3%)	
-negative	[mean ± SD]	13±22.6	25±20	0.06
- Anti- ds DNA. Ab titer	[mean ± SD]	40±16	53±26.8	0.11
- ESR (mm)	[mean ± SD]	113±99	65±31.7	0.002
- C_3 (mg/dl)	[mean ± SD]	29.8±22.5	24.7±19.6	0.5
- C4 (mg/dl)				
• **Renal disorder**	[mean ± SD]	1.1±0.6	5.8±1.9	<.001
- S.cr (mg%)	[mean ± SD]	83.4±24.5	18.3±19.8	<.001
- Cr.Cl (ml/min)	[mean ± SD]	0.8±0.7	2+1.1	<.001
- Protein 24h (gm/day)	[mean ± SD]	1.3±0.6	2.2±0.8	<.001
- Haematuria (call/cmm)	[mean ± SD]	3.3±0.5	2.8±0.7	0.02
- serum albumin (gm/dl)				

Table (14)

•Comparison of biopsy data between patients with improved serum creatinine and patients without improvement after 12 month (n:75 case)

Variable	Improved group	Not improved group	P
• WHO Type III	23(95.3%)	1 (4.2 %)	0.07
Type IV	41(80.4%)	10 (19.6 %)	
• Proliferation			
- <25% of glomeruli affected	15 (88.2%)	3 (11.8%)	.005
- 25-50% of glomeruli affected	31(96.9%)	1 (3.1%)	
- 50 %of glomeruli affected	18(72%)	7 (28 %)	
• Cellular Crescent			
- No	21(95.5%)	1 (4.5%)	0.02
- <25 % of Glomeruli affected	25(83.3%)	5 (16.7%)	
- <25 -50 % of Glomeruli affected	12(70.6%)	5 (29.4 %)	
- >25 % of Glomeruli affected	6(100%)	0	
• Fibriniod necrosis			
- No	38(92.8%)	3 (7.3 %)	
- <25 % of Glomeruli affected	23(74.2%)	8 (25.8 %)	0.15
-25-50% of glomeruli affected	2(100%)	0	
- 50 %of glomeruli affected	1(100%)	0	
• Hyaline deposit			
- No	21(84%)	4 (16%)	
- <25 % of Glomeruli affected	22(84.6%)	4 (15.5%)	0.9
- <25 -50 % of Glomeruli affected	11(91.7%)	1 (8.3%)	
- >50 %of glomeruli affected	10(83.3%)	2 (16.7%)	

Table (14). Cont.

Variable	Improved group	Not improved group	P
• **Neutrophils infiltration**			
- No	30 (88.2 %)	4 (11.8 %)	0.29
- + 2/ glomerulous	21 (87.5 %)	3 (15.2 %)	
- + 3/ glomerulous	8 (88.9 %)	1 (11.1 %)	
- > 4/ glomerulous	5 (62.5 %)	3 (37.5 %)	
• **Interstitial inflammation**			
- No	8 (90 %)	1 (10 %)	0.6
- < 20 % of interstitum affected	34 (81 %)	8 (19 %)	
- 20- 40 % of interstitum affected	17 (89.5 %)	2 (10.5 %)	
- > 40 % of interstitum affected	4 (100 %)	0	
• **Glomerular Sclerosis**			
- No	31 (96.9 %)	1 (3.1 %)	0.005
- < 20 % of glomeruli affected	26 (76.5 %)	8 (23.5 %)	
- 20- 40 % of glomeruli affected	7 (77.8 %)	2 (22.2 %)	
- > 40 % of glomeruli affected	0	0	
• **Fibrous Crescent**			
- No	50 (92.6 %)	4 (7.4 %)	0.017
- < 20 % of glomeruli affected	10 (66.7 %)	5 (33.3 %)	
- 20- 40 % of glomeruli affected	4 (66.7 %)	2 (33.3)	
- > 40 % of glomeruli affected	0	0	
•**Interstitial fibrosis**			
- No	14(87.5%)	2 (12.5 %)	0.009
- <20 % of interstitum affected	38(84.4%)	7 (15.5 %)	
- 20-40% of interstitum affected	12(92.3%)	1 (7.7%)	
- 40 %of interstitum affected	0	1 (100%)	

Table (14). Cont.

Variable	Improved group	Not improved group	P
• **Tubular atrophy**			0.4
- No	16(94.1%)	1(5.9%)	
- <20 % of cortical affected	40(81.6%)	9 (81.4%)	
- <20 -40 % of cortical affected	8(88.9%)	1 (11.1%)	
- >40 %of cortical affected	0	0	
• **Immunofluorescence :**			0.6
-IGG Deposit	46 (85.2%)	6(14.8%)	
Positive	17 (89.5%)	2(10.5%)	
Negative			
-IGA Deposit	37 (84.1%)	7(15.9%)	0.5
Positive	26 (89.7%)	3(10.3%)	
Negative			
-IGM Deposit	52 (83.9%)	10(16.1%)	0.2
Positive	11(100%)	0	
Negative			
-C_1Q Deposit	56 (86.2%)	9(13.8%)	0.9
Positive	7 (87%)	1(12.5%)	
Negative			
-C_3 Deposit	51(85%)	9(15%)	0.5
Positive	12 (92.3%)	1(7.7%	
Negative			

Table (14). Cont.

Variable	Improved group	Not improved group	P
-C_4 Deposit			0.02
Positive	19 (73.1%)	7(26.9%)	
Negative	44 (93.6%)	3(6.4%)	
- Fibrin deposit			0.007
Positive	34 (77.3%)	10 (22.7%)	
Negative	28 (100%)	0	
• **Activity Index**	8 ± 3.7	9.5 ±2.9	0.08
• **chronicity Index**	2.8 ± 1.9	4 ± 1.3	0.12

- **Comparison of demographic , clinical , laboratory , biopsy data, between patients with improved serum creatinine (50% of basal or < 1.4 mg %) and patients without improvement after 12 month in patients treated with I.V-cy. therapy. (n:75 case) - table (12,13,14):-**

At 12 month follow up period (12 month) when the improvement of serum creatinine was considered to classify the patients to identify who had significant improvement at 12 month , it was found that improvement of serum creatinine was associated with significant improvement of arthritis ($p = 0.04$) CNS ($p = 0.002$) and oedema & hypertension ($p < 0.001$) while the improvement in kidney function was not dependant on other demographic or clinical features.

In parallel to that , the improvement in serum creatinine also associated with significant improvement of haemoglobin concentration (11.9 ± 1.3) , platelet count (413 ± 230) , C_3 level (113 ± 99) , protein 24 - hours excretion level (0.8 ± 0.7). Also microscopic Haematuria (1.3 ± 0.6) and improvement of serum albumin (3.3 ± 0.5) ; while the improvement of renal function was not dependant on other laboratory features at 12 month follow up period.

In contract to that the improvement of serum creatinine at 12 month follow up (period) was associated with the degree of proliferation ($p = 0.005$), degree of fibrous crescent ($p = 0.017$) degree of cellular crescent ($p= 0.02$) and degree of interstitial fibrosis ($p= 0.009$) , also , C_4 deposit ($p = 0.02$) and fibrin deposit ($p= 0.007$) in renal biopsy , while improvement in serum creatinine was not dependant on other features in renal biopsy at 12 month follow up period.

Interestingly , improvement of serum creatinine was not dependant on activity or chronicity indices (p: 0.08 & 0.12 respectively) in initial renal biopsy at 12 month follow up period.

Table (15)

•Comparison of activity and chronicity indices between patients with improved serum creatinine and patients without improvement (n:75 case)

Variable	improved group	Not improved group	P
• AI. after 6 months (total)	65 (86.7%)	10 (13.3%)	0.06
-Low ≤7	36 (80%)	9 (20.%)	
-mid / high > 7	29 (96.7%)	1 (3.3%)	
•AI. after 12 month (total)	64 (85.3%)	11 (29.7%)	0.27
- Low ≤7	37 (82.2%)	8 (17.8%)	
- mid / high > 7	27 (90%)	3 (10%)	
• CI. after 6 months (total)	65 (86.7%)	10 (13.3%)	0.3
- low / mid ≤3	47 (88.7%)	6 (11.3%)	
- high > 3	18 (81.8%)	4 (18.2%)	
• CI. after 12 month (total)	64 (86.7%)	11 (14.7%)	0.13
- low / mid ≤3	48 (90.6%)	5 (9.4%)	
- high > 3	16 (72.7%)	6 (27.3%)	

Table (16)

•Comparison of activity and chronicity indices between patients with improved proteinuria and patients without improvement (n:75 case)

Variable	improved group	Not improved group	P
• AI. after 6 months (total)	57 (76%)	18 (24%)	0.052
-Low ≤7	36 (80%)	9 (20.%)	
-mid / high >7	21(70%)	9 (30%)	
•AI. after 12 month (total)	52 (70.3%)	22 (29.7%)	0.65
- Low ≤7	29 (64.4%)	16 (35.6%)	
- mid / high >7	23 (90%)	6 (20.7%)	
• CI. after 6 months (total)	57 (76%)	18 (24%)	0.06
- low / mid ≤3	40 (75.5%)	13 (24.5%)	
- high > 3	17 (77.3%)	5(22.7%)	
• CI. after 12 month (total)	52 (70.3%)	22 (29.7%)	0.14
- low / mid ≤3	39 (75%)	13 (25%)	
- high >3	13 (59%)	9 (41%)	

- **Comparison the degree of pathological activity and chronicity indices between patients with improved serum creatinine (50% of basal or <1.4 mg%) and patients without improvement after 6,12 months in patients treated with I.V-cy. therapy (n:75 case)-Table (15,16)**

when classified according to Austin et al., (1994), the improvement in renal function (serum creatinine value or 24- hour urinary protein excretion rate) was independent on neither AI. nor CI. at any time point (0,6,12) month between improved group and not improved group.

Table (17)

- **Classification results of outcome predicted from logistic regression analysis for all variables (n:75 case)**

Original group	Predicted outcome	
	Improving group	Not improved group
Improved s.cr	64	2
Not improved	3	5

Percent correction (overall) 82.31 %.

Table (18):-

- Logistic regression analysis for outcome predictions in patients treated with I.V-cy. therapy (n:75 case).

Predictor variables	Partial R	Partial R of B	X_2	P	Correlation Coefficient	Odds ratio
• Serum Creatinine	-1.6128	0.5647	8.1565	0.0043	-0.3138	0.1993
• Protein 24 hours	- 1.2124	0.4136	8.5919	0.0034	- 0.3551	0.2975
• Fibrous crescent	-1.2267	0.5447	5.0706	0.0243	-0.2216	0.2933
• Glomerulosclerosis	-1.5375	0.7932	3.7586	0.0052	-0.1834	0.2149

Model X^2 : 18.901

• $P < 0.0001$

- **Logistic regression analysis for outcome predictions in patients treated with I.V-cy. therapy(n:75 case). Table (17,18)**

Initial entery of all variables into the logistic regression equation, it yields 4 important variables that could significantly predicting of those who had and those who didn't have of favorable prognosis according to the pre-sited criteria.

- These 4 variables(serum creatinine value at presentation, 24-hour urinary protein excretion level at presentation, degree of fibrous crescent and degree of glomerulosclerosis in initial renal biopsy) were found could significantly predicting of outcome in the study group by (92.31%, modle x_2 :18.9018, $P < 0.001$) and can be used as indices for using of I.V-cy. therapy in treatment of lupus nephritis patients, These 4 variables have negative partial logistic regression and odds ratio less than one, thus, any decrease in the value of these variables will be associated with good prognosis and vis versa.

Table (19)

- **Logistic regression analysis for outcome predictors interact in patients treated with IV.Cy. therapy (n: 75):-**

Classification models	Prognostic variables			
	Serum creatinine	24-hour protein	Pathology variable	Comparison
1- Laboratory predictors				
Coefficient	- 1.281	- 1.255		
Standradized coefficient	- 0.237	- 0.3192		
P-value	0.018	0.0038		
2- Laboratory and pathological predictors				
Coefficient	- 1.914	- 1.438	- 1.081	
Standradized coefficient	- 0.828	- 0.292	- 0.248	0.0001
P-value	0.008	0.006	0.015	

- **Logistic regression analysis for outcome predictors interact in patients treated with IV.Cy therapy (table 19).**
- For outcome predictions the laboratory predictors (24 hour urinary protein excretion and serum creatinine) were enchanced by addition of renal biopsy predictors (degree of glomerulosclerosis + degree of fibrous crescent) (p= 0.0001).

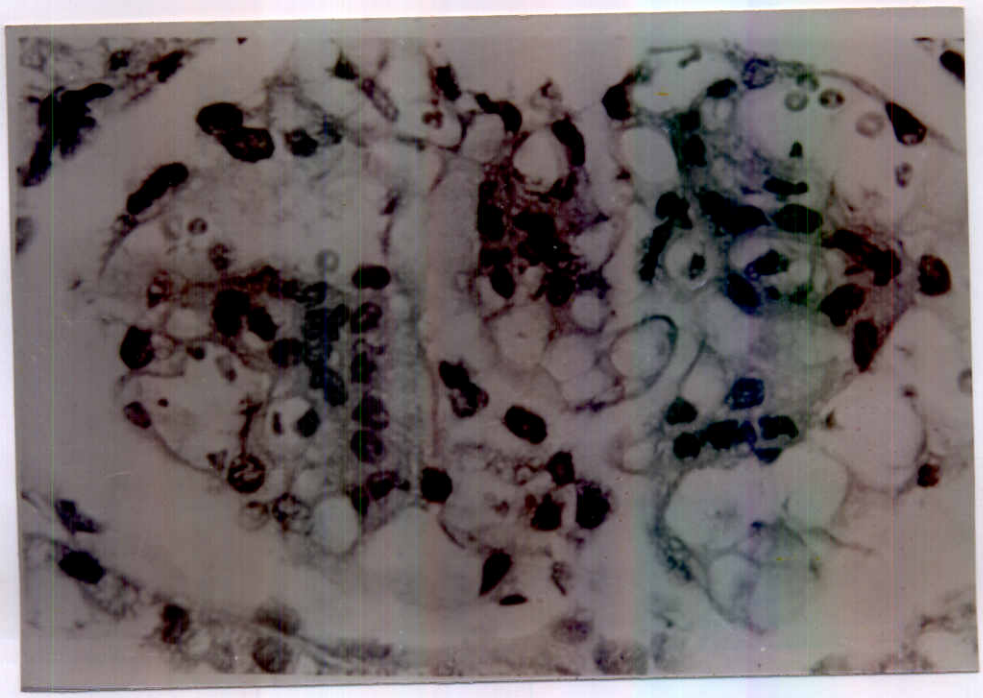

Fig (6): SLE-WHO class II. Mild mesangial hypercellularity (H x & Ex 400).

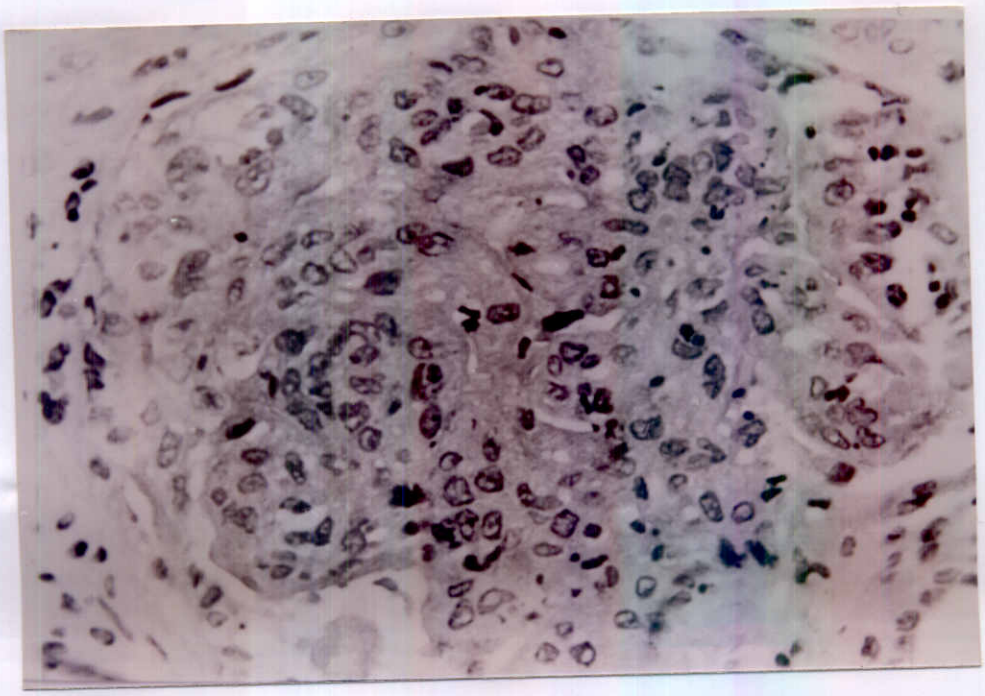

Fig (7): SLE-WHO class III. Showing hypercellularity and fragmented nuclei (necrosis) (Hx XE x 400).

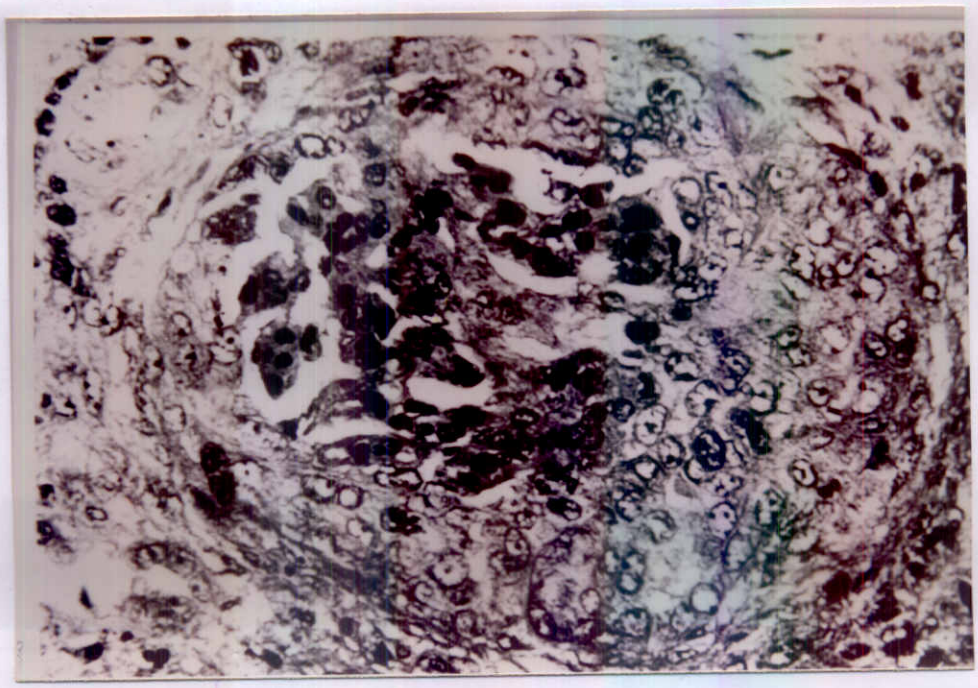

Fig (8): Lupus Nephritis WHO class IV-Glomerulus showing cellular crescent (PAS x 400).

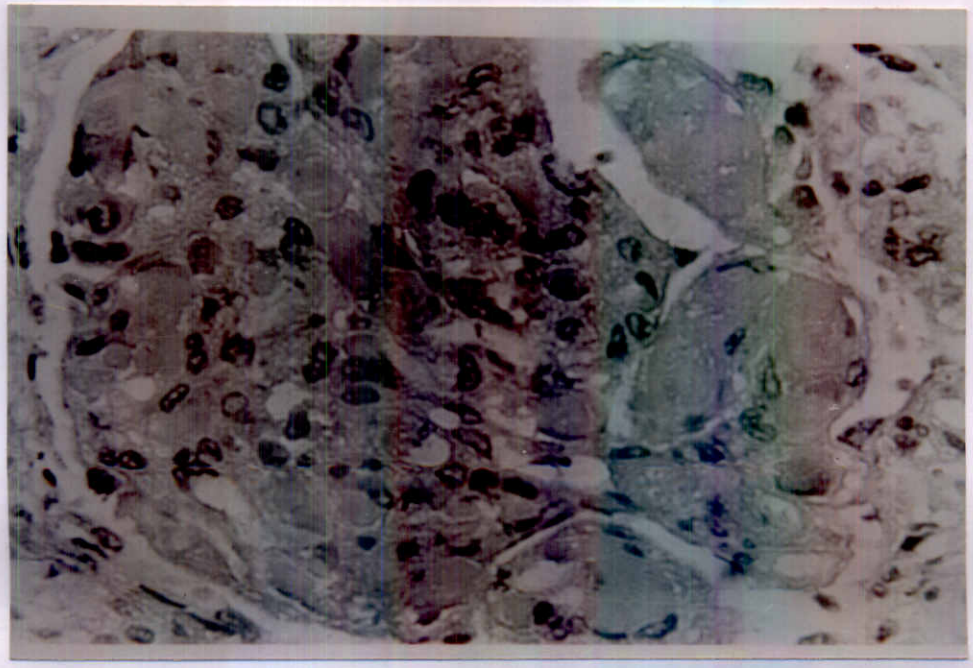

Fig (9): Lupus Nephritis WHO class IV- Hyaline intracapillary thrombi (Hx XE x 400).

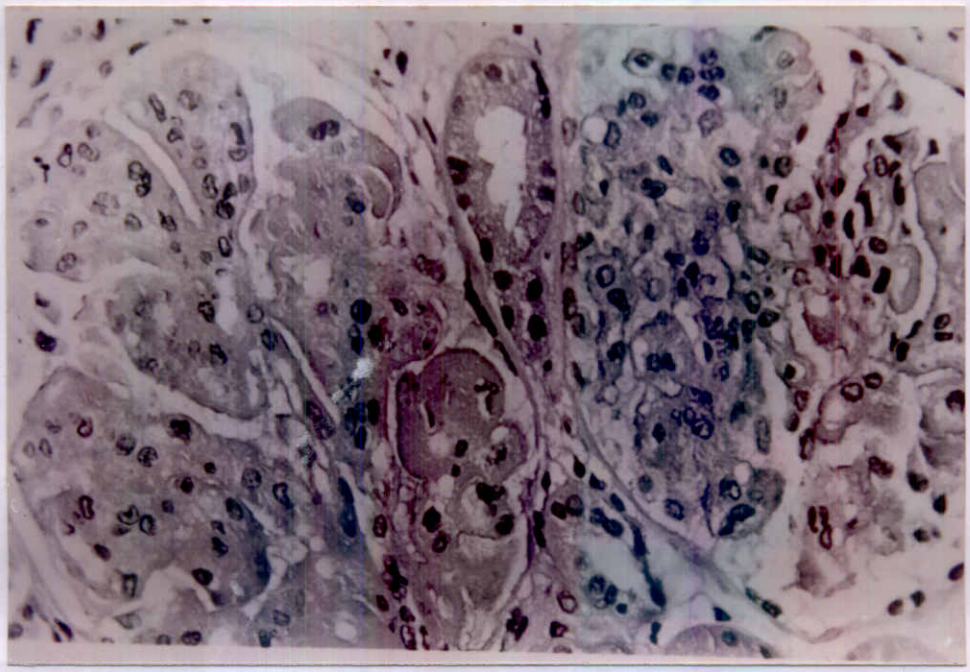

Fig (10): SLE-WHO class IV. Hypercellularity and wire loops (Hx XE x 250).

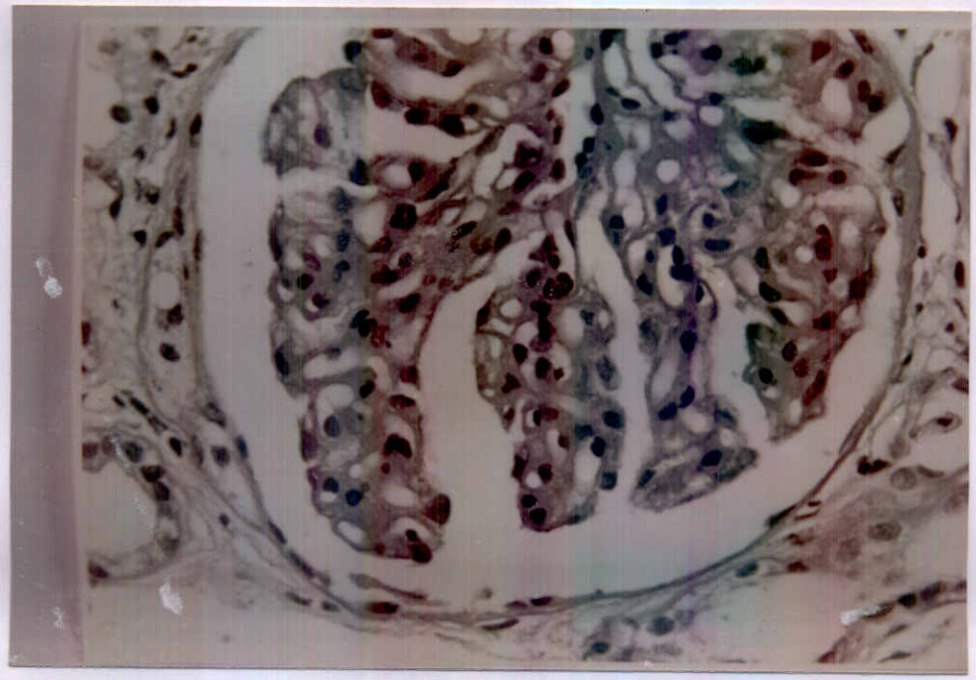

Fig (11): SLE-who class V. Diffuse thickening of glomerular capillaries without associated hypercellularity (DAS x 400).

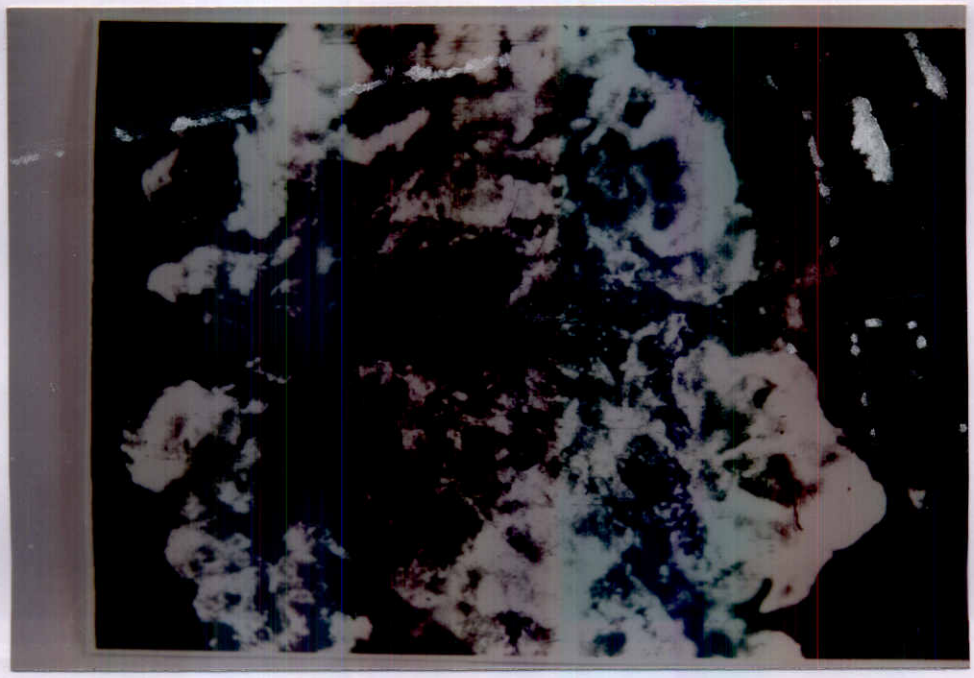

Fig (12): Lupus Nephritis WHO class IV- IgG deposits in capillaries & mesangium (Direct immunofluorescence-antihuman ZgG x 400).

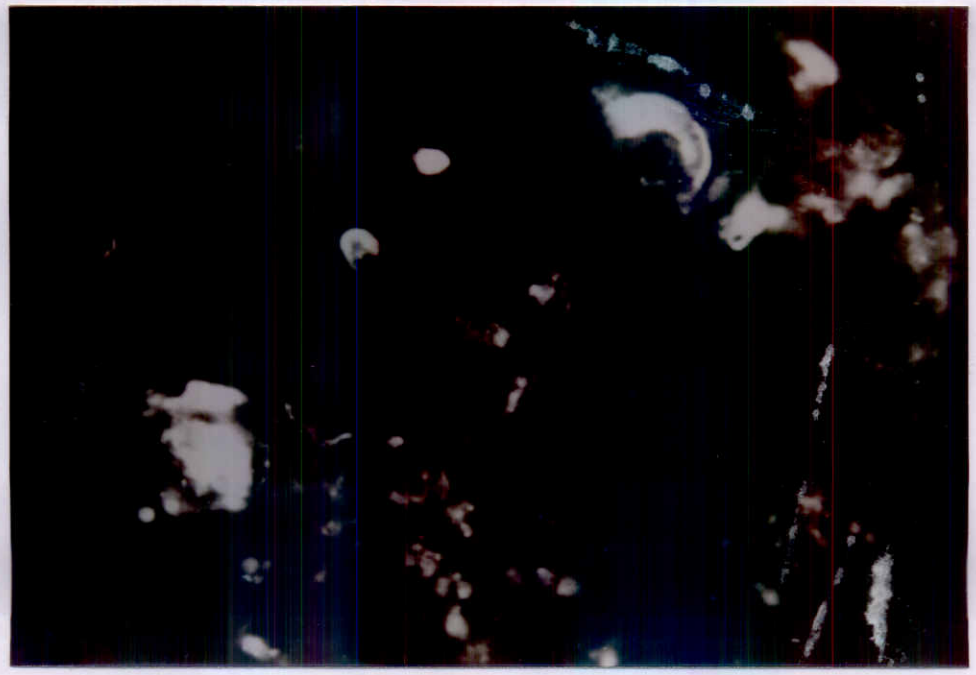

Fig (13): Lupus Nephritis. IgG deposits in the mesangium and in some thicketed capillary loops (Direct immunofluorescence antihuman IgM x 400).

Fig (14): Lupus Nephritis C_3 deposits in peripheral thickened capillaries (Direct immunofluorescence-antihuman C_3 x 400).

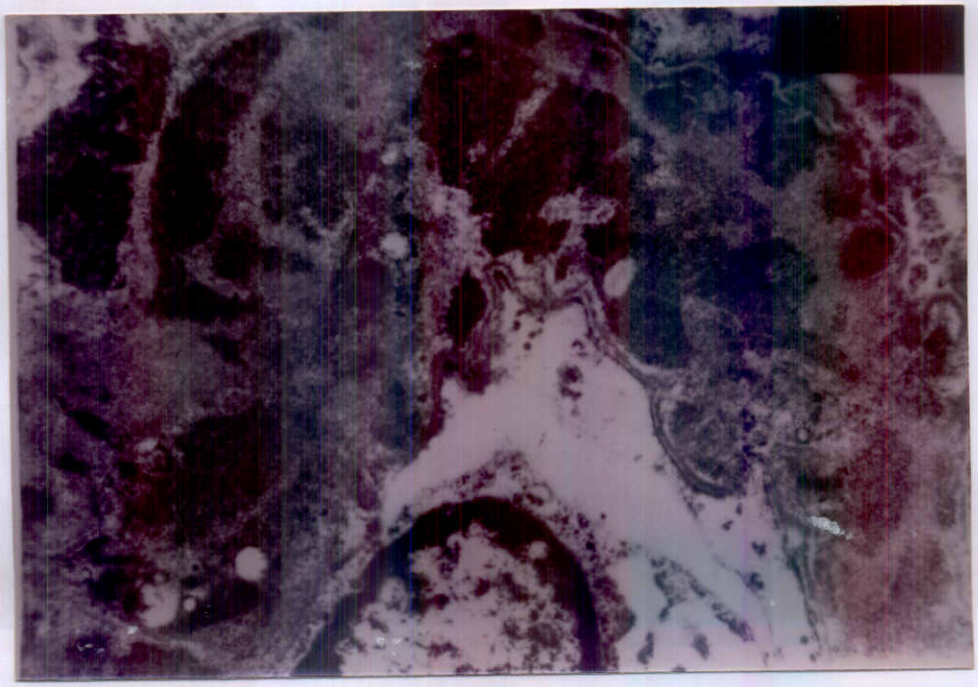

Fig (15): Wire loop lesion examined by E/M. Dense subendo thelial immune complex deposits (Urinyl acetate & lead citrate x 8000).