



Journal Homepage: - [www.journalijar.com](http://www.journalijar.com)  
**INTERNATIONAL JOURNAL OF  
 ADVANCED RESEARCH (IJAR)**

Article DOI: 10.21474/IJAR01/5805  
 DOI URL: <http://dx.doi.org/10.21474/IJAR01/5805>



### RESEARCH ARTICLE

#### IMMUNOSUPPRESSIVE TREATMENT IN LUPUS NEPHRITIS: A COMPARATIVE STUDY COMPARING THE EFFECT OF CYCLOPHOSPHAMIDE OR MYCOPHENOLATE IN NAÏVE OR RELAPSING PATIENTS.

Ragaa Ramadan Mohamed<sup>1</sup>, Khalida El-Refaei El-Refaei<sup>1</sup>, Sahar Mohamed Ismail<sup>1</sup>, Amal Mokhtar<sup>1</sup>, Ahmad El- Seasi<sup>2</sup> and Basma El Tawel<sup>2</sup>.

1. Department of internal medicine, faculty of medicine alazhar university. (girls).
2. Department of nephrology, National institute of urology and nephrology.

#### Manuscript Info

##### Manuscript History

Received: 08 September 2017  
 Final Accepted: 10 October 2017  
 Published: November 2017

##### Key words:-

lupus nephritis ,Cyclophosphamide  
 ,Mycophenolate Mofetile.

#### Abstract

**Background:** Lupus nephritis, one of the most serious manifestations of systemic lupus erythematosus (SLE).

**Objective:** The aim of the study is to compare the outcome of lupus nephritis patients regarding the achievement of complete or partial remission or failure of therapy after six and twelve months of induction therapy using two different immunosuppressive regimens in Egyptian patients.

**Methods:** The study was conducted on eighty patients (40 naive and 40 relapsed) presented with lupus nephritis (Class III, IV and Class V) allocated from the National Institute of Nephrology and Urology (Cairo) and followed up for six and twelve months after induction therapy with two different immunosuppressive regimens (mycophenolate mofetil or cyclophosphamide). Renal response and complications were assessed after six and twelve months.

**Results:** There was significant difference in patients who received either Cyclophosphamide or Mycophenolate mofetil regarding renal response in group B relapsing lupus nephritis patients after 6 month of therapy. There were eight (40%) patients with complete remission, four (20%) patients with partial remission, and only eight(40%) patients that had no remission with cyclophosphamide, whereas no patient who received mycophenolate mofetile entered complete remission, seven(35%) patients with partial remission, and 13(65%) patients that had no remission. while there was insignificant difference in group A naïve lupus nephritis patients.

**Conclusion:** we conclude the usage of cyclophosphamide in induction therapy for treating patients with relapsing lupus nephritis. Due to its superiority over mycophenolate mofetile in short term induction of remission while there was insignificant difference between the two drugs in naïve patients.

Copy Right, IJAR, 2017,. All rights reserved.

#### Introduction:-

Lupus nephritis, one of the most serious manifestations of systemic lupus erythematosus (SLE), usually arises within 5 years of diagnosis (1). It is histologically evident in most patients with SLE, even those without clinical manifestations of

**Corresponding Author:- Ragaa Ramadan Mohamed.**

Address:- Department of internal medicine ,faculty of medicine alazhar university.(girls).

renal disease. The symptoms of lupus nephritis are generally related to hypertension, proteinuria, and renal failure (1). The immunologic mechanisms in SLE include production of autoantibodies directed against nuclear elements. These autoantibodies form pathogenic immune complexes. Deposition of these immune complexes in the kidneys initiate an inflammatory response by activating the complement cascade and recruiting inflammatory cells. (2). Glomerular thrombosis may play a role in pathogenesis of lupus nephritis, and is believed to be the result of antibodies directed against negatively charged phospholipid-protein complexes (2). Renal biopsy should be considered in any patient with SLE who has clinical and laboratory evidence of active nephritis. It may be useful in patients with recurrent episodes of nephritis. Beside revealing the histological pattern and stage of disease (activity and chronicity), renal biopsy is useful in determining prognosis and effect of treatment (3). The principal goal of therapy in lupus nephritis is to normalize renal function as possible. With the advent of more aggressive immunosuppressive and supportive therapy, rates of renal involvement and patient survival are improving. (1). The current treatment of LN includes an induction phase with high-dose steroids associated with pulse cyclophosphamide (CYC) or oral mycophenolate mofetil (MMF) and a maintenance phase with low doses of steroids associated with mycophenolate mofetil or azathioprine (AZA) (4). Immunosuppressive agents, particularly cyclophosphamide, azathioprine, or mycophenolate mofetil, are used if the patient has aggressive proliferative renal lesions, as they improve the renal outcome. They can also be used if the patient has an inadequate response or excessive sensitivity to corticosteroids (5).

**Objective:-**

The aim of the study is to compare the outcome of lupus nephritis patients regarding the achievement of complete or partial remission or failure of therapy after six and twelve months of induction therapy using two different immunosuppressive regimens in Egyptian patients.

**Patients and methods:-**

Eighty patients of whom 40 were naive patients with lupus nephritis (class III, IV, V) were allocated from National institute of nephrology and urology (Cairo) during the period from 2014 to 2016. Of the forty naive patients, 20 of whom were started mycophenolate mofetil plus pulse steroid while the other 20 patients were given pulse cyclophosphamide plus pulse steroid. The same treatment was applied to 40 patients with relapsing lupus nephritis: All patients were followed up for 6 months, then after 12 months

**Studied group were divided according to renal response after six month of induction therapy into:**

1. Complete remission was considered when level of proteinuria was  $\leq 0.33$  g/d and serum creatinine  $\leq 1.4$  mg/dl
2. Partial remission was considered when level was 50% reduction in baseline proteinuria and  $\leq 25\%$  increase in baseline creatinine occurred
3. However failure of therapy was considered when less than 50% reduction in baseline proteinuria and more than 25% increase in baseline creatinine occurred.

**All patients were subjected to the following:-**

Written consent was taken from all patients before inclusion into the study. An approval from the ethical committee of faculty of medicine; AL-Azhar University was also obtained.

Full history and full clinical examination were done for each patient. Laboratory investigations were done including :- Renal function tests (Serum creatinine, BUN, e GFR, urine analysis and 24 hour urinary protein), liver function test, also random blood sugar before and after induction therapy with different immunosuppressive regimens, complete blood count (CBC), determination of erythrocyte sedimentation rate (ESR). Antinuclear antibody (ANA). Anti double strand antibody (anti ds DNA) titer, C3-C4 and CRP were also done.

In relapsed patients history of drug used in previous induction (cyclophosphamide or MMF) and maintenance therapy (MMF or azathioprine) was taken.

Pelvi-abdominal ultrasonography and renal biopsy were done at time of examination.

Patients who had autoimmune diseases and diabetes patients were excluded from this study.

**Statistical analysis:-**

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 22. The qualitative data were presented as number and percentages while quantitative data were presented as mean, standard deviations and ranges when their distribution found parametric. Independent t test was used for comparison between quantitative variables. Paired t test was used for comparison of quantitative variables among two dependent groups. Chi square test was used for comparison of distribution of qualitative variables among different groups. The confidence interval

was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: P > 0.05: Non significant; P ≤ 0.05: Significant and P ≤ 0.01: Highly significant.

### Results:-

There was insignificant difference between the mean serum creatinine levels ( $2.44 \pm 2.38$ ) mg/dl, 24 hours urinary protein ( $3987.50 \pm 1630.47$ ) and eGFR ( $50.98 \pm 38.24$ ) in group A (naïve) patients compared to mean serum creatinine levels ( $2.78 \pm 2.33$ ) mg/dl, 24 hours urinary proteins ( $4247.08 \pm 2048.48$ ) mg/24h and eGFR ( $38.23 \pm 27.34$ ) ml/min of group B (relapsed) patients before two immunosuppressive regimen (table 1). Also There was insignificant decrease in mean serum creatinine level ( $1.288 \pm 0.52$ ) mg/dl and 24 hours urinary protein ( $1262.35 \pm 882.01$ ) in group A (naïve) compared to mean of serum creatinine levels ( $1.403 \pm 0.57$ ) mg/dl, urinary 24 hours urinary protein ( $1464.98 \pm 827.31$ ) mg/24h of group B (relapsed) patients, also there was insignificant increase in mean of eGFR in group ( $61.23 \pm 25.87$ ) ml/min of group A (naïve) compared to eGFR ( $54.33 \pm 25.00$ ) ml/min of group B (relapsing) patients after two immunosuppressive regimen (table 1).

There was a significant decrease in mean serum creatinine levels ( $1.26 \pm 0.52$ ) mg/dl and 24 hours urinary protein ( $1273.73 \pm 936.08$ ) mg/24h after treatment of cyclophosphamide compared to mean serum creatinine levels ( $2.33 \pm 2.28$ ) mg/dl (P value < 0.01) and 24 hours urinary protein ( $3954.50 \pm 1821.98$ ) mg/24h before treatment (P value < 0.01). While there was significant increase in mean eGFR ( $63.35 \pm 28.28$ ) ml/min after treatment with cyclophosphamide compared to mean eGFR ( $52.73 \pm 38.21$ ) ml/min before treatment (p value < 0.01). Table (2). Also there was a significant decrease in mean serum creatinine level ( $1.42 \pm 0.57$ ) mg/dl and 24 hours urinary protein ( $1453.60 \pm 768.51$ ) mg/24h after treatment of Mycophenolate mofetil compared to mean serum creatinine level ( $2.64 \pm 1.86$ ) mg/dl (p value < 0.01) and 24 hours urinary protein ( $4280.08 \pm 1874.91$ ) mg/24 before treatment (p value < 0.01). While there was significant increase in mean of eGFR ( $52.20 \pm 21.35$ ) ml/min after treatment with Mycophenolate mofetil compared to mean of eGFR ( $36.48 \pm 26.41$ ) ml/min before treatment. (p value < 0.01). Table (2)

There was insignificant difference in patients who received either Cyclophosphamide or Mycophenolate mofetil regarding renal response in group (A) naïve lupus nephritis after 6 month of therapy. There were six (30%) patients with complete remission, four (20%) patients with partial remission, and 10 (50%) patients that had no remission with cyclophosphamide, whereas seven (35%) patients who received mycophenolate mofetil entered complete remission, nine (45%) patients with partial remission, and four (20%) patients that had no remission. Table (3).

There was significant difference in patients who received either Cyclophosphamide or Mycophenolate mofetil regarding renal response in group B relapsing lupus nephritis patients after 6 month of therapy. There were eight (40%) patients with complete remission, four (20%) patients with partial remission, and only eight (40%) patients that had no remission with cyclophosphamide, whereas no patient who received mycophenolate mofetil entered complete remission, seven (35%) patients with partial remission, and 13 (65%) patients that had no remission Table (3).

The number of patients using cyclophosphamide 16 patients class III, 10 patient class IV and 14 patients class V, while the number of patient using mycophenolate mofetil, 14 patients class III, 15 patient class IV and 11 patients class V. There was insignificant difference in patients who received Cyclophosphamide or Mycophenolate mofetil regarding renal response in class III lupus nephritis patients. There were seven (43.75%) patients who had complete remission with cyclophosphamide, two (12.5%) patients with partial remission and seven (43.75%) patients with no remission, whereas two (14.28%) patients who received mycophenolate mofetil enter complete remission, three (21.42%) patients with partial remission and nine (64.28%) patients with no remission. Table (4).

There was significant difference in patients who received either Cyclophosphamide or Mycophenolate mofetil regarding renal response in class IV lupus nephritis patients (p value < 0.05). There were four (40%) patients who had complete remission with cyclophosphamide, four (40%) patients with partial remission and two (20%) patients with no remission, whereas no patient who received mycophenolate mofetil enter complete remission, nine (60%) patients with partial remission and six (40%) patients with no remission. Table (5). There was insignificant difference in patients who received either Cyclophosphamide or Mycophenolate mofetil regarding renal response in class V lupus nephritis patients. There were three (21.42%) patients had complete remission with cyclophosphamide, two (14.28%) patients with partial remission and nine (64.28%) patients with no remission, while five (48.46%) patients who received mycophenolate mofetil enter complete remission, four (36.36%) patients with partial remission and two (18.18%) patients with no remission. Table (6).

There was insignificant difference in patients who received either cyclophosphamide and mycophenolate mofetil regarding renal response in naïve(A) patients after 12 month of therapy .there were four (20%) patient had complete remission with cyclophosphamide, seven(35%) patients with partial remission and two (10%) patient with no remission, whereas two (10%) patients who received mycophenolate mofetil enter complete remission and eight (40%) patients with partial remission and five (25%) patients with no remission. Table (7).

There was insignificant difference in patients who received either cyclophosphamide or mycophenolate mofetil regarding renal response in relapsed (group B) lupus nephritis patients after 12 month of therapy .there were three (15%) patients who had complete remission with cyclophosphamide therapy, six(30%) patients partial remission ,seven (35%) patients with no remission, whereas none of the patients who received mycophenolate mofetil enter complete remission ,seven (35%) patients with partial remission and 10(50%) patients with no remission. Table (7).

There was insignificant difference in patients who received either cyclophosphamide or mycophenolate mofetil regarding rate of incidence of complications .seven (17.5%) patients had chest infection with cyclophosphamide versus three (7.5%) patients with mycophenolate mofetil . Neutropenia occurred only with cyclophosphamide in three (7.5%) patients while gastroenteritis occurred only with mycophenolate mofetil in one (2.5%) patient. table (8).

**Table (1):-** serum Creatinine level, eGFR and 24 hours protein in 40 relapsed lupus nephritis patients(group A) and 40 naïve lupus nephritis patients(group B) before and after treatment with two immunosuppressive regimen

Before treatment					After treatment		
Parameters	group	Mean ±SD	T value	P value	Mean ±SD	T value	P value
S.creat (mg)	relapsed	2.78 ± 2.33	0.64	0.52 (NS)	1.403 ± 0.57	0.94	0.35 (NS)
	Naïve	2.44 ± 2.38			1.288 ± 0.52		
e.GFR (ml/min)	relapsed	38.23 ± 27.34	1.72	0.09 (NS)	54.33 ± 25.00	1.21	0.23 (NS)
	naive	50.98 ± 38.24			61.23 ± 25.87		
Urinary protein 24hr	relapsed	4247.08 ± 2048.48	0.63	0.53 (NS)	1464.98 ± 827.31	1.06	0.29 (NS)
	naive	3987.50 ± 1630.47			1262.35 ± 882.01		

\*creat, creatinine \*\*eGFR, estimated glomerular filtration rate.

**Table (2):-** serum creatinine level, eGFR and 24 hours protein in 40 lupus nephritis patients treated with cyclophosphamide and 40 patients treated with mycophenolate mofetile before and after treatment.

Cyclophosphamide treatment				Mycophenolate mofetil treatment			
Parameters	Mean ±SD	T value	P value	Mean ±SD	T value	P value	significance
Screat1(mg/dl)	2.33 ± 2.28	5.42	0.001	2.64 ± 1.86	3.45	0.001	HS
Screat2(mg/dl)	1.26 ± 0.52			1.42 ± 0.57			
e.GFR1(ml/min)	52.73 ± 38.21	3.16	0.001	36.48 ± 26.41	5.87	0.001	HS
e.GFR2(ml/min)	63.35 ± 28.28			52.20 ± 21.35			
Urinaryprote in 24hr1(mg/24hr)	3954.50 ± 1821.98	12.67	0.001	4280.08 ± 1874.91	10.87	0.001	HS
Urinaryprote in 24hr2(mg/24hr)	1273.73 ± 936.08			1453.60 ± 768.51			

Screat, serum creatinine: eGFR, estimated serum creatinine: urinaryprotein 24h,urinary protein in 24h.

**Table (3):-** the renal response of naïve patients group (A) and relapsed patients group (B) who received cyclophosphamide or who received mycophenolate mofetil after 6 month of therapy.

Target	Induction therapy (naïve)		X <sup>2</sup>	P value	Induction therapy (relapsed)		X <sup>2</sup>	P (Sig)
	Group I cyclophosphamide	Group II Mycophenolate mofetile			Group I cyclophosphamide	Group II Mycophenolate mofetile		
Complete remission	6(30%)	7(35%)	4.57	0.10 (NS)	8(40%)	0(0%)	10.01	0.01 (S)
Partial remission	4(20%)	9(45%)			4(20%)	7(35%)		

No remission	10(50%)	4(20%)			8(40%)	13(65%)		
--------------	---------	--------	--	--	--------	---------	--	--

**Table (4):-** the renal response of class III lupus nephritis patients who received cyclophosphamide or who received mycophenolate mofetil.

Renal biopsy Class III		Induction therapy		X <sup>2</sup>	p
		Group(I) Cyclophosphamide	Group (II) Mycophenolate mofetil		
Target	Complete remission	7(43.75%)	2(14.28%)	3.11	0.21 (NS)
	Partial remission	2(12.5%)	3(21.42%)		
	No remission	7(43.75%)	9(64.28%)		

**Table (5):-** The renal response of class IV lupus nephritis patients who received cyclophosphamide or who received mycophenolate mofetil.

Renal biopsy Class IV		Induction therapy		X <sup>2</sup>	p
		Group (I) Cyclophosphamide	Group (II) Mycophenolate mofetil		
Target	Complete remission	4(40%)	0(0%)	7.21	0.03 (S)
	Partial remission	4(40%)	9(60%)		
	No remission	2(20%)	6(40%)		

**Table (6):-** The renal response of class V lupus nephritis patients who received cyclophosphamide or who received mycophenolate mofetil.

Renal biopsy Class V		Induction therapy		X <sup>2</sup>	P
		Group (I) Cyclophosphamide	Group (II) Mycophenolate mofetil		
Target	Complete remission	3(21.42%)	5(45.45%)	5.34	0.07 (NS)
	Partial remission	2(14.28%)	4(36.36%)		
	No remission	9(64.28%)	2(18.18%)		

**Table (7):-** The renal response of naïve(group A) patients and relapsed (group B)patients who received cyclophosphamide or who received mycophenolate mofetil after 12 month of therapy.

Target	Induction therapy(naïve)		X <sup>2</sup>	P Sig)	Induction therapy(relapsed)		X <sup>2</sup>	P Sig)
	Group (I) Cyclophosphamide	Group (II) Mycophenolate mofetil			Group (I) Cyclophosphamide	Group (II) Mycophenolate mofetil		
Complete remission	4(20%)	2(10%)	1.89	0.39 (NS)	3(15%)	0(0%)	3.58	0.17 (NS)
Partial remission	7(35%)	8(40%)			6(30%)	7(35%)		
No remission	2(10%)	5(25%)			7(35%)	10(50%)		

**Table (8):-** The incidence of complications in patients who received cyclophosphamide or who received Mycophenolate mofetil .

Complications	Induction therapy		X <sup>2</sup>	P (Sig.)
	Group (I) Cyclophosphamide	Group (II) Mycophenolate mofetil		
Chest infection	7(17.5%)	3(7.5%)	6.15	0.11 (NS)
Neutropenia	3(7.5%)	0(0%)		
Gastroenteritis	0(0%)	1(2.5%)		
Negative	30(75%)	36(90%)		

**Discussion:-**

In comparing the effect of cyclophosphamide against mycophenolate mofetil in the treatment of patients with lupus nephritis there was no significant difference in the number of patients who showed complete or partial remission ( $p$  value  $> 0.05$ ) table(1). Similar results were reported previously by chan and his colleagues (2000) and by Appel and his colleagues (2014). (7) (6).

Also, Appel and his colleagues (2005) (8) did not notice superiority of mycophenolate mofetil over the intravenous cyclophosphamide as induction therapy in lupus nephritis patients treated for 24 weeks (8)(9).

However, Hu and his colleagues(2002)(10) reported reduction of proteinuria , urinary sediment activity ,serological activity and granular immune deposits in the renal biopsy after mycophenolate mofetil compared to intravenous cyclophosphamide in 46 patients with diffuse proliferative lupus nephritis .Also, in a multicenter prospective trial in 140 patients (the majority with class IV) lupus nephritis patients, randomized to either mycophenolate mofetile or cyclophosphamide over six months ,along with tapering corticosteroid dosage, reported fewer treatment failures and more complete or partial remission with MMF compared to cyclophosphamide.(11)

In a retrospective study by Angela and her colleagues (2014)(12) noticed a better response to mycophenolate mofetile over cyclophosphamide in the treatment of lupus nephritis class III and IV.However that study was conducted on African ,American and Hispanic patients. The same authors reported that mycophenolate mofetile tends to achieve higher remission rates in Black and is at least Caucasians and Asians in the Indian subcontinent with fewer adverse effects (12). Also David and his colleagues(2010)(13) reported that more black and Hispanic patients responded better to mycophenolate mofetile but did not find significant difference in side effects between mycophenolate mofetile and intravenous cyclophosphamide. In the presented study, we did not find significant difference in the incidence or severity of side effects in patients treated with either drugs(table8). Moreover, none of the patients were withdrawn treatment due to sever adverse effects.

The adverse effect to both drugs is summarized in table (8). The insignificant difference in adverse effect in patients treated with either drug was previously reported by Appel and his colleagues (6), Whereas, other authors reported less incidence and milder forms of side effects in patients treated with mycophenolate mofetile compared to those treated with cyclophosphamide.(14), This difference in the different reports could be due to the ethnicity ,age and doses of drugs used. During these years follow up ,there were lower incidence in renal failure or death and in the twice to renal failure with mycophenolate mofetile compared to cyclophosphamide ,but these differences did not reach significant level (14).

In patients with class IV lupus nephritis in the presented study we noticed cyclophosphamide treatment showed better response in inducing complete and partial remission( $p<0.05$ )respectively than mycophenolate mofetil (table5).While in patients with class III lupus nephritis there was insignificant differences between both drugs in inducing complete or partial remission (table 4).

In patients with class V lupus nephritis , there was insignificant difference in the response to either drugs (table 6).However, Roberts and his colleagues (2004) (15) stressed that cyclophosphamide combined with steroids preserved renal function in patients with diffuse proliferative lupus nephritis (DPLN) and by using the smallest effective dosage during steroid duration, could avoid toxicities from the drugs, also Andrwe and his colleagues(2012)(16) stated that mycophenolate mofetil has emerged as a viable alternative to cyclophosphamide for induction therapy of both proliferative and membranous lupus nephritis ,Meantime ,Keith and his colleagues(2009) (17) reported that mycophenolate mofetile was better than cyclophosphamide in children patients with class III nephritis and with less toxicity.

In the presented study we reported that in class IV lupus nephritis could give better result with cyclophosphamide in remission induction but there is no differences in the effect of either cyclophosphamide or mycophenolate mofetil in other classes of lupus nephritis .The adverse dissimilar and with low incidence mild severity ,None of our patients was withdrawn from the study due to adverse effect the differences in the literature, in the effect between these two drugs could be attributed to ethnicity ,geographical areas ,age of patients and differences in doses of the drugs used.

**Conclusion:-**

According to presented study we conclude the usage of cyclophosphamide in induction therapy for treating patients with relapsing lupus nephritis due its superiority over mycophenolate mofetile in short term induction of remission while there was insignificant difference between the two drugs in newly diagnosed patients.

**Recommendations:-**

1. Usage of cyclophosphamide for induction of remission in patients with relapsing lupus nephritis.
2. More trials with more numbers of patients from different races at different ages and followed up for longer periods to ensure the results of our study or opposing it.
3. More trials to be done for evaluating the value of more recent drugs e.g. Rituximab in induction of remission in patients with lupus nephritis with no response to treatment.

**Reference:-**

1. **Dooley MA.(2013):** Clinical and epidemiologic features of lupus nephritis. Wallace DJ, Hahn BH, eds. Dubois' Lupus Erythematosus and Related Syndromes. 8th ed. Philadelphia, PA: Elsevier Saunders;. 438-54.
2. **D'Agati VD and Appel GB. (2007):** Lupus Nephritis: Pathology and Pathogenesis. In: Wallace DJ, Hahn BH, eds. Dubois' Lupus Erythematosus. 7<sup>th</sup> ed. Philadelphia, PA: Lippincott Williams & Wilkins: 1094-111.
3. **Dooley MA. (2007):** Clinical and Laboratory Features of Lupus Nephritis. Dubois' lupus erythematosus. Wallace, D. J., Hahn, B., Dubois, E. L. and Ovid Technologies Inc. Philadelphia, PA, Lippincott Williams & Wilkin. P1112-30.
4. **Ortega LM, Schultz DR, Lenz O. (2010):** Review: Lupus nephritis: pathologic features, epidemiology and a guide to therapeutic decisions. *Lupus* 19(5): 557-574.
5. **Houssiau FA and Ginzler EM. Current treatment of lupus nephritis. *Lupus*. 2008. 17(5):426-30.**
6. **Appel GB., Gabriel Contreras, Mary Anne Dooley,. (2014):** Mycophenolate Mofetil versus Cyclophosphamide for Induction Treatment of Lupus Nephritis. *J Am SocNephrol*. May; 20(5): 1103–1112.
7. **Chan TM, Li FK, Tang CS. (2000):** Efficacy of mycophenolatemofetil in patients with diffuse proliferative lupus nephritis. Hong Kong-Guangzhou Nephrology Study Group. *N Engl J Med*; 343: 1156–1162.
8. **Appel, G. B., Cook, H. T., Hageman, G. (2005).** Membranoproliferative glomerulonephritis type II (dense deposit disease): An update. *Journal of the American Society of Nephrology*, 16(5), 1392-1403.
9. **Contreras G, Mattiazzì A, Guerra G. (2010):** Recurrence of lupus nephritis after kidney transplantation. *J Am SocNephrol*: JASN 21(7): 1200-1207.
10. **Hu W, Liu Z, Chen H. (2002):** Mycophenolatemofetilvs cyclophosphamide therapy for patients with diffuse proliferative lupus nephritis. *Chin Med J (England)*; 115: 705–709.
11. **Ginzler EM, Dooley MA, Aranow C. (2005):** Mycophenolatemofetil or intravenous cyclophosphamide for lupus nephritis. *N Engl J Med*; 353: 2219–2228.
12. **Anglea P, Ravindra R, Michael Sh. (2014):** Influence of Ethnicity on Efficacy of Current Immunosuppressive Protocols in Proliferative Lupus Nephritis; *Rheumatology (Oxford)*; 49(1): 128–140.
13. **David S, Appel GB, Contreras G. (2010):** Influence of race/ethnicity on response to lupus nephritis treatment: the ALMS study. *Rheumatology* 49(1): 128-140.
14. **Ginzler E and Tayar J.(2015):** Lupus. American College of Rheumatology. Available at [http://www.rheumatology.org/practice/clinical/patients/diseases\\_and\\_conditions/lupus.pdf#search=sle](http://www.rheumatology.org/practice/clinical/patients/diseases_and_conditions/lupus.pdf#search=sle). June 2015; Accessed: September 25, 2015.
15. **Robert S Flanc, Matthew A Roberts, Giovanni F. M Strippoli,. (2004):** Treatment of diffuse proliferative lupus nephritis: a meta-analysis of randomized controlled trials. *AJKD*; Volume 43, Issue 2, Pages 197–208
16. **Andrew S. Bombback ,Gerald B. Appel. (2012):** Updates on the Treatment of Lupus Nephritis *JASN*: Volume 43, Issue 2, Pages 197–208.
17. **Kith K. Lau, Bettina H. Ault, Deborah P. Jones. (2009):** Induction Therapy for Pediatric Focal Proliferative Lupus Nephritis: Cyclophosphamide Versus Mycophenolate Mofetil. *Pedhc*; Volume 22, Issue 5, Pages 282–288.