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RESEARCH ARTICLE

# IMPACT OF MYCOPHENOLATEMOFETIL VERSUS IV CYCLOPHOSPHAMIDE AS INDUCTION THERAPY ON PROTEINURIA IN LUPUS NEPHRITIS

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**ABSTRACT**

**Background:** Sever lupus nephritis is a serious complication of systemic lupus erythematosus (SLE) which carries significant morbidity and mortality and requires an aggressive immunosuppressive therapy. **Objective: To** evaluate the effect of induction treatment by Mycophenolatemofetil(MMF) versus IV Cyclophosphamide (IVC) on 24h urinary protein and S.Creatininein lupus nephritis patients.**Patient and Methods:** Retrospective cohort study in single center, Cairo, Egypt, 100 patients had enrolled with proliferative lupus nephritis. Data extraction sheet was designed to collect clinical and laboratory data retrospectively from records of patients whom received induction therapy during the period (October 2010 – November 2014) and follow up data fora period of 3 months after induction. Complete remission was considered when (Proteinuria ≤0.33 g/d and serum creatinine ≤1.4 mg/dl) and partial remission was (50% reduction in baseline proteinuria to ≤1.5 g/d and ≤25% increase in baseline creatinine).**Results: The** study included 81% females and 19% males with mean of age was 30.40±7.45 and range (16 - 46) year, 29% of all patients had class III lupus nephritis and 71% had class IV. 48 patients received MMF and 52 patients received IVC. In MMF group of patients, 12(25%) patients had complete remission, 8(16.6%) had partial remission and 28(58.3%) showed failure of remission versus IVC group, 10(19.2%) had complete remission, 15(28.8%) had partial remission and 27(51.9%) failed to enter remission. There was a non-significant statistical difference ($X^2$=2.17, $P$=0.337) between both groups regarding rate of remission. The mean of S.Creatinine and 24h urinary protein after 3 months of induction treatment in MMF group was (2.89±10.9, 1466.78±902.07) respectively versus (1.49±0.641, 1466.78±902.07) in IVC group of patients, with no significant statistical difference between both groups (P>0.05).**Conclusion:** MMF and IV cyclophosphamide both with corticosteroid showed similar efficacy as short term induction treatment of proliferative lupus nephritis.



## INTRODUCTION

Lupus nephritis (LN), is one of the most serious manifestations of Systemic lupus erythematosus SLE. The LN is more common in certain racial groups,Asian (55%), African (51%), and Hispanic (43%) ancestry compared with Caucasians (14%) *(Ortega et al., 2010)*

Although the survival of patients with lupus nephritis has increased during recent decades,20–30% of LN patients eventually progress to end stage renal disease (ESRD)within 10 years after LN onset *(Moon et al., 2011)*.The 5- and 10-year renal survival rates of LN in the 1990s ranged between 83–93% and 74–84%, respectively *(Anaya et al., 2011)*. The prognosis of lupus nephritis depends on a large number of demographic, racial, genetic, histopathological, immunological, and time-dependent factors*(Mok,2005)*

LN results from a complex interaction between autoantibodies in association with anti-dsDNA, nucleosomes and histones that end up forming kidney immune complexes and permanently activated inflammatory cells that stimulate and induce proliferation in local cells, which, in turn, stimulate complement, cytokines and chemokines *(Salgado1 et al.,2012)*. Proliferative lupus nephritis (class III and IV or mixed III/V and IV/V) and more serious class V (Nephrotic range of proteinuria or deteriorating renal function) disease require more aggressive induction regimens that combine glucocorticoid and a non-glucocorticoid immunosuppressive agent *(Andrew ,2010)*

The standard induction therapy for severe lupus nephritis has been a combination of high-doseglucocorticoid and cyclophosphamide (CYC). Although the optimal route and duration of (CYC) therapyin lupus nephritis remains uncertain, recent evidence supportsthe use of a shorter course and lower dose of CYCto minimize toxicities *(Mok ,2001) (Moc 2002)*.

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Mycophenolatemofetil (MMF) is considered an alternative to intravenous cyclophosphamidefor induction therapy in severe lupus nephritis (ISN classes IIIA, IIIA/C, IVA, and IVA/C). Recent randomized clinical trials showed that mycophenolatemofetil compared favorably with cyclophosphamide for remission induction *(M Chiu Mok,2012)*,MMF alsoreduces the risk of ovarian failure, leucopenia and alopecia compared with IV cyclophosphamide (IVC) (*Webster, 2013*).

We aimed to study the impact of IVC versus MMF as induction treatment on proteinuria and serum creatinine in proliferative lupus nephritis.

## PATIENTS AND METHODS

This a retrospective cohort study was conducted on 100 patients with proliferative lupus nephritis in the National Institute of Nephrology and Urology, Cairo, Egypt. Data extraction sheet was designed to collect data retrospectively from records of patients whom received induction therapy during the period (October2010 –November 2014) and follow up of patients was done for the period 3 months after induction therapy.

Clinical data were collected which included age, sex, BMI, mean arterial blood pressure (MAP) and comorbidities (e.g .hypertension, diabetes mellitus, cardiovascular diseases or cerebrovascular diseases. Results of renal pathology at the time of presentation were recorded. Laboratory data were included serum creatinine , serum albumin and total protein ,complete blood cells counts ,cholesterol, triglycerides, erythrocyte sedimentation rate (ESR) , C-reactive protein ( CRP) titer, immunological markers (ANA, Anti Ds DNA titre ,C3 and C4),HCV Ab ,HBsAg, urine analysis and 24h urinary protein .Estimated glomerular filtration rate ( eGFR) were calculated using MDRD equation:

$GFR = 175 \times SerumCr^{-1.154} * age^{-0.203} * 1.212$ (if patient is black) * 0.742(if female)

All laboratory data were done before induction therapy and after the induction by only 3 months.

Patients were divided randomly into two main groups regarding type of induction treatment of lupus nephritis which included Methylprednisolone 0.5-1g /day for three successive days then decreased to 60 mg/day plus Mycophenolatemofetil (MMF) 2g /day( MMF group) or IVCyclophosphamide (IVC) 0.75 $g/m^2$ per month (IVC group ).

We observed the impact of both regimens on the proteinuria and S.Creatinine after three months of induction treatment, complete remission was considered when (Proteinuria ≤0.33 g/d and serum creatinine ≤1.4 mg/dl) and partial remission was (50% reduction in baseline proteinuria to ≤1.5 g/d and ≤25% increase in baseline creatinine).

Analysis of data was done by IBM computer using SPSS (Statistical Program for Social Science version 18). Quantitative data were presented as range, mean and SD.Qualitative data were presented as number and percent. Chi-square test was used to compare qualitative variables between groups. Student t-test was used to compare quantitative variables between two groups. One way ANOVA (analysis of variance) test was used to compare quantitative variables between more than two groups.*P*values less than 0.05 was considered significant.

## RESULTS

This study was conducted upon100 patients with lupus nephritis (LN), 81% of the patients were females and 19% were males,their age was ranging between (16 - 46) years with meanwas 30.40±7.45 year. 48 patients received induction treatment in the form of pulse Steroids and MMF and 52 patients received Steroids+ IVC.

At baseline all patients enrolled had active proliferative lupus nephritis as baseline renal biopsy showed class III lupus nephritis in 29% of all patients and class IV in 71% of total patients. The mean of serum creatinine at the start of induction therapy in all studied patients was2.848±2.577, the mean of eGFR was 44.16±33.59 and the mean of 24h urinary protein was 4077.50±2028.59 mg/day. The baseline patient's characteristics inMMF group andIVC group was shown in table (1). Baseline laboratory results reported retrospectively for both patients groups was shown in table (2) .As no significant differences between two groups regarding renal biopsy results or the systemic lupus markers. But there was differences regarding mean Age of the patients, mean of BMI and mean GFR retrospectively.

The impact of the induction treatment was reported after 3 months follow up regarding serum creatinine and 24hr urinary protein. In MMF group patients we observed 12(25%) patients with complete remission, 8(16.6%) with partial remission and 28(58.3%) showed failure of remission, figure (1). In IVC group patients we found that 10(19.2%) patients with complete remission,15(28.8%) patients with partial remission and 27(51.9%) patients failed to enter remission., figure(2).There was a non-significant statistical difference ($X^2$=2.17,*P*=0.337) between both groups regarding response to induction after 3 months.

There was no significant difference between both studied groups regarding baseline S.Creatinine or 24h urinary protein.(*P*>0.05).The mean of S.Creatinine and 24h proteinuria after 3 months of induction treatment with MMF were (2.89±10.9, 1466.78±902.07) respectively versus (1.49±0.641,1466.78± 902.07) in patients with IVC, with no significant statistical difference (*P*>0.05).

There was statistically significant difference regarding mean of eGFR post induction between MMF group (64.82±30.26) and IVC group (51.40±23.99) (*P*=0.016).

**Table 1** Demographic and baseline disease characteristics

| | MMF group (n=48) | | IVC group (n=52) | | *t* | *P* |
|---|---|---|---|---|---|---|
| | **Mean** | **±SD** | **Mean** | **±SD** | | |
| Age (year) | 25.79 | 6.64 | 34.65 | 5.36 | -7.37* | <0.01 |
| BMI (Kg/m$^2$) | 24.66 | 2.91 | 27.58 | 4.07 | -4.10* | <0.01 |
| MAP (mmHg) | 95.48 | 12.98 | 99.12 | 13.51 | -1.37 | 0.17 |
| e.GFR(mL/min/1.73 m$^2$) | 53.35 | 38.14 | 35.67 | 26.39 | 2.67* | 0.01 |
| C3 (mg/dL) | 70.80 | 28.86 | 67.34 | 31.21 | 0.58 | 0.57 |
| C4 ( mg/dL) | 7.85 | 3.72 | 8.52 | 3.70 | -0.90 | 0.37 |
| | **n** | **%** | **N** | **%** | **Chi Square test** | ***P* value** |
| Sex | | | | | | |
| Male | 11 | 22.9 | 8 | 84.6 | 0.927 | 0.337 |
| Female | 37 | 77.1 | 44 | 15.4 | | |
| Renal biopsy class | | | | | | |
| Class III | 14 | 29.2% | 15 | 28.8% | 0.00 | 0.97 |
| Class IV | 34 | 70.8% | 37 | 71.2% | | |
| ANA | | | | | | |
| Positive | 47 | 97.9% | 50 | 96.2% | 0.27$^+$ | 1.00 |
| Negative | 1 | 2.1% | 2 | 3.8% | | |
| Anti Ds DNA | | | | | | |
| Positive | 37 | 77.1% | 43 | 82.7% | 0.49 | 0.48 |
| Negative | 11 | 22.9% | 9 | 17.3% | | |
| HCV Negative | 47 | 97.9% | 49 | 94.2% | 0.88$^+$ | 0.62 |
| HCV Positive | 1 | 2.1% | 3 | 5.8% | | |

** Significant P value<0.05*
*$^+$ Done by Fisher exact test.*

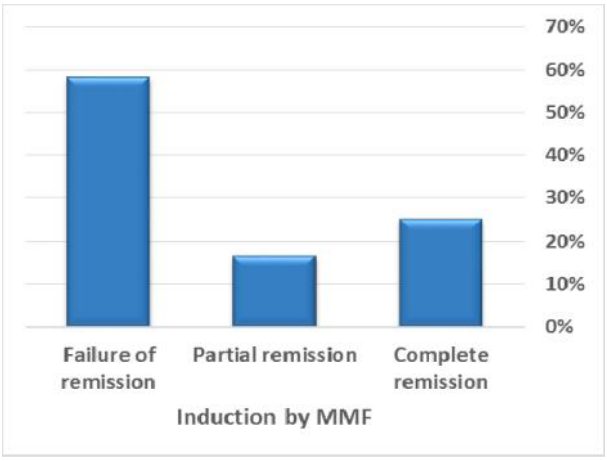


**Figure 1**Response to the induction treatment in MMF group

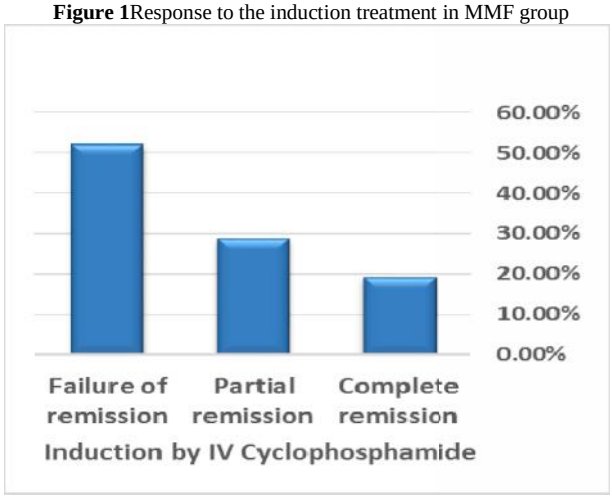


**Figure 2**Response to induction treatment in IVC group

As regards patients with complete remission , we reported no statistically significant differences between patients received MMF and patients with similar response to IVC as regards eGFR, 24h urinary protein before the induction therapy (P>0.05) but there was significant difference regarding BMI and ESR as shown in table(3).

**Table 3** Comparison between patients with complete remission by MMF group versus IVC group regarding baseline characteristics

| **Studied parameters** | **MMF (Complete remission) (n=12)** | | **IVC (Complete remission) (n=10)** | | **t** | ***P* value** |
|---|---|---|---|---|---|---|
| | **Mean** | **SD±** | **mean** | **±SD** | | |
| Age (year) | 29.00 | 8.53 | 34.30 | 5.19 | -1.715 | .102 |
| BMI (Kg/m2) | 23.37 | 2.10 | 25.94 | 3.20 | -2.268* | .035 |
| MAP (mmHg) | 95.67 | 13.58 | 95.00 | 11.36 | .123 | .903 |
| S.Creatinine (mg/dl) | 3.67 | 3.85 | 2.03 | .88 | 1.430 | .178 |
| eGFR(mL/min/1.73 m$^2$) | 46.58 | 29.20 | 39.00 | 20.97 | .686 | .501 |
| S.Albumin (g/dl) | 2.21 | .43 | 2.10 | .54 | .525 | .606 |
| Total proteins (g/dl) | 5.87 | .56 | 5.79 | .49 | .337 | .740 |
| 24 hr. protein in urine (mg/day) | 2688.33 | 1043.56 | 3150.00 | 1048.83 | -1.031 | .315 |
| CRP titer (mg/L) | 6.00 | 14.91 | 2.4000 | 7.58947 | .577 | .435 |
| ESR ( mm/h) | 85.92 | 10.15 | 100.90 | 17.90 | -2.46* | .023 |

**Significant P value<0.05*

**Table 4** Comparison between patients with partial remission by MMF versus partial remission subgroup by IVC induction treatment regarding baseline characteristics

| **Studied parameters** | **MMF (Partial remission) (n=8)** | | **IVC (Partial remission) ( n=15)** | | **t** | ***P* value** |
|---|---|---|---|---|---|---|
| | Mean | SD± | Mean | SD± | | |
| Age (year) | 22.88 | 4.12 | 33.40 | 6.00 | -4.41* | <.01 |
| BMI (Kg/m2) | 23.36 | 1.53 | 25.45 | 2.58 | -2.09* | .049 |
| MAP (mmHg) | 90.00 | 6.26 | 102.80 | 13.51 | -3.09* | .005 |
| S.Creatinine (mg/dl) | 2.35 | 1.76 | 2.55 | 1.79 | -.26 | .797 |
| eGFR(mL/min/1.73m$^2$) | 46.13 | 32.07 | 39.13 | 27.23 | .52 | .587 |
| S.Albumin (g/dl) | 1.91 | .48 | 2.87 | 4.26 | -.62 | .539 |
| Total proteins (g/dl) | 5.96 | .60 | 5.83 | .92 | .374 | .712 |
| 24 hr. protein in urine (mg/day) | 3071.25 | 728.02 | 4074.67 | 2124.11 | -1.28 | .213 |
| CRP titer (mg/L) | 0.00 | 0.00 | 13.60 | 11.80 | 1.08- | .067 |
| ESR( mm/h) | 90.50 | 29.07 | 88.33 | 17.52 | .224 | .825 |

**Significant P value<0.05*

We studied patients with partial remissionas shown in (Table 4) and we found no significant difference between partial remission subgroups with MMF and IVC induction asregards baseline characteristics and laboratories except regarding age, BMI and mean arterial BP was significantly higher in IVC subgroup with partial remission.

Patients failed to achieved remission in IVC group were with significantly higher baseline age, BMI and lower baseline eGFR than patient failed to remit after induction with MMF (P <0.05) (Table 5).

**Table 5** Baseline characteristics of patients with failure of remission by MMF or IVC

| Studied parameters | MMF (Failure of remission) (n=28) | | IVC (Failure of remission) ( n=27) | | t | *P* value |
|---|---|---|---|---|---|---|
| | Mean | SD± | Mean | SD± | | |
| Age (year) | 25.25 | 5.94 | 35.48 | 5.10 | -6.84* | < .01 |
| BMI (Kg/m2) | 25.58 | 3.19 | 29.37 | 4.28 | -3.72* | < .01 |
| MAP (mmHg) | 96.96 | 14.02 | 98.59 | 14.16 | -.428 | .670 |
| S.Creatinine (mg/dl) | 2.81 | 3.22 | 3.13 | 2.16 | -.430 | .669 |
| eGFR(mL/min/1.73 $m^2$) | 58.32 | 43.09 | 32.52 | 28.17 | 2.63* | .011 |
| S.Albumin (g/dl) | 1.58 | .85 | 1.63 | .76 | -.267 | .790 |
| Total proteins (g/dl) | 8.20 | 15.48 | 5.30 | 1.07 | .969 | .337 |
| 24 hr. protein in urine (mg/day) | 4954.81 | 2144.13 | 4460.85 | 2239.47 | .828 | .412 |
| CRP titer (mg/L) | 2.40 | 7.58 | 7.29 | 14.52 | 4.51 | .683 |
| ESR( mm/h) | 94.64 | 10.40 | 91.30 | 17.31 | .873 | .387 |

**Significant P value<0.05*

We compare patients with different response to induction therapy in each group regarding baseline disease characteristics to study factors may affect impact of induction treatment on proteinuria and S. Creatinine in lupus nephritis. In MMF group ,we observed retrospectively that patients with failure of remission had significantly higher BMI ,baseline 24h urinary proteins and lower C3and serum albumin than patients with complete remission by LSD post hoc test ($P$<0.05).But no significant difference between subgroups regarding sex ($X^2$=1.91, $P$=0.18) orclass of lupus nephritis ($X^2$=2.67,$P$=0.32) *(P value>0.05* ),and no significant difference regarding baseline creatinine or eGFR*(P>0.05)*(Table 6).

Comparison between patients with different response achieved byIVC induction revealed that no statistically significant differences between the patients subgroups regarding sex($X^2$= 2.068,$P$=0.356) or class of lupus nephritis($X^2$=4.001,$P$= 0.135) *(P value>0.05)*,and no significant difference regarding other baseline studied parameters except as regards BMI ,as shown in (Table 7).

We also reported statistically significant negative correlation between 24h urinary protein and C3($r$=-0.318,$P$=0.001),C4($r$=-0.222,$P$=0.027),serum albumin ($r$=-0.313,$P$=0.002) and serum creatinine($r$= -0.425,$P$=0.000) ,and statistically significant positive correlation with eGFR($r$=0.468,$P$=0.000),serum cholesterol($r$=0.719,$P$=0.000) ,TG($r$=0.628,$P$=0.000) and ESR($r$=0.203,$P$=0.044).

**Table 6**Comparison between studied patients with different response to MMF regarding baseline characteristics

| Studied parameters | Complete remission (n=12 ) | | Partial remission (n=8) | | Failure of remission (n=28) | | F | *P* value |
|---|---|---|---|---|---|---|---|---|
| | Mean | SD± | Mean | SD± | Mean | ±SD | | |
| **Age** (year) | 29.00 | 8.53 | 22.88 | 4.12 | 25.25 | 5.94 | 2.404 | 0.102 |
| **BMI** (Kg/m2) | 23.37 | 2.10 | 23.36 | 1.53 | 25.58 | 3.19 | 3.803* | 0.030 |
| **MAP** (mmHg) | 95.67 | 13.58 | 90.00 | 6.26 | 96.96 | 14.02 | 0.894 | 0.416 |
| **S.Creatinine**(mg/dl) | 3.67 | 3.85 | 2.35 | 1.76 | 2.81 | 3.22 | 0.436 | 0.632 |
| **eGFR** (mL/min/1.73 m2 ) | 46.58 | 29.20 | 46.12 | 32.07 | 58.32 | 43.09 | .559 | .575 |
| **S.Albumin**(g/dl) | 3.63 | 0.19 | 1.91 | .48 | 1.58 | .85 | 3.395* | 0.042 |
| **Total proteins** (g/dl) | 5.87 | .56 | 5.96 | .60 | 8.20 | 15.48 | 0.213 | 0.809 |
| **24 hr. protein in urine** (mg/day) | 2688.33 | 1043.56 | 3071.25 | 728.02 | 4954.81 | 2144.13 | 8.463* | 0.01 |
| **CRP titer** (mg/L) | 6.00 | 14.91 | 0.00 | 0.00 | 9.42 | 21.99 | .826 | .444 |
| **ESR**( mm/h) | 85.91 | 10.14 | 90.50 | 29.07 | 94.64 | 10.40 | 1.479 | .239 |
| **C3** (mg/dL) | 71.00 | 23.39 | 93.25 | 17.75 | 64.30 | 30.85 | 3.456* | .040 |
| **C4** ( mg/dL) | 7.41 | 3.15 | 9.82 | 2.81 | 7.47 | 4.08 | 1.366 | .266 |

**Statistically significant P value<0.05.LSD post hoc test showed the significant difference regarding BMI ,S.Albumin between (Complete,&Failure of remission ) ,regarding 24hour protein in urine was between (Complete&Failure and Partial &Failure ) subgroups.*

**Table 7** Comparison between studied patients with different response to IVC regarding baseline characteristics

| Studied parameters | Complete remission (n= 10) | | Partial remission (n=15) | | Failure of remission (n= 27) | | F mean | *P* value |
|---|---|---|---|---|---|---|---|---|
| | Mean | SD± | Mean | SD± | Mean | ±SD | | |
| **Age** (year) | 34.30 | 5.19 | 33.40 | 6.00 | 35.48 | 5.10 | 0.746 | 0.479 |
| **BMI** (Kg/m2) | 25.94 | 3.20 | 25.45 | 2.58 | 29.37 | 4.28 | 6.708* | 0.003 |
| **MAP** (mmHg) | 95.00 | 11.36 | 102.80 | 13.51 | 98.59 | 14.16 | 1.044 | 0.360 |
| **S.Creatinine**(mg/dl) | 2.03 | .88 | 2.55 | 1.79 | 3.13 | 2.16 | 1.374 | 0.263 |
| **eGFR** (mL/min/1.73 m2 ) | 39.00 | 20.97 | 39.13 | 27.23 | 32.51 | 28.17 | .392 | 0.678 |
| **S.Albumin**(g/dl) | 2.10 | .54 | 2.87 | 4.26 | 1.63 | .76 | 1.324 | 0.275 |
| **Total proteins** (g/dl) | 5.79 | .49 | 5.83 | .92 | 5.30 | 1.07 | 1.866 | 0.166 |
| **24 hr. protein in urine** (mg/day) | 3150.00 | 1048.83 | 4074.67 | 2124.11 | 4460.85 | 2239.47 | 1.511 | 0.231 |
| **CRP titer** (mg/L) | 2.40 | 7.58 | 13.60 | 18.62 | 7.29 | 14.52 | 1.795 | 0.177 |
| **ESR( mm/h)** | 100.90 | 17.90 | 88.33 | 17.52 | 91.29 | 17.31 | 1.640 | 0.204 |
| **C3** (mg/dL) | 80.40 | 20.53 | 74.06 | 33.72 | 58.76 | 31.36 | 2.363 | 0.105 |
| **C4** ( mg/dL) | 9.92 | 3.07 | 9.07 | 3.80 | 7.69 | 3.76 | 1.588 | 0.215 |

**Statistically significant P value<0.05.LSD post hoc test showed that the difference in BMI was between (Complete& Failure) and (Partial &Failure) subgroups.*

But no significant correlation between 24h urinary protein and hemoglobin ($r$=0.002,$P$=0.987),total proteins ( $r$ = 0.022,$P$=0.828) or CRP titer ( $r$ = -0.383, $P$ = 0.071)($P<0.05$).No significant correlation between 24h urinary protein and age($r$= -0.118, $P$ = 0.246), BMI($r$ = 0.134,P = 0.186) ,mean arterial BP ( $r$ = -0.073, $P$ =0.473), sex ($t$= 0.74,$P$=0.45) or HCV infection($t$=1.93,$P$=0.056) ($P$ >0.05)in all patients with lupus nephritis in the study .

## DISCUSSION

Effective induction therapy for suppressionof active immune-mediated inflammatory processes in severe proliferative lupus nephritis is of great importance to preserve renal function and decrease progression to ESRD and ultimately to decreasemortality. Mycophenolatemofetil selectively inhibits lymphocyte proliferation, and thus targets an instrumental step in the pathogenesis of systemic lupus erythematosus. There is accumulating evidence that the combined use of mycophenolatemofetil and corticosteroid presents an effective treatment for severe proliferative lupus nephritis in different ethnic groups, and is associated with much fewer adverse effects compared with cyclophosphamide-based regimens *(Chan ,2005).*

We studied the impact of induction therapy by MMF versus IVC on serum creatinine and 24h urinary protein in Egyptian patients with active proliferative lupus nephritis in a single center retrospectively ,and we reported that no statistically significant difference between MMF and IVC patients groups regarding rate of complete remission, partial or failure of remission in patients with proliferative lupus nephritis after 3 months of the induction *(P>0.05)*.No significant difference between both studied main groups regarding means of post induction S.Creatinine or 24h urinary protein *(P>0.05).*

Our results in agreement with (*Contereras et al., 2010)* study who found that MMF did not show superiority over IVC for the induction therapy of LN, as measured by renal response rate after 24 wk of treatment. The complete remission was achieved by 86 (63.7%) of 135 patients in the MMF group compared with 89 (57.1%) of 156 patients in the IVC group.

In another *(Appel et al., 2009)*trial that randomized 370 patients with severe LN and an average serum creatinine of 1.1 mg/dl to receive prednisone plus either MMF (average dose 2.6 gm/d) or NIH-protocol IVC for 24 weeks as induction therapy, the response to treatment at the end of induction therapy was similar in the MMF and IVC groups, with 56% and 53% of patients responding to treatment, respectively In contrast to a trial from China**,***(Hu et al.,2002)* reported that Patients randomized to MMF had greater reduction of proteinuria compared to conventional IVC for 6 months induction therapy in 46 patients with diffuse proliferative lupus nephritis (DPLN) In comparison to our trial *(Ginzler et al,. 2005 )* is a multi-center, prospective trial, 140 patients (the majority with class IV LN) were randomized to standard six monthly pulses of IVC or MMF . The study allowed crossover at 3 months for treatment failure or toxicity. At the 6-month end point, there were fewer treatment failures, and more complete and partial remissions with MMF (22 and 52%, respectively) compared to IVC (4 and 30%, respectively). Crossover to the alternate arm was more common with IVC than with MMF (20 vs 8%, respectively).

Other controlled trials, and subsequent meta-analyses, establish MMF as one of the recommended, first-choice regimens for inducing a remission in severe active proliferative lupus nephritis *(Chan et al., 2000) (Lee Y et al., 2010).*

In our retrospective study the patients in MMF group had significantly lower age ,BMI and higher eGFR as baseline characteristics may explain rate of complete remission in MMF group versus IVC (25% VS 19.2%) and explain the significant difference between main groups regarding post induction eGFR ($P$<0.05).

We compare between patients with complete, partial or failure of remission subgroups received MMF induction and similar subgroups with IVC induction regarding baseline means of S. Creatinine, S. Albumin, 24h urinary protein and complements and we observed no significant differences. Although IVC reduce proteinuria (partial and complete remission) in25(48.1 %) patients versus 20 (41.7%) in MMF group there was no statistically significant difference ($P$>0.05). So we considered MMF is effective as IVC to reduce proteinuria and achieve remission as induction therapy.

In *(Rovin B, 2013)*study considered MMF and cyclophosphamide are about equal in inducing remissionin the short term. However, long-termoutcomessuggest better preservation of kidney function and fewer relapses with cyclophosphamide therapy. Therefore,MMF should not yet be considered the induction drug of choice for severe lupus nephritis.
We observed that patients failed to achieve remission were with significantly higher BMI, lower S.Albumin and massive proteinuria than patients with remission in MMF group. In IVC group, patients with significantly higher BMI had poorer response. This association between high BMI and poorer outcome for induction therapy in both groups may be postulated to the detrimental effect of higher BMI on proteinuria. .

We also reported statistically significant negative correlation between 24h urinary protein and C3,C4,serum albumin and serum creatinine , and significant positive correlation with eGFR. Persistent depression of C3 complement has been associated with the activity and progression of kidney disease in patients with LN*(Swaak etal.,1990).*

**Limitation**

Retrospective study with limited number of patients with difficulties in collecting data and non-adherence of the patients to the regular follow up with treating center.

## CONCLUSION

MMF and IV cyclophosphamide both with corticosteroid showed similar efficacy as short term induction treatment of

proliferative lupus nephritis and we need further prospective cohort studies on large number of saver lupus nephritis.

## REFERENCES


1. AnayaJ.-M., Cañas C, Mantilla R. D. *et al*.,2011. "Lupus nephritis in colombians: contrasts and comparisons with other populations," Clinical Reviews in Allergy and Immunology,40 (3) :199–207.
2. Andrew S.Bomback and Gerald B,2010. Appel .Updates on the Treatment of Lupus Nephritis *J Am SocNephrol*,21: 2028–2035.
3. Appel GB, Contreras G, Dooley MA, *et al*.,2009. Mycophenolatemofetil versus cyclophosphamide for induction treatment of lupus nephritis. J Am SocNephrol , 20 : 1103 – 12 .
4. Chan TM, Li FK, Tang CS, Wong RW,2000.Efficacy of mycophenolatemofetil in patients with diffuse proliferativelupus nephritis. Hong Kong-GuangzhouNephrology Study Group. N EnglJ Med 343: 1156–1162.
5. Chan TM.,2005 . Lupus nephritis: induction therapy. Lupus.,14 (1):s27-32.
6. Chiu MokC ,2012. Understanding lupus nephritis: diagnosis, management, and treatment options. International Journal of Women's Health, 4 :213–222.
7. Contreras G,Mattiazzi A, Guerra G, *et al*.,2010: Recurrence of lupus nephritis after kidney transplantation. J Am SocNephrol ,JASN 21(7): 1200-1207.
8. Ginzler EM, Dooley MA, Aranow C, *et al*., 2005. Mycophenolatemofetil or intravenous cyclophosphamide for lupus nephritis. N Engl J Med , 353 : 2219 – 28 .
9. Hu W, Liu Z, Chen H *et al*.,2002 . Mycophenolatemofetil vs cyclophosphamide therapy for patients with diffuse proliferative lupus nephritis. Chin Med J (England) , 115: 705–709.
10. Lee Y, Woo JH, Choi S, Ji J, Song G,2010 : Inductionand maintenance therapy for lupus nephritis:a systematic review and meta-analysis.Lupus ,19: 703–710.
11. Mok CC, Ho CT, Siu YP, *et al*.,2001. Treatment of diffuse proliferative lupusglomerulonephritis: a comparison of two cyclophosphamide-containingregimens. Am J Kidney Dis., 38:256–264.
12. Mok CC, Ho CTK, Chan KW, *et al*.,2002. Outcome and prognostic indicatorsof diffuse proliferative lupus glomerulonephritis treated with sequentialoral cyclophosphamide and azathioprine. Arthritis Rheum. ,46:1003–1013.
13. Mok CC., 2005. Prognostic factors in lupus nephritis. Lupus.,14: 39–44.
14. Moon SJ, Kwok SK, Ju JH, *et al*., 2011. Predictors of chronic kidney disease in Korean patients with lupus nephritis. J Rheumatol, 38: 2588–2597.
15. Ortega L. M, SchultzD. R. Lenz, V. *et al*., 2010. Contreras, "Lupus nephritis: pathologic features, epidemiology and a guide to therapeutic decisions," Lupus, 19 (5): 557–574.
16. Rovin, B, Parikh S, Hebert L, Chan T,2013.Lupus Nephritis: Induction Therapy in Severe Lupus Nephritis—Should MMF Be Considered the Drug of Choice?.Clin J Am SocNephrol ,8: 147–153.
17. SalgadolA, and Herrera-Diaz C,2012. Lupus Nephritis: An Overview of Recent Findings. Autoimmune Diseases J, 849684 :21 .
18. Swaak AJ, Huysen V, Nossent JC, 1990. Antinuclear antibody profiles in relation to specific disease manifestations of systemic lupus erythematosus. ClinRheumatol,9:82-94.
19. Webster A, Masson P, 2013. Induction and maintenance treatment of proliferativelupus nephritis Nephrology , 18 :71–72.


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