SMGroup

SM Journal of Nephrology and Kidney Diseases

Research Article

Lupus Nephritis: Clinical Characteristics and Prognostic Factors

Yosra Ben Ariba*, Faida Ajili, Mouna Maïza, Bassem Louzir and Jannet Labidi

Department of nephrology and internal medicine, UR17DN02, Tunisian Miltary Hospital, Tunisia

Article Information

Received date: Oct 15, 2018
Accepted date: Oct 22, 2018
Published date: Oct 26, 2018

***Corresponding author**

Yosra Ben Ariba, Department of Nephrology and Internal medicine, UR17DN02, Tunisian Miltary Hospital, Mont Fleury, Tunis, Tunisia,
Tel: +216 97566616;
Email: yosrabenariba@yahoo.fr

Keywords Nephritis; Systemic Lupus Erythematosus; Corticosteroids; Immunosuppressive Therapy

Article DOI 10.36876/smjnkd.1017

Abstract

Lupus nephritis is a severe organic manifestation of systemic lupus erythematosus. We studied 120 cases of patients diagnosed with systemic lupus erythematosus. Lupus nephritis was found in 41 patients (34.1%) with a mean age of 34 years and including 32 women and 9 men. Nephritis was the first sign of lupus in 66%. Renal clinical features were: swelling (39%), hypertension (25%), hematuria (25%), proteinuria (95%), nephrotic syndrome (46%) and renal failure (29%). Renal biopsy was contributive in 30 cases and showed glomerular nephritis class I in 2%, class III in 7%, class IV in 42%, class V in 15% and class IV+V in 7% of all cases. Induction therapy consisted of high dose corticosteroids in all patients, associated with IS therapy in 78% of the cases: cyclophosphamide in 29 patients and MMF in 3 patients. Maintenance therapy included low doses of corticosteroids in all patients in addition to cyclophosphamide in 3 cases, MMF in 10 cases and azathioprine in 10 patients. A complete remission was observed in 17 cases (41%), a partial remission in 20 cases (49%), a renal relapse in 20 patients (49%) and an end-stage renal failure in 9 patients (22%). Two patients died. Predictor factors of better outcome were achieving complete remission and a longer duration of maintenance therapy. Swelling, high rates of proteinuria, nephrotic syndrome, partial remission and short duration of maintenance therapy were identified as poor prognostic predictors.

Introduction

Systemic Lupus Erythematosus (SLE) is an autoimmune systemic disease affecting several organs. Renal involvement is one of the most common and severe manifestations of this disease [1]. The existence of a Lupus Nephropathy (LN) is a poor prognosis factor. Its management depends closely not only on its clinico-biological presentation but mainly on histological findings. The therapeutic modalities are variable but the prognosis of the disease remains difficult to predict.

The aim of this work was to study the clinical, biological and histological characteristics of patients with LN and the different therapeutic modalities and to deduce the factors influencing the prognosis of the disease.

Patients and Methods

We realize a descriptive retrospective study carried out in the department of internal medicine of the Military Hospital of Tunis during a period of 13 years from 1999 to 2012. We included in this study the patients who met the corrected criteria of the American College of Rheumatology for the diagnosis of SLE. The LN was diagnosed on the basis of the International Society of Nephrology (ISN) criteria. We have adopted the histological classification of the 2004 ISN. We excluded from this study patients with SLE without renal involvement.

We reviewed 120 cases of patients with SLE and retained 41 cases of patients with LN. We analyzed epidemiological, clinical, biological, immunological, histological, and therapeutic and outcome parameters of these patients.

We have adopted the following definitions:

Complete remission: normal urinary sediment, normal renal function, normal blood pressure with or without antihypertensive treatment, absence of extra-renal manifestations for at least 6 months.

Incomplete remission: an improvement of the renal function, the disappearance of the nephrotic syndrome with persistence of proteinuria <2 g / 24h.

Relapse: elevation or reappearance of proteinuria, degradation of renal function, elevation of native anti-DNA antibodies and/or decreased serum complement levels, existence of extra-renal relapse manifestations.

Aggravation: worsening of renal function with decreased plasma creatinine clearance.

Moderate renal insufficiency: 30 ≤ glomerular filtration rate (GFR) <59 ml / min per 1.73 m^2 of body surface area.

OPEN ACCESS
ISSN: 2576-5450

Severe renal insufficiency: 15 ≤ GFR <29 ml / min per 1.73 m^2 of body surface area.

End-stage renal insufficiency: GFR <15 ml / min per 1.73 m^2 of body surface area.

To define the factors of poor renal prognosis, we divided the studied population into two groups:

Group 1 included patients in total remission at the last visit (proteinuria = 0 and normal renal function).

Group 2 included all other patients.

We performed a comparative study between the two groups according to the clinical, biological, immunological, histological, and therapeutic and outcome parameters.

SPSS 19 software was used for statistical analysis. The results are expressed either in terms of the number of cases and / or percentage for categorical variables and in terms of mean for quantitative variables. The Chi^2 test was used to compare percentages. If the conditions for applying this test were not valid, we used the Fischer test. The Student test was used for the comparison of 2 means. P less than 0.05 were considered significant.

Results

Our work revealed a prevalence of LN of 34.1% and an incidence of LN of 2.4 cases per year. There were 32 women (78%) and 9 men (22%), with a median age at diagnosis of 34.1 years (12-70 years), with a peak between 30 and 40 years of age. In 12.2% of our patients, the LN was late-onset (50 years or older). Nephropathy had inaugurated lupus disease in 27 of our patients (66%). For the other cases, it occurred within an average of 28 months (2 months to 29 years) after diagnosis of lupus disease. One (or more) trigger factor was found in 25 cases (61%). These were mainly infections in 18 cases (44%), pregnancies or postpartum period in 5 cases (12%), sun exposure in 2 cases (5%), corticosteroid unintentional interruption in one case and a beta-blocker medication use in one other. The table 1 resumes the clinical and biological signs observed in our patients at initial presentation. The most frequent clinical manifestation was edema, which was revealing LN in 39% of cases. Proteinuria was almost constant (95%) with an average value of 3.72g/24h (0.84-10.5 g/24h) nephrotic in 46%, aseptic leukocyturia was noted in 71% of patients and hematuria was present in 54% of cases. Mean serum creatinine was 145.4 µmol/l (39-541 µmol/l). Renal Failure (RF) was observed in 12 patients (29%). It was moderate in 4 patients, severe in 7 patients. One patient has an end stage renal disease. Four of our patients have a Hemolytic Uremic Syndrome (HUS).

Table 1: Clinico-biological features at lupus nephritis diagnosis.

Renal Manifestations	Number of patients	Percentage (%)
Edema	16	39
HT	9	25
Proteinuria	39	95
Nephrotic Syndrome	19	46
Hematuria	22	54
Aseptic leucocyturia	29	71
Renal failure	12	29

Table 2: Frequency of lupus extra-renal signs.

Signs	Number of patients	Percentage (%)
Photosensibility	17	41
"Vespertilio" Erythema	18	44
Discoïd Lupus erythematosus	5	12
Mouth Ulcers	3	7
Polyarthritis	32	78
Seritis	17	41
Seizure	7	17

Extra-renal signs were present in all patients and were dominated by articular and muco-cutaneous manifestations (Table 2).

The remainder of clinical, biological and immunological data is summarized in Table 3. Renal biopsy was contributive in 30 cases. We found a contraindication to PBR in 9 cases, a single kidney in 2 cases, severe thrombocytopenia in 3 cases, anticoagulant treatment in 3 cases and a pregnancy with uncontrolled HTA in 1 case. The renal histology revealed a LN class I in one case, a class III in 3 cases (7%), a class IV in 17 cases (42%), a pure class V in 6 cases (15% V + IV in 3 cases (7%). Tubulo-interstitial lesions were noted in 22% of cases and vascular lesions in 10% of cases.

Nephrotic Syndrome (NS) was more frequent in proliferative forms of LN (47% of IV classes, 100% of classes III and IV + V). It was observed in 50% of the membranous lupus nephritis. Hematuria was often present in proliferative and membranous nephritis (67% in class III and class IV + V, 50% in class V and 41% in class IV) and that RF was noted in 67% of class IV + V and in 35% of class IV but it was absent in classes I and III. We also Hypertension was common in diffuse proliferative nephritis (29% of class IV and 33% of class IV + V) and it was constant in patients with HUS.

Treatment included corticosteroid therapy in all patients initially with high dose (oral and/or IV) with progressive decrease. Immunosuppressive (IS) therapy was associated in 78% of patients, mainly in proliferative LN. Cyclophosphamide (CYC) was prescribed as an induction treatment in 29 patients (71%) according to different therapeutic protocols: oral CYC in one case, CYC IV in monthly boli at a dose of 600 mg/1.73 m^2 of body surface area in 15 cases and CYC IV according to the EUROLUPUS protocol from 2004 in 13 cases (Table 3). Mycophenolate Mofetil (MMF) was prescribed as induction IS therapy in 3 cases (class IV = 1, class V = 1,

Table 3: Different protocols of cyclophosphamide in induction treatment of lupus nephritis.

	Before 2004		After 2004
Therapeutic protocols	Oral CYC	Monthly IV CYC	Eurolupus
Number de patients	1	15	13
Percentage (%)	3	52	45
Class III	0	1	2
Class IV	1	8	6
Class V	0	2	1
Class IV+V	0	1	2
Not classified	0	3	2

Citation: Ariba YB, Ajili F, Maïza M, Louzir B and Labidi J. Lupus Nephritis: Clinical Characteristics and Prognostic Factors. J Nephrol Kidney Dis. 2018; 2(2): 1017.
https://dx.doi.org/10.36876/smjnkd.1017

non-contributive histology with no response to corticosteroid alone = 1). Rituximab (RTX) was used in a 17-year-old patient with active LN class IV + V associated with autoimmune hemolytic anemia, thrombocytopenia and pericardial effusion, due to lack of response to CYC IV. Concerning maintenance IS therapy, azathioprine (AZA) and MMF were used in 10 cases each; CYC was used in 3 patients, in oral form at the dose of 100 mg per day in one case and in the form of quarterly boli in 2 cases. Maintenance treatment was used for a long period with an average of 36 months.

We used plasma exchange sessions, IV immunoglobulin infusions and dialysis sessions in severe forms of LN, particularly in patients with associated HUS.

Remission was observed in 90% of the patients: total remission was obtained in 17 cases (41%) and partial remission in 20 patients (49%). Twenty patients (49%), including 4 men and 16 women, had one or more renal relapses (1-5 relapses per patient) in an average of 43 months (6 to 96 months). One or more triggers of relapse were identified in 10 cases (50%): infection in 6 cases, treatment interruption in 5 cases and pregnancy in 3 cases. Nine of our patients (22%) had reached end stage renal disease after an average of 36 months with extremes ranging from 40 days to 8.5 years. Three of our chronic dialysis patients had an extra-renal lupus flare: articular flare associated with pericarditis in one case, joint flare associated with autoimmune hepatitis in one other and articular, hematological, with macrophage activation syndrome in one case. Only two of our patients died.

Seven patients improved a complete renal remission. A steady state of renal function was obtained in 8 cases. Aggravation was noted in 9 cases with end stage renal disease in 22% of cases, 8 in hemodialysis and one patient in peritoneal dialysis. Renal survival was 88% at 5 years and 78% at 10 years. Overall survival was 97% at 5 and 10 years.

Comparing the 2 groups of patients (group 1=16 patients and group 2 =25 patients), some factors were significantly associated with a good evolution: a longer duration of maintenance treatment ($p = 0.033$) and achieving total remission ($p < 0.001$).

Other factors were significantly associated with renal aggravation: edema ($p = 0.033$), high initial proteinuria ($p = 0.021$) and especially greater than 3 g/24h, NS ($p = 0.028$), partial remission ($p < 0.001$) and short duration of maintenance therapy ($p = 0.033$).

The different clinical, biological, histological and therapeutic correlations according to the renal prognosis are illustrated in Table 4.

Discussion

Our study, although retrospective, was carried out on a cohort of 41 cases followed in a single center. In our series, we have a predominance of occurrence in young women. The LN inaugurated the lupus disease in more than half of the cases, it was mainly proliferative forms. Treatment was based on corticosteroids and IS therapy. Induction and maintenance treatments have been described and several therapeutic protocols have been used.

In our series, remission was observed in the majority of cases (90%) and the factors of poor and good prognosis were confirmed by multicentric prospective studies.

Table 4: Epidemiological, clinical, biological, histological and therapeutic correlations according to the renal prognosis.

	Group 1	Group 2	Difference p
Average of age	38,4	30,9	0,064
Age < 30	16-Apr	25-Dec	0,141
Age > 30	16-Dec	13/25	
Age < 50	13/16	24/25	0,120
Age≥50	16-Mar	25-Jan	
Female gender	13	3	0,501
Male gender	3	7	
Edema	**16-Mar**	**13/25**	**0,033**
hypertension	4	5	0,704
Average of Proteinuria	**2,59**	**4,57**	**0,021**
Proteinuria >3g	**4**	**15**	**0,029**
Proteinuria <1g	3	1	0,113
Average of albumin	27,9	25,2	0,228
Nephrotic syndrome	**4**	**15**	**0,028**
Average of creatinine	112,37	150,72	0,278
Initial renal failure	16-May	25-Oct	0,507
Hematuria	16-Sep	25-Dec	0,606
Leucocyturia	14-Sep	20/25	0,281
Anemia	16-Dec	20/25	1,000
Thrombopenia	15-May	25-Jul	0,722
Average of C Reactive Protein	42,6	33,7	0,629
Hypocomplementemia C3	14-Jun	13/21	0,26
Hypocomplementemia C4	14-Nov	15/21	0,635
AAN (+)	16/16	24/25	0,418
Ac anti DNA (+)	14-Dec	17/21	0,714
Ac anti Sm (+)	10-Jan	18-Jun	0,172
Ac anti-phospholipides (+)	10-May	14-Oct	0,285
Not biopsied	16-May	25-Jun	0,413
Class I	0	1	0,438
Class III/A	0	3	0,164
Class IV/A	8	9	0,17
Class V	2	5	0,611
Class IV+V	1	1	0,685
Signs of activity	11-Oct	14/19	0,364
Signs of Chronicity	0	3	0,206
CYC (induction treatment)	16-Nov	19/25	0,31
MMF (induction treatment)	16-Feb	25-Jan	
Absence of immunosuppressive treatment	3	5	0,92
Duration of maintenance treatment	**32,81**	**15,75**	**0,033**
Initial total remission	**14/16**	**23-Mar**	**<0,001**
Initial partial remission	**16-Feb**	**18/23**	**<0,001**

Citation: Ariba YB, Ajili F, Maïza M, Louzir B and Labidi J. Lupus Nephritis: Clinical Characteristics and Prognostic Factors. J Nephrol Kidney Dis. 2018; 2(2): 1017.
https://dx.doi.org/10.36876/smjnkd.1017

LN is one of the most frequent involvements of SLE. It was observed in 20-65% of lupus patients [1]. This frequency becomes very important (> 90%) if we take into account the silent LN of histological discovery [2].

LN occurs at all ages with a significantly higher prevalence in young subjects before 40 years [3,4]. LN can inaugurate lupus disease in 16 to 60% of cases [3]. This was the case for 66% of our patients, where the other signs of SLE were unrecognized or taken for another disease.

In our series, articular and cutaneous manifestations were the most frequent, joining the results of other studies [3-7].

Hypertension is reported in 13 to 62% of the literature [3,5,8]. In our series, it was present in 24% of patients. Hematuria, noted in 71% of our cases, varies between 50 and 80% in the literature.

RF, of varying degrees, is part of the initial presentation of LN in 11.9 to 44.3% of published cases. It was present in 29% of our patients. Nephrotic syndrome, present in 46% of our patients, is observed in 17.8% to 67.1% of LN [3, 5].

In the majority of series, as in ours, there is a predominance of diffuse proliferative nephritis whose frequency varies from 27 to 53% [8,9]. Class V is less frequent, noted in 7 to 25% [8,9]. Classes I and II remain the least frequent.

Although the most severe clinical manifestations tend to associate with the more severe histological forms, the clinical signs are not necessarily correlated with the histological lesions. However, in our series a certain anatomo-clinical correlation was found: nephrotic syndrome and hematuria; were more frequent in proliferative forms and in membranous nephritis. Hypertension was common in diffuse proliferative LN and was constant in HUS, and RF was noted in 67% of Class IV + V and in 35% of Class IV when it was absent in classes I and III.

The treatment of LN depends on the histological lesions observed. In Classes I and II, corticosteroids are the basis of treatment and indication of IS therapy was based in this cases on extra-renal manifestations. Class V is no longer an indication for corticosteroid therapy alone, but the MMF is currently associated with a recommendation level A of the Task Force Pannel. Proliferative nephropathies are a classic indication of IS therapy associated with high-dose corticosteroids during lupus disease. CYC is the most widely used: initially prescribed by the oral route, which resulted in several iatrogenic complications [10], its prescription according to the protocol of monthly high-dose boli IV was born in the 1970s and 1980s following the trials of the group " NIH "which have shown great efficacy with markedly less iatrogenicity. In the Eurolupus Nephritis Trial (ELNT), the classic regimen (CYC in 6 boli monthly high doses) was compared to the European low dose regimen (CYC in 6 boli 500mg/15j). Houssiau FA et al, in this study (ELNT), included patients with severe LN with proliferative GN in all cases and presence of glomerular crescents in 47% of cases and showed that after a follow-up of 41 months, the rate of complete remission was better with the 500 mg/15j regimen (71% versus 54%), the failure rate was lower (16% *versus* 20%), and relapses (27% *versus* 29%) [11,12]. After a follow-up of 73 months, no difference was noted on renal survival. The persistence of renal dysfunction was noted in 20% versus 23% [13]. We used high-dose CYC IV in 15 of our patients and CYC according to Eurolupus in 13 of our patients and we obtained good results with remission in 90% of our cases with more complete remissions with the Eurolupus group (7 cases) than the high dose CYC IV group (4 cases).

MMF is increasingly taking a place in the treatment of LN induction. Different authors agree on the non-inferiority to see the superiority of the MMF with respect to the CYC. Chan TM et al. compared MMF therapy with oral CYC in patients with proliferative LN with hypo-albuminemia and found comparable efficacy in the degree of improvement in proteinuria, albuminemia, and serum creatinine as well as the rate of relapse [13,14]. Similarly, Appeal GB et al, in the ALMS study that included a multi-ethnic cohort with active or membranous proliferative LN, showed MMF and CYC IV equivalence in total or partial remission induction, or within obtaining remission (56.2% in the MMF arm and 53% in the CYC arm) with an MMF advantage over CYC in non-Caucasian/non-Asian patients; In addition, analysis of LN cases with creatinine clearance <30ml / min showed that MMF is not less effective than CYC IV in the treatment of these severe LN [15,16]. Ginzler et al., in their randomized trial of 140 cases of LN class III, IV or V, of which more than half were africo-americans, demonstrated MMF superiority to monthly CYC IV in induction of 6-month remissions with 22.5% complete remission in MMF versus 5.8% in CYC [16] Hu W et al showed that MMF is more effective than CYC IV in reducing proteinuria, hematuria, and d autoantibodies and a clear reduction in glomerular necrosis, croissants and vascular abnormalities in MMF-treated patients who were re-biopsied [17]. Regarding treatment tolerance, Chan TM et al showed that infectious complications and the occurrence of amenorrhoea were less with MMF [13]. We used MMF in 3 patients (class V, class IV + V, without histology) with a remission in all cases (total = 2, partial = 1).

Rituximab, an anti-B lymphocyte monoclonal antibody directed against the CD20 molecule, was used in a single patient of our series in front of a proliferative LN that was refractory to CYC IV but evolution to end stage renal disease could not be avoided in this case. In the literature, indications are refractory, recurrent or first-line treatment. In the randomized "LUNAR" study, treatment of proliferative LN class III or IV with RTX associated to MMF at an average dose of 2.4 g/d and corticosteroids was compared to MMF treatment at the mean dose of 2.7 g/day associated with corticosteroids. In spite of complete B-cell depletion in all patients in the RTX arm, there was no significant difference between the two arms [18]. A recent review of the literature by Ramos-Casal resulted in the collection of 106 patients with lupus nephropathy in a common analysis. A total or partial response was observed in 70% of patients, 80% of class III and 67% of class IV [19]. The passage of proliferative LN to terminal renal insufficiency could not be avoided in 26.6% of cases [20].

Concerning maintenance therapy, corticosteroid therapy remains the cornerstone associated or not with IS treatment. Contreras et al compared the short- and long-term efficacy of CYC, AZA and MMF as maintenance therapy in relay of high-dose CYC IV induction therapy. They found increased mortality in patients receiving CYC IV (compared with AZA), more iatrogenic side effects in this subgroup (compared to AZA and MMF groups) and, more surprisingly, an increased rate of recurrence (compared to patients receiving MMF) [21]. The MAINTAIN study, including caucasian patients treated with

CYC induction according to Eurolupus with relay either by MMF or AZA in maintenance, found a comparable efficacy between MMF and AZA in maintenance treatment (19% renal relapses for MMF and 25% for AZA without significant difference) with comparable adverse events except for the occurrence of transient cytopenia which was more common in the AZA-treated group [22]. A histological re-evaluation by renal biopsy, after 2 years, on a representative sample of these patients showed no benefit of either of these two molecules in terms of histological lesions of activity or chronicity [22]. In the maintenance phase of the "ALMS" study, patients who responded to induction therapy by either CYC IV monthly or MMF had been re-randomized to receive MMF or AZA as maintenance IS treatment. This study showed the superiority of MMF compared to AZA with less therapeutic failure (16.4% for MMF versus 32.4% for AZA) and less severe adverse effects (23.5% For MMF versus 33% for AZA) [23]. Currently, AZA and MMF are the most prescribed in LN maintenance therapy in most literature series [22,23]. They were equally prescribed in our patients (24%); MMF was more effective in maintaining remission since 80% of AZA patients had a renal relapse whereas only 20% of MMF patients had relapsed.

The rate of renal remission (total or partial) after an initial therapeutic line is at best 81% in the literature [3,11,21]. However, 27% to 66% of patients suffering from proliferative LN will relapse according to Sidiropoulos et al [24]. The relapse rate was 49% in our series. According to the literature, the rate of relapse depends on the treatment. Thus, the probability of relapse is 72% at 50 months of progression in patients treated with corticosteroids alone, and decreases to 30% when CYC is combined in induction therapy [25]. Ginzler et al reported a similar relapse rate in the group of patients who received MMF induction (8 of 71 or 11.2%) and CYC induction (8 of 69, 11.5%) [16]. The IS therapy also influences the recurrence rate, which varies from 11% to 37% in AZA [25-27], 15% in MMF [13] and 30% in CYC [25].

Despite therapeutic advances, the incidence of end stage renal insufficiency in LN does not appear to decrease. Indeed, a study published by Ward had shown a stable rate over time: 4.4 per million inhabitants in 1996 and 4.9 per million inhabitants in 2004 [28]. The prevalence of end RF varies between 6.5% and 30% [3,29,30], it was 22% in our series. The average delay of end RF, which was 3 years in our patients, varies in the literature between 1.9 and 2.3 years [31].

Renal involvement in lupus is an important prognostic factor. The survival rate of patients with LN improved significantly from 70% in ten years in the 1970s to 92% in the 1990s [8,32]. In our series, overall survival was 97% at 5 and 10 years. Mortality due to infections (often early) and renal disease has decreased at the expense of late cardio-vascular mortality [7].

As regards renal survival, recent data show an improvement in renal survival estimated at 86% at 10 years in the membrano-proliferative forms [33].

In the literature, some factors have been identified by various authors as predictive factors for renal poor prognosis such as hypertension, nephrotic syndrome, initial RF, anemia, thrombocytosis, hypocomplementemia [6,12,33-34]. The predictive value of class IV remains controversial in the literature: some authors correlated it with a poor renal prognosis [9,35]; Chrysochou correlated it with a good evolution of the LN, this can be explained by the important use of the IS [6]. Our work identified certain factors of poor renal prognosis: edema ($p = 0.033$), high initial proteinuria ($p=0.029$), nephrotic syndrome ($p=0.028$), partial remission $P <0.001$) and a short duration of maintenance treatment ($p = 0.033$).

Following our patients at the end RF stage, we noted an extra-renal relapse in 3 of our patients. Beji et al reported 5 cases of lupus relapses under chronic dialysis (19.5% of their chronic dialysis patients) [3].

Conclusion

The LN is a frequent occurrence during the SLE. Despite therapeutic progress, refractory forms are sometimes observed. End-stage RF is the frightening complication of this disease, its frequency has decreased due to the generalization of the renal biopsy and the widening of indications of IS therapy.

References

1. Alarcón GS. Multiethnic lupus cohorts: what have they taught us? Reumatol Clin. 2010; 7: 3-6.
2. Zabaleta-Lanz M, Vargas-Arenas RE, Tápanes F, Daboin I, Atahualpa Pinto J, Bianco NE. Silent nephritis in systemic lupus erythematosus. Lupus. 2003; 12: 26-30.
3. Béji S, Kaaroud H, Ben Moussa F, Abderrahim E, Goucha R, Ben Hamida F et al. Néphropathie lupique : à propos de 211 cas. Rev Med Interne. 2005; 26: 8-12.
4. Dhakal SS, Sharma SK, Bhatta N, Bhattarai S, Karki S, Shrestha S et al. Clinical features and histological patterns of lupus nephritis in Eastern Nepal. Saudi J Kidney Dis Transpl. 2011; 22: 377-380.
5. Kammoun K, Jarraya F, Bouhamed L, Kharrat M, Makni S, Hmida MB et al. Poor prognostic factors of lupus nephritis. Saudi Kidney Dis Transpl. 2011; 22: 727-732.
6. Chrysochou C, Randhawa H, Reeve R, Waldek S, Wood GN, O'Donoghue DJ, et al. Determinants of renal functional outcome in lupus nephritis: a single centre retrospective study. QJM. 2008; 101: 313-316.
7. Zheng ZH, Zhang LJ, Liu WX, Lei YS, Xing GL, Zhang JJ, et al. Predictors of survival in Chinese patients with lupus nephritis. Lupus. 2012; 21: 1049-1056.
8. Huong DL, Papo T, Beaufils H, Wechsler B, Blétry O, Baumelou A, et al Renal involvement in systemic lupus erythematosus. A study of 180 patients from a single center. Medicine. 1999; 78: 148-166.
9. Sharon LK, James B, Albert DA. What do we know about lupus membranous nephropathy? An analytic review. Arthritis and Rheumatism. 2002; 47: 450-455.
10. Flanc RS, Roberts MA, Strippoli GFM, Chadban SJ, Kerr PG, Atkins RC. Treatment of diffuse proliferative lupus nephritis: a meta-analysis of randomized controlled trials. Am J Kidney Dis. 2004; 43: 197-208.
11. Houssiau FA, Vasconcelos C, D'Cruz D, Sebastiani GD, Garrido Ed Ede R, Danieli MG, et al. Immunosuppressive therapy in lupus nephritis: the Euro-Lupus Nephritis Trial, a randomized trial of low-dose versus high-dose intravenous cyclophosphamide. Arthritis Rheum. 2002; 46: 2121-2131.
12. Houssiau FA, Vasconcelos C, D'Cruz D,Sebastiani GD, de Ramon Garrido E, Danieli MG et al. Early Response to Immunosuppressive Therapy Predicts Good Renal Outcome in Lupus Nephritis. Arthritis. Rheum. 2004; 50: 3934-3940.
13. Chan TM, Tse KC, Tang CS, Mok MY, Li FK. Hong Kong Nephrology Study Group: Long-term study of mycophenolate mofetil as continuous induction and maintenance treatment for diffuse proliferative lupus nephritis. J Am Soc Nephrol. 2005; 16: 1076-1084.

Citation: Ariba YB, Ajili F, Maïza M, Louzir B and Labidi J. Lupus Nephritis: Clinical Characteristics and Prognostic Factors. J Nephrol Kidney Dis. 2018; 2(2): 1017.
https://dx.doi.org/10.36876/smjnkd.1017

14. Chan TM, Li FK, Tang CS,Wong RW, Fang GX, Ji YL et al. Hong Kong-Guangzhou Nephrology Study Group. Efficacy of mycophenolate mofetil in patients with diffuse proliferative lupus nephritis. N Engl J Med. 2000; 343:1156-1162.

15. Appel GB, Contreras G, Dooley MA, Ginzler EM, Isenberg D, Jayne D et al. Aspreva Lupus Management Study Group. Mycophenolate versus cyclophosphamide for induction treatment of lupus nephritis. J Am Soc Nephrol. 2009; 20: 1103-1112.

16. Ginzler EM, Dooley MA, Aranow C, Kim MY, Buyon J, Merrill JT et al. Mycophenolate mofetil or intravenous cyclophosphamide for lupus nephritis. N Engl J Med. 2005; 353: 2219-2228.

17. Hu W, Liu Z, Chen H, Tang Z, Wang Q, Shen K, et al. Mycophenolate mofetil vs cyclophosphamide therapy for patients with diffuse proliferative lupus nephritis. Chin Med J. 2002; 115: 705-709.

18. Rovin BH, Furie R, Latinis K, Looney RJ, Fervenza FC, Sanchez-Guerrero J et al. Efficacy and safety of rituximab in patients with active proliferative lupus nephritis: the Lupus Nephritis Assessment with Rituximab study. Arthritis Rheum. 2012; 64: 1215-1226.

19. Ramos-Casals M, Diaz-Lagares C, Soto-Cardenas MJ, Brito-Zeron P, Cuadrado MJ, Sanna G et al. Rituximab Therapy in Lupus Nephritis: Current Clinical Evidence. Clin Rev Allergy Immunol. 2011; 40: 159-169.

20. Melander C, Sallée M, Trolliet P, Candon S, Belenfant X, Daugas E et al. Rituximab in Severe Lupus Nephritis: Early B-Cell Depletion Affects Long-Term Renal Outcome. Clin J Am Soc Nephrol. 2009; 4: 579-587.

21. Contreras G, Pardo V, Leclercq B, Lenz O, Tozman E, O'Nan P, et al. Sequential therapies for proliferative lupus nephritis. N Engl J Med. 2004; 350: 971-980.

22. Stoenoiu MS, Aydin S, Tektonidou M, Ravelingien I, le Guern V, Fiehn C, et al. MAINTAIN Nephritis Trial Group. Repeat kidney biopsies fail to detect differences between azathioprine and mycophenolate mofetil maintenance therapy for lupus nephritis: data from the MAINTAIN Nephritis Trial. Nephrol Dial Transplant. 2012; 27: 1924-1930.

23. Dooley MA, Jayne D, Ginzler EM, Isenberg D, Olsen NJ, Wofsy D et al. ALMS Group. Mycophenolate versus azathioprine as maintenance therapy for lupus nephritis. N Engl J Med. 2011; 365:1886-1895.

24. Sidiropoulos PI, Kritikos HD, Boumpas DT. Lupus nephritis flares. Lupus. 2005; 14: 49-52.

25. Donadio JV, Holley KE, Ferguson RH, Ilstrup DM. Treatment of diffuse proliferative lupus nephritis with prednisone and combined prednisone and cyclophosphamide. N Engl J Med. 1978; 299: 1151-1155.

26. Chan TM, Li FK, Wong RW, Wong KL, Chan KW, Cheng IK. Sequential therapy for diffuse proliferative and membranous lupus nephritis: cyclophosphamide and prednisolone followed by azathioprine and prednisolone. Nephron. 1995; 71: 321-327.

27. El Hachmi M, Jadoul M, Lefèbvre C, Depresseux G, Houssiau FA. Relapses of lupus nephritis: incidence, risk factors, serology and impact on outcome. Lupus. 2003; 12: 692-696.

28. Ward MM. Changes in the incidence of end-stage renal disease due to lupus nephritis in the united states, 1996-2004. J Rheumatol. 2009; 36: 63-67.

29. Singh S, Zhou XJ, Ahn C, Saxena R. Lupus Nephritis. A Retrospective Analysis of Clinical Presentation and Outcomes from a single center. Am J Med Sci. 2011; 342: 467-473.

30. Mok CC, Ying KY, Tang S, Leung CY, Lee KW, Ng WL, et al. Predictors and Outcome of Renal Flares after Successful Cyclophosphamide Treatment for Diffuse Proliferative Lupus Glomerulonephritis. Arthritis Rheum. 2004; 50: 2559-2568.

31. Croca SC, Rodrigues T, Isenberg DA. Assessment of a lupus nephritis cohort over a 30-year period. Rheumatology. 2011; 50:1424-1430.

32. Wallace DJ, Podell TE, Weiner JM, Cox MB, Klinenberg JR, Forouzesh S, et al. Experience with 230 patients in a private practice from 1950 to 1980. Am J Med. 1982; 72: 209-220.

33. Moroni G, Quaglini S, Gravellone L, Gallelli B, Leoni A, Messa P et al. Membranous Nephropathy in Systemic Lupus Erythematosus: Long-term Outcome and Prognostic Factors of 103 Patients. Semin Arthritis Rheum. 2012; 41: 642-651.

34. Adler M, Chambers S, Edwards C, Neild G, Isenberg D. An assessment of renal failure in an SLE cohort with special reference to ethnicity, over a 25-year period. Rheumatology. 2006; 45: 1144-1147.

35. Martens HA, Bijl M, Kallenberg CG. Prognostic value of renal hemodynamic characteristics in patients with proliferative lupus nephritis. Kidney Blood Press Res. 2007; 30: 175-181.

Citation: Ariba YB, Ajili F, Maïza M, Louzir B and Labidi J. Lupus Nephritis: Clinical Characteristics and Prognostic Factors. J Nephrol Kidney Dis. 2018; 2(2): 1017.
https://dx.doi.org/10.36876/smjnkd.1017