

RENAL BIOPSY IN LUPUS NEPHROPATHY: GENERAL FEATURES AND PREDICTORS OF BAD PROGNOSIS

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ABSTRACT

Introduction: Lupus nephritis is one of the most serious manifestations of systemic lupus erythematosus (SLE). It's responsible for a high morbid-mortality in young subjects. The aim of our study is to establish lupus nephritis epidemiology in our population, histological features and predictive factors of proliferative and active injuries and predictors of bad prognosis.

Results: Were enrolled 71 biopsies finding lupus nephritis among 700 kidney biopsies conducted in our nephrology department during the period of 6 years (10.14%). The average age of patients was 32.69 ± 11.48 years. A female predominance was observed (sex-ratio =0.2). The main indication for biopsy was the concomitant existence of proteinuria, hematuria and renal failure (48%). In univariate analysis, we retained as predictive factors of proliferative and active form: spring season flare with a maximum in June, pre-existing lupus nephritis, lymphopenia and nephrotic syndrome. Risks of progression to chronic renal failure were: female gender in 90% of cases ($p < 0.001$), hypertension at admission ($p < 0.004$), positive anti-Nuclear and anti- DNA Antibodies ($p < 0.04$), renal failure at admission ($p < 0.0001$). Morbidity associated with lupus nephritis is related to female gender ($p < 0.001$), hypertension ($p < 0.001$), renal failure at admission ($p < 0.001$) and need for hemodialysis ($p < 0.001$).

Conclusion: Lupus nephritis is severe in our series of 71 biopsies, with a high frequency of proliferative forms. Looking out the stigma of renal involvement during the disease progression and largest reflection of renal biopsy indications could improve the diagnosis and the management of LN.

Keywords: Classification, Lupus Nephritis, Renal Biopsy, Spring, Predictive Factors, Prognosis.

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INTRODUCTION

The systemic lupus erythematosus is a polymorphic autoimmune systemic disease. It is characterized by a succession of outbreaks leaving various effects depending on the severity of outbreak and injury type.

Lupus nephritis is one of the most serious manifestations of systemic lupus erythematosus (SLE). It is responsible of a high morbi-mortality in young subjects.

Renal biopsy is an essential step in lupus nephritis management strategy. It contributes to diagnosis, prognosis evaluation and therapeutic choice. It specifies histological injury and their extent; establish their classification and determine active and chronic signs. Greater precision is ensured by

immunological labeling techniques providing a better approach to this disease.

Lupus Kidney damages are mostly glomerular. They are defined by the International Classification ISN / RPS 2003. However, tubular, interstitial and vascular injuries can be found. Hormonal, immunological and genetic factors in lupus pathogenesis has been suggested by several studies, but the environmental nature is poorly understood and few studies have been able to establish causal links, particularly solar exposure, geographical and seasonal distribution of outbreaks.

The aims of our study were:

- 1 Establish lupus nephritis epidemiology.
- 2 Analyze histological features especially their proliferative and active distribution.
- 3 Look for predictive factors of proliferative and active injuries.
- 4 Identify predicting factors of bad prognosis.

MATERIAL AND METHODS

Study Diagram

This study was retrospectively conducted in both nephrology- transplant -hemodialysis department and Pathology Laboratory of Hassan II^d University Hospital for a period of six years, from January 2008 until December 2013.

Patients

We selected patient records with lupus nephritis injuries in renal biopsy in order to study clinical, biological, immunological and outcomes parameters. Subsequently, Clinical, biological and histological showdown has been carried out to confirm the renal impairment of lupus.

Inclusion criteria: Were enrolled all patients older than 16 years and whose clinical and biological data meet at least four criteria of "the American College of Rheumatology (ACR)" for diagnosis of systemic lupus erythematosus and whose renal biopsy concluded lupus nephritis.

Exclusion criteria: Were excluded from our study

- Children under 16 years
- Renal biopsies performed in other hospitals.
- Patients followed in other health services.

Compiling data

Were selected all renal biopsies concluding for lupus nephritis from the anatomo-pathologic registry of our nephrology departement. The histo-immunologic and pathologic data were collected from renal biopsies records.

All biopsies were examined within the Anatomic pathology laboratory by light microscopy and direct immune-fluorescence technique.

Demographic, clinical and laboratory Data were collected from medical records and the HOSIX-NET information system installed since 2011.

Variables

We studied the following parameters:

- Date of renal biopsy: month, year, seasons. The four seasons were defined as follows: Winter (22 December- March 21), Spring (22 March-

21 June), Summer (22 June-21 September) and Fall (September 22 -December 21).

- Medical background: High blood pressure, Miscarriages, lupus.
- Discovery Circumstances:
- Already known lupus:

 - 1 Lupus nephritis is newly suspected or relapse of a preexisting renal impairment.
 - 2 Onset lupus: revealed by an acute renal injury, nephrotic syndrome, non-nephrotic proteinuria.

 - At admission we sought:

 - 1 Hypertension: defined by a systolic and / or diastolic blood pressure 140/90 mmHg.
 - 2 Microscopic hematuria on dipstick then confirmed by cytological examination of urine defined by the presence of 5 RBCs/mm³ without any urinary tract infection and menstruation.
 - 3 Proteinuria on dipstick and confirmed by dosing on two 24 hours urine samples. It is considered positive if the flow is >300 mg / day and nephrotic if the flow is >3 g / day.
 - 4 Renal impairment defined by a serum creatinine 12mg / l.

 - Among extra-renal lupus group, we noted all cutaneous, arthritis, hematological, neurological and cardiac impairment occurred during the follow-up period.
 - Laboratory tests for SLE disease activity include the following:

 - 1 Antibodies to double-stranded DNA (ds DNA), antinuclear antibodies and anti-phospholipid antibodies.
 - 2 Complement (C3, C4) seeking hypocomplementemia

Lupus nephritis is staged according to the classification revised by the International Society of Nephrology (ISN) and the Renal Pathology Society (RPS) in 2003[1], as follows:

- Class I – Minimal mesangial lupus nephritis
- Class II – Mesangial proliferative lupus nephritis
- Class III – Focal lupus nephritis (active and chronic; proliferative and sclerosing)
- Class IV – Diffuse lupus nephritis (active and chronic; proliferative and sclerosing; segmental and global)
- Class V – Membranous lupus nephritis
- Class VI – Advanced sclerosis lupus nephritis

Lupus nephritis activity is classified according to the HILL score:

Glomerular Activity Index	
Glomerular proliferation	0-3
Polymorphonuclear leucocytes	0-3
Fibrinoid necrosis	(0-3)x2
Cellular crescents	(0-3)x2
Hyaline deposits	(0-3)
glomerular monocytes	(0-3)
Maximum	24
Tubular-interstitial Activity Index	
Tubular cell pyknosis	0-3
Tubular nuclear activation	0-3
Tubular cell necrosis	0-3
Tubular cell flattening	0-3
Macrophages in tubular lumens	0-3
Epithelia cells in tubular lumens	0-3
Interstitial inflammation	0-3
Maximum	21
Chronic Lesions Index	
Glomerulonecrosis	0-3
Glomerular scars	0-3
Fibrous crescents	0-3
Tubular atrophy	0-3
Interstitial fibrosis	0-3
Maximum	15
Immunofluorescence Index	
Glomerular capillary IF	(0-4)x6
Glomerular mesangial IF	(0-4)x6
Tubulointerstitial IF	(0-4)x6
Vascular IF	(0-4)x6
Maximum	96

We have defined three groups of patients based on:

- Histological class: two groups were defined. A group of patients with proliferative lupus nephritis (Class III+ IV). The second with a non-proliferative lupus nephritis (Class I, II, V and VI).
- Activity signs on renal biopsy defining an active form group and a non-active form group.
- Concomitant proliferative injuries and active lesions defining a group of active and proliferative form.
- Unfavorable evolution is evaluated by searching death and renal function assessment at the last consultation. Chronic renal failure is defined by a creatinine clearance <60 ml / min / 1.73 m².

Statistical analysis

Statistical analysis is performed in laboratory of epidemiology and clinical research of the Medicine and Pharmacy school of Fez. We used the SPSS version 17.0 software. This study is initially descriptive and analytic. Quantitative variables are expressed as mean ± standard deviation of the mean, and were compared using the Student test. Categorical variables were expressed as numbers and percentage and compared by Chi tests 2. A p value <0.05 was considered significant. Univariate analysis is then used to determine the predictive criteria of active lesions and / or proliferative renal biopsy and the risk factors for adverse developments.

Results

Since 2008, 71 patients were followed in our nephrology department for confirmed lupus nephritis on renal biopsy, it represent 10.14% of all renal biopsies performed in our department during this period (n = 700). The average age of patients was 32.69 ± 11.48 years, with extremes ranging from 16 years to 70 years. A female predominance was observed (sex-ratio 12H/59F (0.2)). The number of patients recruited for renal biopsy increase by years with the increasing number of patients hospitalized in the department since its opening in 2009. Maximum of biopsies is noted in 2011 (Fig. 1).



Fig. 1: Distributions of renal biopsies according to the execution year

The largest number of biopsy is performed during June with a total of 13 biopsies, followed by March with 9 biopsies (Fig. 2). In spring-time season, we noted the largest number of kidney biopsies concluding for lupus nephritis (Fig. 3).

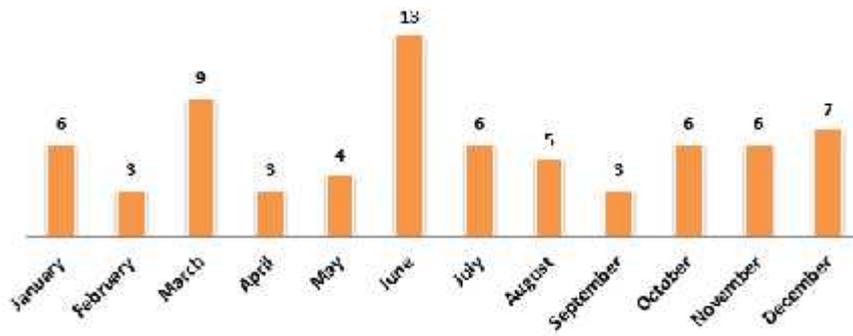


Figure 2: Distribution of biopsies by month

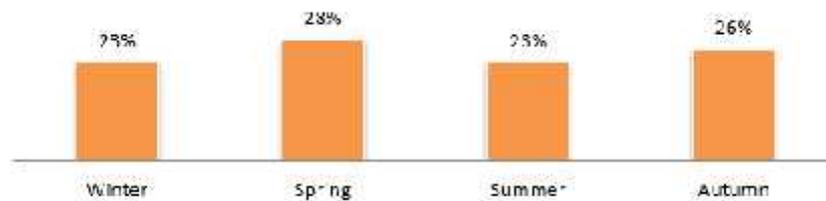


Figure 3: Distribution of patients according to seasons

Renal biopsy allowed the diagnosis and classification of lupus nephritis:

- De novo in an already diagnosed lupus in 13 patients (18.3%)
- Relapsed lupus nephritis in 32.4 % of cases.
- Concomitant systemic lupus and lupus nephritis diagnosed in 49.3% of cases (35 patients).

Among the histological classes of lupus nephritis, proliferative classes are mostly founded: class IV in 32.4% of cases and class III in 18.3% of cases. Membranous nephropathy was found in 9 patients while mixed membranous and proliferative lupus nephritis was described in a single patient (Table I). Histological activity was found in 36 renal biopsies (50.7% of cases).

Table I: Distribution of patients according to their lupus nephritis class

Lupus Nephritis Class	n	%
I	8	11,3
II	14	19,7
III	13	18,3
IV	23	32,4
V	9	12,7
V+IV	1	1,4
VI	3	4,2

Nephrotic syndrome is the first reason of reference to nephrologists (32.4% whose 3 are pure), followed by non-nephrotic proteinuria (6 patients) and acute renal failure (5 patients). Lupus nephritis is suspected in 13 patients during the follow-up of their systemic lupus while a relapse is suspected in 23 patients (Fig. 4).

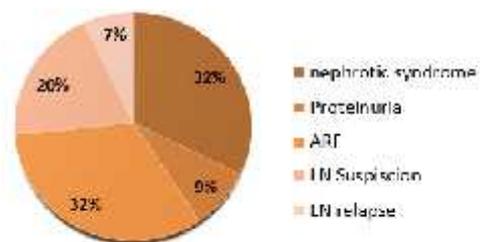


Figure 4: Distribution of patients according to their consultation pattern

On admission, 37 patients (61%) had nephrotic syndrome and 6 (50%) had rapidly progressive glomerulonephritis. Extra-renal symptoms was dominated by hematological damages in 84% of cases and whose anemia was mostly present (95%). Hypocomplementemia for free fractions of C3 and / or C4 complement was found in 50 patients (70%), antinuclear antibodies in 54 patients (76%) and anti-DNA antibodies in 50 patients (70%). The clinical and biological characteristics are shown in Table II.

Table II : Clinical and biological parameters

Parameters	Results n (%)
Renalimpairment	
Hypertension	26 (36,6)
Microscopic hematuria	26 (52,1)
Nephrotic proteinuria	37 (61)
Proteinuria (g/j)	3,4 ± 2,2
Creatinine (g/l)	22,37 ± 25,5
Renal Failure	38 (53,5)
Extrarenal impairment	
Skin	50 (70)
Articular	50 (70)
Haematological	59 (84,2)
Cardiac	13 (18,3)
Neurologic	5 (7)
Immunological tests	
Hypocomplementemia	50 (70)
Antinuclear	54 (76)
Anti-DNA	50 (70)
Antiphospholipid	9 (12,6)

The main indication for renal biopsy in our series is the association of proteinuria, hematuria and renal failure (34 patients=47.8%), while it was motivated by an isolated proteinuria in 17 (23.9%) patients. The different indications of renal biopsy are summarized in **Fig. 5**.

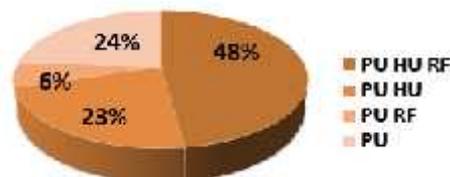


Fig. 5: Kidney biopsy indications

PU:proteinuria HU: hematuria RF: renal failure

The progression of Renal function until the end of the study is marked by persistence of chronic renal failure in 26 (36.6%) patients, hemodialysis setting in 9 patients (12.6%) including 8 (11.26%) in end stage of renal disease. However, a death occurred among 9 patients (12.6%) (3 pulmonary embolisms, 2 cardiogenic shocks, 1 septic shock and one patient died in an array of seizures).

In univariate analysis, proliferative forms are statistically linked to an active form in 43.7% of patients ($p < 0.001$) (**Table III**).

Table III : Histological Correlations

Histological form	Active form	Non active form	Total
Non proliferative form	7%	41%	48%
Proliferative form	44%	8%	52%
Total	51%	49%	100%

To find predictive factors of proliferative and active form, we compared clinical and biological parameters between the two groups (**Table IV**). In univariate analysis, the following factors were sustained: spring season flare with a maximum in June, pre-existing lupus nephritis, lymphopenia and nephrotic syndrome. In multivariate analysis, predictive factors of an active and proliferative form are: spring season flare [6] ($p < 0.04$; OR = 4.4, CI (1.4-18.8)) with a significant female predominance, and nephrotic syndrome ($p < 0.06$; OR = 2.6, CI (0.9-7.4)).

However, the clinical, pathological and biological correlations demonstrate that proliferative forms occur most often with renal failure (31%), hematuria (39%), hypocomplementemia (46.7%) and positive immunological tests. These parameters are not statistically significant. There was no statistical significance in the correlation between biopsy indication and histological classes.

In univariate analysis, risks of progression to chronic renal failure were: female gender in 90% of cases ($p < 0.001$), hypertension at admission ($p < 0.004$), positive anti-Nuclear and anti-dsDNA Antibodies ($p < 0.04$), renal failure at admission ($p < 0.0001$). Needs hemodialysis for ESRD is correlated to female sex ($p < 0.004$), hypertension and renal failure at admission ($p < 0.02$ and $p < 0.002$ respectively).

In univariate analysis, Morbidity associated with lupus nephritis is related to female gender ($p < 0.001$), hypertension ($p < 0.001$), renal failure at admission ($p < 0.001$) and need for hemodialysis ($p < 0.001$). 32.4% of patients have consulted for lupus nephritis relapse but only 17 (23.94%) have already received a first kidney biopsy. These relapses occur particularly in winter ($p = 0.039$). There was no significant difference between patients of this group neither on clinical symptoms or biological ones and neither on renal function progression or mortality.

However, they presented a statistically significant low rate of c3 ($p = 0.021$). 64.7% ($n = 11$) of cases showed a proliferative form at the first renal biopsy (8 cases of class IV) of which 54.5% of cases remained proliferating on the second kidney biopsy but not statistically significant (**Table V**). In Two cases, nephropathy has progressed from non proliferative class to proliferative one.

Table IV: Clinical, biological and evolutionary parameters

Parameters	Proliferative forms n= 37	Active forms n= 36	Active and proliferative forms n=31	
Seasons	Winter n=16	9,86%	9,86%	7,04%
	Spring n =20	18,31%	19,72%	18,31%
	Summer n=16	15,49%	12,68%	11,27%
	Autumn n=19	8,45%	8,45%	7,04%
Age	Under 24 years	15,49%	15,49%	14,08%
	Over 24 years	36,62%	35,21%	29,58%
Gender	Female n=52	43,66%	40,85%	38,03%
	Male n=12	8,45%	9,86%	5,63%
MiscarriageATCD n=10	8,45%	8,45%	7,04%	
Known Lupus n=36	26,76%	26,76%	21,13%	
Known LN n=23	14,08%	15,49%	9,86%	
Hypertension n=26	18,31%	18,31%	14,08%	
Skin n=50	36,62%	35,21%	29,58%	
Cardiac n=13	8,45%	5,63%	5,63%	
Articular n=50	36,62%	36,62%	29,58%	
Neurologic n=5	2,82%	1,41%	1,41%	
Haematological n=59	46,48%	42,25%	38,03%	
Neutropenia n=7	5,63%	5,63%	5,63%	
Lymphopenia n=17	15,49%	14,08%	14,08%	
Anemia n=56	43,66%	39,44%	35,21%	
Thrombocytopenia n=15	11,27%	14,08%	11,27%	
AAN n=54	38,03%	38,03%	33,80%	
DNA n=50	35,21%	35,21%	30,99%	
APL n=9	7,04%	7,04%	7,04%	
C3 consumed n=48	39,44%	38,03%	33,80%	
C4 consumed n=33	25,35%	23,94%	22,54%	
RF n=38	30,99%	29,58%	23,94%	
Hematuria n=51	39,44%	36,62%	30,99%	
NephroticPu n=37	32,39%	30,99%	28,17%	
HD n=9	8,45%	9,86%	7,04%	
CRF n=26	21,13%	21,13%	16,90%	
Death n=7	5,63%	7,04%	5,63%	

Table V: Iterative biopsies

First biopsy	Second biopsy	Activity	Chronicity
GNMP	IV	+	-
I	II	-	-
I	IV	+	-
II	II	-	-
II	I	-	+
II	III	+	+
III	III	+	+
III	III	-	+
IV	V	+	+
IV	III	-	+
IV	V	-	-
IV	II	-	-
IV	II	-	+
IV	IV	-	+
IV	V+IV	+	-
V	V	-	-
V+IV	V	+	+

DISCUSSION

Renal damages occur in 30-75% of SLE patients according to criteria used to define renal disease [2, 3]. Early onset lupus nephritis happened in 50% of cases; however, it can occur late in the history of the disease. Lupus signs were previously unknown, unexplored or mistaken for another illness in 49.3% of our patients. The female prevalence and more

particularly in youth is reported by several national and international studies and also in our series (83% of cases). (Table VI^o) reports the female prevalence and the average age in different series of literature. However, age less than 33 years and male gender are considered as factors of early and severe renal impairment whose are not be found in our series in which the female gender is significantly related to worse kidney outcomes[4-6].

Table VI: Female prevalence and the average age in different series in the literature

Autors	Country/City	LN Cases	Female %	Age Average (Yr)
Constans [36]	Bordeaux	61	-	33
Sidappa [37]	India	62	79	30
E-F.Ka [38]	Dakar	43	93	33
Béji [39]	Tunis	211	93	29
Benhmida [40]	Sfax	20	-	31
Saidi [41]	Sfax	31	87	30
Arzour [42]	Algeria	278	92	33
Zellama [43]	Sousse	47	75	32
Lemrini [44]	Casablanca	16	-	35
Nasri [45]	Marrakech	105	95	-
Zbiti [35]	Rabat	114	89	30
Our Series	Fez	71	83	32.69

In our study, we investigated the possibility of influence of seasonal and climatic variations on the occurrence of severe lupus flare associated with renal impairment. We found that there is a clear predominance of relapses during the spring and more particularly in proliferative and active forms of LN. This predominance tends to progressively

increase during the spring, reaching a maximum on the first fortnight of June. This seasonality is always present even in the absence of cutaneous flare. Similar results were published in the study L. Chiche and al (Marseille) and the Hasan and al (Finland), which suggest a worsening activity disease during the summer uncorrelated with

photosensibility or skin involvement [7, 8]. They refer in their studies that the first sun exposure could have a greater impact on the occurrence of relapses compared to prolonged exposure during the summer. In other words, never UV exposed patients are more prone to develop a lupus flare than patients how have been broader exposed to UV especially in summer. In contrast, previous work by Amit and al. [9] and Hagat and al [10], could not show any seasonal pattern of lupus flares except for photosensitivity. In the United States, Schlesinger and al found a higher number of patients with LN class V during spring and winter seasons compared to summer and autumn [11]. However, the Stetzo and al study found seasonal variation in the incidence of the LN thrust class V with a peak incidence in December and January. [12]

Proteinuria is the most common manifestation of lupus nephritis, observed in 100% of cases and reaching the nephrotic syndrome (> 3 g / 24 hours) in 45-65% of cases. Microscopic hematuria was noted in 80% of lupus kidney disease, it may appear

at any time of disease progression [4, 13]. In our study, nephrotic syndrome was the most common mode of revelation (53.2%) and significantly correlated with active and proliferative kidney damage and with a worse vital and renal prognosis. Extra-renal symptoms frequency in our series is similar to the other series with or without nephropathy; it is dominated by articular, mucosal and cutaneous symptoms [14, 15]. However, in our study, we described more frequent hematologic disorders which the lymphopenia was found as a predictive factor for active and proliferative form. A high frequency of renal failure was found in our series (53.5% of cases), it reflect the seriousness and severity of the LN. Indeed, renal failure is frequently occur in 40 to 80% of patients depending on the cohorts. This RF is often chronic, only 1 to 2% of patients had an acute kidney failure and 30% had rapidly progressive kidney failure [4,13,16]. It mostly occurs late in SLE evolution. (Table VII) summarizes the frequency of renal symptoms reported by some studies.

Table VII : Extra-Renal Symptoms

Authors	Proteinuria g/24h	Nephrotic syndrome %	Hematuria %	RF %	HTA %
Constans [36]	-	-	-	41	-
Sidappa [37]	3,64	-	-	11	-
E-F.Ka [38]	2,01	-	-	17	-
Arzour [42]	-	-	15	70	-
Benhmida [40]	3,6	55	60	45	20
Béji [39]	3,47	47,7	75,3	51,6	32,3
Lemrini [44]	-	-	-	81,2	-
Zbiti [35]	3,5	88	-	60,2	70
Our Series	3.4	61.5	52.1	53.5	36.6

Serological parameters observed in patients with severe LN reach up the hypothesis of immune complex pathogenesis. Almost all patients with severe forms of LN especially IIIrd or IVth Classes have active serology: high titers of auto antibodies and hypocomplementemia [17,18]. In our study, more than half of patients have positive tests; their presence is correlated with active and proliferative forms.

Kidney biopsy [1, 19] is worthwhile in all patients with lupus who have abnormal urine and/or reduced renal function. Renal histology cannot be predicted with any certainty from the clinical picture, although severe glomerular forms of nephritis have a tendency to result in more severe clinical manifestations. Renal biopsy should be performed at any suspicion of renal disorder in lupus disease [20]. In renal failure cases, biopsy is not discussed. Most authors recommend biopsy in cases with a proteinuria greater than 500 mg / 24h [21]. A retrospective study found that 77% (16 of 21) of SLE patients with proteinuria <1000 mg / 24h had an authentic LN. In addition 37.5% of patients with

proteinuria <500 mg / 24H had a Class III LN. The latest KDIGO recommendations published in 2012 "KDIGO Clinical Practice Guideline for Glomerulonephritis" do not specify the proteinuria threshold from which the renal biopsy should be performed in a lupus patient. However, they define proteinuria by a rate between 0.3-1.5 g per 24 hours, and it becomes nephrotic if it exceeds 3.5g / day associated with hypoalbuminemia[22]. Confirmed microscopic hematuria without urinary infection, is also suggestive of kidney damage and often signs his proliferative character.

We believe that the realization of a reactive dipstick looking for proteinuria and hematuria, and an assay of plasma creatinine must be systematically monitored at least by 6 month during lupus systemic remission. The "silent nephropathy" is rare and its significance is not certain. In our series, the concomitant presence of proteinuria, hematuria and renal failure was the most frequent indication for renal biopsy (48% vs 24% of isolated proteinuria). Histological distribution is similar between our study and other series. Diffuse proliferative forms

are predominating varying from 27 and 53% of cases, the classes I and II reach maximum 19% and Class V between 7 and 25% [23, 24].

In our study, there was no statistically significant correlation between clinical and anatomic damages except the nephrotic syndrome whose is correlated with active and proliferative form. However, in the series S. Beji, nephrotic syndrome is more common in classes IV and V and kidney failure is more common in classes IV and III [23]. Renal failure is more common in proliferative form in our study than the other groups (34% vs 29% and 24% in active form and proliferative active form) it can be explained that pure forms cause renal failure more than mixed forms.

Frequency of Histological changes is difficult to determine, it is reported in 10-54% of cases (50% in the series of S. Béji [23] and 64.7% in our series). These transitions are more common from Class III to class IV in 20 to 40% of cases. The passage of a Class V to Class III or IV is described in only 7% of cases [25].

Lupus nephritis leads to kidney failure in 10-15% of cases despite immunosuppressive therapy developed in recent decades [19]. In a French retrospective study, [14,26] renal failure or hypertension, the presence of proliferative lupus GN (Class III and IV), and a non-Caucasian ethnicity are correlated to a poorer prognosis of lupus nephritis. In our series, 36.6% of patients progressed to chronic renal failure which 11.2% goes in chronic hemodialysis.

Several observations show that SLE goes off when the renal disease leads to kidney failure. SLE dialysis patients have the same survival rate if comparing to other dialysis patients (14). The mortality rate is 12% in our series and 17% in S. Béji [23] study. Several factors of bad renal prognosis have been reported in different studies. These are: age <24 years, male gender, hypertension, nephrotic syndrome, initial renal failure, anemia, low levels of C3, anti-DNA (+), class IV, interstitial fibrosis, activity index > 9 [27]. Some of these factors were found in our series.

CONCLUSION

Lupus nephritis is severe in our series of 71 biopsies, with a high frequency of proliferative forms. The main indication for renal biopsy was the concomitant existence of proteinuria, hematuria and renal failure. Looking out the stigma of renal involvement during the disease progression and largest reflection of renal biopsy indications could improve the diagnosis and the management of LN. Seasonality of active and proliferative forms found in our study and in several series in the literature confirms the polymorphism of this

autoimmune disease and supports the need for an overall and complete approach. The diagnosis of LN must be a real reflection conducted jointly by nephrologists and pathologists.

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