Long Term Outcome of Lupus Nephritis in SLE in Oman

DR TASNEEM AL RASHDI, DR JUMA AL KAABI

¹[Department of Rheumatology, Sultan Qaboos University Hospital]

ABSTRACT

- **Objective.** To study the histopathological pattern of lupus nephritis, long term outcome and identify the predictors of poor outcome among SLE patients in Oman.
- **Methods.** This retrospective study included 94 patients diagnosed with biopsy proven lupus nephritis hospitalized between 1995 and 2016 at a single center. The revised WHO classification of lupus nephritis was used to score the type of lupus nephritis on renal biopsy. Patients were treated as per standard protocol. Demographic, clinical, laboratory, therapeutic and end-point data were collected. Data are shown as the mean+/- SD. Kaplan-Meier survival curves and long rank test were used for survival analysis. Predictors of poor outcome are identified using the Cox regression analysis.
- **Results.** 94 patients were included in the study with a female to male ratio of 5.7:1. The majority had nephritis at presentation or within 6 months of diagnosis of SLE. The long-term outcome was calculated for all 94 patients and the median duration of follow up was 8 years interquartile range [IQR] 6-14 years during which 16 patients developed ESRD and 7 patients died. Treatment response was based on PCR and creatinine level on last follow up, hence, 50% achieved complete remission, 9.5% had partial remission and 16% had active nephritis. The overall renal survival at 5, 10 and 15 years was 86.9%, 73.8% and 68.6% respectively. There is a statistically significant difference in survival distribution between histological class II and class V (p=0.036). However, there is no difference in renal survival between patients who had a renal biopsy and nonbiopsied patients. Risk factors for poor outcome (CKD, ESRD or death) on multivariate cox regression analysis were onset to nephritis, elevated dsDNA and presence of infection.
- **Conclusion.** our study is the first in Oman to address the outcome of lupus nephritis in Omani population. Results showed similar outcome to what reported in different parts of the worlds and the most common histopathological class was class IV. Duration of SLE till onset of nephritis, dsDNA and infection were risk factors for poor outcome.

BACKGROUND

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the production of various autoantibodies directed against self-antigens. Tissue injuries and subsequent organs damaged ensue resulting in various clinical manifestations of the disease. Renal involvement is quite common and up to 60% of patients with SLE will develop renal disease during the course of their disease and progression to end stage renal disease (ESRD) can occur in up to 48% of patients at 5 years. The presentation of lupus nephritis (LN) is highly variable ranging from clinically silent nephritis to rapidly progressive disease with acute renal failure. In 3% to 6% of cases LN constitute the initial presentation of SLE and this may precede the other symptoms of lupus by years.

Despite the improved over all SLE survival over the last decays, patients with LN still succumb into chronic renal failure and death. Several studies have shown consistently, the mortality rate is higher in SLE patients with LN than those without renal involvement.

Epidemiological studies in SLE with LN, have pointed out demographic, clinical and histological features associated with worse prognosis.

Among the strong predictors of poor outcome is the histological pattern of LN. Diffuse proliferative (WHO class IV) of LN usually follows a progressive course to CRF without early and adequate treatment. A 17% 5-year survival without treatment has been reported. Further outcome analysis published between 1990-2013, WHO class IV still leads to ESRD in 10-26% of patients.

OBJECTIVES

We have no published data about LN in Omani patients yet. Thus, this study aims to provide information on the histological pattern, overall renal survival and the predictors of poor outcome of lupus nephritis patients in Oman and compare them with studies from other parts of the world.

SUBJECTS AND METHODS

- It is a retrospective study that was carried out at a tertiary hospital, Sultan Qaboos University Hospital, in Oman.
- Total of 103 patients presented between 1995 and 2016 and fulfilled the American College of Rheumatology classification criteria for SLE with evidence of lupus nephritis were included. (This included patients who did and did not have a histologically proven biopsy, however 9 patients who had their biopsy done in another center were excluded from the study).
- From the laboratory tests protein/creatinine ratio (PCR), creatinine, glomerular filtration rate at the time of nephritis and yearly till last follow up were obtained
- Histological class of lupus nephritis was defined based on the WHO classification of lupus nephritis.
- The response of treatment: based on laboratory records on last follow up patients were categorized using the EULAR criteria into
- 1) **complete response:** defined as PCR <0.5 and normal or near normal GFR (within 10% of normal GFR if previously abnormal),
 - 2) **partial response:** >50% reduction in proteinurea to sub-nephrotic level and normal or near normal GFR,
 - 3) **active renal disease:** neither 1 or 2 with normal creatinine,
 - 4) **chronic renal failure:** serum creatinine >1.5mg/dl for more than 3 months.
- Long-term outcome:
- Poor renal outcome measure were:
- CKD (serum creatinine >1.5mg/dl for >3months),
- ESRD (dialysis dependent)
- and death.
- Immunosuppressive medications used for induction therapy included corticosteroids, cyclophosphamide or mycophenolate mofetil and for maintenance therapy, majority of our patients received mycophenolate mofetil.

RESULTS

Table 1. Baseline characteristics of the patients with lupus nephritis (n=94)

Variable	n (%)
Sex	
Male	14 (14.9)
Female	80 (85.1)
Age at diagnosis of SLE, Mean±SD years	20.65±8.60
SLE to nephritis duration, median (min-max) years	0.50 (0-20)
Low C3 (<0.9 g/dl)	64 (68.1)
Low C4 (<0.1 g/dl)	35 (37.2)
Elevated dsDNA (>100 IU/L)	71 (75.5)
Elevated creatinine (>1.5mg/dl)	2 (2.1)
High PCR (>3g)	33 (35.1)
Low Hb (<11.5 g/dL)	85 (90.4)
Low PLT (<150 10 ⁹ /L)	12 (12.8)
Biopsied	
Class II	11 (11.7)
Class III	7 (7.4)
Class IV	40 (42.6)
Class V	23 (24.5)
Class VI	0 (0)
Nonbiopsied	13 (13.8)

Table 1.

The mean age at diagnosis of SLE was 20 years and the majority had nephritis at presentation or within 6 months of diagnosis of SLE.

Laboratory investigations collected at onset of nephritis showed that 64% of the patients had low complement level 3 < 0.9g/dl, 70% had elevated dsDNA >100IU/L, 33% had high PCR >3 and only 2% had elevated creatinine > 1.5mg/dl at onset of nephritis. Percutaneous renal biopsy was available for 81 (86.2%) out of 94 patients and the most common histopathological class was class IV (42.6%).

RESULTS

•Figure 1. Kaplan-Meier curve for renal survival (CKD, ESRD and death were considered as the hard end points). The overall renal survival at 5, 10 and 15 years was 86.9%, 73.8% and 68.6% respectively.

•Figure 2. Kaplan-Meier curves for renal survival in the different histologic classes and non-biopsied patients. P<0.05 by the log rank test between class II and V. There is however, no difference in renal survival between patients who had a renal biopsy and non-biopsied patients.

RESULTS

Table 2. Final outcome in different histologic classes (n=94)

	Total	Class II	Class III	Class IV	Class V	Non biopsied
Total	94	11	7	40	23	13
Complete remission	47	11	7	15	8	6
Partial remission	9	0	0	6	1	2
Active nephritis	15	0	0	7	7	1
Chronic renal failure	16	0	0	9	4	3
Death	7	0	0	3	3	1

•Table 2. The long-term outcome was calculated for all 94 patients and the median duration of follow up was 8 years interquartile range [IQR] 6-14 years during which 16 patients (17%) developed CKD and 7 patients (7.4%) died. Treatment response was based on PCR and creatinine level on last follow up, hence, 50% achieved complete remission, 9.5% had partial remission and 16% had active nephritis. All patients with class II and III LN achieved complete remission compared to patients with class IV and V LN whom around 35% achieved complete remission. 30% of class IV lupus nephritis had poor outcome (defined as CKD, ESRD and death).

Table 3. Cox regression analysis of risk factors leading to poor outcome (CKD, ESRD or death)

Variable	HR (95% CI)	p value
Female sex	0.329 (0.116 - 0.930)	0.036*
Age at diagnosis of SLE, years	1.032 (0.976 - 1.091)	0.267
Onset to nephritis duration, years	1.211 (1.081 - 1.356)	0.001*
Low C3 (<0.9 g/dl)	2.414 (0.696 - 8.378)	0.165
Low C4 (<0.1 g/dl)	0.645 (0.218 - 1.904)	0.427
Elevated dsDNA (>100 IU/L)	8.107 (1.247 - 52.711)	0.028*
Elevated creatinine (>1.5mg/dl)	3.192 (0.315 - 32.305)	0.326
High PCR (>3)	0.838 (0.327 - 2.152)	0.714
Low Hb (<11.5 g/dL)	0.508 (0.040 - 6.517)	0.603
Low PLT (<150 10 ⁹ /L)	0.256 (0.049 - 1.328)	0.105
Presence of infection	4.975 (1.428 - 17.336)	0.012*

Table 3. Risk factors for poor outcome on multivariate cox regression analysis were **onset to nephritis, elevated dsDNA and presence of infection**. There is a 21.1% increase in the expected HR relative to a year increase in onset of SLE to nephritis duration, holding all other factors constant (p=0.001). The expected hazard is 8.1 times higher in patients with elevated dsDNA (p=0.028) and 4.9 times higher in patients who had an infection as compared to patients who did not have (p=0.012).

CONCLUSIONS

Our study is the first in Oman to address the outcome of lupus nephritis in Omani population. Results showed similar outcome to what reported in different parts of the worlds and the most common histopathological class was class IV. SLE to onset of nephritis duration, high dsDNA and infection were risk factors for poor outcome.