In the name of God

Shiraz E-Medical Journal

Vol. 6, No. 1 & 2, January and April 2005

http://semj.sums.ac.ir/vol6/jan2005/lupusnephritis.htm

The Clinical and Pathological Findings Among Patients with Lupus Nephritis in Shiraz, Southern Iran.

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Abstract:
Systemic lupus erythematosus is a chronic, debilitating autoimmune disorder that involves multiple organ systems. Nephritis is a component of systemic lupus erythematosus that influence the long-term outcome of the patients and remains the leading cause of death in theses patients. This study was performed to evaluate the demographic, clinical, and histopathological features of Iranian patients with lupus nephritis in Shiraz, Iran. A retrospective survey was performed on 200 patients with renal involvement and SLE who referred to Rheumatology Research Center of Shiraz University of Medical Sciences since 1976. Among 35 patients (17.5%), renal biopsy was not performed and excluded from the study. Patients' medical recording files were reviewed for demographic, clinical presentation of SLE, development of nephritic syndrome, renal failure, end stage renal disease (ESRD) during nephritis, the mortality rate and probable causes of death. The mean age of the patients was 23.36±9.2 years at the time of diagnosis of SLE. Among the 200 performed biopsies, 35 cases had failure. The remaining 165 patients had the following WHO classification: class I in one, class II in 30, class III in 33, class IV in 58, and class V in 43 patients. The most frequent clinical presentations of SLE were arthralgia, edema, and skin rash. The mean value of SLE activity index (SLEAI) was 8.9. There may be differences of clinical and histopathological manifestations of SLE and lupus nephritis considering geographical distribution of the patients.

Key Words: Systemic lupus erythematosus, Lupus nephritis, Clinical manifestations, Renal biopsy.

Introduction:

Systemic lupus erythematosus is a chronic, debilitating autoimmune disorder with unknown etiology that is characterized by the involvement of multiple organ systems[1]. Some systems that are more commonly involved include the central and peripheral nervous systems, lungs, heart, skin, serous membranes, hematological system, and the kidneys[1]. Other systems

were reported to be involved too, but the prevalence of their involvement was too much lower. The disorder occurs more commonly in women especially in the childbearing ages[2], with a female to male ratio between 8-13 to one[3].

William Osler was the first one who described nephritis as a component of systemic lupus erythematosus (SLE)[4]. Despite the great improvements in the diagnosis and treatment of SLE in the past 50 years, including the emergence of corticosteroids, antihypertensive drugs, antibiotics, dialysis, immunosuppressive drugs (such as cyclophosphamide, etc), and renal transplantation, nephritis remained the leading cause of death among patients with SLE[4]. Today, lupus nephritis is responsible for growing percentages of cases with end stage renal failure that need dialysis or renal transplantation.

Glomerulonephritis is a frequent complication of SLE and the presence and severity of renal involvement greatly influence the long-term outcome of the patients. Lupus nephritis has been extensively studied during the last 20 years5-8 and renal biopsy results were classified according to WHO[9] and other institutes (such as National Institute of Health [NIH][10]) descriptions. The WHO classification system, consider six histological classes and their subtypes for renal involvement in SLE patients[9]. It has one of the worst outcomes of the other lupus subsets and despite aggressive therapies frequently results in end stage renal disease and shortens the life expectancy of the patients[11]. The frequencies of the histopathological classes have been reported to be different among Iranian patients, with higher than expected frequency of membranoproliferative glomerulonephritis[12].

Considering the above-mentioned facts and considering the fact that there was no exact data about these disorders and its subtypes in our geographical region, we decided to evaluate the demographic, clinical, and histopathological factors among the Iranian patients with lupus nephritis and their probable differences with the WHO reports.

Materials and Methods:

This study, which was a retrospective survey, was performed on 200 patients with renal involvement and SLE who referred to Rheumatology Research Center of Shiraz University of Medical Sciences since 1976. In 35 patients (17.5%), renal biopsy was not performed and was excluded from the study. The suggested criteria of American College of Rheumatology (ACR) were used to diagnose the patient who had lupus nephritis.

Patients' medical recording files were reviewed and data about their sex, place of birth, age at diagnosis of SLE and lupus nephritis and at the time of biopsy, WHO histological classes of biopsy specimens, and SLE activity index (SLEAI)[13] at the time of renal biopsy were obtained.

The patients' clinical presentation of SLE, development of nephritic syndrome, renal failure, and end stage renal disease (ESRD) during nephritis, mortality rate and the probable cause of death were obtained too.

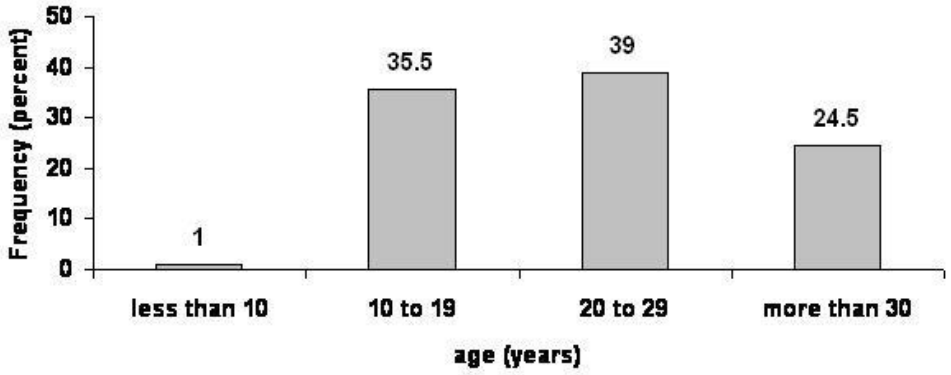
The obtained data about patients' clinical symptoms and their histopathological manifestations of biopsy specimens were entered a PC and analyzed by Chi Square and Analysis of Variance tests using SPSS WIN 10.0 software. P value less than 0.05 was considered as significant.

Results:

Among the 200 patients with lupus nephritis, 170 patients (85 percent) were female and 30 patients (15 percent) were male (female to male ratio 5.7:1). The mean age of the patients was 23.36±9.2 years at the time of diagnosis of SLE and 24.35±9.2 at the time of onset of lupus nephritis (With a range of 5 to 70 years). There were no statistically significant differences between male and female patients considering their ages at the time of diagnosis of SLE and onset of lupus nephritis (P value >0.05). The mean interval between diagnosis of SLE and onset of lupus nephritis was one year with a

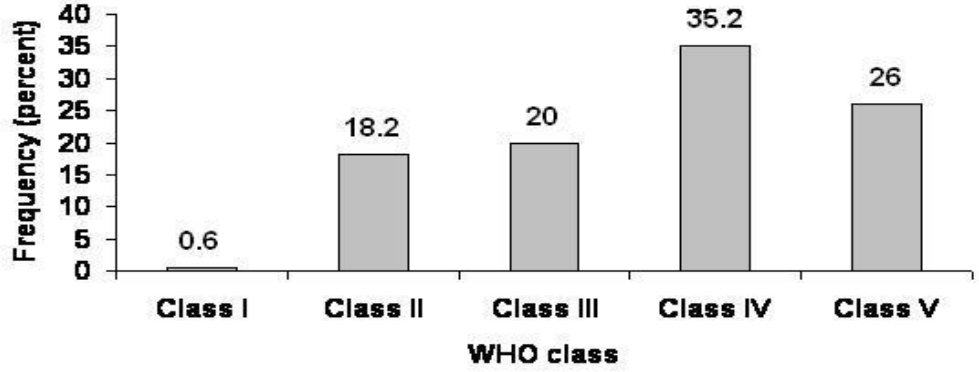
minimum of about four months. The peak age of diagnosis of lupus nephritis was 20 to 29 years (Figure 1).

Figure 1. Age distribution of the studied patients



Among the 200 performed biopsies, 35 cases showed failure. The remaining 165 patients had the following WHO classification: class I in one (0.6%); class II in 30 (18.2%); class III in 33 (20%); class IV in 58 (35.2%); and class V in 43 patients (26%; Figure 2).

Figure 2. Frequency of different who classes in the studied patients.



The most frequent clinical presentations of SLE were arthralgia (23.2 percent), edema (23 percent), and skin rash (13.5 percent; Table 1). The most frequent combination of symptoms was arthralgia and skin rash.

Table 1. Clinical manifestations of SLE in the 200 studied patients with lupus nephritis.

Manifestation	Frequency (Percent)
Arthralgia	88 (23.3)
Edema	87 (23)
Rash	57 (13.5)
Fever	49 (12.9)
Ascitis	21 (5.5)
Fatigue	16 (4.2)
Dyspnea	15 (4)
Flunk pain	6 (1.6)
Diarrhea	5 (1.3)
Weight loss	4 (1)
Alopecia	4 (1)
Hematuria	4 (1)
Dysuria	3 (0.8)
Psychosis	3 (0.8)
Pleural effusion	3 (0.8)
Abdominal pain	3 (0.8)
Convulsion	2 (0.5)

Chest pain	2 (0.5)
Purpura	2 (0.5)
Vomiting	2 (0.5)
Myalgia	1 (0.3)
Bone pain	1 (0.3)
Oral ulcer	1 (0.3)
Headaches	1 (0.3)
Dizziness	1 (0.3)
Pneumonia	1 (0.3)
Heart failure	1 (0.3)
Epistaxis	1 (0.3)
Raynauds' phenomenon	1 (0.3)

The mean value of SLE activity index (SLEAI) was 8.9 (8.72-9.84). There was no statistically significant difference between SLEAI in different histological classes of SLE nephritis. Prognosis of the patients in the class IV groups was worse than the patients in other groups. Among 5 patients who died during the study, 4 patients had class IV lupus nephritis. The frequencies of some clinical conditions in different classes were presented in Table 2.

Table 2. Frequency of some manifestations of lupus nephritis in the studied patients.

	Class I	Class II	Class III	Class IV	Class V
Hyper tension (%)	-	13.3	48.5	41.4	32.6
Renal Failure (%)	-	3.3	3	10.3	9.3
Nephrotic syndrome (%)	-	10	27.3	32.8	37.3
End stage renal disease (%)	-	-	3	5.2	7
Death (%)	-	-	-	6.9	2.3

Discussion:

Among the 200 patients who underwent renal biopsies in our study, 85 percent were female and 15 percent were male. This male to female ratio was approximately equal to other reports about sex ratio of SLE11, 14-17. The mean age of the patients at the time of diagnosis of SLE in our study was lower than the similar reports[6, 8, 11, 18]. The mean age of the patients at the time of onset of SLE nephritis was lower compared to other reports[6, 11, 19, 20]. In our study, there were not any statistically significant differences between mean age of male and female patients at the time of diagnosis of SLE and onset of lupus nephritis. This finding was in contrast with the report of another study, in which the lupus nepthritis occurred earlier in female patients than male ones[15]. The mean time interval between diagnosis of SLE and onset of nephritis in our study was lower than the reports made by Neumann et al. (1 year vs. 2.8±0.4 years, respectively)[11].

Distribution of different renal pathology classes in the above-mentioned study was comparable to other studies[6, 7, 11]. In majority of these studies, the patients in class IV lupus nephritis outnumbered other classes. The clinical manifestations of SLE in our patients were similar to other studies, performed by Leaker et al.[15] and Houman et al.[17,] but different with two other studies in which the most frequent clinical manifestations of SLE on the onset of SLE were arthritis and malar rash[21, 22]. These differences may be due to ethnic differences or difference in precision of the studies[17].

Although the SLE activity indices were different among patients in different pathology classes, these differences were not statistically significant. Considering this index, nothing was found in the literature to compare these values in different pathological classes of lupus nephritis.

The other evaluated clinical factors in the studied patients and their correlation with histopathological classes of lupus nephritis, the findings of this study were comparable with other studies[6, 8, 10, 11, 15, 17, 19].

Finally, considering the findings of this study and the findings of similar studies, it

is suggested that this study to be repeated with a larger sample size and with more clinical precision to find possible correlations between these clinical presentations and histopathological classes of lupus nephritis.

Acknowledgements:
The authors would like to thank the Office of Vice-Chancellor for Research of Shiraz University of Medical Sciences for financial support and Dr. Davood Mehrabani, Dr. SA Alavi, the Center for Development of Clinical Research of Nemazee Hospital for editorial and statistical assistance.

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