Original Article

Comparison Study on the Effect of Treatment Decision Based on Renal Biopsy and Clinical Symptoms in the Outcome of Patients with Recurrent Lupus Nephritis

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Abstract

Background: Renal involvement in systemic lupus erythematous is one of the most serious complications. The aim of this study was to compare the effects of treatment decisions based on clinical symptoms and renal biopsy on the outcome of patients with recurrent lupus nephritis. **Materials and Methods:** This descriptive study was conducted in 2012–13 in the Alzahra hospital on patients with lupus nephritis who had referred to the rheumatology clinic of this center due to lupus nephritis relapse. All lupus nephritis patients were diagnosed with renal biopsy and had gone into remission by treatment but due to the discontinuation of treatment and other causes had relapsed. The patients were divided randomly into two groups of 26, the first group was treated without renal biopsy and based on clinical and laboratory symptoms and the second group was re-biopsied through considering the ethical points. Then their relationship with laboratory findings (BUN, Cr, ANA, ds-DNA, C3, C4, CH50, U/A, cast, and proteinuria), treatment and recurrence outcome were compared between the two groups. **Results:** The mean of SLEDAI-2K index before initial treatment, after the first round of treatment and after the second round of treatment in single biopsy group and twice biopsy group is not significantly different (P = 0.27). **Conclusions:** Treatment decisions based on clinical and laboratory findings or re-biopsy of the kidney in patients who relapsed after initial treatment had no significant effect on the recovery of patients. Adoption of a treatment plan in patients with lupus nephritis is recommended based on clinical and laboratory finding and the discretion of the physician and if possible, kidney re-biopsy should be avoided.

Keywords: *Biopsy, lupus nephritis, recurrent*

Introduction

Systemic lupus erythematous (SLE) is an autoimmune disease of unknown etiology in which tissues and cells are injured by immune complexes and pathogenic autoantibodies. Renal involvement is one of the most serious and most common problems of patients in lupus susceptibility so that in America, approximately 35% of patients with SLE blurt lupus nephritis symptoms at the time of initial diagnosis, and 50–60% during the first 10 years of their disease.[1-4] Today, the World Health Organization classification methods for lupus nephritis have been accepted by most renal and pathology experts and severity of lupus nephritis which is assessed with SLEDAI-2K standard is the estimator of patients' future, but for the diagnosis of lupus nephritis patients we can't only rely on clinical findings such as proteinuria, increases in serum creatinine, and urinary active sediment, since clinical signs are not sufficient and reliable predictors to determine the nature of lupus nephritis.[6,7] Other kidney diseases that damage the kidneys tissue and create clinical symptoms should be evaluated and ruled out.[5] Renal biopsy is an essential step in determining the nature of renal involvement in SLE. The classification of lupus nephritis decision of treatment is strongly related to renal biopsy findings of these patients. According to the International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification, six conflict classes are defined for lupus nephritis.[8] However, some physicians believe that the clinical diagnosis of lupus nephritis is easily possible and without having histological evidences, we can evaluate the treatment and patient's prognosis.[8] Of course, this issue is controversial, and another group of physicians consider repeated renal biopsy

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as an obligatory for the certainty of disease even on proven lupus nephritis.[8] In addition, relapse occurs even after an initial complete remission in lupus nephritis.[9] A group of experts suggests renal biopsy as a proper approach for recurrent lupus nephritis[5,11-14] and others consider the need for repeating the biopsy, depending on the lupus nephritis in initial biopsy.[9] Patients with proliferative lesions in the initial biopsy rarely in recurrent lupus nephritis change into pure non-proliferative lesions and therefore do not need re-biopsy. But in patients with non-proliferative lesions on initial biopsy in the recurrence of lupus nephritis transfer to other classes is commonly observed and repeated biopsy is justifiable.[10] In addition, from the view point of treatment guidelines, there is no distinction between classes III and IV, thus class change of proliferative has no significant impact on treatment proceedings. Similarly, the addition or unperceptive of class V in second biopsy in a person who has a previous proliferative injury does not have significant impact on the treatment of choice.[15] Thus, the disease prognosis depends largely on proliferative lesions,[15,16] so only changing from proliferative form into non-proliferative forms i.e. class III to class V or vice versa which has treatment differences and different consequences and doing a biopsy enhance the chances of their detection and reinforces the biopsy theory. When attempt to re-biopsy is still controversial, continuous follow-up of patient along with periodic review (urine protein/creatinine ratio, increased creatinine and increased proteinuria) has great importance.[17,18] Therefore, based on the controversies that exist about the effectiveness of biopsy repetition, the present study was performed to determine the impact of treatment decisions and outcome of patients with lupus nephritis relapsed disease and its comparison with clinical symptom-based decisions.

Materials and Methods

This study is a descriptive analytical study which was conducted in 2012–13 in the Alzahra hospital. The population studies included patients with lupus nephritis who had referred to the rheumatology clinic of this center due to nephritis relapse treatment. Inclusion criteria were known risk for SLE according to the American College of Rheumatology (ACR) criteria, lupus nephritis on biopsy, relapse after previous remission, renal insufficiency at the time of reference, non-pregnant and the patient agreement to participate in the study. Also, in the case of patient withdrawal from further participation in the study and the absence of patients before the end of the treatment (e.g., death, immigration, etc.) they were excluded.

In this study, 52 patients with lupus nephritis who previously treated during the year 2012 and 2013 and their disease had relapsed again were divided into two groups of 26 each and assessment of disease severity and treatment program in the first group was determined based on clinical and laboratory feature and in the second group was determined based on re-biopsy of the kidney. All patients were studied after 3 and 6 months.

All lupus nephritis patients were diagnosed with renal biopsy and had gone into remission by treatment but due to the discontinuation of treatment and other causes have relapsed. The relapse of disease was determined due to the existence of proteinuria more than 0.5 g per day or more than 3+ on dipstick, cell casts like red blood casts in the survey of urinary sediment, random samples of urine protein to creatinine ratio was greater than 0.5 and active urinary sediment. The procedure was in a way that at the beginning, demographic data, clinical and laboratory symptoms and pathology results were extracted from the patients' files and registered in the special check list.

The first group was treated based on clinical and laboratory symptoms and the second group was treated based on re-biopsy. Biopsy specimens were studied with the light microscopy and divided based on Weber ISN/RPS (2003) criteria by a pathologist without the knowledge about the patients' status.[5]

Both groups, depending on the class of patients, underwent proper treatment so that at Class I and II or mild to moderate flares (stable SCr, subnephrotic proteinuria), prednisolone (0.5 to 1 mg/kg/day) for 4 to 6 weeks then if patient had gone to going to remission, the alternate day was reduced from 0.125 to 0.25 mg/kg if remission occurs. + azathioprine (AZA) 1–2 mg/kg/day + hydroxychloroquine 400 mg daily if after 3 months the patient did not remit, aggressive treatment was started.

In class IV ISN, class III or class IV + III, severe nephritic flares aggressive treatment was done with cytotoxic drugs including +1 gram methylprednisolone, MMF or IV cyclophosphamide therapy for 6 months and induction therapy +1 mg/kg/day prednisolon or equivalent for at least 4 weeks. In this method, a dose of cyclophosphamide 0.5–0.75/m^2 up to 1 g/m^2 with maintaining the levels of white blood cells higher than 3000/ml (for 7 to 10 days after infusion) for 6 months or mycophenolate mofetil MMF (cellcept) with doses of 250 to 500 mg started twice daily and increased to the dose of 2–3 gram per day. Then for the maintenance treatment of patients CsA (cyclosporin A), MMF, and AZA drugs were used. In order to treat of class V in the case of mild to moderate (pure membranous and proteinuria <2 g/day), low dose corticosteroids + ACE inhibitor and if mixed membranous and proliferative histology or the amount of creatinine in plasma during relapses increased 30% than before offensive treatment started. Then their relationship with laboratory findings (BUN, Cr, ANA, ds-DNA, C3, C4, CH50, U/A, cast and proteinuria), and treatment and recurrence outcome were compared between the two groups. It should be noted that in this study, data study were entered into the computer and analyzed by SPSS version 20 and *t* test and Chi-square test.

Results

In this study, 52 patients were selected and randomly divided into two groups of 26, the first group was treated without kidney re-biopsy and based on clinical and laboratory symptoms and the second group patients were re-biopsied. The mean age of patients in both groups the initial biopsy and repeated biopsy were 29.5 ± 13.38 and 24.65 ± 6.97 years, respectively (P = 0.11). Male/female ratio in above the two groups was 4/22 and 3/23 (P = 0.99), respectively. In Table 1, the treatment regime offered to patients in the two groups is shown. Based on the above table, 14 (53.8%) of one biopsy group and 8 (30.8%) of the two biopsy group were treated by cys + hcq + pred. Also, in one biopsy and two biopsy groups, nine patients (34.6%) were treated by "cellcept + Hcq + pred" and the frequency distribution of the treatment type in this group was not significant (P = 0.21)

The mean of SLEDAI-2K index before initial treatment, after the first round of treatment and after the second round of treatment in single biopsy group and twice biopsy group is shown in Table 2. According to this table, before the initial treatment, the mean of disease activity index in both single and double biopsy groups showed no significant difference (P = 0.27). The treatment plan was adopted for patients in both groups based on the severity of the disease. Three months after the treatment, mean of disease activity index decreased in both groups and no significant differences were observed between the two groups (P = 0.39), but 6 months after the treatment disease activity index had statistical significant differences and was significantly higher in two biopsy groups (P = 0.007).

Also, repeated measures ANOVA showed that changes in disease severity until 6 months after starting the treatment had no significant difference in two groups (P = 0.33). The distribution of SLEDAI-2K index in the two groups is shown in Figure 1.

In Figure 2, the percentage of biopsy frequency class before treatment is shown divided into two groups. According to this chart, the most common class in pre-treatment at single biopsy class V with the frequency of 14 cases (53.8%) and in the two biopsied group class IV was the most prevalent class of 9 cases frequency (34.6%) and according to the Fisher exact test, the difference between the two groups was significant (P = 0.043).

Also in Table 2, the mean and standard deviation of protein, BUN and 24-hour urinary protein and GFR of patients 6 and 3 months after treatment are shown in two and one biopsy groups. According to this table, no significant difference was observed between the average protein levels, BUN and creatinine (24 hours) and GFR in the two

Table 1: Drug regimen used in the two groups of patients

Groups	1 biopsy		2 biposy	
Drugs	***n***	**%**	***n***	**%**
Cellcept+Hcq+Pred	10	38.5	10	38.5
Aza+Hcq+pred	2	7.7	4	15.4
CYC+hcq+pred	12	46.1	9	34.6
CsA+HCQ+pred	2	7.7	3	11.5
Total	26	100	26	100

P=0.24

Table 2: The mean and standard deviation of 24-hour protein, BUN and urinary creatinine and GFR of patients 6 months after treatment

Variables	Groups time	1 biopsy	2 biopsy	*P* (between two groups in each time)
Disease activity index	Before treatment	18.19±8.08	20.29±7.95	0.27
based on SLEDAI-2K	3 months after	11.35±7.83	15.29±7.81	0.39
	6 months after	5.15±4.7	10.24±6.96	0.007
	P (between 2 groups in all time)	0.33		
Protein	Before treatment	1241.9±874.3	1729.6±1395.3	0.063
	3 months after	1245.9±1044.7	1191.8±1001.4	0.79
	6 months after	830.1±152.7	736.2±677.6	0.82
	P (between 2 groups in all time)	0.69		
Active UA	Before treatment	21 (80.8)	21 (80.8)	1
	3 months after	18 (69.2)	17 (65.4)	0.77
	6 months after	8 (30.8)	9 (34.6)	0.77
	P (between 2 groups in all time)	0.47		
Creatinine	Before treatment	1.019±0.44	1.07±0.7	0.38
	3 months after	0.99±0.46	0.98±0.30	0.27
	6 months after	0.90±0.35	1.43±1.76	0.19
	P (between 2 groups in all time)	0.24		
GFR	Before treatment	92.45±39.02	81.57±3426	0.29
	3 months after	95.79±44	90.72±97.7	0.29
	6 months after	98.41±11.16	96.33±48.42	0.67
	P (between 2 groups in all time)	0.67		

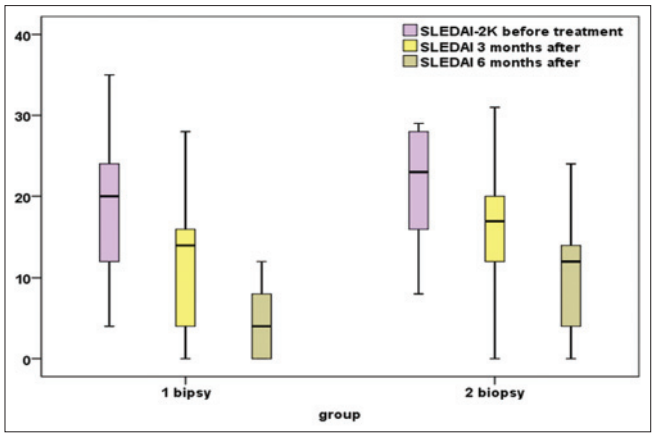

Figure 1: Distribution of SLEDAI score between two groups

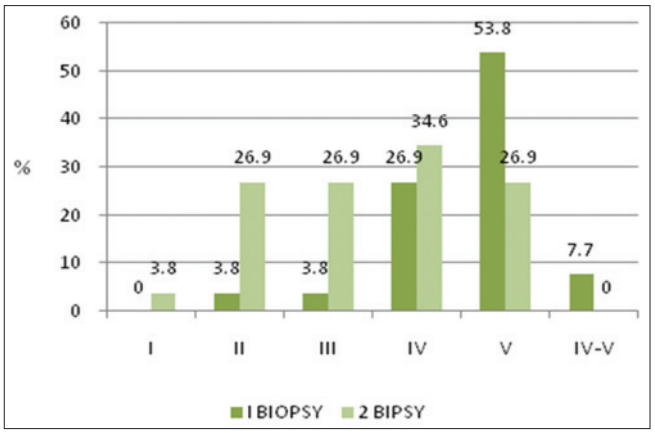

Figure 2: Frequency distribution of biopsy class in two groups

groups patients before the treatment, and 3 and 6 months after the treatment between once and twice a biopsy. Also, according to ANOVA with repeated observations the changes of the mentioned parameters before and 6 months after the treatment was not significantly different between the two groups.

Urine analysis of patients at three studied periods showed that the severity of proteinuria in the 3 and 6 months after the treatment in all studied patients dropped and 6 months after the treatment, the reduction of proteinuria severity in two biopsied groups was significantly higher than the single biopsy group (P = 0.03). The existence of blood in the urine during the treatment period in both groups had reduction, and despite the fact that at the beginning of treatment there were significant differences between the two groups but 3 and 6 months after treatment, no significant differences were observed between the two groups. According to the mentioned table, other parameters such as WBC, RBC, and cast were decreased in both groups during the treatment period but no significant difference was observed between the two groups. Finally according to Table 3, frequency distribution of remission in the first 3 months after the treatment, no statistically difference between one biopsy and two biopsies were seen (P = 0.52), but in the second 3 month follow-up, frequency distribution of remission in the one biopsy group was higher than the two biopsy (P = 0.012).

Frequency distribution of proliferative versus non-proliferative in the two biopsy group is shown in Table 4. Based on this table, no statistically difference between the before and after secondary biopsy (P = 0.13).

Regarding the urinary parameters and re-biopsy (in group II patients) at 3 months after the treatment, 8 patients from a single biopsy and 11 patients from two biopsied group went into complete remission (30.8% vs. 42.3%); in contrast, disease was still active in five patients of single biopsy group and six patient in two biopsied group (19.2% vs. 23.1%), but reduction in disease activity in 3 months after treatment in

Table 3: Frequency distribution of remission during study

Time	Groups level	1 biopsy *N* (%)	2 biopsy *N* (%)	*P*
3 months after	No remission	5 (19.2)	6 (23.1)	0.52
	Partial	13 (50)	9 (34.6)	
	Complete	8 (30.8)	11 (42.3)	
	4+	0 (0)	2 (7.7)	
6 months after	No remission	2 (7.7)	0 (0)	0.012
	Partial	5 (19.2)	14 (53.8)	
	Complete	19 (73.1)	12 (46.2)	

Table 4: Proliferative versus non-proliferative in two biopsy group

Reference Repeat	Non-proliferative *N* (%)	Proliferative *N* (%)
Non-proliferative	2 (20)	0 (0)
Proliferative	6 (60)	14 (87.5)
Glomerulosclerosis	2 (20)	2 (12.5)
Total	10 (100)	16 (100)

P=0.13

once or twice biopsy was not significant (P = 0.52). Six months after the treatment, 19 patients of a single biopsy group and 12 of two biopsied groups went to complete remission (73.1% vs. 46.2%) and there was statistical difference between the two groups seen (P = 0.0012). It should be noted that in following up the patients, 6 months after the treatment a patient of the two biopsied group, and a patient of the single biopsy group, despite the remission of patients in the second quarter, the disease relapsed again.

Discussion

The overall objective of this study was to compare the effects of treatment decisions based on clinical symptoms and renal biopsy on the outcome of patients with recurrent lupus nephritis. Previous studies and experiences have shown that renal biopsy due to the invasive nature, time consuming and expense is hardly accepted by the patients.

Many rheumatologists believe that initial biopsy is necessary to determine the pathology of kidney tissue, the grade of disease and extent of damage to the kidney tissue and the patient's treatment plan is arranged according to laboratory findings, pathologic and physical examination of patients due to various reasons such as the lack of continuity of treatment and follow-up release, etc. In many patients with lupus nephritis, the disease re-ignites and causes acute symptoms such as urea and creatinine and proteinuria and reduced renal function (GFR).[1]

According to our study, transforming from relapse to remission in 3 months after intervention, in the one or two biopsy groups was similar but 6 months later, in the one biopsy group was higher than the two biopsy group. Various rheumatologists believe that kidney re-biopsy is necessary in order to determine the severity of disease but there is no consensus since other rheumatology specialists believe that therapeutic decisions on recurrence level based on clinical and laboratory findings is sufficient for controlling the disease and pushing it to remission mode. On the other hand, studies have shown that approximately 35% of patients with SLE, show the symptoms of lupus nephritis at the time of initial diagnosis, and 50 to 60% at first 10 years of their disease[1-4] and for the detection of lupus nephritis usually one cannot only rely on clinical findings such as proteinuria, increase in serum creatinine, urinary active sodium in other words, these are not reliable clinical predictor for lupus nephritis nature.[6,7]

Based on the results of our study, the severity of the disease in both single and double biopsy regarding to treatment programs in the 3 and 6 months after the treatment was almost similar in the two groups, therefore, renal re-biopsy was not significant in the adoption of treatment provided to patients, thus according to the clinical findings and laboratory one can adopt an appropriate treatment for the patient and no need is felt for re-biopsy of the kidney.A study conducted by Yazdi *et al*. (2010) has also shown no significant difference between laboratory findings and histological findings of renal involvement in lupus nephritis.[21] Other results of our study showed that class switches during lupus nephritis flares were more frequent in patients with non-proliferative lesions in their re-biopsy but no proliferative lesions in the original biopsy switch to pure non-proliferative lesions in re-biopsy and no statistically difference between the first and second biopsies. One study that done by Daleboudt *et al*. showed that patients with proliferative lesions in the original biopsy rarely switch to a pure non-proliferative nephritis during a flare.[10] Therefore, a repeat biopsy during a lupus nephritis flare is frequently not necessary if proliferative lesions were found in the reference for over 25 years to perform a biopsy before treating renal flares.[19]

Our study showed that decrease in the severity of proteinuria, urine sediment and SCr and increase in GFR during the treatment period had similar results in both groups.

Providing a treatment program based on repeated biopsy or based on laboratory and clinical findings had no effect on patient remission. However, similar results were also obtained by Wang *et al*. and according to their study, repeated biopsy had no effect on the outcome of patients and no need was felt to repeat it. However, in the study of Wang, Yao and Hsieh it has been concluded that re-biopsy in patients with lupus nephritis may be beneficial in adopting the proper treatment.[19-21] Urinary parameters such as proteinuria, hematuria, WBC, RBC, and cast in both groups showed during the treatment period that there are no significant changes in these parameters. Finally, providing treatment based on renal re-biopsy in first group and clinical and laboratory findings in the second group had the same results in the treatment of patients, so that 3 months after treatment 13 patients from a single biopsy group and 9 of the twice biopsy group had gone on complete remission and review on 6 months after the treatment showed that in one biopsy group 19 patients and in two biopsy group 24 patients had gone into complete remission and in this interval the non-responders were 5 patient in the biopsy group and 6 patient in the two biopsy group.

Conclusion

Therefore, the overall conclusion that can be driven from this study is that treatment decisions based on re-biopsy of the kidney or clinical and laboratory findings in patients who relapsed after initial treatment had no significant effect on the recovery of patients and based on the results of this study the outcome was similar in the two groups and since re-biopsy damage the tissue of kidney thus is hardly accepted by patient and in addition to the expenses sometimes consumes the time and cause the resumption of therapy, adoption of a treatment plan in patients with lupus nephritis is recommended based on clinical and laboratory finding and the discretion of the physician and if possible, kidney re-biopsy should be avoided.

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Conflicts of interest

There are no conflicts of interest.

References

1. Dooley MA, Aranow C, Ginzler EM. Review of ACR renal criteria in systemic lupus erythematosus. Lupus 2004;13:857-60.
2. Kasitanon N, Magder LS, Petri M. Predictors of survival in systemic lupus erythematosus. Medicine (Baltimore) 2006;85:147-56.
3. Ward MM, Pyun E, Studenski S. Mortality risks associated with specific clinical manifestations of systemic lupus erythematosus. Arch Intern Med 1996;156:1337-44.
4. Alarcón GS, McGwin G Jr, Petri M, Reveille JD,

Ramsey-Goldman R, Kimberly RP; PROFILE Study Group. Baseline characteristics of a multiethnic lupus cohort: PROFILE. Lupus 2002;11:95-101.

5. Bihl GR, Petri M, Fine DM. Kidney biopsy in lupus nephritis: Look before you leap. Nephrol Dial Transplant 2006;21:1749-52.
6. Gladman DD, Urowitz MB, Cole E, Ritchie S, Chang CH, Churg J. Kidney biopsy in SLE: I. A clinical-morphologic evaluation. Q J Med 1989;73:1125-33.
7. Nossent JC, Henzen-Logmans SC, Vroom TM, Huysen V, Berden JH, Swaak AJ. Relation between serological data at the time of biopsy and renal histology in lupus nephritis. Rheumatol Int 1991;11:77-82.
8. Hsieh YP, Wen YK, Chen ML. The value of early renal biopsy in systemic lupus erythematosus patients presenting with renal involvement. Clin Nephrol 2012;77:18-24.
9. Sidiropoulos PI, Kritikos HD, Boumpas DT. Lupus nephritis flares. Lupus 2005;14:49-52.
10. Daleboudt GM, Bajema IM, Goemaere NN, van Laar JM, Bruijn JA, Berger SP. The clinical relevance of a repeat biopsy in lupus nephritis flares. Nephrol Dial Transplant 2009;24:3712-7.
11. Bajaj S, Albert L, Gladman DD, Urowitz MB, Hallett DC, Ritchie S. Serial renal biopsy in systemic lupus erythematosus. J Rheumatol 2000;27:2822-6.
12. Esdaile JM, Joseph L, MacKenzie T, Kashgarian M, Hayslett JP. The pathogenesis and prognosis of lupus nephritis: Information from repeat renal biopsy. Semin Arthritis Rheum 1993;23:135-48.
13. Lee HS, Mujais SK, Kasinath BS, Spargo BH, Katz AI. Course of renal pathology in patients with systemic lupus erythematosus. Am J Med 1984;77:612-20.
14. Moroni G, Pasquali S, Quaglini S, Banfi G, Casanova S, Maccario M, *et al*. Clinical and prognostic value of serial renal biopsies in lupus nephritis. Am J Kidney Dis 1999;34:530-9.
15. Sloan RP, Schwartz MM, Korbet SM, Borok RZ. Long-term outcome in systemic lupus erythematosus membranous glomerulonephritis. Lupus Nephritis Collaborative Study Group. J Am Soc Nephrol 1996;7:299-305.
16. Renal Disease Subcommittee of the American College of Rheumatology *Ad Hoc* Committee on Systemic Lupus Erythematosus Response Criteria. The American College of Rheumatology response criteria for proliferative and membranous renal disease in systemic lupus erythematosus clinical trials. Arthritis Rheum 2006;54:421-32.
17. Moroni G, Quaglini S, Maccario M, Banfi G, Ponticelli C. "Nephritic flares" are predictors of bad long-term renal outcome in lupus nephritis. Kidney Int 1996;50:2047-53.
18. Wiener C, Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, Loscalzo J. Harrison's principles of internal medicine, self-assessment and board review. McGraw Hill Professional; 2008 Jul 20.
19. 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 (Baltimore) 1999;78:148-66.
20. Wang GB, Xu ZJ, Liu HF, Zhou QG, Zhou ZM, Jia N. Changes in pathological pattern and treatment regimens based on repeat renal biopsy in lupus nephritis. Chin Med J (Engl) 2012;125:2890-4.
21. Rezaeieyazdi Z, Ghareh S, Ghaffarzadegan K, Maboodi A, Maboodi A. Correlation between histological findings, activity & choronicity indices and laboratory data in patients with lupus nephritis. JQUMS, 2010;14:5-11.