



# Lack of differences between morphological variables in age below 40 years versus more than 40 years in lupus nephritis patients

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## Abstract

This is a cross-sectional investigation, which was carried out on 127 kidney biopsy proven lupus nephritis cases by lupus nephritis classification of ISN/RPS 2003. We studied demographic data of all individuals comprising serum creatinine, 24 hours proteinuria, age and gender. Our study showed no difference of serum creatinine and 24 hours proteinuria and lupus nephritis (LN) classes between age below or equal to 40 versus more than 40 years old. In this study also, we found no significant difference of antibody deposited intensity of IgG, C3 and C1q in immunofluorescence study in age below or equal to 40 versus more than 40 years old. Accordingly, no significant difference of LN classes, activity or chronicity percent between ages below or equal to 40 versus more than 40 years old. Moreover, no significant difference of number of sclerotic glomeruli or crescents among patients with ages below or equal to 40 versus more than 40 years old were detected.

**Keywords:** Lupus nephritis, Systemic lupus erythematosus, Proteinuria

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## Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease which recognized by production of antibodies especially against nuclear antigens that involve multiple organs (1). SLE is more prevalent in women particularly in childbearing ages (2).

Kidney involvement is one of the most serious and frequent manifestation which involved 30-75% of patients and increase mortality and morbidity (3). The common features in lupus nephritis (LN) include raising in creatinine, proteinuria, hematuria, pyuria, urinary casts, and hypertension. Renal biopsy indicated as soon as observing decline in renal function. It is also indicated for follow-up (4). Multiple factors affect severity of SLE and LN (4). Age-onset is proved to impress activity, chronicity, severity, and even response to treatment (5). Researches from different countries estimated association between age-onset and activity, severity and chronicity of SLE and LE. Although there are controversies between the results (5-9). For example, in Portugal (6), Spain (8) and Korea (10) studies showed higher risk of activity, severity and chronicity of renal involvement due to SLE in childhood. However, in Canadian population. Various factors affect the outcome and treatment of LN for example we have a

gender difference (11). Accordingly, the length of the time between starting and treatment may have a prognostic affect (4). More over LN in old age versus young age may have prognostic implication regarding the intensity of morphologic lesions, demographic data and biochemical parameters. Thus in this study designed to compare a group of LN regarding age below and equal 40 and more than 40 years old.

## Objectives

We aimed to investigate the biochemical and morphological variables in age below 40 years versus more in a group of LN cases undergoing kidney biopsy.

## Patients and Methods

### Study design

This is a cross-sectional investigation that was conducted on kidney biopsies with the diagnosis of SLE to assess the LN classes and consequently selecting the proper treatment. This research followed our previous study (12), which was conducted on medical documents of cases that were diagnosed with LN at the beginning of treatment. The participants fulfilled the revised American College of Rheumatology (ACR) criteria for SLE as determined

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### ■ Implication for health policy/practice/research/medical education

Our study on 127 renal biopsy proven lupus nephritis showed no significant difference of lupus nephritis classes, activity or chronicity percent between ages below or equal to 40 versus more than 40 years old.

by their physicians (13). LN biopsies were classified corresponding to the 2003 ISN/RPS LN classification (14). This study was directed from January 2008 to January 2020.

The total number of our cases was 127 whose SLE was confirmed by rheumatologist or nephrologist based on SLICC (Systemic Lupus International Collaborating Clinics) SLE criteria and by kidney biopsy. For LN classes we conducted ISN/RPS 2003 criteria (15). This study is a continuation of the previously published article by the researchers of this report. However, the new analysis was focused on the impact of age on the LN, which was not addressed in the previous study, therefore the details of method and patients' selection was explain in the study by Tavassoli et al (16). For the statistical analysis, here we conducted student *t* test to analyze the age groups ( $\leq 40$  and  $>40$  years). Accordingly, a *P* value less than 0.05 was considered significance.

### Results

Medical records of 127 patients were assessed in which the mean age of the subjects was  $33.51 \pm 12.91$  years [78% females ( $n=99$ ) and 22% males ( $n=28$ )].

In the assessment of proteinuria and serum creatinine, means were  $1.56 \pm 0.91$  mg/dL and  $2369.18 \pm 1453.42$  mg/day, respectively.

According to results, the most common one was IV-G LN class ( $n=51$ ) followed by class III ( $n=27$ ). Our study had no significant difference between the LN classes of two ages of  $\leq 40$  years versus more than 40 years old group (Table 1).

We evaluated the data containing IgM, IgG, C1q, and C3 immunofluorescence results and their correlation with age. Evaluation of IgM, IgG, C1q, and C3 antibodies did not indicate meaningful relationship between their intensity with age ( $P > 0.05$ ; Tables 2-5). Accordingly, glomerular sclerosis, serum creatinine, crescent, disease chronicity, proteinuria and disease activity were not different across age group and genders ( $P > 0.05$ ; Table 6).

### Discussion

In study which designed by Wen et al in China, they compered 797 Chinese juvenile-onset, adult-onset, and late-onset SLE. They classified patients under 18 years of age in juvenile-onset, patients with the age between 18 to 50 in adult-onset and over 50 in late-onset group. They found that proteinuria was significantly higher in younger patients. Risk of rising in serum creatinine and hematuria is higher in juvenile-onset and adult-onset. Accordingly,

**Table 1.** Frequency of different lupus nephritis classifications by age group ( $\leq 40$  versus  $>40$  years)

Variable	$\leq 40$ Years	$>40$ Years	<i>P</i> value
I	2	0	
II	4	4	
III	23	4	
IV-G	36	15	
Lupus nephritis classes			0.759
IV-G+V	1	0	
IV-S	2	0	
IV-S+V	1	0	
V	17	5	
V+II	4	1	
V+III	5	2	
VI	1	0	

they showed younger patients are more susceptible to renal dysfunction (9).

Another study from Spain with 3619 patients diagnosed with SLE showed that LN are more common in younger patients. They also showed kidney involvement in form of proteinuria and urine cast are more common in younger group. However, they did not assess other biomarkers to estimate chronicity, severity and activity (8).

Additionally, Kim et al on childhood and adult onset indicated no significant association between age and renal disorders, proteinuria and cast in SLE patients (7).

Our study showed no significant difference of serum creatinine and 24 hours proteinuria and LN classes between both age group. We also found no significant difference of antibody deposited intensity of IgG, C3 and C1q in immunofluorescence study. Accordingly, no significant difference of LN classes, activity or chronicity percent between ages below or equal to 40 versus more than 40 years old. Moreover, no significant difference of number of sclerotic glomeruli or crescents among patients with ages below or equal to 40 versus more than 40 years old were detected.

### Conclusion

Our study also showed no difference of serum creatinine and 24 hours proteinuria and LN classes between ages below or equal to 40 versus more than 40 years old. In this study also, we found no significant difference of antibody deposited intensity of IgG, C3 and C1q in immunofluorescence study in age below or equal to 40 versus more than 40 years old. Accordingly, no significant difference of LN classes, activity or chronicity percent between ages below or equal to 40 versus more than 40 years old. Moreover, no significant difference of number of sclerotic glomeruli or crescents among patients with ages below or equal to 40 versus more than 40 years old were detected.

### Limitations of the study

This investigation was conducted in a single laboratory and requires further investigations by larger studies.

**Table 2.** Relationships between IgG grade by age groups ( $\leq 40$  versus  $>40$  years)

Variable		Score 0	Score 1	Score 2	Score 3	P value
Age group, No.	$\leq 40$ years	4	2	18	52	0.909
	$>40$ years	0	1	6	18	

**Table 3.** Relationships between IgM grade by age groups ( $\leq 40$  versus  $>40$  years)

Variable		Score 0	Score 1	Score 2	Score 3	P value
Age group, No.	$\leq 40$ years		30	26	20	0.349
	$>40$ years		5	12	8	

**Table 4.** Relationships between C3 deposit score by age groups ( $\leq 40$  versus  $>40$  years)

Variable		Score 0	Score 1	Score 2	Score 3	P value
Age group, No.	$\leq 40$ years	1	13	23	39	0.898
	$>40$ years	0	6	6	13	

**Table 5.** Assessments of C1q grade by age groups ( $\leq 40$  versus  $>40$  years)

Variable		Score 0	Score 1	Score 2	Score 3	P value
Age group, No.	$\leq 40$ years	3	19	27	27	0.939
	$>40$ years	0	8	8	9	

**Table 6.** Assessments of 24h proteinuria, serum creatinine, disease activity and chronicity by age groups ( $\leq 40$  versus  $>40$  years)

Variable		Mean	Std. Deviation	P value
24h proteinuria	$\leq 40$ years	2341.99	1514.62	0.712
	$>40$ years	2453.41	1264.10	
Serum creatinine	$\leq 40$ years	1.52	0.80	0.389
	$>40$ years	1.68	1.21	
Activity (%)	$\leq 40$ years	50.69	31.41	0.960
	$>40$ years	51.09	33.95	
Chronicity (%)	$\leq 40$ years	14.81	18.61	0.924
	$>40$ years	15.23	15.29	
Crescents	$\leq 40$ years	1.94	3.85	0.722
	$>40$ years	1.67	2.99	
Sclerotic glomeruli	$\leq 40$ years	1.93	4.67	0.171
	$>40$ years	3.54	7.99	

### Authors' contribution

Conceptualization, validation, resources, data curation, supervision, project management, funding acquisition: HN.

Methodology, formal Analysis: RV.

Investigation: NS and HN.

Writing—original draft preparation, writing—reviewing and editing: NT, HN, EM, RV and YR.

Visualization: HN and RV.

### Conflicts of interest

The authors declare that they have no competing interests.

### Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Isfahan University of Medical Sciences approved this study (IR.MUI.MED.REC.1399.1075). Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from M.D., thesis of Nasrin Tavassoli at this university (Thesis# 399973). The main part of this research was published previously; however, in this paper we only focused on the demographic, some biochemical and morphologic

variables of our patients below and over 40 years old, which was not mentioned in our previous publication (16). Additionally, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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