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Assessment of Interleukin-34 Serum level In Children with Systemic lupus Erythematosus

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ABSTRACT

Background: Pediatric-onset systemic lupus erythematosus (pSLE) is an autoimmune disease with multiorgan involvement and accounts for 15% to 20% of all systemic lupus erythematosus (SLE) cases. Systemic lupus erythematosus (SLE) is a multifactorial autoimmune disease characterized by variable immune dysregulation, disabling symptoms, and progressive organ damage. Interleukin (IL) -34 is a newly discovered cytokine that has no significant amino acid sequence homology to other cytokines.

Objective: This study aimed to assess interleukin-34 serum level in children with systemic lupus erythematosus.

Patients and Methods: This was a case-control study performed on 39 individuals divided into control group containing 13 healthy children and diseased group containing 26 children, which further subdivided into two diseased groups (one group classified as active SLE group and another group classified as inactive SLE group each group contained 13 children).

Results: In our study the age of the participant children were distributed as 9.46 ± 2.93, 9.07 ± 2.9 and 10.0 ± 3.22 for the control group, inactive and active SLE groups respectively with no significant difference among the studied groups regarding age. But regarding sex, females were majority among all the studied groups with no significant difference between all groups. Our study showed that malar rash was significantly associated with the active lupus nephritis (LN) group. In the current study, we found that serum Interleukin 34 was significantly higher among the active LN group followed by the inactive LN group and the control group was significantly lower.

Conclusion: The serum IL-34 level was significantly elevated in the SLE patients. IL-34 could be a potential disease activity marker, and this study might have revealed new insight for the study of SLE disease activity.

Keywords: Metabolic syndrome, Uric acid, Evaluation.

INTRODUCTION

Pediatric-onset systemic lupus erythematosus (pSLE) is an autoimmune disease with multiorgan involvement and accounts for 15% to 20% of all systemic lupus erythematosus (SLE) cases [1, 2]. SLE is a multifactorial autoimmune disease characterized by variable immune dysregulation, disabling symptoms, and progressive organ damage [3].

Although many of the clinical manifestations were similar with the adult onset form, lupus nephritis (LN) among the pediatric population has been suggested to differ from the adult onset cases for its abrupt onset, high prevalence, and relative poor response to current treatment regimen [4].

According to previous studies, as high as 50% to 78% of pediatric-onset systemic lupus erythematosus (pSLE) cases suffered renal damages [5] and 18% to 50% of these cases subsequently progressed to end-stage renal disease (ESRD) [6]. Additionally, WHO class IV diffuse proliferative glomerulonephritis, the subgroup known with the worst outcome, is the most common histopathological findings of LN among pSLE patients accounting for half (40%–55%) of the cases [7].

To date, invasive renal biopsy remains the gold standard in determining LN classification, directing therapeutic strategy and predicting treatment outcome [2].

Interleukin (IL) -34 is a newly discovered cytokine that has no significant amino acid sequence homology to other cytokines. [8] Currently, knowledge regarding this cytokine is limited. IL-34 shares a common receptor with macrophage-colony stimulating factor (M-CSF) [9]. Because IL-34 is an alternative ligand of the colony-stimulating factor-1 receptor (CSF-1R), IL-34 binds to CSF-1R and promotes the differentiation and proliferation of lymphocytes and the expression of cytokines, leading to inflammatory lesions and autoimmunity [8]. The study aimed to assess interleukin-34 serum level in children with systemic lupus erythematosus.

PATIENTS AND METHODS

This study was a case-control study that included 39 individuals. This study was conducted at Pediatric Department (Nephrology Unit), Zagazig University Hospitals.

Selected children were divided into two groups: Group A: healthy controls, and Group B: diseased children with SLE.

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Diseased children with SLE were subdivided into two groups: Group B1: children with active SLE disease, and Group B2: children with inactive SLE disease.

SLE children were diagnosed according to the revised American College of Rheumatology (ACR) classification criteria for SLE. They fulfilled at least 4 of the 11 criteria. SLE disease activity were determined using SLE disease activity index (SLEDAI) and renal biopsy.

Inclusion criteria:

1. Age: 2-18 years.
2. Gender: both males and females.

Exclusion criteria:

1. Age < 2 or > 18 years.
2. Children with systemic lupus erythematosus suffering any other autoimmune diseases, infectious diseases, tumors, diabetes and obesity.

Selected children were subjected to the following:

1. Full history taking.
2. Full general examination.
3. Laboratory investigations.
4. Serum interleukin-34 level.

Ethical approval:

An approval of the study was obtained from Zagazig University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation.

Statistical Analysis

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures were coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. According to the type of data, qualitative were represented as number and percentage, quantitative continues groups were represented as mean ± SD.

The following tests were used to test differences for significance; difference and association of qualitative variable by Chi square test (X^2). Differences between quantitative independent multiple by ANOVA and correlation by Pearson's correlation. P value was set at ≤ 0.05 for significant results & < 0.001 for highly significant result.

RESULTS

Age was distributed as 9.46 ± 2.93, 9.07 ± 2.92 and 10.0 ± 3.22 years respectively with no significant difference among the studied groups, also there was no significant difference regarding BMI, while females were majority among all the studied groups with no significant difference among all groups regarding the distribution of sex (Table 1).

Table (1): Age and sex distribution among the studied groups

			Control	Inactive SLE	Active SLE	F/X^2	P
Age (years)			**9.46 ± 2.93**	**9.07 ± 2.92**	**10.0 ± 3.22**	**0.298**	**0.744**
BMI (kg/m^2)			**25.87 ± 2.9**	**26.1 ± 4.25**	**25.74 ± 3.98**	**1.245**	**0.125**
Sex	**Male**	**N**	**5**	**3**	**2**		
		%	**38.5%**	**23.1%**	**15.4%**		
	Female	**N**	**8**	**10**	**11**	**1.88**	**0.39**
		%	**61.5%**	**76.9%**	**84.6%**		
Total		**N**	**13**	**13**	**13**		
		%	**100.0%**	**100.0%**	**100.0%**		

Table (2) showed that oral ulcers and fever were significantly associated with the active group and SLEDAI was significantly higher among the active group than the inactive group.

Table (2): Disease activity parameters findings among the diseased groups

			Group		$X^{2\ fisher}$	P
			Inactive SLE	Active SLE		
Malar Rash	**-VE**	**N**	**11**	**8**		**0.181**
		%	**84.6%**	**61.5%**		
	+VE	**N**	**2**	**5**	**1.75**	
		%	**15.4%**	**38.5%**		
Oral Ulcers	**-VE**	**N**	**13**	**8**		**0.038***
		%	**100.0%**	**61.5%**		
	+VE	**N**	**0**	**5**	**4.15**	
		%	**0.0%**	**38.5%**		
Arthritis	**-VE**	**N**	**12**	**9**		**0.112**
		%	**92.7%**	**69.2%**		
	+VE	**N**	**1**	**4**	**2.68**	
		%	**7.6%**	**30.8%**		
Vasculitis	**-VE**	**N**	**13**	**10**		**0.311**
		%	**100.0%**	**76.9%**		
	+VE	**N**	**0**	**3**	**1.98**	
		%	**0.0%**	**23.1%**		
Fever	**-VE**	**N**	**13**	**3**		**0.00****
		%	**100.0%**	**23.1%**		
	+VE	**N**	**0**	**10**	**22.11**	
		%	**0.0%**	**76.9%**		
CNS (seizures)	**-VE**	**N**	**13**	**11**		**0.55**
		%	**100.0%**	**84.6%**		
	+VE	**N**	**0**	**2**	**0.46**	
		%	**0.0%**	**15.4%**		
CVS (pericarditis)	**-VE**	**N**	**13**	**12**		**0.78**
		%	**100.0%**	**92.3%**		
	+VE	**N**	**0**	**1**	**0.33**	
		%	**0.0%**	**7.7%**		
Pulmonary (pleuritis)	**-VE**	**N**	**13**	**11**		**0.55**
		%	**100.0%**	**84.6%**		
	+VE	**N**	**0**	**2**	**0.46**	
		%	**0.0%**	**15.4%**		
Visual (Retinal vasculitis)	**-VE**	**N**	**13**	**12**		**0.78**
		%	**100.0%**	**92.3 %**		
	+VE	**N**	**0**	**1**	**0.33**	
		%	**0.0%**	**7.7%**		
SLEDAI			**4.29±0.18**	**18.21±2.85**	**7.87**	**0.00****
Total		**N**	**13**	**13**		
		%	**100.0%**	**100.0%**		

Table (3) and figure (1) showed that serum interleukin-34 levels were significantly higher among the active group followed by the inactive group and the control group was significantly lower.

Table (3): Serum interleukin- 34 levels among all groups

	Control	Inactive SLE	Active SLE	F	P
Interleukin 34	**42.83 ± 4.38**	**94.53 ± 31.9**	**658.84 ± 225.6**	**37.551**	**0.00****

P control with inactive =0.00** P control with active =0.00** P inactive with active =0.00**

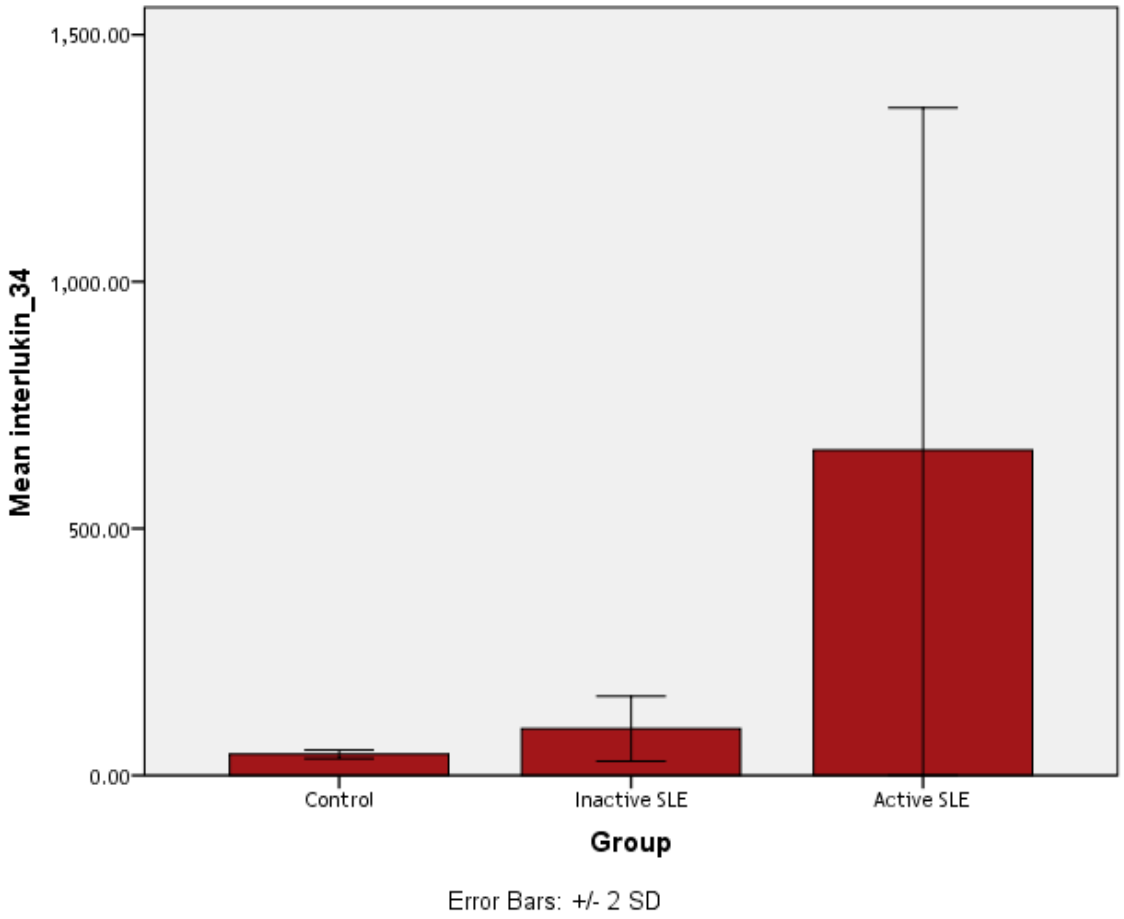

Figure (1): Serum interleukin- 34 levels among all groups

DISCUSSION

In our study the age of the participant children were distributed as 9.46 ± 2.93, 9.07 ± 2.9 and 10.0 ± 3.22 years in the control group, inactive and active SLE groups respectively with no significant difference among the studied groups regarding the age, but regarding the sex, females were majority among all the studied groups with no significant difference between all groups. This is consistent with the pSLE cohort of 96 patients of **Wu *et al.*** [(2)] who reported that there were 87 female and 9 male patients and the mean age of overall enrolled pSLE patients at the time of diagnosis was 12.74 ± 3.01 years (range, 4.07–14.80 years).

Our study showed that, malar rash was significantly associated with the active LN group and this agree with a longitudinal study of 241 pediatric SLE patients with skin disease, including malar rash, which showed higher renal and hematologic involvement both at the time of diagnosis and during follow-up [(10)]**. Živković *et al.*** [(11)] reported that the frequency of individual clinical manifestations at the time of examination was for arthritis/arthralgias 69.41%, skin changes 65.88%, serositis 24.70%, hematologic manifestations 24.70%, lupus nephritis 37.56%, and neuropsychic manifestations 18.82%, compared to 69% for arthritis/arthralgia, 61% for skin changes, 23% for serositis 60% for lupus nephritis 15% for neuropsychic manifestation in our study.

In the current study, we found that serum Interleukin 34 was significantly higher among the active LN group followed by the inactive LN group and the control group was significantly lower. This agrees with the study of **Xie *et al.*** [(12)] on 110 SLE patients that reported that serum IL-34 level was significantly elevated in the SLE patients compared to that in the healthy controls.

CONCLUSION

The serum IL-34 level was significantly elevated in the SLE patients. IL-34 could be used as a potential disease activity marker, and this study might have revealed new insight for the study of SLE disease activity.

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