Clinical and sub-clinical features in patients with systemic lupus erythematosus

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Abstract

Objectives: To describe the clinical and sub-clinical features in patients with Systemic Lupus Erythematosus (SLE) according to the criteria of the ACR/SLICC 2015, studying the relationship between clinical and sub-clinical features. **Methods:** This was a descriptive cross - sectional study of 74 SLE patients admitted to Nephrology – Rheumatology Department of Hue Central Hospital and General Medicine - Endocrinology Department of Hue University of Medicine and Pharmacy Hospital from March 2020 to March 2021. **Results:** Malar rash 70.3%, photosensitivity 66.2%, discoid rash 18.9%, non – scarring alopecia 75.7%, oral ulcers 21.6%, arthritis 54.1%, serositis 2.7%, neurology and/or psychosis damage 5.4%, kidney involvement 75.7%, hematologic: leukopenia 40.5%, lymphopenia 56.8%, thrombocytopenia 41.9%, hemolytic anemia 16.2%, positive ANA 74.3%, positive anti-dsDNA 64.9%. Positive ANA in non – scarring alopecia group was higher than the group without ($p < 0.05$); positive anti-dsDNA in malar rash group was higher than the group without ($p < 0.05$); the risk of kidney involvement was higher in the group with positive anti-dsDNA (OR = 3.1; $p < 0.05$), the rates of anemia and thrombocytopenia in kidney involvement groups were higher than the group without ($p < 0.05$). **Conclusions:** In this study cohort, the clinical, subclinical features according to the criteria of the ACR/SLICC 2015 that had the highest rate were non – scarring alopecia and kidney involvement, followed by malar rash, photosensitivity. ANA positivity in the non-scarring alopecia group was higher. Anti-dsDNA positivity in malar rash group was higher. The risk of potential kidney disorders was higher in the group with positive anti-dsDNA. The rates of anemia and thrombocytopenia in the potential kidney disorders group were higher.

Key words: *Systemic Lupus Erythematosus, ACR/SLICC 2015, ANA, anti ds DN.*

1. BACKGROUND

Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease with multisystem involvement characterized by antinuclear antibodies and other antigens. Organs that are often injured include joints, skin, kidneys, hematologic abnormalities, heart, lungs, nerves,... More than 90% of cases of SLE occur in women, frequently starting at childbearing age, between 20 and 40- year-olds [4].

Previously, the diagnosis of systemic lupus erythematosus was based on the criteria of the American College of Rheumatology 1997 (ACR 1997) [8]. This criteria was mainly based on clinical organ damages. Therefore, it tended to diagnose the disease at the late stage, when organ damages were already shown. In 2012, the Systemic Lupus International Collaborating Clinics (SLICC 2012) published new criteria [7], classified into two groups of clinical and biological manifestations, emphasizing immunological criterion, which allowed to diagnose systemic lupus erythematosus even when there were only immunological changes without clinical organ damages. In 2015, the ACR/SLICC published criteria, based on the framework of the 2012 SLICC criteria. Criteria were scored by points, emphasizing the role of common symptoms. Therefore, if a patient was admitted to the hospital with many clinical symptoms pointing to systemic lupus erythematosus without laboratory tests, the diagnosis could be based on this criteria [6].

The early detection and diagnosis of systemic lupus erythematosus based on clinical symptoms will help early treatment for patients. Therefore, we conduct the project: "Clinical and sub-clinical features of patients with systemic lupus erythematosus" with the following objectives:

1. To describe the clinical and sub-clinical features in patients with systemic lupus erythematosus according to ACR/SLICC 2015 criteria.

2. To study the relationship between clinical and subclinical features in patients with systemic lupus erythematosus

2. METHODS

2.1. Patients

It was a descriptive cross - sectional study

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including 74 SLE patients diagnosed in the Nephrology – Rheumatology Department of Hue Central Hospital and General Medicine - Endocrinology Department of Hue University of Medicine and Pharmacy Hospital during the period from March 2020 to March 2021.

All patients satisfied at least four of ACR/SLICC 2015 criteria for the classification of SLE [16].

2.2. Methods

Descriptive Cross - sectional study.

* Clinical variables

- Malar rash
- Photosensitivity
- Discoid rash
- Oral/nasal ulcers
- Arthritis
- Serositis
- Neurology and/or psychosis damage
- Non – scarring alopecia
- Kidney involvement
- Hemolytic anemia

*Sub-clinical variables:

- Complete blood count: anemia, hemolytic anemia, leukopenia, lymphopenia, thrombocytopenia
- 24 hour urine protein
- ANA and anti-dsDNA

Methods of data processing: The collected data were processed according to medical statistical algorithms, using SPSS 26.0 software.

3. RESULTS

3.1. Clinical and sub-clinical features in patients with systemic lupus erythematosus

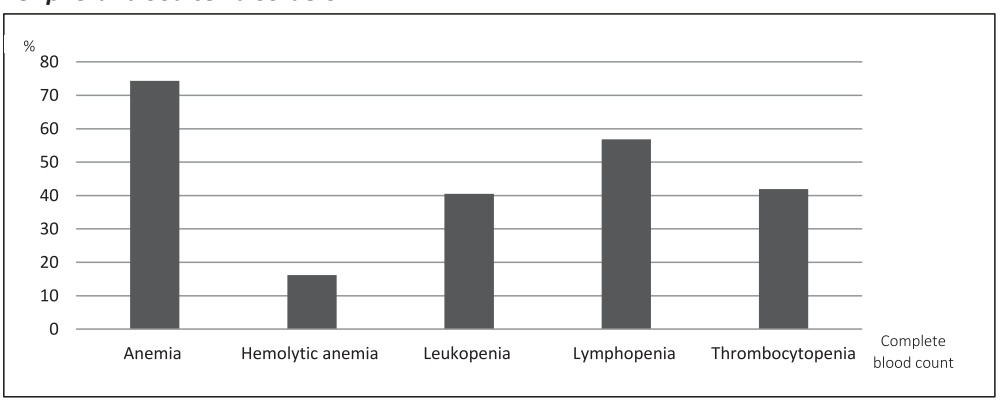
3.1.1. Clinical features

Table 1. Clinical features

Symptoms	n	%	Symptoms	n	%
Malar rash	52	70.3	Non – scarring alopecia	56	75.7
Photosensitivity	49	66.2	Arthritis	2	2.7
Discoid rash	14	18.9			
Oral/nasal ulcers	16	21.6	Kidney involvement	56	75.7
Arthritis	40	54.1	Neurology and/or psychosis damage	4	5.4

Comment: Kidney involvement and non – scarring alopecia accounted for 75.7%, malar rash accounted for 70.3%, photosensitivity accounted for 66.2%, arthritis accounted for 54.1%.

3.1.2. Peripheral blood cell disorders



Bar chart 1. Peripheral blood cell disorders

Comment: Anemia accounted for 74.3%, hemolytic anemia accounted for 16.2%, leukopenia accounted for 40.5%, lymphopenia accounted for 56.8%, thrombocytopenia accounted for 41.9%.

3.1.3. 24-hour proteinuria

Table 2. 24-hour proteinuria

24-hour proteinuria (g/24h)	n	%	± SD
< 0.5	18	24.3	0.2 ± 0.13
0.5 – 3.5	27	36.5	7.12 ± 9.45
> 3.5	29	39.2	

Comment: 56/74 patients who had proteinuria level > 0.5 g/24h accounted for 75.7% and the average of 24-hour proteinuria concentration in this group was 7.12 ± 9.45 g.

3.1.4. Distribution of ANA and anti-dsDNA

Table 3. Distribution of ANA and anti-dsDNA

Tests	Positive			Negative	
	n	%	± SD	n	%
ANA (OD ratio)	55	7.3	2.92 ± 4.09	19	25.7
Anti-dsDNA (U/ml)	48	64.9	76.49 ± 104.75	26	35.1

Comment: Positive ANA accounted for 74.3% and the average of OD ratio was 2.92 ± 4.09; positive anti-dsDNA accounted for 64.9% and the average concentration was 76.49 ± 104.75 U/ml

3.2. The relationship between clinical and subclinical features in patients with systemic lupus erythematosus

3.2.1. The relationship between clinical features and immunological tests

Table 4. The relationship between clinical features and immunological tests

Symptoms		ANA positivity		p	Anti-dsDNA positivity		p
		n	%		n	%	
Malar rash	Yes	37	67.3	0.337	30	62.5	**0.047**
	No	18	32.7		18	37.5	
Photosensitivity	Yes	35	63.6	0.425	28	58.3	0.051
	No	20	36.4		20	41.7	
Discoid rash	Yes	11	20.0	0.686	12	25.0	0.070
	No	44	80.0		36	75.0	
Oral/nasal ulcers	Yes	14	25.5	0.173	10	20.8	0.823
	No	41	74.5		38	79.2	
Non – scarring alopecia	Yes	45	81.8	**0.036**	37	77.1	0.701
	No	10	18.2		11	22.9	
Arthritis	Yes	32	58.2	0.225	25	52.1	0.644
	No	23	41.8		23	47.9	
Serositis	Yes	2	3.6	0.399	2	4.2	0.291
	No	53	96.4		46	95.8	
Neurology damage	Yes	4	7.3	0.227	3	6.3	0.662
	No	51	92.7		45	93.8	

Comment:

+ Positive ANA in non – scarring alopecia group was higher than the group without (81.8% và 18.2%) ($p < 0.05$).

+ Positive anti-dsDNA in the malar rash group was higher than the group without (62.5% và 37.5%) (p < 0.05).

3.2.2. The relationship between potential kidney disorders and immunological tests

Table 5. The relationship between potential kidney involvement and immunological tests

Antinuclear antibodies		Potential kidney disorders		OR	p
		n	%		
ANA positivity	Yes	44	78.6	2.333 (0.744 – 7.314)	0.140
	No	12	21.4		
Anti-dsDNA positivity	Yes	40	74.4	3.125 (1.045 – 9347)	0.037
	No	16	28.6		

Comment: The risk of potential kidney disorders was higher in the group with positive anti-dsDNA (OR = 3.1; p < 0.05).

3.2.3. The relationship between potential kidney disorders and peripheral blood cell disorders

Table 6. The relationship between potential kidney disorders and peripheral blood cell disorders

	Kidney disorders		Non-kidney disorders		p
	n	%	n	%	
Anemia	46	83.6	9	164	0.007
Leukopenia	24	80.0	6	20.0	0.474
Lymphopenia	34	81.0	8	19.0	0.225
Thrombocytopenia	19	613	12	38.7	0.014

Comment:

+ The rate of anemia in the group with kidney disorders was higher than the group without (83.6% và 16.4%) (p < 0.05).

+ The rate of thrombocytopenia in the group with kidney disorders was higher than the group without (61.3% và 38.7%) (p < 0.05).

4. DISCUSSIONS

Dermatological manifestations are one of the most typical symptoms in SLE includes malar rash, photosensitivity, discoid rash, oral/nasal ulcers, non-scarring alopecia. In this study, we recorded the rate of malar rash at 70.3%, higher than the study of Ngo Thi Thuy Thanh (54.7%) [2]. Photosensitivity accounted for 66.2%, similar to the study of Nguyen Thi Kim Thanh (57.6%) [3]. Discoid rash accounted for 18.9%, which is similar to the study of Nguyen Thi Kim Thanh (19.5%) [3], but higher than the study of Ngo Thi Thuy Thanh (3.8%) [2]. Oral/nasal ulcers accounted for 21.6%, the oral mucosal ulcer is the most popular one. As noted by author Abdulrahman Maryam, who conducted a study at Nephrology – Rheumatology Department of Ain Sham University, Greece in 2019 on 110 SLE patients reported the rate of nasal/oral ulcers was 35.5% [5]. In our study, 75.7% of patients showed non – scarring alopecia, higher than some relative studies: Ngo Thi Thuy Thanh (71.7%) [2], Mai Thu Huyen (43.8%) [1].

Musculoskeletal involvement: Arthralgia and true synovitis are very common in SLE. In this study, we recorded that 54.1% of patients had arthritis symptoms, compared to some other studies: Ngo Thi Thuy Thanh (57.0%) [2], Nguyen Thi Kim Thanh (55.9%) [3]. This may be explained by the fact that when the patients had joint pain, they had self-treated with corticosteroids or analgesic drugs at home, so when they came to the hospital, the arthritis symptoms have been reduced significantly.

In 74 patients studied, we recorded 2 cases of serositis, accounting for 2.7%, including 1 case of pleurisy, 1 case of pericarditis. Serositis was shown to be significantly lower in our series than that reported in the study of Nguyen Thi Kim Thanh (5.1% pleurisy, 5.1% pericarditis) [3].

Potential kidney disorders was diagnosed when 24- hour urine protein ≥ 3+ or > 0.5 g or hematuria or lupus nephritis on histopathology [6]. We recorded 75.7% of cases met the criteria. This result is similar to the study of Abdulrahman Maryam (72.7%) [5]

and higher than the study of Nguyen Thi Kim Thanh (57.6%) [3].

A wide array of neuropsychiatric manifestations have been associated with SLE. However, only a few of them are more specific for SLE and are helpful for diagnosis. More importantly, these require the exclusion of other known causes. Neurological symptoms were not common in our study, accounting for 5.4% (2 cases of cerebral infarction, 2 cases of unexplained seizures), compared to the study of Ngo Thi Thuy Thanh (15.1%) [2]. This difference might be due to the small sample size and only a cross-sectional study, which leads to limitations in detecting other various types of neuropsychiatric manifestations.

Anemia is a common hematological abnormality in SLE, with many forms such as nonspecific anemia, iron deficiency anemia, autoimmune hemolytic anemia, chronic renal failure. In this study, we recorded 74.3% of patients with anemia, while hemolytic anemia was 16.2%. Compared to some other studies: Mai Thu Huyen (anemia 70.8%, hemolytic anemia 4.2%) [1], Ngo Thi Thuy Thanh (anemia 83.0%, hemolytic anemia 7.5%) [2].

Leukopenia in patients with SLE may be due to immune mechanisms, drugs (such as cyclophosphamide or azathioprine), bone marrow disorders,… In the classification criteria of ACR/SLICC 2015 defined as WBC count < 4000/mm^3 or lymphocyte count < 1500/mm^3 on ≥ 2 occasions or WBC count < 4000/mm^3 and along with lymphocyte count < 1500/mm^3 in one occasion [6]. Thus, the rate of leukopenia was 40.5%, lymphopenia was 56.8% in our study. These figures are higher than the study of Mai Thu Huyen (33.3% and 45.8%) [1], Nguyen Thi Kim Thanh (13.6% and 16.9%) [3]

Thrombocytopenia accounted for 41.9%, which was higher than other studies: Mai Thu Huyen (18.8%) [1], Nguyen Thi Kim Thanh (13.6%) [3], this could be explained by the difference in test kits used and sample size.

ANA and anti-dsDNA are two very valuable immunological tests in the diagnosis of SLE, in which ANA has a sensitivity of 98-99%, considered the best screening test and anti-dsDNA has a high specificity, allowing the assessment of disease activity of SLE [14]. According to table 3, the positivity rates of ANA and anti-dsDNA were 74.3% and 64.9%, respectively. This result was lower than other studies: Ngo Thi Thuy Thanh (84.9% and 71.7%) [2], Nguyen Thi Kim Thanh (98.3% and 72.9%) [3]. This could be explained by the difference related to methods used in antibody detection, thresholds for positive determinations and the ethnic origin.

According to table 4, ANA positivity in non – scarring alopecia group was higher than the group without (81.8% and 18.2%) ($p < 0.05$). Anti-dsDNA positivity in malar rash group was higher than the group without (62.5% và 37.5%) ($p < 0.05$). A relative study by V. Pradhan et al. showed the result was the significant relationship between malar rash ($p = 0.046$), oral/nasal ulcers ($p = 0.0014$), and anti-dsDNA positivity [9]. This difference may be due to the limitation of the study sample size, the variability of sensitivity related to methods used in antibody detection, and ethnic origin.

The risk of potential kidney disorders was higher in the group with positive anti-dsDNA (OR = 3.1; $p < 0.05$), compared to other studies: in the study of Nguyen Thi Kim Thanh: the rate of potential kidney disorders was higher in the group with positive ANA, anti-dsDNA ($p > 0.05$) [3], the study of V. Pradhan et al., the risk of potential kidney disorders was higher in the group with ANA, anti-dsDNA positivity (OR = 10, $p = 0.0026$) [9]. This could be explained by the deposition of autoantibodies on renal tissue in patients with lupus nephritis and anti-dsDNA is primarily associated with the pathogenesis of lupus nephritis.

The study also showed that the rates of anemia, thrombocytopenia in groups with kidney involvement were higher than the groups without (83.6% and 16.4%), (61.3% and 38.7%) ($p < 0.05$). These figures were similar to the study of Nguyen Thi Kim Thanh: the rates of anemia, lymphopenia, and thrombocytopenia in groups with kidney involvement were higher than the groups without ($p < 0.05$) [3].

5. CONCLUSIONS

Through the study of 74 patients diagnosed with systemic lupus erythematosus according to the 2015 ACR/SLICC classification criteria, we have some conclusions:

- Non – scarring alopecia 75.7%
- Potential kidney disorders 75.7%
- Malar rash 70.3%, photosensitivity 66.2%, discoid rash 21.6%.
- Oral/nasal ulcers 21.6%
- Arthritis 54.1%
- Pleurisy and/or pericarditis 2.7%
- Neurology and/or psychosis damage 5.4%
-Hematologic abnormalities: leukopenia 40.5%, lymphopenia 56.8%, thrombocytopenia 41.9%,

hemolytic anemia 16.2%

- Positive ANA 74.3%
- Positive anti-dsDNA 64.9%
- Positive ANA in non – scarring alopecia group was higher than the group without ($p < 0.05$)
- Positive anti-dsDNA in malar rash group was higher than the group without ($p < 0.05$)
- The risk of kidney involvement was higher in the group with positive anti-dsDNA (OR = 3.1; $p < 0.05$).
- The rate of anemia and thrombocytopenia in the group with potential kidney disorders was higher than the groups without ($p < 0.05$).

REFERENCES

1. Mai Thu Huyen (2019), Studying hematological characteristics of patients with systemic lupus erythematosus, Master's thesis in medicine, Hue University of Medicine and Pharmacy

2. Ngo Thi Thuy Thanh (2016), Studying application of SLICC 2012 criteria and SLEDAI index in diagnosis, assessment of severity and treatment outcome of systemic lupus erythematosus, Master's thesis in medicine by resident doctor, Hue University of Medicine and Pharmacy.

3. Nguyen Thi Kim Thanh (2020), Studying the correlation between NLR and PLR in peripheral blood with kidney involvement in patients with systemic lupus erythematosus, Graduation Thesis Specialization II, Hue University of Medicine and Pharmacy.

4. Nguyen Ngoc Vinh (2020), "Systemic Lupus Erythematosus", Textbook of Internal Medicine, Hanoi, Medical Publisher, Hanoi, pp. 132 – 143.

5. Abdulrahman Maryam A, Afifi Naglaa, Al – Ashry Marwa (2020), "Neutrophil/ lymphocyte and platelet/ lymphocyte ratios are useful predictors comparable to serum IL6 for disease activity and damage in naive and relapsing patients with lupus nephritis", The Egyptian Rheumatologist, pp. 107 – 112.

6. Iraj Salehi-Abari (2015), "2015 ACR/SLICC Revised Criteria for Diagnosis of Systemic Lupus Erythematosus", Autoimmune Diseases and Therapeutic, pp. 1 – 4.

7. Petri M, Orbai AM, Alarcon GS et al. (2012), "Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for Systemic Lupus Erythematosus", Arthritis Rheum, 64(8), pp. 2677 – 2686.

8. Tan E.M et al. (1997), "The 1997 revised criteria for the classification of systemic lupus erythematosus", Arthritis Rheum, 25(11), pp. 1271 – 1277.

9. V.Pradhan, M.Patwardhan et al. (2015), "Association of clinical presentation with anti-nuclear antibody specificities among patients with Systemic Lupus Erythematosus", Indian Journal of Nephrology, pp. 391–392.