Egyptian Rheumatology and Rehabilitation

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Nailfold capillaroscopy in Egyptian systemic lupus erythematosus (SLE) patients: correlation with demographic features and serum levels of IL 17A and IFNs I

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Abstract

Background In SLE patients, cytokines are linked to endothelial cell damage. Nailfold capillaroscopy (NFC) is a simple method for evaluating micro-vascular abnormalities in different connective tissue diseases (CTDs). The study aimed to detect the levels of interleukin 17A (IL 17A), type I interferons (IFNs I) in the serum, and NFC changes in Egyptian SLE patients compared to a control group and to correlate NFC findings with patients' demographic features and serum levels of IL 17A and IFNs I.

Results Serum levels of IL 17A, IFN α, and IFN β were significantly higher in SLE patients than in control group ($P < 0.0001$). About thirty nine patients (73.6%) of the 53 SLE patients showed abnormal NFC changes. Egyptian SLE patients had a high prevalence of the NFC non-specific pattern, with 32 (60.4%) patients showing non-specific changes and 7 (13.2%) patients showing scleroderma pattern, including 3 (5.6%) patients with active scleroderma pattern and 4 (7.55%) patients with late scleroderma pattern. Furthermore, Raynaud's phenomenon (RP) was observed in 8 (15.1%) SLE patients, with 3 (5.6%) having normal NFC pattern and 5 (9.4%) having scleroderma pattern. All controls ($n = 20$) showed normal hairpin shape capillaries. Except for SLEDAI ($P = 0.03$) and the presence of RP ($P < 0.0001$), there were no significant differences in demographic and laboratory parameters between the three NFC patterns (normal, non-specific, and scleroderma); additionally, NFC score correlated significantly with SLEDAI ($P = 0.021$).

Conclusion As a result of the high disease activity, Egyptian SLE patients had elevated serum levels of IL 17A and IFNs I. The most common NFC pattern in Egyptian SLE patients was a non-specific pattern. NFC abnormalities in Egyptian SLE patients were correlated with disease activity but not with patients' ages, disease duration, or serum levels of IL 17A and IFNs I. SLE patients with scleroderma NFC pattern and RP should be closely followed for the possibility of appearance of anti-U1 RNP antibodies and MCTDS.

Keywords NFC, SLEDAI, IL 17A, IFN α, IFN β

Background

Systemic lupus erythematosus (SLE) is an inflammatory autoimmune disease with a wide range of clinical symptoms and a chronic course with flares and remissions. The pathophysiology of SLE is significantly influenced by the activation of endothelial cells, as well as immunological abnormalities [1]. Endothelial cells produce a variety of substances that regulate vascular tone, the immune

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system, and the coagulation system; they are also a goal for cytokines produced during the inflammatory process [2]. Vascular injury has been considered as the origin of tissue damage in SLE pathogenesis [1].

IL 17A and IFNs I, including IFN α and IFN β, are cytokines that damage endothelial cells [3, 4]. Many studies in SLE patients [4–7] found high serum levels of these cytokines. Recent studies suggests that IL 17A is associated with SLE pathogenesis and also has a crucial role in initiating angiogenesis by stimulating vascular endothelial growth factor (VEGF), an essential factor in the process of new vessels formation [8, 9]. IFN-α and β have anti-proliferative and anti-angiogenic activity [10], and their high levels reduce levels of endothelial progenitor cells (EPCs) [3], which are important in endothelial repair and contribute to endothelial dysfunction.

Nailfold capillaroscopy (NFC) is a highly effective, low-cost, and simple imaging method used in the morphological analysis of capillaries in the nailfold area [11], with the added benefit of detecting micro-vascular changes early in some inflammatory CTDs. While NFC has been widely utilized for diagnosing systemic sclerosis and scleroderma-like diseases [12], there is a growing body of evidence suggesting its potential utility in detecting early microangiopathic changes in SLE [13]. Moreover, recent studies have indicated a correlation between microcapillary pathological alterations and the clinical progression of SLE [13].

Few studies have been conducted on the correlation between serum cytokine levels and microvascular abnormalities observed by NFC in SLE patients. Therefore, the study aimed to detect the levels of IL 17A, IFNs I in the serum, and NFC changes in Egyptian SLE patients compared to a control group and to correlate NFC findings with patients' demographic features, IL 17A and IFNs I levels.

Patients and methods

Fifty-three SLE patients (46 women and 7 men, mean age 32.5 ± 10.6 years) were recruited for the study, according to the updated 1982 American College of Rheumatology (ACR) criteria for SLE [14], from the out-patient clinics of immunology and rheumatology department from January 2021 to August 2022. The local ethics committee approved the study (D-1–2022) and all participants received informed consent before the beginning of the study. Patients with any of the following diseases were excluded from the study: diabetes mellitus, uncontrolled hypertension, overlap syndrome, malignancy, and chronic infections. On the same day of collecting blood samples, the physicians applied the physical examination for the patients and the rheumatologist performed NFC measurements for all subjects. The patients were also evaluated for the existence of Raynaud's phenomenon (RP). The systemic lupus erythematosus diseases activity index (SLEDAI) was used for the assessment of disease activity [15] with a maximum score of 105 points and a score more than or equal to 12 points was considered an active case. The control sera were obtained from 20 healthy volunteers matched for age and sex.

The blood samples were obtained from all subjects and the serum was isolated and stored as frozen at −80 °C for later ELISA experiments. The laboratory investigations were performed for all subjects. Serum complement levels (C3 and C4) were determined by using a quantitative competitive fluorescent probe technique, AssayLite™ Multiplex EFCIA Kit. Serum level of anti-phospholipid antibody (APL) (lupus anticoagulant) was measured by ELISA assay (MYBIOSOURCE kit). Serum levels of anticardiolipin antibody (ACL) were measured by using ELISA assay (DIAPHARMA kit); in addition, anti-double strand deoxyribonucleic acid (anti-dsDNA) and antinuclear antibody (ANA) concentrations were determined by using ELISA assay (SIGNOSIS kit). Serum levels of IL-17A, IFN-α and β were measured by using ELISA assay (ELABSCIENCE kit and RAYBiotech kit, respectively).

NFC measurements

NFC was performed for all subjects by a rheumatologist with a background in NFC using an XW 880 USB digital microscope with LED light, magnification power × 400, an 8 inch LCD monitor, and a 0.38 megapixel camera (Hefei Golden Brains optical instrument Co., China). Before the examination, each of the included subjects sat for 20 min in a room with a temperature of 20–24 °C. Both the middle and ring fingers from the right and left hands were examined to detect NFC abnormalities in Egyptian SLE patients. A drop of immersion oil was added to the nailfold bed to improve visualization. The following parameters were recorded: capillary density (number of capillaries counted in 1 mm area), capillary length (normal or elongated ≥ 300 μm), apical loop diameter including dilated capillaries (20–50 μm) and giant capillaries (> 50 μm), capillary morphology (shape of subject capillaries), and presence or absence of hemorrhages [16, 17]. According to Smith et al. [18], a qualitative analysis was adopted to evaluate capillaroscopic changes. The qualitative analysis includes three patterns: normal (pattern of typical hairpin-like capillaries with a regular distribution), non-specific (pattern with density, dimension, and morphological abnormalities but not meeting the definition of a 'scleroderma pattern'), and scleroderma (pattern with giant capillaries, hemorrhages, and avascularity). Scleroderma pattern was divided into three subgroups (early, active, late) according to the degree of NFC abnormalities, where "early scleroderma pattern"

was described as a pattern with normal density and capillary morphology, but has giant capillary(> 50 μm) with or without occurrence of hemorrhages, “active scleroderma pattern” was explained as a pattern with lowered density (4–6 capillary/mm), giant capillary (> 50 μm), abnormal morphology, and with presence or absence of hemorrhages, “late scleroderma pattern” was defined as a pattern with very low density (≤ 3 capillary/mm), abnormal morphology, and with absence of hemorrhages and giant capillaries. According to Sulli et al. [19], a semi quantitative analysis was also adopted which rates capillaroscopic changes from 0 to 3 (0 = no changes, 1 = ≤ 33% of capillary alterations/reduction, 2 = 33–66% of capillary alterations/reduction, 3 = ≥ 66% of capillary alterations/reduction, per linear mm).

Statistical analysis

The data were analyzed by t-test for unpaired samples and one way ANOVA to evaluate the significance of difference between means. The probability difference in frequency distributions was measured by using chi-square test or Fisher’s exact test. The correlation between data was performed by using Spearman’s rank coefficient. *P* value was considered significant when it was less than 0.05.

Results

The study contained 53 SLE patients with mean disease duration of 65 ± 30.6 months. SLEDAI ranged from 2 to 18 points, with a mean of 8.8 ± 3.7. 19 (35.85%) patients developed lupus nephritis. Arthritis was found in 14 (26.4%) patients and 8 (15.1%) patients showed malar rash. Five (9.4%), 21 (39.6%), and 2 (3.77%) SLE patients had alopecia, neurologic manifestations, and serositis, respectively. RP was observed in 8 patients (15.1%) of the 53 SLE patients. Leukopenia, defined as a total leukocyte count of less than 4000 cells/l, was found in 8 (15.1%) patients, and thrombocytopenia, defined as a low platelet count of less than 150,000 cells/l, was found in 9 (17%) patients. Fifteen patients (28.3%) tested positive for APL antibody. ACL antibody was discovered in 10 (18.9%) of the patients. There were 34 (64.15%) patients who took azathioprine drug, 21 (39.6%) patients who took hydroxychloroquine drug, and 51 (96.2%) patients who took prednisone drug. Table 1 presents the features of SLE patients.

Table 1 Detailed demographic, clinical, laboratory features and drug history of 53 SLE patients

Parameters	Values
Sex (M/F)	7/46
Age (years; mean ± SD)	32.5 ± 10.6
Disease duration (months; mean ± SD)	65 ± 30.6
SLEDAI (mean ± SD)	8.8 ± 3.7
Lupus nephritis (*n*/%)	19/35.85
Arthritis (*n*/%)	14/26.4
Malar rash (*n*/%)	8/15.1
Alopecia (*n*/%)	5/9.4
Neurologic manifestations (*n*/%)	21/39.6
Serositis (*n*/%)	2/3.77
RP^+ (*n*/%)	8/15.1
Anemia (hemoglobin < 12 g/dl) (*n*/%)	37/69.8
Leukopenia (*n*/%)	8/15.1
Thrombocytopenia (*n*/%)	9/17
ANA (*n*/%)	53/100
Anti-dsDNA (*n*/%)	51/98
APL^+ (*n*/%)	15/28.3
ACL^+ (*n*/%)	10/18.9
Low complement level (C3 < 80 mg/dl, C4 < 12 mg/dl) (*n*/%)	20/37.3
ESR (> 20 mm/h) (*n*/%)	35/66.04
Treatment	
Azathioprine (*n*/%)	34/64.15
Hydroxychloroquine (*n*/%)	21/39.6
Prednisone (*n*/%)	51/96.2

SLEDAI systemic lupus erythematosus disease activity index, RP^+ positive for Raynaud’s phenomenon, *ANA* anti-nuclear antibody, *Anti-dsDNA* anti-double strand DNA, APL^+ positive for anti-phospholipid antibody, ACL^+ positive for anticardiolipin antibody, *ESR* erythrocyte sedimentation rate. *SD* standard deviation. Data were presented by mean ± standard deviation and number/percentage (*n*/%)

NFC changes were observed in 39 of 53 (73.6%) SLE patients, with 32 (60.4%) showing non-specific changes (Fig. 1) and 7 (13.2%) showing scleroderma pattern, including active scleroderma pattern in 3 (5.6%) (Fig. 2a), and late scleroderma pattern in 4 (7.55%) (Fig. 2b). Controls were compared to SLE patients in terms of age, sex, serum cytokine levels, and NFC changes as shown in Table 2. Serum levels of IL 17A, IFN α, and β were significantly higher (*P* < 0.0001) in SLE patients than in the control group. According to Table 2, most of SLE patients had elongated, crossed, tortuous, and dilated capillaries. In the control group, NFC changes were normal, with hairpin shape capillaries. When the previous two groups were compared in terms of NFC changes, there was a significant difference in capillary density (*P* = 0.02), capillary length (*P* = 0.0073), capillary elongation (*P* < 0.0001), capillary dilation (*P* = 0.015), and capillary tortuosity (*P* < 0.0001).

As shown in Table 3, NFC score has significant positive correlation with SLEDAI (*P* = 0.021). SLEDAI, on the other hand, showed significant positive correlations with disease duration, IL 17A, IFN α, and IFN β.

Table 4 shows the demographic and laboratory features of SLE patients based on NFC patterns (normal, non-specific, and scleroderma). RP was seen in three (21.43%) of SLE patients with a normal pattern and five (71.4%)

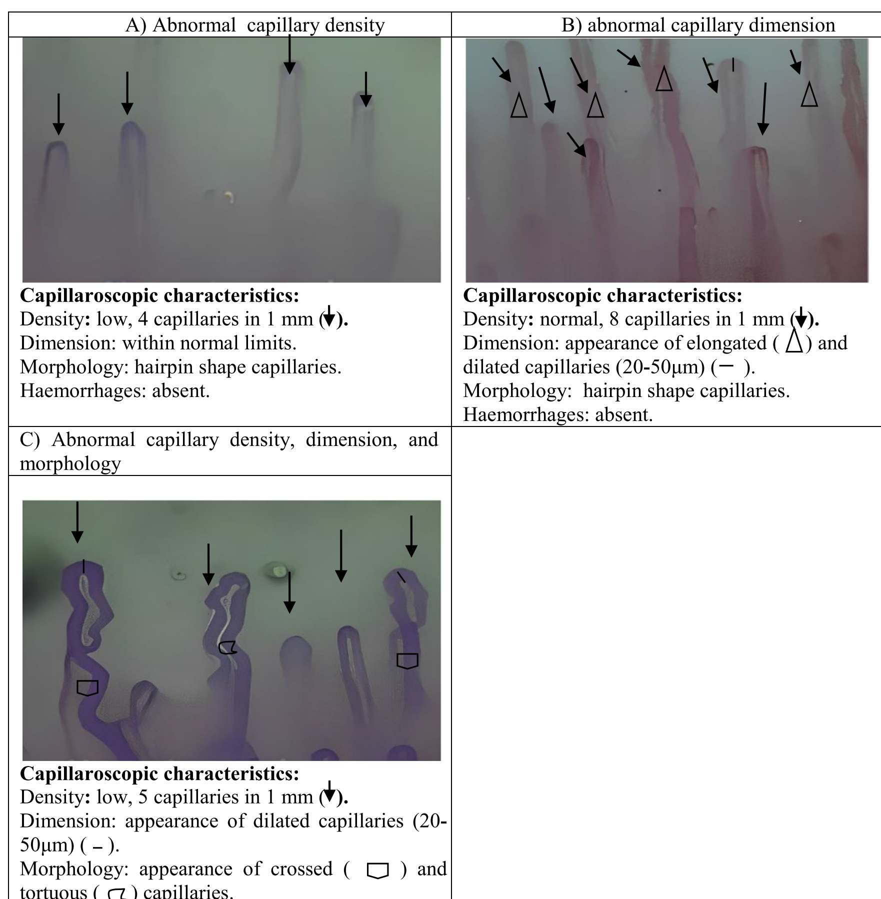

Fig. 1 Examples of non-specific pattern in SLE patients. **A** Abnormal capillary density. **B** Abnormal capillary dimension. **C** Abnormal capillary density, dimension, and morphology

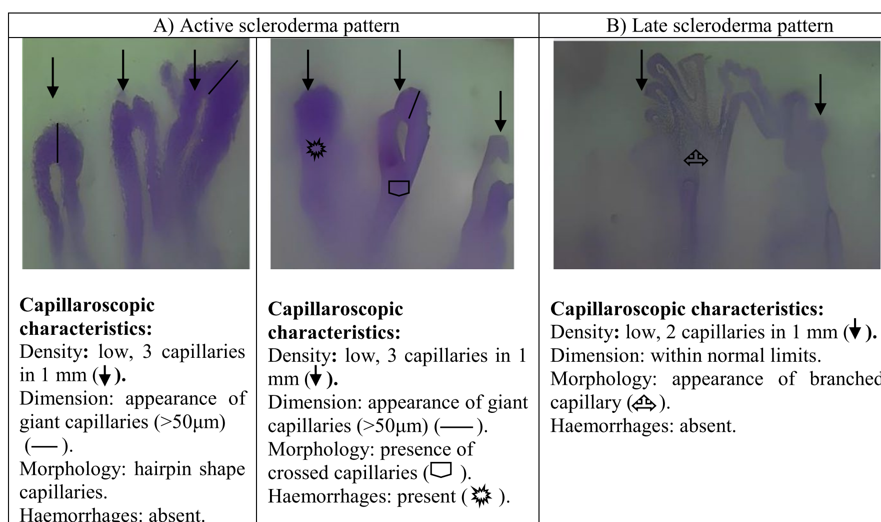

Fig. 2 Examples of scleroderma patterns in SLE patients. **A** Active scleroderma pattern. **B** Late scleroderma pattern

Table 2 Differences in the age, sex, serum cytokines level, and NFC changes between SLE patients and control group

Parameters	Controls ($n=20$)	SLE patients ($n=53$)	P value
Age (years)	34.21 ± 11.4	32.5 ± 10.6	NS
Sex (M/F)	6/14	7/46	NS
IL-17A (ng/ml)	1.23 ± 0.16	3.137 ± 0.7	< 0.0001
IFN-α (ng/ml)	0.185 ± 0.019	0.371 ± 0.081	< 0.0001
IFN-β (ng/ml)	0.173 ± 0.019	0.441 ± 0.081	< 0.0001
Capillary density (/mm)	8.6 ± 1.13	7 ± 1.23	0.02
Capillary length (μm)	231.1 ± 13.84	276.2 ± 43.5	0.0073
Elongated capillaries (*n*/%)	0/0	35/66	< 0.0001
Dilated capillaries (*n*/%)	0/0	13/24.5	0.015
Giant capillaries (*n*/%)	0/0	3/5.66	NS
Avascular area (*n*/%)	0/0	4/7.55	NS
Branched capillaries (*n*/%)	0/0	7/13.2	NS
Crossed capillaries (*n*/%)	0/0	18/34	0.0017
Tortuous capillaries (*n*/%)	0/0	30/56.6	< 0.0001
Sluggish capillaries (*n*/%)	0/0	4/7.55	NS
Hemorrhages (*n*/%)	0/0	6/11.32	NS

IL-17A interleukin 17A, *IFN-α* interferon alpha, *IFN-β* interferon beta, *NS* non-significant. Data were presented by mean ± standard deviation and number/percentage (*n*/%). *P* was considered significant when it was ≤ 0.05 and non-significant when more than 0.05

Table 3 NFC score and SLEDAI correlations with age, disease duration, and serum cytokines levels in SLE patients

Parameters	NFC score (P value)	SLEDAI (P value)
Age (years)	NS	NS
Disease duration (months)	NS	0.03
SLEDAI	0.021	–
IL-17A (ng/ml)	NS	0.04
IFN-α (ng/ml)	NS	0.036
IFN-β (ng/ml)	NS	0.038

NFC nailfold capillaroscopy, *SLEDAI* systemic lupus erythematosus disease activity index, *IL-17A* interleukin 17A, *IFN-α* interferon alpha, *IFN-β* interferon beta, *NS* non-significant. *P* was considered significant when it was ≤ 0.05 and non-significant when more than 0.05

of those with a scleroderma pattern. All patients with active scleroderma pattern ($n=3$, 100%) and only two patients (50%) of four patients with late scleroderma pattern developed RP. Except for SLEDAI ($P=0.03$) and the presence of RP ($P<0.0001$), no significant differences in demographic and laboratory parameters of SLE patients were found between different capillaroscopic patterns. Patients with positive APL had different NFC patterns without any statistically significant difference.

Discussion

Many studies have recently focused on microvascular endothelial damage and its role in the pathogenesis of systemic organ involvement in rheumatic diseases like

Table 4 Demographic and laboratory differences in SLE patients according to NFC patterns

Parameters	Normal pattern ($n=14$)	Non-specific pattern ($n=32$)	Scleroderma pattern ($n=7$)	P value
Age (years)	27 ± 12.9	31 ± 8.9	34 ± 9.8	NS
Sex (M/F)	3/11	4/28	0/7	NS
Disease duration (months)	18 ± 34.8	24 ± 40.4	30 ± 40.1	NS
SLEDAI	7.5 ± 5.74	13.1 ± 6.3	19.3 ± 2.41	0.03
RP^{+} (*n*/%)	3/21.43	0/0	5/71.4	< 0.0001
IL-17A (ng/ml)	2.67 ± 0.65	3.2 ± 0.56	2.96 ± 0.5	NS
IFN-α (ng/ml)	0.4 ± 0.081	0.33 ± 0.08	0.38 ± 0.062	NS
IFN-β (ng/ml)	0.47 ± 0.084	0.4 ± 0.082	0.45 ± 0.07	NS
APL^{+} (*n*/%)	6/42.9	8/25	1/14.3	NS

SLEDAI systemic lupus erythematosus disease activity index, RP^{+} positive for Reynaud's phenomenon, *IL-17A* interleukin 17A, *IFN-α* interferon alpha, *IFN-β* interferon beta, APL^{+} positive for anti-phospholipid antibody, *NS* non-significant. Data were presented by mean ± standard deviation and number/percentage (n/%). *P* was considered significant when it was ≤ 0.05 and non-significant when more than 0.05

SLE [20]. Cytokines have a critical role in the development of SLE because they are important regulators of SLE pathogenesis and are linked to immune dysfunction and organ damage. The present study investigated the correlations between demographic, laboratory parameters, including IL 17A, IFN α, and IFN β, and NFC changes in Egyptian SLE patients to determine whether these parameters contribute to microvascular abnormalities, where the previous studies pointed to the great diagnostic value of NFC in rheumatic diseases, but there have been few studies on the association of immune system alterations with capillaroscopic abnormalities.

IL 17 cytokines are produced by many lymphocytes, including CD 4^+ Th 17 cells, CD 8^+ cells, γδ T cells, and natural killer T cells [21]. IL 17 family consists of six members (IL 17A to IL 17F) and the previous studies has found that IL 17A and IL 17F, in particular, can initiate tissue injury through the secretion of chemokines that cause monocytes recruitment, maturation, and proliferation. [22]. IL 17A is a cytokine with inflammatory properties that participates in the host defenses against bacterial and fungal infections as well as autoimmunity and tumors [23]. Studies reported that IL 17A is associated with SLE pathogenesis because it can activate B cells and cause local inflammation and tissue injury, which are associated with different events in the pathophysiology of SLE [24]. It can also magnify the immune response by increasing the secretion of autoantibodies by B lymphocyte activation, making it an appealing therapeutic target [25]. The present study demonstrated that individuals diagnosed with SLE and exhibiting active disease displayed elevated levels of IL-17A in comparison to those with mild or moderate disease and control subjects. Furthermore, a notable significant positive correlation was observed between IL 17A and SLEDAI. This correlation suggests that raised IL-17A levels contribute to increased disease activity or vice versa. These findings were consistent with previous studies' findings [26–29].

Type I IFNs, which are primarily secreted by plasmacytoid dendritic cells (pDCs), participate in the pathogenesis of SLE [30]. It was found that most of SLE symptoms are related to elevated levels of IFNs I. There are two types of cells that control vascular repair: bone marrow-derived EPCs and myelomonocytic circulating angiogenic cells (CACs) [31, 32]. Type I IFNs have a possibility of disrupt EPC/CAC function by decreasing pro-angiogenic factors such as VEGF and increasing IL-18 [32]. An in vitro study that found that blocking IFN-α in SLE patients' peripheral blood mononuclear cells (PBMCs) restored the normal angiogenic phenotype [31] provides evidence that type I IFNs promote abnormal vascular repair. The present study found elevated serum levels of type I IFNs in SLE patients when compared to the control group, with a significant positive correlation with SLEDAI, implying that as serum levels of IFNs I increase, disease activity increases, which is in agreement with the previous studies [33–35].

NFC has been used as a non-invasive method for detecting microvascular involvement in rheumatic diseases [11]. Capillary abnormalities have been reported in a variable prevalence in SLE patients [36–38]. Furthermore, the capillaroscopic changes in the nailfold appear to be related to the disease activity score [36]. Both the middle and ring fingers from the right and left hands were examined in the current study, as the previous multicenter studies showed that these fingers have a high sensitivity to detect capillary abnormalities [39, 40]. According to the findings of this study, 39 out of 53 (73.6%) SLE patients have NFC abnormalities, with non-specific pattern being the most prevalent pattern in SLE patients, followed by normal and scleroderma patterns; additionally, patients with scleroderma pattern showed only active and late pattern. The previous findings were consistent with other studies [41, 42] that found that the majority of SLE patients have a non-specific NFC pattern with rare occurrence of scleroderma pattern.

The tortuosity of capillaries exhibited a statistically significant increase in individuals diagnosed with SLE compared to the control group in this study. Tortuosity has been described as a normal variation in some studies [43, 44], but it has also been defined as an SLE pattern in others [11, 38]. Moreover, a notable significant difference in capillary density was obtained between the control group and the patient group. Specifically, a majority of individuals diagnosed with systemic lupus exhibited capillary density of below 7 capillary/mm. The prevailing NFC alterations observed in the Egyptian individuals with SLE include dilatation, elongation, and capillary crossing. These findings provide evidence to demonstrate that most SLE patients have non-specific abnormalities.

In addition, there was a correlation observed between changes in NFC and SLEDAI scores, whereas discernible variations in scleroderma patterns were observed between patients with inactive SLE and those with active SLE. Patients diagnosed with inactive SLE exhibited normal NFC, whereas active SLE patients had an abnormal pattern. These findings are consistent with many other studies that have found a correlation between capillary abnormalities and disease activity in SLE [45, 46]. Furthermore, the occurrence of hemorrhages was higher in active SLE cases than in inactive cases, which is consistent with the previous studies that demonstrated a higher frequency of hemorrhages in SLE patients with higher disease activity [47]. In contrast to the findings of Nakajima et al. [48], who found that NFC patterns correlated with subjects' age, the current study found no significant

correlation between NFC score and the ages of SLE patients.

The study found that SLE patients with different NFC patterns, including normal, nonspecific, and scleroderma, had no significant difference in IL 17A, IFN α, and β levels. Furthermore, there was no significant correlation between NFC score and previous serum cytokine levels, indicating that there was no clear relationship between NFC abnormalities and immunologic markers. When the previous three NFC patterns were compared based on the presence of RP, a significant difference was found, with scleroderma pattern patients having a higher occurrence of this phenomenon than the other two patterns, which was consistent with the findings of Furtado et al. [49], who discovered a significant correlation between the presence of RP and the scleroderma NFC pattern. Because no clinical signs of scleroderma were observed in the SLE patients with RP, these patients need close follow up for the possibility of the development of anti-U1 ribonucleoprotein antibodies (anti-U1 RNP) and mixed connective tissue diseases (MCTDs), as the previous studies [50, 51] discovered that the development of anti-U1 RNP antibodies is related to the presence of RP, which may lead to MCTDs in these patients. Moreover, no significant difference in antiphospholipid antibodies was found in the current study between different NFC patterns, which agrees with Raeeskarami et al. [52] who demonstrated that there was no significant correlation between antiphospholipid antibodies and capillary alterations and contrasts with other studies that used capillaroscopic changes as a diagnostic test for the antiphospholipid syndrome in rheumatic disease [42, 53, 54]. Our findings suggest that IL 17A and IFNs I have essential roles in the pathogenesis of SLE, but they may not have a specific effect on SLE microvascular abnormalities; additionally, NFC changes in Egyptian SLE patients are affected by disease activity rather than age or disease duration. NFC abnormalities in SLE can act as a mirror for microvascular involvement and disease activity.

Conclusion

The present study found that patients with SLE had elevated levels of IL 17A and IFNs I in their serum due to increased disease activity. Furthermore, the study's findings revealed that non-specific NFC patterns were more common in SLE patients. Notably, there was a significant positive correlation between NFC changes and disease activity but no correlation between NFC changes and studied cytokines. SLE patients with scleroderma NFC pattern and RP should be closely followed up for the possibility of appearance of anti-U1 RNP antibodies and MCTDS.

Abbreviations

SLE	Systemic lupus erythematosus
NFC	Nailfold capillaroscopy
CTDs	Connective tissue diseases
IL 17A	Interleukin 17A
IFN α	Interferon alpha
IFN β	Interferon beta
SLEDAI	Systemic lupus erythematosus disease activity index
VEGF	Vascular endothelial growth factor
pDCs	Plasmacytoid dendritic cells
EPCs	Endothelial progenitor cells
CACs	Myelomonocytic circulating angiogenic cells
PBMCs	Peripheral blood mononuclear cells
RP	Raynaud's phenomenon
APL	Anti-phospholipid antibody
ACL	Anticardiolipin antibody
ESR	Erythrocyte sedimentation rate
Anti-U1 RNP	Anti-U1 ribonucleoprotein antibodies
MCTDs	Mixed connective tissue diseases

Acknowledgements

The authors thank all staff members and colleagues in the Rheumatology and Immunology Department, Faculty of Medicine, Cairo University Hospitals, Egypt, for their helpful cooperation and all the study participants for their patience and support.

Authors' contributions

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Mary Wadie and Mohamed Nasser. The first draft of the manuscript was written by Mohamed Nasser and revised by Azza El Amir and Alyaa Farid and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

The current research has been conducted in accordance to the Declarations of Helsinki and after approval of the local Ethics Committee of Faculty of Medicine, Cairo University (Ethical approval code: D-1–2022). Written informed consents were obtained from all participants enrolled in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Received: 2 August 2023 Accepted: 8 September 2023
Published online: 19 September 2023

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