Research Article

Association of Antinuclear Antibody Staining Pattern with Antinuclear Antibody Immunofluorescence Titer and Clinical Manifestation in Pediatric Systemic Lupus Erythematosus

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ABSTRACT

Background: Pediatric systemic lupus erythematosus (pSLE) has become increasingly prevalent in pediatric wards, accounting for 10%-20% of all SLE patients. While the clinical significance of antinuclear antibody (ANA) immunofluorescence (IF) staining patterns has been reported in relation to disease presentation, limited research has explored whether different ANA IF staining patterns are associated with distinct clinical features in pSLE.

Aim: This study aimed to investigate the association between ANA IF staining pattern and clinical manifestations, as well as ANA titer, in pSLE patients.

Methods: ANA-positive pSLE subjects were recruited from the Prof. Ngoerah General Hospital between 2015 and 2022. The association between ANA IF staining pattern and ANA titer was analyzed using the likelihood ratio test. The association between ANA IF staining pattern with organ involvement and specific clinical manifestation was analyzed using the contingency coefficient test. A p-value less than 0.05 was considered significant.

Results: A total of 130 ANA-positive pSLE subjects were included in the study. The female-to-male ratio was 3.3:1, and the median age at diagnosis was 14 ± 3.5 years. Eight types of ANA IF staining patterns were identified, with speckled and homogenous patterns being the most common. The majority of subjects had ANA titers higher than 1:1000. The speckled pattern was evenly distributed across a wide range of titers, while the homogenous pattern tended to be concentrated at higher ANA titers ($p=0.004$). The gastrohepatology system showed a significant association with ANA IF staining patterns (contingency coefficient 0.720, $p<0.001$). Additionally, ANA IF staining patterns were significantly associated with ascites, photosensitivity, colitis, and lymphopenia (contingency coefficient 0.372, $p=0.007$; 0.401, $p=0.002$; 0.720, $p<0.001$; 0.348, $p=0.022$, respectively).

Conclusion: The findings suggest that ANA IF staining patterns are associated with ANA titers, organ involvement, and specific clinical manifestations in pSLE, with potential diagnostic implications.

Keywords: pediatric SLE, antinuclear antibody, ANA IF staining pattern, clinical manifestation, organ system

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by the involvement of multiple organ systems, resulting from a complex interplay of environmental, hormonal, and genetic factors.[1] Pediatric systemic lupus erythematosus (pSLE) has exhibited a significant rise in prevalence within pediatric healthcare settings, accounting for approximately 10-20% of all SLE cases.[2] Compared to adult-onset SLE, pSLE is known to present with a more

severe clinical course, higher disease activity, and a greater likelihood of major organ involvement. Consequently, early and accurate diagnosis of pSLE is crucial for improved prognosis; however, it remains challenging due to its relatively low prevalence and diverse clinical manifestations.[3–7]

Antinuclear antibodies (ANA) are autoantibodies that target various cellular constituents and play a crucial role in screening and diagnosing systemic autoimmune rheumatic diseases (SARDs), including SLE. Despite the longstanding recognition of autoantibodies in SLE, their precise role in the pathogenesis, diagnosis, and prognosis of the disease is still an active area of investigation.[5,6]

Patterns of ANA staining has been associated with specific nuclear antigens, which in turn have implications for the clinical presentation of SLE. However, there have been limited reports regarding the clinical significance of ANA staining patterns specifically in pSLE patients, and even fewer studies have explored whether different ANA immunofluorescence (IF) staining patterns may correlate with distinct clinical features in this population. Therefore, the aim of this study is to describe the ANA IF staining patterns observed in pSLE patients and investigate the potential associations between these patterns, ANA titers, and the clinical manifestations of pSLE. The findings from this study are expected to enhance our understanding of pSLE and contribute to the improvement of early diagnosis and treatment strategies.

METHODS

This retrospective observational study was conducted at Prof. Ngoerah General Hospital, a tertiary teaching hospital and referral center for pSLE patients in Bali, Indonesia, and nearby provinces. The study included all patients below 18 years old who were diagnosed with SLE between 2015 and 2022. Data was collected retrospectively from the Bali Pediatric Systemic Lupus Erythematosus (BEATLES) database.

Subjects with positive ANA test were included in the study, while those with incomplete medical records or comorbidities including infectious or non-infectious causes such as metabolic or congenital disease that could interfere with clinical presentation at the time of diagnosis were excluded. Subject characteristics, including gender, age at diagnosis, year of diagnosis, referral status, origin, ANA titer, and ANA IF staining pattern at diagnosis were documented.

Clinical manifestations recorded at the time of diagnosis were recorded to define the clinical spectrum of the disease. Manifestations were categorized based on system organ involvement or specific within-organ system manifestations, defined as follow:

- Hematology organ involvement comprised of specific clinical manifestations including

leukopenia (WBC count < 4000/mm^3), lymphopenia (lymphocyte count < 1500/mm^3), anemia (hemoglobin below normal range based on age; below 11 g/dL up to 5 years, below 11.5 g/dL from 5-11 years, below 12 g/dL from 12-14 years or female teenager > 15 years, and below 13 g/dL for male teenager > 15 years old) and thrombocytopenia (thrombocyte count < 100.000/mm^3).[8,9]

- Neuropsychiatric system involvement comprised of specific clinical manifestations, including seizures, headache, acute confusional state, peripheral neuritis, intracranial bleeding.
- Cardiology involvement comprised of specific clinical manifestations including pericarditis / pericardial effusion, abnormal valve involvement, cardiomegaly / cardiomyopathy.
- Pulmonary involvement comprised of specific clinical manifestations including pleuritis / pleural effusion.
- Gastrohepatology involvement comprised of specific clinical manifestations including raising of liver enzymes with or without liver enlargement, abdominal pain or abdominal bleeding unexplained by other condition.
- Skin and mucocutaneous involvement comprised of specific clinical manifestations including malar rash, discoid rash, subcutaneous chronic lupus erythematosus (SCLE) rash, alopecia, oral ulcers, photosensitivity, Raynaud phenomenon.
- Musculoskeletal involvement comprised of specific clinical manifestations regarding any sign of myositis or arthritis, including swelling, warmth, tender, redness range of movement limitation on the joint / muscle.
- Fever: any raising temperature reported by parents from history taking, documented by prior hospital or our hospital. As fever might represent certain infectious disease, we also collect data on the chronicity of the fever onset, pattern of raising temperature, particularly during the evening or night.
- Electrolyte imbalance: any out of normal range of electrolyte level, including sodium imbalance, potassium imbalance and calcium imbalance.

The presence of at least one clinical presentation in a particular organ was considered as involvement of the organ system. Subtypes of ANA IF staining pattern along with its titer found in our subjects were documented in this study. Descriptive statistics were used to summarize subject characteristics as numbers and percentages. The association between ANA IF staining pattern and ANA titer was analyzed using likelihood ratio test. The association between ANA IF staining pattern and organ involvement, as well as specific clinical

manifestations, was analyzed using contingency coefficient test. Statistical Package for Social Sciences (SPSS) version 25.0 was utilized for data analysis. A p-value less than 0.05 was considered statistically significant.

Ethical clearance was obtained from the Health Research Ethics Committee of the Faculty of Medicine Universitas Udayana, and approval was also obtained from Prof. Ngoerah General Hospital.

RESULTS

Demographic and Clinical Characteristics

A total of 130 subjects who met the study criteria were included in the analysis. The study population had a female-to-male ratio of 3.3:1, and the median age at diagnosis was 14 ± 3.5 years. The majority of subjects were referred from other hospitals and from outside the city of Denpasar.

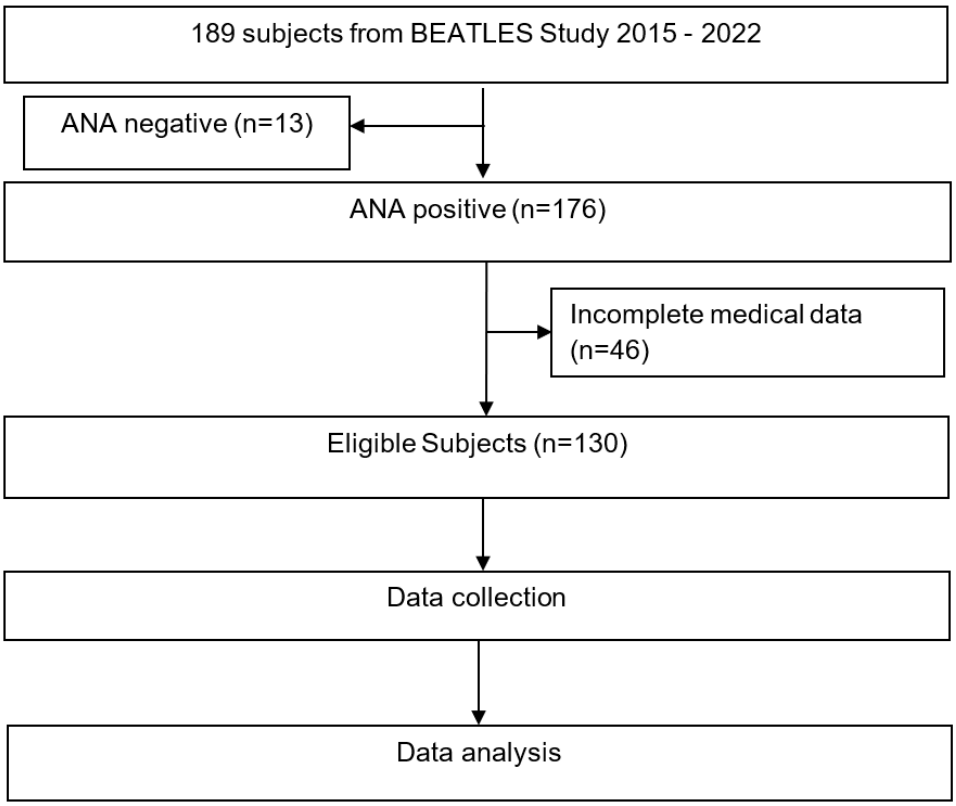

Figure 1. Research flow

Hematology involvement was the most common organ involvement, observed in 103 subjects (85.4%). Anemia was the most common clinical presentation, occurring in 70% of subjects.

ANA immunofluorescence (IF) staining patterns were classified into eight types, including nuclear (homogenous, speckled, nucleolar, discrete nuclear dots, and nuclear envelope), cytoplasmic (speckled and fibrillar), and mitotic patterns (spindle fibers). The most frequently observed pattern among our subjects was nuclear speckled, and the majority had an ANA titer of more than 1:1000. Most subjects presented with a single ANA IF staining pattern, although one subject exhibited three patterns at the time of diagnosis.

Table 1. Subject characteristics

Subject characteristics	Value n(%)
Gender	
Male	30 (23.1)
Female	100 (76.9)
Age (years)	
≤ 5	3 (2.3)
6 - 11	35 (26.9)
12-18	92 (70.8)
Referral	
Other hospital	78 (60.0)
Other division	28 (21.5)
Not referral	24 (18.5)
Origin	
Denpasar	30 (23.1)
Outside Denpasar	84 (64.6)
Outside Bali	16 (12.3)
Year of Diagnosis	
2015	1 (0.8)
2016	4 (3.1)
2017	5 (3.8)
2018	17 (13.1)
2019	37 (28.5)
2020	28 (21.5)
2021	13 (10.0)
2022	25 (19.2)
ANA titer	
1:100	39 (30.0)
1:320	11 (8.4)
1:1000	39 (30.0)
>1:1000	69 (53.1)
ANA pattern	
Homogenous	56 (43.1)
Speckled	68 (52.3)
Nucleolar	6 (4.6)
Cytoplasmic speckled	20 (15.4)
Cytoplasmic fibrillar	2 (1.5)
Spindle fibers	1 (0.8)
Discrete nuclear dots	3 (2.3)
Nuclear envelope	1 (0.8)
Number of patterns	
Single pattern	103 (79.2)
Two patterns	26 (20.0)
Three patterns	1 (0.8)

Associations of ANA IF staining patterns with ANA titer and clinical manifestations

Our findings revealed a significant association between ANA IF staining patterns and ANA titer. The homogenous pattern tended to be more prevalent at higher ANA titers, while the speckled pattern was evenly distributed across all ANA titer groups (p=0.01) (Table 2). The distribution of ANA IF staining patterns across organ involvement categories showed no notable variation (Table 3). However, a significant association was found between the gastrohepatology system and ANA IF staining pattern (contingency coefficient 0.720, p <0.001). Furthermore, specific clinical manifestations, including ascites (0.372, p=0.007), photosensitivity (0.401, p=0.002), colitis (0.720, p <0.001), and lymphopenia (0.348, p=0.022), were significantly associated with ANA IF staining pattern.

Table 2. Association between ANA IF staining pattern and ANA titer

ANA titers	Homogenous (%)	Speckled (%)	Nucleolar (%)	Cytoplasmic speckled (%)	Cytoplasmic fibrillar (%)	Spindle fiber (%)	Discrete nuclear dots (%)	Nuclear envelope (%)	n (%)	p-value
1:100	6 (10.7)	26 (38.2)	1 (16.7)	3 (15)	N/A	N/A	1 (33.3)	1 (100)	39 (30.0)	0.01
1:320	3 (5.4)	6 (8.8)	N/A	N/A	1 (50)	N/A	1 (33.3)	N/A	11 (8.5)	
1:1000	19 (33.5)	12 (17.6)	1 (16.7)	4 (20)	1 (50)	1 (100)	1 (33.3)	N/A	39 (37.7)	
>1:1000	28 (50)	24 (35.3)	4 (66.6)	13 (65)	N/A	N/A	N/A	N/A	69 (53.1)	
N (%)	56 (100)	68 (100)	6 (100)	20 (100)	2 (100)	1 (00)	3 (100)	1 (100)		

*N/A: not available

Table 3. Association between ANA IF staining pattern and system organ involvement

Organ Involvements	Homogenous (%)	Speckled (%)	Nucleolar (%)	Cytoplasmic speckled (%)	Cytoplasmic fibrillar (%)	Spindle fiber (%)	Discrete nuclear dots (%)	Nuclear envelope (%)	Homogenous-Speckled (HS) (%)	n (%)	Contingency Coefficient	p - value
Cardiology	16 (38.1)	19 (36.5)	3 (50)	7 (53.8)	N/A	1 (100)	1 (33.3)	N/A	7 (63.6)	54 (41.5)	0.237	0.461
Pulmonary	28 (66.7)	32 (61.5)	5 (83.3)	9 (69.2)	N/A	1 (100)	1 (33.3)	N/A	8 (72.7)	83 (63.8)	0.228	0.522
Neuropsychiatry	11 (26.2)	8 (15.4)	1 (16.7)	3 (23.1)	N/A	N/A	N/A	N/A	2 (18.2)	25 (19.2)	0.159	0.908
Kidney	31 (73.8)	29 (55.8)	3 (50)	9 (69.2)	1 (50))	1 (100)	1 (33.3)	1 (100)	10 (90.9)	85 (65.4)	0.299	0.690
Hematology	35 (83.3)	52 (84.6)	6 (100)	11 (84.6)	2 (100)	1 (100)	1 (33.3)	1 (100)	11 (100)	111 (85.4)	0.269	0.257
Gastrohepatology	17 (40.5)	16 (30.8)	N/A	5 (38.5)	N/A	N/A	N/A	1 (100)	1 (9.1)	40 (30.8)	0.720	<0.001
Skin and mucocutaneous	26 (61.9)	32 (61.5)	5 (83.3)	9 (69.2)	2 (100)	1 (100)	3 (100)	N/A	10 (90.9)	87 (66.9)	0.258	0.320
Musculoskeletal	25 (59.5)	26 (50)	5 (83.3)	8 (61.5)	1 (50)	1 (100)	2 (66.7)	N/A	6 (54.5)	75 (57.5)	0.229	0.969

*N/A: not available

Table 4. Association between ANA IF staining pattern and clinical manifestation

Clinical Manifestations	Homogeneous	Speckled	Nucleolar	Cytoplasmic speckled	Cytoplasmic fibrillar	Spindle fiber	Discrete nuclear dots	Nuclear envelope	Homogenous-speckled/ HS	n (%)	Contingency coefficient	p-value
Cardiology												
Pericarditis	4 (9.5)	3 (5.8)	0	3 (23.1)	N/A	N/A	N/A	N/A	4 (36.4)	14 (10.8)	0.384	0.092
pericardial effusion	7 (16.7)	6 (11.5)	3 (50)	1 (7.7)	N/A	1 (100)	1 (33.3)	N/A	2 (18.2)	21 (16.2)	0.402	0.069
Abnormal valve involvement	2 (4.8)	7 (13.5)	1 (16.7)	3 (23.1)	N/A	1 (100)	1 (33.3)	N/A	2 (18.2)	17 (13.1)	0.291	0.149
Cardiomegaly	4 (9.5)	5 (9.6)	N/A	4 (30.8)	N/A	N/A	N/A	N/A	1 (9.1)	14 (10.8)	0.329	0.472
Cardiomyopathy	1 (2.4)	2 (9.6)	N/A	N/A	N/A	N/A	1 (33.3)	N/A	1 (9.1)	5 (3.8)	0.335	0.421
Pulmonary												
Pleurisy	12 (28.6)	23 (34.6)	2 (33.3)	6 (46.2)	N/A	N/A	N/A	N/A	7 (63.6)	46 (35.4)	0.327	0.487
Pleural effusion	16 (38.1)	16 (26.9)	3 (50)	3 (23.1)	N/A	N/A	N/A	N/A	1 (9.1)	37 (28.5)	0.324	0.504
Neuropsychiatry												
Headache	1 (2.4)	2 (3.8)	N/A	N/A	N/A	N/A	N/A	N/A	2 (18.2)	5 (3.8)	0.231	0.499
Seizures	3 (7.1)	5 (7.7)	1 (16.7)	N/A	N/A	N/A	N/A	N/A	1 (9.1)	10 (7.7)	0.097	0.996
Psychosis	8 (19)	4 (7.7)	1 (16.7)	1 (7.7)	N/A	N/A	N/A	N/A	1 (9.1)	15 (11.5)	0.178	0.833
Acute confusional state	3 (7.1)	2 (3.8)	1 (16.7)	N/A	N/A	N/A	N/A	N/A	N/A	7 (5.4)	0.293	0.728
Intracranial hemorrhage	N/A	N/A	N/A	1 (7.7)	N/A	N/A	N/A	N/A	N/A	1 (0.8)	0.175	0.999
Kidney												
Proteinuria	26 (61.9)	24 (46.2)	2 (33.3)	4 (30.8)	N/A	N/A	1 (33.3)	N/A	8 (72.7)	65 (50.0)	0.278	0.208
Hematuria	18 (42.9)	17 (32.7)	2 (33.3)	6 (46.2)	N/A	N/A	N/A	N/A	7 (63.6)	50 (38.5)	0.243	0.418
Pyuria	16 (38.1)	6 (11.5)	2 (33.3)	2 (15.4)	N/A	N/A	N/A	N/A	3 (27.3)	29 (22.3)	0.293	0.143

Urinary casts	4 (9.5)	10 (19.2)	1 (15.7)	2 (15.4)	N/A	N/A	N/A	N/A	2 (18.2)	19 (14.6)	0.148	0.939
Peripheral edema	15 (35.7)	10 (19.2)	N/A	4 (30.8)	N/A	1 (100)	1 (33.3)	N/A	6 (54.5)	37 (28.5)	0.298	0.123
Ascites	12 (28.6)	4 (7.7)	N/A	5 (38.5)	N/A	N/A	N/A	1 (100)	N/A	22 (16.9)	0.372	0.007
Hypertension	8 (19)	3 (5.8)	N/A	N/A	N/A	N/A	N/A	N/A	4 (46.4)	15 (11.5)	0.311	0.084
Hematology												
Leukopenia	14 (33.3)	12 (23.1)	3 (50)	4 (30.8)	N/A	N/A	N/A	N/A	3 (27.3)	36 (27.7)	0.194	0.750
Lymphopenia	23 (54.8)	22 (42.3)	6 (100)	7 (53.8)	N/A	N/A	1 (33.3)	N/A	10 (90.9)	69 (53.1)	0.348	0.022
Anemia	31 (73.8)	34 (65.4)	3 (50)	11 (84.6)	2 (100)	1 (100)	N/A	1 (100)	9 (81.8)	91 (70.0)	0.294	0.138
Thrombocytopenia	11 (26.2)	9 (17.3)	1 (16.7)	1 (7.7)	N/A	N/A	N/A	N/A	3 (27.3)	25 (19.2)	0.182	0.813
Gastrohepatology												
Transaminitis	17 (40.5)	16 (30.8)	N/A	N/A	N/A	N/A	N/A	N/A	1 (9.1)	39 (30.0)	0.268	0.259
Colitis	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1 (100)	N/A	1 (0.8)	0.707	<0.001
Skin and mucocutaneous												
Malar rash	13 (31)	20 (38.5)	4 (66.7)	4 (30.8)	N/A	N/A	N/A	N/A	7 (63.6)	48 (36.9)	0.291	0.741
Discoid rash	1 (2.4)	1 (1.9)	N/A	2 (15.4)	N/A	N/A	N/A	N/A	N/A	5 (3.8)	0.236	0.470
SCLE rash	5 (11.9)	13 (25)	1 (16.7)	3 (23.1)	N/A	1 (100)	1 (33.3)	N/A	3 (27.3)	27 (20.8)	0.235	0.475
Alopecia	19 (45.2)	23 (44.2)	3 (50)	7 (53.8)	1 (100)	N/A	1 (33.3)	N/A	8 (72.7)	62 (47.7)	0.218	0.592
Oral ulcer	12 (28.6)	14 (26.9)	3 (50)	3 (23.1)	1 (100)	N/A	N/A	N/A	3 (27.3)	36 (27.7)	0.213	0.626
Photosensitivity	5 (11.9)	4 (7.7)	2 (33.3)	1 (7.7)	N/A	N/A	3 (100)	N/A	3 (27.3)	18 (13.8)	0.401	0.002
Raynaud phenomenon	1 (2.4)	2 (3.8)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	3 (2.3)	0.162	1.000
Epistaxis	1 (2.4)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1 (0.8)	0.150	1.000

Musculosceletal												
Arthritis	25 (59.5)	26 (50)	5 (83.3)	8 (61.5)	1 (50)	1 (100)	2 (66.7)	N/A	6 (54.5)	74 (56.9)	0.229	0.969
Myositis	N/A	1 (1.9)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1 (0.8)	0.229	0.969
Electrolyte imbalance												
Sodium imbalance	10 (23.8)	10 (19.2)	2 (4.8)	N/A	N/A	N/A	N/A	N/A	1 (9.1)	25 (19.2)	0.232	0.965
Potassium imbalance	7 (16.7)	8 (15.3)	N/A	3 (23)	N/A	N/A	N/A	N/A	1 (9.1)	19 (14.6)	0.214	0.985
Calcium imbalance	19 (45.2)	15 (28.8)	2 (33.3)	6 (46.2)	N/A	N/A	N/A	N/A	2 (18.2)	44 (33.8)	0.243	0.417
Fever	18 (42.9)	22 (42.3)	4 (66.7)	3 (23.1)	N/A	N/A	N/A	N/A	4 (36.4)	51 (39.2)	0.236	0.467

*N/A: not available

DISCUSSION

This restrospective study aimed to investigate the association between ANA IF staining patterns, ANA titers, and clinical manifestations in order to identify potential diagnostic and prognostic implications for pSLE. We documented 130 ANA positive pSLE cases from 2015 to 2022, with a median age at diagnosis of 14 ± 3.5 years old and a female to male ratio of 3.3:1. Consistent with previous studies, our results revealed a high prevalence of anemia and hematology involvement in pSLE patients, followed by skin/mucocutaneous and kidney involvement.[7,10–12]

The International Consensus on ANA Patterns (ICAP) has divided ANA IF staining pattern into 29 discrete HEp-2 cell IIF patterns on expert level and 13 subtypes on competent level. The distribution of ANA patterns in SLE may vary depending on clinical and ethnic differences, as reported in earlier studies.[13] Eight types of ANA IF staining pattern were identified in our study, distributed into three main types of patterns: nuclear, cytoplasmic, and mitotic patterns. This study demonstrated that the speckled and homogenous patterns were the most common ANA IF staining patterns, which aligns with findings in both adult and pediatric SLE populations.[14–16] Rare ANA IF staining patterns (frequency less than 1%) were also found in our subjects, including nuclear envelope and spindle fibers.[17]

We observed a significant association between ANA IF staining patterns and ANA titers. The speckled pattern was distributed across a wide range of titers, whereas the homogenous pattern was more concentrated at higher titers, particularly at 1:1000 or higher. This finding suggests a potential association between the intensity of ANA staining which indicated by higher titers, and organ involvements in pSLE.

Previous studies have suggested that ANA-IF staining pattern is correlated with specific autoantibodies, which may be related to particular clinical symptoms. Our findings showed associations between ANA IF staining patterns and specific clinical manifestations. Notably, the gastrohepatology organ system showed a significant association with ANA staining patterns, specifically the nuclear envelope pattern. This association may be linked to clinical manifestations such as colitis and differences in the distribution of ANA patterns in transaminitis. We also found significant associations were found between ANA staining patterns and clinical manifestations, including photosensitivity, colitis, ascites, and lymphopenia.

Photosensitivity was commonly presented with homogenous, speckled, or HS pattern and in all discrete nuclear dots pattern (100%). Colitis was probably associated with nuclear envelope pattern, and mixed pattern was more likely presented along with lymphopenia, though it could be presented as homogenous or speckled pattern alone. Ascites was commonly distributed in homogenous pattern, similar to serositis in other organs such as pericardial effusion or pleural effusion. These findings were statistically significant (p value < 0.05). These findings align with previous reports and highlight the potential diagnostic and prognostic value of ANA IF staining patterns in pSLE.[18,19]

The association between ANA IF staining pattern and clinical manifestation was statistically significant in accordance with Frodlund, et al. who showed that central nervous system was less often associated with homogenous pattern compared to other staining patterns, whereas arthritis and organ damage respectively were

less often associated with speckled pattern and photosensitivity was significantly associated with anti-Ro/SSA antibodies which was more often associated with mixed (HS pattern).[18]

Previous studies have reported that lymphopenia is associated with increased disease activity and organ damage indices, as noted by Faddah et al.[20] Additionally, Mughales et al. found that the mixed pattern was associated with the highest levels of lupus anticoagulant.[14] Consistent with these findings, our study found that lymphopenia was frequently presented in HS pattern, although presentation with homogenous or speckled pattern was also possible. This may suggest that more antibodies were involved in the development of lymphopenia, which could reflect a more aggressive course of the disease.

Study Limitations

- As our study was retrospective, some clinical features could not be specifically identified from the medical records, such as cardiomegaly without further evaluation with echocardiography.
- The association of ANA IF staining pattern to a particular clinical manifestation in our study may reduce its clinical utility. Analyzing the association between staining pattern and a collection of symptoms as included in the disease activity index (SLEDAI) or damage index (SDI) may help extend its clinical relevance.

Implication and Recommendations

- Children and adolescents with homogenous ANA IF staining pattern should be evaluated for ascites and serositis in lungs and heart, as these may be related to severe manifestations that increase the risk of mortality.
- Children and adolescents with discrete nuclear dots ANA IF staining pattern should be informed about the risk of excessive activity under sunlight, and adequate protection should be provided to prevent photosensitivity.
- Children and adolescents with rare patterns should be evaluated for the possibility of unusual presentations, such as colitis with nuclear envelope pattern.
- Children and adolescents with presentations of more than one pattern, especially with the combination of the two most common patterns (homogenous and speckled - HS pattern), should raise awareness of the possibility of a more severe clinical course and lead to the investigation of lymphopenia.

CONCLUSION

Our study highlights the association between ANA IF staining patterns, ANA titer, and clinical manifestations in pSLE. These findings suggest potential diagnostic implications to a certain extent. Further exploration of these relationships and their potential clinical significance is warranted.

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