The presentations and outcomes of patients with positive ANA test.

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ABSTRACT:

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Background: In general practice, antinuclear antibody (ANA) test is often used as an initial screening for connective tissue diseases (CTDs). Even though positive test can be detected in most of the autoimmune diseases, it can also be found in other inflammatory or infectious conditions, and even in healthy individuals.

Objective: To evaluate the patients who had positive antinuclear antibody (ANA) test in relation to clinical presentation and presence of connective tissue diseases (CTDs).

Methods: A retrospective collection of data was done in patients who underwent the ANA test at Phramongkutklao Hospital between May 1, 2013 and March 30, 2015. Patients older than 15 years old with ANA titer ≥1:160 were enrolled into the study. The demographic data, clinical presentations, relevant laboratory evaluations and final diagnosis were collected.

Results: There were 320 patients, 59 were male and 261 were female with the mean age of 48.5 years. The final diagnoses of connective tissue diseases (CTD) and non-connective tissue diseases (non-CTD) were found in 154 (48.12%) and 166 (51.88%) of patients respectively.

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ANA patterns of “homogeneous”, “coarse speckled” and “nucleolar”, especially in high titer (≥1:1280) were significantly correlated with the diagnosis of CTD (P< 0.05). No correlation of ANA patterns and major organ involvement was found. Nevertheless, the presence of anti-centromere pattern was associated with less number of major organ involvements.

Conclusion: Among patients with positive ANA test, the patients with high titers of “homogeneous”, “speckled” and “nucleolar” ANA patterns were more likely to have CTDs. The presence of anti-centromere pattern was less likely to have major organ involvement.

Key words: Anti-nuclear antibody, connective tissue disease

บทคัดย่อ :

กาญจนา เหลืองรังษิยากุล กอบกุล อุณหโชค ชุติกา ศรีสุทธิยากร อาการ อาการแสดง การวินิจฉัย และการดำเนินโรคในกลุ่มผู้ป่วยที่การตรวจ ANA ให้ผลบวก วารสารโรคผิวหนัง 2560; 33: 195-208.

แผนกผิวหนัง และกามโรค กองอายุรกรรม โรงพยาบาลพระมงกุฎเกล้า

หลักการและเหตุผล: การตรวจ ANA มักใช้เป็นการตรวจเบื้องต้นเพื่อช่วยในการตรวจคัดกรองโรคเนื้อเยื่อเกี่ยวพัน (CTDs) แต่อย่างไรก็ตามผลการตรวจที่เป็นบวกสามารถตรวจพบได้ในโรคการอักเสบอื่นๆ, กลุ่มโรคติดเชื้อบางชนิด หรือในคนปกติ ไม่เฉพาะ แต่โรคภูมิคุ้มกันต่อต้านตนเอง

วัตถุประสงค์: เพื่อประเมินอาการ อาการแสดง และการวินิจฉัยโรค ของผู้ป่วย ที่ให้ผลทดสอบ ANA เป็นบวก

วิธีการศึกษา: เป็นการเก็บข้อมูลย้อนหลังในผู้ป่วยที่ได้รับการตรวจ ANA ในโรงพยาบาลพระมงกุฎเกล้าระหว่างวันที่ 1 พฤษภาคม 2556 ถึงวันที่ 30 มีนาคม 2558 โดยผู้ป่วยที่เข้าร่วมการศึกษามีเกณฑ์ดังต่อไปนี้ ได้แก่ ผู้ป่วยที่มีอายุมากกว่า 15 ปีที่มีระดับ ANA ≥ 1: 160 ผู้ป่วยจะถูกเก็บข้อมูลในด้านต่างๆ ในแง่อาการและอาการแสดง, การประเมินผลห้องปฏิบัติการที่เกี่ยวข้องและการวินิจฉัยขั้นสุดท้าย

ผลการศึกษา: จากผู้ป่วย 320 รายเป็นผู้ชาย 59 ราย และผู้หญิง 261 ราย อายุเฉลี่ย 48.5 ปี อาการที่พบบ่อยที่สุดคืออาการปวดข้อตามด้วยอาการทางผิวหนัง ผู้ป่วย 154 (48.12%) รายได้รับการวินิจฉัยเป็นโรคเนื้อเยื่อเกี่ยวพัน (CTD) ส่วนผู้ป่วย 166 (51.88%) ราย ได้รับการวินิจฉัยเป็นโรคอื่นที่ไม่ใช่โรคเนื้อเยื่อเกี่ยวพัน

รูปแบบของ ANA ชนิด "homogenous", "coarse speckled" และ "nucleolar" โดยเฉพาะอย่างยิ่งใน titer ที่สูง (≥1: 1280) มีความสัมพันธ์อย่างมีนัยสำคัญกับการได้รับการวินิจฉัยโรคเนื้อเยื่อเกี่ยวพัน (CTD) (P <0.05) แต่ไม่พบความสัมพันธ์ของรูปแบบ ANA และมีความผิดปกติของอวัยวะภายในที่สำคัญร่วมด้วย อย่างไรก็ตามการศึกษานี้พบว่า ANA รูปแบบ anti-centromere มีความเกี่ยวข้องกับความผิดปกติของอวัยวะภายในน้อยกว่าการพบใน ANA รูปแบบ อื่นๆ

สรุปผล: ในการศึกษานี้พบว่าผู้ป่วยที่มีการทดสอบ ANA เป็นบวกโดยเฉพาะผู้ป่วยที่มี titers สูงและมีรูปแบบ ANA "homogenous", "speckled" และ "nucleolar" จะมีความสัมพันธ์อย่างมีนัยสำคัญกับการวินิจฉัยเป็นโรคเนื้อเยื่อเกี่ยวพัน

(CTD) อีกทั้งการพบ ANA รูปแบบ “anti-centromere” จะมีความเกี่ยวข้องกับความผิดปกติของอวัยวะภายในน้อยกว่าการพบใน ANA รูปแบบ อื่นๆ

คำสำคัญ: แอนตี้นิวเคลียร์ แอนตี้บอดี้, โรคเนื้อเยื่อเกี่ยวพัน

Introduction

The ANA test is the most useful and important test for evaluation, diagnosis and follow-up in patients with connective tissue diseases (CTDs).[1] ANA test has low positive predictive value but high negative predictive value in general populations.[2,3,4,5] The sensitivity and specificity were high in CTDs, especially in systemic lupus erythematosus (SLE) corresponding to 90-100% and 86-89%, respectively.[3,5,6] The sensitivity and specificity were lower in other CTDs at 42% and 85% respectively.[3,5,6] Several conditions can induce positive result of ANA test including physiological and pathological factors such as pregnancy, advanced age, pre-pubertal period, family history of autoimmune diseases, HIV infection, chronic infections, liver diseases, thyroid diseases and malignancies.[1,2,3,4,7]

In general, the diagnosis of CTDs is made by fulfilling the clinical and laboratory criteria including the ANA test.[8] The result of positive ANA test without any strong clinical manifestations of CTDs was very limited.[4] A small number of patients, with no evidence of CTDs but had positive ANA test, developed CTDs in the follow-up period.[9,10]

In Thailand, there was a single report in the prevalence of ANA in healthy individuals without any study of relationship between positive ANA test, clinical presentations and final diagnosis.[5]

The purpose of this study is to evaluate the relationship between the positive antinuclear antibodies (ANA) and the presence of CTDs together with the association of signs and symptoms that bring about the request for the ANA test.

Materials and methods

This study was approved by the Ethics Committee of the Institutional Review Board of the Royal Thai Army Medical Department, Bangkok, Thailand. The medical records of patients who underwent ANA test between May 1, 2013 and March 30, 2015 were reviewed. All patients aged 15 years or older who had ANA titer $\geq$1:160 were included into the study. The exclusion criteria were patients who have already been diagnosed as CTDs, patients who received medications that could induce positive ANA tests, patients who received phototherapy and patients who had incomplete medical records. The list of medications are shown in **Table 7**.

Demographic data including clinical presentations, relevant laboratory evaluations and final diagnosis of all patients were retrospectively reviewed. Incomplete medical records or those with unclear diagnosis were excluded from this study.

The final diagnoses were classified as connective tissue disease (CTD) and non-connective tissue disease (non-CTD). The CTD included lupus erythematosus (LE), rheumatoid arthritis (RA), scleroderma, CREST syndrome, Sjogren syndrome, overlapping syndrome, mixed connective tissue disease (MCTD), unclassified connective tissue disease (UCTD) and Kikuchi disease.

The presence of cutaneous lesions was defined as CTD-specific skin lesions and CTD non-specific lesions. The CTD-specific skin lesions included acute/sub-acute/chronic cutaneous lupus erythematosus (LE), hallmark skin lesions in dermatomyositis (Gottron papules, heliotrope, V-sign, shawl sign, pre-pubertal telangiectasia and dystrophic cuticle) and skin lesions in scleroderma (sclerotic skin change, scleradactyly, Raynaud's phenomenon and mask-like facial appearance).[11,12]

The CTD non-specific skin lesions were defined as lesions that were not compatible with the CTD-specific skin lesions, for example alopecia, pigmentary change, livedo reticularis, leukocytoclastic vasculitis (LCV), urticaria and pannicultis.

The severity of diseases in this study depended on the presence of major organ involvement, such as lupus nephritis, neuropsychiatric SLE, significant cytopenia and interstitial lung diseases. Serositis, musculoskeletal, mucocutaneous and constitutional symptoms were defined as minor organ involvement.[13,14]

Statistical analysis

The differences between groups in categorical variables were examined using the Chi-square test. The odd ratio was calculated by applying the statistic methodology of logistic regression. A p-value ≤ 0.05 was considered statistically significant.

Results

Demographics

Among 2,596 patients who underwent the ANA test during the study period, 1,777 patients had ANA titer < 1:160 and 819 patients had ANA titer ≥ 1:160. From 819 patients who had ANA titer ≥ 1:160, 499 patients had prior diagnosis as CTD. Finally 320 patients were qualified for this study. All patients were Thai. Fifty nine patients were male and 261 patients were female (male to female ratio=1:4.4). The age of patients ranged from 15.6 to 92.0 years (mean age 48.5years) (Table 1).

The initial presentations leading to the ANA test are shown in **Table 1**. The most common initial presentation was joint pain (28.8%), followed by dermatologic manifestations (25.3%) and abnormal laboratory tests such as hepatitis, thrombocytopenia and anemia (9.4%) (Table 1).

Table 1. The demographic data, initial presentations and final diagnosis in 320 patients

Clinical presentations	**CTD*** (N=154)	**Non-CTD** (N =166)	**P-value**	**Odd-ratio(CI)**
Gender				
Male: Female	25: 129	34: 132	0.387	0.86 (0.62-0.68)
Mean age (years)	42±17.2	52.9±18.1	**<0.001***	0.97 (0.95-0.98)
Initial presentations				
Joint pain	54	38	**0.013***	1.36(1.09-1.71)
Dermatologic	41	40	0.61	1.07(0.83-1.38)
Abnormal laboratory tests	6	24	**0.002***	0.39(0.19-0.81)
Nephrologic*	23	7	**0.001***	1.69(1.34-2.15)
Neurologic*	8	17	0.10	0.65(0.36-1.16)
Gastrointestinal*	2	16	**0.001***	0.22(0.06-0.82)
Ophthalmologic*	8	8	1.00	1.04(0.63-1.72)
Fever	5	6	1.00	0.94(0.48-1.81)
Hematologic*	3	5	0.725	0.77(0.31-1.91)
Pulmonary*	2	3	1.00	0.83(0.28-2.44)
Endocrinologic*	0	2	0.49	0(0-1)
Cardiologic*	1	0	0.48	2.08(1.86-2.34)
Gynecologic*	1	0	0.48	2.08(1.86-2.34)

*(Nephrologic symptoms: edema; Neurologic symptom: paresthesia; Gastrointestinal symptoms: jaundice, abdominal pain; Ophthalmologic symptoms: sicca, eye pain, blur vision;Hematologic symptoms: bleeding; Pulmonary symptoms: dyspnea; Endocrinologic symptoms: constipation, weight loss; Cardiologic symptom: dyspnea; Gynecologic symptom: multiple abortions.)

The younger age of the patient, the presentations with joint pain, and nephrologic symptoms were significantly correlated with the final diagnosis of CTD (Table 1). On the contrary, the presence of abnormal laboratory tests and gastrointestinal symptoms were significantly correlated with the final diagnosis of non-CTD (Table 1).

One hundred and fifty four (48.12%) patients were diagnosed as CTDs and 166 (51.87%) patients were diagnosed as non-CTDs. Lupus erythematosus, rheumatoid arthritis and

overlapping syndrome were the three most common diseases in CTD group (Table 2). Musculoskeletal diseases, hepatic disease and dermatologic diseases were the three most common diseases in non-CTD group (Table 2).

Table 2. The final diagnoses of 320 patients in CTD group and non-CTD group

Final diagnosis	N = 320 (%)
CTD* (n = 154)	
SLE/DLE/LN (lupus group)	83(25.94%)
RA	19(5.94%)
Overlapping syndrome	16(5.00%)
Undifferentiated CTD	13(4.06%)
Scleroderma/CREST	9(2.81%)
Sjogren syndrome	7(2.19%)
Dermatomyositis	3(0.94%)
Mixed CTD	2(0.63%)
Kikuchi disease	2(0.63%)
Non-CTD* (n = 166)	
Musculoskeletal diseases	37(11.56%)
Hepatic diseases	36(11.25%)
Dermatologic diseases	36(11.25%)
Neurologic diseases	16(5.00%)
Hematologic diseases	15(4.69%)
Nephrologic diseases	10(3.13%)
Ophthalmologic diseases	6(1.81%)
Malignancies	4(1.25%)
Endocrinology diseases	4(1.25%)
Pulmonary diseases	2(0.63%)

*CTD = connective tissue disease

The correlations of ANA patterns, titers and the final diagnosis of CTD and non-CTD are shown in Table 3**.** The high titer of “homogeneous”, “fine speckled”, "coarse speckled" and “nucleolar” ANA patterns, especially titer ≥ 1:1280, were significantly associated with the final diagnosis of CTDs ($P<0.05$).

Table 3. The correlations of ANA patterns, titers and the final diagnosis

ANA patterns and titers		CTD, N = 154		Non-CTD, N = 166		P-value
		n	%	n	%	
Homogenous	1:160	12	19.35	16	36.36	0.693
	1:320	16	25.81	12	27.27	0.330
	1: 640	6	9.68	8	18.18	0.788
	1:1280	28	45.16	8	18.18	**<0.001***
Rim	1:1280	0	0.00	1	100.00	**NA**
Fine speckled	1:160	14	19.72	30	37.04	0.023*
	1:320	11	15.49	28	34.57	0.010*
	1: 640	11	15.49	13	16.05	0.835
	1:1280	35	49.30	10	12.35	**<0.001***
Coarse speckled	1:160	1	3.03	1	14.29	1.00
	1:320	1	3.03	2	28.57	1.00
	1: 640	1	3.03	2	28.57	1.00
	1:1280	30	90.91	2	28.57	**<0.001***
Nucleolar	1:160	8	21.05	16	47.06	0.143
	1:320	3	7.89	7	20.59	0.340
	1: 640	5	13.16	8	23.53	0.577
	1:1280	22	57.89	3	8.82	**<0.001***
Cytoplasmic	1:160	6	20.00	14	40.00	0.109
	1:320	11	36.67	11	31.43	1.00
	1: 640	5	16.67	1	2.86	0.109
	1:1280	8	26.67	9	25.71	1.00
Centromere	1:160	1	10.00	3	17.65	0.624
	1:320	0	0.00	1	5.88	1.00
	1: 640	2	20.00	1	5.88	0.610
	1:1280	7	70.00	12	70.59	0.351

The skin lesions were found in 132 (41.25%) patients. Sixty nine (52.27%) patients had CTD-specific skin lesions and 63 (47.73%) patients had CTD non-specific skin lesions. The presence of CTD-specific skin lesions was significantly correlated with the diagnosis of CTDs, compared to the presence of CTD non-specific skin lesions (Table 4). Almost all patients with CTD-specific skin lesions were diagnosed as CTD (Table 4). On the contrary, around one-third of the patients

(34.92%) with CTD non-specific skin lesion had the final diagnosis of CTD. The sensitivity and specificity of the CTD-specific skin lesions and the diagnosis of CTDs were 75.6% and 97.6% respectively. The positive predictive value (PPV) was 98.6%.

Non-scarring alopecia and xerosis were the CTD non-specific skin lesions that were significantly associate with the final diagnosis of CTD. On the other hand, chronic urticaria was significantly associated with the final diagnosis of non-CTD (Table 5).

There was no correlation of ANA patterns and the presence of major organ involvement, except the centromere pattern (Table 6). The presence of centromere pattern is less frequently associated with major organ involvement as compared to other patterns ($p < 0.05$).

Table 4. The correlation of CTD-specific/ non-specific skin lesions and the final diagnosis

	CTD-specific skin lesions, N= 69 (%)	**CTD non-specific skin lesions, N = 63 (%)**	**P-Value**
CTD	68 (98.55%)	22 (34.92%)	**<0.001***
Non- CTD	1 (1%)	41 (65.07%)	

Table 5. The correlations of CTD non-specific skin lesions and the final diagnosis

CTD non- specific skin lesions	**CTD*** N = 154	**Non-CTD** N = 166	**P-value**	**Odd-ratio (CI)**
Non-scarring alopecia	6	1	**0.006**	3.0 (1.8-5.01)
Non-specific oral ulcers	2	0	0.118	3.05(2.13-4.37)
Xerosis	3	0	**0.039**	3.16 (2.18-4.58)
Chronic urticaria	3	22	**0.003**	0.24 (0.08-0.73)
Leukocytoclastic vasculitis	3	3	0.413	1.5(0.62-3.62)
Subcutaneous nodules	0	2	0.538	0(0-1)
Petechiae	0	3	0.546	0(0-1)
Blue toe	0	1	1.000	0(0-1)

Table 6. The correlation of ANA patterns and major organ involvement

ANA patterns		Major organ involvement				
		Yes		No		
		n	%	n	%	p-value
Homogenous	Yes	13	30.2%	7	15.6%	0.101
	No	30	69.8%	38	84.4%	
Fine speckle	Yes	9	20.9%	13	28.9%	0.389
	No	34	79.1%	32	71.1%	
Coarse speckle	Yes	12	27.9%	10	22.2%	0.538
	No	31	72.1%	35	77.8%	
Nucleolar	Yes	5	11.6%	4	8.9%	0.736
	No	38	88.4%	41	91.1%	
Cytoplasmic	Yes	3	7.0%	4	8.9%	1
	No	40	93.0%	41	91.1%	
Centromere	Yes	1	2.3%	8	17.8%	**0.030***
	No	42	97.7%	37	82.2%	

Discussion

In general practice, antinuclear antibody (ANA) test is often used as an initial screening for connective tissue diseases (CTDs). Positive ANA test is detected in most of the autoimmune diseases including systemic lupus erythematosus (SLE), scleroderma (SSc), Sjögren's syndrome, rheumatoid arthritis (RA) and mixed connective disease (MCTD).[9,10] Nevertheless, ANA positivity can also be found in organ-specific autoimmune diseases including autoimmune thyroiditis, autoimmune hepatitis as well as other disorders including chronic infections (mononucleosis, tuberculosis, and subacute bacterial endocarditis).[1,3,4,7,10]

ANA positivity in the general population varies depending on the titers. Up to 32% of normal individuals have a positive ANA test at 1:40, whereas only 8% and 4% of healthy controls have ANA ≥1:80 and ≥ 1:160, respectively.[1,15,16] In Thailand, the prevalence of ANA positivity in healthy individuals was 11.6%, compared to 97%, 31.7% and 90.4% in patients with SLE, RA, SSc, respectively.[5] The sensitivity and specificity of ANA titer ≥ 1:160 was highest in SLE which was 92% and 96% respectively.[16] In other CTDs, the sensitivity and specificity varied between 41-85% and 56-63%, respectively.[17]

Only half of the patients in our study with ANA titer ≥ 1:160 had the final diagnosis of CTDs. This finding confirmed the importance of using

other criteria in combination with ANA test for the diagnosis of CTDs. Among these patients, the three most common diseases were lupus erythematosus, rheumatoid arthritis and overlapping syndrome. This finding was similar to the previous studies.[4,9]

Table 7. The medications that could induce positive ANA tests [34-37]

Antiarrhythmic	Antihypertensives	Antipsychotics	Antibiotics	Anticonvulsants
• Procainamide (15–20%)	• Hydralazine (5–8 %)	• Chlorpromazine	• Isoniazid	• Carbamazepine
• Quinidine (<1 %)	• Methyldopa	• Chlorprothixene	• Minocycline	• Ethosuximide
• Disopyramide	• Captopril	• Lithium carbonate	• Nitrofurantoin	• Phenytoin
• Propafenone	• Acebutol	• Phenelzine	• Cefepime	• Primidone
	• Clonidine			• Trimethadione
	• Enalapril			
	• Labetalol			
	• Minoxidil			
	• Pindolol			
	• Prazosin			

Diuretics	Anti-thyroidal	Anti-inflammatories	Biologicals
• Chlorthalidone	• Propylthiouracil	• D-penicillamine	• Etanercept
• Hydrochlorothiazide		• Sulfasalazine	• Infliximab
		• Phenylbutazone	• Adalimumab
		• NSAIDs	• IL-2
			• IFN-a
			• IFN-1b

The most common initial presenting symptom in our patients leading to ANA test was joint pain, followed by dermatologic manifestations. As we all know, arthritis or arthralgia and skin lesions were the common presenting signs in many CTDs.[4,10, 18,19] Our study found that the younger age of the patients, initial symptoms of joint pain and nephrologic symptoms were significantly associated with the final diagnosis of CTDs. The presence of these symptoms in the patients emphasized that suspected individuals need to be investigated for CTDs.

Considering ANA titers and patterns, our study showed that the high titer of “homogeneous”, “speckled” and “nucleolar” ANA patterns, particularly if the titer ≥ 1:1280, were significantly associated with CTDs ($P < 0.05$). This finding was

compatible with the previous reports of the association between specific ANA patterns and CTDs.[1,15,16,20] The presence of homogenous and speckled ANA patterns was associated with the diagnosis of SLE, Dermatomyositis and rheumatoid arthritis.[21,22,23] Concurrently, speckled, homogenous and centromere patterns were commonly present in systemic sclerosis.[24,25] There were no correlation of ANA patterns and titer with major organ involvement in our study. The result was different from previous reports which showed correlation of high titer anti-Ro with the disease activity in SLE patients, evaluated by SLEDAI score.[26,27] Homogenous and nucleolar ANA patterns indicated critical organ involvements and reduced survival in systemic sclerosis patients.[24] In Dermatomyositis/ polymyositis, the presence of ANA was not associated with the risk of developing interstitial lung disease (ILD), while the significant association of ILD was shown in anti-Jo and anti-MDA5 antibodies.[28]

Our study showed the presence of anti-centromere antibody was correlated with less number of patients with major organ involvement. Anti-centromere antibody is associated with CREST syndrome that usually has less systemic involvement compared to other CTDs.[29,30] There were 9 patients with positive centromere antibody in our study. Eight out of 9 patients showed no major organ involvement, of which 5 patients had systemic sclerosis and CREST syndrome, 2 patients had rheumatoid arthritis and 1 patient had overlapping syndrome. The only one patient with positive anti-centromere antibody who had renal involvement was finally diagnosed as undifferentiated connective tissue disease (UCTD).

Concerning dermatologic manifestations, CTD-specific and CTD non-specific skin lesions were found in 21.56% and 19.69% of the patients, respectively. The presence of CTD-specific skin lesions were significantly correlated with the CTDs ($p < 0.05$) and our study confirmed the high sensitivity and specificity of the CTD-specific skin lesions and the final diagnosis of CTDs. This finding emphasized the importance of skin lesions that would help diagnose CTDs. However, 22 patients who had CTD non-specific skin lesions also had the final diagnosis of CTDs. The presence of non-scarring alopecia and xerosis was significantly associated with CTDs (Table 5). These would support the inclusion of non-scarring alopecia as one of the diagnostic criteria in the 2012 SLICC classification criteria for systemic lupus eryhematosus.[31] Nevertheless, the number of patients with non-scarring alopecia and xerosis was low. Further data collections and studies will be required.

The presence of chronic urticaria was significantly associated with the diagnosis of non-

CTD in our study. In contrast to previous reports of higher incidence of autoimmune diseases in chronic urticaria.[32,33] The highest incidence was in autoimmune thyroid disease. Confino-Cohen R et al. mentioned that 15-20% of the patients with chronic urticaria were associated with rheumatoid arthritis, Sjogren syndrome and SLE.[32] The odd ratio in their study were 13.25, 15.17 and 14.59, respectively.[32] Our study found lower odd ratio of 0.24 for chronic urticaria and CTDs. These may be explained by the small number of our study populations, difference in population group and shorter follow-up period. In our study, the follow-up period was only 1-3 years compared to 10 years in previous reports. Additionally, the population group in our study was all ethnically Thai patients with ANA titer ≥ 1:160.

Study limitations

Our study had a number of limitations. Firstly, some data were lost and incomplete due to the retrospective study method. Secondly, there was relatively small number of the cases. Finally, the short duration of follow up period ranged only 1-3 years.[9,10]

Conclusion

The positive ANA test can be found in both CTDs and healthy individuals, even in high titers. In our study, we found that many factors were associated with the diagnosis of CTDs and the presence of major organ involvement. The younger age of the patients, initial symptoms of joint pain and nephrologic symptoms were significantly associated with the final diagnosis of CTDs. The patients with high titers of "homogeneous", "speckled" and "nucleolar" ANA patterns were more likely to be associated with CTDs. Nevertheless, the presence of anti-centromere pattern was more likely to associate with less major organ involvement. Our study confirmed a well-established knowledge that the presence of CTD specific skin lesions were associated with the diagnosis of CTDs. Interestingly the CTD non-specific lesions of non-scarring alopecia and xerosis were also associated with the final diagnosis of CTDs.

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