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Sicca Symptoms in Thai Patients with Rheumatoid Arthritis, Systemic Lupus Erythematosus and Scleroderma: A Comparison with Age-Matched Controls and Correlation with Disease Variables

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SUMMARY This study was performed to determine the prevalence of ocular and oral sicca symptoms in Thai patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and scleroderma (Scl). The ocular symptoms and sign (the Schirmer's 1 test) and the oral sicca symptoms and sign (the Saxon's test) in each of 50 RA, SLE and Scl patients were compared with their age-matched controls. The correlation between the presence of sicca symptoms and signs with their clinical activity was also determined. Ocular sicca symptoms were found more common in patients with RA (38% *vs* 18%, $p < 0.05$), SLE (36% *vs* 14%, $p < 0.05$) and Scl (54% *vs* 16%, $p < 0.01$), and oral sicca symptoms were found more common in SLE (22% *vs* 0%, $p < 0.01$), and Scl (16% *vs* 4%, $p < 0.05$) than their controls. However, only RA patients had a significantly higher proportion of positive Schimer-1 test compared with their controls ($p < 0.01$). There was no strong correlation between sicca symptoms or signs and other clinical or laboratory variables (age, disease duration, disease activity, disease severity, and antibody to Ro and La antigens) in these three groups. In conclusion, sicca symptoms were seen significantly more common in Thai patients with connective tissue diseases, but the symptoms did not show a good correlation with the clinical and laboratory variables.

Sjögren's syndrome or sicca syndrome is a slow progressive inflammatory autoimmune disease characterized by lymphocytic infiltration of the exocrine glands, leading to decreased exocrine secretions. Lacrimal and salivary glands are most commonly affected in this condition, resulting in decreased tear (dry eyes or xeropthalmia) and salivary production (dry mouth or xerostomia). Antibodies to Ro and La antigen are usually present. Sjögren's syndrome can be classified into primary Sjögren's syndrome and secondary Sjögren's syndrome – the sicca syndrome that is associated with well defined connective tissue diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), scleroderma (Scl), etc.[1]

Recently, a revised international classification for Sjögren's syndrome was developed in order to classify clearly patients with primary and secondary Sjögren's syndrome.[2] This revised criteria were composed of six items: I) ocular sicca symptoms (composed of three questions), II) oral sicca symptoms (composed of three questions), III) ocular sicca signs (positive Schirmer's I test or Rose Bengal staining), IV) typical histopathology of minor salivary gland biopsy, V) oral sicca signs (decreased

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salivary flow or positive sialography or salivary scintigraphy), and VI) the presence of autoantibodies (anti-Ro or La or both). Primary Sjögren's syndrome may be defined if a) any four of the six items are present (must include item IV and VI, or b) three of the four objective findings are present (item III, IV, V and VI). Secondary Sjögren's syndrome may be defined if it has a well defined connective tissue disease and the presence of item I or II, plus any two of items III, IV, and V.

The prevalence of sicca symptoms in autoimmune disease has been reported as 27% to 66.7% in various studies.[3-7] However, these symptoms are usually under diagnosed in clinical practice. Moreover, there had never been systematically study in the Thai population. We, therefore, performed this study to determine the prevalence of ocular and oral sicca symptoms and sicca findings in Thai patients with RA, SLE, and Scl, and compare the findings with those of age-matched controls. The correlation between clinical variables and the sicca symptoms and signs were also determined.

MATERIALS AND METHODS

This cross sectional study included 50 patients in each RA, SLE and Scl group, who regularly followed up at the Rheumatology Clinic of Chiang Mai University Hospital. The diagnosis of RA, SLE, and Scl was based on the ACR revised criteria for classification of RA,[8] the American College of Rheumatology (ACR) revised criteria for the classification of SLE,[9,10] and the ACR criteria for Scl,[11] respectively. One hundred medical personnel (79 females and 21 males) of Chiang Mai University Hospital participated in the study as controls. From these controls, 50 subjects, who were of the same age (± 5 yr) as the patients in each group, were chosen. All of them were healthy and none had any significant rheumatic complaints.

The patients were excluded if they were less than 15 or over 60 years of age, had a functional status of class IV, or currently using xerogenic drugs including beta blocker, diuretic, antihistamine, pseudoephredine, antidepressant, neuroleptic, parasympatholytic, and clonidine. Those with underlying human immunodeficiency virus (HIV) infection, graft versus host disease, amyloidosis, lymphoma, prior head and neck radiation, sarcoidosis, chronic active hepatitis, renal insufficiency and vasculitis were also excluded. All patients were screened for antibody to hepatitis C virus (HCV) by an enzyme-linked immunosorbent assay (ELISA) and they had negative results. We did not perform anti-HCV tests in the control group, as they did not a have previous history of blood transfusion and intravenous drug abuse, thus being low risk for HCV infection. Those who used a tear substitute were not excluded from the study, but the last tear substitution should not have been used within one hour before the tear measurement was carried out.

Data were collected from all consenting participants and included in self reported questionnaires, hospital records, clinical examination and laboratory analysis. The self reported questionnaires[2] comprised six questions about oral and ocular sicca symptoms. The interview included smoking habits, and previous and current use of xerogenic drugs. The self reported questionnaire, clinical and laboratory examination, and the tests for ocular and oral sicca symptoms and signs were performed in all participants at the same time on the day of the visit (between 8.00-10.00 a.m.).

The Schirmer-1-test (S1T)[12] without topical anesthesia was used to identify the ocular sicca sign, and the Saxon's test[13] was used to identify the oral sicca sign. These two tests were performed by one trained rheumatologist (SW). The European League of Association for Rheumatology (EULAR) response criteria for RA or the Disease Activity Score (DAS28),[14] modified Systemic Lupus Erythematosus Disease Activity Index (modified-SLEDAI),[15] and modified Rodnan's skin score[16] were used to determine the disease activity of RA, SLE and Scl, respectively. The Sharp score[17] was used to determine joint destruction in patients with RA.

The study was approved by the Ethic Committee of the Faculty of Medicine, Chiang Mai University, Thailand.

Assessment and instruments

The S1T was performed according to the guidelines.[12] The standardized tear test strips were placed at the medial, two thirds from the medial part

of the lower eyelid, with no preceding use of anesthetic eye drops. The patients sat with their eyes closed for five minutes before the strips were removed. The length of wet area starting from the notch corresponding to the lower eyelid margin was measured. Pathological S1T (ocular sicca sign) was determined if the wet areas were less than 5 mm at one or both eyes.

Saxon's test[13] was performed by chewing 5 x 5 cm sterile paraffin paper for 2 minutes. Saliva production was quantitated by subtracting the original weight from the weight obtained after chewing. Weight was measured on a weight recorder (OHAUS: TP2K), which was accurate to 0.01 gm. All participants were told not to eat, smoke, swallow liquid, or rinse their mouths for at least one hour before the test. Pathological Saxon's test (oral sicca sign) was recorded if the saliva production was less than 2.75 gm.

All participants were asked questions in the Thai language on oral and ocular sicca symptoms, which were translated from the revised international classification criteria for Sjögren's syndrome[2] (three questions each on eyes and mouth). Keratoconjunctivitis sicca (KCS) was defined as one or more ocular sicca symptoms in combination with the pathological S1T, and xerostomia as one or more oral sicca symptoms in combination with the pathological Saxon's test.

DAS28[14] was calculated by program execution of the total joint count (swelling and tenderness in 28 joints), serum erythrocyte sedimentation rate (ESR) and global health assessment score to determine disease activity for RA.

The SLEDAI[15] containing 24 descriptions in nine organ systems, which included clinical and laboratory measurements, was used to determine disease activity for SLE. In this study, we used a modified SLEDAI score; as anti-dsDNA was determined by the *Crithidia luciliae* indirect immunofluorescent test instead of the Farr assay, as described by the original description.

The modified Rodnan's skin score[16] divided the body into 22 regions and the degree of skin involvement in each region was quantitated by numerical unit. The extent of skin thickness in scleroderma was reported to be correlated with the degree of internal organ involvement.

The participating sera were tested for the presence of antinuclear antibody (ANA) by indirect immunofluorescence method using an HEP-2 cell as a substrate (Euroimmun Company, Lubeck, Germany). A dilution of ≥ 1:160 was considered significant. The presence of antibody to Ro and La antigens were detected by ELISA (Euroimmun Company). Rheumatoid factor was determined by the nephelometry method (Dade Behring Company, Deerfield, Illinois, USA).

The Sharp score[17] (summation of the score of joint space narrowing scores and joint erosion scores of both hand joints) was recorded from the hand radiographs of patients with RA. The hand radiographs were performed within the visiting day and seen by a radiologist who did not know the patient's clinical status.

Disease onset was defined as the time when the patients fulfilled the criteria for their respective disease, and disease duration as the period from the disease onset to the time of this study.

Statistical analyses

The SPSS version 10 statistical program (SPSS Inc., Chicago, Illinois, USA) was used for statistical analyses. Continuous variables were described as mean with standard deviation (S.D.). Categorical variables were described as percentages. The proportion of sicca symptoms and sicca findings for the patients was compared with their age-matched healthy controls. Comparisons were made using the Student's t-test for parametric continuous variables, Mann-Whitney U test for nonparametric continuous variables and Chi-square or Fisher's exact test for qualitative variables. Correlation was examined by the Pearson correlation coefficient when comparing continuous variables. The Spearman correlation coefficient was used when comparing categorical variables. The Eta test was used when comparing continuous with categorical variables. A correlation was considered as strong if the correlation coefficient (r) was > 0.7, moderate at 0.3-0.7, and weak if < 0.3. A p-value of < 0.05 was considered clinically significant.

RESULTS

Demographic and clinical variables for 50 patients with RA, SLE, and Scl, and 50 age-matched controls (± 5 yr) assigned to each group of patients are shown in Table 1. There was a significantly higher proportion of females in RA and SLE patients than in their controls. A significantly higher proportion of positive antinuclear antibody (ANA) was found in the three groups of patients than in their controls. SLE patients also had a significantly higher proportion of positive antibody to Ro antigen than the controls. Although three persons (6%) in the SLE control group were smokers, this finding did not show statistical significance.

Sicca symptoms and signs in RA, SLE, and Scl patients and aged-matched controls

Details of sicca symptoms and signs in RA, SLE, and Scl patients, and their aged-matched controls are shown in Table 2. RA patients had significantly higher (≥ 1) ocular sicca symptoms (38% *vs* 18%; $p = 0.03$). In comparison, RA patients produced less tear (13.6-15.7 mm *vs* 20.7-23.2 mm; $p < 0.01$), less saliva (2.8 gm *vs* 3.5 gm; $p = 0.01$), and had more pathological S1T (54% *vs* 22%; $p < 0.01$), than their controls. However, there was no difference in the incidence of KCS (18% *vs* 8%; $p = 0.14$) and xerostomia (6% *vs* 0%; $p = 0.24$). SLE patients had significantly higher (≥ 1) ocular and oral sicca symptoms than their controls (18% *vs* 0%; $p < 0.01$). They also produced less saliva than their controls (2.8 ± 1.4 gm *vs* 3.9 ± 1.8 gm; $p < 0.01$). Patients with Scl had significantly higher (≥ 1) ocular sicca (54% *vs* 16%; $p < 0.01$) and oral sicca (16% *vs* 4%; $p = 0.04$) symptoms than their controls. They also produced less tear and saliva than their controls, but these findings did not reach statistical significance. All groups had more KCS and xerostomia than their controls, but only SLE patients significantly had KSC higher than their controls (18% *vs* 2%; $p < 0.01$).

Correlation between sicca symptoms and signs, and clinical variables in RA, SLE and Scl

Correlation between sicca symptoms and findings, and clinical variables in RA are shown in Table 3. Age showed a weak correlation with the sicca symptoms, sicca signs (pathological S1T, pathological Saxon's test), and the presence of antibody to Ro and La antigens. Sicca symptoms showed a weak correlation with sicca signs, disease

Table 1 Demographics and clinical variables of 50 matched patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), scleroderma (Scl) and their age-matched controls

	RA		SLE		Scl	
	Cases (n = 50)	**Controls** (n = 50)	**Cases** (n = 50)	**Controls** (n = 50)	**Cases** (n = 50)	**Controls** (n = 50)
Sex, Female (%)	94	64**	100	72**	74	66
Age (years)	46.6 ± 8.8	45.5 ± 8.3	39.1 ± 9.6	39.1 ± 9.6	46.6 ± 7.9	46.2 ± 7.3
Smokers (current; %)	6	8	0	6	10	10
Disease duration (years)	8.5 ± 7.1	NA	6.12 ± 5.9	NA	5.1 ± 4.6	NA
Anti-Ro (%)	20	10	50	2**	18	10
Anti-La (%)	4	2	10	0	6	2
ANA positive (%)	34	14*	100	6**	100	14**
Anti-dsDNA positive (%)	NA	NA	38	NA	NA	NA
DAS28	6.1 ± 1.5	NA	NA	NA	NA	NA
RF positive (%)	90	NA	NA	NA	NA	NA
Sharp score	85.3 ± 56.5	NA	NA	NA	NA	NA
Modified-SLEDAI score	NA	NA	5.8 ± 4.4	NA	NA	NA
Modified Rodnan's skin score	NA	NA	NA	NA	15.0 ± 11.1	NA

*$p < 0.05$, **$p < 0.01$, NA, not applicable.

Table 2 Comparison of sicca symptoms and signs in matched patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), scleroderma (Scl) and their age-matched controls. (Mean±SD for continuous, proportion (%) for categorical variables)

	RA			SLE			Scl		
	RA (n = 50)	**Controls** (n = 50)	***p***	**SLE** (n = 50)	**Controls** (n = 50)	***p***	**Scl** (n = 50)	**Controls** (n = 50)	***p***
Subjective sicca symptoms (%)									
≥1 ocular sicca symptoms	38	18	0.03	36	14	< 0.05	54	16	< 0.01
≥1 oral sicca symptoms	6	4	1.00	22	0	< 0.01	16	4	0.04
≥1 ocular and oral sicca	6	2	0.62	18	0	< 0.01	8	2	0.36
Objective assessment of ocular involvement									
Tear production in mm									
Right eye	15.7 ± 16.4	23.2 ± 16.4	0.01	26.2 ± 17.9	25.7 ± 15.5	0.73	18.6 ± 16.6	21.7 ± 16.3	0.45
Left eye	13.6 ± 14.7	20.7 ± 14.9	< 0.01	25.8 ± 17.4	21.7 ± 15.3	0.23	15.7 ± 14.7	19.6 ± 16.1	0.30
Pathological S1T (%)	54	22	< 0.01	22	20	0.80	32	32	1.00
Keratoconjunctivitis sicca (%)	18	8	0.14	18	2	< 0.01	18	8	0.14
Objective assessment of oral involvement									
Saliva production in gm	2.8 ± 1.8	3.5 ± 1.7	0.01	2.8 ± 1.4	3.9 ± 1.8	< 0.01	3.5 ± 1.8	3.7 ± 1.7	0.49
Pathological Saxon's test (%)	56	38	0.07	50	32	0.06	38	32	0.53
Xerostomia (%)	6	0	0.24	8	0	0.12	14	0	0.01

S1T = Schirmer's 1 test

duration, disease activity (DAS28), disease severity (Sharp score), and the presence of antibody to Ro and La antigens. However, oral sicca signs (Saxon's test) showed a moderate correlation with the DAS28 ($r = 0.44$) and Sharp score ($r = 0.34$).

In patients with SLE (Table 4), age had a mild to moderate correlation with sicca symptoms and sicca signs, and showed a weak correlation with disease activity (m-SLEDAI), and antibody to Ro and La antigens. Ocular sicca symptoms had a moderate correlation with their signs (pathological S1T) ($r = 0.51$) and m-SLEDAI ($r = 0.32$). Oral sicca symptoms showed a weak correlation with their signs (pathological Saxon's test), disease duration, m-SLEDAI, and antibody to Ro and La antigens.

In patients with Scl (Table 5), age again showed a weak correlation with sicca symptoms, sicca signs, skin score, and antibody to Ro and La antigens. The ocular sicca symptoms correlated weakly with their signs (pathological S1T), disease duration, skin score, and antibody to Ro and La antigens. The oral sicca symptoms correlated moderately with their signs (pathological Saxon's test) ($r = 0.55$); however, they had a weak correlation with disease duration, skin score and antibody to Ro and La antigens.

Overall, there was no strong correlation between sicca symptoms, signs, and disease activity and severity, and the presence of antibody to Ro and La antigens.

DISCUSSION

In this study, we found that the patients with RA, SLE and Scl had significantly more ocular symptoms than their controls. SLE and Scl patients also had significantly more oral sicca symptoms compared with controls. The prevalence of subjective ocular and oral sicca symptoms was 38% and 6% in patients with RA, 36% and 22% in patients with SLE, and 54% and 16% in patients with Scl, respectively. A higher proportion of patients with RA had significantly more ocular symptoms and pathological S1T (54%) than their controls, but it showed only a mild to moderate correlation with DAS28 and Sharp score. A higher proportion of patients with SLE had significantly more ocular and oral sicca symptoms and KCS (18%) than their controls, but it showed only a mild to moderate correlation with the

Table 3 Correlation between ocular and oral sicca symptoms and findings, and clinical variables in rheumatoid arthritis

	Age	Duration	Dry eye	S1T	KCS	Dry mouth	Saxon's test	Xerostomia	DAS 28	Sharp score	Anti-Ro	Anti-La
Age	1											
Duration	0.45**	1										
Dry eye	0.002	0.03	1									
S1T	0.16	0.04	-0.10	1								
KCS	0.01	0.05	0.60**	0.43**	1							
Dry mouth	0.08	0.03	0.32*	0.23	0.54**	1						
Saxon	0.16	0.14	-0.05	0.39**	0.21	0.22	1					
Xerostomia	0.08	0.03	0.32*	0.23	0.54**	1**	0.22	1				
DAS28	0.27	0.11	0.03	0.33	0.11	0.03	0.44	0.03	1			
Sharp score	0.33*	0.59**	0.14	0.16	0.03	0.05	0.34	0.05	0.36*	1		
Anti-Ro	0.02	0.08	0.12	0.26	0.16	-0.13	0.14	-0.13	0.19	0.19	1	
Anti-La	0.04	0.19	0.26	0.19	0.44**	-0.05	0.18	-0.05	0.18	0.31	0.41**	1

* = p < 0.05, ** = p < 0.01, S1T = Schirmer-1-test, KCS = keratoconjunctivitis sicca, DAS = disease activity score

Table 4 Correlation between ocular and oral sicca symptoms and findings, and clinical variables in systemic lupus erythematosus

	Age	Duration	Dry eye	S1T	KCS	Dry mouth	Saxon's test	Xerostomia	m-SLEDAI	Anti-Ro	Anti-La
Age	1										
Duration	.07	1									
Dry eye	0.43	0.04	1								
S1T	0.54	0.06	0.51**	1							
KCS	0.50	0.01	0.62**	0.88**	1						
Dry mouth	0.28	0.14	0.51**	0.30*	0.38**	1					
Saxon	0.26	0.13	0	0.24	0.16	-0.14	1				
Xerostomia	0.21	0.13	0.39**	0.37**	0.44**	0.55**	0.29*	1			
m-SLEDAI	-0.26	0.21	0.32	0.28	0.21	0.05	0.29	0.19	1		
Anti-Ro	0.19	0.20	0.08	0.24	0.16	-0.05	0.04	0.15	0.14	1	
Anti- La	0.05	0.22	0.17	-0.02	0.02	0.14	0.07	0.39**	0.12	0.2	1

* = p < 0.05, ** = p < 0.01, S1T = Schirmer-1-test, KCS = keratoconjunctivitis sicca, m-SLEDAI = modified SLEDAI score

m-SLEDAI. A higher proportion of patients with Scl had significantly more ocular and oral sicca symptoms and xerostomia (14%) than their controls; however, it correlated weakly with modified Rodnan's skin score.

The prevalence of subjective xeropthalmia in RA, SLE and Scl patients (36-54%) in this study was comparable to that previously described (27-55.5%),[3,5,7] whereas subjective xerostomia (6-22%) was less common than in other reports (42-66.7%).[4,6] Such differences might be due to the different patients studied and assessment methods used. The finding that a higher proportion of patients with RA and SLE had more sicca symptoms than controls was similar to previous reports.[3] As there was no strong correlation between sicca symptoms and signs in this study, and it was not surprising that all three groups of patients had a higher proportion of subjective ocular and oral sicca symptoms than that of KCS and xerostomia.

Age is otherwise known to influence both tear and saliva production and composition.[18-21] Patients with advancing age tend to produce less tears and saliva. In this study, controls were matched with

Table 5 Correlation between ocular and oral sicca symptoms and findings, and clinical variables in scleroderma

	Age	Duration	Dry eye	S1T	KCS	Dry mouth	Saxon's test	Xerostomia	Skin score	Anti-Ro	Anti-La
Age	1										
Duration	0.22	1									
Dry eye	0.05	0.01	1								
S1T	0.06	0.18	0.03	1							
KCS	0.09	0.19	0.43**	0.68**	1						
Dry mouth	0.23	0.21	-0.03	-0.06	0.08	1					
Saxon	0.13	0.29	0.06	0.26	0.38**	0.44**	1				
Xerostomia	0.31	0.28	0.02	-0.03	0.11	0.92**	0.51**	1			
Skin score	0.18	-0.22	0.11	0.11	0.21	0.20	0.21	0.16	1		
Anti-Ro	0.06	0.02	-0.09	0.12	0.05	-0.06	0.06	-0.04	0.01	1	
Anti-La	0.03	0.2	-0.10	0.19	0.10	0.12	0.15	0.14	0.04	0.32*	1

* = $p < 0.05$, ** = $p < 0.01$, S1T = Schirmer-1-test, KCS = keratoconjunctivitis sicca

age (± 5 yr) to the cases, and this could help exclude demographic variables that might explain the difference in ocular and oral dryness. However, in contrast to previous reports, we found no strong correlation between age and sicca symptoms, sicca signs, disease activity, disease severity and the presence of antibody to Ro and La antigens in all groups of patients.[18-21] The concomitant factors that may contribute to dryness in all participants, especially xerogenic drugs, was excluded from this study. Although smoking can be associated with a decrease in saliva secretion, the proportion of smokers was comparable in all groups of patients studied, and showed no statistically significant difference. Therefore, the effect of smoking on the oral sicca symptoms and findings between cases and controls could be excluded.

In this study, we found no strong correlation between the presence of sicca symptoms, and sicca signs, and the presence of antibody to Ro and La antigens. These findings were in-line with previous reports.[3,5,22,23] However, the correlation between the presence of sicca symptoms and that of antibody to Ro and La antigens has been noted in patients with SLE and Scl in some reports.[3,24] Our finding that the presence of sicca symptoms and signs showed no strong correlation with the disease activity determined by the DAS28 score was similar to that of Uhlig *et al*.[5] Also, no strong correlation was observed between the sicca symptoms and signs and the disease activity in SLE (determined by the modified SLEDAI score) and Scl (determined by the modified Rodnan's skin score). This may imply that sicca symptoms and signs in RA, SLE and Scl patients do not have a good correlation with disease activity and severity.

There were several limitations in this study. Firstly, there was a relatively small number of sample patients and controls. Secondly, patients with RA and SLE had a significantly higher proportion of females than in the controls; this gender-related difference might have affected statistical results. Previous studies found that dry eye was more prevalent in women than men.[25-27] Thirdly, the Saxon's test was chosen to assess oral dryness instead of using the un-stimulated salivary flow, as described in criteria for the diagnosis of Sjögren's syndrome. The Saxon's test is an unsophisticated method for stimulating salivary production, and easy to perform in an out-patient clinic setting. It is used in some epidemiological studies. The cut-off value for a positive Saxon's test is saliva of less than 2.75 gm in 2 minutes. However, our age-matched controls for the RA, SLE and Scl patients had a positive Saxon's test of 38%, 32% and 32%, respectively. The reasons for this high incidence of pathological Saxon's test in these control groups were not clear. This might be due to the small body size of Thai people, or the saliva production of Thais might be lower than that of western people. A further study of the cut-off point of salivary production in Thais is of interest. Fourthly, as we did not perform Rose Bengal ocular staining, un-stimulated salivary flow, minor salivary gland biopsy and the parotid sialography or salivary scintigraphy, some patients who might have positive results of these tests might have been missed. Thus,

the actual incidence of secondary Sjögren's syndrome in our patients was not determinable.

Lastly, it should be noted that there was a rather high percentage of positive ANA and antibody to the Ro antigen. The incidence of positive ANA at a titer of ≥ 1:160 in 6-14% of normal controls in this study was higher than that in western countries (5%),[28] and Thailand (4.1%).[29] The reason for this was not clearly understood. Moreover, our controls also had a high incidence of ocular symptoms, pathological S1T and pathological Saxon's test. However, these subjects were healthy and did not have any signs or symptoms that suggested the presence of any connective tissue diseases. It would be of interest to follow these subjects to see if they would develop certain connective tissue diseases in the future.

In conclusion, a higher proportion of sicca problems were observed in Thai patients with RA, SLE, and Scl when compared with their age-matched controls. However, both sicca symptoms and signs did not show a good correlation with clinical and laboratory variables. Patients with connective tissue diseases should be carefully evaluated to document the presence of objective sicca findings for appropriate treatment and follow-up.

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