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## **ORIGINAL ARTICLE**

# The Prevalence of Sicca Symptoms and Secondary Sjogren in Patients with Rheumatoid Arthritis and it is Association to Disease Activity

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#### **Abstract**

Background: Sjogren disorder (SS) is a persistent foundational immune system sickness of obscure etiology that can happen alone prevalently Sjogren or in relationship with a fundamental connective tissue illness, most regularly rheumatoid joint pain (RA) or lupus erythematosus.

Aim: To determine the commonness of dryness side effects and optional SS in patients with RA and their relationship with illness movement.

Patients and methods: This cross-sectional review was directed at 100 patients with RA chosen from the people who went to the short-term branch of the Division of Restoration and Rheumatology of Al-Azhar College Clinic in Asyut from January 2022 to December 2022.

Results: The study group had an incidence of 8 % of secondary Sjogren's syndrome (sSS). Disease activity score 28 (DAS - 28) cases analyzed were 36 (36 %) strange and 64 (64 %) ordinary. With a P-value of 0.003, there was a statistically significant correlation between sSS and DAS - 28, and the cases with 100 % sSS had the highest activity. 23 (23 %) with Schirmer result + ve and 77 (77 %) negative. Genuinely critical connection between sSS and Schirmer test with P-value ( $<0.001^*$ ), salivary organ ultrasound score of 39 (39 %) unusual, and 61 (61 %) ordinary. There was a genuinely huge relationship between sSS and salivary organ ultrasound score with a P-value of ( $0.013^*$ ).

Conclusion: The incidence of sSS is not affected by disease duration, whereas the reported role of disease activity has been demonstrated. Secondary SS was found in a secondary subset of RA patients.

Keywords: Autoimmune, Rheumatoid arthritis, Secondary sjogren's

#### 1. Introduction

R heumatoid joint inflammation (RA) is a diligent sickness of the heterogeneous safe framework described by painful joint bothering that can prompt bone harm. 1

RA is characterized by joint inflammation and tenderness, as well as destruction of the synovial joints, resulting in severe disability and premature death.<sup>2</sup>

RA pain affects multiple organs and affects vision, particularly dry eyes. The disquietude, utilization, the sensation of obliviousness about the body and

the heaviness of the eyelids affect regular daily existence at work and on the psyche.<sup>3</sup>

Sjogren's disorder (SS) is an ongoing immune system infection that essentially influences the exocrine organs. Xerosis and keratoconjunctivitis sicca are the disease's main features. SS sickness can be essential or elective when joined by other insusceptible framework issues like scleroderma and RA.<sup>4</sup>

The particular pervasiveness of sSS in RA shifts altogether relying upon the significance of sSS, span of RA, and geographic area. The effect of sSS in RA is reflected in a two-overlap expanded chance of

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non-Hodgin's lymphoma contrasted with non-Hodgin's lymphoma patients, Dryness is a side effect of RA that is normal and related to how well the disease works.<sup>5</sup>

Therefore, the purpose of this study is to ascertain the prevalence of sicca symptoms and sSS in RA patients and the relationship between these conditions and disease activity.

#### 2. Patients and methods

This cross-sectional review was conducted on 100 patients with RA those going to rheumatology and transient recovery offices at Al-Azhar School Clinical Center in Assiut from January 2022 to December 2022. People over the age of 18 made up the review. RA that persists into old age. While, earlier radiation of the head and neck, hepatitis C, helps, lymphoma, sarcoidosis, throat sicknesses, and the utilization of anticholinergic medications were restricted. Complete clinical and feminine anamneses were recorded for every patient. In light of the evaluation of joint side effects: stiffness, pain, swelling, fever, weakness, and exhaustion, as well as their transmission. Unusual side effects and previous use of other drugs Span of ailment: affirmation before crises, clinical issues. Joint pain and related conditions general assessment: evaluation of the patient's general health, major bodily functions, pallor, hepatitis, cyanosis, skin, lymph nodes, stomach, heart, and head and neck, as well as their neurological condition. Outer muscle evaluation: each joint or reference case in which the woman's assessment showed an irregularity was given this level of evaluation. The straightforward visual scale was used to measure anguish. Utilizing the Sickness Action Score (DAS-28), the 100 R A patients remembered for the review were partitioned into three classifications: gentle, moderate and serious. A DAS-28 score of more than 5.1 indicates a disease that is very active, a DAS-28 score of less than 5.1 and more than 3.2 indicates a disease that is moderately active, a DAS-28 score of less than 3, 2 indicates a disease that is indolent, and a DAS-28 score of less than 2.6 indicates remissions. Audits from research foundations: complete urinalysis, complete blood count, erythrocyte sedimentation rate (ESR), polymerase chain reaction, blood urea nitrogen and serum creatinine, liver function catalysts, component of gout, and hostile to Ro and La. The amino acid sequence of Ro60 does not connect Ro52 to Ro52. In any case, the primary SS will hunt Ro52 enemies less frequently than Ro60 enemies. The La protein capabilities as an RNA III polymerase and is once in a while related with the Ro60-hiRNA complex. A typical postero-anterior projection of the hands is shown on the radiograph. Sicca's side effect survey incorporates: problematic dry eyes every day for over 90 days, repetitive sensation of sand in the eyes, different day to day utilization of fake tears, normal liquid admission to swallow dry food varieties, and a day to day dry eye sensation. Clogged. For over 90 days. Examine your eyes: For the Schirmer test, standardized filter paper strips were utilized. The Schirmer test was run for 5 min (mm/ 5 min) at millimeter stickiness. Objective visual dryness was deemed reliable with a Schirmer test result of less than 5 mm/5 min. Highlights from a salivary organ ultrasound: an ultrasound examination of the salivary organs was performed: MSUS material was (Toshiba Xario200), with direct test 10-12 MHz. From 0 (homogeneity) to 3 (severe lack of homogeneity), the parenchyma's homogeneity was evaluated. A support of Al-Azhar Assiut staff of medicine moral warning gathering was obtained before the start of the survey. Verbal and made consent was gotten from individuals who agree to partake in the survey.

The collected data were tabulated and statistically analyzed using statistical package for social sciences (SPSS) version 23.0 for windows. Data are presented as the Mean  $\pm$  standard deviation (SD), frequency, and percentage. The level of significance was accepted if the P value less than 0.05 Figs. 1 and 2.

#### 3. Results

The mean age was range (25-66), 88 (88 %) females and 12 (12 %) male, there were 87 (87 %) from Assiut, 4 (4 %) from Minia and 9 (9 %) from Suhag, illness term was range (2-20) and occupation there were 5 (5 %) ranchers, 90 (90 %) housewives and 5 (5 %) laborers. 6 (6 %) with diabetes, 8 (8 %) with hypertension, 3 (3 %) with Over powered, 46 (46 %) with dry. The mean un-stimulated whole salivary collection (USWC) was range (1-5.5), were 20 (20 %)unusual and 80 (80 %) ordinary. sSS was found in 8 % of the cases studied. No statistically significant connection between personal data and sSS. Significant huge connection among sSS and diabetes, dry eve greater than 3month, regular beverage fluid during eating and dry mouth greater than 3 months. Significant huge connection among sSS and Hemoglobin, plateletes (PLT) and creatinine. High significant critical connection among sSS and Schirmer test. Significant critical connection among sSS and salivary organ ultrasound score (SGUS). Significant critical connection among sSS and DAS-28 Tables 1–13.



Fig. 1. Ultrasound images of left parotid gland in rheumatoid patient according to Hocevar scoring systems illustrating: Example of decreased echogenicity in parotid gland in comparison with thyroid gland.

### 4. Discussion

The most common connective tissue disease associated with SS, RA may cause extra-articular manifestations known as sicca symptoms, such as keratoconjunctivitis sicca, also known as dry eyes, and xerostomia, also known as dry mouth. The goal of this study was to determine the prevalence of sicca symptoms and sSS in patients with RA, as well as the relationship between sicca symptoms.

In our study, there were 88 (88 %) females and 12 (12 %) males in the current study, with a mean age

of 45.27 ( $\pm$ 10.8 SD) and a range of 25–66. 87 (87 %) were from Assiut, 4 (4 %) from Minia, and 9 (9 %) from Suhag. The mean duration of the disease was 8.17 ( $\pm$ 3.83 SD) and ranged from 2 to 20, and according to occupation there were 5 (5 %) farmers, 90 (90 %) housewives and 5 (5 %) workers.

Hassold *et al.*<sup>7</sup> exhibited that 210 ladies (68.4 %) and 97 men (31.6 %) of the 307 patients who were welcome to take part in the review session. The mean age at appraisal was 62.5 years (19–87 years), and the time since determination of RA was 10.6



Fig. 2. Ultrasound images of right submandibular gland in rheumatoid patient according to Hocevar scoring systems illustrating: ill-defined borders.

Table 1. Distribution of the studied cases according to personal data.

	8 1	
	Cases (no = 10	0)
Age		
Range	25-66	
Mean $\pm$ SD.	$45.27 \pm 10.8$	
Sex		
Female	88	88.0
Male	12	12.0
Residence		
Assiut	87	87.0
Minia	4	4.0
Suhag	9	9.0
Disease duration		
Range	2-20	
Mean $\pm$ SD.	$8.17 \pm 3.83$	
Occupation		
Farmer	5	5.0
House wife	90	90.0
Worker	5	5.0

Table 2. Distribution of the studied cases according to history data.

	Cases (1	no = 100)
Diabetes mellitus	6	6.0
Hypertension	8	8.0
Osteoporosis	3	3.0
Dry eye >3month	46	46.0
Sand sensation	9	9.0
Use of artificial tear>3times daily	4	4.0
Frequent drink liquid during eating	37	37.0
Dry mouth >3 months	20	20.0

Table 3. Distribution of the studied cases according to lab investigation.

	Cases (no = 100)
RBCS	$4.89 \pm 0.73$
НВ	$11.42 \pm 1.06$
WBCS	$7.22 \pm 3.29$
PLT	$298.23 \pm 84.09$
ESR	$51.61 \pm 31.57$
CRP	$20.92 \pm 33.03$
RF	$33.1 \pm 37.11$
ALT	$16.51 \pm 8.46$
AST	$18.64 \pm 9.11$
Urea	$27.8 \pm 8.25$
Creatinine	$0.78 \pm 0.22$

ALT, alanine aminotransferase; ESR, erythrocyte sedimentation rate; PLT, plateletes; RF, rheumatoid factor.

Table 4. Distribution of the studied cases according to lab investigation.

	ě ě
Urine analysis	Cases (no = 100) No. (%)
Nil	90 (90.0)
Protein ≫ trace	6 (6.0)
Pus 15-20	4 (4.0)
Anti-RO	$22.33 \pm 38.79$
Anti-LA	$10.33 \pm 14.21$

years (0-50 years). Positive rheumatoid part was found in 248 (80.6 %) patients.

Hernández-Molina *et al.*<sup>8</sup> definite that of 83 individuals in this exploratory audit, 90.4 % (75 from 83) were female. They averaged 48.313 years old.

Table 5. Distribution of the studied cases according to Schirmer test.

	Cases (no $= 100$ )	
Schirmer test		
≫ +ve	23	23.0
≫-ve	77	77.0

Table 6. Distribution of the studied cases according to un-stimulated whole salivary collection (USWC).

	Cases (no = 10	0)
USWC		
Range	1-5.5	
Mean ± SD	$2.8 \pm 1.23$	
Abnormal	20	20.0
Normal	80	80.0

Table 7. Prevalence of Secondary sjogrens syndrome (sSS) among the studied cases.

	Cases (no = 100)	<u>,                                      </u>	
sSS	8	8.0	
Not-sSS	92	92.0	

The duration of RA was 36.1 % for less than 5 years, 21.9 % for 5–10 years, 12.1 % for 11–15 years, and 289.9 % for more than 15 years.

In the ongoing review, 6 (6 %) with diabetes mellitus, 8 (8 %) with hypertension, 3 (3 %) with Osteoporosis, 46 (46 %) with dry eye greater than 3 month, 9 (9 %) with sand sensation, 4 (4 %) with use of fake tear greater than 3 times every day, 37 (37 %) with progressive drink liquid during eating and 20 (20 %) with dry mouth greater than 3 months.

Eldaly *et al.*<sup>9</sup> a recurring sensation of sand in the eyes (17.9 %) and a dry mouth (18.6 %) were the most common complaints, but only 2.6 % used artificial tear substitutes.

Fragoulis *et al.*<sup>10</sup> grievances of dry mouth and dry eyes were tracked down in 29 of 82 (35.3 %) patients, and A minor salivary organ biopsy was performed on 46 of 82 (56.0 %) patients.

The review cases had a mean red blood cells of 4.89 ( $\pm$ 0.73 SD), mean hemoglobin of 11.42 ( $\pm$ 1.06 SD), mean white blood cells of 7.22 ( $\pm$ 3.29 SD), mean PLTs of 298.23 ( $\pm$ 84.09 SD), mean ESR of 51.61 ( $\pm$ 31.57 SD), mean C-reactive protein of 20.92 ( $\pm$ 33.03 SD), mean rheumatoid factor (RF) of 33.1 ( $\pm$ 37.11 SD), mean alanine aminotransferase (ALT) of 16.51.

Smolen *et al.*<sup>11</sup> ESR was most frequently affected when SS and hypergammaglobulinemia overlapped. Notwithstanding, covering SS inescapably affected an extra individual part of the composite RA illness action score. The impact of covering SS on the assessment of RA ailment activity was practically identical regardless of what the composite score applied.

Table 8. Relation between Secondary sjogrens syndrome (sSS) and personal data.

	Cases		Test of	P
	Not-secondary Sjogren's syndrome ( $n = 92$ )	Secondary Sjogren's syndrome ( $n = 8$ )	Significance	
Age (y)				
Range	25-66	40-65	t = 0.950	0.345
Mean ± SD	$44.97 \pm 10.8$	$48.75 \pm 10.94$		
Sex	No. (%)	No. (%)		
Female	80 (87.0)	8 (100.0)	$\chi^2 = 1.186$	0.276
Male	12 (13.0)	0		
Disease duration				
Range	2-20	5-20	t = 1.415	0.160
Mean $\pm$ SD	$8.01 \pm 3.54$	$10 \pm 6.37$		

Table 9. Relation between secondary Sjogren's syndrome and history data.

	Cases		$\chi^2$	P
	Not-secondary Sjogren's syndrome ( $n = 92$ ) No. (%)	Secondary Sjogren's syndrome ( $n = 8$ ) No. (%)		
Diabetes	4 (4.3)	2 (25.0)	5.566	0.018*
Hypertension	8 (8.7)	0	0.756	0.385
Osteoporosis	3 (3.3)	0	0.269	0.604
dry eye >3month	38 (41.3)	8 (100.0)	10.208	0.001*
sand sensation	7 (7.6)	2 (25.0)	2.718	0.099
use of artificial tear>3- times daily	4 (4.3)	0	0.362	0.547
frequent drink liquid dur- ing eating	29 (31.5)	8 (100.0)	14.806	<0.001*
dry mouth >3 months	16 (17.4)	4 (50.0)	4.891	0.027*

Table 10. Relation between secondary sjogrens syndrome and laboratory investigation.

	Cases		Test of	P
	Not-secondary sjogrens syndrome ( $n = 92$ )	Secondary sjogrens syndrome ( $n = 8$ )	Significance	
RBCS				
Range	3.85-6.7	3.5-5.4	t = 1.908	0.059
Mean $\pm$ SD	$4.93 \pm 0.72$	$4.43 \pm 0.72$		
HB				
Range	8.5-13.3	8-11.6	t = 2.203	0.030*
Mean $\pm$ SD	$11.49 \pm 0.97$	$10.65 \pm 1.64$		
WBCS				
Range	4-25	6-10.7	t = 0.859	0.393
Mean $\pm$ SD	$7.13 \pm 3.37$	$8.18 \pm 1.94$		
PLT				
Range	150-511	179-315	t = 2.732	0.007*
Mean ± SD	$304.79 \pm 83$	$222.75 \pm 58.22$		
ESR				
Range	7-140	30-110	U = 303.0	0.408
Median (IQR)	45 (30-61)	50 (33.75-76.25)		
CRP				
Range	0-192	0-96	U = 262.0	0.176
Median (IQR)	12 (2-24)	2.4 (0.75-26.85)		
RF				
Range	8-128	8-32	U = 351.0	0.989
Median (IQR)	16 (8-32)	22 (14-29)		
ALT				
Range	4-53	10-30	U = 272.0	0.218
Median (IQR)	14 (12–19)	19 (14.5-24)		
Median (IQR) RF Range Median (IQR) ALT Range	12 (2-24) 8-128 16 (8-32) 4-53	2.4 (0.75–26.85) 8–32 22 (14–29) 10–30	U = 351.0	

(continued on next page)

Table 10. (continued)

	Cases		Test of	P
	Not-secondary sjogrens syndrome ( $n = 92$ )	Secondary sjogrens syndrome ( $n = 8$ )	Significance	
AST				
Range	6-66	13-35	U = 356.0	0.345
Median (IQR)	17 (14-20)	16 (13.75–22.25)		
Urea				
Range	15-51	28-38	t = 1.236	0.878
Mean $\pm$ SD	$27.5 \pm 8.46$	$31.25 \pm 4.23$		
Creatinine				
Range	0.4-1.2	0.7-1.2	t = 2.022	0.046*
Mean $\pm$ SD	$0.77 \pm 0.21$	$0.93 \pm 0.24$		

ALT, alanine aminotransferase; ESR, erythrocyte sedimentation rate; PLT, plateletes; RF, rheumatoid factor.

Table 11. Relation between secondary sjogrens syndrome and Schirmer test.

	Cases		Test of Sig.	P
	Not-secondary sjogrens syndrome ( <i>n</i> =92)	Secondary sjogrens syndrome ( $n = 8$ )		
Schirmer test	No. (%)	No. (%)		
≫-ve	77 (83.7)	0	$\chi^2 = 29.112$	<0.001*
≫ +ve	15 (16.3)	8 (100.0)		

Table 12. Relation between secondary sjogrens syndrome and salivary organ ultrasound Score.

	Cases		Test of	P
	Not-secondary sjogrens syndrome ( $n = 92$ )	Secondary sjogrens syndrome ( $n = 8$ )	Significance	
SGUS Score				
Range	0-40	18-35	U = 173.50	0.013*
Mean ± SD	5 (1-23)	22.5 (19-24.25)		

Table 13. Relation between secondary sjogrens syndrome and disease activity index (DAS-28) Score.

	Cases		Test of	P
	Not-secondary sjogrens syndrome ( $n = 92$ )	Secondary sjogrens syndrome ( $n = 8$ )	Significance	
DAS-28				
Range	2.2-6.69	5.2-6.67	t = 3.055	0.003*
Mean ± SD	$4.69 \pm 1.1$	$5.9 \pm 0.59$		
Classification	No. (%)	No. (%)		
Remission	4 (4.3)	0	$\chi^2 = 15.459$	0.001*
Low activity	10 (10.9)	0		
Moderate activity	50 (54.3)	0		
High activity	28 (30.4)	8 (100.0)		

Lee *et al.*<sup>12</sup> demonstrated that 581 of the 820 R A patients who underwent RF testing came back positive. Among the RF-positive RA patients (n=581), 61 (10.5 %) patients had rheumatologist investigated SS. Only 11 (4.6 %) of the 239 RF-negative RA patients had rheumatologist-analyzed SS.

In the ongoing survey, 6 (6 %) with protein follow and 4 (4 %) with release, the mean Adversary of RO focused on cases was 22.33 (±38.79 SD) and the mean Foe of LA was 10.33 (±14.21 SD).

Alani *et al.* <sup>13</sup> only 48 % of people had anti-La, and only 83 % had anti-Ro (of which 59 % also had anti-La), Antinuclear antibodies and rheumatoid component were positive in 95 % and 67 % independently. 22 (38 %) and 10 (17 %) had low C4 and C3.

Brown *et al.*<sup>14</sup> reported that really two patients of 829 patients have against Ro and threatening to La negatives (they had xerostomia and xerophthalmia, parotid breadth and biopsy feasible with the end).

There were 10 cases of the disease, 2 of which were large growths and 4 of which were hematologic.

There were 23 (23 %) positive Schirmer test results and 77 (77 %) negative test brings about this review. There were 20 (20 %) abnormal cases and 80 (80 %) normal cases, with a mean USWC of 2.8 ( $\pm$ 1.23 SD) and a range of 1–5.5.

Haga *et al.*<sup>15</sup> brought up that 11 patients had positive Schirmer I and USWC tests. This shows that sSS has a base predominance of 3.6 %.

Brkic *et al.*<sup>16</sup> reported that the Schirmer test result ranged from 0 to 35 mm and was less than 5 mm in 34 of 82 cases (41.4 %). Ceratitis was also present in five (6 %) patients.

Our continuous disclosures the mean SGUS of focused on cases was 12.49 ( $\pm$ 12.89 SD) with range (0–40) and 39 (39 %) uncommon and 61 (61 %) standard. The average DAS for the 28 cases that were examined ranged from 2.2 to 6.69, and 36 (36 %) of them were unusual and 64 (64 %) were ordinary.

Goodchild *et al.*<sup>17</sup> saw that DAS-28 varied from 0.6 to 6.99 (mean  $3.22 \pm 1.41$ ). Twenty patients (24.39 %) met the American-European criteria for sSS.

Tan *et al.*<sup>18</sup> demonstrated that at the first visit, the median age, duration of RA, and DAS-28-C-reactive protein were 51 (IQR 45–61), 24 (IQR 8–120), and 3.86 (IQR 2.78–4.74) years, respectively.

There was a genuinely huge connection among sSS and diabetes, sSS and Hb, PLT and creatinine, sSS and SGUS Score, sSS and DAS - 28, and sSS and Schirmer test, yet there was no significant critical connection among sSS and individual information.

In simultaneousness with our review, Das *et al.*<sup>19</sup> definite that Focusing on DAS-28 according to the presence of discretionary SS, we found a mean worth of  $2.81 \pm 1.14$  in those with SS and  $3.35 \pm 1.47$  in those without it (P = 0.13).

On the other hand, Hajiabbasi *et al.*<sup>20</sup> The occurrence of sSS is unaffected by the duration of the disease, despite the fact that a role registered to the activity of the disease has been observed that there was no significant connection between UWSC and DAS-28, nor between UWSC and the quantity of delicate and enlarged joints. A small number of RA patients had sSS. There was no statistically significant relationship between sSS and personal data, but there were statistically significant relationships between sSS and diabetes, Hb, PLT, and creatinine, SGUS Score, DAS-28, and sSS and Schirmer test.

## 4.1. Conclusion

The incidence of sSS is not affected by disease duration, whereas the reported role of disease

activity has been demonstrated. Secondary SS was found in a secondary subset of RA patients.

#### Conflicts of interest

There are no conflicts of interest.

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