

The Incidence of Secondary Sjogren Syndrome in Relation to Disease Activity & Disease Duration of Rheumatoid Arthritis Patients

Fatma A. Abdulkareem¹, Fawaz D. AL-Aswad², Mohammed H. Alasami³

^{1,2}Baghdad University, College of Dentistry, Baghdad, Iraq

³Baghdad University, College of Medicine, Baghdad, Iraq

Abstract: Background: Secondary sjogren syndrome is a chronic autoimmune disease that associated with connective tissue disorders most commonly Rheumatoid arthritis. Aim of the work: to evaluate the incidence of secondary Sjogren syndrome in relation to disease activity & disease duration of Rheumatoid arthritis. Methods: 61 Rheumatoid arthritis patients of either gender with age range (25- 60) y., of them (31 patients with Secondary sjogren syndrome diagnosed according to American-European Consensus Group criteria (AECC) & 30 Rheumatoid arthritis patients diagnosed clinically by rheumatology specialists) both of them evaluated clinically by DAS28-score & subjected to questionnaire including duration of the disease. Result: a comparison between two studied diseased groups using ROC curve, showed highly significant differences at $p = 0.018$ regarding disease duration, and secondary sjogren group revealed long duration than Rheumatoid arthritis group .while no relation could be found between DAS28 & occurrence of secondary Sjogren syndrome. Conclusion: the occurrence of secondary sjogren syndrome affected by disease duration but independent of DAS28 Rheumatoid arthritis.

Keywords: secondary Sjogren syndrome, Rheumatoid arthritis, Disease duration, Disease Activity 28

1. Introduction

Sjögren syndrome (SS) is a chronic autoimmune inflammatory disease that initially involves the exocrine glands, resulted in their functional defacement. Sjögren syndrome can present either alone (primary Sjögren's syndrome (pSS)) or in association of an underlying connective tissue disease, most commonly rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE) (secondary Sjögren's syndrome (sSS)). (1) Clinically the hallmarks of Sjögren's syndrome are keratoconjunctivitis sicca and xerostomia, or named sicca complex.(2)

Sjögren's syndrome is an autoimmune disease related to the group of collagenases. that is manifested by lymphocytic infiltration of the exocrine glands, leading to their functional impairment . The inflammatory process involves cells of the lacrimal or salivary glands. However, other organs and systems can be affected. (3)

The chief pathogenesis of primary Sjögren's syndrome is the distribution of T cells and B cells regulation, with central contributors from innate pathways of inflammation. So that many of these same concepts may be relevant to the pathogenesis of secondary Sjogren's syndrome; although, most researching into the mechanisms of the disease was focusing on patients with the primary form of the disease, & may be many of the immunologic features of secondary Sjögren's syndrome are determined by the pathogenic mechanisms involving the associated disorders. (2)The present study aims to study if the occurrence of secondary Sjogren syndrome have any association with disease duration &/or disease activity of Rheumatoid arthritis.

2. Patients & Methods

A comparative study was performed in Baghdad Teaching Hospital / Department of Rheumatology .This study was conducted on patients after approval of the research protocol by the Research Scientific Committee .The study samples consist of ninety patients,60 Rheumatoid arthritis (RA) patients of either gender with age range (25- 60), of them (30 patients with secondary Sjogren syndrome (sSS) diagnosed according to American-European Consensus Group criteria (AECC) (4) & 30 RA patients diagnosed clinically by rheumatology specialists) and both of them evaluated by disease activity depending on DAS 28 "Disease Activity Score in 28 Joints (DAS28)" & 30 Healthy control subjects.

The study sample divided into three groups:

Group I: (n=30) sSS patients with RA.

Group II: (n=30) RA patients .

Group III: (n=30) healthy control subjects.

Exclusion Criteria

Past head and neck radiation treatment; hepatitis C infection; acquired immunodeficiency syndrome (AIDS); preexisting lymphoma; sarcoidosis; graftvs.-host disease; use of anticholinergic drugs (since a time shorter than fourfold the half-life of the drug)

Diagnoses of the secondary Sjogren syndrome patients according to American-European Consensus Group criteria (AECC), all included patients subjected to Schirmer test "Cutoff for abnormally low tear production is 5 mm distance or less usually".(2), whole unstimulated salivary flow rate "a less than 1.5mL is considered abnormal or xerostomia". (4). Also those patients should have (+ve ocular symptoms & oral symptoms) then evaluation of the (DAS 28)

carried out by specification of the no. of swollen & tender joints in 28 joints encompassing the small joints in the hands, wrists, elbows, shoulders, and knees". The score is derived from a complicated formula, (5). DAS28 is carried on both studied groups (RA & sSS).

Statistical analysis:

All data were interpreted in a computerized database structure. "Statistical Package for Social Sciences" (SPSS) version 20 was applied. Comparisons were done using Contingency Coefficient (CC) test for the cause's correlation ship of the association tables; P value was considered statistically significant when < 0.05. The Receiver operating Characteristic (ROC) analysis was done for ranking quantitative parameters in descending manner according to their area under the curve (AUC), to figure out the most affected parameters by the disease status.

3. Results

Results demonstrated that, vast majority of a diseased groups are reported at (40 – 49) yrs., and at (60 – 70) yrs. for the RA, and sSS with mean and standard deviation (48.30 ± 10.02) yrs., and (52.65 ± 9.88) yrs. respectively, and highest percentages of the diseased groups were found at females, and they are accounted 28(93.3%), and 31(100%), in RA, and sSS groups respectively.

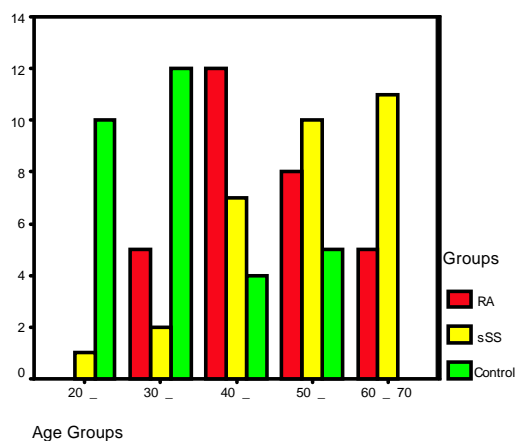


Figure 1: Distribution of the sample according to age

Table1: Distribution of studied groups according to age

Age Groups	Groups			
	RA		sSS	
	No.	%	No.	%
20 _	0	0	1	3.2
30 _	5	16.7	2	6.5
40 _	12	40	7	22.6
50 _	8	26.7	10	32.3
60 _70	5	16.7	11	35.5
Total	30	100	31	100
Mean ± SD	48.30 ± 10.02		52.65 ± 9.88	

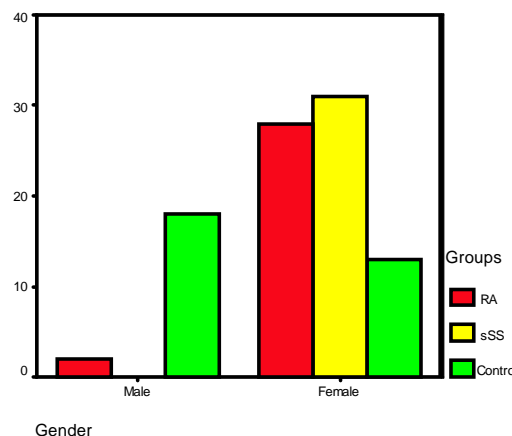


Figure 2: Distribution of the samples according to gender

Table 2: Distribution of the studied groups according to gender

Gender	RA		sSS	
	No.	%	No.	%
Male	2	6.7	0	0.00
Female	28	93.3	31	100
Total	30	100	31	100

Distribution of DAS-28 results in two diseased groups

With respect to "DAS28-Result levels", result showed that relationship are reported (CC=0.279) in light of increases mainly low level of DAS 28-Result in RA group, and MDA level in both groups, especially regarding sSS group, then followed by HAD level similarly. In addition to that, rather than no significant difference at P>0.05 are accounted between the two diseased groups in light of DAS28-Result responding, but according to low calculated significant level, it make more informative for that level to be reported, rather than simply stating that statistical significant was not achieved.(6)that illustrated in figure & table 3

Table 3: Distribution of DAS28-Result levels responding according to studied groups with comparisons significant

Parameter	DAS 28-Result	Groups No. & %	Groups		Total	C.S. (*) P-value
			RA	sSS		
DAS28-Result levels	(Remission)	No.	4	0	4	C.C.=0.279 P=0.161 NS
		% Group	13.30%	0.00%	6.60%	
	(LDA)	No.	2	2	4	
		% Group	6.70%	6.50%	6.60%	
	(MDA)	No.	13	19	32	
		% Group	43.30%	61.30%	52.50%	
(HDA)	No.	11	10	21		
	% Group	36.70%	32.30%	34.40%		

(*) NS: Non Sig. at P>0.05; C.C.; Contingency Coefficients.

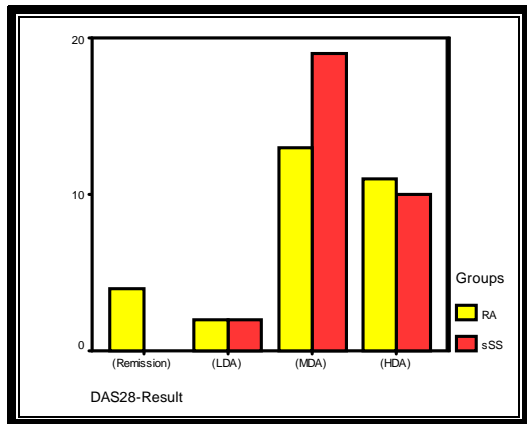


Figure 3: Cluster Bar Chart for redistribution

"DAS28 Result" outcomes in the studied disordered groups

Diseased Groups Duration sSS revealed highly significant difference comparing with RA group, at $p < 0.01$ in Receiver operating Characteristic curve (ROC). which illustrated in figure & table 4

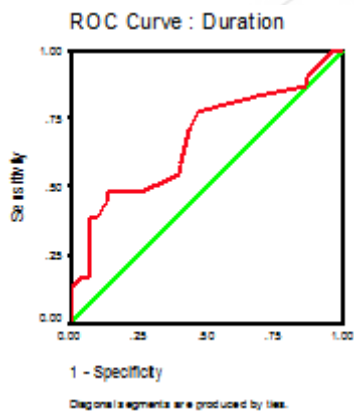


Figure 4: ROC Curve Plots for the diseases (sSS : RA) groups in light of studied disease Duration.

Table 4: Statistics of ROC Curve in contrasts of diseases (sSS : RA) groups in light of studied (disease Duration)

Test Result Variable(s)	Area Under the Curve				
	Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Duration/m	0.676	0.069	0.018*	0.54	0.812

(*) HS: Highly sig. at $P < 0.01$; S:Sig. at $P < 0.0$; NS: Non Sig. at $P > 0.05$

4. Discussion

Sjogren's syndrome considered to be one of the chronic autoimmune disease that characterized by symptoms of ocular and oral dryness, exocrine dysfunction, destruction of the exocrine glands & lymphocytic infiltration. SS mainly affects "women in the fourth and fifth decade with female to male ratio 9:1". (7)

Sjogren's syndrome occasionally coexists with other systemic autoimmune diseases, such that SLE and RA. Since 1965 several studies have been focusing on RA associated with SS. (8) Unfortunately Sjogren syndrome is a common

autoimmune disease but till now it remain underdiagnosed inflammatory disease that have significant impact on "oral health" Oral physicians should be the first health care providers meeting the early stage.

Disease Activity

Regarding disease activity which measured by DAS28-Score the finding result of the present study explained that the occurrence of sSS was unaffected by disease activity, also studies done by (9, 10, 11) are agreed with the current study. In the other hand (8, 12, 13) they found that the occurrence of sSS are increased in RA patients who had higher disease activity.

There were many variations between studies regarding relationship between sSS & disease activity, however one of the suggested reasons is using different or non-standard regimes "such as steroids or nonsteroidal anti-inflammatory medications", disease modifying Rheumatoid arthritis drugs that can affect the severity of the disease, second reasons estimated that even though DAS28-ESR formula is quantitative measure but part of the formula is depending on patient's tolerance to pain which is considered as subjective criteria. So this in turn affects the accuracy of DAS28 formula in determining severity of RA.

Duration of the disease

Our results showed that there was a significant difference in disease duration between RA & sSS which illustrated in ROC curve, so this lead to the suggestion that secondary SS occurrence may relate to disease duration. This results in line with study done by (8); they proposed that patients with sSS have old age & long duration of the disease than those with RA only &/or pSS. While on the other hand studies done by (11, 12, 14); they found that no relations between duration of the disease & sSS occurrence.

The variations in the results of these studies may be related to the size of the sample, ethnic &/or genetic background.

5. Conclusion

The occurrence of secondary Sjogren syndrome is affected by the duration of the disease, while no role registered to the disease activity.

References

- [1] Peri Y, Agmon-Levin N, Theodor E, Shoenfeld Y. Sjögren's syndrome, the old and the new. Best Practice & Research Clinical Rheumatology. 2012 Feb 29;26(1):105-17.
- [2] Clair WS. Sjogren syndrome .In : Firestein GS, Budd R, Gabriel SE, McInnes IB, O'Dell JR. editors. Kelley's textbook of rheumatology. Elsevier Health Sciences; 2012 Aug 31;P1169-11913
- [3] Pryczynicz A, Guzinska-Ustymowicz K, Wakulewska A, Ducher M, Lewczuk L, Kisielewski W, Ustymowicz A, Ziolo M, Famulski W. Fine needle aspiration cytology in

the diagnosis of Sjögren's syndrome. Progress in Health Sciences. 2013 Jul 1;3(2):178.

- [4] Vitali C, Bombardieri S, Jonsson R, Moutsopoulos HM, Alexander EL, Carsons SE, Daniels TE, Fox PC, Fox RI, Kassan S, Pillemer SR. Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. *Annals of the rheumatic diseases*. 2002 Jun 1;61(6):5
- [5] Van der Heijde DM, Van't Hof M, Van Riel PL, Van de Putte LB. Development of a disease activity score based on judgment in clinical practice by rheumatologists. *The Journal of rheumatology*. 1993 Mar;20(3):579-81.
- [6] Nordness RJ. Epidemiology and biostatistics secrets: questions you will be asked: top 100 secrets, key points and web sites. In *Epidemiology and biostatistics secrets: questions you will be asked: top 100 secrets, key points and web sites* 2006. Mosby Elsevier.
- [7] Glick M. *Burket's Oral Medicine*, 12e. PMPH-USA; 2015
- [8] He J, Ding Y, Feng M, Guo J, Sun X, Zhao J, Yu D, Li Z. Characteristics of Sjögren's syndrome in rheumatoid arthritis. *Rheumatology*. 2013 Feb 4;kes374.
- [9] Antero DC, Parra AG, Miyazaki FH, Gehlen M, Skare TL. Secondary Sjögren's syndrome and disease activity of rheumatoid arthritis. *Revista da Associação Médica Brasileira*. 2011 May 1;57(3):319-22.,
- [10] Zakeri Z, Parsa M, Zanjani H, Ansarimoghaddam A, Sandoughi M, Aminifard M, Shahbakhsh S, Pour AB. Relationship Between Severity of RA and Dry Eye Syndrome. *Health Scope*. 2013 Feb;1(4):184-6.
- [11] Abdelghani KB, Mahmoud I, Chatelus E, Sordet C, Gottenberg JE, Sibilia J. Clinical and Serological Features of Sjogren Syndrome in Patients with Rheumatoid Arthritis. *British Journal of Medicine and Medical Research*. 2015 Jan 1;5(10):1287.
- [12] Uhlig T, Kvien TK, Jensen JL, Axéll T. Sicca symptoms, saliva and tear production, and disease variables in 636 patients with rheumatoid arthritis. *Annals of the rheumatic diseases*. 1999 Jul 1;58(7):415-22.
- [13] Wolfe F, Michaud K. Prevalence, risk, and risk factors for oral and ocular dryness with particular emphasis on rheumatoid arthritis. *The Journal of rheumatology*. 2008 Jun 1;35(6):1023-30.
- [14] Antero DC, Parra AG, Miyazaki FH, Gehlen M, Skare TL. Secondary Sjögren's syndrome and disease activity of rheumatoid arthritis. *Revista da Associação Médica Brasileira*. 2011 May 1;57(3):319-22.



Prof. Dr. Fawaz Dawad Abdulrazaq, Graduated from college of Dentistry/Baghdad University at 1991, he gained B.D.S degree. In 1999 gained M.Sc. in oral medicine and in 2004 gained Ph.D. in oral medicine from College of Dentistry/Baghdad University. Now he is full Prof. in oral medicine in the oral diagnosis department at college of Dentistry/Baghdad University.



Dr. Mohammed H. Alosami received the M B Ch B FROM the college of Medicine / Al-Mustanserreyia University at 1993 .Then he received the certificate of Iraqi Board of internal medicine at 2000& Arabic Board in internal medicine at 2002 CABM, and the fellowship of and the certificate of subspeciality in rheumatology and medical rehabilitation from the Iraqi board of medical specialization FICMS(Rheumatology) at 2003, then he joined the staff of the college of Medicine of Baghdad at 2010 and now he is assistant Prof. of medicine and consultant Rheumatologist and head of Rheumatology unit at Baghdad teaching hospital.

Author Profile



Dr. Fatma A. Abdulkareem received the B.S. in Dental and Maxillofacial surgery and M.S. degrees in Oral Medicine from College of Dentistry/Baghdad University in 2002 and 2012 respectively. During 2002-2012 stayed in different institutions at Iraqi Ministry of Health. Now study to award the Doctor of Philosophy degree in Oral Medicine.