OPEN ACCESS

Research Paper

Estimation of Prevalence Rate of Sjogren's Syndrome among Rheumatology Clinic Patients in Iraq

Ziad S. AL Rawi,[1] Mohammed H AL Osmi,[1] Elaff A Jebur,[1]
Shna A Mohammed Amin,[2] Mariwan Esmaeel.[2]

ABSTRACT:

BACKGROUND:

Primary Sjogren's syndrome is a system chronic autoimmune disorder, it's a etiology is still not well understood. The syndrome is characterized by lymphocytic infiltrates in exocrine organs. There has been no previous prevalence study about Sjogren's syndrome in Iraq.

OBJECTIVE:

To determine the prevalence rate of primary Sjogren's syndrome among Rheumatology clinic patients in Iraq.

PATIENTS AND METHODS:

A cross –sectional Rheumatology clinic – based survey was performed on 1000 consecutive patients aged 18-70 years attending rheumatology clinic during the first 9 months of the year 2019. Patients fulfilling the 2002 criteria for the classification of Sjogren's syndrome, and those fulfilling the 2010 criteria for classification of rheumatoid arthritis were recorded to estimate the prevalence of primary Sjogren's syndrome.

RESULTS:

Among the 1000 studied adult rheumatic disease pateints attending the rheumatology clinic, there were 98 pateints diagnosed as primary Sjogren's syndrome and 165 patients diagnosed as rheumatoid arthritis. By compairing the prevalence of primary Sjogren's syndrome with that of rheumatoid arthritis and extrapolating of data, we found that the estimated prevalence of pSS is 0.59% of population, which is more common in elderly females. It comes next only to rheumatoid arthritis in frequency among connective tissue diseases in Iraq.

CONCLUSION:

Primary Sjogren's estimated prevalence is 0.59% of the population, and was more common in elderly females.

KEYWORDS: Sjogren's syndrome , Epidemiology, Cross-sectional study

[1] *College of Medicine , University of Baghdad, Baghdad, Iraq*
[2] *Kurdistan Board for Medical Specialties –Rizgari Teaching Hospital, Erbil, Iraq*

Iraqi Postgraduate Medical Journal, 2024; Vol. 23(2): 231-237
DOI: 10.52573/Ipmj.2023.136801, Received: November 24, 2022, Accepted: December 27, 2022

INTRODUCTION:

Primary sjogren's syndrome(pSS) is a systemic chronic autoimmune disorder, its aetiology is still not well understood.[1-3] The syndrome is characterized by lymphocytic infilterates in exocrine organs. Most individuals with pSS present with dry eyes (xerophthalmia) dry mouth(xerostomia) and parotid gland enlargement [4,5] The disease is also a systemic disorder that may involve several body systems [6-12] like arthritis, raynauds phenomenon, myalgia, pulmonary and gastro intestinal manifestations, heamatological, neurological, cutaneaous manifestation and fatigue. When the disease diagnosed in the absence of another underlying autoimmune disease its termed pSS and when it occur in combination with another auto-immune disease it's termed secondsry Sjogren's syndrome (sSS), the disease most often affect women and the median age of onset is around 50 to 60 years.[13] The prevalence rate of pSS varies widly round the world. Published studies using various classification criteria reported wide range of prevalence which was reported between (0.04%-6.50%).[14,15] There is a great feeling among Iraqi physicians and General practionars that pSS is a rare disease without a reference. Rheumatologist working in the main teaching hospitals do not share this feeling with their colleugues, so we aimed in this study to clarify this point by estimating the prevalence rate of pSS among Iraqi population.

PATIENTS AND METHODS:

A cross –sectional Rheumatology clinic- based survey was performed on 1000 consecutive patients aged 18-70 year attending the rheumatology clinic between first of January to the 30th of September 2019 . Patients fulfilling the AECG- 2002 criteria for classification of pSS,[16] and those fulfilling the 2010 criteria for classification of rheumatid arthritis(RA)[17] were recorded in order to estimate the prevalence of PSS. Patients were excluded from the study if they have one of the followings: 1. Other collagen disease and or vasculitidis 2. Post head- and –neck irradiation 3.Hepatitis C virus infection. 4.Diabetis mellitis. 5. Sarcoidosis 6. Use of anticholenergic drugs or diuretics. Full history was taken from all patients suspected to have pSS or RA and complete clinical examination was made for patients in both groups. Schrimer's test, as well as measurment of Unstimulated Salivery flow were done for patients in both groups. ESR, CBC, with Xray both hands and feet AP views were done for patients in both groups. Autoantibodies: Anti Ro (SSA), Anti La (SSB), Rheumatoid factor (RF), Anti neuclear antibodies (ANA) were done for patients with possible pSS. If the autoantibodies are negative in suspected pSS group of patients, then labial salivery gland biopsy was performed and sent for histopathological studies. RF and Anti-ccp antibodies were tested in suspected patients with RA.

Patients ethical and consent approval:

1. Ethical approval was obtained from local authorized committee for doing the study.
2. Statistical analysis:Microsoft Excel was used for data organizations and analysis. Continuous variables were presented as mean +/- Standard Deviation (SD) and categorical variables were presented as frequency and relative frequency. Confidence Interval for proportion was calculated to estimate the frequency of the disease among 1,000 patients with various rheumatic diseases. All data were arranged and tabulated in number and percent, which was performed to measure association between different variables by using EPI-Info version 16 by Chi-Square and Fisher's Exact tests and results were tested at 0.05 level of statistical significance.
3. A signed consent was taken from all patients studied.

RESULTS:

During the study period 1000 patients with various rheumatic diseases were studied. There were 661 female and 339 male patients with a female to male ratio of (2/1) as shown in Table 1.

Table 1: Distribution of 1000 RD patients by gender

Gender	No.	%
Males	339	33.9
Females	661	66.1
Total	1000	100.1

On calculating the 95% confidence interval (CI) for the population proportion, it was found that the 95% confidence interval for the population proportion of the PSS ranged from 0.08-0.116 where as that of RA ranged from 0.142-0.188 as shown in table (2).

Table 2: Proportion of PSS and RA among the studied patients

Variable	No. Total No=1000	%	95%CI
PSS	98	9.8	(0.08-0.116)
RA	165	16.5	(0.124-0.188)

There were 98 patients with PSS, 92 female and 6 male patients with a female to male ratio of 92/6 =(15/1), (P< 0.05). And 165 patients diagnosed as RA, 125 female and 40 male patients with a ratio of (3/1) (P<0.05). The differences between female and male groups were statistically significant among both diseases, as shown in table 3.

Table 3: Distribution of pSS & RA patients by gender

Gender	pSS Patients	RA Patients	Total	P value
Males	6	40	46	0.0002*
Females	92	125	217	
Total	98	165	263	

**The association was statistically significant (Chi-s= 13.99, DF=1,P<0.05)*

The 1000 patients with various RD age ranged between 18-70 years with a mean age of 47.26 ±12.8 standard deviation (SD). when they are subdivided into two age groups, patients number whom they are less than 50 year old are more frequent compared to the group whom they are 50 years old and over, but the difference were insignificant. (P>0.05) as shown in Table 4.

Table 4: Distribution of RD patients by age group.

Age (in years)	Patients with RD		Total	P value
	Males	Females		
<50	191	339	530	0.13*
≥50	148	322	470	
Total	339	661	100	

**The association was not statisically significant (Chi-squared=2.3, P>0.05)*

When the 98 patients with PSS were sub-divided also into two age groups. Patients 50 year old and over group, there mean age and SD are 58.9±12.8 for 53 female and 58.7±13.03 for 4 male patients (total 57) compared to those group whom they are less than 50 year old, there mean age and SD are 36.8±12 for 39 female and 37±12 for 2 male patients (total 41). Although the number of patients with PSS aged 50 and over were more frequent than those whom they are below the age of 50 year, but the differences were insignificant (P> 0.05), as shown in table 5.

Table 5: Distribution of pSS patients by age group.

Age (in years)	Patients with pSS		Total	P value
	Males	Females		
<50	2	39	41	1*
≥50	4	53	57	
Total	6	92	98	

**This association was statistically not significant Fisher's Exact Test, P>0.05*

One hundred sixty-five patients with RA were sub-divided also into two age groups. Patients under 50 year old group, there mean age and SD are 35.5±7.8 for 59 female and 36.7±8.12 for 15 male patients compared to those group whom they are 50 year old and over, there mean age and SD are 59.8±5 for 66 female and 59.4±21.8 for 25 male patients. Although the number of patients with RA aged less than 50 year old were more frequent than those whom they are 50 year old and over, but the differences were insignificant (P> 0.05), as shown in table 6.

Table 6: Distribution of RA patients by age group.

Age (in years)	Patients with RA		Total	P value
	Males	Females		
<50	25	66	91	0.28*
≥50	15	59	74	
Total	40	125	165	

**The association was statistically not significant (Chi-squared=1.15, P>0.05)*

Patient occupations are shown in table (7) which did not show any effect on the diseases studied.

Table 7: Employment of pSS and RA patients studied

Occupation	pSS Patients	RA Patients	Total	P value
Housewives	45	71	116	
Civil Servant	21	37	58	
Employee	20	38	58	0.98*
Unemployed	5	8	13	
Others (Retired, students)	7	11	18	
Total	98	165	263	

**The association was statistically not significant (Chi-squared=1.15, P>0.05)*

Among the 1000 studied adult rheumatic diseases patients attending the rheumatology clinic there were 98 patients diagnosed as PSS and 165 patients diagnosed as RA. In a population study sample in Iraq [17] definite RA patients were observed in 1% of 6999 individuals studied. By comparing the prevalence of PSS with that of RA and extrapolating the data, we found that the estimated prevalence of PSS is 0.59% of adult population which comes next only to RA in frequency among connective tissue diseases in Iraq.

All patients with PSS have positive symptoms and signs of dry eyes and dry mouth.

Parotid gland enlargement was reported in 39(39.8%) patients. Autoantibodies were reported as follows ANA was positive in 72 patients, RF was positive in 65 patients, SSA was positive in 55 patients and SSB was positive in 31 patients. Both SSA and SSB were negative in 22 patients, for whom labial tissue biopsy were done and histopathological examination was consistent with Sjogren's syndrome. Labial salivary gland biopsy has been considered for long duration as gold standard for diagnosing Sjogren's syndrome with sensitivity of 83.5% and specificity of 81.8%.[13] The prevalence of the disease was significantly higher among female {92(93.88%)} patients compared to male 6 (6.12%) patients (P< 0.05). The frequency of PSS is higher among patients aged 50 year and over (57) compated to those less than 50 year old (41), but the differences were insignificant (P> 0.05)

DISCUSSION:

Primary Sjogren's syndrome is an autoimmue disease of unknown aetiology. The burden of this disease is substantail because of lack of theraputic options. The disease has a significant burden to patient quality of life and the health care system.[19] Until today no epidemiological study which investigated the prevalence of pSS in Iraq .

However there were earlier studies done in various parts of the world which yields a wide range of incidence and prevalence rates in Asia,[19-21] America,[22,23] and Europe.[24-28] This variation is attributed to many factors, partly because different studies have used different criteria to classify patients, study design and methodology, population sample studied, ethnicity ,age and sex of individuals studied. Mild cases may be overlooked or misdiagnosed. Comparison of our results with those from other population surveys has been hampered by methodological problems mentioned above. The difficulties with usage of so many classification criteria should become less with the publication of EU- USA consensus -2002 (AECG) criteria which is widely used in clinical and prevalence studies during the last two decades. In this study the estimated prevalence of pSS is reported as 0.59% of the adult population.

Although comparison of the prevalence rate of our results and others which were reported from various parts of the world is quite difficult, not only because of the presence of genetic, environmental and major methodological differences among these studies but also because of uses of different classification criteria. Among published series there were wide range of prevalence of PSS which were reported between (0.04% -6.5%) [14,15]. This high wide range of prevalence, declined dramatically to (0.01-0.72%) [27,21] when one set of criteria (AECG-2002) was used in all surveys as shown in

table (8), and for that we decided to compare our findings with other published surveys using the same classification (AECG-2002) criteria to minimize these variations.

Table 8: Prevalence estimates of primary Sjögren's syndrome in published studies using AECG-2002 classification criteria in comparison to the present study

Author	Year	Country	Clinical examination	Study design	PSS no.	Population no.	Female/ male no.	Prevalence (100%)
Bowman S. J., et al.(24)	2004	UK	Questionnaire Clinical examination	Cross-sectional female population survey	2	846 Females	2	0.1-0.4%
Trontzas P. I., et al.(28)	2005	Greece	Questionnaire Clinical examination	Cross-sectional population based	13	8740	12/1	0.15%
Alamanos Y., et al.(25)	2006	Greece	Medical record search	Population based	422	500	20/1	0.09%
Kabasakal Y., et al.(21)	2006	Turkey	Questionnaire Clinical examination	Cross-sectional population survey	6	831 females	6	0.72%
Birlik M., et al,(19)	2008	Turkey (Balcova)	Questionnaire Clinical examination	Cross-sectional population survey	6	2837	6/0	0.21%
Anagnostopoulos L., et al.(29)	2010	Greece (Prefecture)	Questionnaire Clinical examination	Cross-sectional population survey	4	3528	NR	0.23%
Goransson L. G., et al.(26)	2011	Norway	Medical record search	Population based	424	852 342	396 / 28 93% / 7%	0.05%
Valim V., et al.(23)	2013	Brazil	Questionnaire Clinical examination	Cross-sectional population survey	2	1205	2/0	0.17%
Maldini C., et al.(27)	2013	France (Paris)	Comprehension methods	Population based	133	1 172 4	126/7	0.01-0.09%
Al-Rawi Z. S., et al. Present study	2022	Iraq	Clinical examination	Cross-sectional Rheumatology clinic survey	98	1000 patients	92/6	0.59%

There were two surveys (Haugen-Norway)[14] and (Birlik-Turkey)[19] whom they were using two sets of criteria by each of them, during the same survey .The preliminary European criteria (EU C-1993) [30] and the revised European criteria (EU C-1996) [31] were used in Haugen study, while the (EU C-1993) and the (AECG-2002) criteria were used in Birlik study. It was found that in Haugen survey the prevalence was double (0.44%) when (EU C-1993) was used compared to (0.22%) when revised (EU C-1993) criteria were used, which is very much comparable to the results of Birlik which shows 10 patients with PSS When (EU C -1993) criteria was used compared to 6 patients with PSS when (AECG-2002 criteria) was used.

The findings in these two studies confirms how much usage of various classification criteria can affect the results of each survey. It's well known from all surveys that females are much more frequently affected by the disease compared to male individuals [19,25,26,27,28] and this could explain why Kabasakal survey [21] from Turkey gives the highest prevalence among the compared studies in the above table (8) because it was conducted on adult female individuals only. In order to decrease the possibilities of under estimation of PSS we have to keep in mind that patients who are accompanied by extra ordinary fatigue, pain and arthralgia following structural approach would best facilitate and favor the recognition and diagnosis of PSS.

Better estimation of prevalence rates of PSS in various countries using uniform methodology and accepted one classification criteria will improve the assessment of the magnitude of health burden caused by pSS in various community surveys. In conclusion the estimated prevelence of primary Sjogren's syndrome is 0.59% of adult population, which is reported more frequently in elderly females.

REFERENCES:

1. Binard A, Devauchelle-Pensec V, Fautrel B, et al. Epidemiology of Sjogren's syndrome: where are we now? Clin Exp Rheumatol 2007;25:1–4.
2. Larche MJ. A short review of the pathogenesis of Sjogren's syndrome. Autoimmun Rev 2006;5:132–35.
3. Segal BM, Nazmul-Hossain AN, Patel K, et al. Genetics and genomics of Sjogren's syndrome: research provides clues to pathogenesis and novel therapies. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:673–80.
4. Jacobsson LT, Axell TE, Hansen BU, et al. Dry eyes or mouth--an epidemiological study in Swedish adults, with special reference to primary Sjögren's syndrome. J Autoimmune .1989;2: 521-27.
5. Fox P C, Busch K A, Baum B J. Subjective reports of xerostomia and objective measures of salivary gland performance. J Am Dent Association. 1987;115:581-84.
6. Kraus A, Caballero-Uribe C, Jakez J, et al. Raynaud's phenomenon in primary Sjogren's syndrome. Associations with other extraglandular manifestations. J Rheumatol 1992; 19: 1572-74.
7. Moutsopoulos HM, Youinou P. New developments in Sjogren's syndrome. Curr Opin Rheumatol 1991;3: 815-22.
8. Escudero D, Latorre P, Codina M, et al. Central nervous system disease in Sjo gren's syndrome. Ann Med Interne 1995;146: 239-42.
9. Alexander EL. Neurologic disease in Sjogren's syndrome: mononuclear inflammatory vasculopathy affecting central/peripheral nervous system and muscle. A clinical review and update of immunopathogenesis. Rheum Dis Clin North Am 1993;19: 869-908.
10. Alexander E. Central nervous system disease in Sjogren's syndrome. New insights into immunopathogenesis. Rheum Dis Clin North Am 1992;18: 637-72.
11. Calabrese LH, Davis ME, Wilke WS. Chronic fatigue syndrome and a disorder resembling Sjogren's syndrome: preliminary report. Clin Infect Dis 1994;18 (suppl. 1):S28-31.
12. Gudbjornsson B, Broman JE, Hetta J, Hallgren R. Sleep disturbances in patients with primary Sjogren's syndrome. Br J Rheumatol 1993;32:1072-76.
13. William E, Clair ST, Leverenz L. Sjögren's Syndrome. In: Firestein GS, Budd RC, Gabriel SE, et al, Editors. Kelley and Firestein's Textbook of Rheumatology. 11th ED, Philadelphia: Elsevier,2021 :1284-1306.
14. Haugen AJ, Peen E, Hulten B, et al. Estimation of the prevalence of primary Sjogren's syndrome in two age-different community-based populations using two sets of classification criteria: the Hordaland Health Study. Scand J Rheumatol 2008;37: 30–34.
15. Vitali C, Bombardieri S, Jonsson R, et al. Classification criteria for Sjogren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. Ann Rheum Dis 2002;61: 554–58.
16. Aletalia D, Neogi T, Silman A J, et al. Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum. 2010;62:2569-81.
17. Al-Rawi Z S, Alazzawi A J, Alajili F M, Alwakil R. Rheumatoid arthritis in population samples in Iraq. Ann Rheum Dis. 1978;37:73-75.
18. Brito-Zeron P, Siso-Almirall A, Bove A, et al. Primary Sjogren syndrome: an update on current pharmacotherapy options and future directions. Expert Opin Pharmacother 2013;14: 279–89.
19. Birlik M, Akar S, Gurler O, et al. Prevalence of primary Sjogren's syndrome in Turkey: a population-based epidemiological study. Int J Clin Pract 2009;63: 954–61.

20. See LC, Kuo CF, Chou IJ, et al. Sex- and age-specific incidence of autoimmune rheumatic diseases in the Chinese population: A Taiwan population-based study. Semin Arthritis Rheum 2013;43: 381–86.

21. Yu KH, See LC, Kuo CF, et al. Prevalence and incidence in patients with autoimmune rheumatic diseases: a nationwide population-based study in Taiwan. Arthritis Care Res (Hoboken) 2013;65: 244–50.

22. Pillemer SR, Matteson EL, Jacobsson LT, et al. Incidence of physician-diagnosed primary Sjogren syndrome in residents of Olmsted County, Minnesota. Mayo Clin Proc 2001;76: 593–99.

23. Valim V, Zandonade E, Pereira AM, et al. Primary Sjogren's syndrome prevalence in a major metropolitan area in Brazil. Rev Bras Reumatol 2013;53: 24–34.

24. Bowman SJ, Ibrahim GH, Holmes G, et al. Estimating the prevalence among Caucasian women of primary Sjogren's syndrome in two general practices in Birmingham, UK. Scand J Rheumatol 2004;33:39–43.

25. Alamanos Y, Tsifetaki N, Voulgari PV, et al. Epidemiology of primary Sjogren's syndrome in north-west Greece, 1982–2003. Rheumatology (Oxford) 2006;45:187–91.

26. Goransson LG, Haldorsen K, Brun JG, et al. The point prevalence of clinically relevant primary Sjogren's syndrome in two Norwegian counties. Scand J Rheumatol 2011;40: 221–24.

27. Maldini C, Seror R, Fain O, et al. Epidemiology of primary Sjogren's syndrome in a French Multi-Racial/Ethnic area. Arthritis Care Res (Hoboken) 2014;66: 454–63.

28. Tronyas PI, Andrianakos AA. Sjögren's syndrome: a population-based study of prevalence in Greece. The ESORDIG study. Ann Rheum Dis 2005;64:1240-41

29. Anagnostopoulos I, Zinzaras E, Akexiou I, et al. The prevalnce of rheumatic diseases in Central Greece: a population survey. BMC Musculoskeletal disord 2010; 11:98.

30. Vitali C, Bombardieri S, Moutsopoulos HM, et al. Preliminary classification criteria for Sjögren's syndrome. Results of a prospective concerted action supported by the European Community. Arthritis Rheum 1993;36:340-47.

31. Vitali C, Bombardieri S, Moutsopoulos HM, et al. Assessment of the European classification criteria for Sjögren's syndrome in a series of clinically defined cases: results of a prospective multicentre study. The European Study Group on Diagnostic Criteria for Sjögren's syndrome. Ann Rheum Dis 1996;55:116-21.