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Prevalence of Inflammatory Rheumatic Diseases in a Rheumatologic outpatient clinic: analysis of 12626 cases

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Inflammatory rheumatic diseases are a heterogeneous class of often chronic autoimmune disorders. They are among the most common chronic diseases. They cause major health problems in the general population. This study assessed the distribution of inflammatory systemic rheumatic diseases in a rheumatologic outpatient clinic. The medical records of patients diagnosed with any type of inflammatory rheumatic disease between January 1, 2006 and December 31, 2016 in a non-hospital-based rheumatologic outpatient practice in Mashhad, Iran were retrospectively studied. Diagnoses were made using the agreed-upon classification criteria. Data regarding each patient's diagnosis, age at onset of disease, and gender was extracted from their files. The total number of patients was 12,626. The most common diseases were rheumatoid arthritis (47.30%), spondyloarthropathies (17.23%), systemic lupus erythematosus (8.10%), gout (7.84%), and vasculitis (6.84%). Patients were aged from 1 to 93 years, with a mean age of 41.17±39.70 years. Most patients were in the third, fourth, and fifth decade of life. Sixty-four percent of all patients were female. The overall sex ratio (women to men) was 1.8:1. The proportion of women was 95% in Takayasu's arteritis, 92% in systemic lupus erythematosus, 87% in Sjögren's syndrome, 78% in rheumatoid arthritis, and 24% in ankylosing spondylitis. The age at onset of inflammatory rheumatic diseases in Mashhad, Iran is lower than that in some other regions. The frequency of Behcet's disease, systemic lupus erythematosus, and systemic sclerosis was greater in this study than in most other studies, but gout, polymyalgia rheumatica, and psoriatic arthritis were less frequent in the current study.

Keywords: arthritis, epidemiology, inflammatory, rheumatic diseases, rheumatology.

Introduction

Rheumatic disorders are among the most prevalent chronic diseases of the musculoskeletal system and connective tissue, and they can affect a wide range of age groups. Encompassing a large number of arthritis and autoimmune diseases, they can affect the bones, joints, and other components of the musculoskeletal system, causing morbidity or disability with resultant healthcare utilization [1]. Rheumatic disorders are mainly responsible for an inability to work and early retirement, a fact which highlights their enormous social and economic impact [2]. The economic burden of rheumatic diseases is often more substantial than other chronic conditions, including cardiovascular diseases and cancer [3]. Unfortunately, despite the growing disease burden associated with rheumatic diseases, inadequate attention has been paid to them and to arthritis in the scientific literature [4].

There are more than 150 classified rheumatic disease conditions with specific pathogenesis, clinical picture, treatment, and prognosis. For successful treatment, identifying each condition and its variations is essential [1]. Rheumatic diseases can be divided into two major groups: inflammatory rheumatic diseases (IRDs) and non-inflammatory rheumatic diseases. As the most common rheumatic diseases, non-inflammatory rheumatic diseases are highly age-dependent and usually have a better prognosis [5]. About 5% of the population, however, suffer from a chronic inflammatory rheumatic disease [6]. Statistics show that, in America, a higher number of disabilities are caused by inflammatory rheumatic diseases with arthritis than by heart disease, cancer, or diabetes [7].

As a heterogeneous group of often chronic immune-mediated disorders, inflammatory rheumatic diseases cause inflammatory reactions in various body tissues. The primary target is the musculoskeletal system; these disorders cause joint pain (arthralgia) and restricted mobility, leading to irreversible damage and disability. Some internal organs, including the heart and kidneys,

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can also be affected [8, 9]. There are over 30 autoimmune rheumatic diseases; some of the most common ones are rheumatoid arthritis, lupus, scleroderma, juvenile idiopathic arthritis, Sjögren's syndrome, spondyloarthropathies, polymyalgia rheumatica, and systemic vasculitis [10].

The epidemiological and demographic features of vasculitis [11], giant cell arteritis [12], Takayasu's arteritis [13], and sarcoidosis [14] in northeastern Iran have previously been reported. This study aimed to analyze the inflammatory rheumatic disease profile of patients visiting an outpatient rheumatology practice in Mashhad, Iran and compare the prevalence and distribution of different inflammatory rheumatic diseases.

Materials and Methods

The medical records of patients diagnosed with any type of inflammatory rheumatic disease between January 1, 2006 and December 31, 2016 in a non-hospital-based rheumatologic outpatient practice in Mashhad, Iran were retrospectively studied.

The following disorders were defined as inflammatory rheumatic diseases: rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (SSc), spondyloarthropathies, Sjogren's syndrome (SS), dermatomyositis/ polymyositis, relapsing polychondritis, sarcoidosis, vasculitides, adult onset Still's disease, juvenile idiopathic arthritis (JIA), antiphospholipid antibody syndrome (APS), crystal-induced arthritis, familial Mediterranean fever (FMF), acute rheumatic fever, polymyalgia rheumatica (PMR), SAPHO (Synovitis–acne–pustulosis–hyperostosis–osteitis), RS3PE (remitting seronegative symmetrical synovitis with pitting edema), mixed connective tissue disease (MCTD), and palindromic rheumatism.

The following conditions were defined as noninflammatory conditions and were excluded from this study: osteoarthritis, osteoporosis, non-inflammatory back pain, soft tissue rheumatism, complex regional pain syndrome, fibromyalgia, malignancy and hypertrophic osteoarthropathy. Patients with infectious arthritis were also excluded.

The agreed classification criteria were used to make the diagnosis (Table 1). Data regarding diagnosis, age at disease onset, and gender was extracted from the patients' files.

Statistical analysis

SPSS software (Statistical Package for the Social Sciences) 20 was used for data entry and analysis. Continuous data was shown as mean and standard deviation (mean±SD), and categorical variables were shown as percentages.

Results

The total number of patients with inflammatory rheumatic disease was 12,626. Table 2 presents the distribution of patients separately grouped based on their diagnoses. The most common diseases were RA (47.30%), spondyloarthropathies (including ankylosing spondylitis, psoriatic arthritis, reactive arthritis and enteropathic arthritis) (17.23%), SLE (8.10%), gout (7.84%), and vasculitis (6.83%).

Patients' ages ranged from 1 to 93 years, with a mean of 41.17± 39.70 years. Most patients were in the third, fourth, or fifth decade of life. Figure 1 shows the distribution of age at disease onset in the studied patients.

Sixty four percent of all patients were female. The overall sex ratio (women to men) was 1.8:1. The proportion of women was 95% in Takayasu's arteritis, 92% in SLE, 87% in Sjögren's syndrome, 78% in RA, and 24% in AS. The most common age of onset for AS, reactive arthritis (ReA), Takayasu's arteritis, Still's disease, Behcet's disease, and SLE was in the twenties, whereas the most common age of onset for Granulomatosis with polyangiitis (GPA), sarcoidosis, psoriatic arthritis (PsA), APS, inflammatory bowel disease (IBD), palindromic rheumatism, and systemic sclerosis was in the thirties. The most common age of onset for RA was in the forties. The total number of patients with JIA was 359 (2.8%).

Discussion

The exact etiology and pathogenesis of inflammatory rheumatic diseases remain unclear today. However, among a host of factors, a variable combination of individual genetic predisposition, environmental factors, and dysregulated immune responses have been singled out as the underlying causes of these autoimmune diseases [15]. The role of genetic predisposition, in particular the influence of distinct HLA haplotypes, has been highlighted in most of these diseases. Moreover, environmental factors including nutrition, infection, and exposure to sunlight have been pinpointed as being responsible for the development of the disease [16].

A number of reports on the epidemiology and prevalence of rheumatic diseases seen in rheumatology practices have been published [17-20]. The inflammatory rheumatic patients in this study were compared with other populations in Germany [17], the Netherlands [18], Belgium [19], and Nigeria [20] (Table 3).

Table 1. The used classification criteria for inflammatory rheumatic diseases

Disease	Classification criteria
Acute rheumatic fever	2004 World Health Organization Criteria for the Diagnosis of Rheumatic Fever and Rheumatic Heart Disease
Adult onset Still's disease	Yamaguchi criteria
Antiphospholipid antibody syndrome	Revised Sapporo Classification Criteria for Anti-phospholipid Syndrome
Ankylosing Spondylitis	Modified New York, 1984
Behcet's disease	Revised International Criteria for Behçet's Disease
Cryoglobulinemic vasculitis	Preliminary classification criteria for the cryoglobulinaemic vasculitis
CPPD	McCarty and colleagues
Dermatomyostis/ Polymyositis	Bohan and Peter Criteria for Polymyositis and Dermatomyositis
Eosinophilic granulomatosis with polyangiitis	ACR 1990 criteria for Churg-Strauss syndrome
Familial Mediterranean Fever	Tel Hashomer Medical Center
Giant cell arteritis	American College of Rheumatology Classification Criteria for Giant Cell Arteritis
Gout	ACR/EULAR
Granulomatosis with polyangiitis	ACR criteria
Hypocomplementemic urticarial vasculitis	1982 Schwartz et al.
Inclusion body Myositis	The proposed European Neuromuscular Centre (ENMC) 2011
IgA Vasculitis	American College of Rheumatology 1990 Criteria for the Classification of Henoch-Schönlein Purpura
Juvenile Idiopathic Arthritis	IL AR Classification Criteria for Juvenile Idiopathic Arthritis
Microscopic polyangiitis	ACR 1990
Mixed Connective Tissue Disease	Alarcón-Segovia Criteria
Palindromic rheumatism	Pasero and Barbieri
Polyarteritis nodosa	American College of Rheumatology Criteria for Classification of Polyarteritis Nodosa
Polymyalgia Rheumatica	ACR/EULAR 2012 provisional classification criteria for Polymyalgia rheumatica
Polychondritis	Modified (Damiani) criteria
Psoriatic Arthritis	CASPAR Classification Criteria for Psoriatic Arthritis
Reactive arthritis	French Society of Rheumatology (FSR)
Rheumatoid arthritis	ACR/EULAR 2010
RS3PE	Olive criteria
SAPHO	Benhamou criteria
Sarcoidosis	Visser's Criteria for Sarcoidosis in Patients with Arthritis and Bihilar Lymphadenopathy
Sjogren's syndrome	Revised International Classification Criteria for Sjogren's Syndrome
Systemic lupus erythematosus	SLICC criteria for the classification of systemic lupus erythematosus
Systemic sclerosis	American College of Rheumatology/European League against Rheumatism Classification Criteria for the Classification of Systemic Sclerosis
Takayasu' arteritis	American College of Rheumatology Classification Criteria for Takayasu's Arteritis
Undifferentiated seronegative spondyloarthropathy	ESSG criteria
Vasculitis	Revised International, Chapel Hill Consensus Conference Nomenclature of Vasculitides

CPPD: Calcium-Pyrophosphate-Deposition; ACR: American College of Rheumatology; EULAR: European League Against Rheumatism; ILAR: International League Against Rheumatism; CASPAR: Classification of Psoriatic Arthritis; RS3PE: Remitting seronegative symmetrical synovitis with pitting edema; SAPHO: Synovitis–Acne–Pustulosis–Hyperostosis–Osteitis; SLICC: Systemic Lupus International Collaborating Clinics; ESSG: European Spondyloarthropathy Study Group

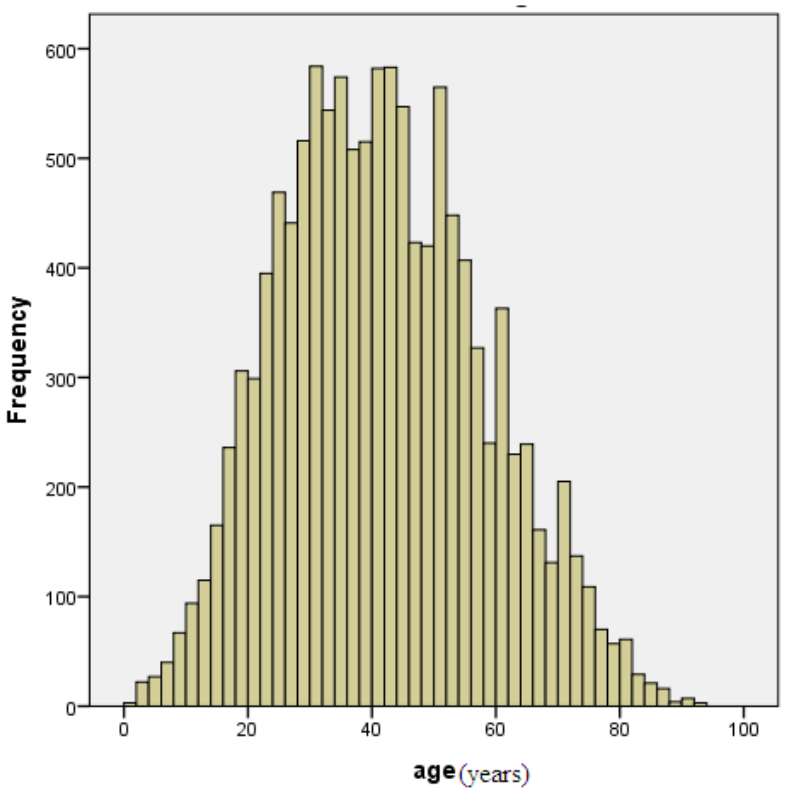

Fig. 1. Age distribution of the patients

Table 2. Distribution of patients and their diagnoses, female % and ages

Disaese			Frequency no. (%)	Female (%)	Age (years)		
					Minimum	Maximum	Mean
RA			5973 (47.30)	78.5	16	90	46.69
SLE			1023 (8.10)	92.0	3	74	31.74
SPA	Total		2176 (17.23)	42.0	3	76	33.44
	AS		665 (5.26)	24.2	9	75	34.12
	ReA		113 (0.89)	32.7	8	71	28.45
	PsA		373 (2.95)	59.0	3	76	38.47
	Enterpathic		104 (0.82)	57.7	17	74	37.06
	USPA		921 (7.29)	1.37	5	72	31.12
Inflammatory myopathies	Total		167 (1.32)	60.2	3	74	36.29
	DM		67 (0.53)	48.1	3	68	38.43
	PM		99 (o.78)	78.1	8	70	34.75
	IBM		1 (0.00007)	100	74	74	74.00
SSc			299 (2.36)	79.9	4	85	40.25
SS			111 (0.87)	87.4	16	75	46.44
PMR			52 (0.41)	51.9	40	84	66.42
Vasculitidies	Total		864 (6.84)	51.5	5	86	34.54
LVV	Total		95 (0.75)	72.9	17	83	45.49
	TAK		50 (0.38)	95.7	17	48	28.33
	GCA		45 (0.35)	46.2	44	83	64.19
MVV	Total		23 (0.18)	53.4	11	82	41.00
	PAN		23 (0.18)	50.0	11	82	41.00
	KD		0 (0)	-	-	-	-
SVV	Total		138 (1.09)	48.5	5	66	34.23
	AAV	Total	83 (0.65)	51.5	11	66	35.90
		GPA	49 (0.38)	50.0	11	61	33.00
		EGPA	23 (0.18)	33.3	23	66	51.07

		MPA	11 (0.08)	75.1	19	35	27.00
		Total	55 (0.43)	48.3	5	54	21.40
		AGBM	0 (0)	-	-	-	-
	ICV	CV	3 (0.0002)	75.1	35	43	39.00
		IGAV	52 (0.41)	37.5	5	54	20.50
		HUV	0 (0)	-	-	-	-
	Total		529 (4.18)	47.3	11	78	33.40
VVV	BD		529 (4.18)	47.1	11	78	33.40
	CS		0 (0)	-	-	-	-
	Total		79 (0.62)	45.4	5	86	34.5
	CLA		71 (0.56)	45.0	11	86	38.00
SOV	CA		0 (0)	-	-	-	-
	PCNSV		0 (0)	-	-	-	-
	IA		0 (0)	-	-	-	-
	OTHERs		8 (0.0006)	50.0	18	30	24.00
Sarcoidosis			307 (2.4)	65.8	15	81	40.57
	Total		994 (7.78)	14.9	8	93	52.59
Crystal induced arthritis	Gout		991 (7.84)	14.9	8	93	52.52
	CPPD		3 (0.0002)	33.3	70	86	78.00
Relapsing polychodritis			3 (0.0002)	33.3	22	55	43.00
Juvenile idiopathic arthritis			359 (2.84)	49.3	1	16	10.60
Familial Mediterranean fever			8 (0.0006)	50.0	7	37	18.25
Antiphospholipid antibody syndrome			22 (0.17)	72.7	16	80	33.77
Acute rheumatic fever			76 (0.6)	46.1	4	40	16.88
Still's disease			95 (0.8)	58.9	17	80	30.42
Mixed connective tissue disease			2(0.0001)	100	28	52	40.00
Palindromic rheumatism			17 (0.13)	76.5	25	71	41.65
RS3PE			1 (0.00007)	100	23	23	23.00
SAPHO			1 (0.00007)	0	16	16	16.00
	Total		76 (0.28)	86.8	16	70	36.86
	RA+SLE		32 (0.25)	96.8	16	60	35.75
	RA+SSc		18 (0.14)	94.4	16	59	37.11
	RA+DM		3 (0.0002)	100	43	61	54.67
	RA+PM		1 (0.00007)	100	30	63	44.00
	RA+PBS		1 (0.00007)	100	45	45	45.00
	SLE+SSc		3 (0.0002)	100	27	42	34.50
Overlaps	SLE+PM		1 (0.00007)	100	24	24	24.00
	SLE+IBD		1 (0.00007)	100	23	23	23.00
	SLE+Taka		1 (0.00007)	100	20	20	20.00
	PSA+Gout		2 (0.0001)	50.0	52	54	53.00
	IBD+DM		1 (0.00007)	100	64	64	64:00
	IBD+Takayasu		1 (0.00007)	100	20	20	20.00
	DM+PSA		1 (0.00007)	0	29	29	29.00
	DM+SSc		4 (0.0003)	50	28	70	49.50
	PM+SSc		4 (0.0003)	0	30	65	44.00
Total			12626 (100)	64.20	1	93	41.17

RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythamtosus; SPA: spondyloarthropathies; AS: Ankylosing Spondylitis; ReA: Reactive Arthritis, PsA: Psoriatic Arthritis; USPA: undifferentiated spondyloarthropathies; DM: dermatomyositis; PM: polymyositis; IBM: Inclusion Body Myositis; SS: Sjogren's Syndrome; SSc: Systemic Sclerosis; PMR: polymyalgia rheumatica; LVV: Large Vessel Vasculitis; TAK: Takayasu arteritis; GCA: Giant Cell Arteritis; MVV: medium vessel vasculitis; PAN: polyarteritis nodosa; KD: Kawasaki Disease; SVV: Small Vessel Vasculitis; AAV: antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis; MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis (Wegener's); EGPA: eosinophilic granulomatosis with polyangiitis (Churg-Strauss); ICV: Immune Complex Vasculitis; SVV: small vessel vasculitis; AGBM: anti-glomerular basement membrane disease; CV: Cryoglobulinemic Vasculitis; IGAV: IgA vasculitis (Henoch-Schonlein); HUV: Hypocomplementemic Urticarial Vasculitis; VVV: Variable Vessel Vasculitis; BD: Behcet's Disease; CS: Cogan's Syndrome; SOV: Single-Organ Vasculitis; CLA: Cutaneous Leukocytoclastic Angiitis; CA: Cutaneous Arteritis; PCNSV: Primary Central Nervous System Vasculitis; IA; Isolated Aortitis; CPPD: calcium-pyrophosphate-deposition; RS3PE: Remitting seronegative symmetrical synovitis with pitting edema; SAPHO: Synovitis–Acne–Pustulosis–Hyperostosis–Osteitis

Table 3. Comparative data of patients with inflammatory rheumatic diseases

Variable	Germany [17] N= 25653	Netherland [18] N=33076	Iran N= 12626	Belgium [19] N=1566	Nigeria [20] N=82
Female %	71.00	-	64.20	-	-
Mean age at onset (years)	51.50	-	41.17	-	-
Rheumatoid arthritis%	50.6	45.2	47.30	45.8	25.6
Systemic lupus erythamtosus %	4.72	1.7	8.10	1.9	12.1
Systemic sclerosis %	1.2	0.6	2.36	-	7.3
Spondyloarthropathies (total) %	22.61	20.8	17.23	-	4.8
Ankylosing spondylitis %	5.79	8.6	5.26	10.2	-
Reactive arthritis %	0.2	2.5	0.89	2.6	2.4
Psoriatic arthritis %	8.26	6.1	2.95	8.2	2.4
Sjogren's syndrome %	1.7	2.2	0.87	1.5	7.3
Vasculitides %	2.1	1.3	6.83	-	-
Behcet’s disease %	-	-	4.18	-	-
Juvenile idiopathic arthritis %	-	1.3	2.82	-	-
Dermatomyositis/ polymyositis %	-	-	1.32	-	1.2
Gout %	8.5	1.3	7.78	3.5	39.0
Polymyalgia rheumatica %	3.8	5,6	0.41	5.6	2.4
Overlap syndromes %			0.6		

In Nigeria [20], a study was performed to examine the prevalence and distribution of rheumatic diseases in a tertiary hospital outpatient practice. The study consisted of a small number of patients restricted to a tertiary institution in southwestern Nigeria, which, however, cannot represent the true prevalence of each rheumatologic disorder in the general community of the studied region.

Overall, inflammatory rheumatic diseases are more common in females than in males [21, 22]. In the current study, the proportion of women was lower compared to the study carried out in Germany (64% versus 71%).

Inflammatory rheumatic diseases can occur at any age [23] (age range in the current study was 1-93 years). In this study, the mean age at disease onset was 41 years, which was lower than in the study carried out in Germany (51 years). The reason for this difference may lie in the fact that the population of Iran is younger than the population of Germany.

About half of the patients with inflammatory rheumatic diseases have RA. The frequency of RA in this study (47.5%) was slightly lower than that in the German study (50.6), but it was higher than its level in studies performed in Belgium (45.8%) and the Netherlands (45.2%).

The percentage of SLE (the second most common disease) was higher in the present study (8.1%) than in the three other above-mentioned studies.

This difference can also be explained by the lower age of the Iranian population, since SLE is a disease of young adults.

The frequency of spondyloarthropathies was slightly lower in this study than in studies in Germany and the Netherlands. The most common subtype of spondyloarthropathies in this study was undifferentiated spondyloarthropathy, whereas the prevalence of ankylosing spondylitis in this study corresponded to its level reported in a study performed in Germany, i.e. less frequent than in the other two studies. The prevalence of arthritis in patients with psoriasis is 9.1% in Iran [24]. The frequency of PsA in the current study was less than three other studies.

Systemic sclerosis was seen more frequently in this study (2.36%) than in three other studies.

The prevalence of Behcet's disease (BD) in Iran was 68 per 100,000 inhabitants, which is the second highest prevalence after Turkey (80–370 per 100,000) worldwide [25]. The frequency of Behcet's disease among patients in the present study was 4.18%. The three other studies did not report any patients with Behcet's disease due to the rarity of BD in these countries. Behcet's disease is classified as a vasculitis [26]. It is possible that, in the aforementioned studies, BD was considered a vasculitis, and, therefore, its rate was not reported separately.

PMR was much less frequent in Iran (0.4%) in comparison with other studies (Germany, 3.8%; the Netherlands and Belgium, 5.6%). PMR is a disease of the elderly. Thus, its current low prevalence can be associated with the younger population of Iran.

The prevalence of gout in Iranian population is 0.13% [25]. The frequency of gout in the present study matched its rate in the study carried out in Germany;

however, it was higher than the other two studies.

Juvenile idiopathic arthritis (JIA) is the most common chronic pediatric rheumatologic disease. Only 359 cases of juvenile idiopathic arthritis were recorded here. The small number of such cases can be explained by the fact that the database is maintained in adult rheumatology units. During the last decade, the number of pediatric rheumatologists has increased in Iran; at present, most pediatric patients with rheumatologic problems are visited by pediatric rheumatologists.

Some patients who fulfill the criteria for a diagnosis of an autoimmune disease have overlapping features of a second autoimmune illness. In 30%–52% of patients with SLE, RA, or Sjögren's syndrome, the second autoimmune disease, rheumatic or nonrheumatic, will occur [27]. Sjogren's syndrome and APS can develop in many other IRDs. If SS or APS develops in patients with other IRDs, the diseases are called secondary Sjogren's syndrome or secondary APS. In this study, the association of these 2 disorders with any other IRDs as overlap syndromes was not taken into account. About 0.6% of patients in the current study had overlap syndromes. The most common overlap syndromes (2 IRDs) were RA-SLE (rhupus) and RA-SSc.

The database used in this study had several limitations: it only included patients visited by rheumatologists; it did not give information on the situation of patients who never reached the specialized sector. There is no information on how the diseases are diagnosed and treated at the level of the general population.

Conflicts of interest

The authors declare no conflicts of interest.

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