Frequency of musculoskeletal conditions among patients referred to Italian tertiary rheumatological centers

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Abstract

Objective

To describe the occurrence of different rheumatic diseases and to examine the characteristics of patients referred to six Italian rheumatological units. To compare these data with those from other countries.

Methods

Six Italian rheumatological tertiary referral centers participated in the study. Diagnoses of in- and outpatients aged over 16 years were classified according to the International Classification of Diseases, ninth revision.

Results

Three thousand, five hundred and thirty-seven patients with mean age 56 ± 14.8 years, of which 2604 (73.6%) were women, were studied. Inflammatory joint and spine diseases were diagnosed in 40.4%, connective tissue diseases in 14.4%, degenerative joint and spine diseases in 21.4%, soft tissue rheumatisms in 18.5%, and metabolic bone diseases in 5.3%. There was a significant difference among centers in the frequency of most diagnoses: non-academic centers cared for more patients with arthritis and connective tissue diseases and for less patients with degenerative diseases, soft tissue rheumatisms and metabolic bone diseases. Connective tissue diseases were constantly seen more often in Italian centers, whereas soft tissue rheumatisms were seen more often abroad.

Conclusion

Our data emphasize the great variability of the diagnostic case-mix in different centers from the same country, an observation that raises some concerns of the results of descriptive multicenter studies. Studies on the breakdown of diagnoses made in rheumatological centers could be helpful to determine the burden of rheumatic diseases on the health system, and for the planning of health interventions by both the national rheumatological societies and health authorities.

Key words

Rheumatic diseases, Italy, frequence.

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Introduction

Information on the frequency and causes of in- and outpatient visits for rheumatic conditions is scanty in the Mediterranean area. Conversely, these data have been studied more precisely in other European countries (1-2) and in the US (3). More than 150 rheumatic diseases are estimated to affect approximately 40 million patients (15% of the whole population) in the US. By the year 2020, this figure is expected to reach 60 million (4). In Italy, 27% of the population over 16 years reports to have or have had musculoskeletal pain for at least one month (5). Rheumatic diseases are often underestimated because they are mistakenly considered an inescapable consequence of aging. This belief reflects the preponderance of osteoarthritis among elderly individuals. However, most other rheumatic diseases affect patients at any age (6-8). In a recently published report on the burden of musculoskeletal conditions, the World Health Organization concluded that "although the diseases that kill attract much of the public's attention, musculoskeletal or rheumatic diseases are the major cause of morbidity throughout the world, having a substantial influence on health and quality of life, and inflicting an enormous burden of cost on health systems"(9). This is the reason why the international effort denominated Bone and Joint Decade 2000-2010 is aiming to rise awareness on rheumatic diseases in the general public and the political arena.

The aim of our study was to describe the occurrence of different rheumatic diseases and to examine the characteristics of patients referred to six Italian rheumatological units. An additional aim was to compare the case mix observed in different centers and to test its homogeneity. If the patients' composition varies between centers, doubts about the feasibility of multicenter studies on disease frequency could be raised. The data observed in Italy were also compared with those seen in similar studies from other Countries.

Patients and methods

Six Italian rheumatological centers located in Northern (Genoa and Reggio Emilia), Central (Florence and Rome), and Southern (Cagliari and Naples) Italy participated in the study. These units are all tertiary referral centers, of which four are university based. All in- and outpatients aged more than 16 years seen between May 1 and December 31, 1996 were considered. In Italy, access to rheumatology consultation is granted through the National Health System and necessarily requested by the patients' general practitioner (GP). All Italian citizens are registered with a GP. Accordingly, all patients were sent for rheumatological consultation by their GPs. However, the number of patient-to-patient referrals, where patients directly asked to their GP to be sent to a rheumatologist, is not known. Clinical diagnoses were made according to currently used criteria, which included the ACR criteria for rheumatoid arthritis (RA) (10), the ESSG criteria for seronegative spondyloarthropaties, psoriatic arthritis (PsA) and reactive arthritis (11), the ACR criteria for gouty arthritis (12), systemic sclerosis (13), systemic lupus erythematosus (SLE) (14), and fibromyalgia (15), the EU community criteria for Sjögren's syndrome (16), the criteria for polymyalgia rheumatica by Chuang *et al.* (17), the ACR criteria for osteoarthritis of the hand (18), hip (19), knee (20), the radiological criteria for diffuse idiophatic skeletal hyperostosis (DISH) (21) and those for osteoporosis (22). In addition, arthralgia was defined as pain in or around the joint in absence of objective signs of inflammation; undifferentiated polyarthritis was defined as a poliarticular arthritis not fulfilling one of the previously cited criteria set; undifferentiated connective tissue disease was diagnosed when signs of a connective tissue disease were present in association with positive antinuclear antibodies, but without the fulfillment of criteria for a specific condition; spine OA was defined as axial pain associated with radiological osteophytes of the column; generalized OA was diagnosed when 2 or more OA localizations were present; Paget's disease of bone when the typical radiological features were seen on a radiograph; low back pain was defined

as pain of the back extending between the gluteal folds and the lower limits of the chest; carpal tunnel syndrome was defined as numbness and pain in the median nerve territory associated with positive response to the Tinel's or Phalen's signs; periarthritis scapulohumeralis was defined as shoulder pain with limitation of its abduction. Only the main diagnosis was recorded. All patients were classified according to the International Classification of Diseases, ninth revision (ICD9) (23). A standard registration form was used, which included identification of the patient, sex, date of birth, nationality, ICD9 disease code, date of the visit, and type of referral (in- or outpatient). The patient's privacy was ensured by coding all data. Identifying information was kept only in the rheumatological center responsible for the patient's follow-up. Four centers provided data of patients admitted to the ward, day-care and outpatient clinic, whereas two centers contributed only outpatients.

Data were expressed as means ± standard deviation. The student's t-test or the chi square test were used for comparisons. Logistic regression modeling was applied to the proportion of the study diseases on the whole patients population to assess the joint predictive role of the study variables (24). In particular, odds ratio point estimates (ORs) were calculated in order to assess the magnitude of multivariate associations among disease outcome and study variables. For each OR, asymptotic 95% confidence interval (95% CI) were computed to highlight the sampling variability of each OR. Model adequacy was checked by performing a graphical approach based on plotting residual, leverage and influence measures as diagnostic quantities.

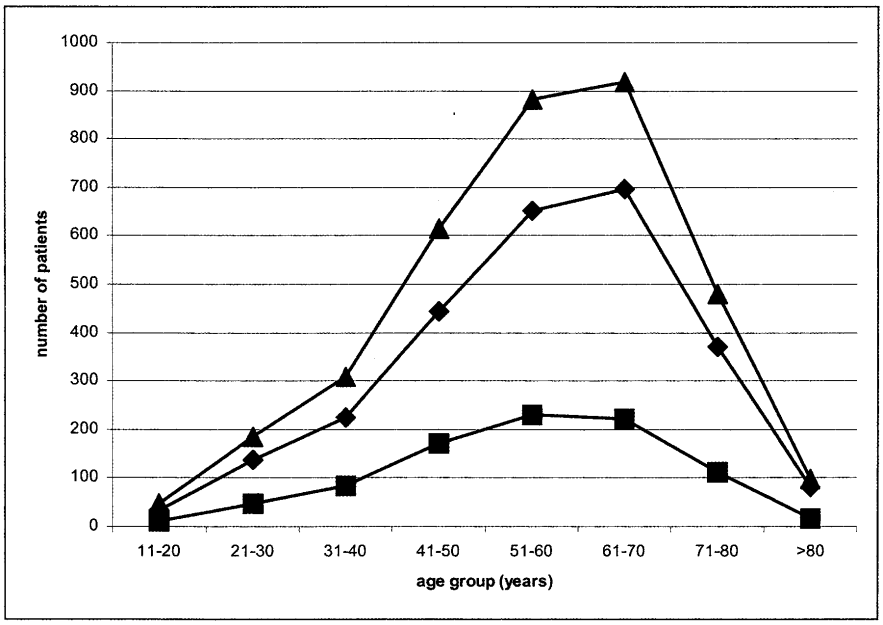

Fig.1. Age distribution of the patients divided according to gender (squares = men; diamonds = women; triangles = total).

Results

A total of 3,695 patients were seen. Eighty-nine patients were excluded because they were not affected by a musculoskeletal condition and 69 because their data were incomplete. Of the remaining 3,537 patients, 2,239 (63.3%) were outpatients, 859 (24.3%) were seen in day care, and 439 (12.4%) were inpatients. All but four (one each from US, Sweden, Greece, and Peru) were Italian citizens. The age range was comprised between 16 and 100 years with mean age 56 ± 14.8 years. Figure 1 shows the age and sex distribution of the patients. There were 2,604 (73.6%) women and 933 (26.4%) men with a sex ratio of 2.8:1. Sex distribution was similar in the six centers with a percentage of women ranging from a minimum of 71.7% in Cagliari to a maximum of 76.4% in Naples. The mean age varied between 54.9 ± 15.6 years in Genoa and 63.2 ± 13 years in Reggio Emilia.

Table I reports the age- and sex-related prevalence of rheumatic diseases grouped in inflammatory joint and spine diseases, connective tissue diseases, degenerative joint and spine diseases, soft tissue rheumatisms, and metabolic bone diseases. Inflammatory joint and spine diseases were diagnosed in 40.4% of patients (women to men ratio 2:1; mean age 56.2 ± 15 years), connective tissue disease in 14.4% (women to men ratio 6.8:1; mean age 56.4 ± 16.8 years), degenerative joint and spine diseases in 21.4% (women to men ratio 3.5:1; mean age 60.7 ± 11.1 years), soft tissue rheumatisms in 18.5% (women to men ratio 3.1:1; mean age 48 ± 13.9 years), and metabolic bone disease in 5.3% (women to men ratio 4.6:1; mean age 63.1 ± 11.3 years). As expected, mean age was significantly higher in patients with degenerative joint and spine disease and metabolic bone disease in comparison with the other groups ($p < 0.0001$). In addition, patients with metabolic bone disease had a higher mean age than those with degenerative joint and spine disease ($p = 0.009$). In our group of patients, the odds ratio of being affected by connective tissue disease (OR = 2.58, 95% CI 2.18 to 3.04) and degenerative bone and spine disease (OR = 1.32, 95% CI 1.19 to 1.48) was higher for women, whereas it was higher for men for inflammatory joint and spine disease (OR = 2.17, 95% CI 1.98-2.37). The probability of being affected by soft tissue rheumatism (OR = 1.15, 95% CI 0.80 to 1.65) or metabolic bone disease (OR = 1.53, 95% CI 0.86 to 2.72) was not associated with gender. As expected, patients with inflammatory joint and spine disease and connective tissue disease were significantly more common in the ward and day care than in the outpatient clinic, whereas the opposite was true for those with degenerative disease. No significant difference was seen for patients with soft tissue rheumatism and metabolic bone disease as far as the setting of the visit was concerned. The

odds ratio of being seen in the ward in comparison with the outpatient clinic was 1.4 (95% CI 0.6-3.1) for inflammatory joint and spine disease, 2.4 (95% CI 1.3-4.7) for connective tissue disease, 0.3 (95% CI 0.2-0.4) for degenerative joint and spine disease, 0.4 (95% CI 0.2-0.9) for soft tissue rheumatism, and 1 (95% CI 0.8-1.3) for metabolic bone disease.

In the subclass of inflammatory joint and spine disease, RA was more frequent, with 57.2% of diagnoses followed by PsA (11.1%). Among connective tissue diseases, SLE was the most frequent diagnosis (23.8%) followed by polymyalgia rheumatica (17.7%). In the subclass of degenerative joint and spine disease, generalized osteoarthritis was the most common diagnosis (34.3%) followed by hand osteoarthritis (14.4%). Unspecified arthralgia and fibromyalgia were the most frequently recorded diagnoses (31.9% and 29.4% respectively) among soft tissue rheumatisms. Finally, osteoporosis and Paget's disease accounted for the majority of the diagnoses in the category of metabolic bone disease (77.4% and 15.6% respectively).

The top ten diagnoses were RA, generalized osteoarthritis, unspecified arthralgia, fibromyalgia, PsA, osteoporosis, SLE, hand osteoarthritis, unspecified polyarthritis, and knee osteoarthritis.

There was a significant difference among centers in the frequency of several diagnoses as shown in Table II, where the odds ratio of having specific rheumatic diseases (compared to that of the Genoa group, arbitrarily assumed to be 1) was corrected for sex, age, and the type of setting (outpatient clinic, inpatient clinic, day care). The two non-academic centers cared for more patients with inflammatory joint and spine disease (OR 2.7, 95% CI 2.3 to 3.2) and connective tissue disease (OR 1.8, 95% CI 1.6 to 2.1), but fewer patients with degenerative joint and spine disease (OR 0.3, 95% CI 0.2 to 0.4), soft tissue rheumatisms (OR 0.5, 95% CI 0.4 to 0.5), and metabolic bone disease (OR 0.5, 95% CI 0.4 to 0.6).

Our results have been compared with those obtained abroad in other studies (2,3,12-14) in Table III, where only outpatients were considered because comparison studies were performed on the same population type.

Table I. Distribution of patients and their diagnoses. (UCTD: undifferentiated connective tissue disease; DISH: diffuse hydiopathic skeletal hyperostosis; SD: standard deviation).

Diagnostic groups	Number of patients (n = 3537)	% of patients (n = 3537)	% within groups	Sex distribution F/M	Mean age (years)	SD
Inflammatory joint and spine disease	1428	40.4%		2/1	56.2	15
Rheumatoid arthritis	817	23.1%	57.2%	3.6/1	60.5	13.2
Psoriatic arthrits	159	4.5%	11.1%	0.9/1	52.8	12.2
Undifferentiated polyarthritis	95	2.7%	6.7%	2.4/1	48.3	14.2
Gouty arthritis	68	1.9%	4.8%	0.1/1	61.6	9.2
Spondyloarthropaties	41	1.2%	2.9%	1.3/1	45.1	13
Reactive arthritis	40	1.1%	2.8%	1/1	43.7	16.1
Connective tissue disease	509	14.4%		6.8/1	56.4	16.8
Systemic lupus erythematosus	121	3.4%	23.8%	19.2/1	49.8	15
Polymyalgia rheumatica	90	2.5%	17.7%	4/1	71.1	10.6
Sjögren's syndrome	62	1.8%	12.2%	6.7/1	62.2	14.9
UCTD	61	1.7%	12.0%	6.6/1	50.9	15.5
Systemic sclerosis	40	1.1%	7.9%	4/1	55.0	14.7
Degenerative joint and spine disease	758	21.4%		3.5/1	60.7	11.1
Generalized osteoarthritis	260	7.4%	34.3%	5/1	65.1	9.8
Hand osteoarthritis	109	3.1%	14.4%	5.4/1	56.1	10.4
Knee osteoarthritis	83	2.3%	10.9%	2.2/1	60.2	8
DISH	63	1.8%	8.3%	2/1	63.4	7.7
Hip osteoarthritis	48	1.4%	6.3%	3.8/1	63.6	9.4
Cervical spine osteoarthritis	44	1.2%	5.8%	2.1/1	56.7	9.5
Soft tissue rheumatism	656	18.5%		3.1/1	48.0	13.9
Unspecified arthralgia	209	5.9%	31.9%	2.3/1	44.6	13.8
Fibromyalgia	193	5.5%	29.4%	15.1/1	47.8	14.9
Periarthritis scapulohumeralis	70	2.0%	10.7%	2.3/1	57.2	9.4
Low back pain	52	1.5%	7.9%	2.5/1	47.2	12.1
Carpal tunnel syndrome	40	1.1%	6.1%	5.7/1	49.4	13.9
Metabolic bone disease	186	5.3%		4.6/1	63.1	11.3
Osteoporosis	144	4.1%	77.4%	10.1/1	63.3	9.7
Paget's disease	29	0.8%	15.6%	1.1/1	65.5	11.6

Table II. Relative frequency of diagnostic classes among centers, expressed as odds ratio compared to that of the center of Genova, arbitrarily assumed to be 1, corrected for sex, age, and type of setting (outpatient clinic, inpatient clinic, day-care).

Diagnostic group	Genoa	Naples	Rome	Cagliari	Florence	Reggio Emilia
Inflammatory joint and spine disease	1	0.53 (0.48-0.60)	0.36 (0.27-0.48)	1.16 (0.87-1.54)	1.03 (0.87-1.54)	2.29 (1.69-3.09)
Connective tissue disease	1	1.42 (1.23-1.65)	0.29 (0.20-0.40)	2.20 (1.94-2.49)	1.84 (1.71-1.97)	1.50 (1.08-2.09)
Degenerative joint and spine disease	1	0.97 (0.78-1.19)	3.37 (2.44-4.67)	0.88 (0.61-1.26)	0.66 (0.51-0.85)	0.47 (0.33-0.65)
Soft tissue rheumatism	1	1.50 (1.31-1.71)	1.06 (0.67-1.68)	0.54 (0.41-0.70)	0.69 (0.44-1.07)	0.47 (0.29-0.76)
Metabolic bone disease	1	1.51 (1.45-1.58)	1.51 (1.13-2.02)	0.10 (0.09-0.11)	1.28 (1.13-1.45)	0.22 (0.17-0.29)

Table III. International comparison of the diagnoses' frequency. (NL: The Netherlands; B: Belgium; CDN: Canada).

Diagnostic group	Country	%	Difference compared fo Italy	p
Inflammatory joint and spine disease	NL	50.50	10.79	<0.001
	B	36.76	-2.95	0.023
	CDN	50.93	11.22	<0.001
Connective tissue disease	NL	8.10	0.02	0.973
	B	4.99	-3.09	<0.001
	USA	3.99	-4.09	<0.001
Degenerative joint and spine disease	NZ	33.40	5.98	0.007
	NL	18.00	-9.42	<0.001
	B	36.31	8.89	<0.001
	USA	19.46	-7.96	<0.001
	CDN	18.61	-8.81	<0.001
Soft tissue rheumatism	NL	27.60	8.26	<0.001
	B	37.00	17.66	<0.001
	CDN	21.32	1.98	0.282
Metabolic bone disease	B	16.98	11.53	<0.001

Discussion

This paper describes the pattern of rheumatic diseases seen in Italian tertiary referral centers. The distribution of diagnoses according to age and sex shown in Table I is in keeping with what is known of the epidemiology of rheumatic diseases. In multivariate analysis, the only difference was the increased OR of inflammatory joint and spine disease seen in men after correction for age and type of setting. This finding is due to the fact that 53% of men seen in Italian centers were affected by this class of diseases in comparison with only 36% of women. Another surprising finding was the low number of patients with low back pain seen in Italian centers, which contrasts with the high incidence of this condition in the general population. Possible explanations are that low back pain patients are commonly managed by GPs or that they are referred by GPs to other specialists of the musculoskeletal system. This last possibility is confirmed by the observation that fewer patients with soft tissue rheumatism are seen by Italian than by Belgian and Dutch rheumatologists (Table III).

Our study shows that there was a large variation between centers as far as the percentage of patients per diagnostic group is concerned. This fact seems to be only partially explained by the type of center, i.e. academic versus non academic, or outpatient versus inpatient care. The largest proportion of patients with degenerative diseases was seen in Rome, a center with outpatients facilities only. However, this was not the case for Reggio Emilia, the other center with the same characteristic. Alternative explanations include the extent to which rheumatic patients are referred to other specialists, such as orthopedic clinics, the specific research interests and reputation of the clinicians concerned, and the different referral area of the involved units. It is unlikely, although not known, that they reflect real geographical differences in the prevalence of rheumatic conditions. This finding has been reported also by Grahame and Woolfe (1) in their auditing work on clinical activities of rheumatology practice in 30 European centers, and by Miedema *et al*. (2) in the Dutch Standard Diagnosis Register of rheumatic diseases. According to these data, the spectrum of patients seen in different centers can be remarkably different not only between countries, but also in the same country or even in the same town.

Although all participating centers were tertiary referral units, two of them were not academic and two evaluated only outpatients. Results were analyzed after grouping for these variables. Non academic centers cared for more patients with arthritis and connective tissue diseases and for less patients with degenerative diseases, soft tissue rheumatisms and metabolic bone diseases. This may be due to the bias of academic centers to select a wider range of rheumatic patients for teaching purposes. Moreover, the two non academic centers were the only rheumatological centers in a large area, whereas the academic ones coexisted with other rheumatological units in the same town. This fact could have modified the diagnostic case mix.

Another possible limitation is the variable accuracy of recording. The participants agreed to apply the standard classification for diagnosis, but no attempt was made to validate individual diagnoses. We feel that the quality of the recorded data was sufficiently high because all the involved clinicians were expert rheumatologists who were greatly interested in participating in this study.

Our data have been compared with those obtained in other countries (2, 3, 25-27). Again, there was much variation in the frequency of the different diagnoses (Table III), in an apparently random fashion. Only connective tissue diseases were constantly seen more often in Italian centers, whereas soft tissue rheumatisms were seen more often abroad. This may be due differences in the health organization model. For instance, in Italy, connective tissue diseases are probably seen more frequently by rheumatologists than by internists, and soft tissue rheumatisms are more often seen by orthopedic surgeons than by rheumatologists.

The international comparison of the diagnoses' frequency is also affected by many limitations. Patients were seen in different settings such as private rheumatology practices (28), academic rheumatology outpatient clinics (27), non-hospital based outpatient practices (25) and university hospitals. In addition, only the main diagnosis or all rheumatological comorbidities could be recorded and new referrals or review visits could be considered. The published papers lack clear indications on how clinical criteria for rheumatic diseases were applied. The observed differences are therefore more probably due to different referral patterns rather than to real differences in rheumatic diseases occurrence among Countries. In spite of all these restraints, there are a few findings that are remarkably constant in all published papers. The mean age of the patients varied only slightly between 50 and 55 years, 60% to 70% of the patients were women, and RA represented more than 50% of the inflammatory conditions in all series.

Our data could be used to evaluate the relative frequency of diseases the epidemiology of which is largely unknown, such as PsA. The rate between the number of patients with PsA and the number of patients with RA was calculated at 0.2. This figure is much higher than those of 0.04 and 0.02 observed in outpatients seen in private practices in the US (28) and in Mexico (29). The same rate was 0.09 for ambulatory care visits in the US (3). The hypothetical prevalence of PsA was calculated by considering the rate between patients with RA, whose prevalence figures are known for many countries, and those with PsA, after adaptation for the specific prevalence of RA. By this method, the "inferred prevalence" of PsA was 0.08% in Italy, in comparison with 0.18% in Germany (30), 0.16% in The Netherlands (2) and 0.11% in Belgium (25). The first study on PsA prevalence comes from Olmsted County, Mn, US and shows a value of 0.1% (31). These calculations as well as the clinical impression of several European rheumatologists support the view that the prevalence of PsA in Europe is higher than in the US and probably similar to that of RA. During the preparation of this article, the first European paper on the prevalence of PsA was published (32). Salaffi *et al.* showed that it is 0.42% in the Marche region of Italy, confirming the figures suggested by our study.

In conclusion, studies on the breakdown of diagnoses made in rheumatological centers could be helpful to determine the burden of rheumatic diseases on the health system, and for the planning of health interventions by both the national rheumatological societies and health authorities. These data cannot be used to answer formal epidemiological questions, but could be important to formulate hypotheses for future epidemiological studies.

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