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The prevalence of rheumatic diseases in central Greece: a population survey

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Abstract

Background: Rheumatic diseases are a major health and financial burden for societies. The prevalence of rheumatic diseases may change over time, and therefore, we sought to estimate the prevalence of rheumatic diseases in an adult population of central Greece.

Methods: In this prospective cross-sectional population survey, a random sample of adult population was drawn from poll catalogues of a region in central Greece. A postal questionnaire was sent to 3,528 people for the presence of any rheumatic disease. All positive cases were further confirmed by clinical examination using the American College of Rheumatoloy criteria. Multiple regression analysis was used to assess risk factors for rheumatic diseases.

Results: The response rate was 48.3% (1,705 answers). Four hundred and twenty individuals (24.6%) had a rheumatic disease. The prevalence of rheumatoid arthritis was 0.58% (95% confidence interval [CI], 0.32-0.87), of psoriatic arthritis was 0.35% (95% CI, 0.33-1.13), of ankylosing spondylitis was 0.29% (95% CI, 0.28-0.94), of primary Sjögren's syndrome was 0.23% (95% CI, 0.22-0.75) and of systemic lupus erythematosus was 0.11% (95% CI, 0.11-0.37). One individual had systemic sclerosis (prevalence, 0.058%), 1 individual had dermatomyositis (prevalence, 0.058%; 95% CI, 0.05-0.18), 2 individuals had vasculitis (prevalence 0.11%; 95% CI, 0.11-0.37), 81 individuals had gout (prevalence, 4.75%; 95% CI, 4.41-5.13), and 304 individuals had osteoarthritis (OA) (prevalence 17.82%; 95% CI, 16.50-19.34). Gout was associated with male gender, diabetes mellitus, and hypertension, and OA was associated with age, female gender, and hypertension.

Conclusions: Rheumatic diseases are common in central Greece, affecting nearly a quarter of adult population. OA and gout are the most common joint disorders.

Background

Rheumatic diseases are a common cause of disability, and a large public health burden [1]. However, they may vary considerably in prevalence, mainly due to environmental factors. For example, the prevalence of systemic lupus erythematosus (SLE) or systemic sclerosis (SSc) differ in ethnic populations living in different geographical regions [2,3]. Also, the prevalence of the rheumatic diseases may change over time. In a US population, the incidence of rheumatoid arthritis (RA) progressively declined since early 1960s, while the prevalence of gout doubled from 1969 to 1985, and it further increased by 80% from 1990 to 1999 [4]. In Greece, two older studies on the

prevalence of rheumatic diseases have taken place mainly in the north-west of the country [5,6]. Therefore, we conducted a population survey for the prevalence of rheumatic diseases in central Greece.

Methods

A prospective two-step population-based cross-sectional survey was conducted from April 2007 to June 2008 in the Prefecture of Magnesia, a coastal region of central Greece. This region consists of a mainland with plains, mountains, and islands. The study involved a mailed questionnaire followed by confirmation clinical examination and tests, when needed, of individuals with a positive reply.

A sample of adults was drawn from poll catalogues of the Prefecture of Magnesia by systematic random sam-

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pling. The study involved 3,528 subjects (2% of the total 176,433 adult population in poll catalogues), consisting of 2% of the population in each sub-region, urban, rural, highlander, and islander population. According to their sub-region of residence, our sample consisted of 2,216 persons living in urban regions (2% of urban adult population), 723 persons living in rural regions (2% of rural adult population), 335 persons living in mainland highlands (2% of adult highlanders), and 254 persons living in islands (2% of islander adult population). Persons who could not be traced by mail (n = 200) were replaced using the same randomization process.

A postal questionnaire aimed at detecting any individual with current or previous diagnosis of a rheumatic disease. An explanatory letter was sent along with the questionnaire in a stamped self-addressed envelope to each one of randomly selected individuals. Persons were asked directly to report any diagnosis of: rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), systemic lupus erythematosus (SLE), primary Sjogren's syndrome (pSS), systemic sclerosis (SSc), polymyositis (PM), dermatomyositis (DM), gout, osteoarthritis (OA), and vasculitis (e.g Do you suffer from rheumatoid arthritis? yes or no; Do you suffer from psoriatic arthritis? yes or no; etc). These "self-reported doctor-diagnosed" questions seemed to provide the best estimate for overall arthritis prevalence, with acceptable sensitivity and specificity, according to cognitive and validation studies [4].

The questionnaire also contained questions about demographic and life-style variables. Social-demographic variables included age, sex, and working status (employed - current occupation, out of work [unemployed, early retirement] and retirement). A qualitative score (0 and 1) was given for the degree of mechanical stress to joints according the particular occupation (Table 1). Lifestyle variables included: smoking status, recorded as any current and/or in the past daily smoking (yes) or not (no); alcohol consumption, classified into 4 categories: no use (no more than 3 drinks per year), light drinking (less than 2 drinks per day), moderate drinking (2-4 drinks per day) and heavy drinking (more than 4 drinks per day). Financial and family problems were self-reported as yes/no variables. The utilization of classical disease modifying anti-rheumatic drugs (DMARDs) and biologics were also recorded.

Case detection through questionnaire was followed by case confirmation. Individuals who responded positively for any disease item were called in for evaluation by one rheumatologist (IA). A medical history was recorded and a careful clinical examination was carried out. Any previous laboratory test results or imaging findings were taken into account during the diagnostic procedure. For each rheumatic disease, established classification criteria of the American College of Rheumatology were used [7-15]. The study was approved by the Ethics Committee of our Hospital. All data remained confidential.

Statistical analysis

Statistical analysis was carried out using the SPSS v.13.0 statistics package. Categorical parameters were compared using the Fisher's exact test or Pearson chi-square test. Rheumatic diseases were tested for associations with gender, age, or other confounding parameters using univariate and multivariate logistic regression analysis. Associations were expressed in terms of unadjusted or adjusted odds ratio (OR) with 95% confidence interval (CI). An effect was considered significant, when $p < 0.05$.

Results

One thousand seven hundred and five individuals (48.3%) (females, 54.1%; mean age ± standard deviation [SD], 51.08 ± 15.25 years) responded to questionnaire. Four hundred and twenty individuals (24.6%) reported a rheumatic disease and were invited for confirmation of diagnosis. Diagnoses had been made by Rheumatologists at University Hospitals, and private practice offices. All cases were confirmed.

Ten individuals had RA (7 women, 3 men; mean age ± SD, 46.82 ± 14.9 years; prevalence, 0.57% [95% CI, 0.32-0.87]). Eleven individuals had spondylartropathies (SpA): five individuals had AS (1 woman, 4 men; mean age ± SD, 43.46 ± 15.04 years; prevalence, 0.29% [95% CI, 0.28-0.94]), and six individuals had PsA (4 women, 2 men; mean age ± SD, 41.56 ± 2.2 years; prevalence, 0.35% [95% CI, 0.33-1.33]). Two individuals had SLE, (prevalence, 0.11%), four individuals had pSS (prevalence 0.23%; 95% CI, 0.22-0.75), one individuals had SSc (prevalence, 0.058%), and one individual had DM (prevalence 0.058%). Two individuals had vasculitis (prevalence, 0.11%): one with giant cell arteritis, and one with hypocomplementemic urticarial vasculitis syndrome (HUVS) (Table 2).

Eighty one individuals had gout (mean age ± SD, 63.0 ± 7.8 years; prevalence, 4.71% [95% CI, 4.41-5.13]). The prevalence of gout was 10.0% in men and 0.3% in women. It was 0.0% in the < 40 year-age group, 5.3% in the 40-65 year-age group and 9.6% in the > 65 year-age group. By univariate logistic regression analysis, age, male gender, diabetes mellitus, hypertension, smoking, and manual work were risk factors associated with gout (Table 3).

Three hundred and four individuals had OA (mean age ± SD, 65.54 ± 12.9 years; prevalence, 17.82 [95% CI, 16.5-19.34]). The overall prevalence in women was 12.96% (95% CI, 11.85-14.23; mean age ± SD, 72.39 ± 8.25 years), and in men 4.86% (95% CI, 4.35-5.43; mean age ± SD, 65.97 ± 7.57 years). The prevalence of symptomatic knee OA (knee symptoms verified by a positive radiograph) was 11.3% (95% CI, 9.76-13.09) in women, and 2.99%

Table 1: Demographic and lifestyle variables included in the questionnaire

Variable	Definition
Gender	Male/Female
Age	≥ 50 years
Residence	Urban, Rural, Highland, Island
Drinking situation	No use: ≤ 3 drinks per year Light drinker: < 2 drinks per day Moderate drinker: 2-4 drinks per day Heavy drinker: > 4 drinks per day
Current occupation	nonmanual: clerks, small business owners, merchants, university graduates, students, artists manual: Industry workers, construction workers, cleaning, farmers, ranchers, fishermen, transporters Out of work: unemployed, early retired Age retirement
Smoking status	Yes: Current and/or in the past daily smoking
	No: not ever daily smoking
Financial problems	Yes/No
Diabetes Mellitus	Yes/No
Hypertension	Yes/No

(95% CI, 2.6-3.42) in men. Also, the prevalence of hand OA was 0.99% (95% CI, 0.76-1.25) in women, and 0.70% (95% CI, 0.56-0.86) in men. Finally, the prevalence of symptomatic hip OA was 0.64% (95% CI, 0.43-0.89) in women, and 1.17% (95% CI, 0.99-1.38) in men. By univariate logistic regression analysis, age, diabetes mellitus, hypertension, and living in island were risk factors associated with OA (Table 4).

Discussion

Our study is a population-based postal survey using a random population sample. In Manchester, UK, a study by questionnaire followed by examination conducted in early 1990s, showed that the prevalence of RA was 0.3% in blacks and 0.8% in whites [16]. In Halmstad, Sweden, a study using a questionnaire of 3,928 persons and review of medical records of persons who did not reply, found a prevalence of RA to be 0.51% [17]. In Spain and Italy, the prevalence of RA was 0.3-0.5% [18,19]. In our study, the prevalence of RA lies between those found by a retrospective study (0.35%) [5] and a cross-sectional study (0.68%) [20] in Greece.

The prevalence of AS varies according to the frequency of HLA-B27 in the general population. It has been reported 0.1% in African blacks and Eskimos, 0.5%-1% in whites of the USA and UK, and 6.0% in Amerindians [21]. In a retrospective study, using medical records of a University hospital in northern Norway in 1990, the prevalence of AS was 0.21% [22]. In Ancona, Italy, a study, using a questionnaire followed by review of medical

Table 2: Prevalence of rheumatic diseases in central Greece

Disease	Prevalence(%) (95% CI)	Age(years) (mean ± SD)	Women:men ratio
Rheumatoid arthritis	0.57 (0.32-0.87)	46.8 ± 14.9	2.3: 1
Ankylosing spondylitis	0.29 (0.28-0.94)	43.5 ± 15.0	1: 4
Psoriatic arthritis	0.35 (0.33-1.33)	41.6 ± 2.2	2:1
Sjogren syndrome	0.23 (0.22-0.75)		
Systemic lupus erythematosus	0.11		
Systemic sclerosis	0.06		
Dermatomyositis	0.06		
Vasculitis	0.11		
Gout	4.71 (4.41-5.13)	63.0 ± 7.8	0:8
Osteoarthritis (OA)	17.82 (16.5-19.34)	65.6 ± 7.7	2.7:1

Table 3: Variables assessed for association with gout

Variable		Gout		Unadjusted OR	P-value	Adjusted OR
		Yes	No	(95% CI)		95% c.i.
Gender	Male	10.0%	90.0%	33.926 (10.664-107.932)	<0.01	25.873 (7.811-85.699)
	Female	0.3%	99.7%			
Age	≥66	9.6%	90.4%	Non-applicable	<0.01	
	≥40 & <66	5.3%	94.7%			
	<40	0.0%	100.0%			
Residence	Island	6.2%	93.8%	1.446 (0.805-2.599)	0.346	1.107 (0.580-2.113)
	Mountain	6.1%	93.9%	1.016 (0.433-2.384)		0.738 (0.296-1.839)
	Urban and suburban	4.4%	95.6%	Reference		Reference
Alcohol	Yes	7.8%	92.2%	3. 357 (2.060-5.471)	<0.01	1.654 (0.819-3.342)
	No	2.5%	97.5%			
Smoke	Yes	7.4%	92.6%	2.589 (1.633-4.105)	<0.01	1.035 (0.540-1.984)
	No	3.0%	97.0%			
Financial problems	Yes	4.0%	96.0%	0.799 (0.490-1.305)	0.400	0.842 (0.489-1.450)
	No	5.0%	95.0%			
Manual work	Yes	6.5%	93.5%	1.680 (1.040-2.713)	0.044	0.973 (0.569-1.664)
	No	3.9%	96.1%			
Diabetes mellitus	Yes	11.1%	88.9%	2.972 (1.711-5.161)	<0.01	2.634 (1.350-5.138)
	No	4.0%	96.0%			
Hypertension	Yes	10.2%	89.8%	3.508 (2.218-5.547)	<0.01	2.780 (1.649-4.686)
	No	3.1%	96.9%			

records and examination in 2007, showed a prevalence of AS of 0.37%, and that of SpA of 1.1% [23]. In north-west Greece a study, using medical records of hospitals and Rheumatology Private Practices between 1983 and 2002, has found AS prevalence to be 0.03%, with HLA-B27 positivity present in 80.5% of patients [24]. Another study in Greece in 2002 showed a prevalence of AS of 0.24% and that of SpA of 0.49% [6]. In Izmir, Turkey, the prevalence of AS was 0.49% and that of SpA was 1.05% [25].

The prevalence of PsA in a study based on medical records in the Olmsted county, Minesota, USA in 1992 was 0.1% [4,26] and in another study conducted by phone in a random US population sample was 0.25% [27]. In the latter study, the prevalence of psoriasis was 2.2% [27]. In western Norway, a study using medical records of Rheumatology centers covering 442,000 persons between 1999 and 2002, found the prevalence of AS to be 0.19% [28]. In Ancona, Italy, a study using questionnaire in 2007 showed

Table 4: Variables assessed for association with osteoarthritis

Variable		Osteoarthritis		Unadjusted OR	P-value	Adjusted OR
		Yes	No	(95% CI)		95% c.i.
Gender	Male	11.3%	88.7%	0.411 (0.314-0.538)	<0.01	0.430 (0.306-0.604)
	Female	23.6%	76.4%			
Age	≥66	39.7%	60.3%	265.240 (36.807-1911.358)	<0.01	173.679 (23.714-1271.983)
	≥40 & <66	18.4%	81.6%	2.926 (2.220-3.857)		2.140 (1.541-2.974)
	<40	0.2%	99.8%	Reference		Reference
Residence	Island	23.8%	76.2%	1.546 (1.113-2.148)	0.033	1.186 (0.810-1.737)
	Mountain	18.2%	81.8%	1.397 (0.838-2.329)		1.656 (0.919-2.983)
	Urban & suburban	16.8%	83.2%	Reference		Reference
Alcohol	Yes	9.9%	90.1%	0.352 (0.264-0.468)	<0.01	0.827 (0.534-1.283)
	No	23.7%	76.3%			
Smoke	Yes	9.2%	90.8%	0.334 (0.247-0.451)	<0.01	0.667 (0.425-1.045)
	No	23.3%	76.7%			
Financial problems	Yes	20.8%	79.2%	1.353 (1.049-1.745)	0.020	1.316 (0.984-1.759)
	No	16.3%	83.7%			
Manual work	Yes	13.8%	86.2%	0.649 (0.477-0.882)	0.006	1.044 (0.727-1.499)
	No	19.8%	80.2%			
Diabetes	Yes	29.0%	71.0%	2.045 (1.420-2.946)	<0.01	0.739 (0.488-1.117)
	No	16.7%	83.3%			
Hypertension	Yes	36.7%	63.3%	3.987 (3.051-5.210)	<0.01	2.131 (1.553-2.926)
	No	12.7%	87.3%			

a prevalence of PsA of 0.42% [23]. Our PsA prevalence estimate is similar to that reported earlier in Greece (0.17%) [6].

Our estimate of SLE prevalence (0.11%) is slightly higher than that reported in a study using medical records of Hospitals and rheumatology practices in northwest Greece in 2001 (0.009% for men, 0.069% for women) [29]. The prevalence of SLE was 0.05% in a study using physician billing and hospital database in Quebec, Canada [30], and 0.01% in males and 0.071% in females in a study using General Practice Research Database in UK [31]. In northern Spain, a study using database of the single Immunology laboratory of a region, found SLE prevalence to be 0.034% [32], and in Northern Italy, a study using hospital medical records reported SLE prevalence 0.058% [33].

The prevalence of pSS in our study (0.23%) is in agreement with those of two previous community-based stud-

ies in Greece [34,35]. In Norway, the prevalence of pSS, as detected by postal questionnaire, was 0.22% in adult ages 40-44 years and 1.4% in the adult ages 71-74 years [36], and in UK the prevalence of pSS was 0.33% [37].

Our finding that only one person was diagnosed with SSc, DM, giant cell arteritis, hypocoplementemic urticarial vasculitis precludes any comment on the prevalence of these diseases. However, it is worth mentioning that there are geographical clusters of SSc which suggest an environmental aetiology for the disease [3].

The prevalence of gout increases with age, is higher in men than women, and is on the increase. In adult age >75 years in USA, the prevalence of gout increased from 2.1% in 1990, to 4.1% in 1999 [38]. The respective values for men were 2.5%, and 6.4% [38]. In the US National Health and Nutrition Examination Survey (NHANES) III between 1988 and 1994, the highest prevalence (8%; males, 11.6%; females, 5.2%) was found in adult ages 70-

79 years [39,40]. In a UK study using General Practitioner database, the prevalence of gout was 0.3% in the 1970s, and 0.95% in the 1990s [41]. Results from the UK General Practice database during the period 1990-1999 showed relatively constant incidence rates. In 1999 the prevalence of gout was 1.4% in adult population, and 7.0% in males over 65 years of age [42]. A retrospective study using medical records of General Practitioners in UK and Germany between 2000 and 2005 found the prevalence of gout to be 1.4% (mean age, 60 years) [43]. In China, the prevalence of hyperuricemia and gout varied among different regions. The prevalence of gout was 11.7% in Taiwanese aborigines and 3.0% in ethnic Taiwanese [44]. Our estimate of the prevalence of gout is much higher than that reported in the general Greek population (0.47%) a few years ago [6]. This may be explained by the relatively old age of our gouty patients (mean age, 63 years), and the changing diet and lifestyle. High seafood consumption, which is a risk factor for gout [45], is prevalent in this coastal region of Greece. Our study has found gout to be associated with male gender, hypertension, and diabetes mellitus. Since hypertension and type II diabetes mellitus are components of the metabolic syndrome or insulin resistance syndrome, our gouty men are likely to have this syndrome that carries an increased cardiovascular risk [46].

Epidemiological studies of OA have inherent problems due to lack of association between symptoms and radiographic findings that may underestimate OA prevalence. Generally, the prevalence of OA is associated with age and is higher in women. The prevalence of symptomatic hand OA, verified by x-rays, in the Framingham study was 6.8% (3.8% in men, 9.2% in women) whereas in adults age > 71 years was 13.4% in men and 26.2% in women [47]. The prevalence of symptomatic knee OA was 4.9%, and increased to 6.7% (5.9% in men, 7.2% in women) in adults aged > 45 years [48]. In the US NHANES III study, the prevalence of symptomatic knee OA in adults age >60 years was 12.1% [49], and in the Jonston county, northern Carolina, USA, it was 16.7% in adults age > 45 years [50]. In the latter study, the prevalence of symptomatic hip OA was 9.2% [40]. In British Columbia, Canada, database from Health centers and Hospitals between 1991 and 2001 showed a prevalence of symptomatic OA in 2001 of 10.0% in adult ages 45-49 years, whereas 32% of men and 40% of women aged 70 years had OA [51]. In France, a phone survey in a random population sample of adults aged 40-75 years found the prevalence of knee OA and hip OA to be 7.6% and 5%, respectively [52]. In Spain, the frequency of symptomatic hand OA was 6.2% and knee OA 10.2% [53]. In our study, there is a low frequency of hand OA. Individuals with hand OA may have mild symptoms and do not seek medical advice. Therefore, these patients did not report their condition. The rela-

tively low prevalence of OA in manual workers, compared to non-manual workers, may be attributed to women as house-wives. These women, included in non-manual workers, may have not only house duties but they may also work manually in the fields, a common practice in the country. A previous study in Greece showed a prevalence of symptomatic hand OA of 2.0%, knee OA 6.0%, and hip OA of 0.9% [54].

Radiographic OA, defined by the presence of osteophytes is much prevalent than symptomatic OA. In the Framingham study, the prevalence of radiographic hand OA was 27.2% (25.9% in men, 28.2% in women) [47]. The prevalence of radiographic knee OA was 13.8%, and increased to 19.2% in the > 45 year-old age group [48]. In the Jonston county study, the prevalence of radiographic OA in the >45 year age group was 27.8% (24.3% in men, 30.15% in women) and hip OA was 27.8% [40,50]. In the US NHANES III study, the prevalence of radiographic knee OA was 37.4% (31.2% in men, 42.1% in women) in the > 60 year-old age group [49]. In Holland, radiographic hand OA was found in 67% of women and 54.8% of men > 55 years of age [55].

As with other studies, our study has limitations to consider. Firstly, our study relied on patient self-reporting of a physician diagnosis of a disease as opposed to ascertaining a diagnosis through medical records. Additionally, our study may have missed patients with mild arthritis, such as OA, that did not come to medical attention. However, our estimates are generally close to those studies that used medical records to ascertain rheumatic disease diagnoses. Furthermore, self-report of chronic disease has been found accurate [56]. Secondly, our study had a relatively low response rate. However, similar response rate has also been reported by other postal surveys [57] and may be attributed to the increasingly use of questionnaires (postal or by phone) in public marketing.

Conclusions

Rheumatic diseases are common in central Greece, affecting nearly a quarter of adult population. OA and gout are the most common joint disorders.

ing of the manuscript, and in the decision to submit the manuscript for publication.

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