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Original Article

The Low Prevalence of Rheumatoid Arthritis in Two Regions of Serbia Based on Evidence-Based Data

Kanıta Dayalı Verilere Göre Sırbistan'ın İki Bölgesinde Romatoid Artritin Düşük Prevalansı

Roksanda STOJANOVIC,[1,2] Radmila JOVICEVIC,[3] Branka GLOGOVAC,[4]
Natasa RADOSAVLJEVIC,[5] Mirjana Zlatkovic SVENDA[1]

[1]*Institute of Rheumatology, Belgrade, Serbia*
[2]*University of Belgrade, School of Medicine, Belgrade, Serbia*
[3]*General Hospital Uzice, Serbia*
[4]*Primary Health Care Service, Department Dobanovci, Zemun, Belgrade, Serbia*
[5]*Institute for Rehabilitation, Department Mladenovac, Belgrade, Serbia*

Objectives: This study aims to present the results of three consecutive regional studies concerning the prevalence of rheumatoid arthritis (RA) based on medical documentation in two regions of Serbia.

Patients and methods: Two representative regions of Serbia were chosen for the survey. The first region selected was the Zlatibor region located in the mountainous part of Western Serbia with a predominantly rural population. This study included patients registered in 1997. Two studies were also carried in the region of Belgrade, the capital. One of these studies was conducted in 2001 in the northern part of the city in Dobanovci, an urban suburb. The other took place in 2007 in Mladenovac, a southern suburb of Belgrade with a combined rural and urban population. The medical documentation for all patients diagnosed with chronic polyarthritis was reviewed to verify the diagnosis of RA according to the American Rheumatology College (ARC) 1987 revised criteria. The prevalence of RA was estimated based on the entire population over the age of 18 for Zlatibor region and over the age of 20 in the two studies in the Belgrade area.

Results: The prevalence of RA in region Zlatibor was 0.253% (95% CI=0.217-0.288). In Dobanovci, the prevalence was 0.224% (95% CI=0.214-0.234), and it was 0.220% (95% CI=0.18-0.27) in Mladenovac. The estimated total number of patients with RA in Serbia was 14,445 out of an estimated 5,778,102 adult inhabitants in Serbia in 2009.

Conclusion: The previous prevalence of RA obtained in a population study of Belgrade in the 1990s along with the data from these three studies demonstrates low values. These results are consistent with the values obtained in surrounding countries in the Mediterranean region.

Key words: Epidemiology; medical records; prevalence study; rheumatoid arthritis; Serbia.

Amaç: Bu çalışmada tıbbi kayıtlara göre romatoid artrit (RA) prevalansına ilişkin iki ardışık bölgesel çalışmanın sonuçları sunuldu.

Hastalar ve yöntemler: Araştırma kapsamında Sırbistan'ı temsil eden iki bölge seçildi. Bunlardan biri, kırsal nüfusun hakim olduğu Batı Sırbistan'ın dağlık kesimi olan Zlatibor bölgesiydi. Bu çalışmaya 1997 yılında bu bölgeden hastalar dahil edildi. Başkent Belgrad'da ise iki çalışma yürütüldü. Çalışmalardan biri 2001 yılında Belgrad'ın kuzeyindeki Dobanovci kentinde ve varoşlarında yapıldı. Belgrad'ın güneyindeki hem kırsal hem de kentli nüfusu barındıran Mladenovac'ta ise, 2007 yılında bir başka çalışma yapıldı. Kronik poliartrit tanısı konulan tüm hastaların tıbbi kayıtları, Amerikan Romatoloji Derneği'nin (ARC) 1987 kriterlerine göre, RA tanısını doğrulamak amacıyla yeniden gözden geçirildi. Romatoid artrit prevalansı, Zlatibor bölgesinde 18 yaş üzerindeki nüfusun tümünü ve diğer iki çalışmada (Belgrad bölgesinde) 20 yaş üzerindeki nüfusun tümünü dikkate alarak hesaplandı.

Bulgular: Zlatibor bölgesindeki RA prevalansı, %0.253 idi (%95 GA 0.217-0.288). Dobanovci'de RA prevalansı %0.224 (%95 GA 0.214-0.234) iken, Mladenovac'ta %0.220 idi (%95 GA 0.18-0.27). Sırbistan'da tahmin edilen RA'lı hasta sayısı 14.445 idi (2009 yılında Sırbistan'da yaşayan erişkin sayısı 5.778.102 idi).

Sonuç: Kayıt çalışmaları ve tıbbi kayıtlara göre 1990'lı yıllarda Belgrad'da yapılan bir nüfus çalışmasında ve bu üç çalışmada elde edilen RA prevalansı, düşük değerler göstermektedir. Bu bulgular, komşu ülkeler ve Akdeniz bölgesinde yapılan çalışmalardan elde edilen değerler ile uyumludur.

Anahtar sözcükler: Epidemiyoloji; tıbbi kayıt; prevalans çalışması; romatoid artrit; Sırbistan.

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Correspondence: Roksanda Stojanovic, M.D., PhD. Institute of Rheumatology, Resavska 69, 11000 Belgrade, Serbia.
Tel: +381113600860 e-mail: roksandastojanovic@yahoo.com

The prevalence of rheumatoid arthritis (RA) in many countries of Europe in the last two decades was considerably lower in comparison to the earlier published data. Studies in Central European countries as well in the Mediterranean area demonstrated the prevalence of RA to be between 0.3 and 0.8.[1-5] The reasons for the overall decrease in the number of patients might be related to a better definition of RA, the precise use of classification criteria, the use of the same methodology to investigate the different populations, and extrinsic factors such as better health conditions and improved nutrition and lifestyle.

The first population study of RA in Serbia performed in the 1990s demonstrated a lower prevalence of RA (0.183%) in comparison to that found in other European countries.[6] The lower value was explained due to the strict use of the American Rheumatism Association (ARA) 1987 revised criteria for the classification of RA since the 1958 ARA criteria or the Rome criteria had been used in some earlier studies.[7]

In order to further elucidate the prevalence of RA in Serbia, we used evidence-based medical documentation and established local registries of the patients with RA.

The aim of this study was to present the results of three studies on the prevalence of RA based on medical documentation and to contextualize these results in a wider comparative framework for further research.

PATIENTS AND METHODS

Studies were performed during the 1990s and early in this century in two different regions of Serbia. The first study was done in 1997 in the Zlatibor region, the mountainous part of Western Serbia with a predominantly rural population, and it included patients from nine out of 10 local municipalities who were registered and treated in hospitals and primary care units. The municipality of Sjenica, which is on the border of the region, was not included since patients from there receive part of their medical care from other regions. Rheumatologists in the primary care units and local hospitals reviewed the documentation of patients diagnosed with RA or chronic polyarthritis. When no certain diagnosis of RA was evident based on the available documentation, they were sent to a regional hospital in Uzice where an experienced rheumatologist confirmed or rejected the diagnosis of RA. On the basis of the total number of patients (exceptions from the registry were not included), the prevalence of RA was determined for the Zlatibor region, and the details were published in the national journal of rheumatology - Acta rheumatologica Belgradensia.[8]

Two further studies were performed in the suburbs of the capital Belgrade. One of these was carried out in 2001 in Dobanovci, a suburb located in the northern part of Belgrade. It utilized the data that was available from personal health charts in general practice primary health service units and occupational medicine units. All patients diagnosed with RA or chronic polyarthritis were examined by a rheumatologist, and additional laboratory and/or radiographic examinations were performed to confirm the final diagnosis of RA. The next study was conducted in Mladenovac, a municipality with a combination of urban and rural residents in the southern part of Belgrade. The medical documentation of all patients diagnosed with chronic polyarthritis or RA in the primary health service units, occupational medicine units, and the general hospital were reevaluated by a rheumatologist to verify the diagnosis of RA. Based on the available data, a registry of patients was formed, and the prevalence of RA was determined in 2007.

For the study in the Zlatibor region, the subjects needed to be more than 18 years old. This age was chosen based on the proposed number of inhabitants in 1997 according to the data from the 1991 census. In the second and third studies, residents older that 20 years old were included. In Dobanovci this age was based on the proposed number of inhabitants in 2001 according to the data from the same census, and in Mladenovac, the data from the 2002 census was used to determine the appropriate age for inclusion.[9] The prevalence of people with RA with a 95% confidence interval (CI) was then calculated.

RESULTS

The total number of adult inhabitants and the number of male and female patients in the three studies is presented on Table 1. In the Zlatibor region, 563 persons with RA (114 males and 449 females with a male to female ratio of 1:4) were included in the registry and treated. Moreover, 388 of those patients (70 males and 318 females) received treatment in the hospital.

In Dobanovci, 18 patients were determined to have RA based on the medical data, but after reevaluation by a rheumatologist at the Institute of Rheumatology in Belgrade, RA was confirmed in only 14 of the participants (1 male and 13 females).

In Mladenovac, according to the medical records in the primary medical care units, occupational medical centers, and home care, 187 persons were diagnosed

Table 1. The adult population in three studies of two regions in Serbia regarding gender and the number of rheumatoid arthritis patients

	Population		Gender				Number of RA patients		
	≥20 years old		Male		Female		Male	Female	*Total*
	n	%	n	%	n	%	n	n	n
Zlatibor*	222,408	100*	109,315	49.2	113,093	50.8	114	449	563
Dobanovci**	6,245	100	3,191	51.1	3,054	48.9	1	13	14
Mladenovac**	40,715	100	19,580	48.1	21,135	51.9	14	75	89

RA: Rheumatoid arthritis; * Without the municipality of Sjenica, the population was over 18 years old; ** Belgrade area.

with RA or chronic polyarthritis, but reevaluation by a rheumatologist only confirmed RA in 89 of these cases (47.6%) (14 males and 75 females with a male to female ratio of 1:5.3).

The prevalence of RA in the investigated areas is shown in Table 2. The results obtained in the three studies demonstrated a similar low prevalence in the adult population with a male to female ratio of 1:4-5 (with the exception of Dobanovci). There was no discrepancy in the results regarding RA prevalence in the central parts of Belgrade, as had previously been demonstrated.[6]

The estimated number of adult inhabitants in Serbia in 2009 was 5,778,102. Calculations based on the higher prevalence value of 0.253[9] revealed the total number of patients with RA in Serbia (not including Kosovo) to be 14,445.

DISCUSSION

The prevalence of RA in the center of Belgrade as determined by a study conducted in 1989 and 1990 was lower than the results for other European populations.[10] When these results were analyzed, no genetic variables were incorporated, and further consideration of epidemiological/clinical studies involving chronic arthritis yielded no special determinants for RA.[11] Since we had no previous experience with regard to the prevalence of RA in our residents, there was no basis for comparison; therefore, we assumed that the low prevalence was due to the strict use of the ARA 1987 revised criteria. In our study, all patients who were candidates for RA were examined by an experienced rheumatologist, and the diagnosis of RA was confirmed only if a minimum of four ARA criteria were met. If the patients were discovered to have less than four of the ARA criteria, they were diagnosed with chronic polyarthritis. This approach was proven correct since after three years, none of the patients that had been previously diagnosed with chronic polyarthritis showed any characteristics of RA.

At the time of our population study in the 1990s, little was known about RA prevalence in the surrounding countries. In a study by Turkish authors published in 1968, the epidemiology of infective and rheumatoid syndromes was investigated in the Sagmalcilar district, a part of Istanbul which had mainly been settled by immigrants from Balkan countries.[12] Out of the 5,020 inhabitants included in the study, 2,789 (55%) were originally from different regions of the former Yugoslavia. The prevalence of RA in Sagmalcilar district residents was found

Table 2. The prevalence of rheumatoid arthritis in three studies of two regions in Serbia and in the central Belgrade population study

Region/area of study	Total	Male	Female
Zlatibor*	0.253	0.104	0.397
Registry	(0.217-0.288)◆	(0.0478-0.155)	(0.352-0.442)
Dobanovci**	0.224	0.033	0.407
Health chart	(0.214-0.234)	(0.027-0.039)	(0.389-0.424)
Mladenovac**	0.220	0.070	0.350
Health chart	(0.18-0.27)	(0.04-0.12)	(0.28-0.44)
Belgrade++	0.183	0.087	0.287
Population study	(0.169-0.197)	(0.071-0.101)	(0.259-0.314)

* Reference[8]; ** Belgrade area; ++ Reference[6]; ◆ 95% confidence interval (CI).

to be 0.22%. These results are similar to our data (irrespective of the methods used), which suggests that genetic background might be responsible for the low prevalence of RA found by the Turkish authors.

Recent studies in other regions of Turkey with different population structure have determined the prevalence of RA to be 0.36% in Antalya, 1% in the eastern Black Sea region and 3.7% in the city center of Trabzon, a town on the Black Sea coast.[13-15]

In Bulgaria, the prevalence of definitive RA was found to be 0.9%, whereas it was 0.4% in the former Czechoslovakia and 0.3% in Italy according to ARA 1958 criteria. On the other hand, the rates were higher in Northern European countries and North America (1-1.9%).[16]

The presented studies in Serbia, based on documentation from the public health services units, occupational medical units, and hospitals concerning chronic arthritis might count as control studies for the prevalence of RA in our population. Since population studies are expensive and require a great number of investigators, and having in mind the needs of the local health services, registry was formed in the Zlatibor region. It was useful for planning the distribution of personal and financial resources for the treatment of patients with RA and other rheumatic diseases in the region.

The results obtained in Dobanovci were similar to those in the Zlatibor region, although the male to female ratio was higher (1:13). The accepted male to female ratio for RA (1:3-4) is commonly found, but similar exceptions have been reported in İzmir (1:7).[3] In Mladenovac, the RA prevalence was slightly lower than in the other investigations and a slightly higher than normal male to female ratio (1:5.5) was discovered.

A number of studies concerning the prevalence of RA have been published in the last two decades (1988-2005) based on the ARA 1987 criteria,[10] and the results were comparable for the regions that were investigated (North America, Northern Europe, Southern Europe, and developing countries). For the Southern European countries (including our population study), it was evident that the prevalence of RA was lower than in other parts of the world.[17]

Recent studies on RA prevalence in the Mediterranean region and the surrounding areas have also demonstrated lower values than in Northern Europe. The reported prevalence rates were 0.31% in France,[1] 0.33% in Italy,[2] and 0.37% in Turkey.[3] Another study on the prevalence of RA in the Southern part of Hungary (the border area with Serbia) demonstrated a value of 0.37%.[4] In addition, the results of a studies from Spain showing an RA prevalence of 0.5%,[5] the Czech Republic with a rate of 0.6%,[18] and, more recently, from Greece with a rate of 0.58%[19] demonstrate the difference in the values between Southern and Northern Europe, where the prevalence of RA is higher as demonstrated by the rates of 0.8% in Finland and 0.85% in England.[20,21]

In order to further investigate the prevalence of RA in Serbia, a study is in progress that is using a tested questionnaire prepared in cooperation with the European League Against Rheumatism (EULAR).[22] The results will be comparable to those published in France[23] and Lithuania[24] where the same methodology was used.

In conclusion, our study showed that the prevalence of RA for the urban population of Belgrade in 1990 was lower than what was found in most other European studies at that time. The three studies in Serbia that were based on a local registry of RA patients and medical documentation demonstrated and confirmed the low prevalence values of RA in two parts of Serbia. These results are in line with the values obtained in the surrounding countries and the Mediterranean region. Our results should be accepted as valid and could prove to be beneficial for the planning of health services related to RA. Furthermore, the estimated number of RA patients in our study could be used for establishing hospital facilities and for determining the amount of finances needed for treatment and rehabilitation. Additionally, our results could be used in further investigations concerning the prevalence of RA.

- The low prevalence of rheumatoid arthritis in Serbia.
- The data presented is in line with the prevalence of RA in the Mediterranean region.
- The estimated number of RA patients in Serbia is approximately 15,000.

Declaration of conflicting interests

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