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## ORIGINAL PAPER

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# Epidemiology of Rheumatoid Arthritis in Southern Albania

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**ABSTRACT****Objectives:** The aim of this study was to assess the prevalence, incidence and the burden of rheumatoid arthritis (RA) in the Southern Albania.**Material and Methods:** This is an epidemiologic observational study with cross-sectional analyses of all patients with RA who lived in Southern Albania during the 1995-2011 years. The RA prevalence, incidence and disability-adjusted life years (DALY) were assessed. **Results:** During the 1995-2011 years, 194 patients (154 females and 40 males) with RA living in Southern Albania were identified. The prevalence of RA in 2011 was 0.25% in general population and 0.34% in adult (>14 years) population. The incidence of RA in 2011 was 0.012% (12 new cases per 100000 inhabitants) and 0.016% (16 new cases per 100000 adults). The prevalence increased (from 0.036% in 1996 to 0.25% in 2011) and the incidence did not change over the study period. The mortality was 3.2% (n=7 deaths). The DALY due to RA was 823 years per 100000 inhabitants during 1995-2011 years. **Conclusion:** RA in Southern Albania has a prevalence of 0.25% and an annual incidence of 0.012% in the general population in 2011. RA was responsible for a considerable burden on the health of population during the 1995-2011 years.**Keywords:** Rheumatoid arthritis; incidence; prevalence; Albania**1. INTRODUCTION**

Rheumatoid Arthritis (RA) is a chronic inflammatory disease with unknown etiology that is characterized by articular damages, concomitant involvement of other systems, increased work-related disability and socioeconomic deterioration (1). Worldwide, RA affects 0.5% to 1% of the adult population (2). The prevalence of the disease increases with age in men and women (1). The women to men ratio has been reported to be 2:1 or higher (3). The RA prevalence and incidence, as well as the clinical manifestations have no clear geographic borders, potentially due to the complexity of the genetic, environmental and socioeconomic factors (4). In the North American and European countries the annual incidence varies between 20 and 50 cases per 100 000 inhabitants (2, 5). Overall, in Europe the prevalence of RA decreases from north to south (6, 7). Although, few studies have investigated the incidence and prevalence of RA in the Southern European countries, they indicate a lower annual incidence, in general, between 10 and 20 new cases per 100 000 inhabitants (8, 9).

RA, like other muscle-skeletal diseases, contributes to the general disease burden in the population. The burden that RA causes in the population is linked more to the years lost due to the disability it causes, than to the premature death (4). According to the World Health Organization (WHO) Global Burden

of Disease 2009, the disability-adjusted life year (DALY), attributed to the RA was highest in Europe and North America and lowest in the African, Eastern Mediterranean and Southeast Asian Regions (10). There are no studies that have assessed the incidence, prevalence and the indicators of the burden of RA in Southern Albania.

The aim of this study was to assess the prevalence, incidence and the burden of RA in the Southern Albania during the 1995-2011 years.

**2. MATERIAL AND METHODS**

This is an epidemiologic observational study, with cross-sectional analyses to study the prevalence, incidence and burden of RA in Southern Albania. The study included all patients with RA who lived in the region of Gjirokaster between January 1995 and December 2011. The region of Gjirokaster is situated in the Southern Albania and is close to Greece. The region includes 3 districts and has a surface of 2884.26 km<sup>2</sup> and a population of 75,172 inhabitants in 2011 (according to the National Institute of Statistics data). Urban residents comprise 42.3% of the total population and they live in 6 municipalities; the remaining 57.7% of population live in rural areas (26 communes and 273 villages). The climate of the region is Mediterranean.

### Data collection and inclusion criteria

Data on the general population were obtained from the regional register of statistics and the National Institute of Statistics. The RA was diagnosed according to the criteria of the American College of Rheumatology of 1987 (11). In order to identify all patients with RA living in the region, the documentation from the regional hospital, ambulatory clinics, health centers, family practitioners and regional medical committee for work disability was analyzed. All patients were diagnosed and treated by the Service of Rheumatology, Regional Hospital of Gjirokastër. The final diagnoses of the patients were confirmed by the Service of Rheumatology, University Hospital Center in Tirana (145 patients), or rheumatology clinics abroad (49 patients).

For every patient included in this study, the following information was collected: general information (name, gender, birthday); demographic data (place of birth, residence, urban or rural area, education, profession); data on the history of the disease (age at the onset of the disease, duration, stages, disability and death) and data on the risk factors (relatives with the disease, smoking or alcohol consumption). The stage of the disease was assessed using the classification of global functional status according to the American College of Rheumatology 1991, where patients were classified into 4 functional stages, based on their ability of self-care, professional and nonprofessional activity (12). The disability was defined according to the 1991 and 2010 national medical criteria for determination of the ability to work (13).

### Epidemiologic Data

Point prevalence—the ratio of the total number of cases diagnosed in a certain time point with the total number of the population in that time point—was assessed at the end of the 1996, 2001, 2006, and 2011 years, for the general population, as well as for adult population (>14 years of age), female and male population(s). The incidence—number of new cases during a certain period of time over the population “at risk” at the beginning of the period—was calculated as a cumulative 1-year and 5-year incidence, based on the total population, as well as adult, female and male population(s).

DALY estimates the healthy years lost due to the disease. One unit of DALY is equal to 1 year of healthy life lost due to the disease under consideration. It consists of two components: years lost due to deaths or years of life lost (YLL) and years lived with disability (YLD) (4). YLL shows the years lost in patients with a disease from premature death and it is calculated as the sum of the differences between expected and real patient's ages. Expected age represents the average life expectancy of the generation born in the same year with the patient. The expected age was considered the average life expectancy of the population in the Southern Albania in the years in which the death(s) occurred. YLD are years lived with the disability due to the disease. It indicates the healthy years of life lost due to the disability that the disease causes. The calculation of the YLD is performed using the following formula:  $YLD = I \times DW \times L$ , where I is the number of incidental cases in the study period; DW (disability weight) is a coefficient that is used to determine the disability that causes the disease and L is the average duration of the disease in years (14). A DW value of 0.2 was used for calculation, as recommended by the World Health Organization. This parameter was calculated by Murray and Lopez in 1996

and is used extensively for the calculation YLD from RA (15). YLD was determined for one year (2011) and for the 15-year period of the study (1995-2011) in the general population and in female and male populations.

### Statistical analysis

Continuous data with normal distribution are represented as mean  $\pm$  1 standard deviation. Data with skewed distribution are presented as median with 25<sup>th</sup>-75<sup>th</sup> percentiles. The normality of data distribution was tested with the one-sample Kolmogorov-Smirnov test. Categorical variables (proportions) are presented as absolute numbers (percentages) and are compared with the chi-square test. The data are analyzed with the SPSS statistical package (version 15). A 2-sided P value of less than 0.05 was considered to indicate the statistical significance.

## 3. RESULTS

### Baseline data

The study included 194 patients with RA living in Region of Gjirokaster during the time period from 1995 until the end of 2011. The demographic characteristics of the patients are presented in Table 1.

| Variables                       | Values          |
|---------------------------------|-----------------|
| Age (years)                     | 56.5 $\pm$ 12.0 |
| Onset age (years)               | 44.1 $\pm$ 12.0 |
| Females                         | 154 (79.4)      |
| Living in urban area            | 128 (66)        |
| Education                       |                 |
| ≤ 8 years                       | 114 (58.8)      |
| 8-12 years                      | 64 (33)         |
| > 12 years                      | 16 (8.2)        |
| Profession (physical work)      | 146 (75.3)      |
| Positive family history         | 32 (16.5)       |
| Smoking                         | 33 (17%)        |
| Alcohol consumption             | 10 (5.2)        |
| Duration of the disease (years) | 12.3 $\pm$ 9.7  |
| Diagnosis delay (years)         | 1.8 $\pm$ 1.9   |
| Functional stages               |                 |
| I                               | 19 (9.8)        |
| II                              | 86 (44.3)       |
| III                             | 80 (41.2)       |
| IV                              | 9 (4.6)         |
| Disability, number (%)          | 69 (35.6)       |
| Disability duration (years)*    | 0.0 [0.0-6.0]   |
| Deaths, number (%)              | 7 (3.6)         |

Table 1. Demographic data. The data are presented as number of patients (%), mean  $\pm$  1 standard deviation or median with 25<sup>th</sup>-75<sup>th</sup> percentiles. \* The disability years have a non-Gaussian distribution so they are presented as median with 25<sup>th</sup>-75<sup>th</sup> percentiles. The mean  $\pm$  standard deviation for this variable is 4.2 $\pm$ 7.3 years (range from 0 to 41 years).

As seen in the Table 1, most of the patients were females (n=154) and the female/male ratio was 4:1. Nearly 2/3 of the patients live in urban areas. Three-fourth of the patients practiced professions qualified as physical work and only 8.2% of the patients had a high education. More than one-third of the patients (35.6%) were disabled. The patients with disability were disabled for a mean of 9.5 $\pm$ 8.5 years. Eighty-nine patients (45.8%) were in stages III and IV of the disease.

During the study years, 7 patients (3.2%) died. The causes of death were as follows: chronic renal insufficiency (3 patients), acute renal failure (2 patients), lung cancer (1 patient) and road

accident (1 patient). Six of the dead patients were women.

### Prevalence

In 2011, the RA prevalence was 0.25% or 249 cases per 100 000 inhabitants. In adult population, female and male population, the RA prevalence in 2011 was 0.34% (341 cases/100,000 adult population), 0.40% (400 cases for 100,000 females) and 0.10% (102 cases for 100,000 males), respectively. Expectably, the RA prevalence increased over time from 0.036% in 1996 to 0.25% in 2011 (Table 2).

| Prevalence | General population | Adults (>14 years of age) | Female | Male   |
|------------|--------------------|---------------------------|--------|--------|
| 1996       | 0.036%             | -*                        | 0.057% | 0.016% |
| 2001       | 0.097%             | 0.13%                     | 0.16%  | 0.039% |
| 2006       | 0.14%              | 0.18%                     | 0.24%  | 0.054% |
| 2011       | 0.25%              | 0.34%                     | 0.40%  | 0.10%  |

Table 2. Prevalence in the general population as well as in the adult, female and male populations from 1996 to 2011. \*Data on adult population for 1996 were not available

The RA point prevalence was higher in females than in males throughout the study period and it increased progressively in both genders, particularly in females (Figure 1).

### Incidence

The RA annual incidence in 2011 was 0.012%, or 12 new cases per 100,000 inhabitants. According to gender, the RA annual incidence in 2011 was 0.024% in females (24 new cases per 100,000 females) and 0.010% in males (10 new cases for 100,000 males). In adults, the annual RA incidence in 2011 was 0.016% (16 new cases for 100,000 adults). The 5-year cumulative incidence in general population, adult, female and male populations, is shown in Table 3. As seen in the Table 3, the incidence did not change over the time.

| Cumulative Incidence | Five-year intervals |             |             | P value |
|----------------------|---------------------|-------------|-------------|---------|
|                      | 1997-2001           | 2002-2006   | 2007-2011   |         |
| Total                | 49 (0.029%)         | 42 (0.037%) | 43 (0.014%) | 0.259   |
| Adults               | 49*                 | 42 (0.051%) | 43 (0.052%) | 0.914   |
| Females              | 39 (0.047%)         | 36 (0.064%) | 32 (0.062%) | 0.356   |
| Males                | 10 (0.012%)         | 6 (0.011%)  | 11 (0.021%) | 0.278   |

Table 3. Five-year incidence of RA in general population and adult, female and male populations. Data are numbers of new cases with RA (%). \*Data on adult population in this 5-year interval were not available.

### The RA burden during the 1995-2011 Years

Overall there were 194 patients with RA during the study period. Of them, 7 patients (6 women and 1 man) died. The YLL, or total years of life lost from premature death caused by RA during the 1995-2011 was 141.6 years.

YLD caused by RA for 2011, in the general population was 22.14 years (12.14 years in women and 10 years in men). YLD calculated for the whole period of the study (1995-2011) was 477.2 years (378.4 years in females and 100 years in males).

DALY or the sum of YLL (141.6 years) plus YLD (477.2 years) was 618.8 years. Standardized for 100 000 inhabitants, the DALY due to RA between 1995 and 2011 was 823 years.

## 4. DISCUSSION

The main findings of present study are as follows: 1) The prevalence of RA in the general population of the Southern Albania was 0.25% in 2011. The RA prevalence was higher

in women than in men. 2) The RA annual (2011) and 5-year incidence (2007-2011) in general population was 12 new cases and 43 new cases per 100 000 inhabitants, respectively. The RA incidence remained stable during the 1995-2011 years. 3) There appears to be a considerable burden caused by RA in the general population; the DALY due to RA during the study period (1995-2011 years) was 823 years per 100 000 inhabitants.

The RA prevalence varies among countries and areas of the world. Worldwide, the RA prevalence based on the studies that used the American College of Rheumatology 1987 criteria varies between 0.2% and 1.2%. Studies from the Northern Europe have shown a higher RA prevalence compared to the rest of the world (6). In Southern Europe, the RA prevalence was reported to vary from 0.33% in Italy in 1998 (16), to 0.7% in Greece in 2003 (17). Despite these studies, the number of studies investigating the RA epidemiology in Southern Europe remains limited. By reporting epidemiological data for RA in Southern Albania, the present study helps to better understand the RA epidemiology in Southern Europe. The RA prevalence of 0.34% and the annual incidence of 16 new cases per 100 000 adult inhabitants are similar to those reported by Drosos et al. (9) in the Ioannina population (geographically continuous with Southern Albania). In this study, the total prevalence of RA for men and women was 205 and 478 cases/100 000 inhabitants, respectively. Furthermore, the annual incidence rates varied between 15 and 36/100 000 inhabitants (9).

Although within the range of reported values for Southern European countries, the RA prevalence and incidence found in the present study were low. It is generally accepted that RA is a multifactorial disease and its occurrence and severity are related to both genetic and environmental factors (2). However, the relative contribution of these factors or their interaction in causing RA remains unknown. Accumulating evidence points out to a relationship between HLA-DRB1 alleles (called also the shared epitope alleles) and the susceptibility to RA. Evidence available suggests that genetic associations with RA are different in Southern European populations versus Northern Europe and United States populations (18). The shared epitope alleles are found in approximately three quarters of Northern Europeans and in about half of Southern European patients (19). A recent genetic study investigated the HLA-DRB1 and HLA-DQB1 first-level allele frequencies in Albanian patients with RA, taking into account their rheumatoid factor (RF) and anticitrullinated peptide antibodies (ACPA) serologic subgroups. The study found relatively low frequencies of DRB1\*04 and high DRB1\*11 in the Albanian population that may explain the rather low positivity rate of ACPA and RF antibodies among Albanian patients with RA (20). Since both ACPA and RF antibodies are frequently associated with RA and causally involved in the genesis of the disease (21), the frequency of these alleles may explain the low occurrence of RA in our patients. Apart from genetic factors, environmental and life-style factors appear to be associated with increased RA risk. Although, the impact of the environmental and life-style factors was not investigated in the setting of present study, considering the Mediterranean geographic position of our region, milder climate, immune-suppressive effect of ultra-violet light, as well as dietetic factors, particularly Mediterranean diet (increased olive oil and fish consumption) may decrease the risk for RA (22).

The socioeconomic status may be associated with social

and/or environmental factors that may modify the sensibility towards RA (23). An inverse association between socioeconomic status assessed by education and profession and the risk for RA has been observed (1). By reporting that nearly 60% of the our RA patients had a lower level of education and 75% of them exerted professions considered as physical work, the present study corroborates these studies. With regard to gender differences in the association with the risk of RA, a 4:1 female/male ratio was found. Although, the specific mechanisms responsible for the increased sensibility of women to develop RA remain unknown (3), this finding coincides with the widely-held view and ample evidence that RA is an autoimmune disease that predominantly affects women.

Data on the trends in the incidence and prevalence of RA over time are limited. However, in some Northern countries, a decline in both the prevalence and the incidence of the disease after the 60s has been suggested. Data on time trends of the occurrence of RA for Southern Europe are missing (24). The present study found that the RA prevalence increased and the RA incidence remained stable during the 1995-2011 years. The exact reasons for the increasing RA prevalence in the present study remain unknown. However, demographic changes, particularly, a reduction in the general population caused by emigration of mostly healthy population in this time period may offer an explanation for the upward trending of RA prevalence in the present study.

It has been reported that RA causes modest global disability with severe consequences for the individuals affected. In one study that have analyzed 291 conditions, RA was ranked as the 42nd highest contributor to global disability. Moreover, the DALY due to RA continues to increase mostly due to a growth in population and increase in aging (25). This study was the first one to report the RA burden in Albanian population. In the present study the DALY due to RA was estimated to be 823 years per 100 000 inhabitants. The total DALYs per 100,000 Albanians for cardiovascular disease and stroke was estimated to be 2,997 years (26). In the face of lacking of the data on the DALYs due to other diseases, the contribution of RA in total disease burden remains unknown.

## 5. CONCLUSION

The data of this study showed that RA in the Southern Albania has a prevalence of 0.25% and an annual incidence of 12 new cases per 100 000 inhabitants in 2011. The RA prevalence increased and the incidence remained stable during the 1995-2011 years. RA appears to cause a considerable burden on the health of the population. These data may help the interested institutions dealing with morbidity, disease burden, costs and planning policies in the region.

CONFLICT OF INTEREST: NONE DECLARED.

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