## **ORIGINAL RESEARCH**

## Correlates of rheumatoid arthritis among women in Albania

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#### Abstract

**Aim:** Our aim was to assess the association of rheumatoid arthritis with socio-demographic characteristics and lifestyle factors among women in transitional Albania.

**Methods:** A cross-sectional study was carried out in 2012-2013 including a sample of 2198 women aged 30 years and above who attended the Rheumatology services at primary health care clinics in Tirana municipality (mean age: 60.2±9.7 years; overall response rate: 95%). The diagnosis of rheumatoid arthritis was based on the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) 2010 criteria. In addition, a structured questionnaire was administered to all study participants including information on demographic and socioeconomic characteristics and behavioral factors. Binary logistic regression was used to assess the association of rheumatoid arthritis with covariates.

**Results:** Overall, 437 (19.9%) women were diagnosed with rheumatoid arthritis (both incident and prevalent cases). In multivariable-adjusted models, rheumatoid arthritis was positively and significantly related to older age (OR=1.8, 95%CI=1.3-2.6), a lower educational attainment (OR=1.4, 95%CI=1.1-1.9), smoking (OR=1.5, 95%CI=1.1-2.0), alcohol intake (OR=1.9, 95%CI=1.2-3.1) and overweight and obesity (OR=1.5, 95%CI=1.2-2.0 and OR=1.6, 95%CI=1.2-2.0, respectively).

**Conclusion:** This study provides useful evidence about selected correlates of rheumatoid arthritis among women attending specialized primary health care services in Albania. Health professionals and policymakers in Albania should be aware of the magnitude and consequences of this chronic condition in the adult population.

*Keywords:* Albania, behavioral factors, rheumatoid arthritis, socio-demographic factors, Western Balkans.

Conflicts of interest: None.

## Introduction

Rheumatoid arthritis is currently considered a clinical syndrome across several disease subsets (1), involving inflammatory flows (2), leading to an ultimate common pathway in which persistent synovial inflammation and associated damage to articular cartilage and underlying bone are present (3). Overproduction of the tumor necrosis factor is the principal inflammatory process in the pathophysiology of the rheumatoid arthritis (1,4). This leads to overproduction of many cytokines such as interleukin 6, which causes persistent inflammation and joint destruction (1,5).

Regarding the etiology, genetic factors account for about 50% of the risk of developing rheumatoid arthritis (6,7). These factors are primarily related to either autoantibody-positive disease (ACPA-positive) or ACPA-negative disease (1). As for the lifestyle factors, smoking is considered the main environmental risk factor (1,8), doubling the risk for development of rheumatoid arthritis (9).

Rheumatoid arthritis affects 0.5%-1.0% of adults in developed countries (1). Women are three times more affected than men (1). However, the prevalence of this condition is positively related to age in both men and women (1). In women, hormonal factors play an additional role as the prevalence of rheumatoid arthritis is highest among individuals over 65 years (10). Regarding the incidence of rheumatoid arthritis in developed countries, it varies from 5 to 50 cases per 100,000 adults (11). On the other hand, the prevalence of rheumatoid arthritis displays significant geographical variations (12). The prevalence of this condition is higher in Northern Europe and North America compared to developing countries (13). Such geographical variations have been linked both to different genetic inclinations as well as to different environmental factors which expose individuals from different regions to different levels of risk for rheumatoid arthritis (1).

The information about rheumatoid arthritis in former communist countries of the Western Balkans including Albania is scarce. In general, the burden of musculoskeletal disorders has increased in Albania in the past few decades (14). The proportion of musculoskeletal disorders comprised only 8.5% of the total burden of disease in Albania in 1990, whereas in 2010 it increased to 11.0% (14). There is evidence of a steeper increase in women than in men (3.7% vs. 2.0%, respectively) (14).

In this context, the aim of our study was to assess the association of rheumatoid arthritis with demographic and socioeconomic characteristics and lifestyle/behavioral factors among women attending specialized primary health care services in transitional Albania.

## Methods

This was a cross-sectional study which was carried out in 2012-2013.

## Study population

This study included a sample of 2198 women aged 30 years and over who attended the Rheumatology services at primary health care clinics in Tirana municipality. Beforehand, the required sample size was estimated at 1870 women in order to obtain sufficient cases of rheumatoid arthritis among women who attended the Rheumatology services in different polyclinics of Tirana. In order to increase the study power and account for potential non-response, we decided to include 2500 consecutive women aged $\geq$ 30 years who attended t he Rheumatology services. Of these, 198 women were ineligible (too sick to participate), whereas 104 further women refused to participate. The final study sample consisted of 2198 eligible women who agreed to participate (overall response rate: 2198/2302=95%). Of 2198

women who participated in the study, 437 (19.9%) were diagnosed with rheumatoid arthritis (both incident and prevalent cases).

#### Data collection

The diagnosis of rheumatoid arthritis was based on the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) 2010 criteria (15). These criteria consist of joint involvement, serology, acute-phase reactants and duration of symptoms (15).

In addition, a structured questionnaire was administered to all study participants including information on selected demographic and socioeconomic characteristics and lifestyle/behavioral factors. Socio-demographic factors included age (which in the analysis was dichotomized into:  $\leq$ 50 years vs.  $\geq$ 50 years), marital status (dichotomized into: married vs. not married), employment status (employed and/or retired vs. unemployed) and educational attainment (trichotomized into: low, middle and high). Conversely, lifestyle/behavioral factors included smoking, alcohol intake, coffee consumption and tea consumption – all dichotomized into: no vs. yes), as well as the body mass index (BMI, trichotomized into: <25, 25-29.9 and  $\geq$ 30).

#### Statistical analysis

Independent samples t-test was used to compare the mean ages between women with and without rheumatoid arthritis. Conversely, Fisher's exact test was used to compare the distribution of socio-economic characteristics and behavioral factors between women with and without rheumatoid arthritis. On the other hand, binary logistic regression was used to assess the association of rheumatoid arthritis (outcome variable) with socio-economic characteristics and behavioral factors (independent variables). Initially, crude (unadjusted) odds ratios (ORs) and their respective 95% confidence intervals (95%CIs) were calculated. Subsequently, multivariable-adjusted models controlling simultaneously for all covariates were run. Multivariable-adjusted ORs and their respective 95%CIs were calculated. In all cases, a p-value of  $\leq 0.05$  was considered as statistically significant. Statistical package for Social Sciences (SPSS, version 15.0) was used for all the statistical analyses.

#### Results

Overall, mean age of study participants was  $60.2\pm9.7$  years; median age was 60.0 years (interquartile range: 54.0-67.0 years). On the other hand, the age range was 30-92 years. Women diagnosed with rheumatoid arthritis were older than those without rheumatoid arthritis (mean age:  $62.0\pm9.8$  years vs.  $59.8\pm9.7$  years, respectively; P<0.001) [not shown in the tables].

The distribution of socio-demographic characteristics and lifestyle/behavioral factors of women by rheumatoid arthritis status is presented in Table 1. As expected, the proportion of older individuals (over 50 years of age) was higher among women with rheumatoid arthritis compared with their counterparts without this condition (91% vs. 85%, respectively, P<0.001). The proportion of a lower educational level was more prevalent in women with rheumatoid arthritis than in those without rheumatoid arthritis (20% vs. 16%, respectively, P=0.02). Conversely, no differences were evident for marital status or employment between the two groups of women. Regarding behavioral factors, the prevalence of smoking and alcohol intake were significantly higher in women with rheumatoid arthritis than in those without rheumatoid arthritis than in those of smoking: 15% vs. 11%, respectively, P=0.02; for alcohol consumption: 7% vs. 4%, respectively, P=0.01). Similarly, the prevalence of coffee

consumption was higher among women with rheumatoid arthritis, but this finding was not statistically significant. The prevalence of tea consumption was similar in the two groupings. On the other hand, the prevalence of overweight and obesity were significantly higher in women with rheumatoid arthritis compared with those without this chronic condition (for overweight: 35% vs. 29%, respectively, whereas for obesity: 30% vs. 25%, respectively; overall P<0.001) [Table 1].

Age-group: $\leq 50$ years $298 (13.6)^*$ $37 (8.5)$ $261 (14.8)$ $<0.$ $>50$ years $1900 (86.4)$ $400 (91.5)$ $1500 (85.2)$ Employment:Employed and/or retired $1746 (79.4)$ $342 (78.3)$ $1404 (79.7)$ $0.5$ Unemployed $452 (20.6)$ $95 (21.7)$ $357 (20.3)$ Marital status:Married $1793 (81.6)$ $363 (83.1)$ $1430 (81.2)$ $0.4$ Not married $405 (18.4)$ $74 (16.9)$ $331 (18.8)$ Educational level:Low $364 (16.6)$ $89 (20.4)$ $275 (15.6)$ $0.0$	
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Low 364 (16.6) 89 (20.4) 275 (15.6) 0.0	
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Middle/high 1834 (83.4) 348 (79.6) 1486 (84.4)	
Smoking:	
No 1947 (88.6) 372 (85.1) 1575 (89.4) 0.0	)15
Yes 251 (11.4) 65 (14.9) 186 (10.6)	
Alcohol intake:	
No 2105 (95.8) 407 (93.1) 1698 (96.4) 0.0	)05
Yes 93 (4.2) 30 (6.9) 63 (3.6)	
Coffee consumption:	
No 758 (34.5) 136 (31.1) 622 (35.3) 0.1	03
Yes 1440 (65.5) 301 (68.9) 1139 (64.7)	
Tea consumption:	
No 1200 (54.6) 242 (55.4) 958 (54.4) 0.7	/47
Yes 998 (45.4) 195 (44.6) 803 (45.6)	
BMI:	
Normal weight 971 (44.2) 155 (35.5) 816 (46.3)	.001
Overweight 655 (29.8) 151 (34.6) 504 (28.6) <0.	.001
Obesity 572 (26.0) 131 (30.0) 441 (25.0)	

Table 1. Distribution of socio-demographic characteristics and lifestyle/behavioral factors in a
sample of Albanian women by rheumatoid arthritis status

\* Absolute numbers and their respective *column* percentages (in parentheses).

<sup>†</sup> P-values from Fisher's exact test.

Table 2 presents the association of rheumatoid arthritis with demographic and socioeconomic characteristics and behavioral factors. In crude (unadjusted) models, there was a positive association of rheumatoid arthritis with older age (OR=1.9, 95%CI=1.3-2.7), a lower educational attainment (OR=1.4, 95%CI=1.1-1.8), smoking (OR=1.5, 95%CI=1.1-2.0), alcohol intake (OR=2.0, 95%CI=1.3-3.1) and overweight and obesity (OR=1.5, 95%CI=1.2-2.0 and OR=1.6, 95%CI=1.3-2.3, respectively). Furthermore, there was a weak and

borderline statistically significant relationship with coffee consumption (OR=1.2, 95%CI=1.0-1.5). On the other hand, there was no association with employment, marital status, or tea consumption.

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<b>X7 • 11</b>	Crude (unadjusted) models		Multivariable-adjusted models	
Variable	<b>OR (95%CI)</b> *	<b>P</b> *	OR (95%CI)*	<b>P</b> *
Age-group:				
≤50 years	1.00 (reference)	0.001	1.00 (reference)	0.001
>50 years	1.88 (1.31-2.70)		1.82 (1.26-2.62)	
Employment:				
Employed and/or retired	1.00 (reference)	0.497	1.00 (reference)	0.522
Unemployed	1.09 (0.85-1.41)		1.08 (0.84-1.43)	
Marital status:				
Married	1.00 (reference)	0.369	1.00 (reference)	0.654
Not married	0.88 (0.67-1.16)		0.94 (0.71-1.24)	
Educational level:				
Middle/high	1.00 (reference)	0.017	1.00 (reference)	0.008
Low	1.38 (1.06-1.80)		1.44 (1.10-1.89)	
Smoking:				
No	1.00 (reference)	0.012	1.00 (reference)	0.017
Yes	1.48 (1.09-2.01)		1.46 (1.07-2.00)	
Alcohol intake:				
No	1.00 (reference)	0.003	1.00 (reference)	0.005
Yes	1.99 (1.27-3.11)		1.93 (1.22-3.05)	
Coffee consumption:				
No	1.00 (reference)	0.099	1.00 (reference)	0.210
Yes	1.21 (0.97-1.51)		1.16 (0.92-1.46)	
Tea consumption:				
No	1.00 (reference)	0.714	1.00 (reference)	0.421
Yes	0.96 (0.78-1.19)		0.92 (0.74-1.14)	
BMI:		< <b>0.001</b> (2) <sup>†</sup>		<0.001 (2) <sup>†</sup>
Normal weight	1.00 (reference)	-	1.00 (reference)	-
Overweight	1.54 (1.23-2.02)	0.001	1.53 (1.18-1.98)	0.001
Obesity	1.59 (1.29-2.28)	< 0.001	1.57 (1.22-2.02)	< 0.001

Table 2. Association of rheumatoid arthritis with socio-demographic characteristics and lifestyle
factors

<sup>\*</sup>Odds ratios (OR: rheumatoid arthritis vs. no rheumatoid arthritis), 95% confidence intervals (95%CIs) and p-values from binary logistic regression.

<sup>†</sup> Overall p-value and degrees of freedom (in parentheses).

Upon multivariable-adjustment for all covariates entered simultaneously into the logistic regression models, rheumatoid arthritis was positively and significantly related to older age (OR=1.8, 95%CI=1.3-2.6), a lower educational attainment (OR=1.4, 95%CI=1.1-1.9), smoking (OR=1.5, 95%CI=1.1-2.0), alcohol intake (OR=1.9, 95%CI=1.2-3.1) and overweight and obesity (OR=1.5, 95%CI=1.2-2.0 and OR=1.6, 95%CI=1.2-2.0, respectively) [Table 2].

#### Discussion

This study provides evidence on selected socio-demographic and lifestyle correlates of rheumatoid arthritis among women seeking specialized primary health care in post-communist Albania. Older age, low education, smoking, alcohol intake and overweight and obesity were strong and significant "predictors" of rheumatoid arthritis in this sample of adult women in Albania.

The positive association of rheumatoid arthritis with age which was found in our study is in line with several previous reports (1). On the other hand, the positive relationship with a lower educational attainment is appealing and deserves further investigation in population-based samples.

Regarding the environmental factors, we found that, in multivariable-adjusted models, smoking was related to a 50% increase in the risk of rheumatoid arthritis. Several studies have indicated that smoking is the main environmental risk factor which increases twice the risk of developing rheumatoid arthritis (9). It has been demonstrated that the effect of smoking is confined to patients with ACPA-positive disease (8). Nonetheless, at a population level, the risk associated with smoking is quite low and has limited clinical relevance regardless of the pathogenetic importance of this factor (1).

In our study, we found a positive relationship between rheumatoid arthritis and alcohol consumption. The risk in women who reported to consume alcohol was about 90% higher than in those who did not report alcohol intake. This finding is generally compatible with previous studies conducted elsewhere (1,16). Other potential environmental risk factors for development of rheumatoid arthritis may include coffee intake, vitamin D status, and oral contraceptive use (1,16). We did not assess the effect of vitamin D, or oral contraceptive use, but found a weak and borderline significant relationship with coffee consumption in unadjusted logistic regression models only. In any case, smoking excluded, the effect of environmental factors in the risk of rheumatoid arthritis is controversial (1).

At present, there are many unresolved difficulties for individuals suffering from rheumatoid arthritis. Yet, the constant introduction of innovative and ground-breaking treatments can overcome many of these difficulties and challenges (1). One of the main requirements involves the characterization of disease subsets in individuals with early onset of rheumatoid arthritis in order to target intensive treatment regimens for those who need them most and are also likely to respond (1). From this perspective, it is suggested that that the new direction of treatment and management of rheumatoid arthritis should be towards short intensive therapeutic courses that result in remission instead of the traditional approach which consist of long-term suppressive treatment strategies (1).

This study may have several limitations. The study sample may not be representative of all women who attend Rheumatology services at the primary health care level in Tirana. Nonetheless, we included consecutive women who fulfilled the eligibility criteria in order to ensure, to the extent possible, a representative sample of female primary health care users seeking Rheumatology services in Tirana municipality. Yet, as our study was conducted in Tirana only, the sample may not be necessarily representative of all the Albanian women. Assessment of rheumatoid arthritis was based on the ACR/EULAR 2010 criteria (15), which is reassuring. However, the information related to lifestyle/behavioral factors of women included in this study may have been biased in the context of a traditional and patriarchal society such as Albania. Notwithstanding this possibility, there is no plausible reason to assume different reporting of behavioral factors in women with and without rheumatoid arthritis.

In conclusion, this study provides useful information about important correlates of rheumatoid arthritis among women attending specialized primary health care services in postcommunist Albania. Health professionals and policymakers in Albania should be aware of the magnitude and consequences of this chronic condition in the adult population.

## References

- 1. Scott DL, Wolfe F, Huizinga TWJ. Rheumatoid arthritis. Lancet 2010;376:1094-108.
- 2. van der Helm-van Mil AHM, Huizinga TWJ. Advances in the genetics of rheumatoid arthritis point to sub-classification into distinct disease subsets. Arthritis Res Ther 2008;10:205.
- 3. van Oosterhout M, Bajema I, Levarht EW, Toes RE, Huizinga TW, van Laar JM. Differences in synovial tissue infiltrates between anti-cyclic citrullinated peptide-positive rheumatoid arthritis and anti-cyclic citrullinated peptide-negative rheumatoid arthritis. Arthritis Rheum 2008;58:53-60.
- 4. Feldmann M, Brennan FM, Maini RN. Rheumatoid arthritis. Cell 1996;85:307-10.
- 5. Choy EH, Isenberg DA, Garrood T, et al. Therapeutic benefit of blocking interleukin-6 activity with an anti-interleukin-6 receptor monoclonal antibody in rheumatoid arthritis: a randomized, double-blind, placebo-controlled, dose-escalation trial. Arthritis Rheum 2002;46:3143-50.
- 6. van der Woude D, Houwing-Duistermaat JJ, Toes RE, et al. Quantitative heritability of anti-citrullinated protein antibody-positive and anti-citrullinated protein antibody-negative rheumatoid arthritis. Arthritis Rheum 2009; 60:916-923.
- 7. Barton A, Worthington J. Genetic susceptibility to rheumatoid arthritis: an emerging picture. Arthritis Rheum 2009; 61:1441-1446.
- 8. Källberg H, Padyukov L, Plenge RM, et al, and the Epidemiological Investigation of Rheumatoid Arthritis (EIRA) study group. Gene-gene and gene-environment interactions involving HLA-DRB1, PTPN22, and smoking in two subsets of rheumatoid arthritis. Am J Hum Genet 2007;80:867-75.
- 9. Carlens C, Hergens MP, Grunewald J, et al. Smoking, use of moist snuff, and risk of chronic inflammatory diseases. Am J Respir Crit Care Med 2010;181:1217-22.
- Charbonnier LM, Han WG, Quentin J, et al. Adoptive transfer of IL-10-secreting CD4(+)CD49b(+) regulatory T cells suppresses ongoing arthritis. J Autoimmun 2010;34:390-99.
- 11. Pedersen JK, Kjaer NK, Svendsen AJ, Hørslev-Petersen K. Incidence of rheumatoid arthritis from 1995 to 2001: impact of ascertainment from multiple sources. Rheumatol Int 2009;29:411-5.
- 12. Costenbader KH, Chang SC, Laden F, Puett R, Karlson EW. Geographic variation in rheumatoid arthritis incidence among women in the United States. Arch Intern Med 2008;168:1664-70.
- 13. Kalla AA, Tikly M. Rheumatoid arthritis in the developing world. Best Pract Res Clin Rheumatol 2003;17:863-75.
- 14. Albanian Institute of Public Health. National health report: Health status of the Albanian population. Tirana, Albania; 2014. http://www.ishp.gov.al/wpcontent/uploads/2015/01/Health-report-English-version.pdf (accessed: March 10, 2016).
- 15. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO 3<sup>rd</sup>, et al. 2010 Rheumatoid arthritis classification criteria: an American College of

Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum 2010;62:2569- 81.

16. Liao KP, Alfredsson L, Karlson EW. Environmental influences on risk for rheumatoid arthritis. Curr Opin Rheumatol 2009;21:279-83.

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