Prevalence and Risk Factors of the Rheumatoid Arthritis in Herzegovina Region in 2003–2005

Vesna Damjanović[1], Ivan Vasilj[1], Tonko Vlak[2] and Diana Zelenika[3]

[1] School of Medicine, University of Mostar, Mostar, Bosnia and Herzegovina
[2] Institute of Rehabilitation, University Hospital Center Split, Split, Croatia
[3] Department of Internal Medicine, University Clinical Hospital Mostar, Mostar, Bosnia and Herzegovina

A B S T R A C T

In this study we evidenced prevalence of the rheumatoid arthritis (RA) in Herzegovina region of the Bosnia and Herzegovina and studied selected RA risk factors. Sample of subjects comprised RA diagnosed subjects which were compared to randomly selected controls. In diagnosing the RA we used criteria for the classification of rheumatoid arthritis suggested by The American College of Rheumatology. Risk factors of RA included in this investigation were (1) educational status, (2) quality of nutrition, and (3) socioeconomic status. Average prevalence of the RA in our sample was 0.46/100, ranged from 0.36/100 to 0.64/100, which is comparable to other European samples. The RA occurrence is six times more often in females than in males. We have found indices that the Mediterranean diet has to be considered as protective factor against RA. Although RA occurrence is more frequent in the low socioeconomic samples of subjects, because of the methodological reasons we can not undoubtedly support the socioeconomic status as significant risk factor of the RA. Finally, it is interesting that we have found education level as risk factor significantly related to RA occurrence in our sample. All evidenced should be more precisely studied in some future study, while accurately controlling all relevant factors.

Key words: non-inflammatory rheumatic disorders, rheumatoid arthritis, education, nutrition, socioeconomic status

Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disease which is characterized by chronic inflammation of the joints resulting in joint destruction. Patients experience chronic pain and suffering, impairment of function, and increasing disability, and without treatment there is a reduction in life expectancy[1–3]. The availability of effective previous therapies makes it imperative to identify patients early so that control of inflammation can prevent joint destruction and disability.

Prevalence data for RA are now becoming available for many of the developing countries around the world, and prevalence rate of 0.4–1% could be estimated, and taking into account a female/male ratio of 8:1. National societies in many parts of the world are engaged in gathering information on the burden of RA and developing management strategies in the context of their own local conditions[4,5]. The prevalence of RA is estimated to be about 1% in most European populations, with a lower prevalence reported for people of Asian and African ancestry. However, recent figures from Spain and France show that the prevalence is now estimated at around 0.5%[6].

Access to basic health-care services are a problem in many developing countries, due to a shortage of finance, physical infrastructure, shortage of skilled nurses and medical professionals, and lack of an adequate number of rheumatologists to meet the needs of the communities[7–10]. Thus many of the patients in developing countries, such as Bosnia and Herzegovina, are unable to receive appropriate medical care, and RA is either unrecognized or inadequately treated[9]. Disease-related costs are also a major challenge in the management of RA in all developing countries, particularly in the context of limited health-care resources. Since RA affects the economically active population, early intervention can reduce both suffering and the economic burden to society[4].

It is still relatively unknown what causes the process that leads to RA. It's likely that RA occurs as a result of a

complex combination of factors, such as genetics, but also lifestyle factors (nutrition, smoking, overweight, etc.). RA is strongly associated with the inherited tissue type Major histocompatibility complex (MHC) antigen HLA-DR4 (most specifically DR0401 and 0404) – hence family history is an important risk factor[11–13]. Consequently, studies dealing with the risk factors which could probably lead to definition of the characteristic predictors of the RA are highly welcomed.

We have found no recent study where epidemiological data of RA and eventual risk factors are evidenced in the population sampled in Bosnia and Herzegovina. The aims of the present study were: (1) to establish the true prevalence of the RA in Herzegovina (part of the Federation Bosnia and Herzegovina), during the period 2003–2005, and (2) to study some of the selected risk factors in RA diagnosis.

Materials and Methods

Sample of subjects comprised two groups: RA diagnosed subjects (see latter text for details), and randomly selected comparable Controls (N=300). The sampling was performed by random selection using the EPI statistical software in the population of western Herzegovina, region of the Republic of Bosnia and Herzegovina. Briefly, in each of the included municipality (Mostar, Stolac, Široki Brijeg, Grude) we sampled subjects from one rural and one urban community, proportionally to number of residents. As a result, we defined sample consisted of 28715 residents of Mostar; 10363 residents of Široki Brijeg; 4933 residents of Stolac, and 6676 residents of Grude.

In diagnosing the RA we used criteria for the classification of rheumatoid arthritis suggested by The American College of Rheumatology[14]: (1) Morning stiffness of >1 hour most mornings for at least 6 weeks; (2) Arthritis and soft-tissue swelling of >3 of 14 joints/joint groups, present for at least 6 weeks; (3) Arthritis of hand joints,

present for at least 6 weeks; (4) Symmetric arthritis, present for at least 6 weeks; (5) Subcutaneous nodules in specific places; (6) Rheumatoid factor at a level above the 95th percentile; (7) Radiological changes suggestive of joint erosion. At least four criteria had to be met for classification as RA.

Risk factors of RA observed in this study were as follows: (1) Educational status (subjects were classified in five groups: No education, Elementary school, High school, Undergraduate, Graduate); (2) Quality of Nutritional Status (two groups of nutrition quality: Good Quality, Poor Quality); and (3) Socioeconomic status (three groups: Low – less than 100 USD monthly *per* family capita; Medium – from 100 to 150 USD; Fair – more than 150 USD). All risk status factors were interviewed at the beginning during the medical intervention program. Nutritional status was tested by means of standard nutritional questionnaire, evidencing the consumption of the Mediterranean diet, mainly related to consumption of the unsaturated and saturated fats (fish, olive oil, fat, etc.), fruit and vegetables, vitamin C and E (for details see Martínez-González et al.[15]; Agudo and Pera[16])

Data were interpreted as counts and proportions (N, %). In defining relations between the observed risk factors and RA occurrence, chi-square test was applied. Coefficients considered significant at $p < 0.05$ (95%).

Results

Average prevalence of the RA in our sample was 0.46/100, ranged from 0.36/100 to 0.64/100 which is similar to prevalence reported for Spain and France[6]. RA occurrence was more frequent in females than in males. According to our results RA affects women six times more often than men. It is evidently higher occurrence in females than previously suggested ratio of three vs. one in the USA[17] and more comparable to ratio of 8:1 presented for Latin America[4].

When observed separately for each age of the study duration, we have found significant differences between RA and Controls in education level (Table 2). However,

TABLE 1

DIAGNOSTIC CRITERIA OF THE RA IN THE PERIOD 2003–2005, SEPARATELY IN MALES (M) AND FEMALES (F)

Diagnostic criteria	2003				2004				2005			
	Evident		Non evident		Evident		Non evident		Evident		Non evident	
	M	F	M	F	M	F	M	F	M	F	M	F
Morning stiffness	10	63	0	0	9	61	0	0	8	69	1	0
Arthritis and soft-tissue swelling of >3 of 14 joints/joint groups	8	62	2	1	8	5	1	2	8	69	1	0
Arthritis of hand joints	10	63	0	0	7	61	2	0	8	67	1	2
Symmetric arthritis	9	60	1	3	7	60	2	1	6	67	3	2
Subcutaneous nodules in specific places	3	16	7	47	2	14	7	47	5	30	4	39
Rheumatoid factor at a level above the 95th percentile	8	49	2	14	7	4	2	13	8	68	1	1
Radiological changes suggestive of joint erosion	8	60	2	3	8	60	1	1	6	67	3	2

TABLE 2
EDUCATION LEVEL AND RHEUMATOID ARTHRITIS PREVALENCE (CHI-SQUARE SIGNIFICANCE – DIFFERENCES BETWEEN RHEU-MATIC AND CONTROL SAMPLE)

	2003		2004		2005		2003–2005		Control	
	N	%	N	%	N	%	N	%	N	%
No education	15	20.54	22	31.43	20	25.64	57	24.89	104	34.69
Elementary school	35	47.94	28	40.00	5	6.45	68	29.69	75	25.14
High school	21	28.76	20	28.57	38	48.71	79	34.50	101	33.55
Undergraduate	2	2.73	0	0.00	5	6.45	7	3.06	9	2.84
Graduate	0	0	0	0.00	10	12.82	10	4.37	11	3.78
Total	73	100	70	100	78	100	221	48.25	300	100
χ^2 (p)	<0.001		<0.001		<0.001		0.44			

this difference was not significant (p=0.44) when the RA sample in total (2003–2005) was compared to the Controls. When comparing the nutrition status between RA and C, we have found significant influence of the nutritional quality on RA prevalence (Table 3). Only one RA subsample (2003) was found as significantly different from Controls in the socioeconomic status (Table 4).

Discussion and Conclusions

One of the aims of this study was to explore some specific variables in prevalence of the RA. The idea was to select those variables related to the fact that the Bosnia and Herzegovina, where the investigation was performed, is developing country. Previous studies noted that

the access to basic health-care services are a problem in many developing countries due to a shortage of finance, physical infrastructure, shortage of skilled nurses and medical professionals, and lack of an adequate number of rheumatologists to meet the needs of the communities[18,19]. Thus many of the patients in developing countries are unable to receive appropriate medical care, and RA is either unrecognized or inadequately treated. Even when RA is suspected or diagnosed, factors such as cultural beliefs, lack of education and insight, and use of complementary therapies further delay the initiation of disease-modifying therapy[20]. Elementary, the idea of the influence of the education level on prevalence of the RA (see for example Moddy et al.[4]) is supported in our study too, since it is evident that there is considerable larger

TABLE 3
NUTRITION QUALITY AND RHEUMATOID ARTHRITIS PREVALENCE (CHI-SQUARE SIGNIFICANCE – DIFFERENCES BETWEEN RHEUMATIC AND CONTROL SAMPLE)

	2003		2004		2005		2003–2005		Control	
Nutrition quality	N	%	N	%	N	%	N	%	N	%
Good quality	24	32.88	20	28.57	21	26.92	65	29.41	130	43.33
Poor quality	49	67.12	50	71.43	57	73.08	156	70.59	170	56.67
Total	73	100	70	100	78	100	221	100	300	100
χ^2	0,04		<0,001		<0,001		0,01			

TABLE 4
SOCIOECONOMIC STATUS AND RHEUMATOID ARTHRITIS PREVALENCE (CHI-SQUARE SIGNIFICANCE – DIFFERENCES BETWEEN RHEUMATIC AND CONTROL SAMPLE)

	2003		2004		2005		2003–2005		Control	
Socioeconomic status	N	%	N	%	N	%	N	%	N	%
Low (<100)	15	20.55	18	25.71	28	35.90	61	27.60	90	30.02
Medium (100 – 150)	47	64.38	41	58.57	43	55.13	131	59.28	179	59.66
Fair (> 150)	11	15.07	11	15.71	7	8.97	29	13.12	31	10.32
Total	73	100	70	100	78	100	221	100	300	100
χ^2	0.05		0.18		0.43		0.62			

Note: Socioeconomic status is presented in USD monthly per family capita

prevalence of the RA in lower education subsamples, and the occurrence of the RA is considerably lower in subjects of the higher education level. In the recent Swedish study[21] authors brought similar conclusion mainly related to the fact that the education level was negatively related to the RA occurrence. The comparable findings were noted in the studies performed on the Mexican population[22], and Eastern European transition economies[23]. But, when we compare data we noted in our results and data from other studies we previously noted briefly, we have to emphasize that investigations we referenced at[21–23] did not compare the education levels between RA and Control samples as we did herein, but simply established the differences in RA occurrence between different education level subgroups. Therefore, we are of the opinion that in future studies the influence of the education level has to be even more specifically and precisely studied in the relation to the RA. It mainly relates to the fact that all relevant factors should be controlled (age, sex, risk factors), and appropriate multivariate methods should be used.

Since in this investigation we considered »Mediterranean nutrition« as good quality of nutrition we were not surprised by the fact that we found evident difference between Controls and RA, and significant influence of the nutrition quality on the RA prevalence (more than two thirds of the RA patients do not consume Mediterranean nutrition, but consume high proportion of the saturated fats). Moreover, when we compared RA and Control sample in their quality of the nutrition, we have found significant differences also. Evidently, Controls are more leaned toward Mediterranean nutrition than RA sample (chi-square is significant). It is generally accepted that Mediterranean diet intervention should be considered as effective in RA treatments[24–26] put special attention to nutritional status, mainly polyunsaturated fish oils, in RA prevalence and interventions. The beneficial properties of fish oil are well known and are related to its fatty acid composition rich in omega-3 polyunsaturated fatty acids. In the last years a variety of epidemiological and clinical studies have demonstrated the efficacy of fish oil supplementation in the rheumatic diseases, in particular in rheumatoid arthritis. The anti-inflammatory effects of fish oil are linked to the production of alternative eicosanoids, to the reduction of proinflammatory cytokines, to the inhibition of the activation of T lymphocytes and of catabolic enzymes. Hansen et al.[27] studied the nutritional status of Danish RA patients and addressed the question of whether or not RA can be directly influenced by dietary manipulation (by means of Mediterranean diet). In this prospective, single-blinded study of 6 months duration, 109 patients with active RA were randomly assigned to either treatment with or without a specialized diet. Study has found significant improvements in the RA status as a result of the intervention diet program. Although in our study we did not carried out the follow-up study with the intervention program, data we have presented strongly support the need for the diet and nutrition control in the RA patients. It is mainly related to the need of increasing the consumption of the polyunsaturated oils and antioxidants. Off course, we must note that the region where the sample of subjects is drawn from have to be considered as culturally leaned toward Mediterranean diet because of the geographical position (because of the geographical position Herzegovina is the only Mediterranean region of the Bosnia and Herzegovina). Therefore, we can hypothesize that the positive influence of the proper nutrition on the RA status is even more obvious in the samples that are not so familiar with Mediterranean diet (e.g. other samples from the Bosnia and Herzegovina).

Socioeconomic status (SES) is regularly studied in relation to RA prevalence and occurrence[28–31]. In the study of Bengtsson et al.[31] authors found association between high SES and lower risk of RA in a population based investigation that was representative for the Swedish population. The study shows that as yet unexplained environmental or lifestyle factors, or both, influence the risk of RA, even in the relatively egalitarian Swedish society. But, contrary to these findings, investigation performed in England[30] examined role of socioeconomic factors in susceptibility to RA. In conclusion, SES variables examined did not explain susceptibility patterns in the population studied. However, it is evident lack of studies examining the influence of the SES on the RA incidence in developing countries. Off course, there is no doubt that incidence of the RA is more frequent in countries with the comparably lower SES[4] but the question which arises is, whether the SES of the residents within the developing countries influences the RA prevalence? As presented in our results, prevalence of RA is evidently lower in subjects of higher SES (13.12% in average). But, this data can not be considered as very indicative, mainly because they are saturated with the current general SES in Bosnia and Herzegovina. Briefly, it is not hard to assume that the percentage of the RA in each socioeconomic group we have observed (low-medium-good) will fluctuate as a result of the percentage of each socioeconomic group in whole population. Consequently, we had to compare the SES of RA patients with SES of adequate Controls. In doing so we have found only one significant difference between RA and Controls, noting relatively poor influence of the SES on the RA occurrence within the Bosnia and Herzegovina. However, there are certain indices that the RA occurrence is more often in the subjects of the low SES, and it has to more accurately studied in some future investigation. In explaining relatively low influence of the SES on the RA we have found one explanation as most intriguing. In previous investigations not exclusively related to RA, authors frequently found Mediterranean diet as more frequent in higher SES[32–34]. Most probably, nutritional status we have previously discussed as potential predictor of the RA is not strongly related to SES in the sample of subjects we have studied herein. This is mainly linked to high availability and tradition in consumption of the Mediterranean food (olive oil and fish mostly) in the Herzegovina region, where we performed our investigation.

REFERENCES

1. SMOLJANOVIĆ T, GRGUREVIĆ L, JELIĆ M, KRESZINGER M, HASPL M, MATIČIĆ D, VUKIČEVIĆ S, PEĆINA M, Coll Antropol, 31 (2007) 923. — 2. RAVLIĆ-GULAN J, GULAN G, NOVAK S, DULE-TIĆ-NAČINOVIĆ A, MATOVINOVIĆ D, RUKAVINA D, Coll Antropol, 29 (2005) 661. — 3. PERIĆ S, CEROVSKI B, PERIĆ P, Coll Antropol, 25 (2001) 67. — 4. MODY GM, CARDIEL MH, Best Pract Res Clin Rheumatol, 22 (2008) 621. — 5. WOOLF AD, BROOKS P, AKESSON K, MODY GM, Best Pract Res Clin Rheumatol, 22 (2008) 759. — 6. ABDEL-NASSER AM, RASKER JJ, VALKENBURG HA, Semin Arthritis Rheum, 27 (1997) 123. — 7. MOOLENBURGH JD, MOORE S, VALKENBURG HA, ERASMUS MG, Ann Rheum Dis, 43 (1984) 40. — 8. BEIGHTON P, SOLOMON L, VALKENBURG HA, Ann Rheum Dis, 34 (1975) 136. — 9. MARTELL RW, STEIN M, DAVIS P, WEST G, EMMANUEL J, DU TOIT ED, Tissue Antigens, 36 (1990) 125. — 10. CADENA J, VINACCIA S, PÉREZ A, RICO MI, HINOJOSA R, ANAYA JM, J Clin Rheumatol, 9 (2003) 142. — 11. WESTHOFF G, RAU R, ZINK A, Arthritis Rheum, 56 (2007) 3575. — 12. VAN LIEROP MJ, DEN HOED L, HOUBIERS J, VENCOV-SKY J, RUZICKOVA S, KRYSTUFKOVA O, VAN SCHAARDENBURG M, VAN DEN HOOGEN F, VANDOOREN B, BAETEN D, DE KEYSER F, SØNDERSTRUP G, BOS E, BOOTS AM, Arthritis Rheum, 56 (2007) 2150. — 13. EMERY P, GABAY C, KRAAN M, GOMEZ-REINO J, Rheumatol Int, 27 (2007) 793. — 14. ARNETT FC, EDWORTHY SM, BLOCH DA, MCSHANE DJ, FRIES JF, COOPER NS, HEALEY LA, KAPLAN SR, LIANG MH, LUTHRA HS, MEDSGER JR, MITCHELL DM, NEUSTADT DH, PINALS RS, SCHALLER JG, SHARP JT, WILDER RL, HUNDER GG, Arthritis Rheum, 31 (1988) 315. — 15. MARTI´NEZ-GONZA´LEZ MA, PE´REZ-GUTIE´RREZ R, MARTI´NEZ-GONZA´LEZ J, GARCI´A-MARTI´N M, BUENO-CAVANILLAS A, Eur J Public Health, 7 (1997) 40. — 16. AGUDO A, PERA G, Public Health Nutr, 2 (1999) 263. — 17. ALAMANOS Y, VOULGARI PV, DROSOS AA, Semin Arthritis Rheum, 36 (2006) 182. — 18. SPINDLER A, BELLOMIO V, BERMAN A, LUCERO E, BAIGORRIA M, PAZ S, GARRONE N, TORRES AI, ROMANO O, CARRACCIO A, LEAL O, BAZZANO A, VAZQUEZ D, PERA O, ARQUEZ G, VALDEZ M, LAZARO H, RENGEL S, ACOSTA E, SANTANA M, J Rheumatol, 29 (2002) 1166. — 19. MODY GM, HAMMOND MG, NAIDOO PD, J Rheumatol, 16 (1989) 1326. — 20. ADEBAJO AO, REID DM, Q J Med, 80 (1991) 633. — 21. LI X, SUNDQUIST J, SUNDQUIST K, J Rheumatol, 35 (2008) 986. — 22. MORALES-ROMERO J, GONZALEZ-LOPEZ L, CELIS A, RODRIGUEZ-ARREOLA BE, CABRERA-PIVARAL CE, GAMEZ-NAVA JI, J Rheumatol, 33 (2006) 1247. — 23. HELASOJA V, LAHELMA E, PRÄTTÄLÄ R, KASMEL A, KLUMBIENE J, PUDULE I, Eur J Public Health, 16 (2006) 8. — 24. KJELDSEN-KRAGH J, Ann Rheum Dis, 62 (2003) 193. — 25. SALES C, OLIVIERO F, SPINELLA P, Reumatismo, 60 (2008) 174. — 26. SALES C, OLIVIERO F, SPINELLA P, Reumatismo, 60 (2008) 95. — 27. HANSEN GV, NIELSEN L, KLUGER E, THYSEN M, EMMERTSEN H, STENGAARD-PEDERSEN K, HANSEN EL, UNGER B, ANDERSEN PW, Scand J Rheumatol, 25 (1996) 325. — 28. PEDERSEN M, JACOBSEN S, KLARLUND M, FRISCH M, J Rheumatol, 33 (2006) 1069. — 29.YOUNG A, WILKINSON P, TALAMO J, DIXEY J, JONES R, HUNT A, COX N, DAVIES P, DEVLIN J, EMERY P, GOUGH A, JAMES D, PROUSE P, WILLIAMS P,WINFIELD J, Ann Rheum Dis, 59 (2000) 794. — 30. BANKHEAD C, SILMAN A, BARRETT B, SCOTT D, SYMMONS D, J Rheumatol, 23 (1996) 2039. — 31. BENGTSSON C, NORDMARK B, KLARESKOG L, LUNDBERG I, ALFREDSSON L; EIRA Study Group, Ann Rheum Dis, 64 (2005) 1588. — 32.TUR JA, PUIG MS, BENITO E, PONS A, Nutrition, 20 (2004) 502. — 33. SCALI J, SIARI S, GROSCLAUDE P, GERBER M, Public Health Nutr, 7 (2004) 513. — 34. SCHRÖDER H, ROHLFS I, SCHMELZ EM, MARRUGAT J, REGICOR INVESTIGATORS, Eur J Nutr, 43 (2004) 77.

V. Damjanović

School of Medicine, University of Mostar, Bijeli brijeg bb, 88000 Mostar, Bosnia and Herzegovina
e-mail: vesnamd@gmail.com

PREVALENCIJA I ČIMBENICI RIZIKA ZA POJAVU REUMATOIDNOG ARTRITISA U PODRUČJU HERCEGOVINE TIJEKOM 2003–2005. GODINE

SAŽETAK

Cilj ovog istraživanja bio je ustanoviti prevalenciju reumatoidnog artritisa (RA) u području Hercegovine te istražiti rizične čimbenike povezane s njegovim nastankom. Uzorak za istraživanje sastojao se od slučajeva i slučajnim odabirom prikupljenih kontrola. U dijagnozi RA korišteni su klasifikacijski kriteriji koje je izradilo Američko udruženje reumatologa (The American College of Rheumatology). Rizični čimbenici uključivali su obrazovni status, kvalitetu prehrane i socioekonomski status. Prosječna prevalencija u uzorku bila je 0,46/100, varirala je od 0,36–0,64/100, što je usporedivo s ostatkom Europe. Slučajevi kod žena bili su šest puta češći nego kod muškaraca. Nismo pronašli dokaza o protektivnom učinku mediteranskog tipa prehrane na pojavnost RA. Iako je RA bio češći kod osoba nižeg socioekonomskog statusa, zbog metodoloških razloga ne možemo jednoznačno potvrditi ovu povezanost. Razina obrazovanja bila je značajan čimbenik rizika za pojavu RA. Dobiveni rezultati zahtijevaju daljnja istraživanja.