The Impact of Smoking on Rheumatoid Arthritis Activity

S. Sokolovic*, A. Kasumagic and S. Kasumagic

Heart and Rheumaticm Clinic, University Clinical Center, Sarajevo, Bosnia and Herzegovina

Abstract: *Introduction*: The Rheumatoid arthritis (RA) is a chronic, inflammatory, systemic disease that is usually the most evident and commonly manifested on diarthrosis joints. The initial etiological factors that trigger the immune-inflammatory response still remains unknown. RA is result of the simultaneous influence of genetic risk factors, external factors and changes in immune system.

Objective: The goal of this study was to determine the mutual correlation between smoking and RA activities expressed by the quantitative values of laboratory and disease activity parameters.

Material and Method: The open clinical retrospective study included 100 RA patients stages from I to IV aged from 21 to 77 ys. There were 85 (85%) females and 15 (15%) males selected by randomization. The study analysed: age, gender, smoking, duration of smoking, sedimentation rate (ESR), rheumatoid factor (RF), C-Reactive Protein (CRP) anti-cyclic citrullinated peptide (anti-CCP) antibodies and X-ray. Statistical analyses was done with SPSS software, Student's t-test and chi-square test.

Results: The quantitative values of laboratory parameters are directly related with the smoking period. All inflammatory markers were increased in both groups, but more elevated in smoker's group. The only statistical significance was found in anti-CCP where this test was significantly higher compared to non-smokers. There was no statistical significance in the onset of disease, gender, ESR, CRP, RF, and radiological changes between two groups, although smokers had some more higher values.

Conclusion: Smoking plays significant role in RA activity and leads to longer duration of symptoms and increased disability. All inflammatory markers were increased in both groups, but more elevated in smoker's group, with the only significancy in anti-CCP level. The cessation of smoking should be part of disease management proccess.

Keywords: RA, Smoking, DAS28, RF, CRP.

INTRODUCTION

Rheumatoid arthritis (RA) is chronic autoimmune systemic inflammatory disease affecting mostly diarthrotic joints. The most common clinical manifestation is polyarticular, persistent, symetric and progressive synovitis leading to irreversible anatomıc damages and disability [1]. The etiology is still unknown, although numerous environmental and genetic factors influence the onset of disease. Prevalence of RA vary from 0,5 – 1,0%, with average of 0,8%. Females predominate 2-3 more frequently than in males [1]. Cigarette smoking is the second major cause of mortality in the world. Also passive smoking has also affect on morbidity and mortality rate. There are about 4 000 chemicals in a single smoke with 400 poisoned and 43 cancerogenic respectively. Many disorders are linked to tobacco smoking as well as cardiovacular, lung and different cancer disease. Nicotine causes endotel dysfunction with production of free radicals which stimulate oxidative stress and onset of acute phase reactants like C-reactive protein, fibrinogen, inflammatory cytokines etc. The immune defense constantly “clean” the body from those chemicals but this cause the vaste of immunity cells leading to decreased natural immunity. This state may provoke the onset of many diseases, including autoimmune ones. It has been observed that smokers who suffer from rheumatoid arthritis have more aggressive and evolutive disease. Definitely, RA smokers suffer more from the systemic complications including cardiovascular and cerebrovascular diseases yhank non-smokers.

The aim of this study was to determine the impact of smoking and RA activities.

MATERIAL AND METHOD

The open clinical retrospective study had included a total of 100 patients with definitive RA anatomical stage I to IV, aged from 21 to 77 years. Period of analysis was 3 years, from 2009 until 2012. There were 85 (85%) females and 15 (15%) males. Two groups were formed: Group I smokers and Group II as non-smokers. Sedimentation rate (ESR), rheumatoid factor (RF), C-Reactive Protein (CRP) anti-cyclic citrullinated peptide (anti-CCP) antibodies were analysed. The degree of the disease disability was estimated based on the radiological changes. Smoking status and disease activity parameters were measured in the same time. Analysis of data was performed using the SPSS

*Address correspondence to this author at the Heart and Rheumaticm Clinic, University Clinical Center, Sarajevo, Bosnia and Herzegovina;
E-mail: sekib@bih.net.ba

E-ISSN: 2310-9874/14

Table 1: Age Distribution and Smoking Duration

	Age				Smoking duration/y		p
	Smokers (n=38)		Non-smokers (n=62)		Smokers (n=38)		
Years	52,3±10,6		53,9±12,8		28±11,5		NS*
	Min.	Max.	Min.	Max.	Min.	Max.	
	32	80	21	77	4	50	

Table 2: Smoker vs Non-Smokers: Gender Distribution

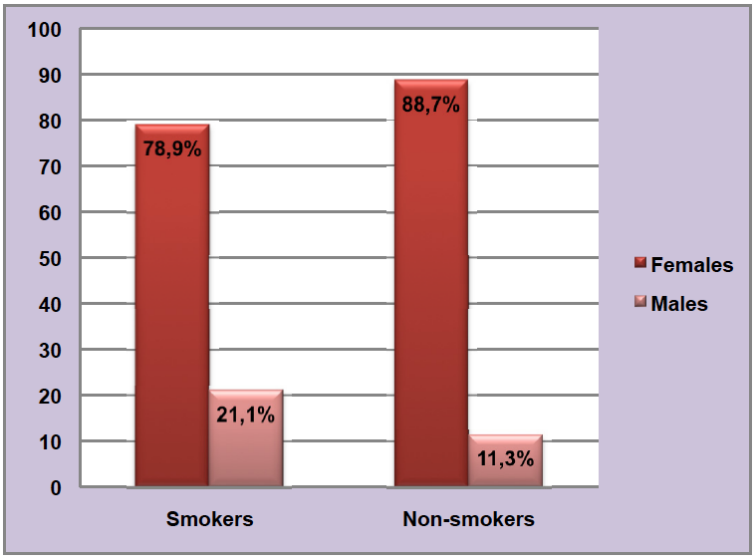


Table 3: ESR Average Values

ESR						
	N	X	SD	SEM	Minimum	Maximum
Smokers	38	33,3200	25,42536	4,12454	5,00	102,00
Non-smokers	62	40,4032	27,61353	3,50692	3,00	118,00
Total	100	37,7116	26,89553	2,68955	3,00	118,00

N: number of subjects, X: mean value of the series, SD: Standard deviation.
SEM: standard error of the mean, No statistical significance in ESR between two groups (p>0,05).

software package with Student's t-test and chi-square test.

RESULTS

There were total 38 RA smokers (38%) with 30 females (78,9%) and 8 males (21,1%). Total number of non-smokers was 62 (62%) with 55 (88,7%) females and 7 (11,3%) males. Average age of smokers was 52,3±10,6 years (minimum 32y and maximum 80y) and they were younger compared to non-smokers with average age of 53,9±12,8 years (minimum 21y and maximum 77y), but without any statistical significance (p= 0,490; p>0,05). Average smoking duration in years was 28±11,5 years (minimum 4 and maximum 50 y). The quantitative values of laboratory parameters are directly related with the smoking period. All inflammatory markers were increased in both groups, but more elevated in smoker's group. The only statistical significance was found in anti-CCP test where average level in smokers was 4,06 compared to non-smokers with 2,81 (p=0,023; p<0,05) There was no statistical significance in the onset of disease, gender, ESR (33,32 vs 40,40 CRP (19,19 vs 18,33), RF (300,77 vs 289,1). Smokers have developed more RA stage III, while non-smokers have developed more RA II stage based on X-ray (p>0,05).

Table 4: CRP Average Values

	Group I		vs	Group II		p
	Smokers (n=38)			Non-smokers(n=62)		
CRP mg/L	19,19 ± 24,3			18,33 ± 22,7		NS
	Min.	Max.		Min.	Max.	
	0,80	116		3,08	126	

CRP was higher in smokers (19,2±24,3; 0,8-116) vs non-smokers (18,3±22,7; 3,08-126,0). No statistical significance (p=0,858; p>0,05).

Table 5: RF Average Values

	Group I		vs	Group II		p
	Smokers (n=38)			Non-smokers (n=62)		
RF IU/mL	300,77±689,4			289,1±746,6		NS
	Min.	Max.		Min.	Max.	
	3,50	2510,00		2,5	5390,00	

Rheumatoid factor was more elevated in smokers than in non-smokers, but without statistical significance. RF (300,77±689,4; 3,5-2510,0) vs (289,1±746,6; 2,50-5390,0) (p=0,457; p>0,05).

Table 6: Anti-CCP Average Values

	Group I		vs	Group II		p
	Smokers (n=38)			Non-smokers (n=62)		
anti-CCP IU/mL	4,06 ± 2,7			2,81 ± 2,6		<0,05
	Min.	Max.		Min.	Max.	
	0,33	8,11		0,30	7,80	

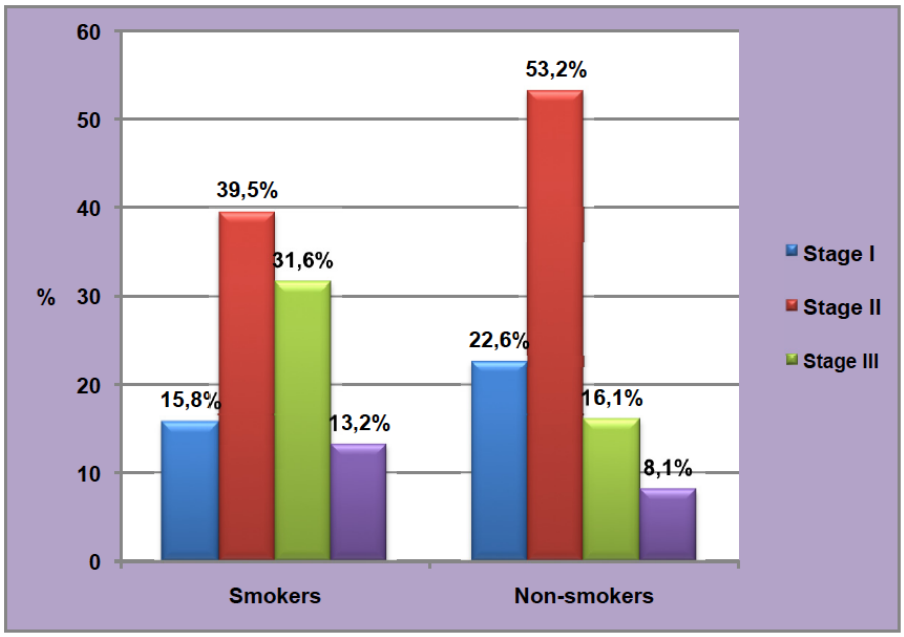
There is statistical significance in anti-CCP antibodies betwen two groups (p=0,023; p<0,05).

DISCUSSION

Our study indicated that smoking is associated with increased risk of higher disease activity in RA patients, with its statistically significancy in anti-CCP level. Also the slighty higher disease activity was seen in RA smokers, but without statistical singificancy in Se, CRP and RF. These results reflect the findings of other previous studies allowing for some slight difference among them. Nicotine increases RF and lymphocytes in RA. Although the interstitial disease in RA is linked to cigarette smoking, the impact of smoking on RA is still unproven. (2). Smokers are more common RF positive than non-smokers. The quantitative level of RF is higher than in non-smokers. Increasing RF levels are in correlation with a longer period of smoking (3). There is a correlation between smoking and X-ray changes. The possibility of development of RA is twice higher than in non-smokers. Risk for RA in ex-smokers is lower than in smokers, but it is higher than in individuals who never smoked. (3). Smoking decrease the estrogen level, thats why devolepment of RA is higher in women. (3). Female who smoke >20years have 39% higher risk to develop RA and 49% seropositive RA (4). ESR raise more in smokers (9.0±2.0) than in non-smokers (4.0±1.0), but without statisticall significance (p>0,05) (5). The CRP is increased in bacterial infections, cystitis, bronchitis, trauma, operations, infarctus myocardii, tuberculosis and sarcoidosis. Smoking increases the CRP (6). RF directly correlate with smoking duration (7). Anti-CCP antibodies in smokers is significantly raised (8). Smoking and HLA–DR gens in RF positive and anti-CCP antibodies are in relationship as well (9). Smoking affect X-ray changes in joints (10). There is a linear correlation between smoking and X-ray changes in RA. Smoking is linked to radiographic changes (11). Anti CCP antibodies are significantly expressed in smokers than in non-smokers. The compliance and treatments of RA smokers is rather difficult than of non-smokers.

Despite the fact that in our study there was no statistical significancy in Se, CRP and RF among two groups, the actual disease RA activity was still higher in

Table 7: RA Stages in Smokers vs Non-Smokers



Stage II of RA was the most common is smokers in 39,5%) as well as in non-smokers in 53,2% and there was no statıstically significance. (p=0,200; p>0,05) Total of 44,8% smokers were in a RA stage III and IV compared with 24,2% non-smokers:

smokers than in RA non-smokers. This slight activity and significant anti-CCP titer had a great impact on the clinical outcome whereas smokers turned into RA stage III from stage II, while RA non-smokers developed mainly RA stage II.

Limitation of this study exist in the rather small number of RA patients. Large size prospective epidemiological study should provide more dispensary data.

CONCLUSION

Our findings showed that 38% of RA patients smoke. Female are 3 times more affected by RA regardless of cigarette smoking. All inflammatory markers were increased in both groups, but more elevated in smoker's group. Cigarette smokers developed RA earlier than smokers, but without significant difference. ESR was increased in RA, but without significant difference between two groups. CRP was increased in RA, but without significant difference between two groups. RF was increased in RA, but without significant difference between two groups. Anti-CCP antibody was increased in both groups with the statistical significance in a smokers compared to non-smokers. Cigarette smokers have developed more RA stage III, while non-smokers have developed more RA stage II based on X-ray.

DISCLOSURES

Sokolovic Sekib: None, Kasumagic Aida: None, Kasumagic Sida: None.

REFERENCES

[1] Stefanovic S. Interna medicina. Medicinska knjiga Beograd 1990; 1406-37.

[2] Kenneth G, Cerhanc J, Kolluric S, Ohashid K, Hunninghakeb G, Schwartzb A. Cigarette smoking and rheumatoid arthritis severity. Ann Rheum Dis 1997; 56: 463-9. http://dx.doi.org/10.1136/ard.56.8.463

[3] Sugiyama D. Impact of smoking as a risk factor for developing rheumatoid arthritis: a meta-analysis of observational studies. Ann Rheum Dis 2010; 69: 70-81. http://dx.doi.org/10.1136/ard.2008.096487

[4] Elizabeth W, Cook N, Manson J, Buring J, Hennekens C. A retrospective cohort study of cigarette smoking and risk of rheumatoid arthritis in female health professionals. Arthritis Rheum 1999; 42: 910-7. http://dx.doi.org/10.1002/1529-0131(199905)42:5<910::AID-ANR9>3.0.CO;2-D

[5] Young B, Gleeson M, Cripps A. C-reactive protein: a critical review. Pathology. Discipline of Pathology. University of Newcastle1991; 36: 1036-44.

[6] Wolfe F. The effect of smoking on clinical, laboratory, and radiographic status in rheumatoid arthritis. J Rheumatol 2000; 27: 630-7.

[7] Klareskog L, Stolt P, Lundberg K, Källberg H, Bengtsson C, Grunewald J. A new model for an etiology of rheumatoid arthritis. Rheumatology Unit. Arthritis Rheum 2006; 54: 38-46. http://dx.doi.org/10.1002/art.21575

[8] Saaga K, Cerhanc J, Kolluric S, Ohashid K, Hunninghakeb G. Cigarette smoking and rheumatoid arthritis severity. Ann Rheum Dis 1997; 56: 463-9. http://dx.doi.org/10.1136/ard.56.8.463

[9] Manfredsdottir F, Vikingsdottir T, Jonsson T. The effects of tobacco smoking and rheumatoid factor seropositivity on disease activity and joint damage in early rheumatoid arthritis. Med Rheumatol 2007; 45: 734-40. http://dx.doi.org/10.1093/rheumatology/kei240

[10] Másdóttir B, Jónsson T, Manfreðsdóttir V, Víkingsson A, Brekkan A, Valdimarsson H. Smoking, rheumatoid factor isotypes and severity of rheumatoid arthritis. Rheumatol Oxford 2000; 39: 1202-5. http://dx.doi.org/10.1093/rheumatology/39.11.1202

[11] Schwedler SB, Filep JG, Galle J, Wanner C, Potempa LA. C-reactive protein: a family of proteins to regulate cardiovascular function. Am J Kidney Dis 2006; 47: 212-22. http://dx.doi.org/10.1053/j.ajkd.2005.10.028

Received on 22-02-2014 Accepted on 19-03-2014 Published on 26-03-2014

DOI: http://dx.doi.org/10.12970/2310-9874.2014.02.01.3