

QUALITY OF LIFE OF PATIENTS WITH RHEUMATOID ARTHRITIS IN BULGARIA

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Abstract. Rheumatoid arthritis (RA) is a chronic, autoimmune, progressive disease which is leading to serious deterioration in patients quality of life (QoL). The goal of this study is to analyze the health related QoL of patients with RA (n=63) in Bulgaria and to evaluate the factors that might influence it. The SF-36 questionnaire was applied for assessment of patients' QoL. The number of the patients on biological treatment has increased with approximately 34% for one year which is the highest expansion in comparison to other treatment regimes. The highest costs are in the group of patients who takes biological drug – 1720.84 BGN and 1523.56 BGN, a year before and at the time of the study, respectively. The average value for QoL for the entire cohort is low – approximately 40 from 100 total scores. Our study confirm that the QoL of patients with RA is not satisfactory. Implementation of the biological therapy could lead to improvement of QoL of the patients, better control of the symptoms and lack of additional medicinal products to relieve the symptoms.

Key Words: Rheumatoid arthritis (RA), quality of life, cost, biologics, biological treatment

Introduction:

Rheumatoid arthritis (RA) is an autoimmune chronic inflammatory disease, which affects joints and surrounding tissues. The treatment is life-long and it is associated with significant consumption of health and economic resources. [1-3]

Health care statistics shows that 0.48% of the Bulgarian population older than 19 years is affected by RA. Approximately 48% of the patients are at the age of 64 or older.[4] 75% of the patients are women and the rest are men.

Several studies conducted from social or health-care perspective explores the cost for treatment of patients with RA as well as quality of life of patients.[5-11] According to the study published by J. Lundkvist et al. the RA total costs to society worth €45.3 billion in Europe and €41.6 billion in the United States.[12]

Published literature review from Cooper (2000) proves the significant economic and social burden of RA and the total average medical costs are reported to be 5720 – 5882 US\$. The share of the indirect costs is also determined.[7] A regression model describes that the odds for high costs increase in case

of greater disability and lower age of the patients.[8]

Infliximab in combination with methotrexate provided clinical benefit, halted the progression of joint damage and improved the health related quality of life (QoL) compared with methotrexate alone.[13] The QoL was increased and the cost-effectiveness ratio of the treatment is in the range of the accepted threshold.[14]

Important role is placed on the education process of RA patients to improve adherence and strengthen the relationship of the patient with the rheumatology team and improvement of their quality of life.[15-17]

The access to biological treatment and the number of prescription of these highly effective treatment options are studied in a Bulgaria from 2011 according to which access to expensive and highly effective treatments with biologic DMARDs is very limited. [18] In addition, studies are necessary to be conducted in order to review the prescription characteristics and practices in our country, as well as their influence on the QoL of the patients.

The goal of this study is to analyze the health related QoL of patients with rheumatoid arthritis in

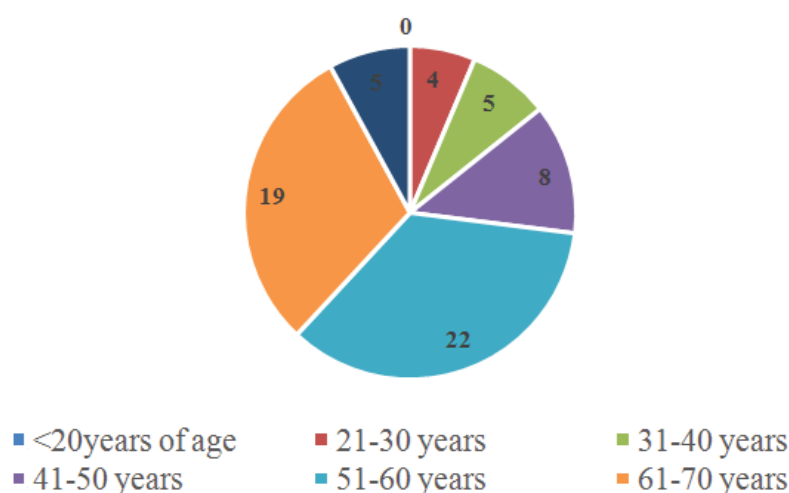


Fig. 1. Distribution of patients in age groups

Bulgaria and to evaluate the factors that might influence it. The age, gender, pharmacotherapy and cost of pharmacotherapy were explored as possible influencing factors.

Materials and methods

Study design

A year study of retrospective phase and prospective follow up was conducted.

Sample size

Rheumatologists recruited patients from all biggest clinical centers in Bulgaria. The Rheumatology Patients' Association (APRA) in Bulgaria supported the process. On total 200 patients were recruited and out of them 63 have filled short form (SF-36) form for assessment of their quality of life. Only patients who agree to participate and who signed the informed consent were included.

Data collection

During the retrospective and prospective phase, information about the demography characteristics of the patients, their pharmacotherapy, frequency of physicians' visits, hospitalizations, and quality of life of patients was collected. Short form for health survey (SF-36) was used for the assessment of the quality of life. The information was collected during patients' routine visit to their rheumatologists. In the retrospective phase, physicians reviewed the previous therapy and prescribe the next one, Additional information was gathered, for some of the patients, via phone call interview. Patients' pharmacotherapy,

past and newly prescribed, was reviewed, and its cost was calculated. Pharmacotherapy cost was calculated based on prices of the medicinal products included in the Positive Drug List, Annex 1.[19]

Statistical analysis

Descriptive statistics were applied towards the data for patients' gender, age, type of therapeutic regimes and quality of life scores. Kruskal-Wallis test, Post-hoc analysis and Mann Whitney tests were applied to evaluate the statistical significance of the relations.

Results and discussions

1. Demography

The total number of patients with RA included in the study is 63 divided as 88.9% (n=56) women and 11.1% (n=7) male. The sample confirms other studies that in the group of the patients with rheumatoid arthritis the number of women prevails. 64% of all included patients are above 50 years old, and the rest are in younger ages. (Figure 1)

2. Pharmacotherapy

The pharmacotherapy includes non-steroid anti-inflammatory drugs (NSAID), corticosteroids and disease modified medicines (DMD). Biological treatment can be prescribed in order to delay deterioration of the disease in combination with methotrexate or other disease-modified drugs. For the purposes of this study biological therapy and distribution of the patients on this treatment are observed and presented separately.

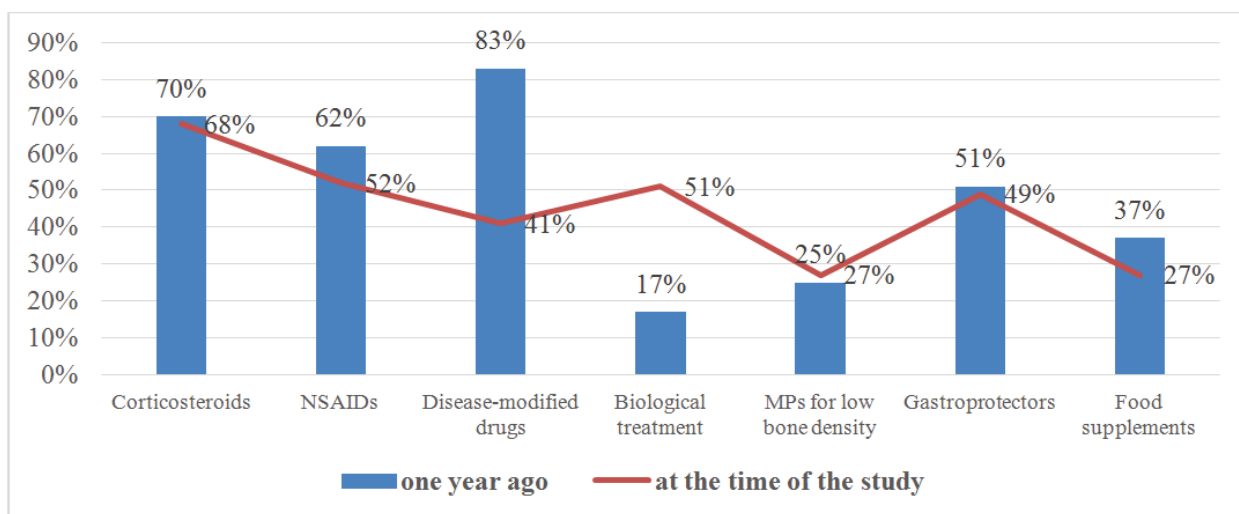


Fig. 2. Distribution of treatment regimens

Distribution of the therapeutic regimens in the past one year and newly prescribed is presented on **Figure 2**.

At the time of the study, more patients received biological treatment (51%) compared to one year ago when the percentage is 17%. The biological INNs prescribed are etanercept, certolizumab, tocilizumab, golimumab, infliximab, adalimumab. Tocilizumab is the most often prescribed modulator of biological response (**Table 1**).

In respect to treatment transition, 36 patients (57%) have not significant change in their treatment regimens: no additional drug or no transition to another drug. Four patients (6%) have switched from NSAIDs or corticosteroids to disease modified drugs, 3 patients (5%) – from NSAIDs or corticosteroids to biological drug, 18 (29%) – from disease modified drugs to biological one (**Figure 3**).

Approximately 70% of patients were on combination therapy without biological drug in the scheme one year ago in comparison to 37% at the time of the study. To the moment of the study more patients are on a treatment with biological drug plus additional medicinal product – 38% in comparison to one year ago (16%).

3. Pharmacotherapy costs

The average monthly pharmacotherapy costs increased fourfold from one year ago -289.53 BGN (SD=582.70) to the moment of the study - 891.94 BGN (SD=880.87). The change in the therapy is associated with switching to biological treatments in more than half of the observed patients. The changes in the average pharmacotherapy cost per age groups is presented on **Table 2**.

Table. 1 Number of patient in different biological treatment before one year and at the time of the study

INN	Number of patients a year before the study	Number of patients at the time of the study
Tocilizumab	5 (7.94%)	12 (19.05%)
Certolizumab	4 (6.35%)	6 (9.52%)
Golimumab	2 (3.17%)	2 (3.17%)
Etanercept	0	6 (9.52%)
Infliximab	0	1 (1.59%)
Adalimumab	0	5 (7.94%)
Total number of patients	11 (17.46%)	32 (50.79%)

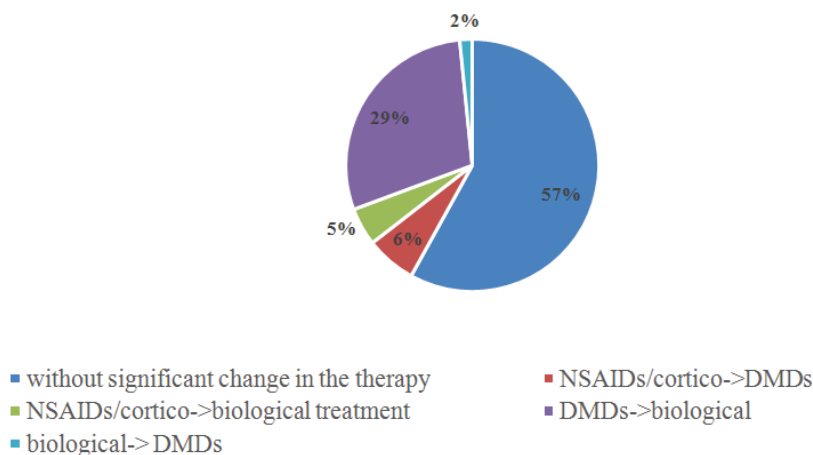


Fig. 3. Percentage of patients switched to another treatment

Table 2. Pharmacotherapy cost per therapeutic group

Treatments scheme	A year before the study			At the time of the study		
	N of patients	Average cost	SD	N of patients	Average costs	SD
Biological treatment +/- other drug	10	1523,56	514,45	32	1720,84	330,62
DMDs	3	13,07	15,27	0		
NSAIDs	2	9,96	10,51	0		
Corticosteroids	2	68,13	62,84	4	15,32	14,05
Combination (no bio)	44	46,64	35,65	23	46,10	34,88

More patients were switched to biological treatment for the period of 1 year (from 10 to 32), while the number of patients on combination therapy without biological drug is decreased (from 44 to 23).

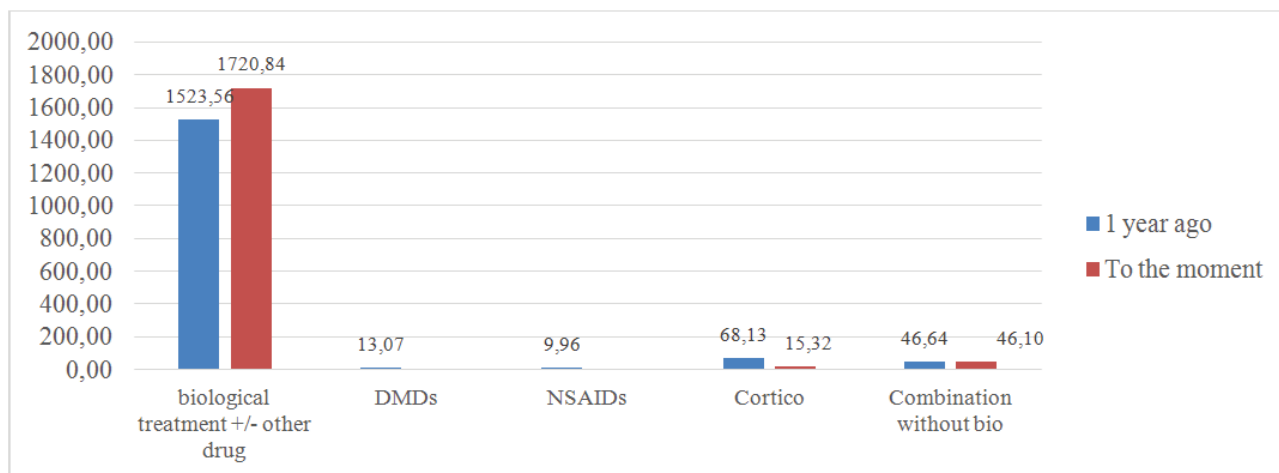
The highest costs are in the group of patients who takes biological medicines – 1720.84 BGN (SD=330.62)

and 1523.56 BGN (SD=514.45), at the time of the study and a year before, respectively (Figure 4).

4. Quality of life of the patients with RA

The average quality of life measured by SF-36 questionnaire for the patients with RA is almost 40

Fig. 4. Average costs for treatment in different therapeutic groups



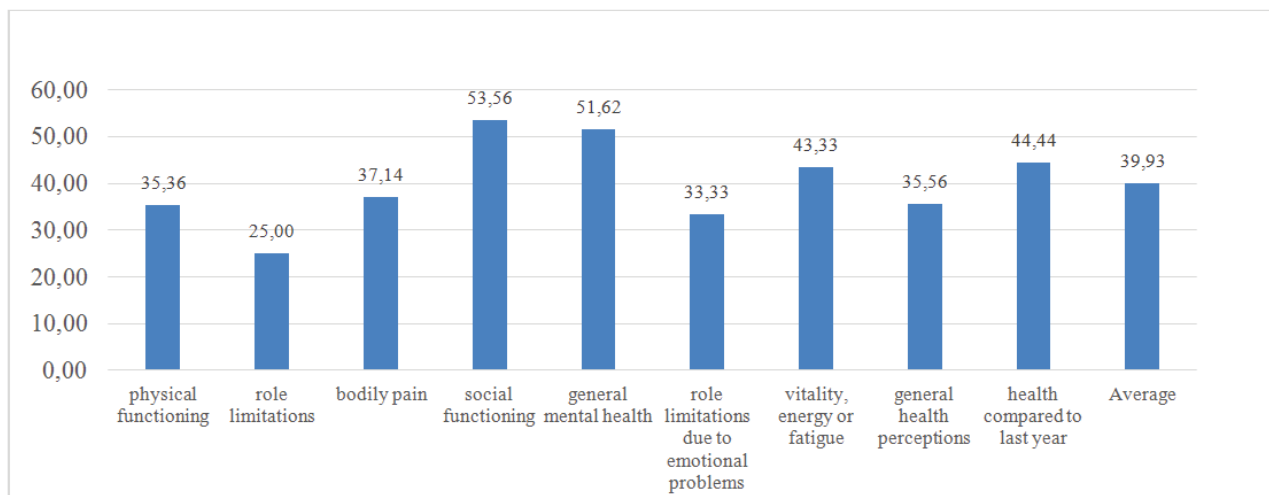


Fig. 5. Values for different scales of SF-36 for the patients with RA

from maximum scores 100. The highest value is for the scale “social functioning” followed by “general mental health” – 53.56 and 51.62, respectively. The lowest value is determined for “role limitations” – 25 (Figure 5).

5. Statistical analysis

The average pharmacotherapy cost, calculated one year ago, is higher in female compared to male group 47.28 BGN and 20.27 BGN ($p=0.042$), respectively (Table 3).

Statistically significant difference is observed between the gender of the patients and treatment costs at the moment of the study as it is shown in Table 4. The costs, calculated during the study, in the male group is higher than in the female group ($p=0.0388$).

Kruskal-Wallis test and Post-hoc analysis define a statistical significant difference in the average values of QoL and the patients in particular age groups. The quality of life of patients in the age group 21-30 years is higher (53.00) than the value for patients' QoL in all age groups over 30 years. The patients between 41 and 50 years have QoL 29.00, followed by 22.32 score for age group 61-70 years, and 29.60 for the age group above 70 years ($p=0.05$). On the opposite, the QoL of patients in the age group 51-60 years is higher (40.86) than the QoL in age groups 41-50 years (23.50) ($p=0.05$).

The youngest patients have the highest quality of life, which could be explained with the early stage of the disease.

The analysis confirms that transition from NSAIDs or corticosteroids to biological treatment is associated

Table 3. Mann Whitney test (independent samples) for the two samples

	Women	Men
Sample size	56	7
Lowest value	2.5300	0.0000
Highest value	1994.6900	46.6500
Median	47.2750	20.2700
95% CI for the median	31.0370 to 74.1794	0.01895 to 46.6339
Interquartile range	21.4650 to 111.5300	12.5950 to 34.6575
Average rank of first group		33.6607
Average rank of second group		18.7143
Large sample test statistic Z		-2.033951
Two-tailed probability		P = 0.0420

Table 4. Mann Whitney test (independent samples) for the two samples

	Women	Men
Sample size	56	7
Lowest value	0.0000	1.9300
Highest value	2023.0100	2049.1200
Median	102.3350	1997.4100
95% CI for the median	46.2393 to 1438.9713	4.2961 to 2049.0818
Interquartile range	27.7250 to 1837.0300	1431.0575 to 2023.8775
Average rank of first group		30.3125
Average rank of second group		45.5000
Large sample test statistic Z		2.066757
Two-tailed probability		P = 0.0388

Table 5. Kruskal-Wallis test and Post-hoc analysis

Test statistic		17.6372	
Corrected for ties Ht		17.6372	
Degrees of Freedom (DF)		5	
Significance level		P = 0.0034	
Factor	n	Average Rank	Different (P<0.05) from factor nr
(1) 2 <u>21-30 years</u>	4	53.00	(2)(3)(5)(6)
(2) 3 <u>31-40 years</u>	5	29.00	(1)
(3) 4 <u>41-50 years</u>	8	23.50	(1)(4)
(4) 5 <u>51-60 years</u>	22	40.86	(3)(5)
(5) 6 <u>61-70 years</u>	19	22.32	(1)(4)
(6) 7 <u>>70 years</u>	5	29.60	(1)

Table 6. Post hoc analysis

Test statistic		28.6900	
Corrected for ties Ht		28.6921	
Degrees of Freedom (DF)		4	
Significance level		P < 0.0001	
Factor	n	Average Rank	Different (P<0.05) from factor nr
(1) 0 no significant change	36	23.42	(3)(4)
(2) 1 NSAIDs/cortico to DMDs	4	17.50	(3)(4)
(3) 2 NSAIDs/cortico to bio	3	44.33	(1)(2)
(4) 3 DMDs to bio	18	49.17	(1)(2)
(5) 4 Bio to DMDs	1	22.00	

with higher direct costs for medicines (44.44 BGN) than to DMDs (17.50 BGN) ($p < 0.0001$) (Table 6).

The QoL score is presented in Table 7. There are statistical significant differences in average values for quality of life for the different treatment regimens.

The quality of life score for patients treated with biological medicines is lower than in case of treatment with NSAIDs. It's the same for QoL of patients on combination therapy (biological + another) in comparison to NSAIDs and higher than combination without biological. The average value for QoL in the

Table 7. Descriptive statistics

Factor	n	Minimum	25th percentile	Median	75th percentile	Maximum
1 biological drug	8	11,2200	22,950	42,140	63,160	71,730
2 bio + additional drug	24	20,0700	31,435	39,115	53,160	77,550
5 NSAIDs	2	71,6900	71,690	77,370	83,050	83,050
6 Cortico	4	33,2500	39,920	47,215	55,580	63,320
7 combination without bio	23	9,4400	19,430	32,110	41,367	66,420

Table 8. Test statistics

Test statistic		11,1526	
Corrected for ties Ht		11,1526	
Degrees of Freedom (DF)		4	
Significance level		p = 0,024901	
Factor	n	Average Rank	Different (p<0,05) from factor nr
(1) 1	8	31,62	(3)
(2) 2	24	34,50	(3)(5)
(3) 5	2	59,00	(1)(2)(5)
(4) 6	4	39,25	
(5) 7	23	23,26	(2)(3)

group on NSAIDs is higher than combination without another drug (**Table 8**).

The treatment with combinations, which do not include biological drugs is associated with lower values for quality of life which could be explained with insufficient control of the symptoms. Inclusion of biological treatment is associated with higher quality of life scores probably due to the better control of the disease.

Conclusions

Our study confirm that the QoL of patients with RA is not satisfactory. Implementation of the biological therapy could lead to improvement of quality of life of the patients, better control of the symptoms and lack of additional medicinal products to relieve the symptoms.

Reallocation of resources in the budget of the health insurance fund should be done in order to provide biological medicines for the patients. The delay of inclusion of biological treatment in the therapeutic regimes could bring additional complications and additional costs in the future.

Further analysis is necessary on the relation of pharmacotherapy with clinical results of the patients.

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