

S.V. Shevchuk^{1,2} , O.V. Zviahina¹ , O.S. Zviahin³ , Y.O. Bezsmertnyi^{1,2} , I.S. Segeda^{1,2} ¹National Pirogov Memorial Medical University, Vinnytsya, Ukraine²Scientific and Research Institute of Invalid Rehabilitation (educational scientific treatment complex) of National Pirogov Memorial Medical University, Vinnytsya, Ukraine³Vinnitsia National Technical University, Vinnytsya, Ukraine

Quality of life in patients with ankylosing spondylitis with anemic syndrome assessed according to the ASQoL questionnaire, the relationship with the course of the disease

For citation: Bol', sustavy, pozvonočnik. 2022;12(2):52-58. doi: 10.22141/pjs.12.2.2022.329

Abstract. Background. Anemia, as a frequent comorbid pathology, increases the severity of the course, reduces the quality of life (QoL), and worsens the prognosis in patients with ankylosing spondylitis (AS). However, studies examining the impact of anemia on the course of the disease and QoL assessed using the ASQoL questionnaire are currently insufficient. **The purpose** was to analyze the QoL indices according to the ASQoL questionnaire in AS patients with anemia and to evaluate its dependence on gender, as well as the form and course of the disease. **Materials and methods.** 118 patients with AS and 26 practically healthy subjects, representative of age and gender, had been examined. QoL index was assessed using the ASQoL questionnaire. **Results.** QoL index in AS patients according to the ASQoL questionnaire was 8.96 ± 0.41 points. In AS patients with anemic syndrome, the QoL parameter was 11.85 ± 0.74 points, QoL index in AS patients without anemia was 7.88 ± 0.44 points. Patients with a peripheral form of AS and anemia have worse QoL index according to ASQoL scores (12.13 ± 0.94), compared to the subjects with a central form of AS and anemia (10.42 ± 1.21). Also, the worst indices of QoL were established in patients with anemia of chronic disease (ACD) (16.27 ± 0.44) and ACD with iron deficiency (11.50 ± 0.92). In the subjects with iron deficiency anemia (IDA), the indices of QoL did not significantly differ from parameters of the patients without anemia (7.16 ± 0.52). Disease activity and the presence of anemic syndrome have a reliable ($p < 0.05$) direct correlation (IL-6: $r = 0.62$; CRP: $r = 0.68$; BASDAI: $r = 0.5$; ASDAS: $r = 0.25$) with deterioration of QoL index according to ASQoL. **Conclusions.** Anemia is a frequent comorbid pathology in patients with AS and worsens the QoL indices of the patients. The degree and pathogenetic type of anemia (in particular, ACD) is closely correlated with the lower QoL index of patients with AS.

Keywords: quality of life; ankylosing spondylitis; anemic syndrome; ASQoL

Introduction

Ankylosing Spondylitis (AS) is seronegative arthritis that affects the axial skeleton and peripheral joints, has a chronic course, and alternates with exacerbations and remissions. Quite often (50-62 %) is combined with comorbid pathology that can modify clinical symptoms, complicate the course of the disease and reduce the effectiveness of treatment [1-3]. One of the frequent comorbid manifestations of AS is an anemic syndrome, which occurs in 15-45.8 % of cases [4-7]. It is known that anemia, namely Anemia of Chronic Dis-

ease (ACD), which is most often detected in AS, is closely related to the activity of the underlying disease. Thus, it can additionally lead to both significant functional impairment and a decrease in quality of life (QoL) [8]. Decreasing QoL in AS patients with anemic syndrome according to SF-36 and HAQ was described in the work of S. V. Shevchuk et al. [9]. The ASQoL questionnaire is another valid tool for assessing QoL in patients with AS [10]. However, in the existing literature, we did not find any information on the assessment of QoL using the ASQoL questionnaire in AS

© 2022. The Authors. This is an open access article under the terms of the Creative Commons Attribution 4.0 International License, CC BY, which allows others to freely distribute the published article, with the obligatory reference to the authors of original works and original publication in this journal.

Для кореспонденції: Шевчук Сергій Вікторович, доктор медичних наук, професор, завідувач кафедри внутрішньої медицини № 2 Вінницького національного медичного університету імені М.І. Пирогова, вул. Пирогова, 56, м. Вінниця, Україна; НДІ реабілітації осіб з інвалідністю Вінницького національного медичного університету імені М.І. Пирогова, вул. Хмельницьке шосе, 104, м. Вінниця, Україна; e-mail: shev.sv76@gmail.com; контактний тел.: +38(067)3978046

For correspondence: Sergij Shevchuk, MD, PhD, Professor, Head of the Chair of internal medicine 2, National Pirogov Memorial Medical University, Scientific and Research Institute of Invalid Rehabilitation (educational scientific treatment complex) of National Pirogov Memorial Medical University, Vinnytsya, Ukraine; e-mail: shev.sv76@gmail.com; contact phone: +38(067)3978046

Full list of authors information is available at the end of the article.

patients with the anemic syndrome. The role of traditional factors of the course of the disease in the violation of QoL in AS patients with anemia is also unknown.

Therefore, based on the information above, the **aim** of this study was to analyze the quality of life according to the ASQoL questionnaire in AS patients with anemia and to assess its dependence on the influence of sexual factors, as well as the form and course of the disease.

Materials and methods

The study included 118 patients with diagnosed AS and 26 age- and sex-representative healthy persons who provided informed consent to participate in the study. The age of the examinees ranged from 19 to 75 years, the average age was 43.67 ± 0.97 years.

The diagnosis of AS was verified according to the ASAS criteria [11]. All patients with AS were treated according to ASAS/EULAR (2016) recommendations: first-line drugs: non-steroidal anti-inflammatory drugs (NSAIDs as monotherapy). Patients with peripheral manifestations of the disease received sulfasalazine (in a dose of 3 g/d), as well as local injections of glucocorticoids. Patients with axial manifestations of the disease without a satisfactory response to NSAIDs and subjects with a peripheral form and ineffective treatment with disease-modifying antirheumatic drugs (DMARDs), as well as with high and very high disease activity, received biological disease-modifying antirheumatic drugs (in particular, inhibitors of tumor necrosis factor α , 8 (6.8 %) persons). The research was conducted in accordance with the ethical principles of the Helsinki Declaration of Human Rights (1964–2000), the Council of Europe Convention on Human Rights and Biomedicine (from 04.04.1997), and the order of the Ministry of Health of Ukraine No. 281 from 01.11.2000. The Bioethics Commission of National Pirogov Memorial Medical University (protocol No. 2 dated February 4, 2016) found that the conducted research corresponds to the ethical and moral, and legal requirements.

Among 118 examined patients with AS, there were 102 men (86.4 %) and 16 women (13.6 %). The quantitative ratio of men to women was 6.4:1. The average duration of the disease was 8.32 ± 0.51 years. The diagnosis of anemia was confirmed in case of a decrease in hemoglobin concentration below 130 g/l in men and below 120 g/l in women [12]. All patients did not take any drugs for the anemia treatment at the time of examination and verification of their anemic syndrome. Patients with AS and anemic syndrome were divided into groups taking into account the severity of anemia [12]. The anemic syndrome was diagnosed in 34 (28.8 %) patients. Anemia in females was established in 11 (68.75 %) subjects. Almost every second woman had the anemic syndrome. Among males, anemia was diagnosed in 23 (22.5 %) subjects. Almost every fourth man had a concomitant anemic syndrome. Depending on the pathogenesis of the development of anemic syndrome, all patients with the anemic syndrome were divided into three clinical groups: patients with ACD, persons with iron deficiency anemia (IDA), and patients with ACD and functional iron deficiency based on the diagnostic criteria of Weiss G. (2005) [13]. The level of

soluble transferrin receptors (sTfR) and ferritin was taken into account for the differential diagnosis of IDA and ACD. sTfR is not an acute-phase inflammatory reagent, unlike ferritin, and provides an accurate estimate of iron content in all tissues. With IDA, their concentration significantly exceeds the norm, and with ACD, it remains within the normal range. ACD with functional iron deficiency was established in the presence of all laboratory signs of ACD, as well as in the presence of a reduced level of serum iron and an increased level of sTfR.

Among patients with anemia, 15 patients (44.1 %) were diagnosed with ACD, 8 (23.6 %) with IDA, 10 (29.4 %) with ACD and iron deficiency. B12-deficiency anemia was confirmed in one patient, confirmed on the basis of hematological blood analysis (hyperchromic, macrocytic, hyporegenerative anemia, megalocytes, Jolly bodies, Cabot rings in erythrocytes, hypersegmentation of neutrophil nuclei). We did not evaluate the impact of basic therapy on the occurrence of an anemic syndrome in this study.

In 84 (71.2 %) patients, a central form of AS was registered, in 34 (28.8 %) – a peripheral one. Among patients with a central form of AS, there were 66 (78.6 %) subjects without anemia and 18 ones (53.0 %) with anemia. Among patients with a peripheral form of AS, there were 18 (21.4 %) persons without anemia and 16 (47.0 %) with anemia.

The control group consisted of 26 healthy subjects, who were representative of the main group in terms of age and sex and were examined as part of the study.

All laboratory indices were determined by commonly accepted methods. Hematological indices were determined using the ERMA PCE-210 device (Japan), biochemical parameters – on a MindrayBS-240 biochemical analyzer, immunoenzymatic indices – using an immunoenzymatic analyzer StatFax 303/Plus according to the manufacturer's method. Among the markers of the activity of the inflammatory process in patients with AS, the content of C-reactive protein (CRP) in the blood serum was quantitatively determined by the immunoenzymatic method using a standard kit from the company "Diagnostic Automation Inc.", USA.

The content of the pro-inflammatory cytokine – interleukin 6 (IL-6) – in the blood plasma was determined by the immunoenzymatic method using the standard kit of the company "IL-6 ELISA", Diaclone, France.

ASDAS (Ankylosing Spondylitis Disease Activity Score) and BASDAI (Bath ankylosing spondylitis disease activity index) questionnaires were used to determine AS activity [14]. The BASFI (Bath ankylosing spondylitis functional index) questionnaire was used to characterize the functional status of patients. The ASQoL (Ankylosing Spondylitis Quality of Life) questionnaire was used to assess the QoL of AS patients [10, 15].

The statistical processing of the results was conducted according to commonly accepted methods of variational statistics using the statistical program package "Microsoft Office Excel 2007" and "Statistica 6.1" using parametric and non-parametric methods. In the case of a parametric distribution of indices, the assessment of their differences between unrelated samples was conducted using the Stu-

dent's t-test, and non-parametric distribution using the Mann-Whitney U-test. Differences between the values were assessed using Fisher's method. The relationship between indices was assessed using Pearson's correlation analysis (r) (differences were considered significant if $p < 0.05$). The percentile method was used to rank individual indices (P5, P10, P25, P75, P90, P95).

Results

According to the ASQoL questionnaire, QoL in patients with AS was 8.96 ± 0.41 points, while in the control group it was 4.87 ± 1.03 points. In the group of AS patients with anemia, the QoL was 33.5 % worse than in patients without anemia and amounted to 11.85 ± 0.74 versus 7.88 ± 0.44 points (Table 1).

QoL indices did not differ significantly in men (9.01 ± 0.94 points) and women (10.44 ± 0.53 points). However, a comparative analysis of the QoL parameters in men and women, depending on the presence of anemia, revealed significantly higher indices were found in patients with anemic syndrome. Thus, in men with anemia, the quality of life was 40.3 % worse than in the group of subjects without anemia. Similar differences were found in the group of women (45.8 %).

The QoL index was significantly worse in patients with a peripheral form of AS (10.44 ± 0.93 points), in subjects with a central form it was 7.72 ± 0.43 points. Differences in QoL indices were also established between groups depending on the presence of the anemic syndrome. Therefore, in patients with central form and anemia, the QoL was 34.7 % worse, and in subjects with peripheral form and anemia (26.3 % worse), than in the corresponding groups of persons without anemia.

Additionally, we analyzed the QoL in patients depending on the pathogenetic variants and the severity of the anemic syndrome (Table 2). It was established that the QoL indi-

ces according to the ASQoL questionnaire were the worst in the group with ACD (16.27 ± 0.44 points) and were significantly higher than in the group of patients with ACD with iron deficiency (by 29.3 %) and in the group with IDA (by 55.9 %, $p < 0.05$). In patients with AS and ASD, the QoL index (7.16 ± 0.52 points) did not differ significantly from the index in subjects with AS without anemia (7.88 ± 0.44 points). It should be noted that patients with ACD and ACD with iron deficiency had higher disease activity, which could directly affect QoL indices. Compared with the group of subjects with IDA, the total activity index of BASDAI was higher by 37 and 25 %, respectively, in persons with ACD and ACD with iron deficiency. Similarly, markers of AS activity, such as IL-6, CRP, and erythrocyte sedimentation rate (ESR), were highest in the group with ACD. Compared to SDA, CRP levels were higher by 43 %, ESR by 19 %, and IL-6 by 91 % in patients with ACD, respectively.

However, the severity of anemia was not associated with higher disease activity. In persons with anemia of the second degree, the values of BASDAI and ASDAS, as well as IL-6, ESR, and CRP were not significantly different from the indices in the group of patients with anemia of the first degree. Comparing the QoL depending on the degree of anemia, it was established that the QoL was 41.9 % worse in subjects with anemia of the first degree than in patients with anemia of the second degree. Among patients with anemia of the first degree, 14 (51.9 %) subjects had ACD and 9 (33.3 %) had ACD with iron deficiency, their QoL was significantly worse, probably due to the high activity of the disease. Among the patients with anemia of second degree, 5 (71.4 %) subjects had IDA, their QoL indices did not differ from the corresponding indices of subjects without anemia.

Further, we analyzed the role of disease activity in the formation of QoL changes according to the QoL questionnaire in men with AS and anemia (Table 3). The

Table 1. Characteristics of the quality of life parameters of AS patients using ASQoL according to sex and form of AS

Groups			ASQoL, points	
All patients with AS, n (%)	118 (100)	with anemia	34 (28.8)	11.85 ± 0.74
		without anemia	84 (71.2)	$7.88 \pm 0.44^*$
According to the sex				
Females, n (%)	16 (13.6)	with anemia	11 (68.7)	12.18 ± 1.51
		without anemia	5 (31.3)	$6.60 \pm 1.17^{\#}$
Males, n (%)	102 (86.4)	with anemia	23 (22.5)	13.09 ± 0.81
		without anemia	79 (77.5)	$7.82 \pm 0.44^{\S}$
According to the form of AS				
Central form of AS, n (%)	34 (28.8)	with anemia	16 (47.0)	12.13 ± 0.94
		without anemia	18 (53.0)	$8.94 \pm 0.37^{\&}$
Peripheral form of AS, n (%)	84 (71.2)	with anemia	18 (21.4)	10.42 ± 1.21
		without anemia	66 (78.6)	$6.80 \pm 0.39^{\circ}$

Notes: results are presented as n (%) and $M \pm \sigma$; * – significant differences ($p < 0.05$) compared to the index of AS patients with anemia; # – significant differences ($p < 0.05$) compared to the index of AS women with anemia; \S – significant differences ($p < 0.05$) with the index of AS men with anemia; $\&$ – significant differences ($p < 0.05$) with the index of patients with a peripheral form of AS and anemia; \circ – significant differences ($p < 0.05$) with the index of patients with a central form of AS and anemia.

group of patients with anemia had significantly higher indices of AS activity, such as CRP, IL-6, and ESR, than persons without anemia. The level of CRP was higher by 34.9 %, ESR by 39.4 %, and IL-6 by 28.5 % in the group of patients with anemia compared to the corresponding indices of subjects without anemia ($p < 0.05$). Since there are no clear gradations of the severity of CRP, IL-6, and ESR, we used a percentile distribution ($P < 25$ optimal levels of CRP, IL-6, and ESR; $P 25-75$ – extremely high level; $P > 75$ – high level).

It was established that with increasing disease activity, QoL worsened both in the group of patients without anemia and with the presence of the anemic syndrome. In particular, the differences in ASQoL indices depending on the levels of

CRP, IL-6, and ESR in patients with anemia were higher than in the group without anemia. Thus, the QoL in subjects with AS, anemia, and IL-6 level of 20.6-32.45 ng/l was 36.29 % worse than in patients with the corresponding IL-6 level, but without anemia ($p < 0.05$). Similar differences were established between the groups of patients with a level of IL-6 > 32.45 ng/l, where the QoL of persons with anemia was 44.26 % worse than the QoL of subjects without anemia ($p < 0.05$). Correlation analysis demonstrated a significant direct relationship between QoL and IL-6 level ($r = 0.62$, $p < 0.05$). Similar results were found in the level of CRP and were somehow lower than in ESR.

The analysis of QoL according to ASQoL in relation to the total indices of AS activity, assessed using the BASDAI

Table 2. Characteristics of the quality of life parameters of AS patients using ASQoL according to the pathogenetic type of anemic syndrome and its degree of severity

Groups	n (%)	ASQoL, points	BASDAI, points	ASDAS, points	IL-6, g/ml	CRP, ng/l	ESR, mm/h
IDA	8 (29.4)	7.16 ± 0.52	5.40 ± 0.46	4.25 ± 0.27	16.15 ± 1.98	13.13 ± 1.60	31.13 ± 2.12
ACD with iron deficiency	10 (23.6)	11.50 ± 0.92 [#]	6.76 ± 0.38	3.89 ± 0.16	24.38 ± 2.39 [#]	12.20 ± 0.69	33.00 ± 4.77
ACD	15 (44.1)	16.27 ± 0.44 ^{#*}	7.42 ± 0.25 [#]	4.38 ± 0.12 [‡]	30.8 ± 1.41 ^{#*}	18.8 ± 0.98 ^{#*}	37.13 ± 3.75
Anemia, 1 st degree	27 (79.4)	13.78 ± 0.71	6.59 ± 0.27	4.06 ± 0.12	25.98 ± 1.54	15.43 ± 0.95	33.11 ± 2.20
Anemia, 2 nd degree	7 (20.6)	8.00 ± 1.00 [*]	7.00 ± 0.49	4.57 ± 0.07 [*]	23.39 ± 3.84	15.00 ± 1.46	38.14 ± 6.95

Notes: results are presented as n (%) and $M \pm \sigma$; IDA – iron deficiency anemia; ACD – anemia of chronic disease; [#] – significant differences ($p < 0.05$) compared to the index of patients with ACD; [‡] – significant differences ($p < 0.05$) compared to the index of patients with ACD and iron deficiency; ^{*} – significant differences ($p < 0.05$) compared to the index of patients with anemia of the 1st degree.

Table 3. Characteristics of the quality of life parameters of AS patients and the correlation between ASQoL and CRP, ESR, and IL-6 indices

Index	ASQoL, points	
	Patients with anemia, n = 34	Patients without anemia, n = 84
CRP, ng/l		
< 12; n = 61	7.75 ± 0.25	6.97 ± 0.79
12-18; n = 37	8.53 ± 0.46	9.50 ± 0.81 [#]
> 18; n = 20	16.00 ± 0.49 [#]	12.60 ± 2.11 [#]
Coefficient of correlation	$r = 0.68$; $p < 0.05$	$r = -0.19$; $p > 0.05$
IL-6, g/ml		
< 20,6; n = 81	7.33 ± 0.50	5.00 ± 1.00
20,6-32,45; n = 26	12.40 ± 1.12 ^s	7.90 ± 0.49 ^{**}
> 32,45; n = 11	14.89 ± 0.65 ^s	8.30 ± 0.92 ^{**}
Coefficient of correlation	$r = 0.62$; $p < 0.05$	$r = 0.012$; $p > 0.05$
ESR, mm/h		
< 30; n = 70	8.00 ± 0.38	7.31 ± 0.40
30-45; n = 25	13.40 ± 0.40 [*]	11.09 ± 1.65 [*]
> 45; n = 23	15.31 ± 1.02 [*]	13.50 ± 3.50 [*]
Coefficient of correlation	$r = 0.17$; $p > 0.05$	$r = -0.02$; $p > 0.05$

Notes: results are presented as $M \pm \sigma$ and correlation coefficient (r) and its significance; [#] – significant differences ($p < 0.05$) compared to the index of patients with anemia and lower CRP index; ^s – significant differences ($p < 0.05$) compared to the index of patients with IL-6 level < 20.6 g/ml; ^{*} – significant differences ($p < 0.05$) compared to the index of patients with anemia and the corresponding index of IL-6; ^{*} – significant differences ($p < 0.05$) compared to the index of patients with an ESR level < 30 mm/h.

and ASDAS questionnaires. As well as according to the functional capacity of patients, assessed using the BASFI questionnaire, revealed similar dependencies (Table 4). Firstly, it was established that the QoL was worse in patients with AS with anemic syndrome than in subjects without anemia. Secondly, with increasing disease activity and a decrease in functional capacity, QoL, accordingly, was getting worse. Thus, in the group with anemia and activity according to BASDAI > 7 points, the QoL was almost twice as bad as in the group of subjects with activity according to BASDAI ≤ 4 points. Similar differences were also found according to the ASDAS and BASFI indices ($p < 0.05$). The confirmation of the above revealed regularities was the receipt of significant correlations between the ASQoL index on the one hand and BASDAI, ASDAS and BASFI on the other.

Discussion

The analysis of our results allows us to state that patients with AS have a significant decrease in the quality of life index (8.96 ± 0.41 points) compared to the indices of the control group (4.87 ± 1.03 points). The ASQoL index was worse in subjects with anemia compared to the indices of patients without it (11.85 ± 0.74 vs. 7.88 ± 0.44 points, respectively, $p < 0.05$). Our results are consistent with recently published work by other scientists. In particular, similar differences were found in the Turkish cohort of patients with AS, where the QoL according to ASQoL in the main group was equal to 13.1 ± 2.5 points, and in the control group – 4.5 ± 1.6 points [16]. In the Egyptian population, the mean value of ASQoL in AS patients was 9.4 ± 3.8 points and was 38 % higher than in the control group [17]. As for the relationship between the QoL index according to ASQoL and the presence and form of anemia, we did not find such studies. At the same time, there are studies where the presence and degree of anemia in AS patients were evaluated with the

physical and mental components of the QoL according to the SF-36 questionnaire. Thus, according to the authors [9], the physical component of the SF-36 questionnaire in patients with anemia was equal to 24.86 ± 1.71 points, and in subjects without it – 33.57 ± 1.23 points. The indices of the mental component of the questionnaire also differed in patients depending on the presence of anemia (47.41 ± 1.96 versus 55.74 ± 1.60 points, respectively, $p < 0.05$).

Analysis of the QoL in patients with AS depending on the degree and type of anemia showed that patients with ACD, ACD and iron deficiency, as well as subjects with the first degree of severity of the anemic syndrome, had significantly higher QoL according to ASQoL than persons with IDA, as well as patients with the second degree of the anemic syndrome. From our standpoint, this pattern is explained by the fact that in the groups with ACD, ACD and iron deficiency, as well as among patients with the first degree of anemia severity, there were patients with higher indices of disease activity, which significantly affected the indices of QoL. The impact of anemia on QoL was also confirmed when comparing disease activity indices in groups depending on the presence of anemia. With increasing levels of markers of the inflammatory process, QoL significantly worsened in both groups, however, was lower in patients with anemia.

In our study, significantly worse QoL indices were established in patients with a peripheral form of AS (ASQoL indicator: 10.44 ± 0.93 points) than in subjects with a central form (respectively, 7.72 ± 0.43 points). Similar patterns were observed in the study [17], in which the ASQoL index was significantly higher in patients with a peripheral form of AS than in subjects with a central form of the disease (11.4 ± 3.1 and 7.3 ± 3.4 , respectively, $p < 0.001$). According to [18], patients with a peripheral form of AS had significantly higher values of ASQoL, night pain, fatigue, and morning stiffness.

Table 4. Characteristics of the quality of life parameters of AS patients and correlation between ASQoL and BASDAI, ASDAS and BASFI indices

Показник		ASQoL, points			
		With anemia		Without anemia	
		n (%)	M ± σ	n (%)	M ± σ
BASDAI, points	< 4; n = 20	3 (15)	7.67 ± 0.33	17 (85)	6.00 ± 0.51
	4–7; n = 71	18 (25.4)	9.50 ± 0.78*	53 (74.6)	9.04 ± 0.55 [®]
	> 7; n = 27	13 (48.1)	15.69 ± 0.57*	14 (51.9)	6.21 ± 1.14 [#]
Coefficient of correlation		r = 0.5; p < 0.05		r = 0.02; p > 0.05	
ASDAS, points	< 3.5; n = 36	5 (13.9)	7.00 ± 0.77	31 (86.1)	6.97 ± 0.57
	> 3.5; n = 82	29 (35.4)	12.54 ± 0.76 [®]	53 (64.6)	8.42 ± 0.60 [#]
Coefficient of correlation		r = 0.25; p < 0.05		r = -0.14; p > 0.05	
BASFI, points	≤ 4; n = 22	5 (22.7)	7.00 ± 0.77	17 (77.3)	6.00 ± 0.51
	> 4; n = 96	29 (30.2)	12.54 ± 0.76 [®]	67 (69.8)	8.36 ± 0.52 [®]
Coefficient of correlation		r = 0.09; p > 0.05		r = 0.1; p > 0.05	

Notes: results are presented as M ± σ and correlation coefficient (r) and its significance; [#] – significant differences (p < 0.05) compared to the index of patients with anemia; * – significant differences (p < 0.05) compared to the index of patients with anemia and lower BASDAI scores; [®] – significant differences (p < 0.05) compared to the index of patients without anemia and BASDAI < 4 points and BASDAI > 7 points; [®] – significant differences (p < 0.05) compared to the index of patients with anemia and lower ASDAS indices; [®] – significant differences (p < 0.05) compared to the index of patients with BASFI scores ≤ 4 points.

We established a significant relationship between QoL indices on the one hand and clinical and laboratory indices of AS activity (CRP, IL-6, ASDAS, BASDAI, and BASFI) on the other. This was also confirmed by the results of correlation analysis. CRP and IL-6 levels were most associated with QoL ($r=0.62$, $r=0.68$, $p<0.05$). The analysis of literature data also clearly confirms the regularities we obtained [18, 19]. Therefore, in the study [20], patients with ASDAS-CRP ≥ 2.1 points had 3 times worse QoL indices according to SF-36 (physical component) than individuals with ASDAS-CRP < 2.1 points.

Consequently, patients with AS with anemia had a significant (66 %) decrease in QoL according to ASQoL, compared to subjects without anemia. Subjects with ACD, ACD and iron deficiency had more profound impairments of QoL and were less pronounced in patients with IDA. QoL according to ASQoL in patients with AS was worse in persons with peripheral form and in persons with high activity of the inflammatory process. Particularly, it is obvious that the anemic syndrome in AS patients is formed partly due to the high activity of the inflammatory process and is a marker of the severity of the course of the disease.

Limitations of the study: the research was performed without taking into account other comorbid pathology in patients with AS. We also did not evaluate the nutritional characteristics of the patients and the effectiveness of the method of correcting the anemic syndrome, which requires further research.

Conclusions

According to the ASQoL questionnaire, the QoL of AS patients with anemia is significantly (66 %) worse than that of AS patients without anemia. More profound disturbances of QoL are found in patients with ACD, ACD and iron deficiency are less pronounced in patients with IDA. In subjects with ASD, the QoL was not significantly different from the indices of patients with AS without anemia. A low level of QoL in subjects with AS and anemic syndrome was associated with high disease activity according to ASDAS ($r = 0.25$, $p < 0.05$), BASDAI ($r = 0.5$, $p < 0.05$) scores, levels of CRP ($r = 0.68$, $p < 0.05$), IL-6 ($r = 0.62$, $p < 0.05$) and the peripheral form of the disease.

References

1. Barnett R, Ingram T, Sengupta R. Axial spondyloarthritis 10 years on: still looking for the lost tribe. *Rheumatology (Oxford)*. 2020 Oct 1;59(Suppl 4):iv25-iv37. doi:10.1093/rheumatology/keaa472.
2. Macfarlane GJ, Rotariu O, Jones GT, Pathan E, Dean LE. Determining factors related to poor quality of life in patients with axial spondyloarthritis: results from the British Society for Rheumatology Biologics Register (BSRBR-AS). *Ann Rheum Dis*. 2020 Feb;79(2):202-208. doi:10.1136/annrheumdis-2019-216143.
3. Nikiphorou E, Ramiro S, van der Heijde D, et al. Association of comorbidities in spondyloarthritis with poor function, work disability, and quality of life: results from the assessment of spondyloarthritis international society comorbidities in spondyloarthritis study. *Arthritis Care*

Res (Hoboken). 2018 Aug;70(8):1257-1262. doi:10.1002/acr.23468.

4. Braun J, van der Heijde D, Doyle MK, et al. Improvement in hemoglobin levels in patients with ankylosing spondylitis treated with infliximab. *Arthritis Rheum*. 2009 Aug 15;61(8):1032-1036. doi:10.1002/art.24865.

5. Bulut Y, Tas DA, Ozturk OG, Karaogullarindan U. SAT0396 Investigation of iron deficiency anemia in ankylosing spondylitis patients. *Ann Rheum Dis*. 2017;76(Suppl 2):921-922. doi:10.1136/annrheumdis-2017-eular.5913.

6. Kim KJ, Cho CS. Anemia of chronic disease in ankylosing spondylitis: improvement following anti-TNF therapy. *Archives of rheumatology*. 2012;27(2):90-97. doi:10.5606/tjr.2012.014.

7. Niccoli L, Nannini C, Cassarà E, Kaloudi O, Cantini F. Frequency of anemia of inflammation in patients with ankylosing spondylitis requiring anti-TNF α drugs and therapy-induced changes. *Int J Rheum Dis*. 2012 Feb;15(1):56-61. doi:10.1111/j.1756-185X.2011.01662.x.

8. Ertenli I, Ozer S, Kiraz S, et al. Infliximab, a TNF- α antagonist treatment in patients with ankylosing spondylitis: the impact on depression, anxiety and quality of life level. *Rheumatol Int*. 2012 Feb;32(2):323-330. doi:10.1007/s00296-010-1616-x.

9. Shevchuk SV, Zviahina OV. Quality of life in patients with ankylosing spondylitis, relationship to the course of the disease and the existing of anemic syndrome. *Ukrainian Journal of Rheumatology*. 2020;(79):76-82. doi:10.32471/rheumatology.2707-6970.79.14825. (in Ukrainian).

10. Doward LC, Spoorenberg A, Cook SA, et al. Development of the ASQoL: a quality of life instrument specific to ankylosing spondylitis. *Ann Rheum Dis*. 2003 Jan;62(1):20-26. doi:10.1136/ard.62.1.20.

11. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis*. 2011 Jun;70(6):896-904. doi:10.1136/ard.2011.151027.

12. Ministry of Health of Ukraine. Order on November 2, 2015 № 709. On Adoption and Implementation of Medical and Technological Documents on the Standardization of Medical Care for Iron Deficiency Anemia. Available from: <https://zakon.rada.gov.ua/rada/show/v0709282-15#Text>. Accessed: November 2, 2015. (in Ukrainian).

13. Weiss G, Goodnough LT. Anemia of chronic disease. *N Engl J Med*. 2005 Mar 10;352(10):1011-1023. doi:10.1056/NEJMra041809.

14. Lukas C, Landewé R, Sieper J, et al. Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. *Ann Rheum Dis*. 2009 Jan;68(1):18-24. doi:10.1136/ard.2008.094870.

15. Masyk OM, Nadashkevich ON, Oleksiv NM. Validation of the ukrainian-language version of BASDAI and BASFI scales. *Ukrainian Journal of Rheumatology*. 2010;(40):51-56. (in Ukrainian).

16. Ali AY, ElTanawy RM, Fawzy RM, Abdel Bary EM. Correlation between different parameters of disease

status and quality of life in patients with ankylosing spondylitis. *Benha Journal of Applied Sciences*. 2021;6(1):67-70. doi:10.21608/БЯС.2021.168488.

17. Sallam RA, Elbahnasawy AS. Health related quality of life (HRQoL) in ankylosing spondylitis patients: Relation to clinical features, disease activity and radiographic damage. *Egyptian Rheumatologist*. 2020;42(4):287-290. doi:10.1016/j.ejr.2020.02.006.

18. Yılmaz O, Tutoğlu A, Garip Y, Ozcan E, Bodur H. Health-related quality of life in Turkish patients with ankylosing spondylitis: impact of peripheral involvement on quality of life in terms of disease activity, functional status, severity of pain, and social and emotional functioning. *Rheumatol Int*. 2013 May;33(5):1159-1163. doi:10.1007/s00296-012-2510-5.

19. Huang JC, Qian BP, Qiu Y, et al. Quality of life and correlation with clinical and radiographic variables in patients with ankylosing spondylitis: a retrospective case series study. *BMC Musculoskelet Disord*. 2017 Aug 15;18(1):352. doi:10.1186/s12891-017-1711-1.

20. Salaffi F, Carotti M, Gasparini S, Intorcchia M, Grassi W. The health-related quality of life in rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis: a comparison with a selected sample of healthy people. *Health Qual Life Outcomes*. 2009 Mar 18;7:25. doi:10.1186/1477-7525-7-25.

Received 08.09.2022

Revised 28.09.2022

Accepted 04.10.2022 ■

Information about authors

Sergii Shevchuk, MD, PhD, Professor, Head of the Chair of the Department of internal medicine 2, National Pirogov Memorial Medical University, Scientific and Research Institute of Invalid Rehabilitation (educational scientific treatment complex) of National Pirogov Memorial Medical University, Vinnytsya, Ukraine; e-mail: shev.sv76@gmail.com; contact phone: +38(067)3978046; <https://orcid.org/0000-0002-5649-2775>.

Oksana Zviachina, MD, PhD, Assistant at the Department of internal medicine 2, National Pirogov Memorial Medical University, Vinnytsya, Ukraine; e-mail: zviachina89@gmail.com; <https://orcid.org/0000-0002-1840-8288>.

Oleksandr Zviachin, candidate of technical sciences, Associate professor at the Department of radio engineering (RT), Vinnytsya National Technical University, Vinnytsya, Ukraine; e-mail: zviachin86@gmail.com; <https://orcid.org/0000-0002-5386-6057>.

Yurii Bezsmertnyi, MD, PhD, Professor of National Pirogov Memorial Medical University, Scientific and Research Institute of Invalid Rehabilitation (educational scientific treatment complex) of National Pirogov Memorial Medical University, Vinnytsya, Ukraine; e-mail: bezsmertnyiyurii@gmail.com; <https://orcid.org/0000-0002-1388-7910>.

Iuliia Segeda, MD, PhD, Assistant of the Department of internal medicine 2, National Pirogov Memorial Medical University, Vinnytsya, Ukraine; e-mail: iuliia.segeda@gmail.com; <https://orcid.org/0000-0001-8282-7703>.

Conflicts of interests. Authors declare the absence of any conflicts of interests and own financial interest that might be construed to influence the results or interpretation of the manuscript.

Information about funding. The scientific work was carried out within the framework of the planned research of the Department of Internal Medicine 2 of the National Pirogov Memorial Medical University in Vinnytsya "To study the role of clinical, molecular genetic, metabolic, immunoinflammatory and hemocoagulation factors in the formation of cardiovascular lesions in rheumatoid arthritis and to develop guidelines for their prevention and treatment", state registration number 0113U000670.

Authors' contribution. S.V. Shevchuk — analysis and processing of the obtained data, writing the text, concept and design of the study; O.V. Zviachina — collection and processing of materials, analysis of the obtained data, writing the text; O.S. Zviachin — statistical processing of results, analysis of the obtained data; Y.O. Bezsmertnyi — analysis of the obtained data, writing the text; I.S. Segeda — analysis of the obtained data, writing the text.

Шевчук С.В.^{1,2}, Звягіна О.В.¹, Звягін О.С.³, Безсмертний Ю.О.^{1,2}, Сеґеда Ю.С.^{1,2}

¹Вінницький національний медичний університет імені М.І. Пирогова, м. Вінниця, Україна

²Науково-дослідний інститут реабілітації осіб з інвалідністю Вінницького національного медичного університету імені М.І. Пирогова, м. Вінниця, Україна

³Вінницький національний технічний університет, м. Вінниця, Україна

Якість життя у хворих на анкілозивний спондиліт з анемічним синдромом за даними опитувальника ASQoL, зв'язок з перебігом захворювання

Резюме. Актуальність. Анемія, як часта коморбідна патологія, посилює тяжкість перебігу, знижує якість життя (ЯЖ) та погіршує прогноз у хворих на анкілозивний спондиліт (АС). Проте досліджень, які вивчали б вплив анемії на перебіг захворювання та ЯЖ, оцінену за допомогою опитувальника ASQoL, на сьогодні недостатньо. **Мета:** проаналізувати ЯЖ з використанням опитувальника ASQoL у хворих на АС з анемією та оцінити її залежність від статевих чинників, а також форми та перебігу захворювання. **Матеріали та методи.** Обстежено 118 пацієнтів із АС та 26 практично здорових осіб групи контролю, репрезентативних за віком та статтю. ЯЖ оцінено за допомогою опитувальника ASQoL. **Результати.** ЯЖ у хворих на АС за даними опитувальника ASQoL становила $8,96 \pm 0,41$ бала. У хворих на АС з анемічним синдромом показники ЯЖ становили $11,85 \pm 0,74$ бала, у хворих на АС без анемії — $7,88 \pm 0,44$ бала. Пацієнти з периферичною формою АС та

анемією мали гірші показники ASQoL ($12,13 \pm 0,94$ бала) порівняно з особами з центральною формою АС та анемією ($10,42 \pm 1,21$ бала). Також найгірші показники ЯЖ відмічені у хворих з анемією хронічного захворювання (АХЗ) ($16,27 \pm 0,44$ бала) та АХЗ з дефіцитом заліза ($11,50 \pm 0,92$ бала). У хворих із залізодефіцитною анемією показники ЯЖ вірогідно не відрізнялись від показників хворих без анемії ($7,16 \pm 0,52$ бала). Активність захворювання та наявність анемічного синдрому мали вірогідний ($p < 0,05$) прямий кореляційний зв'язок (ІЛ-6: $r = 0,62$; СРБ: $r = 0,68$; BASDAI: $r = 0,5$; ASDAS: $r = 0,25$) з погіршенням ЯЖ за даними ASQoL. **Висновки.** Анемія є частою коморбідною патологією у хворих на АС та погіршує ЯЖ пацієнтів. Ступінь та патогенетичний тип анемії (зокрема, АХЗ) тісно корелюють з нижчою ЯЖ хворих на АС.

Ключові слова: якість життя; анкілозивний спондиліт; анемічний синдром; ASQoL