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LETTER TO THE EDITOR

Health-related quality of life in adult patients with chronic immune thrombocytopenia in Serbia

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To the editor,

Chronic immune thrombocytopenia (CIT) in adults is a chronic acquired autoimmune disorder characterized by accelerated platelet destruction, predominantly antibody-mediated, and decreased platelet production [1]. Many patients with CIT present with either no symptoms or minimal bruising, but some experience serious bleeding. The severity of thrombocytopenia correlates to some extent but not entirely with the bleeding risk [2] and is highly variable from one patient to another. These signs and symptoms of the disease and treatment side effects can then affect various domains of health-related quality of life (HRQOL), including emotional and functional health, work life, social and leisure activities, as well as reproductive health. All of these can affect many areas of patient everyday life and overall wellbeing [3–9]. However, the majority of individuals with CIT have a good prognosis, so the most beneficial treatment should not only focus on the platelet count but also on improving their HRQoL.

The aim of this study was to analyze associations between demographic and clinical characteristics including type of therapy and HRQOL in patients with CIT.

A total of 111 patients with primary CIT attending the Clinic of Hematology, Clinical Center of Serbia and the “Bežanijska Kosa” Clinical Hospital either as in-patients or out-patients from 2007 to 2008 were assessed. To be eligible, subjects were required to have active disease and be ≥18 years of age. Exclusion criteria included the presence of cognitive disorders and psychiatric diseases. The study received the approval of the Institutional Review Board and each patient provided written informed consent before enrolling. The demographic data and clinical characteristics were gathered from medical records and presented in Table I. Regarding the effects of the disease on the patients’ life style we evaluated absence from work/school and what bothered patients the most: reduced work ability, fear, fatigue, bleeding, infections or corticosteroid side effects. Their subjective fear of bleeding was recorded on a 4-point scale: (1) no fear at all; (2) a little fear; (3) fear; and (4) extreme fear. SF-36 (Serbian translation) [10] is a self-administered measure of generic health status and was used to assess HRQoL. Anxiety was assessed by the Hamilton anxiety rating scale (HARS); scores were as follows <18 points - no anxiety, 19–25 points - moderate anxiety, and >25 points severe anxiety [11]. Depression was assessed by the Hamilton depression

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rating scale (HDRS); scoring was as follows: <8 points - no depression, 8–13 points - mild depression, 14–18 points - moderate, 19–22 points - severe and >22 points - very severe depression [12]. Non-parametric measures of correlation were evaluated using Spearman’s rank correlation coefficient. Differences between subgroups were analyzed by χ^2 test and ANOVA. The predictive value of variables was assessed by multiple linear regression analysis.

Regarding the effects of the disease and/or its treatment on the patients’ life style 90% reported absence from work/school. The patients were mostly bothered with reduced work ability (26.1%), fear (25.2%), bleeding (19.8%) and fatigue (19.8%). Among them 11 (9.9%) had severe fear of bleeding, 28 (25.2%) moderate fear and 47 (42.3%) a little fear. Over 72.1% of the patients expressed some degree of depression: mild in 63 (35.2%), moderate in 19 (18.9%), severe in 8 (5.4%) and very severe in 14 (12.6%). About a fifth (21%) of the patients was anxious. The impact of CIT and its treatment on patients’ daily functions and HRQoL were studied using SF-36 as shown in Table II. We also investigated the impact of demographic characteristics on HRQoL. Women had lower scores in domains of physical functioning ($p = 0.045$) and bodily pain ($p = 0.042$), while men were more anxious and more depressed ($p < 0.05$). Older patients had worse physical functioning, general health, vitality, emotional functioning, mental health as well as composite scores of physical and mental health. A higher educational level significantly improved HRQoL in all domains. Moreover, married patients exhibited better HRQoL in domains of physical functioning, bodily pain, general health and composite score of physical health compared to the unmarried. Duration of CIT correlated significantly with body pain, while transfusions of both red blood cells and platelets had no impact on HRQoL. Splenectomy did not influence HRQoL, but successful splenectomy markedly ($p < 0.001$) improved general health (patients considered cured by splenectomy) and also significantly

Table I. The demographic and clinical characteristics of the patients.

Characteristics	Values
Mean age (years, range)	
At diagnosis	40.7 (19–74)
At survey	47.6 (19–79)
Gender	
Male	29 (26%)
Female	82 (74%)
Occupation	
No school	7 (6.3%)
Primary school	28 (25.2%)
Manual worker	11 (9.9%)
Clerk	41 (36.9%)
Expert	24 (21.6%)
Employment status	
Employed	43 (38.7%)
Unemployed	31 (27.9%)
Retired	36 (32.4%)
Student	1 (0.9%)
Marital status	
Married/cohabiting	72 (64.9%)
Separated/divorced	8 (7.2%)
Widowed	12 (10.8%)
Never married	73 (18.1%)
Absence from work	100 (90.1%)
Comorbidities	74 (66.7%)
Disease duration (years, range)	4 (1–51)
Platelet count ($\times 10^9/l$) (mean, range)	
At diagnosis	14 (1–137)
At survey	76 (3–500)
Bleeding episodes	
Prior to survey	92 (84%)
At survey	18 (16%)
Prior therapy	
Corticosteroids	87 (78.4%)
Intravenous immunoglobulins	22 (6.3%)
Danazol	20 (18.0%)
Micophenolate-mofetil	12 (10.8%)
Azathioprine	7 (6.3%)
Vincristine	6 (5.4%)
Cy-A	4 (3.6%)
Cyclophosphamide	3 (2.7%)
Dapsone	1 (0.9%)
Therapy at time of survey	
Corticosteroids	36 (32.4%)
Danazol	6 (5.4%)
Micophenolate-mofetil	9 (8.1%)
Refractory patients	17 (14.3%)
Splenectomy	34 (29.7%)
Response to splenectomy	20 (57%)
Time from splenectomy (years, range)	4 (1–42)
Complications of splenectomy	12 (30.3%)
History of transfusions	38 (34.2%)
Treatment side effects	
Corticosteroids	84 (96.5%)
Intravenous immunoglobulins	5 (23.7%)
Splenectomy	12 (30.3%)
Page bleeding score at the moment of hospitalization	
Grade 1	94 (85%)
Grade 2	16 (14%)

improved mental composite score. Platelet count per se did not influence HRQoL, either at diagnosis or at survey. Bleeding episodes significantly decreased HRQoL in the following domains of SF-36: physical functioning, role physical, bodily pain, vitality, social functioning, and composite scores of physical and mental functioning ($p < 0.05$). Bleeding at survey affected HRQoL negatively in the domains of physical functioning, vitality and

Table II. Health-related quality of life, measured using the SF-36 form.

Parameters	Score 0–100	Range
Physical functioning	71.6 $\pm$ 22.0	5.0–100.0
Role limitation due to physical problems	36.7 $\pm$ 40.3	0.0–100.0
Bodily pain	69.4 $\pm$ 29.4	0.0–100.0
General health	48.3 $\pm$ 18.1	0.0–90.0
Vitality	48.6 $\pm$ 22.5	0.0–95.0
Social functioning	78.0 $\pm$ 29.7	0.0–100.0
Emotional functioning	45.3 $\pm$ 43.5	0.0–100.0
Mental health	63.2 $\pm$ 19.3	12.0–100.0
Physical Health Composite	55.0 $\pm$ 21.0	8.0–95.0
Mental Health Composite	56.7 $\pm$ 20.5	7.9–94.00
Total score	57.6 $\pm$ 20.7	8.1–95.2

physical health composite, as well as increasing anxiety. Treatment generally did not influence HRQoL. Side effects of corticosteroids have no influence on HRQoL, while treatment with IVIg increased bodily pain. Conversely, herbs/supplements improved general health. Residence far from the Clinic of Hematology had a marked impact on physical functioning and physical composite score, and also increased the level of depression in our patients. Subjective effects of CIT on the patient's life-style (fear, malaise, bleeding, infections and reduced work ability) significantly influenced physical functioning, role limitations due to physical problems, decreased the composite score of physical functioning ($p < 0.001$) and lowered general health and increased anxiety and depression ($p < 0.05$). Considering the fear of bleeding separately, we found that it increased both HARS and HDRS scores ($p < 0.05$). Highly significant negative correlations were noticed between all domains of HRQoL and HDRS and HARS scores ($p < 0.001$). Univariate linear regression analysis (dependent variable: total SF-36 score) showed that age ($\beta = -0.264$, $p = 0.005$), education ($\beta = 0.453$, $p = 0.001$), employment ($\beta = -0.295$, $p = 0.002$), marital status ($\beta = -0.232$, $p = 0.014$), comorbidities ($\beta = -0.292$, $p = 0.002$), erythrocyte transfusion ($\beta = 0.237$, $p = 0.012$), bleeding episodes ($\beta = 0.262$, $p = 0.006$) and successful splenectomy ($\beta = -0.189$, $p = 0.047$) were the most important predictors of HRQoL in our patients. Using multivariate linear regression analysis, we found that the strongest predictors of HRQoL were bleeding episodes, comorbidities, employment and level of education.

The impact of CIT on HRQoL has not been investigated enough [3–9]. Our study is the first one testing anxiety and depression in an CIT cohort using Hamilton scales. These tests showed that a larger percentage of patients exhibited depression to some degree but only one fifth of them had anxiety. Subjective fear of bleeding enhanced the depression and anxiety and they both significantly decreased all HRQoL domains ($p < 0.001$).

The most important limitation of this study is the lack of normative values of the SF-36 scores for the general population in Serbia. Moreover, further studies should include thrombopoiesis-stimulating agents independently from industry and the number of hospital admissions as that it might serve as a surrogate marker for severe bleeding events.

Our study showed that CIT is not a trivial disease from the perspective of the affected patients. The impact of CIT on patients HRQoL is substantial and to improve it we need a more efficient and less harmful treatment modality.

Declaration of interest

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