

# Health related quality of life in patients with primary biliary cholangitis

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## Abstract

**Aim:** To assess the health related quality of life (HRQOL) in patients diagnosed with primary biliary cholangitis (PBC).

**Material and methods:** A single-centered, prospective, cross-sectional study was conducted among patients diagnosed with primary biliary cholangitis in the Gastroenterology out-patient clinic at Gazi University Hospital, Ankara. Data was collected using a sociodemographic information form, hospital medical database and a PBC-40 questionnaire. Statistical comparison analysis was performed using Chi-square test for categorical variables and Mann-Whitney U test for continuous variables. P values less than 0.05 were considered significant.

**Results:** A total of 37 PBC patients were included in the study. The mean age of the participants was 54.2±8.6. When evaluating the PBC-40 questionnaire scores from each domain in terms of severity, we found that majority of patients in itch %40.4 (n=19) and social %42.6 (n=20) domains had mild severity, as for fatigue %42.6 (n=20), cognitive %36 (n=17), emotional %40.4 (n=19) and other symptoms %44.7 ((n=21) domains had moderate severity. A statistically significant difference was found between AMA positive and AMA negative patient groups in the itch domain (p=0.007).

**Discussion:** With this study on a Turkish based population using the PBK-40 questionnaire we were able to demonstrate that patients with PBC had a significantly impaired HRQOL and fatigue was the most seen symptom.

**Key words:** primary biliary cholangitis, health related quality of life, PBC-40

## Introduction

Primary biliary cholangitis (PBC) is an autoimmune biliary liver disease, it predominantly affects middle-aged women and can progress to cirrhosis [1]. Most patients with PBC suffer from a variety of symptoms, including fatigue, pruritus, jaundice, sleep disturbances, cognitive dysfunction, mood disorders and depression, that can significantly impair their health-related quality of life (HRQOL) [2].

Fatigue has been shown to be the most important symptom affecting the daily activities and lives of individuals at all stages of PBC disease [3]. For this reason, research was needed to evaluate how much the disease affects the quality of life and valid scales specific to this disease were developed. PBC-40, one of which is a health-related quality of life score specific to patients with PBC. PBC-40 was developed with a focus on the course of the disease, its treatment, and its effects on the physical, emotional and functional state of patients. Studies have shown that PBC-40 is a reliable questionnaire that is

useful both in research and in the clinic setting for the evaluation of fatigue, pruritus and other symptoms and indices of emotional, social, and cognitive life [4]. In our study, we aimed to evaluate the HRQOL of the disease by using the PBC-40 questionnaire in PBC patients followed up in our center.

## Materials and methods

Our study was a single-centered, cross-sectional study conducted at Gazi University Medical Faculty Hospital, Gastroenterology outpatient clinic, between December 2020 and October 2021.

Forty-five patients diagnosed with PBC disease, who were regularly monitored at the outpatient clinic, were invited to participate in the study. 3 of the patients did not consent to be included in the study. 5 of them were excluded because they had one or more of the exclusion criteria of the study.

Informed consent was obtained from all patients for participation. The study was conducted in accordance

with the ethical standards stated in the Declaration of Helsinki by the World Medical Association. The study protocol was approved by Gazi University Ethics Committee (Decision no. 819) on 07.12.2020.

### Inclusion and exclusion criteria for the study

Patients between the ages of 18-75 who were diagnosed with PBC were included in the study. Patients with a diagnosis of PBC who were hospitalized for any reason during the study period, those who declared that they wanted to leave the study, those with a history of liver transplantation due to PBC and those with other etiologies of liver diseases, including autoimmune hepatitis or an overlap syndrome, were excluded from the study. In addition, patients with comorbidities such as: Signs of decompensated cirrhosis, severe painful rheumatoid arthritis, severe pruritic atopic dermatitis, patients with end-stage renal disease requiring dialysis and malignant disease, because they had severe symptoms that may greatly affect HRQOL were also excluded from the study.

### Method

Diagnosis of primary biliary cholangitis included two or more of the criteria; Chronic elevation in biliary liver enzymes (ALP and GGT), detectable anti-mitochondrial antibody (AMA) in the serum, and a liver histology compatible with or diagnostic of PBC.

Detailed clinical features, biochemical and imaging findings of the patients were accessed and recorded from the hospital database. These data included the date of diagnosis (in years), liver histological stage at diagnosis if liver biopsy was performed, liver biochemistry, and presence of clinical events (i.e., jaundice, ascites, edema, hepatic encephalopathy, esophageal or gastric varices and hepatocellular carcinoma).

Patients who agreed to participate in the study were asked to fill up the PBC-40 questionnaire adapted into Turkish for the evaluation of symptoms and HRQOL. PBC-40 is a patient-derived, disease specific symptom and HRQOL questionnaire consisting of 6 domains; Other symptoms, pruritus, fatigue, cognitive, social, and emotional [5]. Each domain mentioned contains 7, 3, 11, 6, 10 and 3 items respectively. And since the scores on each item range from 1 to 5 points, the score range in each domain is 7-35, 3-15, 11-55, 6-30, 10-50 and 3-15 respectively.

In this study we defined the severity of each area in four categories as follows; “None” if the score is 0, “mild” if the score is between 0 and one-third of the full score, “moderate” for scores between one-third and two-thirds of full score, and “severe” for scores between two-thirds and full score (Table 1).

**Table 1** Classification of PBC-40 Field Scores by Severity.

	None	Mild	Moderate	Severe
<b>Other symptoms</b> (7-35)	0	0-11	11-24	24-35
<b>Pruritus</b> (3-15)	0	0-5	5-10	10-15
<b>Fatigue</b> (11-55)	0	0-18	18-36	36-55
<b>Cognition</b> (6-30)	0	0-10	10-20	20-30
<b>Social</b> (10-50)	0	0-16	16-32	32-50
<b>Emotional</b> (3-15)	0	0-5	5-10	10-15

### Statistical analysis

All statistical analyzes were performed using SPSS® Statistical version 22 (IBM). Continuous variables are presented as mean (standard deviation) if normally distributed, otherwise as median (interquartile range), categorical variables are presented as numbers and percentages. Chi-square test was used within statistical analysis between categorical variables. The Mann-Whitney U test was used for comparisons between groups for continuous variables. P value less than 0.05 was considered statistically significant.

### Results

#### Clinical and demographic characteristics of the patients

37 patients with PBC were included in the study. 35 (94.6%) of the patients were female and 2 (5.4%) were male. The mean age of the patients was 54 (35-69). The median body mass index (BMI) of the patients was 28 (21.7-39.5) kg/m<sup>2</sup>. The mean disease duration was 6 years, the shortest disease duration was 1 year, and the longest disease duration was 16 years. Education level, marital status, habits and comorbid diseases are summarized in Table 2.

**Table 2** Demographic characteristics of the patients included in the study

Variable	n (%)
Age, Mean ± SD (min-max)	54.24±8.64 (35-69)
Sex	
Female	35 (94.6)
Male	2 (5.4)
BMI, kg/m <sup>2</sup>	28.09 ±4.58 (21.7-39.5)
Duration of disease (yrs.), mean ±SD (min-max)	5.95±3.50 (1-16)
Education level	
Primary	17 (45.9)
Secondary	15 (40.5)
University	5 (13.5)
Marital status	
Married	30 (81.1)
Single	2 (5.4)
Widow	5 (13.5)
Work status	
House wife	26 (70.3)
Working	11 (29.7)
Smoking habit	
Smoker	11 (29.7)
Never smoked	22 (59.5)
Former smoker	4 (10.8)
Presence of other autoimmune disease	
Present	17 (45.9)
Absent	19(51.7)

#### Evaluation of biochemical parameters

In evaluating of biochemical parameters, mean values of AST, ALT, total protein, albumin, total bilirubin, international correction ratio (INR), creatinine, total IgG, erythrocyte sedimentation rate (ESR) values were within the normal limits. The mean value of ALP was 145.05±92.30 U/L and was above the normal limits. The summary of evaluation of the biochemical parameters of the patients is shown in Table 3.

When categorizing patients in terms of autoantibody positivity, 32 patients (86.5%) were found to be AMA positive, 6 patients (16.20%) anti-sp100 positive, 6 patients (16.20%) anti-gp210 positive and 19 patients (51.4%) antinuclear

antibody (ANA) positive. Liver biopsy findings of 20 patients were compatible with PBC. Three of the patients (8.1%) had compensated cirrhosis. The clinical and autoimmune markers of the patients are summarized in Table 4.

Variable	Mean ±SD(min-max)
ALP	145.05±92.30 (63-555)
GGT	59.03±49.95 (16-226)
AST	32.54±27.98 (15-174)
ALT	27.00±18.26 (8-92)
Total bilirubin	0.66±0.25 (0.27-1.55)
Total protein	7.53±0.48 (6.7-8.5)
Albumin	4.21±0.31 (3.5-4.8)
Creatinine	0.67±0.16 (0.33-1.05)
INR	0.97±0.10 (0.61-1.20)
ESH	31.11±14.57 (10-79)
Total Ig G	1400.59±236.50 (962-1900)

Variable	n(%)
AMA positive	32 (86.5)
Anti sp100 positive	6 (16.20)
Anti gp210 positive	6 (16.20)
ANA positive	19 (51.4)
Compensated cirrhosis	3 (8.1)
Liver biopsy compatible	20 (54.1)
Liver size	
Normal	31 (83.8)
>16cm	6 (16.2)

### Evaluation of the patients' performance from the PBC-40 Questionnaire.

The highest and lowest mean field scores were observed in fatigue (24.35±9.47) and itching (3.93±2.80) domains, respectively. Score averages of the 6 domains of the PBC-40 are summarized in Table 5. When evaluating the PBC-40 questionnaire scores from each domain in terms of severity, we found that majority of patients in itch %40.4 (n=19) and social %42,6 (n=20) domains had mild severity, as for fatigue %42.6 (n=20), cognitive %36 (n=17), emotional %40.4 (n=19) and other symptoms %44.7 ((n=21) domains had moderate severity. Classification of the domains of PBC-40 questionnaire in terms of severity is summarized in Table 6.

Variable	mean SD (min-max)
Itching	3.93±2.80 (0-11)
Fatigue	24.35±9.47 (7-44)
Cognitive	13.59±6.31 (6-27)
Emotional	8.22±3.44 (3-15)
Social	16.86±5.85 (9-37)
Other symptom	13.24±4.60 (6-25)

Variable	None n (%)	Mild n (%)	Moderate n (%)	Severe n (%)
Itch	6 (12.8)	19 (40.4)	10 (21.3)	2 (4.3)
Fatigue	0 (0)	12 (25.5)	20 (42.6)	5 (10.6)
Cognitive	0 (0)	13 (27.7)	17 (36.2)	7 (14.9)
Social	0 (0)	20 (42.6)	16 (34)	1 (2.1)
Emotional	0 (0)	6 (12.8)	19 (40.4)	12 (25.5)
Other symptoms	0 (0)	15 (31.9)	21 (44.7)	1 (2.1)

Analyzing of the domains of the PBC-40 questionnaire according to the presence of antibodies is summarized in Table 7. No statistically significant difference was found between the anti gp-210 positive and negative groups among domains of the PBC-40 questionnaire (p>0.05).

When comparing between AMA positive and AMA negative groups, a statistically significant high value in itching was found in the AMA positive group (p=0.007). However, in other PBC-40 domains a statistically significant difference was not found among AMA negative and positive groups.

	Anti gp210 +	Anti gp210 -	P	AMA -	AMA +	P
Itch	5 (0-11)	3.5 (0-11)	0.809	5 (3-11)	3 (0-11)	0.007
Fatigue	26 (11-43)	16.5 (6-26)	0.785	27 (7-44)	25.5 (7-36)	0.508
Cognitive	16 (6-27)	16.5 (6-26)	0.845	18 (6-27)	10.5 (6-24)	0.019
Social	15 (11-37)	19 (9-24)	0.815	14 (11-37)	15.5 (9-30)	0.679
Emotional	9 (3-15)	7 (3-15)	0.410	8 (5-15)	8 (3-15)	0.803
Other symptoms	12 (9-22)	10 (10-20)	0.969	12 (9-22)	11,5 (6-20)	0.360

Mann-Whitney U test was used, p value <0.05 was statistically significant, AMA; anti-mitochondrial antibody.

Correlation analysis evaluating the relationship between itching and biochemical parameters is summarized in Table 8. According to the evaluation, no statistically significant correlation was found between itching and any of the biochemical parameters (p>0.05).

Variable	r	p
Itch		
ALP	0.084	
GGT	-0.060	0.806
AST	-0.042	0.806
ALT	-0.122	0.471
Total bilirubin	-0.136	0.423
Albumin	-0.239	0.155
Creatinine	-0.295	0.076
INR	0.063	0.713
ESR	-0.017	0.922
Total Ig G	0.075	0.658

Spearman correlation was used, p value <0.05 was statistically significant, ALP; alkaline phosphatase, GGT: gamma-glutamyl transferase, AST: aspartate aminotransferase, ALT: alanine aminotransferase, INR: international normalized ratio ESR: erythrocyte sedimentation rate.

### Discussion

PBC is a chronic autoimmune liver disease characterized by progressive inflammation and eventual destruction of the small intrahepatic bile ducts. Symptoms such as itching, cognitive impairment and fatigue negatively affect the quality of life in PBC patients. HRQOL in these patients can be assessed using questionnaires, which may or may not be specific to the disease. One of these questionnaires is PBC-40. PBC-40 questionnaire was developed focusing on the course of the disease, its treatment and the physical, emotional and functional status of the patients.

Studies have shown that evaluation of fatigue, itching and other symptoms, as well as emotional, social and cognitive vitality indices by the PBC-40 questionnaire to be useful and reliable both in research and clinical practice [5]. In this study, using the PBC-40 questionnaire we evaluated the relation between the patients' quality of life and clinical findings, laboratory values, and demographic characteristics. According to our literature review, we did not come across a study evaluating HRQOL in PBC patients from Turkey.

PBC is known to be predominant in women. In our study, 95% of the patients were women. In an epidemiological study, the mean age of patients diagnosed with PBC was 51 years. As for our study, the mean age was found to be 54 years. Our findings, showed almost similar features with previous studies on PBC in terms of both gender and age [6].

Autoimmune injury is inherent in PBC. In addition, PBC may be associated with other autoimmune diseases. In our study, we found that approximately 46% of the patients had an autoimmune disease accompanying PBC. According to the literature, the distribution of autoimmune disease accompanying PBC is variable, although seen frequently, it was similar to the findings we found in our study [7,8].

ALP elevation is typical in PBC. In our study, the mean ALP was found to be 145.05 U/L and it was above the normal limits. Fatigue has been shown to be an important cause in the deterioration of quality of life in PBC patients [4]. Fatigue; Among the symptoms, as shown in other studies also, in our study it had the highest impact on HRQOL [9].

Itching, while an important symptom that affects the quality of life of PBC patients, has a less frequent effect in this study. This is more likely considered to be because of the availability and effectiveness of treatments for itching rather than the weakness of the PBC-40 questionnaire [5]. We also think that itching was less common in the patients included in our study due to the exclusion of decompensated cirrhotic patients and most of the patients were under regular treatment with ursodeoxycholic acid therapy. In this study, we performed a correlation analysis between the itching and biochemical values. However, we did not find any statistically significant correlation. In one study, a positive correlation was found between the emotional domain of PBC-40 with ALP and GGT levels [9]. In another study, itching

was shown to be more common in cirrhotic patients than in non-cirrhotic patient [10].

A study found that anti-gp210 seropositivity was associated with worse itching, cognitive, social and emotional state. In the same study, no difference was found between AMA positive and negative patients among the domains of PBC-40 [10]. In our study, anti-gp210 positivity was not associated with any statistically significant difference among all domains of PBC-40. Also of note is we found that, between AMA positive and negative groups, a statistically significant higher incidence of itching in the AMA positive group.

We found a significant symptom burden and HRQOL disorder associated with PBC disease. In terms of severity, from all domains of the PBC-40 questionnaire, the least (21.3%) in itching and the most in other symptoms domain (44.7%), we found that they were moderately affected. Accordingly, we can say that half or at least a quarter of the patients lived with a significant burden of the disease in their daily life regardless of its severity.

## Limitations

In the beginning of the study, we had planned to include 50 participants to the study but due to the ongoing COVID-19 pandemic the targeted number could not be reached. The limitations of our study were the few number of participants and the study being a single-centered study.

## Conclusion

According to the World Health Organization, health is defined as, not only as the absence of infirmity or sickness but a state of complete physical, mental and social well-being. And if any of these is broken, the person cannot be considered healthy. Therefore, further research, specific to each community, is needed to develop modalities that will increase the quality of life in patients with PBC and minimize the negative effects of the disease.

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