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Original Article

Analysis of Quality of Life in Patients with Primary Biliary Cholangitis: A Cross-Sectional Observational Study

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Abstract

Background and objectives: Primary biliary cholangitis (PBC) significantly impairs health-related quality of life (HRQL), yet the impact of disease stage and fatigue on HRQL and psychological status remains insufficiently quantified. This study aimed to investigate differences in HRQL across disease stages and the impact of fatigue in patients with PBC.

Methods: This cross-sectional study recruited 219 patients with PBC from two Chinese tertiary hospitals (2011–2024). After excluding one preclinical case, 218 patients were analyzed. Quality of life was assessed using the validated Chinese versions of the SF-36 and Chronic Liver Disease Questionnaire (CLDQ); psychological status was assessed using the Self-Rating Anxiety Scale and Self-Rating Depression Scale. Between-group differences were quantified by mean differences (MDs) and odds ratios (ORs) with 95% confidence intervals (CIs). Baseline characteristics were balanced across stages (all $P > 0.05$).

Results: Of the 218 patients (90.4% female; mean age, 57.2 ± 10.3 years), 41 were in the clinical stage, 75 in the fibrosis stage, and 102 in the cirrhosis stage. SF-36 scores were lowest in the cirrhosis stage (e.g., Physical Functioning MD, 17.26; 95% CI, 6.93–27.59 vs. clinical stage), with similar declines in CLDQ domains. Anxiety was highest in the clinical stage (58.5%; OR vs. cirrhosis, 4.13; 95% CI, 1.92–8.92), whereas depression was highest in the cirrhosis stage (55.9%; OR vs. clinical stage, 4.50; 95% CI, 1.95–10.38). Fatigue prevalence was 66.1% and increased with disease stage. Patients with fatigue had lower SF-36 scores in Physical Functioning, Bodily Pain, Vitality, Mental Health, and Physical Component Summary (e.g., Physical Component Summary MD, 38.22; 95% CI, 10.41–66.02).

Conclusions: HRQL declines progressively with PBC stage. Fatigue is strongly associated with impaired HRQL and is closely interrelated with anxiety and depression. Stage-specific psychological patterns suggest the need for tailored supportive interventions.

Introduction

Primary biliary cholangitis (PBC) is a chronic autoimmune liver disease that may progress to cirrhosis and liver failure.[1] Its clinical burden is marked by a substantial decline in health-related quality of life (HRQL). Fatigue represents the most prevalent and distressing symptom.[2] Current clinical treatments may offer limited improvement for the patient-reported symptom burden of PBC, including PBC-related fatigue, particularly in patients with moderate-to-severe pruritus. Even patients receiving standard ursodeoxycholic acid (UDCA) therapy may commonly experience significant fatigue-related impairment. The second-line medication obeticholic acid (OCA) is mainly supported by improvements in surrogate biochemical markers and may not effectively alleviate this symptom burden; some patients even experience worsened discomfort, particularly pruritus, due to drug adverse effects or treatment intolerance. Furthermore, fatigue often persists after liver transplantation.[2-6] International guidelines have explicitly designated fatigue as a key indicator of poor prognosis in patients with PBC. Early assessment and management of fatigue are therefore essential to mitigate HRQL deterioration.[2] With evolving medical concepts, diagnostic advancements, and widespread

Keywords: Primary biliary cholangitis; Clinical staging; Health-related quality of life; Fatigue; Cross-sectional study; SF-36; Chronic Liver Disease Questionnaire; CLDQ; Self-Rating Anxiety Scale; SAS; Self-Rating Depression Scale; SDS.
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chronic disease management, systematic evaluation and enhancement of quality of life (QoL) have become integral to the comprehensive diagnosis and treatment of PBC.

Although fatigue and impaired HRQL are well-recognized concerns in patients with PBC, the stage-specific patterns of HRQL impairment and psychological distress remain insufficiently characterized, particularly in Chinese patients. In addition, the relationship among fatigue, disease stage, anxiety, depression, and HRQL has not been fully quantified. Therefore, this study aimed to evaluate HRQL, fatigue, anxiety, and depression in patients with PBC at different clinical stages, and to clarify the association between fatigue and HRQL, thereby providing evidence for stage-specific comprehensive management of PBC.

Materials and methods

Study design and participants

This questionnaire-based cross-sectional study adhered to the STROBE Statement and systematically assessed HRQL, fatigue, and psychological status in 218 patients with PBC across different clinical stages, recruited from two tertiary hospitals in China. The sample size was determined a priori based on the primary outcome.

Between January 2011 and December 2024, a total of 219 patients with confirmed PBC were recruited from Longhua Hospital Affiliated with Shanghai University of Traditional Chinese Medicine and Hangzhou Xixi Hospital. The study flow diagram is presented in Figure 1. Among them, 171 were outpatients from Longhua Hospital and 48 were inpatients from Hangzhou Xixi Hospital. One preclinical-stage patient was excluded because of the extremely small subgroup size to avoid potential bias. The final 218 patients were included in the statistical analysis (Fig. 1). This cross-sectional study had no loss to follow-up, and all enrolled patients completed the questionnaire assessments.

According to the 2017 European Association for the Study of the Liver Clinical Practice Guidelines for PBC,[1] the diagnosis was confirmed if at least 2 of the following 3 criteria were met:

(1) Antimitochondrial antibody (AMA) titer > 1:40 (or positive AMA-M2);

(2) Alkaline phosphatase (ALP) > 2 × the upper limit of normal (ULN) or γ-glutamyl transferase (GGT) > 5 × ULN;

(3) Histological evidence of nonsuppurative destructive cholangitis and interlobular bile duct destruction on liver biopsy.

Inclusion criteria included:

(1) Meeting the above PBC diagnostic criteria;

(2) Age 18–75 years;

(3) Ability to complete the scale assessment independently or with standardized researcher assistance;

(4) Voluntary participation in the study and provision of written informed consent.

Exclusion criteria included:

(1) Liver disease with concomitant hepatotropic viral infection;

(2) Patients with Child-Pugh class C cirrhosis;

(3) Patients with severe underlying cardiac, renal, pulmonary, endocrine, hematologic, metabolic, or gastrointestinal disorders, or psychiatric disorders;

(4) Pregnant or lactating women;

(5) Patients with allergic constitutions or multiple drug allergies;

(6) Noncooperative patients.

The primary outcome was the prevalence of fatigue. The required sample size was calculated using the single-population proportion formula: $n = Z^2_{\alpha/2} \times p \times (1 - p) / d^2$.

Where $Z_{\alpha/2} = 1.96$ (95% confidence level), p denotes the expected prevalence of fatigue, and d represents the absolute precision. Based on previous studies reporting PBC-related fatigue prevalence between 50% and 70%, a conservative estimate of 60% ($p = 0.60$) was adopted,[1] with d set at 0.065. This yielded a minimum sample size of 218 participants. Given the consecutive enrollment design and the high completion rate of supervised questionnaire administration, no inflation for non-response was applied. Ultimately, 218 patients met the inclusion criteria, provided informed consent, and completed all assessments with valid data, thereby fulfilling the sample size requirement.

The study flow diagram is presented in Figure 1.

Measures and procedures

All scales used in this study were validated Chinese versions with satisfactory reliability and validity. The Chinese version of the SF-36 was reported by Li *et al*.[7] in 2002, with Cronbach's α ranging from 0.72 to 0.88. The Chinese version of the LDQOL 1.0 was reported by Qi *et al*.[8] in 2015 and showed satisfactory reliability and validity overall, although several dimensions had Cronbach's alpha coefficients below 0.70.The Self-Rating Depression Scale (SDS) were originally developed by Zung in 1965,[9] and Self-Rating Anxiety Scale (SAS) were originally developed by Zung in 1971.[10] The Chinese revised version by Wang *et al*.[11,12] in 1984 was adopted in this study, with Cronbach's α ranging from 0.83 to 0.86.

All assessments were conducted in a quiet and independent clinical interview room by trained researchers following unified standard operating procedures. Standardized assistance procedures were provided for patients unable to read and write independently. Researchers read each scale item verbatim, offered no prompts, suggestions, or subjective interpretations, and recorded patient responses accurately and independently.

All investigators completed unified professional training before study initiation, covering scale interpretation, standardized assistance skills, and quality control protocols. All researchers passed post-training assessments with inter-rater consistency (Kappa > 0.85) to ensure reproducibility of the assessment process.

Complete baseline data were collected for all enrolled patients. Missing data were minimal and handled using the mean of completed items within each scale domain when less than 20% of items were missing; otherwise, the domain score was treated as missing. No imputation was performed for missing baseline variables.

HRQL, fatigue, and psychological status in patients with PBC were analyzed according to clinical staging and the presence or absence of fatigue.

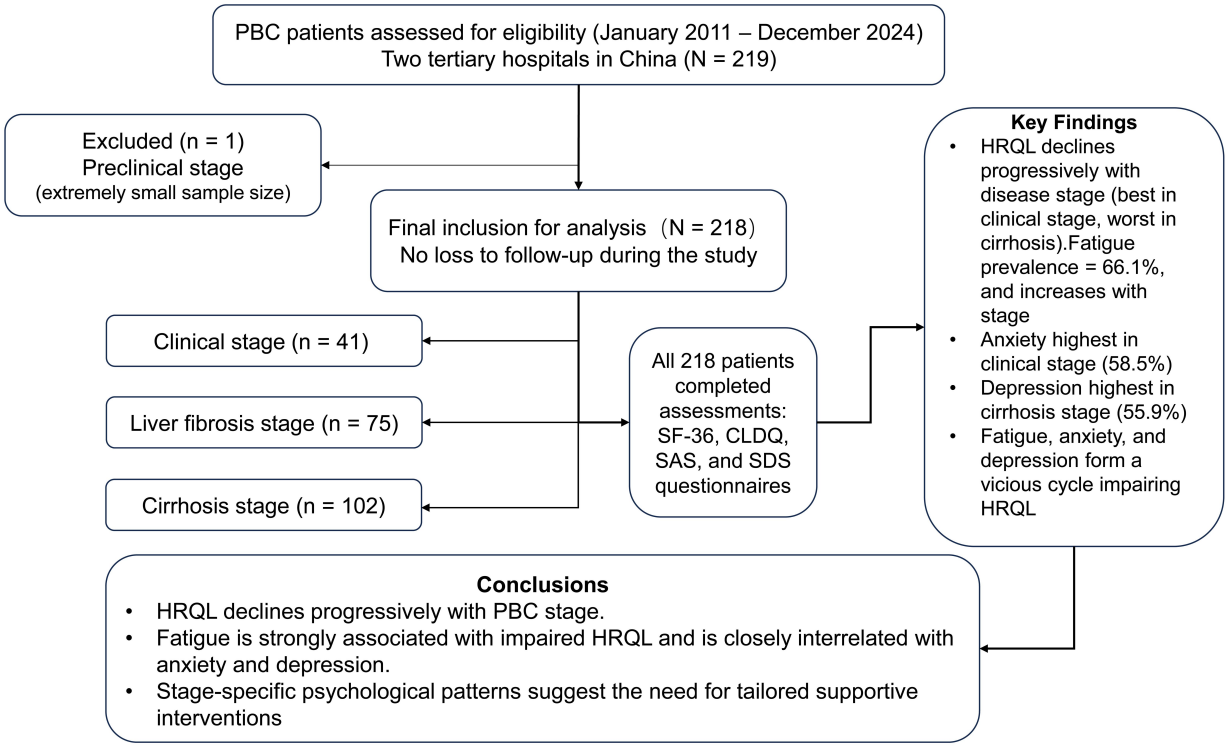

Fig. 1. Study flow diagram of patient enrollment and analysis. This flowchart illustrates the enrollment process of patients with primary biliary cholangitis (PBC) from two tertiary hospitals in China between January 2011 and December 2024. A total of 219 patients were assessed for eligibility. One patient in the preclinical stage was excluded due to the extremely small subgroup size. The remaining 218 patients were included in the final analysis and were classified into three clinical stages: clinical stage (n = 41), liver fibrosis stage (n = 75), and cirrhosis stage (n = 102). All 218 patients completed the SF-36, CLDQ, SAS, and SDS questionnaires. Key findings: HRQL declines progressively with disease stage (best in clinical stage, worst in cirrhosis); fatigue prevalence = 66.1% and increases with stage; anxiety highest in clinical stage (58.5%); depression highest in cirrhosis stage (55.9%); fatigue, anxiety, and depression form a vicious cycle impairing HRQL. CLDQ, Chronic Liver Disease Questionnaire; HRQL, health-related quality of life; SAS, Self-Rating Anxiety Scale; SDS, Self-Rating Depression Scale.

Scale evaluation criteria

SF-36 scale evaluation criteria

The validated Chinese version of the SF-36 was used, covering eight domains: Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role Emotional (RE), and Mental Health (MH). Two summary scores were derived: the Physical Component Summary (PCS) and the Mental Component Summary (MCS).

CLDQ evaluation criteria

The liver disease-specific validated Chinese version of the CLDQ was used, including six domains: Abdominal Symptoms (AS), Fatigue (FA), Systemic Symptoms (SS), Activity (AC), Emotional Function (EF), and Worry (WO). Higher scores reflect better QoL.

SAS and SDS evaluation criteria

The validated Chinese versions of the SAS and SDS were used, both comprising 20 items. The anxiety/depression index (R value) is calculated and stratified to indicate severity: < 0.5 (none), 0.50–0.59 (mild), 0.60–0.69 (moderate), ≥ 0.70 (severe).

Clinical staging of PBC

Based on the natural history of PBC and combined with standardized and operable clinical assessment criteria (imaging, serology, histology),[1] the staging criteria were defined as follows:

(1) Preclinical stage: Normal liver function indicators and no abnormal liver structure on imaging examinations (abdominal ultrasound/ computed tomography (CT)/ magnetic resonance imaging (MRI)), with only positive AMA/AMA-M2;

(2) Clinical stage: Abnormal liver function (persistent elevation of ALP/GGT), with no evidence of liver fibrosis or cirrhosis on abdominal ultrasound/CT/MRI or liver fibrosis serological indicators (hyaluronic acid, laminin, type III procollagen peptide, type IV collagen);

(3) Liver fibrosis stage: Abnormal liver function, with definite evidence of liver fibrosis (abdominal ultrasound/CT showing heterogeneous liver parenchyma, liver fibrosis serological index > 2 × ULN, or liver histology showing S1–S3 fibrosis);

(4) Cirrhosis stage: Abnormal liver function, with definite evidence of liver cirrhosis (abdominal ultrasound/CT showing nodular liver surface, splenomegaly, portal hypertension signs, or liver histology showing S4 fibrosis/cirrhosis).

Fatigue definition

Fatigue was defined by a combination of subjective self-report and objective scale assessment (referring to the optimal cut-off value for PBC fatigue assessment in previous studies[13]): patients self-reported persistent or recurrent fatigue/lethargy for more than 2 weeks (affecting daily life or activities), combined with a CLDQ-FA domain score < 23 points.

Baseline data collection

Standardized collection of complete baseline data for all enrolled patients was conducted by trained researchers, including:

(1) General demographic information: sex, age;

(2) Liver function parameters: ALP, GGT, alanine aminotransferase, aspartate aminotransferase, total bilirubin, albumin;

(3) Comorbidities: hypertension, diabetes, hypothyroidism, sleep disorders, etc.;

(4) Medication use: UDCA, OCA, antihypertensive drugs, antidiabetic drugs, etc.

Statistical methods

Statistical analyses were performed using SPSS version 21.0 (IBM Corp.). Continuous variables were expressed as mean ± standard deviation and compared using one-way ANOVA with post hoc Tukey tests for three-group comparisons or independent-samples t-tests for two-group comparisons, following tests of normality and homogeneity of variance. Non-normally distributed data were analyzed using the Kruskal–Wallis test with Dunn–Bonferroni correction or the Mann–Whitney U test. Categorical variables were presented as counts and percentages and compared using the chi-square test or Fisher's exact test. Between-group differences in HRQL, fatigue, and psychological status across clinical stages were quantified using effect sizes and 95% confidence intervals (CIs), as appropriate.

Results

General information

Of the 219 cases, one preclinical case was excluded due to the small sample size. The remaining 218 patients included 41 in the clinical stage, 75 in the fibrosis stage, and 102 in the cirrhosis stage.

In this study, females accounted for 90.4% of the total cohort and males accounted for 9.6%, with a female-to-male ratio of approximately 9.4:1. This distribution is consistent with the epidemiological characteristics of PBC, which predominantly affects middle-aged and elderly women. The sex distribution was balanced and comparable among the three groups, with no statistically significant difference ($P > 0.05$). Regarding age, the overall mean age was 57.21 ± 10.33 years. Patients in the liver fibrosis stage had a slightly lower mean age (55.45 ± 9.77 years), while those in the cirrhosis stage had a slightly higher mean age (58.70 ± 10.11 years); however, the differences among the three groups were not statistically significant ($P > 0.05$). Age stratification analysis showed that patients in the clinical stage were predominantly aged 60–69 years (36.6%), those in the liver fibrosis stage were predominantly aged 50–59 years (37.3%), and those in the cirrhosis stage were predominantly aged 60–69 years (39.2%). Notably, the proportion of patients aged ≥ 70 years was highest in the cirrhosis stage (18.6%), suggesting that advanced age may be associated with disease progression (Table 1).

HRQL of PBC patients at different clinical stages

Comparison of SF-36 scores among PBC patients at different clinical stages

Scores in the clinical stage were higher than those in the cirrhosis stage across all domains ($P < 0.05$), with significant differences in PF, BP, GH, VT, RE, and MH ($P < 0.001$). The clinical stage also exceeded the fibrosis stage in GH, VT, RE, MH, PCS and MCS ($P < 0.05$). The fibrosis stage exceeded the cirrhosis stage only in BP ($P < 0.05$). PCS and MCS were higher in the clinical stage compared with both the fibrosis and cirrhosis stages ($P < 0.05$) (Table 2).

Comparison of CLDQ scores among PBC patients at different clinical stages

Scores in the clinical stage exceeded those in the cirrhosis stage in AS, FA, SS, AC, and EF ($P < 0.05$). The clinical stage exceeded the fibrosis stage in AS, EF and AC ($P < 0.05$). The fibrosis stage exceeded the cirrhosis stage in SS, AC, and WO ($P < 0.05$) (Table 3).

Psychological status and disease stage of PBC patients

Comparison of anxiety levels among PBC patients at different clinical stages

Analysis of psychological status among 218 patients with PBC revealed distinct stage-specific patterns of anxiety and depression. The overall prevalence of anxiety was 32.6%, with the highest rate observed in the clinical stage (58.5%), followed by the liver fibrosis stage (28.0%) and the cirrhosis stage (25.5%). Patients in the clinical stage had a significantly higher risk of anxiety compared with those in the cirrhosis stage (OR = 4.13, 95% CI: 1.92–8.92, $P < 0.001$) and the fibrosis stage (OR = 3.64, 95% CI: 1.63–7.46, $P = 0.001$) (Table 4).

Comparison of depression levels among PBC patients in different clinical stages

In contrast, the overall prevalence of depression was 43.6%, with rates increasing progressively across disease stages: clinical stage (22.0%), liver fibrosis stage (38.7%), and cirrhosis stage (55.9%). Patients in the cirrhosis stage exhibited a significantly higher risk of depression compared with those in the clinical stage (OR = 4.50, 95% CI: 1.95–10.38, $P < 0.001$) and the fibrosis stage (OR = 2.01, 95% CI: 1.10–3.69, $P = 0.024$) (Table 5).

Impact of fatigue on QoL in PBC patients

This study analyzed 218 patients with PBC (fatigue group: 144, 66.1%; non-fatigue group: 74, 33.9%) and found that the fatigue group scored significantly lower in multiple SF-36 dimensions, with statistically significant differences in BP ($P = 0.001$), PCS ($P = 0.007$), VT ($P = 0.009$), PF ($P = 0.027$), and MH ($P = 0.045$). The impact on physical domains (PCS, PF, BP) was greater than on mental domains, indicating that fatigue primarily impairs physical functional status rather than purely psychological well-being. The two groups showed no significant differences in any CLDQ domains (AS, FA, SS, AC, EF, WO) ($P > 0.05$), suggesting

Table 1. Baseline characteristics of PBC patients by clinical stage

Characteristic	Clinical stage (n = 41)	Liver fibrosis stage (n = 75)	Cirrhosis stage (n = 102)	*P*-value
Age (years, mean ± SD)	56.78 ± 11.05	55.45 ± 9.77	58.70 ± 10.11	0.109
Sex, female (n, %)	37 (90.2%)	68 (90.7%)	92 (90.2%)	0.845
AST (U/L, mean ± SD)	28.44 ± 8.80	29.77 ± 9.08	29.41 ± 9.64	0.73
ALT (U/L, mean ± SD)	23.55 ± 12.04	22.37 ± 11.91	23.55 ± 12.64	0.788
GGT (U/L, mean ± SD)	43.55 ± 26.31	40.61 ± 25.64	47.12 ± 26.78	0.245
ALP (U/L, mean ± SD)	106.86 ± 34.30	103.91 ± 33.46	105.46 ± 51.50	0.93
ALB (g/L, mean ± SD)	42.37 ± 5.65	42.31 ± 5.16	41.33 ± 6.70	0.422
TBil (μmol/L, mean ± SD)	16.00 ± 8.33	15.87 ± 8.21	14.34 ± 7.36	0.279
Comorbidities (n, %)				
Hypertension	8 (19.5%)	16 (21.3%)	28 (27.5%)	0.493
Diabetes	5 (12.2%)	11 (14.7%)	20 (19.6%)	0.485
Thyroid disease	4 (9.8%)	9 (12.0%)	19 (18.6%)	0.288
Medication use (n, %)				
UDCA	41 (100%)	75 (100%)	102 (100%)	-
OCA	2 (4.9%)	5 (6.7%)	9 (8.8%)	0.689

There were no statistically significant differences in age, sex, liver function parameters, comorbidities, or medication use among the three groups ($P > 0.05$), indicating that baseline characteristics were balanced and comparable across groups. Liver function parameters were measured at stable treatment follow-up (not at diagnosis), which explains the relatively normal ALP/GGT levels. Clinical staging was based on diagnostic criteria at initial diagnosis. ALB, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, γ-glutamyl transferase; OCA, obeticholic acid; SD, standard deviation; TBil, total bilirubin; UDCA, ursodeoxycholic acid.

that the impact of fatigue on QoL is more reflected in general health perception than in liver disease-specific symptoms. The fatigue prevalence of 66.1% is consistent with the literature, confirming fatigue as one of the most common symptoms in PBC. Although the CLDQ-FA domain score did not differ between the fatigue and non-fatigue groups as defined by the composite criteria, this may reflect that the subjective self-report component played a dominant role in fatigue classification (Table 6).

Discussion

PBC is a chronic progressive autoimmune liver disease that imposes a clinical burden not only through abnormal biochemical markers and progression toward cirrhosis and liver failure,[1] but more profoundly through multidimensional impairment of patients' HRQL. Adhering to the STROBE Statement, this cross-sectional study systematically analyzed the HRQL, fatigue, and psychological status of 218 patients with PBC at different clinical stages from two tertiary hospitals in China. The findings confirmed a progressive decline in HRQL with disease progression and identified stage-specific characteristics of fatigue and psychological status (anxiety and depression). Furthermore, by calculating MDs and ORs with 95% CIs, this study quantified clinical differences in related indicators and clarified associations with fatigue, thereby supplementing quantitative clinical evidence for HRQL management in the Chinese PBC population.

As a large-sample cross-sectional observational study, this research systematically analyzed QoL and the impact of fatigue in patients with PBC across different clinical stages. The results show that patients' QoL declines progressively as the disease advances. Those in the clinical stage maintain relatively better PF, MH, and emotional well-being due to milder liver damage. In contrast, patients with cirrhosis experience widespread QoL deterioration driven by disease progression and higher complication risk.

These findings align with a prior cross-geographical study by Montali *et al*.,[3] which analyzed patients with PBC from Italy, Japan, the UK, and other regions. That study confirmed a clear, consistent association between disease progression and QoL decline across diverse populations. Our results are also supported by a 2022 systematic review and meta-analysis by Choo *et al*.,[14] which included 11 clinical studies (covering chronic liver disease and liver transplant patients). The review found that physical function and aerobic capacity decrease steadily with advancing disease stage—consistent with our observations in patients with PBC—further validating the negative impact of disease progression on HRQL.

The liver fibrosis stage is a critical transitional phase. While our study found QoL at this stage is better than in cirrhosis, significant declines are already evident in key areas such as general health and mental well-being. This highlights the liver fibrosis stage as a critical window for intervention. Following the stepped management strategy outlined in the 2023 Quality Standards and Recommendations for Primary Biliary Cholangitis Management,[5] initiating comprehensive care at this stage (including antifibrotic therapy, symptom control, and lifestyle modification) may slow

Table 2. SF-36 scores of PBC patients at different clinical stages (mean ± SD, n = 218)

Dimensions	Clinical stage (n = 41)	Liver fibrosis stage (n = 75)	Cirrhosis stage (n = 102)	MD (95% CI)[1]	MD (95% CI)[2]	MD (95% CI)[3]	*P*-value
PF	84.27 ± 21.20	75.13 ± 28.38	67.01 ± 30.70	17.26(6.93-27.59)	9.13(-1.72-19.99)	8.12(-0.37-16.62)	< 0.001
RP	75.00 ± 55.90	56.67 ± 56.10	46.08 ± 47.30	28.92(9.93-47.92)	18.33(-1.62-38.28)	10.59(-5.04-26.21)	0.003
BP	75.63 ± 18.06	71.91 ± 23.23	62.76 ± 23.78	12.87 (4.62-21.12)	3.73 (-4.94-12.39)	9.14 (2.36-15.93)	0.002
GH	49.49 ± 14.78	36.17 ± 15.52	38.07 ± 14.88	11.42 (5.92-16.92)	13.31 (7.54-19.09)	-1.90(-6.42-2.63)	< 0.001
VT	66.95 ± 19.74	57.67 ± 22.9	53.48 ± 23.76	13.47 (5.17-21.77)	9.28 (0.57-18.00)	4.19(-2.64-11.01)	0.002
SF	92.99 ± 22.89	88.17 ± 22.50	80.27 ± 26.64	12.72 (3.75-21.68)	4.82 (-4.60-14.24)	7.90 (0.52-15.27)	0.006
RE	88.62 ± 49.78	67.11 ± 50.67	55.88 ± 45.76	32.74 (15.15-50.32)	21.51 (3.03-39.98)	11.23(-3.24-25.70)	< 0.001
MH	74.83 ± 14.89	63.95 ± 18.71	59.69 ± 21.01	15.14 (8.14-22.15)	10.88 (3.53-18.24)	4.26(-1.50-10.02)	< 0.001
PCS	284.39 ± 84.63	239.88 ± 101.45	213.92 ± 98.92	70.47 (35.05–105.89)	44.51 (7.31–81.71)	25.96 (−3.17–55.09)	< 0.001
MCS	313.14 ± 74.88	268.56 ± 79.73	238.24 ± 91.99	74.90 (42.38–107.42)	44.58 (10.36–78.80)	30.32 (3.13–57.51)	< 0.001

[1]MD (95% CI) for clinical stage vs. cirrhosis stage; [2]MD (95% CI) for clinical stage vs. liver fibrosis stage; [3]MD (95% CI) for liver fibrosis stage vs. cirrhosis stage. BP, Bodily Pain; CI, confidence interval; GH, General Health; MCS, Mental Component Summary; MD, mean difference; MH, Mental Health; PBC, primary biliary cholangitis; PCS, Physical Component Summary; PF, Physical Functioning; RE, Role Emotional; RP, Role Physical; SD, standard deviation; SF, Social Functioning; VT, Vitality.

Table 3. CLDQ scores of PBC patients at different clinical stages (mean ± SD, n = 218)

Dimensions	Clinical stage (n = 41)	Liver fibrosis stage (n = 75)	Cirrhosis stage (n = 102)	MD (95% CI)[1]	MD (95% CI)[2]	MD (95% CI)[3]	*P*-value
Abdominal Symptoms (AS)	16.95 ± 2.17	15.68 ± 3.39	14.57 ± 3.37	2.38 (1.31–3.45)	1.27 (0.20–2.34)	1.11 (0.17–2.05)	< 0.001
Fatigue (FA)	24.05 ± 3.58	23.08 ± 3.99	20.76 ± 4.72	3.29 (1.61–4.97)	0.97 (−0.44–2.38)	2.32 (0.97–3.67)	< 0.001
Systemic Symptoms (SS)	27.29 ± 3.33	26.67 ± 4.06	24.22 ± 4.19	3.07 (1.61–4.53)	0.62 (−0.84–2.08)	2.45 (1.27–3.63)	< 0.001
Activity (AC)	16.37 ± 2.34	15.22 ± 3.31	13.54 ± 3.66	2.83 (1.71–3.95)	1.15 (0.10–2.20)	1.68 (0.70–2.66)	< 0.001
Emotional Function (EF)	42.45 ± 5.17	37.50 ± 6.19	36.25 ± 6.86	6.20 (3.92–8.48)	4.95 (2.75–7.15)	1.25 (−0.70–3.20)	< 0.001
Worry (WO)	22.10 ± 6.36	22.51 ± 4.98	20.18 ± 5.75	1.92 (−0.29–4.13)	−0.41 (−2.61–1.79)	2.33 (0.71–3.95)	0.015

[1]MD (95% CI) for clinical stage vs. cirrhosis stage; [2] MD (95% CI) for clinical stage vs. liver fibrosis stage; [3] MD (95% CI) for liver fibrosis stage vs. cirrhosis stage. CI, confidence interval; CLDQ, Chronic Liver Disease Questionnaire; MD, mean difference; PBC, primary biliary cholangitis; SD, standard deviation.

Table 4. Anxiety status by clinical stage

Clinical stage	No anxiety (n, %)	With anxiety (n, %)	Total	Anxiety prevalence	Group comparison	OR (95% CI)	*P*-value
Clinical stage	17 (41.5%)	24 (58.5%)	41	58.50%	Clinical vs. Cirrhosis	4.13 (1.92-8.92)	< 0.001
Fibrosis stage	54 (72.0%)	21 (28.0%)	75	28.00%	Clinical vs. Fibrosis	3.64 (1.63-7.46)	0.001
Cirrhosis stage	76 (74.5%)	26 (25.5%)	102	25.50%	Cirrhosis vs. Fibrosis	0.88 (0.45-1.72)	0.709
Total	147 (67.4%)	71 (32.6%)	218	32.60%	Overall: $\chi^2 = 15.629$, $P < 0.001$		

CI, confidence interval; OR, odds ratio.

Table 5. Depression status by clinical stage

Clinical stage	No depression (n, %)	With depression (n, %)	Total	Depression prevalence	Group comparison	OR (95% CI)	*P*-value
Clinical stage	32 (78.0%)	9 (22.0%)	41	21.95%	Cirrhosis vs. Clinical	4.50 (1.95-10.38)	< 0.001
Fibrosis stage	46 (61.3%)	29 (38.7%)	75	38.67%	Fibrosis vs. Clinical	2.24 (0.94-5.37)	0.067
Cirrhosis stage	45 (44.1%)	57 (55.9%)	102	55.88%	Cirrhosis vs. Fibrosis	2.01 (1.10-3.69)	0.024
Total	123 (56.4%)	95 (43.6%)	218	43.58%	Overall: $X^2 = 14.816$, $P = 0.001$		

CI, confidence interval; OR, odds ratio.

QoL deterioration and provides a clear timeline for clinical management of PBC.

Fatigue affected 66.1% of patients with PBC in our study, with prevalence increasing with disease progression: 61.0% in the clinical stage, 61.3% in the fibrosis stage, and 72.5% in the cirrhosis stage. Patients without fatigue had significantly better QoL across PF, VT, and MH domains, confirming fatigue as a core driver of impaired QoL in PBC. Recent research suggests that PBC-related fatigue is complex: it is not only a consequence of liver damage but also a syndrome associated with central nervous system dysfunction, inflammatory factor-induced muscle changes, and autonomic nervous system abnormalities.[14,15] A 2018 review by Khanna *et al*.[15] further provided molecular insights, suggesting that bile acid accumulation may activate spinal dorsal horn neuron receptors, directly triggering fatigue. This may explain why traditional hepatoprotective therapies often fail to relieve fatigue, consistent with our findings.

Notably, the psychological status of patients with PBC varies by stage: anxiety is most common in the clinical stage (58.5%), while depression peaks in the cirrhosis stage (55.9%). Anxiety in patients with PBC may stem from uncertainty regarding prognosis and treatment outcomes. In advanced disease or transplant-related contexts, long-term symptom burden, reduced quality of life, and disease-related complications may contribute to depression.[16] Critically, fatigue, anxiety, and depression form a vicious cycle. Düll and Kremer reported that moderate-to-severe pruritus in patients with PBC may substantially impair quality of life, cause sleep deprivation and exhaustion, worsen fatigue, and contribute to depression and suicidal ideation.[17] Psychological distress may amplify the perception of fatigue, further worsening QoL—a finding supported by our data.

The clinical value of this study lies in identifying the pathway of "disease progression → fatigue → psychological distress → QoL decline", providing evidence to reshape PBC care. Clinical management should move beyond a narrow focus on liver function and adopt a patient-centered, comprehensive approach. First, routine fatigue screening using standardized tools such as the FACIT-Fatigue scale should be implemented,[13,18] along with active management of fatigue-exacerbating comorbidities including anemia, thyroid dysfunction, and sleep disorders. Second, psychological support should be tailored to disease stage: health education and cognitive behavioral therapy for early-stage anxiety, and enhanced psychological care with consideration of antidepressants for cirrhosis-related depression.[19] Third, supervised aerobic exercise—30–60 min three times weekly, such as treadmill walking or stationary cycling—is recommended. A 2022 meta-analysis by Choo *et al*.[14] confirmed that this improves aerobic capacity and physical function, indirectly alleviating fatigue. Fourth, emerging targeted therapies offer promise; 2023 guidelines note that ileal bile acid transporter inhibitors may

Table 6. Comparison of dimension scores between fatigued and non-fatigued PBC patients

Dimension	Non-fatigue group (n = 74)	Fatigue group (n = 144)	MD (95% CI)	t-value	*P*-value
PF	78.99 ± 24.49	70.00 ± 30.63	8.99 (1.04, 16.94)	2.231	**0.027**
RP	64.86 ± 53.46	50.17 ± 52.18	14.69 (-0.07, 29.45)	1.96	0.051
BP	75.80 ± 22.48	64.49 ± 22.63	11.30 (4.93, 17.68)	3.497	**0.001**
GH	41.70 ± 15.90	38.47 ± 15.66	3.24 (-1.20, 7.68)	1.439	0.152
VT	63.11 ± 22.19	54.55 ± 23.24	8.56 (2.13, 14.99)	2.621	**0.009**
SF	85.81 ± 23.89	85.16 ± 25.65	0.65 (-6.35, 7.66)	0.184	0.854
RE	72.97 ± 48.94	62.27 ± 49.59	10.70 (-3.22, 24.63)	1.515	0.131
MH	67.78 ± 19.83	62.06 ± 19.75	5.73 (0.13, 11.33)	2.016	**0.045**
HT	50.68 ± 26.81	45.83 ± 31.15	4.84 (-3.42, 13.11)	1.155	0.249
PCS	261.35 ± 95.63	223.13 ± 100.27	38.22 (10.41, 66.02)	2.711	**0.007**
MCS	277.24 ± 77.59	255.31 ± 93.66	21.93 (-2.00, 45.86)	1.807	0.072
AS	15.34 ± 3.69	15.44 ± 3.09	-0.11 (-1.06, 0.85)	-0.219	0.827
FA	22.07 ± 4.71	22.25 ± 4.37	-0.18 (-1.46, 1.09)	-0.284	0.777
SS	25.54 ± 4.92	25.72 ± 3.80	-0.17 (-1.34, 0.99)	-0.295	0.768
AC	14.70 ± 3.62	14.64 ± 3.45	0.06 (-0.93, 1.06)	0.126	0.900
EF	38.39 ± 6.77	37.49 ± 6.63	0.91 (-0.99, 2.81)	0.942	0.347
WO	21.88 ± 6.15	21.08 ± 5.46	0.80 (-0.81, 2.40)	0.978	0.329
Age	57.24 ± 8.94	57.21 ± 10.87	0.03 (-2.78, 2.85)	0.024	0.981

AC, Activity; AS, Abdominal Symptoms; BP, Bodily Pain; EF, Emotional Function; FA, Fatigue; GH, General Health; HT, Health Transition; MCS, Mental Component Summary; MD, mean difference; MH, Mental Health; PBC, primary biliary cholangitis; PCS, Physical Component Summary; PF, Physical Functioning; RE, Role Emotional; RP, Role Physical; SF, Social Functioning; SS, Systemic Symptoms; VT, Vitality; WO, Worry.

alleviate both pruritus and fatigue by disrupting enterohepatic bile acid circulation.[20] The 2025 ITCH-E study by Levy *et al*.[5] further demonstrated that targeted pruritus treatment interrupts the pruritus–sleep loss–fatigue cycle, significantly improving QoL.

However, this cross-sectional study has several limitations. First, the design identifies associations rather than dynamic changes or causal relationships; future prospective cohort studies should evaluate long-term disease progression, symptom evolution, and intervention effects. Second, potential unmeasured confounders—including UDCA or OCA dosage and duration, complication severity, and social support—may have influenced the results and should be incorporated in future studies. Third, fatigue assessment relied on subjective self-report scales without objective measures such as electromyography, neuroimaging, or inflammatory biomarkers; multimodal assessment would improve accuracy. Fourth, the sample was limited to two tertiary hospitals, introducing potential selection bias; multicenter studies with larger samples are needed to confirm generalizability. Fifth, the use of self-report scales may introduce recall bias and social desirability bias. Finally, clinical staging was determined based on medical records and standard diagnostic criteria, and some degree of misclassification cannot be fully excluded.

Conclusions

The QoL of patients with PBC showed a progressive decline with disease progression, with the highest QoL in the clinical stage and the lowest in the cirrhosis stage. Fatigue is significantly associated with impaired HRQL and is closely interrelated with anxiety and depression.

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Conflict of interest

The authors declare that they have no conflict of interest.

Author contributions

Conceptualization (SH), data curation (SH, SY, BZ), formal analysis (SH), writing – original draft (SH), resources (JG), investigation (JG, SY, BZ), supervision (WZ), project administration (WZ), writing – review & editing (WZ), and

funding acquisition (WZ). All authors reviewed and approved the final manuscript.

Ethical statement

This study was conducted in accordance with the Declaration of Helsinki (as revised in 2024) and was approved by the Institutional Review Board (or Ethics Committee) of Longhua Hospital Affiliated to Shanghai University of Traditional Chinese Medicine (Approval Number: 2020LCSY72). Written informed consent was obtained from all individual participants included in the study.

Data sharing statement

The datasets generated and analyzed during the current study are not publicly available due to patient privacy and confidentiality regulations but are available from the corresponding author on reasonable request.

References

[1] European Association for the Study of the Liver. EASL Clinical Practice Guidelines: The diagnosis and management of patients with primary biliary cholangitis. J Hepatol 2017;67(1):145–172. DOI: 10.1016/j.jhep.2017.03.022, PMID: 28427765.

[2] Carey EJ, Ali AH, Lindor KD. Primary biliary cirrhosis. Lancet 2015; 386(10003):1565–1575. DOI: 10.1016/S0140-6736(15)00154-3, PMID: 26364546.

[3] Montali L, Gragnano A, Miglioretti M, Frigerio A, Vecchio L, Gerussi A, *et al*. Quality of life in patients with primary biliary cholangitis: A cross-geographical comparison. J Transl Autoimmun 2021;4:100081. DOI: 10.1016/j.jtauto.2021.100081, PMID: 33554101.

[4] Nevens F, Andreone P, Mazzella G, Strasser SI, Bowlus C, Invernizzi P, *et al*; POISE Study Group. A Placebo-Controlled Trial of Obeticholic Acid in Primary Biliary Cholangitis. N Engl J Med 2016; 375(7):631–643. DOI: 10.1056/NEJMoa1509840, PMID: 27532829.

[5] Levy C, Younossi ZM, Mayo MJ, Kremer AE, Pate J, Ieyoub J, *et al*. Assessment of PBC Pruritus From the ITCH-E Study: Quality of Life, Productivity, and Treatment Experiences. Liver Int 2025;45(9): e70276. DOI: 10.1111/liv.70276, PMID: 40847640.

[6] Kliewer SA, Mangelsdorf DJ. Bile Acids as Hormones: The FXR-FGF15/19 Pathway. Dig Dis 2015;33(3):327–331. DOI: 10.1159/000371670, PMID: 26045265.

[7] Li L, Wang HM, Shen Y. Development and psychometric testing of a Chinese version of the SF-36 Health Survey Scale (in Chinese). Chinese Journal of Preventive Medicine 2002;36(2):109–113. DOI: 10.3760/j:issn:0253-9624.2002.02.011.

[8] Qi MH, Huang H, Dong JX, Hao YT, Zhou YP. Reliability and validity of the Chinese version of the Liver Disease Quality of Life Questionnaire (LDQOL 1.0) (in Chinese). Shijie Huaren Xiaohua Zazhi 2015;23(12):1973–1979. DOI: 10.11569/wcjd.v23.i12.1973.

[9] Zung WW. A Self-rating depression scale. Arch Gen Psychiatry 1965; 12(1):63–70. DOI: 10.1001/archpsyc.1965.01720310065008, PMID: 14221692.

[10] Zung WW. A rating instrument for anxiety disorders. Psychosomatics 1971;12(6):371–379. DOI: 10.1016/S0033-3182(71)71479-0, PMID: 5172928.

[11] Wang ZY, Chi YF. Self-Rating Anxiety Scale (SAS) (in Chinese). Shanghai Archives of Psychiatry 1984;2:73–74.

[12] Wang ZY, Chi YF. Self-Rating Depression Scale (SDS) (in Chinese). Shanghai Archives of Psychiatry 1984;2:71–72.

[13] Koc OM, Toussaint AK, Untas A, Milkiewicz P, Ytting H, Buck L, *et al*. Fatigue in people with primary biliary cholangitis: a position paper from the European Reference Network for Rare Liver Diseases. Lancet Gastroenterol Hepatol 2026;11(1):71–86. DOI: 10.1016/S2468-1253(25)00257-2, PMID: 41082897.

[14] Choo YJ, Cho CW, Chang MC. Effects of supervised exercise on aerobic capacity and quality of life in patients with chronic liver disease and patients who underwent liver transplantation: a systematic review and meta-analysis. Int J Rehabil Res 2022;45(1): 1–11. DOI: 10.1097/MRR.0000000000000502, PMID: 34678843.

[15] Khanna A, Leighton J, Lee Wong L, Jones DE. Symptoms of PBC - Pathophysiology and management. Best Pract Res Clin Gastroenterol 2018;34-35:41–47. DOI: 10.1016/j.bpg.2018.06.007, PMID: 30343709.

[16] Lasker JN, Sogolow ED, Olenik JM, Sass DA, Weinrieb RM. Uncertainty and liver transplantation: women with primary biliary cirrhosis before and after transplant. Women Health 2010;50(4): 359–375. DOI: 10.1080/03630242.2010.498750, PMID: 20711949.

[17] Düll MM, Kremer AE. Evaluation and Management of Pruritus in Primary Biliary Cholangitis. Clin Liver Dis 2022;26(4):727–745. DOI: 10.1016/j.cld.2022.06.009, PMID: 36270726.

[18] Ai X, Yang X, Fu HY, Xu JM, Tang YM. Health-related quality of life questionnaires used in primary biliary cholangitis: a systematic review. Scand J Gastroenterol 2022;57(3):333–339. DOI: 10.1080/00365521.2021.2010800, PMID: 35107052.

[19] Newton JL, Hollingsworth KG, Taylor R, El-Sharkawy AM, Khan ZU, Pearce R, *et al*. Cognitive impairment in primary biliary cirrhosis: symptom impact and potential etiology. Hepatology 2008;48(2): 541–549. DOI: 10.1002/hep.22371, PMID: 18563843.

[20] Mayo MJ, Carey E, Smith HT, Mospan AR, McLaughlin M, Thompson A, *et al*; TARGET-PBC Investigators. Impact of Pruritus on Quality of Life and Current Treatment Patterns in Patients with Primary Biliary Cholangitis. Dig Dis Sci 2023;68(3):995–1005. DOI: 10.1007/s10620-022-07581-x, PMID: 35704252.