

Comparison of Quality of Life in Chronic Liver Disease Patients Based on Indonesian Version of SF-36 Questionnaire

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ABSTRACT

Background: Liver cirrhosis is a chronic progressive disease associated with substantial morbidity and mortality. Although clinical management often emphasizes physical outcomes, assessment of health-related quality of life (HRQoL) provides a more comprehensive evaluation of patient well-being. A validated multidimensional instrument for HRQoL assessment is SF-36 (36-Item Short Form Health Survey). Therefore, this study aims to compare HRQoL among patients with chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma (HCC) using Indonesian version of SF-36. There are limited data from Indonesia comparing HRQoL across different stages of chronic liver disease, particularly including patients with chronic hepatitis.

Methods: A cross-sectional study was conducted at Gastroenterohepatology Clinic of Saiful Anwar General Hospital, Malang, using 273 patients including 156 with chronic hepatitis, 88 with liver cirrhosis, and 29 with HCC. HRQoL was assessed using SF-36 questionnaire, which evaluated eight domains. Data were analyzed through Kruskal–Wallis test followed by Mann–Whitney post hoc analysis.

Results: The results showed that HRQoL differed significantly across all SF-36 domains among the three groups ($p < 0.001$), with the lowest scores observed in patients with HCC. Post hoc analysis showed a progressive decline in quality of life with increasing disease severity. However, no significant difference was found between cirrhosis and HCC groups in role limitations due to emotional problems ($p > 0.05$).

Conclusion: Advanced stages of chronic liver disease are associated with poorer HRQoL. Emotional role limitations appear less dependent on disease severity, signifying the need for psychological support across all stages.

Keywords: Chronic Hepatitis, Hepatocellular Carcinoma, Liver Cirrhosis, Quality of Life, SF-36.

ABSTRAK

Latar Belakang: Penyakit hati kronis seperti hepatitis kronis, sirosis hati, dan karsinoma hepatoseluler (KHS) merupakan kondisi progresif yang tidak hanya menyebabkan kerusakan organ, tetapi juga berdampak besar terhadap kualitas hidup pasien. Penilaian kualitas hidup yang berhubungan dengan kesehatan (HRQoL) menjadi penting untuk memahami beban penyakit secara menyeluruh. SF-36 adalah instrumen yang komprehensif untuk

menilai aspek fisik, mental, dan sosial pasien. Hingga kini, belum banyak studi di Indonesia yang membandingkan kualitas hidup pasien dengan berbagai derajat penyakit hati kronis, khususnya yang melibatkan kelompok hepatitis kronis. Tujuan penelitian ini untuk membandingkan kualitas hidup berdasarkan kuesioner SF-36 versi Indonesia pada pasien hepatitis kronis, sirosis hati, dan KHS.

Metode: Penelitian cross-sectional ini melibatkan 273 pasien rawat jalan di Klinik Gastroenterohepatologi RSUD Saiful Anwar Malang, terdiri dari 156 pasien hepatitis kronis, 88 pasien sirosis hati, dan 29 pasien KHS. Penilaian kualitas hidup dilakukan dengan kuesioner SF-36 yang telah teruji validitas dan reliabilitasnya. Analisis dilakukan menggunakan uji Kruskal-Wallis dan dilanjutkan Mann-Whitney untuk perbandingan antar kelompok.

Hasil: Terdapat perbedaan bermakna pada seluruh domain SF-36 antar kelompok ($p < 0,001$). Kualitas hidup terendah terdapat pada pasien KHS, diikuti sirosis hati, dan tertinggi pada hepatitis kronis. Tidak ditemukan perbedaan bermakna pada domain keterbatasan emosional antara sirosis dan KHS ($p > 0,05$).

Kesimpulan: Derajat penyakit hati kronis yang lebih berat berhubungan dengan penurunan kualitas hidup. Domain keterbatasan emosional tampaknya tidak dipengaruhi oleh beratnya penyakit.

Kata Kunci: Hepatitis kronis, sirosis hati, karsinoma hepatoseluler, kualitas hidup, SF-36.

INTRODUCTION

A chronic condition that significantly affects morbidity and mortality is liver cirrhosis. The most frequent causes include Non-Alcoholic Fatty Liver Disease (NAFLD), excessive alcohol intake, and viral infections.^{1,2} In 2017, the number of liver cirrhosis cases was estimated at 122.6 million worldwide, with a mortality risk 5 to 10 times higher than the general population. Complications arising from cirrhosis, such as ascites, bleeding esophageal varices, hepatic encephalopathy, impaired renal function, infection, and acute or chronic liver failure have become the primary reason for the death of patients. This high burden of disease confirms that liver cirrhosis is a health problem in need of serious attention and comprehensive treatment.^{1,3}

The disease course of cirrhosis is characterized by progressive liver fibrosis that leads to permanent decline in organ function and increased risk of hepatocellular carcinoma (HCC).^{1,2} Management of cirrhosis has focused more on clinical aspects, such as routine screening to detect HCC and monitoring of esophageal varices. However, health-related quality of life (HRQoL) and other individual characteristics of patients frequently receive less attention. Liver cirrhosis affects physical and emotional health, as well as daily quality of life. Frequent symptoms such as muscle cramping, sleep issues, chronic itching, and reduced sexual function may significantly lower patients' quality of life. Therefore, measuring HRQoL is important to understand the extent to which the disease affects the life of an individual, as well as the basis for developing more comprehensive treatment interventions from a medical and psychosocial perspective.^{3,4}

HRQoL is a multidimensional concept that comprises the impact of a disease on the psychological, social, and daily functioning of patients. The assessment of HRQoL is often carried out through questionnaires completed independently by patients and, in necessary cases, by family members. This allows for a subjective assessment of the experience of living with chronic disease. Various instruments have been developed, both generic and specific, to evaluate HRQoL in patients with liver cirrhosis. The 36-Item Short Form Health Survey (SF-36) is among the most widely used generic instruments.^{5,15}

SF-36 is a general quality of life assessment instrument used to evaluate the health of individuals with a variety of chronic conditions, such as liver disease, gastro-oesophageal reflux disease (GERD), and inflammatory bowel disease (IBD). The 36 items on the questionnaire are divided into eight categories representing different aspects of physical and mental health, in addition to two summary scores that provide a general overview of patients' current state of health. SF-36 can provide a comprehensive picture of the quality of life of individuals with chronic conditions, including liver cirrhosis, because of the vast and comprehensive coverage.^{5,6} This study used Indonesian version of SF-36 questionnaire to compare HRQoL of patients with chronic hepatitis, liver cirrhosis, and HCC.⁷

METHODS

This study used a cross-sectional, quantitative, observational strategy, and was carried out from November 2024 to January 2025 at the Saiful Anwar General Hospital's Gastroenterohepatology Outpatient

Clinic in Malang. A total of 273 patients were selected, including 29 with HCC, 88 with liver cirrhosis, and 156 with chronic hepatitis. According to the diagnoses and willingness to participate, patients were selected serially. The study protocol was authorized by Dr. Saiful Anwar General Hospital's Ethics Committee in Malang with reference number 400/053/K.3/102.7/2025.

HRQoL was assessed using the validated Indonesian version of SF-36 questionnaire. Previous studies have reported this questionnaire with good reliability and validity in Indonesian population.

SF-36 consists of eight domains, including physical functioning, role limitations due to physical health, pain, general health, energy/fatigue, social functioning, role limitations due to emotional problems, and emotional well-being. Each domain is scored on a scale from 0 to 100, with higher scores representing better perceived health status. Domain scores in this study were estimated using standard SF-36 calculator.

Questionnaires with missing responses were handled according to SF-36 manual. Domain scores were calculated when a minimum of 50% of items were completed in a domain, and the scores were treated as missing during failure to meet this expectation. Meanwhile, internal consistency reliability of SF-36 in the study population was assessed using Cronbach's alpha coefficients for each domain.

Subjects

Participants in this study included patients with chronic hepatitis, liver cirrhosis, and HCC. The number was determined through consecutive sampling, where participants who met the inclusion and exclusion criteria were kept until the minimum sample size required by the Cochran's formula was attained. The minimum sample size is calculated using the formula below:

$$N = \left(\frac{Z\alpha^2 \cdot P(1 - P)}{\delta^2} \right)$$

$$N = \left(\frac{(1,96^2)(0,2)(1 - 0,2)}{(0,1)^2} \right)$$

$$N = 62$$

Description:

N: Minimum sample size

Z α : Standard deviation alpha (value is 1.96 for alpha = 0.05)

δ 2: Study precision, determined by the researcher at 20% (0.2)

P: Disease prevalence = 10% (0.1)

Inclusion criteria:

1. Patients who are not less than 18 years old
2. Individuals with a diagnosis of HCC, liver cirrhosis, or chronic hepatitis

Exclusion criteria:

1. Patients who are unconscious or in a clinically unstable state (such as those undergoing inotropic and vasopressor treatment or experiencing haemodynamic abnormalities)
2. Individuals with severe mobility disability or a history of stroke and physical limitation
3. Individuals with autoimmune disorders, diabetes mellitus (DM), hypertension, dementia, or other cancers not related to the hepatology system. Patients with DM and hypertension were excluded to minimize potential confounding effects of the comorbidities on HRQoL outcomes.

A consecutive sampling method was used, where all eligible patients attending Gastroenterohepatology outpatient clinic during the investigation period were selected. Considering the exploratory and comparative nature of this study, a formal sample size calculation based on group comparison was not performed. However, the sample size was determined by availability during the period, as only clinically stable patients were included.

Diagnostic Criteria

The diagnoses of chronic hepatitis (HEP), liver cirrhosis (LC), and HCC were established by attending gastroenterology–hepatology consultations based on a combination of clinical assessment, laboratory observations, and imaging studies, in accordance with current clinical practice guidelines. Chronic hepatitis was identified as the presence of persistent liver inflammation for more than 6 months, supported by abnormal liver transaminase levels and positive viral hepatitis markers (hepatitis B or C), with no clinical, laboratory, or imaging evidence of cirrhosis.

Liver cirrhosis was diagnosed based on clinical features of chronic liver disease, laboratory abnormalities, and imaging results suggestive of cirrhosis (such as nodular liver surface, altered liver morphology, splenomegaly, or portal hypertension), with or without confirmation by transient elastography or histopathology when available. HCC was diagnosed with characteristic radiological results on multiphasic contrast-

enhanced CT or MRI, according to established diagnostic criteria, and histopathological confirmation when available. Tumor staging was determined using *Barcelona Clinic Liver Cancer* (BCLC) classification system.

Data Collection

Information on patients was collected during the first visit to Gastroenterology and Hepatology Outpatient Clinic at Dr. Saiful Anwar Hospital Malang. The factors assessed were the same as the factors in SF-36 questionnaire, which enquired about the quality of life of patients with chronic hepatitis, liver cirrhosis, and HCC.

Statistical Analysis

Collected data were analyzed using the median test, followed by Kruskal-Wallis and Mann-Whitney analysis as a comparison test at a significance level of $p < 0.05$. All stages of the analysis were conducted using SPSS software, version 25. Comparative analyses were performed without adjustment for potential confounders. Therefore, age and sex were considered in the interpretation of the results.

Considering the various comparisons across SF-36 domains, adjustment for multiple testing was performed with Holm–Bonferroni method to control the family-wise error rate. Effect sizes were calculated using eta-squared (η^2) for Kruskal–Wallis tests to quantify the magnitude of between-group differences.

RESULTS

A total of 273 patients with HCC (29), liver cirrhosis (88), and chronic hepatitis (156) were included in this study. The gender distribution with statistically significant differences ($p = 0.019$) showed a male preponderance, particularly in the cases of HCC (86.2%), followed by liver cirrhosis (61.3%) and chronic hepatitis (52.5%). Additionally, there was a significant difference ($p < 0.001$) in the mean age of the patients, where those with chronic hepatitis were younger (46 ± 13 years) than counterparts experiencing liver cirrhosis (58 ± 10 years) and HCC (55 ± 11 years). In every group, hepatitis B was the primary cause, with hepatitis C coming in second in lower amounts. **Table 1** shows the entire attributes of the study participants.

According to the classification of liver function, the majority of cirrhotic patients (61.3%) were in Child-Pugh A, and HCC patients were more prevalent in Child B and C, signifying worse liver function. Only 3.4% had early stage HCC, while the majority had advanced stage (stage C at 62.1%). This suggests that the majority arrived with a serious ailment, which significantly affects quality of life.

As liver disease worsened, quality of life measured by SF-36 instrument significantly declined in all dimensions ($p < 0.001$). Liver cirrhosis (65) and HCC (25) showed significant limitations, while the physical functioning of chronic hepatitis patients was comparatively good (median score 100). In liver cirrhosis, the domains of role limitations due to physical health, pain, and general health gradually deteriorated. For example, there was a considerable rise in pain from HCC (40) to chronic hepatitis (70).

Table 1. Qualities of Research Participants

	HEP (n=156)	LC (n=88)	HCC (n=29)	p-value
Sex (male, n(%))	82 (52,5)	54 (61,3)	25 (86,2)	0,019
Age (Mean SD)	46 (13) ^a	58 (10) ^b	55 (11) ^b	< 0,001
Etiology, n(%)				
Hepatitis B	138 (88,4)	69 (78,4)	23 (79,3)	< 0,001
Hepatitis C	18 (11,5)	10 (11,3)	2 (0,06)	< 0,001
Hepatitis B and C	0	8 (0,09)	4 (13,7)	Na
Non Hepatitis	1 (0,006)	1 (0,01)	0	Na
Child Pugh, n(%)				
A		54 (61,3)	14 (48,2)	0,215
B		25 (29,4)	11 (37,9)	0,335
C		9 (10,2)	4 (13,7)	0,734
BCLC, n(%)				
A			1 (3,4)	
B			7 (24,1)	
C			18 (62,1)	
D			3 (10,3)	

Table 2. Comparison of SF-36 Domain Scores Among Patients with Chronic Liver Disease (median [Q1, Q3])

SF-36 Domain, median (Q1, Q3)	Group			p-value
	HEP (n=156)	LC (n=88)	HCC (n=29)	
Physical Component				
Physical Functioning	100 (85, 100) ^a	65 (45, 83) ^b	30 (10, 60) ^c	< 0,001
Role-Physical	100 (75, 100)	55 (25, 100)	25 (25, 50)	< 0,001
Bodily Pain	100 (85, 100)	77 (57, 100)	45 (22, 61)	< 0,001
General Health	75 (60, 85)	55 (45, 68)	25 (15, 40)	< 0,001
Mental Component				
Vitality	70 (60, 80)	55 (50, 73)	40 (22, 52)	< 0,001
Social Functioning	87 (75, 100)	75 (53, 87)	50 (25, 56)	< 0,001
Role-Emotional	100 (66, 100) ^a	66 (33, 100) ^b	33 (5, 100) ^b	< 0,001
Mental Health	80 (68, 88)	62 (52, 76)	44 (32, 68)	< 0,001

Table 3. Comparison of Liver Functions and Quality of Life

SF-36 Domain, Median (Q1, Q3)	Liver Functions			p-value
	Child Pugh A (n=68)	Child Pugh B (n=36)	Child Pugh C (n13)	
Physical Component				
Physical Functioning	72 (50, 85) ^a	40 (26, 65) ^b	50 (10, 67) ^b	< 0,001
Role-Physical	75 (25, 100) ^a	25 (25, 50) ^b	25 (25, 62) ^b	< 0,001
Bodily Pain	77 (55, 100) ^a	56 (45, 77) ^b	45 (22, 72) ^b	< 0,001
General Health	55 (45, 70) ^a	37 (20, 60) ^b	40 (25, 55) ^b	< 0,001
Mental Component				
Vitality	55 (50, 70) ^a	45 (38, 68) ^b	50 (45, 60) ^{a,b}	< 0,001
Social Functioning	75 (53, 87) ^a	50 (37, 84) ^b	62 (37, 75) ^b	0,002
Role-Emotional	66 (33, 100) ^a	33 (0, 91) ^b	33 (21, 66) ^b	< 0,001
Mental Health	64 (52, 80) ^a	54 (38, 68) ^b	56 (40, 68) ^{a,b}	0,025

Notes: Values are presented as median (Q1, Q3). P-values were obtained using the Kruskal–Wallis test. Different superscript letters indicate statistically significant differences between groups (post hoc analysis).

A similar pattern could be observed in the mental component, as chronic hepatitis patients had generally high energy/fatigue, social functioning, and emotional well-being, which declined significantly in cirrhosis and deteriorated in HCC cases. Although there was often no statistically significant difference between cirrhosis and HCC ($p = 0.314$), the role limitations due to emotional problems-category showed impairment at the onset of cirrhosis (median score 66) and worsened in HCC (33). These results support the assertion in **Table 2** that liver disease has a progressive effect on the physical functioning and mental well-being of patients.

The analysis conducted based on the Child-Pugh classification showed that quality of life gradually decreased for Children A, B, and C. There were substantial variations ($p < 0.001$) in the median score for the physical functioning domain, which dropped from 72 (A) to 40 (B) and 50 (C). Additionally, significant decline was observed in the domains of role limitations due to physical health, pain, and general health. **Table 3** presents the emotional well-being categories that did not significantly differ between Children C and A or B, including energy/fatigue and role limitations due to emotional problems.

This study shows that the more advanced the disease stage and the more severe the degree of liver dysfunction, patients' quality of life decreases significantly in nearly all physical, psychological, and social aspects. This emphasizes the importance of a multidisciplinary method that focuses on disease control and supports comprehensive quality of life. Large effect sizes were observed across all SF-36 domains, with eta-squared (η^2) values from 0.14 to 0.41, signifying substantial and clinically meaningful differences in HRQoL between disease groups.

Inter-item correlation analysis showed moderate to strong correlations between SF-36 domains, suggesting good internal coherence while preserving the multidimensional structure of the instrument. After applying Holm–Bonferroni correction for multiple comparisons, differences in HRQoL scores between groups remained statistically significant across all SF-36 domains.

DISCUSSION

This study evaluated HRQoL of patients with chronic hepatitis, liver cirrhosis, and HCC using SF-36 instrument. The results showed a significant

decline in quality of life as liver disease progressed. Chronic hepatitis patients still had relatively high SF-36 scores, representing a better quality of life than cirrhotic and HCC patients. This decline is related to worsening clinical conditions, complications, treatment burden, and psychosocial distress. Previous studies by Orr et al.² and Mustika et al.⁴ supported the observation that decompensated cirrhosis significantly decreased physical functioning, energy/fatigue, and emotional well-being.^{4,6,9}

HCC patients recorded the most extreme deterioration in quality of life, particularly in the domains of physical functioning, pain, and general health perception. This reflects the impact of the disease and the effects of treatments such as chemotherapy or TACE, as well as pain from the tumor mass. The study by Kang et al.¹⁰ reported that patients with HCC experienced a sharp decline in SF-36 and EORTC QLQ-C30 scores, specifically in social functioning, energy/fatigue, and pain, worsened by poor prognosis and emotional distress related to cancer diagnosis.^{8,10} The domain of role limitations due to emotional problems showed no significant difference between cirrhotic and HCC patients, suggesting the experience of heavy psychological burden from the advanced cirrhotic phase, particularly in patients with severe complications. The study by Xiao et al.¹⁰ emphasized the presence of cognitive impairment, anxiety, and sleep disturbances that worsened the emotional state of cirrhotic patients.^{5,11} Although role limitations due to emotional problems did not show a clear gradient across disease severity, the stated result should be interpreted with caution. Several factors may contribute to this observation, including the relatively smaller sample size in HCC group, which has limited statistical power. In addition, potential ceiling effects of SF-36 role-emotional domain and unmeasured psychosocial factors such as coping mechanisms, social support, or psychological adaptation to chronic disease may have influenced the results.

In addition to the extent of disease, age and gender affect quality of life. Cirrhosis and HCC patients tend to be older and predominantly male, with more comorbidities and socio-economic role pressures as head of the family. Devarbhavi et al.³ reported increase of liver disease burden in the elderly and male population, with significant implications for quality of life and social burden.³ Therefore, HRQoL evaluation should be an integral part of patient monitoring to ensure disease management focuses on biochemical aspects, as well as psychosocial interventions and

improvement of subjective well-being. In terms of liver function, this study showed a consistent decline in SF-36 scores with the progression of liver dysfunction based on Child Pugh classification. There was a significant decrease from Child Pugh A to B and C in nearly all domains, specifically physical function and activity limitation. This observation is consistent with the study of Thiele et al.¹², showing that cirrhosis decompensation is characterized by multidimensional deterioration of quality of life due to complications such as ascites, fatigue, and muscle wasting.¹²

Differences between Child Pugh B and C were often insignificant in some domains, possibly due to the “floor effect” phenomenon where the severity of functional decline leads to difficulty in detecting significant additional variation. These results confirm that the transition from the compensated (Child Pugh A) to decompensated (B and C) phase is a critical point of major quality of life decline, while further progression in the decompensation spectrum does not often have a proportionate impact on perceived quality of life. Early intervention in Child Pugh A patients, through multidisciplinary management that includes nutritional improvement, symptom management, and psychosocial support, is an important strategy in preventing more deterioration in quality of life. Routine HRQoL monitoring with SF-36 may help to plan a more comprehensive and individualized treatment.^{5,9,17}

Cultural and health system differences may influence patient perception and adaptation to liver disease. Studies using Indonesian version of SF-36 emphasize the importance of sociocultural context in interpreting HRQoL data. For example, community support and family roles in Indonesia may buffer disease impact on mental health domains, even in advanced disease stages.^{13,14,15} These results suggest that localized HRQoL tools and culturally sensitive methods are crucial in liver disease management.

Finally, integrating quality of life assessment into routine hepatology care can guide clinicians to identify physical and psychosocial unmet needs, leading to a more holistic treatment method. Future studies should explore longitudinal changes in HRQoL and examine the effectiveness of integrated supportive interventions in different liver disease stages. The large effect sizes observed across all SF-36 domains show the clinical relevance of the differences in quality of life across stages of chronic liver disease. The magnitude of effect sizes consistently supported clinically meaningful differences across domains.

Future studies with broader inclusion criteria and adjusted analyses are needed to better reflect real-world clinical populations. The results are expected to be interpreted in the context of a stable patient population. Considering the cross-sectional design of this study, causal inferences cannot be established, and the observed associations should be interpreted accordingly.

CONCLUSION

In conclusion, this study found that individuals with chronic liver disease, including cirrhosis, chronic hepatitis, and HCC, had the lowest quality of life decreasing simultaneously as the disease advanced. The results showed the importance of comprehensive treatment incorporating quality of life support and psychosocial interventions, specifically at advanced stages. Concerning Child Pugh A patients, early intervention was considered crucial to halting subsequent declines in quality of life. Increasing disease severity was associated with progressively lower HRQoL across most SF-36 domains. These results showed the substantial burden of chronic liver disease on patients' physical and mental well-being, while emphasizing the need for cautious interpretation given the cross-sectional design.

LIMITATIONS

This study has several limitations, specifically the cross-sectional design precludes causal inference, and residual confounding from unmeasured clinical and psychosocial factors cannot be excluded. Differences in age and sex distribution between groups, which are not adjusted for, may influence HRQoL outcomes. Consecutive outpatient recruitment, exclusion of common comorbidities, and omission of hospitalized or clinically decompensated patients tend to introduce selection bias and limited generalizability to patients with more severe disease. Additionally, the single-center design and smaller sample size in HCC group may restrict the applicability of the results to other settings.

Conflict of Interest

The authors declare no conflicts of interest regarding the ongoing nature of this study.

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Author Contribution

Conceptualization and study design: S.M., S.N., N.A.J.; data collection: S.M., S.N., N.A.J., S.L.F., R.T.N.; data analysis and interpretation: S.M., S.N., N.A.J.; manuscript drafting: S.M., N.A.J.; critical revision of the manuscript: S.M., S.N., N.A.J.; supervision: C.R.K. The authors read and approved the final manuscript.

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Data Availability

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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