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Status and factors influencing health-related quality of life in patients with non-alcoholic fatty liver disease in Hangzhou: a cross-sectional study

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ABSTRACT

Objective Due to rapid economic development and the unique lifestyles, cultures and customs of Hangzhou, non-alcoholic fatty liver disease (NAFLD) has attracted widespread attention, with a prevalence rate of 35–45%. In this study, we used the Chinese version of the Chronic Liver Disease Questionnaire for NAFLD (CLDQ-NAFLD) to investigate the current health-related quality of life (HRQL) among patients with NAFLD and analyse the influencing factors, which provides a reference for improving the patients' HRQL.

Design A cross-sectional design.

Setting This study was conducted from March 2022 to March 2023 at a tertiary hospital in Hangzhou.

Participants All patients with NAFLD included in this study were diagnosed using FibroScan, with a controlled attenuation parameter ≥248 dB/m.

Primary outcome measures The primary outcome of the study was the HRQL score, which was assessed using the Chinese version of the CLDQ-NAFLD.

Results A total of 502 patients with NAFLD were enrolled in this study (mean age 1.79±13.49 years; 69.7% male). The overall HRQL score was 5.89 (5.33, 6.36), and the fatigue dimension score was the lowest at 5.17 (4.33, 6.00). Multiple linear regression analyses revealed that poor HRQL score was correlated with other marital status (β=−0.096, p=0.036), liver stiffness ≥10.3 (kPa) (β=−0.110, p=0.017), regular exercise (β=−0.121, p=0.006), sex (β=−0.114, p=0.012) and alanine transaminase (ALT) levels (β=−0.139, p=0.002). A monthly income >10 000 (renminbi) was associated with a significantly higher HRQL score.

Conclusions This cross-sectional survey conducted in Hangzhou, China, revealed that HRQL is impaired among patients with NAFLD. This study revealed a significant association between HRQL and sociodemographic factors, including sex, monthly income and marital status, alongside clinical factors such as liver stiffness, regular exercise and ALT level. Emphasising optimal care management is essential to improve HRQL in patients with NAFLD.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study analysed the impact of clinical and sociodemographic factors on health-related quality of life (HRQL) in patients with non-alcoholic fatty liver disease.
⇒ The relatively large sample size in this study enhances the reliability and generalisability of the results.
⇒ Since HRQL assessment relies on patient self-reports, there is a potential risk of subjective bias.
⇒ The cross-sectional design of this study identifies correlations but does not infer causality.

INTRODUCTION

Owing to modern diets and sedentary lifestyles, non-alcoholic fatty liver disease (NAFLD) has rapidly increased in prevalence and has now overtaken chronic viral hepatitis as the most common chronic liver disease worldwide. NAFLD covers the spectrum of fatty liver disease from NAFLD to non-alcoholic steatohepatitis and finally to cirrhosis and hepatocellular carcinoma.[1] NAFLD is a chronic and progressive disorder that can exacerbate both hepatic and extrahepatic conditions. Without timely intervention, irreversible liver damage can occur.[2] Additionally, NAFLD is a multisystem metabolic disease linked to various complications such as cardiovascular diseases, type 2 diabetes, chronic kidney disease and colorectal cancer.[3 4] Moreover, NAFLD contributes to escalating healthcare costs; from 2006 to 2013, total medical expenses for NAFLD soared from $686 million to $1.42 billion, marking a 207% increase, with a 9.8% rise in per capita costs, thus imposing significant financial strain on patients and families.[5 6]

The prevalence of NAFLD varies significantly across different geographical regions and economic conditions.[7] The results of a large-scale meta-analysis in 2019 revealed that the prevalence of NAFLD in mainland China was 29.8%, the incidence was 63.0 per 1000 person-years and the annual mortality rate

was 7.3 per 1000 person-years, all of which are the highest in Asia, and NAFLD has the fastest growing prevalence in the world.[8] According to a meta-analysis, the prevalence of fatty liver in Zhejiang Province is relatively high, ranging from 30% to 35%, which is above the national average.[7] The prevalence of NAFLD in Hangzhou is approximately 35–45% and shows an increasing trend.[9] In Hangzhou, the humid and rainy climate encourages a preference for high-calorie diets. Additionally, as a centre for technology and e-commerce, and as an economically developed area in China, young people in Hangzhou exhibit a faster pace of life, greater work-related stress and increased sedentary behaviour, all of which contribute to a higher incidence of NAFLD.[10 11]

Health-related quality of life (HRQL) is a multidimensional concept, in which all its dimensions together affect the overall quality of life, and the assessment results can reflect an individual patient's physiological function, psychological status and social adjustment ability.[12] It has become an important component in the assessment of patient outcomes in clinical settings or clinical trials. In tackling chronic non-communicable diseases, the European Union has made improving patients' quality of life a top priority.[13] Patients with NAFLD may experience fatigue, impaired emotional health and reduced activity, which can affect their quality of life. Younossi *et al* reported that the quality of life of patients with NAFLD progressively worsens as the disease progresses.[14] Sayiner *et al* reported that patients with NAFLD had a significantly lower quality of life and health utility scores than the healthy population.[15] It is imperative to identify and measure the prevalent and distressing effects specific to each chronic condition as generic assessment tools may not adequately capture the unique issues associated with the diseases.

Additionally, there is a noticeable lack of research on HRQL for patients with NAFLD in Hangzhou. Thus, we selected the Chinese version of the CLDQ-NAFLD, which our team was authorised to localise in 2021.[16] This scale is particularly tailored for patients with NAFLD in China. Therefore, the aim of this study was to assess the impact of NAFLD on HRQL in patients from Hangzhou, China, and investigate whether variables related to sociodemographic and clinical characteristics were independently associated with HRQL. The results may help identify the additional cause of low HRQL, provide a theoretical basis for clinical diagnosis and care, and provide direction and guidance for the development of health education.

MATERIALS AND METHODS

Study design and sample size

This cross-sectional study followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines[17] (online supplemental material 1). This study was conducted among patients with NAFLD attending the liver disease clinic at Hangzhou Normal University Affiliated Hospital. The Metabolic Disease Management Center at the Affiliated Hospital of Hangzhou Normal University is the first multidisciplinary joint clinic for fatty liver in China. Patients with NAFLD who attended this clinic were enrolled in the survey conducted from March 2022 to March 2023. Patient participation in the study was voluntary and anonymous. The inclusion criteria were an age≥18 years, a controlled attenuation parameter (CAP) ≥248 dB/m according to FibroScan[18] and a willingness to provide written informed consent. The exclusion criteria included excessive alcohol consumption (≥210 g/week for males, ≥140 g/week for females),[19] other chronic liver diseases (such as hepatitis B virus, hepatitis C virus and autoimmune hepatitis), malignant tumours, medication-induced hepatic steatosis (such as amiodarone, methotrexate, tamoxifen and corticosteroids), gastrointestinal conditions (such as starvation, malnutrition and total parenteral nutrition), endocrine and metabolic disorders (such as coeliac disease, polycystic ovary syndrome, growth hormone deficiency and hypothyroidism), and hemolysis, elevated liver enzymes and low platelets (HELLP) syndrome, acute diseases and other disorders associated with hepatic fat deposition.

The sample size was calculated using the formula $[Z^2 * P(1-P)]/d^2$,[20] with a significance level of 0.05 and a 95% CI. The estimated prevalence of NAFLD in Hangzhou is approximately 0.4,[9] and the relative precision is set at 0.05. Therefore, the required sample size for the study was approximately 369 patients with NAFLD. Assuming a 10% non-response rate, a minimum of 410 completed questionnaires were required for the study.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Data collection

General data and clinical characteristic variables

Sociodemographic information, including sex, age, marital status, occupation, education level (junior high school and below, high school/junior college, college and above), monthly income and smoking status (yes, no, ceased), was obtained through self-reports. Clinical information gathered from medical records included measurements of height, weight and waist circumference, body mass index (BMI), patterns of regular exercise; and various laboratory indicators, including triglyceride (TG), alanine transaminase (ALT), CAP and liver stiffness, and the presence of any additional comorbidities.

Regular exercise was defined as five physical activities of 30 min or more per week or three vigorous physical activities of 20 min or more per week.[21] Central obesity was defined as a waist circumference ≥85 cm for females or ≥90 cm for males.[22] BMI was calculated as weight in kilograms divided by the square of height in metres. BMI was divided into three categories (normal, 18.5–23.9 kg/m^2; overweight, 24–27.9 kg/m^2; and obese, ≥ 28 kg/m^2).[23] Body fat is classified by the WHO

as a body fat percentage ≥25% for men and a body fat percentage ≥35% for women.[24 25] According to the CAP, the degree of hepatic steatosis was classified as normal (CAP<248 dB/m), mild (CAP 248–267 dB/m), moderate (CAP 268–279 dB/m) or severe (CAP ≥280 dB/m).[26] The degree of liver fibrosis was classified into a non-fibrotic group (liver stiffness<7.0 kPa), a fibrotic group (liver stiffness of 7.0–10.2 kPa) and a cirrhotic group (liver stiffness≥10.3 kPa) according to liver stiffness.[27] The normal range for TG is <1.70 mmol/L, and the normal range for ALT is <40 U/L. In addition, complications (such as diabetes, hypertension, hyperlipidaemia, cardiovascular disease, depression and colon disease) were diagnosed by doctors.

HRQL assessment

In this study, we used the Chinese version of the CLDQ-NAFLD scale, which was the Chinese-language version of the CLDQ-NAFLD scale developed in 2022 by our team. After cultural debugging, the scale showed better reliability and validity, with Cronbach's α coefficients ranging from 0.807 to 0.956 for each dimension.[16] This scale is only applicable to the population with NAFLD in China. The CLDQ-NAFLD includes 36 items divided into six dimensions: abdominal symptoms, fatigue, systemic symptoms, activity capacity, emotional function and anxiety. The scale is scored on a 7-point Likert scale (1 for always and 7 for never), with higher scores indicating better quality of life for patients.

Statistical analysis

The data obtained were checked by two researchers and then included. The data were entered and analysed using the Statistical Package for the Social Sciences (25.0). Continuous variables were presented as the M±SDs (normal distribution) or medians (quartiles) (skewed distribution), and categorical variables were presented as frequencies. For the univariate analysis, an independent t-test was used for comparisons between two groups, and one-way analysis of variance was used for comparisons between multiple groups. In addition, multiple linear regressions were used to analyse the factors influencing HRQL in patients with NAFLD. In this study, p<0.05 was considered to indicate statistical significance.

RESULTS

HRQL of patients with NAFLD

Owing to the lack of data on the key variables, out of 517 participants, 502 were ultimately selected. The total CLDQ-NAFLD score was 5.89 (5.33, 6.36), indicating that the HRQL of patients with NAFLD was impaired in all dimensions; the other scores for each dimension are shown in table 1.

Table 1 Scores and total scores for each dimension of quality of life in patients with NAFLD

Characteristics	Score
Overall CLDQ-NAFLD scores	5.89 (5.33, 6.36)
Abdominal symptoms	6.00 (5.33, 6.67)
Fatigue	5.17 (4.33, 6.00)
Systemic symptoms	6.17 (5.33, 6.67)
Activity capacity	6.20 (5.40, 6.80)
Emotional function	6.11 (5.33, 6.67)
Anxiety	6.14 (5.43, 6.86)

CLDQ-NAFLD, Chronic Liver Disease Questionnaire for Non-alcoholic Fatty Liver Disease.

Sociodemographic characteristics of patients with NAFLD

The participants were aged between 18 and 94 years, and the mean age was 41.79±13.49 years. Most participants were male (69.7%), married (79.1%), had a college education or above (60.8%) and had a monthly income>10 000 (44.2%). In addition, patients who were male (t=−2.051, p=0.041), had a monthly income>10 000 (F=13.348, p<0.001) or were married (t=3.087, p=0.047) were more likely to have a better HRQL (table 2).

Clinical characteristics of patients with NAFLD

Table 3 summarises and compares the clinical characteristics of patients diagnosed with NAFLD. The majority of patients were centrally obese (74.5%), had a high body fat percentage (76.9%), had severe NAFLD (77.3%), had liver stiffness<7.0 kPa (69.7%) and did not have comorbidities (57.2%). Approximately 40% of patients had a BMI categorised as obese (42.4%). The analysis revealed that patients with a higher BMI (F=3.431, p=0.033), severe NAFLD (F=3.312, p=0.037), greater liver stiffness (F=8.140, p<0.001), no regular exercise (t=3.462, p=0.001) and comorbidities (t=1.995, p=0.047) exhibited worse health-related quality of life.

Factors influencing HRQL in patients with NAFLD

The values assigned to each variable are shown in table 4. Multiple linear regression analysis (table 5) was conducted to explore the associations between the demographic and clinical characteristics and HRQL. The results indicated that sex, marital status, income>10 000 (RMB), liver stiffness≥10.3 (kPa), regular exercise and ALT levels were independently associated with HRQL scores. Notably, income was the strongest influencing factor (β=0.162), followed by ALT levels (β=−0.139).

DISCUSSION

This cross-sectional survey provides information on HRQL and its influencing factors in the NAFLD population in Hangzhou, an economically developed area of China. This study revealed that patients with NAFLD have lower HRQL scores, at (5.89 (5.33, 6.36)), particularly in the dimension of fatigue at (5.17 (4.33, 6.00)), which may be influenced by the high proportion of patients with severe NAFLD (77.3%) even though the majority of patients

Table 2 Comparison of the health-related quality of life scores of patients with NAFLD with their sociodemographic characteristics (n=502)

Characteristic	Group	Overall	CLDQ-NAFLD scores	*T/F*	P value
Sex	Male	305 (69.7%)	5.90 (5.37, 6.36)	2.051	0.041
	Female	152 (30.3)	5.80 (5.09, 6.35)		
Age (years)	18–39	226 (45%)	5.85 (5.23, 6.34)	2.029	0.133
	40–59	224 (44.6%)	5.97 (5.38, 6.43)		
	≥60	52 (10.4%)	5.78 (5.24, 6.26)		
Monthly income (RMB)	<5000	92 (18.3%)	5.62 (5.00, 6.21)	13.348	<0.001
	5000–10 000	188 (37.5%)	5.78 (5.22, 6.22)		
	>10 000	222 (44.2%)	6.04 (5.65, 6.50)		
Marital status	Unmarried	92 (18.3%)	5.81 (5.25, 6.32)	3.087	0.047
	Married	397 (79.1%)	5.92 (5.35, 6.41)		
	Other	13 (2.6%)	5.30 (4.82, 6.14)		
Education level	Junior high school and below	103 (20.5%)	5.95 (5.22, 6.35)	2.216	0.110
	High school/junior college	94 (18.7%)	5.82 (5.15, 6.35)		
	College and above	305 (60.8%)	5.90 (5.36, 6.44)		
Smoking	Yes	84 (16.7%)	5.87 (5.33, 6.45)	0.492	0.611
	No	400 (79.7%)	5.89 (5.33, 6.36)		
	Ceased	18 (3.6%)	5.80 (5.03, 6.14)		

P value was determined using the independent t-test and one-way analysis of variance.
CLDQ-NAFLD, Chronic Liver Disease Questionnaire for Non-alcoholic Fatty Liver Disease.;

with NAFLD in our study were asymptomatic. Moreover, Hangzhou, as an important economic hub in Eastern China, experiences a faster pace of life and greater work pressures, both of which could impair HRQL for patients with NAFLD. Additionally, sex, marital status, monthly income, liver stiffness, regular exercise and ALT levels were the key factors influencing HRQL. Therefore, this study conducted in Hangzhou may offer valuable insights into the impact of NAFLD on patients.

Current status of HRQL in patients with NAFLD

The study revealed that HRQL was impacted in all the patients with NAFLD, but the fatigue dimension (5.17 (4.46, 6.00)) was the most impaired, even though the majority of patients with NAFLD included in our study were asymptomatic. The same conclusion was reached by the authors who originally developed the CLDQ-NAFLD.[28] Fatigue, as a complex and multidimensional symptom, is closely linked to physiological dysfunctions and psychological stress, significantly impacting the HRQL in patients with NAFLD.[28] More importantly, fatigue among individuals with NAFLD was significantly associated with increased mortality, where the presence of fatigue increased the risk of mortality by more than twofold.[29]

The central component of fatigue is driven by neuroinflammation, where systemic inflammatory factors such as tumour necrosis factor-α and interleukin-6 cross the blood-brain barrier, disrupting neurotransmitter systems, particularly serotonin and dopamine. This disruption leads to an imbalance in neurotransmitter equilibrium, reducing self-motivation and cognitive functions, which are the key characteristics of central fatigue and are exacerbated by liver disease conditions.[30] Concurrently, peripheral fatigue originates from metabolic dysfunctions and neuromuscular damage associated with NAFLD, with increased inflammatory markers leading to muscle weakness and reduced endurance.[31 32] Additionally, psychological factors such as depression and anxiety, which often arise from the chronic stress of managing a long-term illness, further exacerbating the perception of fatigue.[32 33]

Fatigue is the most frequently reported symptom among patients with NAFLD. Owing to the difficulty in measuring the degree of fatigue and its non-specific, subjective nature, it is often overlooked. However, it has a significant negative impact on the quality of life of patients with NAFLD. Therefore, the treatment of NAFLD, especially in those with fatigue, requires a multidisciplinary team consisting of gastro-hepatologists, cardiologists and behavioural health, exercise, nutrition and sleep experts to address multiple interrelated comorbidities that drive fatigue to improve HRQL and long-term survival.[34–36] Although fatigue is a non-specific, subjective symptom, it merits attention from clinicians and researchers because of its negative impact on the well-being of patients with NAFLD.

Factors influencing HRQL in patients with NAFLD

This study revealed that male patients have higher HRQL scores than female patients. Similar findings from

Table 3 Comparison of the health-related quality of life scores of patients with NAFLD with their clinical characteristics (n=502)

Characteristics	Group	Overall	CLDQ-NAFLD scores	*T/F*	P value
Central obesity	Yes	374 (74.5%)	5.89 (5.34, 6.26)	0.336	0.737
	No	128 (25.5%)	5.89 (5.25, 6.35)		
Body mass index group (kg/m^2)	18.5–23.9	87 (17.3%)	5.97 (5.34, 6.42)	3.431	0.033
	24–27.9	202 (40.2%)	5.94 (5.42, 6.43)		
	≥28	213 (42.4%)	5.83 (5.17, 6.27)		
Body fat (%)	High	386 (76.9%)	5.86 (5.29, 6.34)	−1.326	0.186
	Normal	116 (23.1%)	5.99 (5.46, 6.45)		
Controlled attenuation parameter (dB/m)	248–267	83 (16.5%)	6.05 (5.66, 6.45)	3.312	0.037
	268–279	31 (6.2%)	5.89 (5.57, 6.57)		
	≥280	388 (77.3%)	5.85 (5.28, 6.33)		
Liver stiffness (kPa)	<7.0	350 (69.7%)	5.93 (5.35, 6.42)	8.140	<0.001
	7.0–10.2	112 (22.3%)	5.89 (5.35, 6.25)		
	≥10.3	40 (8.0%)	5.50 (4.75, 6.02)		
Regular exercise	Yes	374 (74.5%)	6.11 (5.56, 6.52)	3.462	0.001
	No	128 (25.5%)	5.86 (5.20, 6.28)		
Comorbidity	Yes	287 (57.2%)	5.80 (5.19, 6.23)	1.995	0.047
	No	122 (42.8%)	5.97 (5.35, 6.42)		
Laboratory examinations					
Alanine transaminase (U/L)	43.00 (25.00, 76.00)			*r*=−0.208	0.000
Triglyceride (mmol/L)	1.87 (1.27, 2.51)			*r*=−0.058	0.197

P value was determined using the independent t-test and one-way analysis of variance.
CLDQ-NAFLD, Chronic Liver Disease Questionnaire for Non-alcoholic Fatty Liver Disease.;

international research indicate that the quality of life of male patients is better than that of female patients with NAFLD.[37] In female patients with NAFLD, HRQL may be affected by physiological and psychological challenges. Fluctuations in hormone levels can disrupt metabolism and body composition, whereas societal expectations regarding body shape may exacerbate psychological pressure.[38] These factors, working together, may lead to a reduction in HRQL. As Hangzhou is the city with the highest permanent population in the province and has a gender ratio lower than the provincial average, women may face greater societal pressures when dealing with physical and psychological challenges. This could further impact their HRQL.[39 40] This study also revealed that married patients also reported higher HRQL scores. This may be due to the emotional support and family responsibilities provided by their spouse.[41] In addition, patients with NAFLD with spouses are more likely to actively adopt healthy lifestyle practices to control disease progression and improve their quality of life.[42] Social support is also an external resource for individuals to combat stress, and good social support can reduce patients' psychological stress response, relieve psychological distress, accelerate disease management behaviours, increase positive emotions and improve HRQL. Therefore, finding these associations would provide clinicians with the opportunity to detect vulnerable populations and provide proper care.

Moreover, we observed a positive correlation between the level of HRQL in patients with NAFLD

Table 4 Assignment of patients' general information

Independent variable	Assignment
Age	18–39 (Z1=0, Z2=0); 40–59 (Z1=1, Z2=0); ≥60 (Z1=0, Z2=1)
Monthly income (RMB)	<5000 (Z1=0, Z2=0); 5000–10000 (Z1=0, Z2=0); >10 000 (Z1=0, Z2=01)
Education level	Junior high school and below (Z1=0, Z2=0); high school/junior college (Z1=1, Z2=0); college and above (Z1=0, Z2=01)
Body mass index (kg/m^2)	18.5–23.9 (Z1=0, Z2=0); 24–27.9 (Z1=1, Z2=0); ≥28 (Z1=0, Z2=1)
Marital status	Unmarried (Z1=0, Z2=0); married (Z1=1, Z2=0); other (Z1=0, Z2=1)
Controlled attenuation parameter(dB/m)	248–267 (Z1=1, Z2=0); 268–279 (Z1=1, Z2=0); ≥280 (Z1=0, Z2=1)
Liver stiffness (kPa)	<7 (Z1=0, Z2=0); 7–10.2 (Z1=1, Z2=0); ≥10.3 (Z1=0, Z2=1)

Table 5 Results of the multiple linear regression analysis of health-related quality of life

Characteristic	*B*	SE	β	*T*	P value
(Constant)	6.831	0.285		23.932	0.000
Education level					
Junior high school and below (ref)					
High school/junior college	0.010	0.095	0.006	0.104	0.917
College and above	0.112	0.082	0.079	1.369	0.172
Marital status					
Unmarried (ref)					
Married	0.076	0.087	0.045	0.867	0.386
Other	−0.416	0.197	−0.096	−2.107	0.036
Monthly income(RMB)					
<5000 (ref)					
5000–10 000	0.025	0.089	0.018	0.286	0.775
>10 000	0.225	0.089	0.162	2.516	0.012
Controlled attenuation parameter (dB/m)					
248–267 (ref)					
268–279	−0.020	0.138	−0.007	−0.145	0.884
≥280	−0.118	0.083	−0.072	−1.420	0.156
Liver stiffness (kPa)					
<7 (ref)					
7–10.2	0.042	0.074	0.026	0.575	0.565
≥10.3	−0.280	0.118	−0.110	−2.386	0.017
Body mass index group (kg/m^2)					
18.5–23.9 (ref)					
24–27.9	0.026	0.090	0.018	0.287	0.774
≥28	−0.090	0.102	−0.065	−0.884	0.377
Age (years)					
18–39 (ref)					
40–59	0.062	0.073	0.045	0.849	0.396
≥60	−0.068	0.113	−0.030	−0.604	0.546
Sex	−0.171	0.068	−0.114	−2.510	0.012
Comorbidity	−0.057	0.064	−0.041	−0.882	0.378
Regular exercise	−0.189	0.068	−0.121	−2.776	0.006
Smoking	−0.076	0.070	−0.048	−1.091	0.276
Abdominal obesity	−0.131	0.079	−0.083	−1.663	0.097
Alanine transaminase (U/L)	−0.002	0.001	−0.139	−3.080	0.002
Triglyceride (mmol/L)	−0.045	0.023	−0.086	−1.914	0.056

R^2 = 0.159; adjusted R^2 = 0.122; significance was set at p<0.05.
P value was determined using the multiple linear regression.
B, unstandardised coefficient; β, standardised coefficient.

and their income level. Research in Brazil and studies by David both indicate that higher socio-economic status is closely associated with improved HRQL.[43 44] NAFLD is a prevalent disease in men in their 40s–50s who are most active in economic activities.[45] Good economic conditions guarantee a material basis and access to medical treatment, and patients with a better economic status have better living conditions and therefore a better quality of life. Patients with poorer economic status may face greater challenges in making dietary and lifestyle changes, which are crucial for the management of NAFLD. However, in Germany, the HRQL of patients with CLD is not associated with their economic status.[46] The results of

previous studies have been inconsistent. This discrepancy might be due to the differences in the type of liver disease, research measurement tools, and other factors.

The findings of this study indicate that patients with NAFLD who engage in regular physical activity exhibit a higher level of HRQL. An interventional study by Abdelbasset *et al* reported that 8-week high-intensity interval aerobic exercise (40 min cycling, 3×/week) improved weight loss and HRQL in obese patients with NAFLD complicated with diabetes.[47] Cuban reported that exercising for >90 min/week positively impacts quality of life.[48] Notably, the positive effect of exercise on reducing the liver fat content is active even in the absence of significant weight loss.[49] Exercise may benefit patients with NAFLD through several mechanisms. On the one hand, exercise can create a metabolically healthy environment by increasing peripheral insulin sensitivity, thereby reducing the transfer of free fatty acids from adipose tissue to liver tissue.[50] On the other hand, exercise can stimulate the brain to release endorphins and other substances that promote relaxing emotions and relieve psychological stress so that patients with NAFLD who exercise regularly have better HRQL. In addition, a meta-analysis revealed that long-term exercise has a beneficial effect on lipid metabolism in Chinese patients with NAFLD.[51] According to the available literature, physical exercise has a beneficial effect on NAFLD.[52] Various regimens of physical exercise have been shown to reduce the hepatic fat content through improvements in insulin resistance, liver fatty acid metabolism, liver mitochondrial function and the activation of inflammatory cascades, thereby delaying the progression of NAFLD and improving patients' quality of life. Therefore, exercise counselling and health education for patients should be strengthened in clinical practice, especially in terms of exercise type, duration and intensity.

The impact of liver stiffness on HRQL was another finding of our study. Some studies using the SF-36 have shown that liver stiffness and various dimensions of quality of life are negatively correlated.[53 54] In our investigation, patients with cirrhosis presented markedly lower HRQL scores than those without cirrhosis, which is consistent with David's research, which yielded concordant findings.[44] Other reports have also shown that the more severe the combination of liver fibrosis is in patients with NAFLD, the greater the risk of cardiovascular events, and cardiovascular disease is one of the leading causes of death in patients with NAFLD.[55] This finding suggests that liver stiffness not only is a significant indicator of liver health but also may have profound implications for a patients' overall health status and lifespan. In this context, effective treatment not only directly improves liver function but also may reduce the risk of cardiovascular events, thereby increasing patients' overall quality of life and life expectancy. Therefore, future prospective studies are warranted.

Furthermore, this study identified the ALT level as a factor influencing patients' HRQL. This finding aligns with a cross-sectional study in Korea.[56] ALT is a commonly used marker to assess hepatocyte damage. In patients with NAFLD, an elevated ALT level is typically associated with liver inflammation and hepatocellular damage.[57] Some prospective cohort studies have shown that patients with NAFLD, including those with unexplained increases in ALT levels, may face a reduced life expectancy, with the main causes of death being malignant tumours, cardiovascular diseases and cirrhosis.[58] However, even patients with normal ALT levels may have significant liver inflammation and fibrosis, which could affect their quality of life and increase the risk of disease progression.[59] Nevertheless, some studies have suggested that the ALT level is not correlated with the quality of life of patients with NAFLD.[60 61] The reasons for these differing conclusions may lie in the differences in the study populations, sample sizes and diagnostic criteria for NAFLD, among other factors. Overall, the impact of blood markers on the quality of life of patients with NAFLD remains uncertain and requires larger cross-sectional studies and interventional research. Therefore, in the management of NAFLD, in addition to monitoring ALT levels, factors such as liver imaging must also be considered to assess and fully manage the patients' conditions.

Limitations

To our knowledge, this study represents the most comprehensive analysis to date of the demographic and clinical characteristics of HRQL in patients with NAFLD, providing guidance and assistance for improving HRQL in clinical practice. Several limitations remain in this study. First, this cross-sectional study could not determine the cause–effect and temporal relationships between independent variables and HRQL changes. Further longitudinal studies are needed to understand how the characteristics of participants may affect HRQL. This study was conducted at a single centre with a relatively small sample size. Second, the subjects of this study population were recruited from the outpatient clinic of a hospital in Hangzhou, China, potentially impacting the results because of the patients' geographical location, lifestyle and dietary habits. Therefore, a more comprehensive research design is needed in the future to fully consider these factors. Third, this study focused on the HRQL of patients with NAFLD without accounting for the potential differences among the various patient subgroups. Therefore, future research should emphasise subgroup analyses to better understand the heterogeneity of NAFLD and provide personalised treatment strategies.

CONCLUSIONS

Currently, the HRQL in patients with NAFLD is impaired. This study revealed that HRQL is not only associated with clinical factors such as liver stiffness, ALT levels and regular exercise, but is also influenced by sociodemographic factors such as sex, marital status and monthly income. Based on these findings, it is important to consider both

clinical and sociodemographic factors when assessing and managing the overall health of patients with NAFLD. Therefore, healthcare providers should adopt a holistic approach to NAFLD management, which includes not only standard medical treatment but also psychological support. Additionally, personalised lifestyle guidance should be provided based on the patient's socio-economic background to ensure the accessibility of treatment.

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REFERENCES

1 Sheka AC, Adeyi O, Thompson J, *et al*. Nonalcoholic Steatohepatitis. *JAMA* 2020;323:1175.
2 Rinella ME. Nonalcoholic fatty liver disease: a systematic review. *JAMA* 2015;313:2263–73.
3 Hagström H, Kechagias S, Ekstedt M. Risk for hepatic and extra-hepatic outcomes in nonalcoholic fatty liver disease. *J Intern Med* 2022;292:177–89.
4 Adams LA. Cardiovascular disease in metabolic-associated fatty liver disease. *Curr Opin Endocrinol Diabetes Obes* 2023;30:81–6.
5 Stepanova M, Henry L, Younossi ZM. Economic Burden and Patient-Reported Outcomes of Nonalcoholic Fatty Liver Disease. *Clin Liver Dis* 2023;27:483–513.
6 Nguyen AL, Park H, Nguyen P, *et al*. Rising Inpatient Encounters and Economic Burden for Patients with Nonalcoholic Fatty Liver Disease in the USA. *Dig Dis Sci* 2019;64:698–707.
7 Wu Y, Zheng Q, Zou B, *et al*. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. *Hepatol Int* 2020;14:259–69.
8 Li J, Zou B, Yeo YH, *et al*. Prevalence, incidence, and outcome of non-alcoholic fatty liver disease in Asia, 1999-2019: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2019;4:389–98.
9 Lu Z-Y, Shao Z, Li Y-L, *et al*. Prevalence of and risk factors for non-alcoholic fatty liver disease in a Chinese population: An 8-year follow-up study. *World J Gastroenterol* 2016;22:3663–9.
10 Pereira MA, Kartashov AI, Ebbeling CB, *et al*. Fast-food habits, weight gain, and insulin resistance (the CARDIA study): 15-year prospective analysis. *Lancet* 2005;365:36–42.
11 Qiu S, Cai X, Sun Z, *et al*. Association between physical activity and risk of nonalcoholic fatty liver disease: a meta-analysis. *Therap Adv Gastroenterol* 2017;10:701–13.
12 Tourani S, Behzadifar M, Martini M, *et al*. Health-related quality of life among healthy elderly Iranians: a systematic review and meta-analysis of the literature. *Health Qual Life Outcomes* 2018;16:18.
13 Kłak A, Mińko M, Siwczyńska D, *et al*. Selected questionnaire methods studying the quality of life. *Postepy Dermatol Alergol* 2015;32:210–5.
14 Younossi ZM, Stepanova M, Lawitz E, *et al*. Improvement of hepatic fibrosis and patient-reported outcomes in non-alcoholic steatohepatitis treated with selonsertib. *Liver Int* 2018;38:1849–59.
15 Sayiner M, Stepanova M, Pham H, *et al*. Assessment of health utilities and quality of life in patients with non-alcoholic fatty liver disease. *BMJ Open Gastroenterol* 2016;3:e000106.
16 Chen YT, Zhang W, Gu YP, *et al*. Chinesization of the quality of life scale and its reliability and validity tests for non-alcoholic fatty liver disease. *Zhonghua Gan Zang Bing Za Zhi* 2022;30:981–5.
17 von Elm E, Altman DG, Egger M, *et al*. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ* 2007;335:806–8.
18 Karlas T, Petroff D, Sasso M, *et al*. Individual patient data meta-analysis of controlled attenuation parameter (CAP) technology for assessing steatosis. *J Hepatol* 2017;66:1022–30.
19 National Workshop on Fatty Liver and Alcoholic Liver Disease, Chinese Society of Hepatology, Chinese Medical Association, Fatty Liver Expert Committee, Chinese Medical Doctor Association. Guidelines of prevention and treatment for nonalcoholic fatty liver disease: a 2018 update. *Zhonghua Gan Zang Bing Za Zhi* 2018;26:195–203.
20 Charan J, Biswas T. How to calculate sample size for different study designs in medical research? *Indian J Psychol Med* 2013;35:121–6.
21 Hwang TI, Han AL. Quality of Life in Adults with Metabolic Dysfunction-Associated Fatty Liver Disease. *Int J Environ Res Public Health* 2021;18:13145.
22 Zhai Y, Fang HY, Yu WT, *et al*. Changes in Waist Circumference and Abdominal Obesity among Chinese Adults over a Ten-year Period. *Biomed Environ Sci* 2017;30:315–22.
23 Department of Disease Control, Ministry of Health, People's Republic of China. Guidelines for the Prevention and Control of Overweight and Obesity in Chinese Adults; People's Health Publishing House; 2006.
24 Koliaki C, Liatis S, Dalamaga M, *et al*. Sarcopenic Obesity: Epidemiologic Evidence, Pathophysiology, and Therapeutic Perspectives. *Curr Obes Rep* 2019;8:458–71.
25 Hung S-P, Chen C-Y, Guo F-R, *et al*. Combine body mass index and body fat percentage measures to improve the accuracy of obesity screening in young adults. *Obes Res Clin Pract* 2017;11:11–8.
26 Seto W-K, Hui RWH, Mak L-Y, *et al*. Association Between Hepatic Steatosis, Measured by Controlled Attenuation Parameter, and Fibrosis Burden in Chronic Hepatitis B. *Clin Gastroenterol Hepatol* 2018;16:575–83.

27 Tao YT, Yan SY, Chen GY, *et al*. Research on life quality in patients with nonalcoholic fatty liver disease. *Chinese Hepatology* 2016;21:1017–22.
28 Younossi ZM, Stepanova M, Henry L, *et al*. A disease-specific quality of life instrument for non-alcoholic fatty liver disease and non-alcoholic steatohepatitis: CLDQ-NAFLD. *Liver Int* 2017;37:1209–18.
29 Younossi ZM, Paik JM, Golabi P, *et al*. The impact of fatigue on mortality of patients with non-alcoholic fatty liver disease: Data from National Health and nutrition examination survey 2005-2010 and 2017-2018. *Liver Int* 2022;42:2646–61.
30 Karshikoff B, Sundelin T, Lasselin J. Role of Inflammation in Human Fatigue: Relevance of Multidimensional Assessments and Potential Neuronal Mechanisms. *Front Immunol* 2017;8:21.
31 Swain MG. Fatigue in liver disease: pathophysiology and clinical management. *Can J Gastroenterol* 2006;20:181–8.
32 Younossi ZM, Kremer AE, Swain MG, *et al*. Assessment of fatigue and its impact in chronic liver disease. *J Hepatol* 2024;81:726–42.
33 Gerber LH, Weinstein AA, Mehta R, *et al*. Importance of fatigue and its measurement in chronic liver disease. *World J Gastroenterol* 2019;25:3669–83.
34 Chalasani N, Younossi Z, Lavine JE, *et al*. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatology* 2018;67:328–57.
35 Nguyen VH, Yeo YH, Zou B, *et al*. Discrepancies between actual weight, weight perception and weight loss intention amongst persons with NAFLD. *J Intern Med* 2021;289:840–50.
36 Kandola A, Ashdown-Franks G, Hendrikse J, *et al*. Physical activity and depression: Towards understanding the antidepressant mechanisms of physical activity. *Neurosci Biobehav Rev* 2019;107:525–39.
37 Assimakopoulos K, Karaivazoglou K, Tsermpini E-E, *et al*. Quality of life in patients with nonalcoholic fatty liver disease: A systematic review. *J Psychosom Res* 2018;112:73–80.
38 Licata A, Russo GT, Giandalia A, *et al*. Impact of Sex and Gender on Clinical Management of Patients with Advanced Chronic Liver Disease and Type 2 Diabetes. *J Pers Med* 2023;13:558.
39 Zhejiang Provincial Bureau of Statistics. Series analysis ii from the seventh population census of zhejiang province: gender and age [EB/OL]. 2022. Available: https://tjj.zj.gov.cn/art/2022/7/22/art_1229129214_4955988.html [Accessed 22 Apr 2024].
40 Zhejiang Provincial Bureau of Statistics. Main population data bulletin of zhejiang province for 2023 [EB/OL]. 2024. Available: https://tjj.zj.gov.cn/art/2024/2/26/art_1229129205_5268394.html [Accessed 22 Apr 2024].
41 Gao R, Gao F, Li G, *et al*. Health-related quality of life in chinese patients with chronic liver disease. *Gastroenterol Res Pract* 2012;2012:516140.
42 Zhou Y, Fang LH, Lin M, *et al*. Self health management level and influencing factors in patients with nonalcoholic fatty liver disease. *Chin J of PHM* 2021;37:469–72.
43 Häuser W, Holtmann G, Grandt D. Determinants of health-related quality of life in patients with chronic liver diseases. *Clin Gastroenterol Hepatol* 2004;2:157–63.
44 David K, Kowdley KV, Unalp A, *et al*. Quality of life in adults with nonalcoholic fatty liver disease: baseline data from the nonalcoholic steatohepatitis clinical research network. *Hepatology* 2009;49:1904–12.
45 Li Z, Xue J, Chen P, *et al*. Prevalence of nonalcoholic fatty liver disease in mainland of China: a meta-analysis of published studies. *J Gastroenterol Hepatol* 2014;29:42–51.
46 Souza N de, Villar LM, Garbin AJÍ, *et al*. Assessment of health-related quality of life and related factors in patients with chronic liver disease. *Braz J Infect Dis* 2015;19:590–5.
47 Abdelbasset WK, Tantawy SA, Kamel DM, *et al*. A randomized controlled trial on the effectiveness of 8-week high-intensity interval exercise on intrahepatic triglycerides, visceral lipids, and health-related quality of life in diabetic obese patients with nonalcoholic fatty liver disease. *Medicine (Abingdon)* 2019;98:e14918.
48 Castellanos-Fernández MI, Borges-González SA, Stepanova M, *et al*. Health-related quality of life in Cuban patients with chronic liver disease: A real-world experience. *Ann Hepatol* 2021;22:100277.
49 Whitsett M, VanWagner LB. Physical activity as a treatment of non-alcoholic fatty liver disease: A systematic review. *World J Hepatol* 2015;7:2041–52.
50 van der Windt DJ, Sud V, Zhang H, *et al*. The Effects of Physical Exercise on Fatty Liver Disease. *Gene Expr* 2018;18:89–101.
51 Gao Y, Lu J, Liu X, *et al*. Effect of Long-Term Exercise on Liver Lipid Metabolism in Chinese Patients With NAFLD: A Systematic Review and Meta-Analysis. *Front Physiol* 2021;12:748517.
52 Oh S, Shida T, Yamagishi K, *et al*. Moderate to vigorous physical activity volume is an important factor for managing nonalcoholic fatty liver disease: a retrospective study. *Hepatology* 2015;61:1205–15.
53 Samala N, Desai A, Vilar-Gomez E, *et al*. Decreased Quality of Life Is Significantly Associated With Body Composition in Patients With Nonalcoholic Fatty Liver Disease. *Clin Gastroenterol Hepatol* 2020;18:2980–8.
54 Lu J, Piao HG, Jin XM, *et al*. Correlation of quality of life with aspartate aminotransferase - to - platelet ratio index, liver stiffness measurement, and histopathology after antiviral therapy for chronic hepatitis B liver fibrosis. *J Clin Hepato* 2021;37:813–6.
55 Lu JG, Yu L. Effect of liver on cardiovascular disease in patients with nonalcoholic fatty liver disease. *Chin J Clin Gastroenterol* 2023;35:38–41.
56 Glantzounis GK, Tsimoyiannis EC, Kappas AM, *et al*. Uric acid and oxidative stress. *Curr Pharm Des* 2005;11:4145–51.
57 Li Q, Han Y, Hu H, *et al*. Gamma-glutamyl transferase to high-density lipoprotein cholesterol ratio has a non-linear association with non-alcoholic fatty liver disease: A secondary prospective cohort study in non-obese Chinese adults. *Front Med (Lausanne)* 2022;9:995749.
58 Yuan YF, Cao Q, Jiang YY. Association of dietary behavior with nonalcoholic fatty liver disease. *J Clin Hepatol* 2023;39:401–7.
59 Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, *et al*. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology* 2023;77:1797–835.
60 Chawla KS, Talwalkar JA, Keach JC, *et al*. Reliability and validity of the Chronic Liver Disease Questionnaire (CLDQ) in adults with non-alcoholic steatohepatitis (NASH). *BMJ Open Gastroenterol* 2016;3:e000069.
61 Dan AA, Kallman JB, Wheeler A, *et al*. Health-related quality of life in patients with non-alcoholic fatty liver disease. *Aliment Pharmacol Ther* 2007;26:815–20.