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EVALUATION OF THE CORRELATION BETWEEN DISEASE SEVERITY AND QUALITY OF LIFE IN NON ALCOHOLIC FATTY LIVER PATIENTS

E. Pavan Kumar[1]*, Thirumaleswara Goud[2]

[1]Research Scholar, Research and Development, Jawaharlal Nehru Technological University, Anantapur, Andhra Pradesh - 515002, India,
Email: dr.e.pavankumar@gmail.com
[2]Professor, Creative Educational Society's College of Pharmacy, NH-7, Chinnatekur, Kurnool - 518218, Andhra Pradesh, India.

ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is a common chronic liver disease strongly linked with obesity, type 2 diabetes mellitus, dyslipidemia and metabolic syndrome. A progression of disease from simple steatosis to severe fibrosis is accompanied by a marked decline in health-related quality of life (HRQoL). So, this study tried to investigate the relationship between the severity of NAFLD and HRQoL with a particular focus on the effect of hepatic fibrosis.

Materials and Methods: This was a prospective observational study involving 466 adult patients with NAFLD at the Government General Hospital, Anantapur. Severity of the disease was evaluated by Fatty liver index (FLI) and Fibrosis-4 (FIB-4) score, and health related quality of life (HRQoL) by validated questionnaires including Chronic Liver Disease Questionnaire for NAFLD (CLDQ-NAFLD) and Short Form-36 (SF-36). Correlation and stepwise multiple linear regression analyses were conducted to assess disease severity in relation to HRQoL.

Results: The average scores of FLI and FIB-4 were 56.4 ± 13.5 and 2.3 ± 0.7, respectively. Among the subjects, high-risk steatosis and fibrosis were 66.5% and 72.3%, respectively. Advanced fibrosis patients had significantly worse HRQoL in all domains measured like physical functioning, fatigue, emotional well-being, activity restriction, and the quality of life in general; $p < 0.001$. The strongest inverse association of fibrosis severity was with overall HRQoL ($r = –0.48$, $p < 0.001$) as followed by steatosis severity ($r = –0.36$, $p < 0.001$). Several linear regression analysis revealed fibrosis severity ($\beta = –0.41$, $p < 0.001$), HbA1c ($\beta = –0.24$, $p = 0.003$), and BMI ($\beta = –0.19$, $p = 0.008$) as significant predictors of poor HRQoL.

Conclusion: Progressive liver fibrosis is independently associated with substantial impairment in HRQoL in NAFLD patients and accounts for the greatest impairment in patient well-being. Early detection of fibrosis by non-invasive techniques in conjunction with optimal metabolic treatment and multidisciplinary approach may have beneficial effects on clinical outcome and quality of life.

KEYWORDS: Fibrosis, Steatosis, Non-alcoholic fatty liver disease, Quality of life

1. INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is one among the most prevalent chronic liver disease worldwide and is poised to become a leading cause of liver transplantation, which is a significant burden on public health [1]. It affects almost one-fourth of the adult population worldwide, and it is more prevalent in those with obesity, insulin resistance, type 2 diabetes mellitus (T2DM), dyslipidemia, and metabolic syndrome [1,2]. NAFLD comprises a wide range of hepatic disorders from isolated steatosis to non-alcoholic steatohepatitis (NASH), advanced fibrosis, cirrhosis and hepatocellular carcinoma [3,4]. Among these stages, liver fibrosis has been shown the best predictor of liver-related events, disease progression and all-cause mortality [5,6].

NAFLD is currently being considered as a multisystem disease rather an isolated liver disease. Patients with NAFLD are at risk of not only hepatic complications but also cardiovascular disease, chronic kidney disease, endocrine dysfunction, and the worst metabolic outcomes [7,8]. However, cardiovascular disease is still the major cause of death in NAFLD patients, especially those with comorbid diabetes and obesity [9]. T2DM is regarded as the most strong risk factor for progression of NAFLD and diabetic patients have a significantly greater likelihood of advanced fibrosis and cirrhosis compared with non-diabetic patients [10,11]. The reciprocal relationship of NAFLD and diabetes further amplifies disease burden, promotes insulin resistance, and deteriorates long-term prognosis [12].

Although the metabolic and clinical implications of NAFLD are now well known, its effect on health-related quality of life (HRQoL) has been explored less. A reflection of patients' view of their physical, emotional, psychological and social well-being, HRQoL is now considered as a crucial outcome in the management of chronic diseases [13]. NAFLD patients commonly experience fatigue, decreased physical functioning, poor sleep, anxiety and depression as well as having restrictions in their daily activities—all of which have negative impact on adherence to treatment and long-term follow-up [14,15]. Prior reports have indicated that NAFLD patients have markedly worse HRQoL scores relative to the general population, particularly in areas of physical health such as energy, mobility and ability to perform daily activities [16].

Severity of the disease is greatly influenced by the extent of HRQoL disruption. Patients with advanced fibrosis have been

reported to have much worse quality of life than patients with simple steatosis in a number of quality of life domains, such as fatigue, physical limitation, emotional well-being, and social functioning [17,18]. Fibrosis development is often clinically unrecognized in its early stages and consequently the prediction of this process and its early detection significantly enhances clinical and patient outcomes. The FLI and Fibrosis-4 (FIB-4) score are non-invasive markers frequently used to evaluate the severity of steatosis and fibrosis in clinical routine and represent credible substitutes to liver biopsy for risk stratification [19].

Evidence from recent studies suggest that chronic systemic inflammation, sarcopenia, and metabolic abnormalities have a negative impact on the HRQoL in NAFLD patients [20]. They also found that sarcopenia was an independent risk factor for advanced fibrosis and reduced physical performance, underlining the systemic burden of the disease. NASH patients with advanced fibrosis have more severe impairment in fatigue, emotional well-being, and activities of daily living than those with early stage disease [21]. These results further support the notion that the extent of fibrosis is not only a surrogate of hepatic progression but also a major driver of patient reported outcomes.

Despite growing awareness of HRQoL deterioration in NAFLD, only few studies have assessed the direct association between disease severity and quality of life in the day-to-day clinical practice, and none in populations at metabolic high-risk. Understanding and knowledge of this association is critical for advancing patient-focused care, for the identification of individuals at high risk for both disease progression and decreased quality of life, and for the development of multidisciplinary management paradigms targeting disease control and quality of life improvement. Thus, the present study was designed to assess the association between disease severity, notably fibrosis, steatosis, and quality of life in subjects with NAFLD, with a particular focus on determining if fibrosis can be a predictor of compromised health-related well-being.

MATERIALS AND METHODS

This prospective observational study was held at Government General Hospital, Anantapur, Andhra Pradesh, India, for a period of 12 months to assess the association of severity of disease with quality of life in NAFLD patients. This study included patients older than 18 years with a confirmed diagnosis of NAFLD either through ultrasonographic findings and/or biochemical evidence indicative of hepatic steatosis. Those who had significant alcohol intake, viral hepatitis, autoimmune liver disease, Wilson's disease, hemochromatosis, decompensated cirrhosis, hepatocellular carcinoma, pregnant, breast feeding and cognitive impaired patients were not included. The Institutional Ethics Committee approved the study, and written informed consent was obtained from all the participants. After satisfying all the criteria, provided written informed consent a total of 466 participants were consecutively enrolled in this study.

Demographic and clinical data includes age, gender, body mass index (BMI), duration of diabetes, blood pressure, glycated hemoglobin (HbA1c), hypertension, and dyslipidemia status were collected from patient interviews, medical records, and laboratory reports. Disease severity was assessed using non-invasive indices including Fatty Liver Index (FLI) for steatosis and Fibrosis-4 (FIB-4) score for fibrosis. Patients were categorized into low-risk and high-risk groups based on standard cut off values for FLI and FIB-4.

Health-related quality of life (HRQoL) was evaluated using validated questionnaires including the Chronic Liver Disease Questionnaire for NAFLD (CLDQ-NAFLD). Domains assessed included physical functioning, fatigue, emotional well-being, activity limitation, and overall quality of life. Higher scores indicated better HRQoL.

The data were entered into a protected database and analyzed using standard statistical software. Continuous variables are mean ± standard deviation and categorical variables are number (percentage). The association between fibrosis score, steatosis score, and HRQoL domains was assessed using Pearson's correlation analysis. Between-group comparisons were performed with independent t-tests and chi-square tests when appropriate. A multivariate linear regression analysis was conducted to determine independent predictors of poor quality of life after controlling for potential confounders such as age, BMI, duration of diabetes and glycaemic control. The significance level was set at $p < 0.05$.

RESULTS

A total of **466** patients diagnosed with non-alcoholic fatty liver disease (NAFLD) were enrolled in the study. The mean age of the participants was **52.1 ± 11.4 years**, with a mean body mass index (BMI) of **27.3 ± 3.6 kg/m²**, indicating a predominantly middle-aged overweight population with a substantial cardiometabolic burden. The mean Fatty Liver Index (FLI) and Fibrosis-4 (FIB-4) scores were **56.4 ± 13.5** and **2.3 ± 0.7**, respectively. Based on disease severity, **310 (66.5%)** participants were categorized as having high-risk hepatic steatosis, while **337 (72.3%)** were classified as having high-risk fibrosis. Patients with advanced fibrosis demonstrated significantly poorer health-related quality of life (HRQoL) across all assessed domains. Correlation analysis revealed a significant inverse relationship between fibrosis severity and overall HRQoL (**$r = -0.48$, $p < 0.001$**). Furthermore, multiple linear regression analysis identified fibrosis severity, HbA1c, and BMI as independent predictors of impaired quality of life.

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants

Parameter	Value
Sample Size	**466**
Age (years)	52.1 ± 11.4
Female	**233 (50.0%)**
Male	**233 (50.0%)**
BMI (kg/m²)	27.3 ± 3.6

HbA1c (%)	6.8 ± 1.1
Blood Pressure (mmHg)	131 ± 18 / 84 ± 10
Hypertension	**220 (47.2%)**
Dyslipidemia	**219 (47.0%)**
Fatty Liver Index (FLI)	56.4 ± 13.5
FIB-4 Score	2.3 ± 0.7

The study population comprised 466 patients with NAFLD and primarily consisted of middle-aged adults (mean age 52.1 ± 11.4 years). There were an equal number of males and females, with 233 (50.0%) subjects in each arm. The mean BMI was 27.3 ±3.6 kg/m2, suggesting that most of the subjects were overweight. The mean HbA1c level was 6.8 ± 1.1%, which is indicative of poor glycaemic control. The Mean blood pressure was 131 ± 18/84 ± 10 mmHg, and hypertension and dyslipidaemia were diagnosed in 220 (47.2%) and 219 (47.0%) subjects, respectively, confirming a high burden of cardiometabolic risk. The mean FLI and the mean FIB-4 were 56.4 ± 13.5 and 2.3 ± 0.7, respectively, representing medium-high hepatic steatosis and a high risk of fibrosis progression.

Table 2. Distribution of Participants Based on Steatosis and Fibrosis Severity

Variable	Category	No. of Participants	Percentage (%)
Fatty Liver Index (FLI)	Low Risk	**156**	33.5
	High Risk	**310**	66.5
FIB-4 Score	Low Risk	**129**	27.7
	High Risk	**337**	72.3

Severity distribution of hepatic disease was that most of the subjects were in the high risk group of both steatosis and fibrosis. According to Fatty Liver Index, 310 (66.5%) of the subjects were at high risk of steatosis, and 156 (33.5%) were at low risk. Similarly, the FIB-4 score identified 337 (72.3%) participants at high risk of fibrosis and 129 (27.7%) at low risk. Prior high risk of fibrosis compared with steatosis suggests end-stage hepatic involvement in the study population and highlights the need for early fibrosis evaluation and appropriate clinical management.

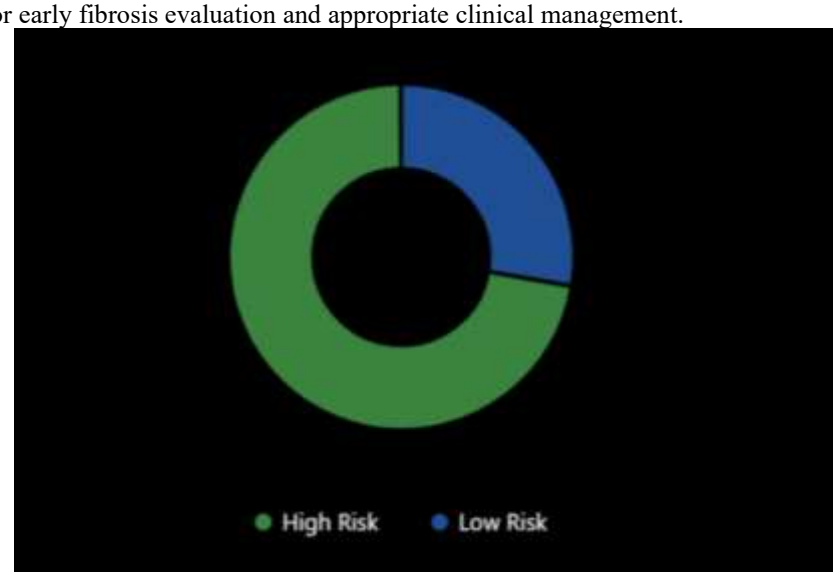

Figure-01: Distribution of FIB-4 Risk categories

The pie chart illustrates the distribution of fibrosis risk among the **466** study participants. Of the total participants, **337 (72.3%)** were classified as having **high fibrosis risk**, whereas **129 (27.7%)** belonged to the **low-risk** category. The predominance of the high-risk group indicates a substantial burden of advanced hepatic fibrosis within the study population, emphasizing the importance of routine fibrosis assessment using non-invasive indices such as the **FIB-4 score** for early risk stratification and timely clinical intervention.

Table 3. Comparison of Quality of Life Scores According to Fibrosis Severity

HRQoL Domain	Low Fibrosis Risk	High Fibrosis Risk	p-value
Physical Functioning	72.4 ± 8.2	58.6 ± 9.4	<0.001
Fatigue	6.1 ± 1.2	4.3 ± 1.5	<0.001
Emotional Well-being	68.2 ± 7.6	55.7 ± 8.3	<0.001
Activity Limitation	5.8 ± 1.1	4.1 ± 1.3	<0.001
Overall QoL Score	69.6 ± 6.8	54.8 ± 7.5	<0.001

Quality of life (QoL) was significantly worse in the high risk fibrosis group in all domains of HRQoL compared to the low risk group (all $p < 0.001$). Consequent with these results, physical functioning scores were significantly lower in the high fibrosis group (58.6 ± 9.4) than the low fibrosis group (72.4 ± 8.2), reflecting more pronounced physical limitations in performing of daily duties [45]. Fatigue scores were also significantly worse in patients with advanced fibrosis (4.3 ± 1.5

vs. 6.1 ± 1.2), indicating greater fatigue and decreased energy. Similar results were obtained for emotional well-being (55.7 ± 8.3 vs. 68.2 ± 7.6), activity limitation (4.1 ± 1.3 vs. 5.8 ± 1.1) and total HRQoL (54.8 ± 7.5 vs. 69.6 ± 6.8), all of which were significantly worse in high risk fibrosis subjects. These results indicate that progressive fibrosis severity profoundly impairs physical and psychosocial functioning.

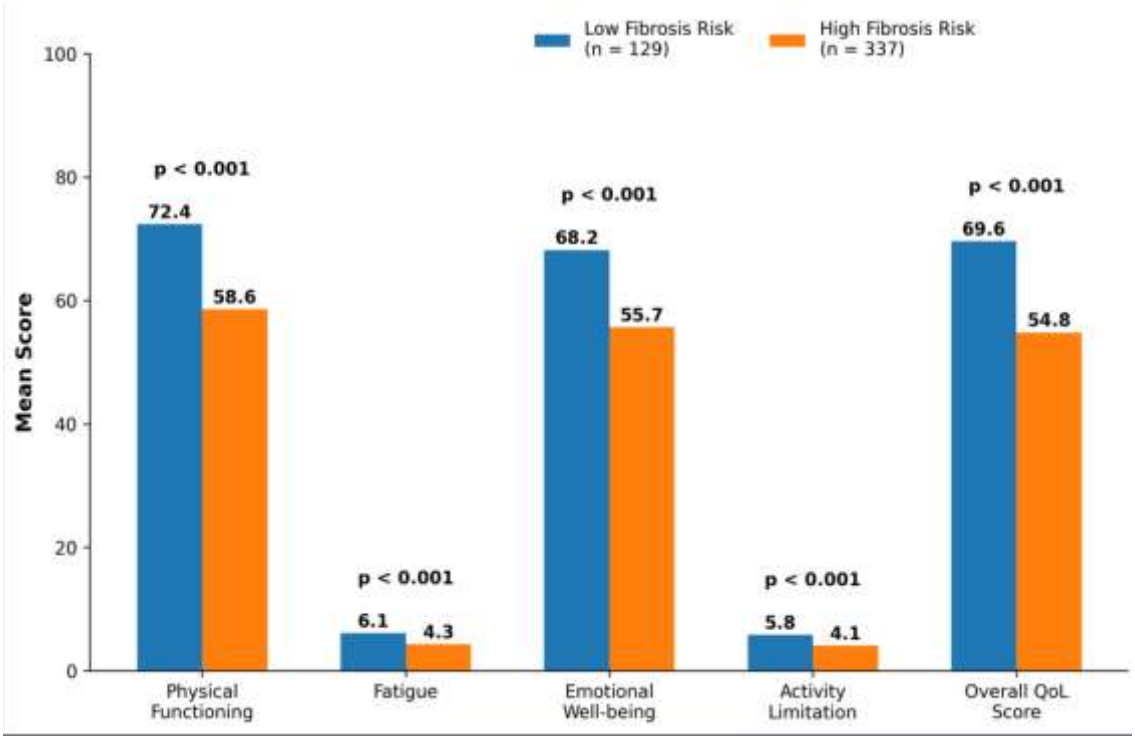

Figure-02: Comparison of HRQoL Domains Between Low and High Fibrosis Risk Groups

Table 4. Correlation and Regression Analysis of Predictors of Quality of Life

Variables	r / β Coefficient	p-value
FIB-4 vs Overall QoL Score	–0.48	<0.001
FLI vs Overall QoL Score	–0.36	<0.001
HbA1c vs QoL Score	–0.29	0.002
BMI vs QoL Score	–0.31	0.001
Duration of Diabetes vs QoL	–0.27	0.004
Fibrosis Severity (Regression β)	–0.41	<0.001
HbA1c (Regression β)	–0.24	0.003
BMI (Regression β)	–0.19	0.008

Correlation analyses revealed inverse association between disease severity and HRQoL. The strongest inverse correlation to all dimensions of quality of life was found for the severity of fibrosis ($r = –0.48$, $p < 0.001$), indicating that increasing fibrosis severity is linked to substantial worsening of patient-reported outcomes. Hepatic steatosis (determined by the Fatty Liver Index) also exhibited a notable inverse association with HRQoL ($r = –0.36$, $p < 0.001$), but this relationship was not as strong as that found for fibrosis. Poorer HRQoL was also significantly associated with higher HbA1c levels ($r = –0.29$, $p = 0.002$), higher BMI ($r = –0.31$, $p = 0.001$), and longer diabetes duration ($r = –0.27$, $p = 0.004$). Multiple linear regression analyses identified fibrosis severity ($\beta = –0.41$, $p < 0.001$), HbA1c ($\beta = –0.24$, $p = 0.003$), and BMI ($\beta = –0.19$, $p = 0.008$) as independent predictors of diminished HRQoL, with fibrosis being the most powerful predictor of a poor quality of life.

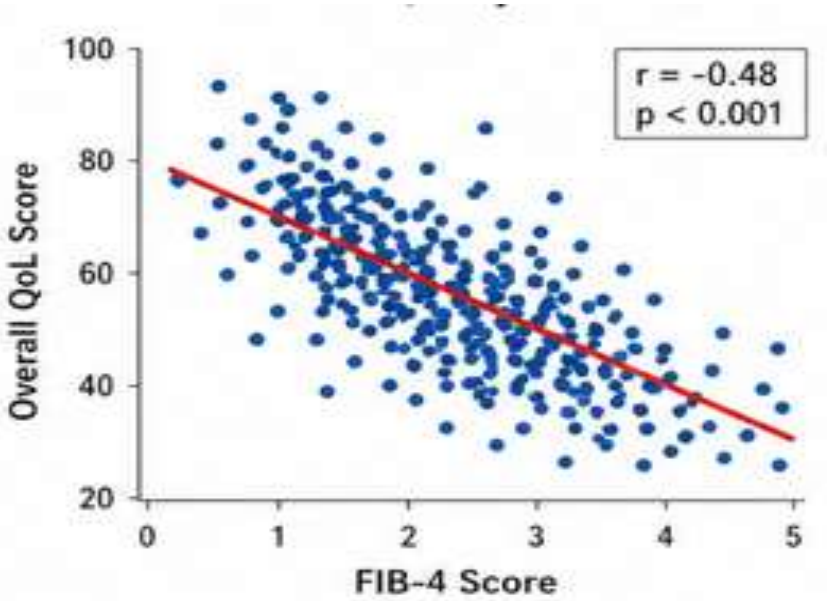

Figure-03: Correlation between FIB-4 Score and Overall Quality of Life Score

The scatter plot demonstrates the correlation between FIB-4 score and overall quality of life score. A significant negative relationship was observed ($r = –0.48$, $p < 0.001$), indicating that as fibrosis severity increased, overall QoL significantly declined. This finding supports the role of fibrosis progression as a major determinant of impaired patient well-being and reduced functional capacity in diabetic NAFLD patients.

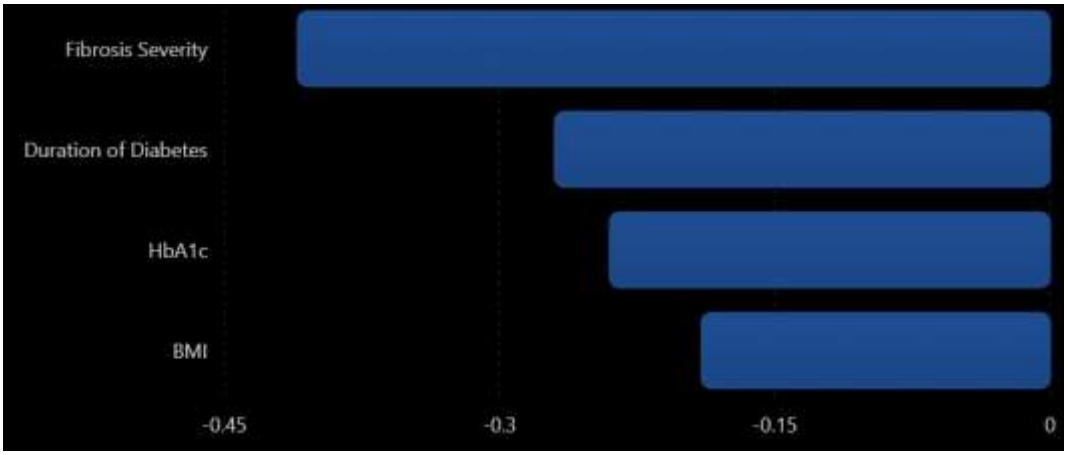

Figure-04: Graph Plot of Multiple Linear Regression Analysis

Above graph summarizes the results of the multiple linear regression analysis. Fibrosis severity demonstrated the strongest independent negative association with HRQoL, followed by HbA1c and BMI, all of which were statistically significant predictors. In contrast, duration of diabetes exhibited comparatively weaker associations. These findings suggest that both hepatic fibrosis and metabolic dysfunction independently contribute to deterioration in quality of life among patients with NAFLD.

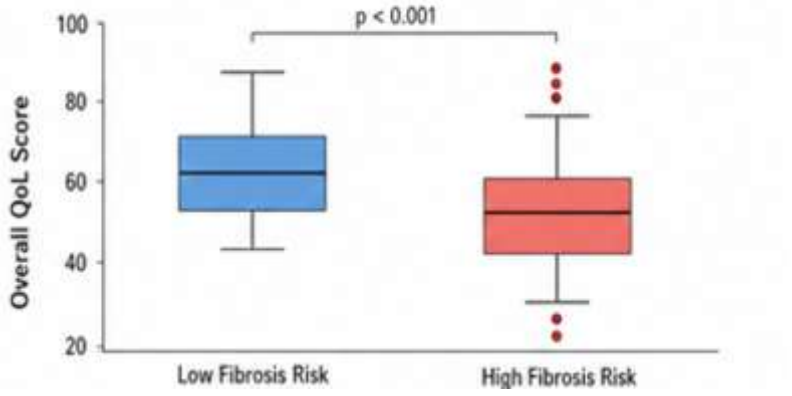

Figure-05: Box Plot Comparing Overall Quality of Life Scores between Low and High Fibrosis Risk Groups

The box plot compares overall quality of life scores between low and high fibrosis risk groups. Patients with high fibrosis risk had significantly lower median QoL scores and greater score variability compared to those with low fibrosis risk ($p < 0.001$). This visual representation strongly supports the statistical findings that advanced fibrosis is associated with substantial deterioration in patient quality of life.

DISCUSSION

This study tried to evaluate the associations of disease severity, including degree of hepatic fibrosis and steatosis, with HRQoL in patients with non-alcoholic fatty liver disease (NAFLD). Results: The results showed that increasing fibrosis severity was significantly correlated with poor quality of life, and reducedphysical function, fatigue, emotional well-being, and activity limitation were observed. Fibrosis negatively affected HRQoL more than steatosis, underscoring that progression of the disease beyond mere fat deposition is a key determinant of patient well-being.

The study sample was predominantly middle-aged adults with overweight or obesity and a substantial burden of cardiometabolic comorbidities, including hypertension, dyslipidemia, and poor glycemic control. The above findings are in line with those of Adams et al. [22] relevant to that NAFLD is a frequent disorder in patients with obesity, insulin resistance and metabolic syndrome and is closely linked with advanced liver disease. Also, insulin resistance and type 2 diabetes mellitus were stated to markedly enhance NAFLD progression and to lead to poor long-term hepatic which is similar to results by Yki-Järvinen [23].

Our study mean FLI and FIB-4 scores reflected a moderate-to-severe steatosis and a clinically relevant fibrosis, with more than two-third of the patients considered at high fibrosis risk. This results are in line with study done by Dulai et al. [24], which suggested that fibrosis stage is the most important determinant of liver-related mortality and all-cause mortality in patients with NAFLD. Ekstedt etal. also observed that fibrosis alone predicts disease-specific mortality, indicating the significance of early fibrosis identification [25].

Quality of life assessment revealed that patients with advanced fibrosis had significantly lower HRQoL scores across all major domains compared to those with low fibrosis risk. Physical functioning and fatigue were the most affected domains, suggesting that fibrosis progression substantially limits daily activities and functional capacity. Similar findings were reported by Dan et al. [26], who showed that NAFLD patients experience significant reductions in vitality, physical functioning, and social well-being compared to healthy controls. Afendy et al. [27] also found that fatigue and reduced physical performance were major contributors to impaired HRQoL in chronic liver disease patients, particularly in those with advanced fibrosis.

In the present study, fibrosis severity showed the strongest negative correlation with overall QoL ($r = –0.48$, $p < 0.001$), followed by steatosis severity ($r = –0.36$, $p < 0.001$). These results suggest that fibrosis contributes more significantly to impaired HRQoL than hepatic fat accumulation alone. Huber et al. [28] similarly demonstrated that hepatic inflammation and fibrosis were independently associated with poorer physical functioning and reduced life satisfaction. Hagström et al. [29] further confirmed that fibrosis progression significantly influences both clinical outcomes and patient-reported quality of life, even in the absence of advanced cirrhosis.

Higher BMI and HbA1c were also associated with significantly worse HRQoL in our study. These results are consistent with Sayiner et al. that showed obesity and poor glycemic control were independent determinants of worsened hepatic and quality of life outcomes among NAFLD subjects [30]. Elwing et al. also found that metabolic load is associated with depression, anxiety and physical inactivity and hence overall patient wellbeing [31] .

Multivariate analysis demonstrated that the impairment of HRQoL was independently predicted by the severity of fibrosis, HbA1c, and BMI, indicating that metabolic abnormalities as well as hepatic advancement have adverse effects on the patient-related outcomes. This suggests the importance of periodic fibrosis evaluation with non-invasive methodologies (e.g., FIB-4 and FLI) and monitoring of quality of life as part of NAFLD care in routine practice.

Overall, our study validates that HRQoL impairment is more closely related to fibrosis severity than to steatosis alone in patients with NAFLD. Early detection of fibrosis, improved metabolic control and patient focused care may dramatically enhance both clinical outcomes and quality of life in long term.

CONCLUSION

Non-alcoholic fatty liver disease in patients with type 2 diabetes mellitus represents a significant clinical challenge due to its progressive hepatic burden and substantial impact on patient well-being. The present study demonstrated that increasing disease severity, particularly hepatic fibrosis, was strongly associated with impaired health-related quality of life, with notable reductions in physical functioning, increased fatigue, emotional distress, and limitations in daily activities. Steatosis also contributed to reduced quality of life, although its impact was less pronounced than fibrosis. Additionally, poor glycemic control, higher body mass index, and longer duration of diabetes were identified as important contributors to worsening patient-reported outcomes. These findings emphasize the importance of early non-invasive assessment of fibrosis and steatosis using indices such as FIB-4 and FLI, along with routine quality of life evaluation. Integrating metabolic control with patient-centered multidisciplinary care may significantly improve both clinical prognosis and long-term quality of life in diabetic NAFLD patients.