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Original article

Impact of Metabolic Associated Fatty Liver Disease on Health-Related Quality of Life

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Abstract

Introduction: Metabolic associated fatty liver disease (MAFLD), the nomenclature major benefit is the shift towards a diagnosis of inclusion based on the presence of metabolic dysfunction. MAFLD has also been associated with impaired health-related quality of life (HRQOL). **Aim**: to assess the impact of MAFLD & degree of hepatic steatosis and fibrosis on patients' HRQOL applying the SF-36 Questionnaire. **Methods**: This cross sectional study was carried out on 250 adult who were subdivided into 2 groups, Group I (GI) comprised 150 consecutive patients with MAFLD while Group II (GII) comprised 100 apparently healthy subjects. Both studied groups had completed the short form-36 (SF-36) questionnaire. **Results**: The mean age among cases group was 43.6 ±10.5 years & females were the predominant. There was a highly statistical significance negative correlation between body mass index (BMI) and all domains of SF-36 questionnaire among GI. Scores of all scales of SF-36 were significantly lower in GI compared to GII). Hepatic steatosis grades with in GI according to CAP values were S1(17.3%), S2(37.3%) and S3(45.3). scores of all scales of SF-36 were significantly lower in S3 patients compared to S2 & S1(P value<0.001). Fibrosis stages within GI according to LSM values were F0(44.7%), F1(32.7%), F2(12.7%), F3(6.7%) & F4(3.3%). scores of all scales of SF-36 were significantly lower in F4 patients compared to F3, F2, F1 & F0(P value<0.001). **Conclusion**: HRQOL is significantly impaired in patients with MAFLD. The higher the grade of steatosis and stage of fibrosis the lower the scales of SF-36 questionnaire.

Keywords: Metabolic associated fatty liver disease (MAFLD), Health-related quality of life(HRQOL), Short form-36 (SF-36) questionnaire.

Introduction

MAFLD is becoming the principal worldwide cause of liver diseases and affects nearly a quarter of the global population [1, 2]. Specific studies suggest that the prevalence range of MAFLD in Egypt is approximately 47.5%, with 56.7% having fibrosis [3]. MAFLD's major benefit is the shift towards a diagnosis of inclusion based on the presence of metabolic dysfunction, the key driver of the disease. Hence, it is possible to diagnose MAFLD coexistence with other liver diseases such as chronic viral hepatitis, alcoholic- and other liver diseases [4, 5]. The diagnosis of MAFLD is based on the detection of liver steatosis (liver histology, non-invasive biomarkers or imaging) together with the presence of at least 1 of 3 criteria that include: overweight or obesity, type 2 diabetes mellitus (T2DM) or clinical evidence of metabolic dysfunction [2].

Beside fatigue, MAFLD patients may also experience other symptoms such as anxiety, depression, cognitive impairment, and loss of self-esteem. These symptoms significantly impact patients' well-being [6]. In the era of patient-centered care, to assess the full burden of MAFLD, it is imperative to consider not only relevant clinical outcomes, but also its economic impact and the effect on patient-reported outcomes (PROs). By definition, PROs are reports that come directly from patients without modification by anyone else. Among PROs, health-related quality of life (HRQOL) typically is linked to patients' well-being and experience with their disease and its management [7].

Quality of life (QOL) is a broad multidimensional concept that usually includes subjective evaluations of both positive and negative aspects of life. HRQOL questionnaires have become an important component of public health surveillance and are generally considered valid indicators of unmet needs and intervention outcomes [8, 9]. The short-form 36 (SF-36) is a questionnaire used to measure general health status. The SF-36 health survey, developed in the United States, is a well-validated, widely used, generic HRQOL assessment tool [10]. The SF-36 has been translated into a number of languages, and psychometric testing of the translated versions provides evidence that the SF-36 is a reliable and valid general health survey measure across diverse cultures or nations [11].

The aim of this work was to assess the impact of MAFLD on patients' HRQOL applying the SF-36 Questionnaire and assess the impact of degree of hepatic steatosis and/or fibrosis on MAFLD patients' HRQOL.

Patients and Methods

This cross sectional study was carried out on 250 adult participants who were subdivided into 2 groups, Group I(cases group, GI) 150 patients with MAFLD while Group II(control group, GII) 100 apparently healthy subjects with normal abdominal ultrasonography, glycaemic & lipid profiles, age and gender matching the cases group. All were attending the Hepatogastroentrology outpatient clinics, Mahalla Hepatology Teaching Hospital, Mahalla, Egypt, during the period from November 2021 to July 2023 after approval from the Ethical Committee, Faculty of Medicine, Benha University,

Benha, Egypt. An informed consent was obtained.

Exclusion criteria were age below 18ys, pregnant females (unfit for Fibroscan and CAP), patients with malignancy, decompensated liver cirrhosis, alternative causes of fatty liver (eg, consumption of amiodarone and tamoxifen), cardiac patients with congestive hepatopathy and patients with neurological & psychological disorders e.g. depression.

All patients were subjected to: thorough history taking and clinical examination, body mass index(BMI), waist circumference, blood pressure was measured on both arms in the sitting position after resting for at least 15 min, laboratory investigations [complete blood count (CBC), HCVAb, HBsAg, Fasting blood glucose(FBG), lipid profile, glycated hemoglobin (HbA1c), liver profile (alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin and serum bilirubin(total & direct) and serum creatinine].

Abdominal ultrasonography

Using Toshiba ultrasound (model USAP-770A, Japan), All subjects were advised to fast for at least 8 h before the procedure. Grading of hepatic steatosis was as follows: normal: no difference in echogenicity between the liver and kidney cortex. mild: increased hepatic echogenicity with visible periportal and diaphragmatic echogenicity.

moderate: increased hepatic echogenicity with imperceptible periportal echogenicity without obscuration of the diaphragm. severe: increased hepatic echogenicity with imperceptible periportal echogenicity and obscuration of the diaphragm **[12].**

Vibration-controlled transient elastography (VCTE)

Using Fibro Scan® Mini+ 430, liver stiffness measurement (LSM) and CAP values were obtained. All subjects were advised to fast for at least 8 h before the procedure.

LSM score was represented by the median of 10 measurements and was considered reliable only if at least 10 successful acquisitions are obtained and the IQR-to-median ratio of the 10 acquisitions were ≤30%. The CAP score was represented by the median value. CAP measurements were considered reliable and included in the final analysis if 10 successful acquisitions were obtained. Hepatic steatosis was graded by CAP using the M probe according to manufacturer provided cut-offs (S1=223-259; S2=260-310 and S3 ≥310 dB/m) [13]. Also, LSM cut-offs were used to define fibrosis stages as fellow (F0=0-5.4, F1=5.5-6.9, F2=7-8.9, F3=9-11.4, F4=11.5-75) [14].

Assessment of HRQOL

Using the SF-36 survey after being translated and adopted in Arabic, participants were asked to provide demographic information related to their age, gender, level of education and socioeconomic status. Afterwards, they complete the questionnaire [15].

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Statistical analysis

All statistical analyses were performed using SPSS for windows version 20.0 (SPSS, Chicago, IL). Continuous data were normally distributed and were expressed in mean ±standard deviation (SD). Categorical data were expressed in number and percentage. One-way analysis

of variance (ANOVA) test was used for comparison among more than two for variables with continuous data. Correlation co-efficient test was used to test for correlations between two variables with continuous data. Post-hoc test was used to identify exactly which groups differ from each other. The reliability (internal consistency) test for the questionnaires used in the study was calculated. Statistical significance was set at $p<0.05$.

Reliability

The Cronbach's alpha value of the SF – 36 Questionnaire was 0.901, and of the LSM Score was 0.893

Results

Regarding BMI and Waist circumference, there was a significantly higher difference between the studied MAFLD patients' group (GI) compared to the control group (GII). **Table 1**

The total scores as well as scores of all scales of SF-36 were significantly lower in Group I compared to Group II. **Table 2**

Scores of all scales of SF-36 were significantly lower in S3 patients compared to S2 and S1 patients. **Table 3**

These tables show that total scores & scores of all scales of SF-36 were significantly lower among diabetic, hypertensive & dyslipidemia patients. **Table 4 & 5**

There was a highly statistical significance negative correlation between BMI and all domains of SF-36 questionnaire among the studied patients group. **Table 6**

There was higher prevalence of female gender in the MAFLD patients group. **Figure 1**

Out of the studied 150 MAFLD patients, 126 were obese while 24 patients were lean (84% & 16% respectively). **Figure 2**

Table 1: Socio-demographic data of studied groups

	Patient group (n=150) (Group I)	**Control group (n=100) (Group II)**	**Student's T-Test**	
K	**Mean ±SD**	**Mean ±SD**	**T**	**P**
Age (ys)	43.6 ±10.5	40.9 ±12.4	1.882	0.061
BMI	34.3 ±6.0	24.5 ±2.7	15.294	**<0.001****
Waist circumference (cm)	110.7 ±12.4	89.1 ±5.5	16.381	**<0.001***

Data are presented as mean ± SD or frequency (%). *Significant p value <0.05, BMI: Body mass index.

Table 2: Comparison of SF-36 questionnaire domains and total score between patients and control groups

	Group I	**Group II**	**Student's T-Test**	
	Mean ±SD	**Mean ±SD**	**T**	**P**
Physical Health Domain				
Physical functioning	80.8 ±19.3	85.8 ±17.1	2.098	**0.036***
Role limitations due to physical health	32.3 ±15.0	54.2 ±18.4	10.364	**<0.001****
Role limitations due to emotional problems	39.0 ±18.2	61.1 ±18.0	9.447	**<0.001****
General health	54.2 ±16.5	58.5 ±13.6	2.161	**0.031***
Physical Health Score	51.6 ±18.8	64.9 ±18.5	5.514	**<0.001****
Mental Health Domain				
Energy/fatigue	47.9 ±11.5	52.8 ±13.8	3.043	**0.002***
Emotional well-being	60.6 ±13.1	64.7 ±15.8	2.230	**0.026***
Social functioning	68.1 ±30.5	81.2 ±21.4	3.725	**<0.001****
Pain	68.0 ±28.2	82.8 ±23.6	4.332	**<0.001****
Mental Health Score	61.2 ±18.2	69.9 ±15.4	3.932	**<0.001****

Data are presented as mean ± SD or frequency (%). *Significant p value <0.05.

Table 3: Association between CAP values of patients and SF – 36 Questionnaire domains

	223 – 259 dB/m (S1)	260 – 310 dB/m (S2)	> 310 dB/m (S3)	One way ANOVA		Post Hoc
	Mean ±SD	Mean ±SD	Mean ±SD	F	P	P
Physical Health Domain						
Physical functioning	82.6 ±17.2	72.3 ±19.0	69.4 ±25.3	3.455	**0.034***	
S3 vs S2						0.479
S2 vs S1						**0.021***
S3 vs S1						0.215
Role limitations due to physical health	65.2 ±15.9	57.7 ±17.8	43.8 ±19.1	16.547	**<0.001****	
S3 vs S2						**<0.001****
S2 vs S1						**0.070**
S3 vs S1						**<0.001****
Role limitations due to emotional problems	64.9 ±18.7	60.3 ±17.7	54.3 ±18.1	3.747	**0.025***	
S3 vs S2						0.066
S2 vs S1						0.285
S3 vs S1						0.013*
General health	58.3 ±14.5	54.6 ±12.7	50.6 ±13.7	3.407	**0.035***	
S3 vs S2						0.097
S2 vs S1						0.244
S3 vs S1						**0.018***
Physical Health Total Score	67.3 ±17.3	61.5 ±17.6	54.8 ±20.4	4.639	**0.011***	
S3 vs S2						0.055
S2 vs S1						0.166
S3 vs S1						**0.007***
Mental Health Domain						
Energy/fatigue	59.0 ±17.9	53.8 ±14.5	50.5 ±11.4	3.613	**0.029***	
S3 vs S2						0.158
S2 vs S1						0.165
S3 vs S1						**0.007***
Emotional well-being	66.1 ±11.7	62.7 ±16.7	56.1 ±22.2	3.402	**0.036***	
S3 vs S2						0.068
S2 vs S1						0.352
S3 vs S1						**0.032***
Social functioning	85.0 ±18.5	81.9 ±21.3	72.4 ±28.1	3.619	**0.029***	
S3 vs S2						**0.039***
S2 vs S1						0.525
S3 vs S1						**0.037***
Pain	86.3 ±22.7	78.8 ±22.5	71.9 ±27.1	3.431	**0.034***	
S3 vs S2						0.130
S2 vs S1						0.165
S3 vs S1						**0.018***
Mental Health Total Score	74.1 ±12.7	69.1 ±15.2	63.4 ±21.4	3.746	**0.025***	
S3 vs S2						0.096
S2 vs S1						0.149
S3 vs S1						**0.019***

Data are presented as mean ± SD or frequency (%). *Significant p value <0.05.

Table 4: Association between DM and SF – 36 questionnaire domains in patients group (Group I)

	Diabetic patients	**Non-diabetic patients**	**Student's T-Test**	
	Mean ±SD	Mean ±SD	T	P
Physical Health Domain				
Physical functioning	76.9 ±20.1	83.2 ±18.0	2.020	**0.045***
Role limitations due to physical health	45.5 ±18.4	61.0 ±17.6	5.248	**<0.001****
Role limitations due to emotional problems	55.1 ±18.4	65.9 ±17.4	3.679	**<0.001****
General health	53.8 ±15.1	58.8 ±11.3	2.319	**0.022***
Physical Health Total Score	57.8 ±18.2	67.3 ±16.3	3.365	**<0.001****
Mental Health Domain				
Energy/fatigue	50.7 ±12.1	55.7 ±15.0	3.365	**<0.001****
Emotional well-being	56.1 ±14.4	63.2 ±16.9	2.723	**0.007***
Social functioning	75.4 ±19.3	82.6 ±22.9	2.898	**0.004***
Pain	75.8 ±24.6	84.0 ±22.3	2.136	**0.034**
Mental Health Total Score	64.5 ±17.0	71.4 ±13.4	3.989	**<0.001****

Data are presented as mean ± SD or frequency (%). *Significant p value <0.05.

Table 5: Association between hypertension and SF – 36 questionnaire domains in patients group (Group I)

	Hypertensive patients (n=65)	**Non-hypertensive patients (n=85)**	**Student's T-Test**	
	Mean ±SD	Mean ±SD	T	P
Physical Health Domain				
Physical functioning	76.3 ±19.6	84.2 ±20.4	2.403	**0.017***
Role limitations due to physical health	29.8 ±13.1	35.5 ±14.7	2.504	**0.013***
Role limitations due to emotional problems	35.9 ±16.9	42.9 ±15.9	2.578	**0.010***
General health	50.1 ±14.9	57.1 ±14.4	2.892	**0.004***
Physical Health Total Score	48.1 ±8.3	54.9 ±7.5	5.182	**<0.001****
Mental Health Domain				
Energy/fatigue	44.2 ±11.5	48.7 ±9.5	2.556	**0.012***
Emotional well-being	58.0 ±14.1	64.6 ±14.3	2.823	**0.005***
Social functioning	64.7 ±17.1	73.8 ±13.5	3.530	**<0.001****
Pain	63.9 ±19.5	70.6 ±16.5	2.226	**0.027***
Mental Health Total Score	57.7 ±11.6	64.4 ±12.8	3.351	**<0.001****

Data are presented as mean ± SD or frequency (%). *Significant p value <0.05.

Table 6: Correlation between BMI and SF – 36 questionnaire domains in patients group (Group I)

	R	P
Physical Health Domain		
Physical functioning	-0.616	**<0.001****
Role limitations due to physical health	-0.564	**<0.001****
Role limitations due to emotional problems	-0.574	**<0.001****
General health	-0.651	**<0.001****
Physical Health Total Score	-0.752	**<0.001****
Mental Health Domain		
Energy/fatigue	-0.548	**<0.001****
Emotional well-being	-0.328	**<0.001****
Social functioning	-0.695	**<0.001****
Pain	-0.667	**<0.001****
Mental Health Total Score	-0.702	**<0.001****

r: Pearson's correlation coefficient **: Highly significant (P<0.001)

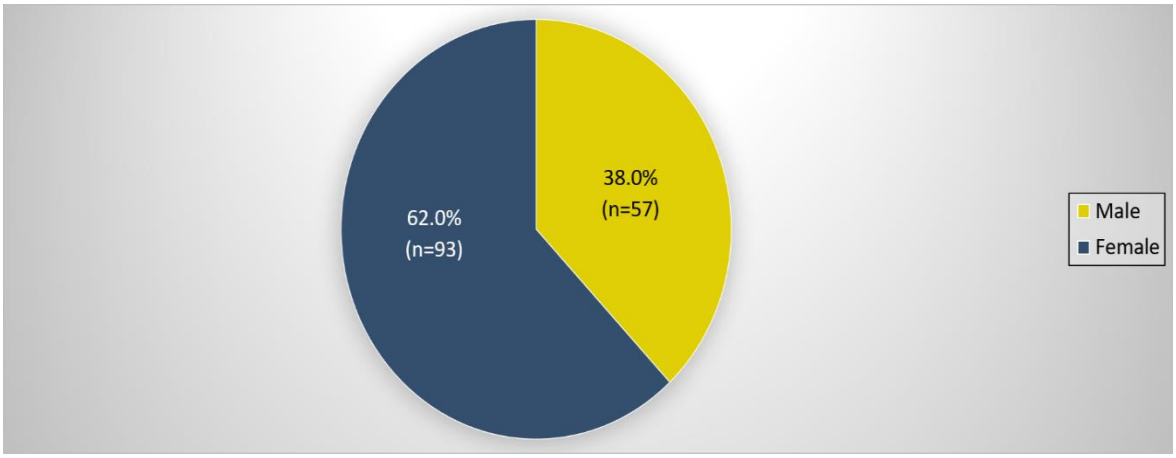

Figure 1: Socio-demographic data regarding the gender in patients group

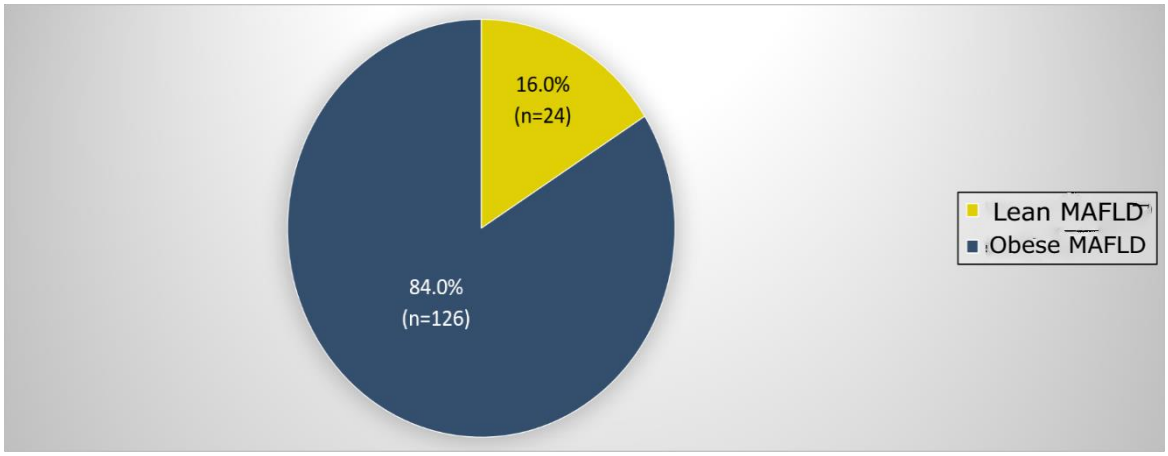

Figure 2: Distribution of MAFLD patients group (GroupI) according to BMI (lean<25, obese>25)

Discussion

In the current study, the mean age among cases group was 43.6 ±10.5 years & females were the predominant representing 62%. **(Table 1)**

This agrees with the previous studies from the literature which stated that most patients are diagnosed with NAFLD in their 40s or 50s [16]. Also in another study showed that [19] , the mean age of MAFLD patient was 48.39 ± 15.20. Moreover, studies showed that there was no statistically significant difference between groups regarding age. [18]

In contrary, study on 228 subjects categorized into two groups: 57 healthy subjects as a control group and 171 cases in the MAFLD group. They found that age was significantly higher in the MAFLD group compared to the control group. [19]

In the current study, there was higher prevalence of female gender in the MAFLD patients' group **(figure 1)**. supporting our results, [20] case-control study on 210 subjects categorized into two groups group I: 105 subjects newly diagnosed with NAFLD by ultrasound examination and group II: 105 healthy individuals without NAFLD. They showed that the female sex represented 58% of cases in NAFLD group. Also, [21] who conducted their cross-sectional comparative study on 139,170 Chinese adults enrolled in their study and diagnosed with MAFLD. They showed that 78,176 subjects (56.2%) were males and 60,994 (43.8%) were females.

In contrary, study showed that in the MAFLD group the males represented the higher prevalence of the included cases (70.8%) compared to (29.2%) females. [19]

These trends differences between sexes suggested that there might be a certain correlation between MAFLD and female menopausal status. It was found that a decrease in estrogen in perimenopausal and postmenopausal women can lead to fat redistribution and thus cause metabolic disorders, including dyslipidemia and glucose intolerance [22] . Also this could be explained due to variations in the inclusion and exclusion criteria in the included cases.

In the current study, BMI and waist circumference were significantly higher in the patients group compared to the control group. **(Table 1)** In accordance with our results, BMI and waist circumference were significantly higher in the fatty liver group compared to the non- fatty liver group. [23] [24] ,

In agreement with our findings, [16] conducted their case-control study on 174 subjects, 87 NAFLD subjects and 87 age- and sex-matched non-NAFLD controls were identified by hepatic ultrasound examination. They found that there was a significant increase in BMI and waist circumference in NAFLD group compared to non-NAFLD group.

In accordance with the current study, [21] studies found that MAFLD is closely associated with metabolic syndrome components, including abdominal obesity, in addition to elevated waist circumference. Also other studies [16] , [25] confirmed the previous findings, as waist circumference was significantly higher in

patient group compared with control group.

In the current study, there are 24 patients (16%) of lean MAFLD & 126 patient (84%) of obese MAFLD**. (Figure 2)** Although overweight/obesity is classically associated with the development and progression of MAFLD, a recent meta-analysis estimated that within the MAFLD population, 40.8% are non-obese and 19.2% are lean, without differences in the histological severity of disease between lean and obese patients [26,27]. Non-obese patients with MAFLD may have a worse outcome and accelerated disease progression [21,28].Insulin resistance and altered body fat distribution rather than BMI could be better indicators of MAFLD in such patients and hence the importance of the new diagnostic criteria of MAFLD [26].

In the current study, 13 out of 150 MAFLD patients (8.7%) were positive HBsAg. Also, 38 out of 150 MAFLD patients (25.3%) had positive HCVAb.

With the high prevalence rates of MAFLD and viral hepatitis in Egypt, it is expected that these disease entities will frequently occur together. In this regard, a recent study of more than 10,000 consecutive patients with HCV from Egypt estimated that nearly half of these patients have coexisting MAFLD, and this group of patients were at a higher risk of hepatic fibrosis compared to those with HCV [29]. Notably, MAFLD may accelerate the progression of liver disease in patients with CHB; a recent study from Thailand suggested that MAFLD was independently associated with increased risk of significant liver fibrosis and advanced liver fibrosis in CHB patients [30].

In the present study, the total scores as well as the scores of all scales of SF-36 were significantly lower in MAFLD compared to controls. **(Table 2)**

In line with our results, all scales of SF-36 were significantly lower in MAFLD compared to controls. [31]

Additionally, 95 patients with NAFLD and 37 controls were enrolled to evaluate the QoL in NAFLD patients. They found that the SF-36 survey yielded lower scores on all subscales compared to controls[32].

In the current study, according to CAP, scores of all scales of SF-36 were significantly lower in S3 patients compared to S2 & S1 patients. **(Table 3)** Also, Scores of all scales of SF-36 were significantly lower in F4 patients compared to other patients and among F3 patients compared to F2, 1 and 0 patients, as well as among F2 patients compared to F1 & 0 patients and finally F1 patients compared to F0 patients.

This came in accordance with study that compared the QoL of patients with various chronic liver diseases (CLDs), including NAFLD, to that of the general population supported that the early stages of CLDs do not affect overall QoL. On the other hand, when the disease progresses to decompensated cirrhosis or HCC, QoL is significantly affected regardless of the etiology. [33]

Importantly, some studies reported that higher fibrosis stages, as well as the presence of cirrhosis, are considered major determinants of reduced QoL in NAFLD populations. This suggests that the negative impact of NAFLD on QoL is mostly apparent at advanced disease stages and is related to development of complications, whereas this is not the case

at early stages, and especially in patients with NAFLD [34].

However, the evidence for association of NASH with QoL is to date conflicting, with some studies showing that the presence of NASH is associated with reduced QoL as compared to individuals without liver disease or patients with NAFLD [35].

Several parameters as older age, female gender, less education, lower income, and coexisting comorbidities, such as obesity, T2DM, Metabolic syndrome, cardiovascular diseases, and malignancies, may worsen QoL in these patients and may complicate the estimation of the net effect of NAFLD on the QoL [33,36].

In the current study, total scores & scores of all scales of SF-36 were significantly lower among diabetic, hypertensive & dyslipidaemia patients. **(Table 4, 5, 6)**

This agreed with study showed that the scores of all domains of SF-36 were significantly lower in diabetic patients especially females. In addition, diabetic patients aged more than 50 years showed significantly lower scores of most domains of SF-36. [37]

Type 2 diabetes mellitus patients with poor glycemic control had lower SF-36 scores[38]. Beside that persons with hypertension report lower scores than the general population on most domains in the SF-36 [39]. Regarding dyslipidaemia, the eight dimensions and the overall QOL score were significantly lower among patients with dyslipidaemia. [40]

In the current study, there was a highly statistically significant negative correlation between BMI and all domains of SF-36 Questionnaire among the studied patients group. **(Table 7)**

This agreed with study that showed the BMI of NAFLD patients was substantially higher than that in the control group, and there were significant negative correlations between BMI and scores on physical functioning (PF), and role limitations due to physical health problems (RP) subscales, both of which were parts of physical component summary (PCS), in the NAFLD group. [32]

Our data are consistent with the results of the National multicentre cross-sectional survey in China, indicating that QoL in patients with NAFLD deteriorated with the increase in BMI, the latter being an independent risk factor. In this study, QoL was measured with Chronic Liver Disease Questionnaire (CLDQ) score. However, even though NAFLD patients with normal BMI had higher CLDQ scores vs. overweight or obese NAFLD patients, their QoL remained poor as well [41].

This agreed with study found that NAFLD prevalence increased with BMI. Steatosis was higher in individuals with overweight with DM versus without DM (USFLI $\geq$ 30: 48.3% vs. 17.4%; $p < 0.01$) and in individuals with obesity with DM versus without DM (USFLI $\geq$ 30: 79.9% vs. 57.6%; $p < 0.01$). DM significantly increased the proportion of individuals at moderate-to-high risk of fibrosis (FIB-4 $\geq$ 1.67: 31.8% vs. 20.1%; $p < 0.05$). In the high risk of advanced fibrosis group (FIB-4 $\geq$ 2.67), the risk almost doubled (3.8% vs. 7.1%). Among individuals with obesity, DM increased the proportion of adults with moderate and high risk of fibrosis by 1.8- and 2.5-fold, respectively ($p < 0.01$ and $p = 0.39$, respectively, vs. without DM). [42]

Another study found that during follow-up, 186 patients progressed to advanced fibrosis (fibrosis-4 index > 2.67). The 3-, 5-, 7-, and 10-year cumulative incidence of progression to advanced fibrosis was 4.4%, 6.7%, 11.0%, and 16.7%, respectively. In the univariate analysis, age, albumin concentration, and type 2 diabetes mellitus (T2DM) were significantly associated with progression to advanced fibrosis. [43]

Limitations of our results were sample size was relatively small, single center study. So, we recommend regular screening for early detection of MAFLD and prevention of the associated complications including the impairment of the QOL.

Conclusions

The presence of MAFLD is associated with impairment of the components of the QOL and the degree of impairment is associated with the increase of the degree of liver fibrosis.

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