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A Clinical Study on Health-Related Quality of Life Burden of Nonalcoholic Steatohepatitis

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Abstract
Nonalcoholic fatty liver disease (NAFLD) is a condition in which excess fat is stored in your liver. This buildup of fat is not caused by heavy alcohol use. Non-alcoholic fatty liver disease (NAFLD), also known as metabolic (dysfunction) associated fatty liver disease (MAFLD), is excessive fat build-up in the liver without another clear cause such as alcohol use. The aim of the study was to determine the quality of life and health utilities in patients with NAFLD with and without cirrhosis for future use. This is Descriptive Observational study. All the patients admitted in the department of General medicine and attending outpatient department of General medicine. Hyderabad during the period of January 2020 to August 2020, who are fitting into the inclusion criteria were included in the study. Patients with chronic liver disease for whom clinical and quality of life data had been collected for our quality-of-life database were considered for this study. We included only patients with an established histological diagnosis of NAFLD with or without cirrhosis who provided an informed consent; the presence of cirrhosis was determined from liver biopsies. Exclusion criteria included pregnant women, breast feeding. A total of 40 patients were enrolled as per inclusion and exclusion criteria, all together 38 patients were participated in this study, and the response was 100%. NASH is the second leading indication of CLD. this study clearly showed that compared to the general population, patients with NAFLD had significantly lower HRQL and health utility scores, which worsen with the advanced stages of the disease.

Keywords
Chronic liver disease (CLD), Nonalcoholic steatohepatitis (NASH), Quality of life.

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INTRODUCTION
Non-alcoholic fatty liver disease (NAFLD) is a very common disorder and refers to a group of conditions where there is accumulation of excess fat in the liver of people who drink little or no alcohol. Non-alcoholic fatty liver disease (NAFLD), also known as metabolic (dysfunction) associated fatty liver disease (MAFLD), is excessive fat build-up in the liver without another clear cause such as alcohol use. The most common form of NAFLD is a non-serious condition called fatty liver. In fatty liver, fat accumulates in the liver cells. Although having fat in the liver is not normal, by itself it probably does not damage the liver. A small group of people with NAFLD may have a more serious condition named non-alcoholic steatohepatitis (NASH). In NASH, fat accumulation is associated with liver cell inflammation and different degrees of scarring. NASH is a potentially serious condition that may lead to severe liver scarring and cirrhosis. Cirrhosis occurs when the liver sustains substantial damage, and the liver cells are gradually replaced by scar tissue, which results in the inability of the liver to work properly. Some patients who develop cirrhosis may eventually require a liver transplant (to remove the damaged liver and replace it with a “new” liver).

Obesity and type 2 diabetes are strong risk factors for NAFLD. Other risks include being overweight, metabolic syndrome (defined as at least three of the five following medical conditions: abdominal obesity, high blood pressure, high blood sugar, high serum triglycerides, and low serum HDL cholesterol), a diet high in fructose, and older age. NAFLD and alcoholic liver disease are types of fatty liver disease. Obtaining a sample of the liver after excluding other potential causes of fatty liver can confirm the diagnosis. Treatment for NAFLD is weight loss by dietary changes and exercise. There is tentative evidence for pioglitazone and vitamin E, bariatric can improve or resolve severe cases. Those with NASH have a 2.6% increased risk of dying per year. NAFLD is the most common liver disorder worldwide and is present in approximately 25% of the world's population. It is also very common in developed nations, such as the United States, and affected about 75 to 100 million Americans in 2017. Over 90% of obese, 60% of diabetic, and up to 20% normal-weight people develop it. NAFLD is the leading cause of chronic liver disease and the second most common reason for liver transplantation in the US and Europe as of 2017.

TYPES

- Non-alcoholic fatty liver (NAFL)
- Non-alcoholic steatohepatitis (NASH), with the latter also including liver inflammation. Non-alcoholic fatty liver disease is less dangerous than NASH and usually does not progress to NASH or liver cirrhosis. When NAFLD does progress to NASH, it may eventually lead to complications such as cirrhosis, liver cancer, liver failure, or cardiovascular disease.

Simple fatty liver

Simple fatty liver, also called nonalcoholic fatty liver (NAFL), is a form of NAFLD in which you have fat in your liver but little or no inflammation or liver cell damage. Simple fatty liver typically does not progress to cause liver damage or complications. Fatty liver disease (FLD), also known as hepatic steatosis, is a condition where excess fat builds up in the liver. Often there are no or few symptoms. Occasionally there may be tiredness or pain in the upper right side of the abdomen. Complications may include cirrhosis, liver cancer, and esophageal varices. There are two types of fatty liver disease: non-alcoholic fatty liver disease (NAFLD) and alcoholic liver disease. NAFLD is made up of simple fatty liver and non-alcoholic steatohepatitis (NASH). The primary risks include alcohol, type 2 diabetes, and obesity. Other risk factors include certain medications such as glucocorticoids, and hepatitis C. It is unclear why some people with NAFLD develop simple fatty liver and others develop NASH.

NASH

NASH is a form of NAFLD in which you have hepatitis inflammation of the liver and liver cell damage, in addition to fat in your liver. Inflammation and liver cell damage can cause fibrosis, or scarring, of the liver. NASH may lead to cirrhosis or liver cancer NIH external link. Experts are not sure why some people with NAFLD have NASH while others have simple fatty liver.

SYMPTOMS

NAFLD usually causes no signs and symptoms. When it does, they may include:

- Fatigue
- Pain or discomfort in the upper right abdomen Possible signs and symptoms of NASH and advanced scarring (cirrhosis) include:
- Abdominal swelling (ascites)
- Enlarged blood vessels just beneath the skin's surface
- Enlarged spleen
- Red palms
- Yellowing of the skin and eyes (jaundice)
- A dull or aching pain in the top right of the tummy (over the lower right side of the ribs)
- Extreme tiredness.
- Unexplained weight loss.
- Weakness.

The majority of individuals with NAFLD have no symptoms and a normal examination. Children may exhibit symptoms such as abdominal pain, which may be in the center or the right upper part of the abdomen, and sometimes fatigue. However, other causes of abdominal pain and fatigue should be considered. On physical examination the liver might be slightly enlarged, and some children may have patchy, dark discoloration of the skin present (acanthosis nigricans) most commonly over the neck and the under-arm area.

People with NAFLD often have no noticeable symptoms, and NAFLD is often only detected during routine blood tests or unrelated abdominal imaging or liver biopsy. In some cases, NAFLD can cause symptoms related to liver dysfunction such as fatigue, malaise, and dull right- upper-quadrant abdominal discomfort. Mild yellow discoloration of the skin may occur, although this is rare. NASH can severely impair liver function, leading to cirrhosis, liver failure, and liver cancer.

Comorbidities

NAFLD is strongly associated with or caused by type 2 diabetes, insulin resistance, and metabolic syndrome (defined as at least three of the five following medical conditions: abdominal obesity,

high blood pressure, high blood sugar, high serum triglycerides, and low serum high-density lipoprotein). It is also associated with hormonal disorders (panhypopituitarism, hypothyroidism, hypogonadism, polycystic ovary syndrome), persistently elevated transaminases, increasing age and hypoxia caused by obstructive sleep apnea, with some of these conditions predicting disease progression. The majority of normal-weight people affected by NAFLD ("lean NAFLD") have impaired insulin sensitivity, are sedentary, and have increased cardiovascular disease risk and increased liver lipid levels. These are the consequences of a decreased capacity for storing fat and reduced mitochondrial function in adipose tissue and increased hepatic de novo lipogenesis.

CAUSES OF NAFLD/NASH

- Overweight or obesity
- Insulin resistance, in which your cells don't take up sugar in response to the hormone insulin
- High blood sugar (hyperglycemia), indicating prediabetes or type 2 diabetes
- High levels of fats, particularly triglycerides, in the blood

These combined health problems appear to promote the deposit of fat in the liver. For some people, this excess fat acts as a toxin to liver cells, causing liver inflammation and NASH, which may lead to a buildup of scar tissue in the liver. Oxidative stress (imbalance between pro-oxidant and antioxidant chemicals that lead to liver cell damage) Production and release of toxic inflammatory proteins (cytokines) by the patient's own inflammatory cells, liver cells, or fat cells Liver cell necrosis or death, called apoptosis. Adipose tissue (fat tissue) inflammation and infiltration by white blood cells. Gut microbiota (intestinal bacteria) which may play a role in liver inflammation.

Fatty liver (FL) is commonly associated with metabolic syndrome (diabetes, hypertension, obesity, and dyslipidemia), but can also be due to any one of many causes:

Alcohol

Alcoholism is one of the causes of fatty liver due to production of toxic metabolites like aldehydes during metabolism of alcohol in the liver. This phenomenon most commonly occurs with chronic alcoholism.

Metabolic

abetalipoproteinemia, glycogen storage diseases, Weber–Christian disease, acute fatty liver of pregnancy, lipodystrophy

Nutritional

obesity, malnutrition, total parenteral nutrition, severe weight loss, refeeding syndrome, jejunoileal bypass, gastric bypass, jejunal diverticulosis with bacterial overgrowth

Drugs and toxins

amiodarone, methotrexate, diltiazem, expired tetracycline, highly active antiretroviral therapy, glucocorticoids, tamoxifen, environmental hepatotoxins (e.g., phosphorus, mushroom poisoning)

Other

celiac disease, inflammatory bowel disease, HIV, hepatitis C (especially genotype 3), and alpha 1-antitrypsin deficiency.

CAUSES OF NAFLD

You are more likely to develop NAFLD either simple fatty liver or NASH if you

- ✓ Are overweight or obese
- ✓ Have insulin resistance
- ✓ Have abnormal levels of fats in your blood, which may include
- ✓ High levels of triglycerides
- ✓ Abnormal levels of cholesterol—high total cholesterol, high LDL cholesterol, or low HDL cholesterol

have metabolic syndrome or one or more traits of metabolic syndrome. Metabolic syndrome is a group of traits and medical conditions linked to overweight and obesity. People with metabolic syndrome are more likely to develop type 2 diabetes and heart disease. Experts think NAFLD may be closely linked to metabolic syndrome. Doctors define metabolic syndrome as the presence of any three of the following:

- ✓ Large waist size
- ✓ High levels of triglycerides in your blood
- ✓ Low levels of HDL cholesterol in your blood
- ✓ High blood pressure
- ✓ Higher than normal blood glucose levels
- ✓ Have type 2 diabetes

Research also suggests that certain genes may make you more likely to develop NAFLD. Experts are still studying the genes that may play a role in NAFLD. In NAFLD, people have a buildup of fat in the liver that is not caused by alcohol use. If you have a history of heavy alcohol use and fat in your liver, your doctor may determine that you have alcoholic liver disease NIH external link instead of NAFLD.

CAUSES OF NASH

Experts are not sure why some people with NAFLD have NASH and others have simple fatty liver. Research suggests that certain genes may play a role. People with NAFLD are more likely to have NASH if they have one or more of the following conditions:

- ✓ Obesity, especially with a large waist size
- ✓ High blood pressure
- ✓ High levels of triglycerides or abnormal levels of cholesterol in their blood
- ✓ Type 2 diabetes
- ✓ Metabolic syndrome
- ✓ Less common causes of NAFLD and NASH

Less common causes of NAFLD and NASH include

- ✓ Disorders that cause your body to use or store fat improperly
- ✓ Rapid weight loss
- ✓ Certain infections, such as hepatitis C
- ✓ Certain medicines, such as

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in the world, and it comprises a spectrum of hepatic abnormalities from simple hepatic steatosis to steatohepatitis, fibrosis, cirrhosis, and liver cancer. NAFLD is a metabolic disorder, and its pathogenesis involves the complex interaction among hormonal, nutritional and genetic factors. While the pathogenesis of NAFLD remains incompletely understood, a multihit model has been proposed that accommodates causal factors from a variety of sources, including intestinal and adipose proinflammatory stimuli acting on the liver simultaneously. Prior cellular and molecular studies of patient and animal models have characterized several common pathogenic mechanisms of NAFLD, including proinflammation cytokines, lipotoxicity, oxidative stress, and endoplasmic reticulum stress. In recent years, gut microbiota has gained much attention, and dysbiosis is recognized as a crucial factor in NAFLD. Although a high-fat diet and inactive lifestyles are typical risk factors for NAFLD, the interplay between diet, gut microbiota, and genetic background is believed to be more important in the development and progression of NAFLD. This review summarizes the common pathogenic mechanisms, the gut microbiota relevant mechanisms, and the major genetic variants leading to NAFLD and its progression. The primary characteristic of NAFLD is the accumulation of lipids in the liver, largely in the form of triglycerides. However, the mechanisms by which triglycerides accumulate and the reasons that accumulation can lead to liver dysfunction are complex and incompletely understood. NAFLD can include steatosis along with varied signs of liver injury, either lobular or portal inflammation (a form of liver injury) or ballooning degeneration. Similarly, NASH can include histological features such as portal inflammation, polymorphonuclear cell infiltrates, Mallory bodies, apoptotic bodies, clear vacuolated nuclei, microvesicular steatosis, megamitochondria, and perisinusoidal fibrosis.

- ✓ NASH increases hepatocyte death via apoptosis or necroptosis is increased in NASH compared with simple steatosis, and inflammation is a hallmark of NASH. One debated mechanism proposes that hepatic steatosis progresses to steatosis with inflammation following some further injury, or second hit. Oxidative stress, hormonal imbalances, and mitochondrial abnormalities are potential causes of this "second hit" phenomenon. A further nutrigenomics model named multiple hits extends the second hit model, suggesting that multiple disease biomarkers and factors such as genes and nutrition influence NAFLD and NASH progression. This model attempts to use these factors to predict the impact of lifestyle changes and genetics for the evolution of the NAFLD pathology. Many researchers describe NAFLD as a multisystem disease, as it impacts and is influenced by organs and regulatory pathways other than the liver.
- ✓ **Fructose consumption**

  Non-alcoholic and alcoholic fatty liver disease share similar histological features, which suggests that they might share common pathogenic pathways. Fructose can cause liver inflammation and addiction similarly to ethanol by using similar metabolic pathways, unlike glucose. Therefore, some researchers argue that non-alcoholic and alcoholic fatty liver diseases are more alike than previously thought. Furthermore, high fructose consumption promotes fat accumulation in the liver by stimulating de novo lipogenesis in the liver and reducing the beta-oxidation of fat. Unlike the sugar glucose, the enzyme fructokinase rapidly metabolizes fructose. This leads to a decreased level of intracellular adenosine triphosphate (ATP). The decrease in ATP increases oxidative stress and impairments in proper protein synthesis and mitochondrial function in the liver.

AIM

The aim of the study was to determine the quality of life and health utilities in patients with NAFLD with and without cirrhosis for future use.

OBJECTIVES

To identify and describe the recent studies on the HRQoL burden of NASH from the patient perspective.

MATERIALS AND METHODS

This is Descriptive Observational study. All the patients admitted in the department of General medicine and attending outpatient department of General medicine. Hyderabad during the period of January 2020 to August 2020, who are fitting into the inclusion criteria were included in the study. Patients with chronic liver disease for whom clinical and quality of life data had been collected for our quality-of-life database were considered for this study. We included only patients with an established histological diagnosis of NAFLD with or without cirrhosis who provided an informed consent; the presence of cirrhosis was determined from liver biopsies. Exclusion criteria included pregnant women, breast feeding, daily use of oral corticosteroids or antimicrobial drugs, diabetes mellitus, alcoholism, history of pulmonary surgery. patients with viral hepatitis, with significant alcohol intake (>20 g/day for men, >10 g/day for women), and with other causes of chronic liver disease. Also, for this study, only patients with a completed SF-36 questionnaire were selected. The study was approved by the medical ethics committee of the University Hospital of ., Hyderabad and all patients gave informed consent. Written informed consent was obtained from patients. We collected data on demographics, risk factors, diagnosis modalities, imaging findings and Nash characteristics were collected at the time of admission, who are fitting into the inclusion criteria were included in the study. Patients with nonalcoholic steatohepatitis from general practices were informed about the study. Physical functioning (PF) domain reflects how much a patient's physical activities are limited because of their health. Role physical (RP) domain reflects how much the patient's physical health impacts their work and daily activities. Bodily pain (BP) domain evaluates the patient's limitations because of pain. General health (GH) domain measures how a patient sees their personal health and the potential for decline. Vitality (VT) domain reflects how tired/full of energy the patient feels. Social functioning (SF) domain measures how much the patient's physical or emotional problems interfere with their normal social activities. The qualitative research suggests that a range of other symptoms are also burdensome, having a broad negative impact on different aspects of patients' lives. In this review, the impact of pharmacological treatment on HRQOL was explored in only two included studies.

INCLUSION CRITERIA

Included age 20 years or older and had BMI in above normal range a positive diagnosis of NAFLD disease included in the study. We included only patients with an established histological diagnosis of NAFLD with or without cirrhosis who provided an informed consent; the presence of cirrhosis was determined from liver biopsies

EXCLUSION CRITERIA

Exclusion criteria included pregnant women, breast feeding, daily use of oral corticosteroids or antimicrobial drugs, diabetes mellitus, alcoholism, history of pulmonary surgery. patients with viral hepatitis, with significant alcohol intake (>20 g/day for men, >10 g/day for women), and with other causes of chronic liver disease.

STATISTICAL ANALYSIS

We compared all collected demographic and clinical parameters, together with all the SF-36 domains, SF-36 summary scores, and SF-6D health utility scores, between patients with cirrhotic NAFLD and non-cirrhotic NAFLD. A non-parametric Mann-Whitney test was used to compare continuous and pseudo-continuous parameters (such as age or HRQOL scores), and a $\chi 2$ test was used for categorical parameters (such as gender). For all tests, p values not exceeding the 0.05 threshold were considered statistically significant. All analyses were performed using SAS software. The study was approved by Institutional Review Board.

RESULTS

A total of 40 patients were enrolled as per inclusion and exclusion criteria, all together 38 patients were participated in this study, and the response was 100%. Table 1 shows the participants were divided into 3 groups by age: 20-30years (n=14, 36.82%), 31-40 years (n=13, 34.24%),.41-50 years (n=11, 28.91%). The majority of patients in the age group between 20- 30years (n=16, 31.61 %).

Age wise distribution of patients		
N= 38	**No. of Patients**	**Percentage**
20-30	14	36.82%
31-40	13	34.24%
41-50	11	28.91%

Graph 1: Age wise distribution of patients

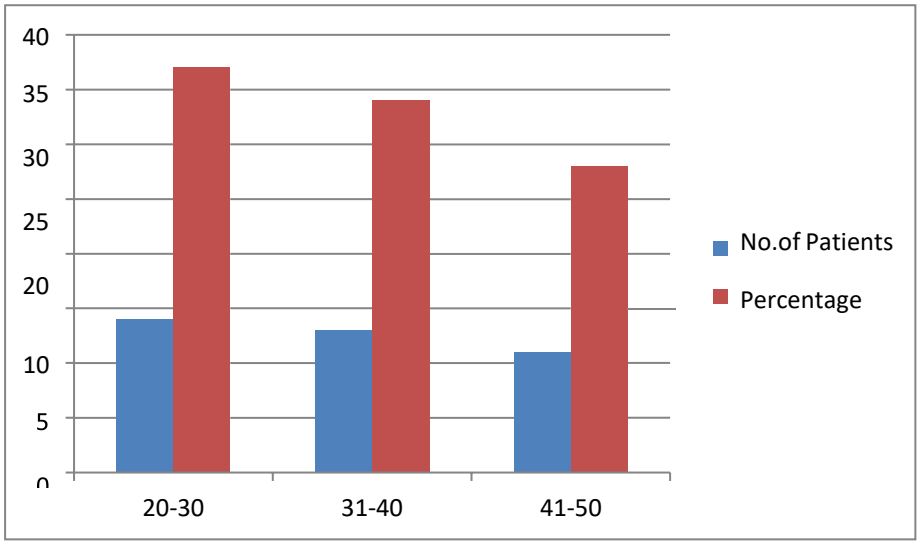


TABLE 2: The diagnosis of hypertension in the study subjects was based on the following clinical symptoms history of Fatigue 32 (23.68 %) (in 100% of subjects), Pain (26%), weakness (21%), sweating (16%), and Headache (13.15%) at the first day of pharmacokinetic assessment.

Symptoms	No. patients (%)
Fatigue	9 (23.68 %)
Pain	10 (26.31%)
weakness	8 (21.05%)
Sweatiness	6 (15.78%)
Headache	5 (13.15%)

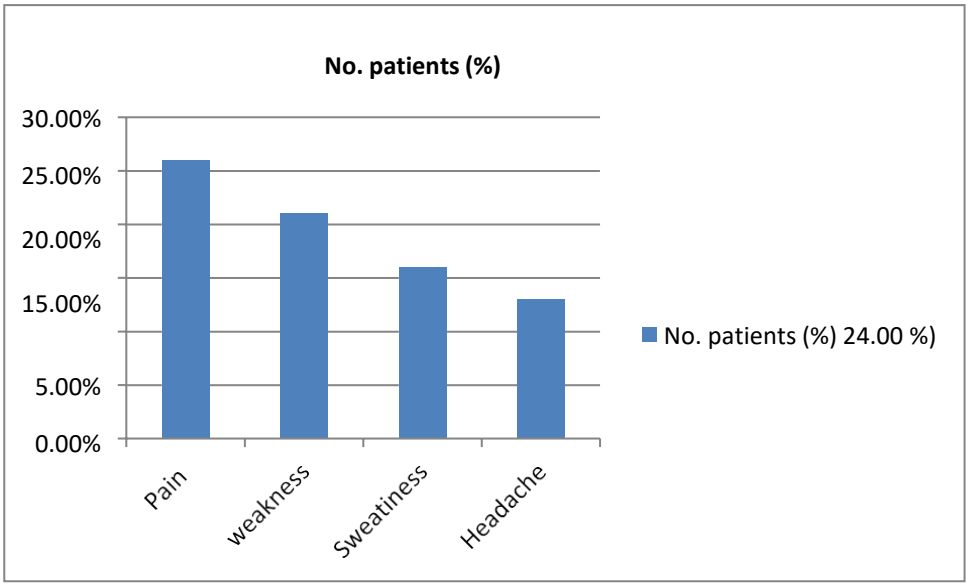
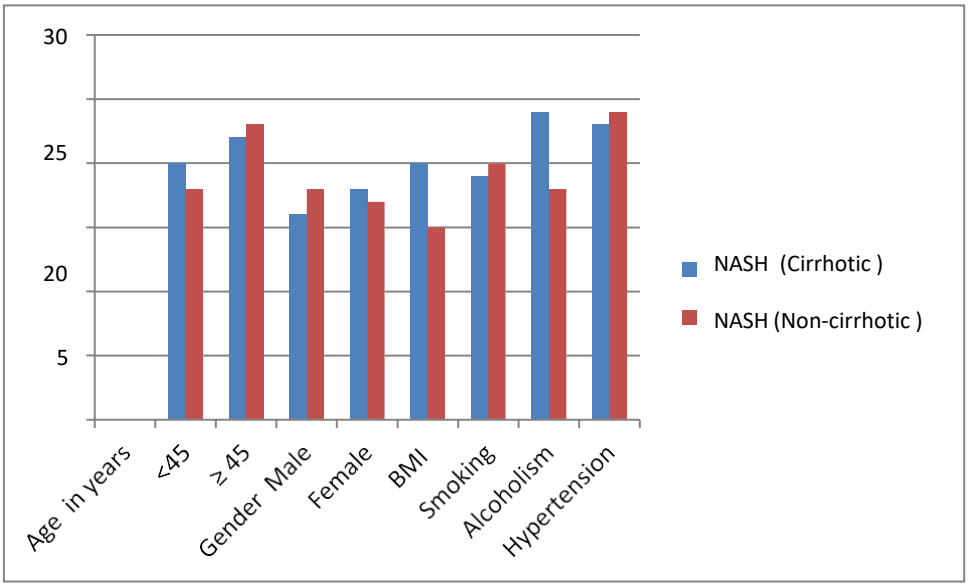


TABLE 3: Comparison of HRQL of patients with and without NASH related cirrhosis

	NASH (Cirrhotic)	NASH (Non-cirrhotic)
Age in years		
<45	20.24±2.8	18.52±2.6
≥ 45	22.21 ±2.4	23.16±2.8
Gender Male	16.24±2.2	18.63±2.8
Female	18.42±2.1	17.28±2.9
BMI	20.16±2.5	15.45±2.8
Smoking	19.45±2.5	20.29±2.7
Alcoholism	24.82±1.8	18.46±2.7
Hypertension	23.67±3.2	24.24±2.2



DISCUSSION

Nonalcoholic steatohepatitis (NASH) is a form of chronic liver disease (CLD). The HRQOL burden is likely to be higher in those NASH patients who have progressed to cirrhosis, HCC, or liver failure. NASH is the second leading indication of CLD. The cross-sectional quantitative studies showed that presence of NASH was associated with a reduced. The comparisons with normative populations, significant impairments in HRQOL were seen in NASH patients HRQOL versus normative populations. It is important to note that the 'NAFLD cohort' comprised a range of patients, including those with simple steatosis, fibrosis, NASH, or cirrhosis. The qualitative research suggests that a range of other symptoms are also burdensome, having a broad negative impact on different aspects of patients' lives. In this review, the impact of pharmacological treatment on HRQoL was explored in only two included studies. NAFLD has increasingly been recognized as one of the most common causes of chronic liver disease worldwide.

The shared pathophysiological mechanisms have established strong linkage between NAFLD and obesity and metabolic syndrome. Besides its substantial epidemiological and economic impacts, NAFLD also causes a significant deterioration of patients' HRQL. Our study revealed that, compared to the general population, patients with NAFLD had lower HRQL and health utility scores, even in the absence of cirrhosis. Our findings supported these data as for physical component domains, patients with cirrhotic and non-cirrhotic NAFLD had significantly lower scores than the general population, whereas for mental component domains, only the scores of cirrhotic patients achieved significance. The impact of disease severity on HRQL was another finding of our study, which was parallel to the findings of previous publications, as patients with cirrhotic NAFLD had significantly lower HRQL and health utility scores than patients with non- cirrhotic NAFLD. In our study, patients with cirrhosis had significantly lower HRQL and health utility scores than patients without cirrhosis and the general population. In conclusion, this study clearly showed that compared to the general population, patients with NAFLD had significantly lower HRQL and health utility scores, which worsen with the advanced stages of the disease.

CONCLUSIONS:

We conclude that the impact of pharmacological treatment on HRQOL was explored in only two included studies. Health utilities and quality of life scores are impaired in patients with cirrhotic NAFLD. These values should be used in cost-effectiveness analysis of the upcoming treatment regimens for advanced NAFLD. NAFLD patients report poor physical QOL. QOL impairment is associated with a variety of disease-related parameters, mostly the presence of fatigue and cirrhosis.

REFERENCE

1. Kashmira S Chawla, Jayant A Talwalkar, Jill C Keach, Michael Malinchoc, Keith D Lindor, Roberta Jorgensen[2], Reliability and validity of the Chronic Liver Disease Questionnaire (CLDQ) in adults with non-alcoholic steatohepatitis (NASH), BMJ open gastroenterology, 2015, vol no: 3, ISSN No: 1, page no. 1-6.
2. Nigel S. Cook, Sarthak H. Nagar, Akanksha Jain , Maria-Magdalena Balp , Miriam Mayla¨nder , Olivia Weiss , Satabdi Chatterjee, Understanding Patient Preferences and Unmet Needs in Non-alcoholic Steatohepatitis (NASH): Insights from a Qualitative Online Bulletin Board Study, ISSN NO: 478–491, page no : 1-14.
3. Maria-Magdalena Balp, Nancy Krieger, Raymond Przybysz, Nate Way, Jennifer Cai, Dion Zappe, Sarah Jane McKenna, Garth Wall, Nico Janssens, Elliot Tapper, The burden of non-alcoholic steatohepatitis (NASH) among patients from Europe, A real-world patientreported outcomes study, JHEP, page no. 1-9.
4. Tessa Kennedy-Martin, Jay P. Bae, Rosirene Paczkowski and Emily Freeman, Health- related quality of life burden of nonalcoholic steatohepatitis, a robust pragmatic literature review, Journal of PatientReported Outcomes, page no: 1-14.
5. Zobair M. Younossi*, Maria Stepanova, Issah Younossi, Andrei Racila, Validation of Chronic Liver Disease Questionnaire for Nonalcoholic Steatohepatitis in Patients with Biopsy-Proven Nonalcoholic Steatohepatitis, clinical gastroenterology and hepatology, Volume 17, Issue 10, September 2019, Pages 2093-2100.
6. M.Balp, N. Krienger, R. Przybysz, N. Way, J. Cai, D. Zappe, S. J Mckenna, G.Wall, N.Janssens, E. Tapper, patients with non-alcoholic steatohepatitis (nash) have worse health related quality of life (hrqol) than matched controls: results from the 2016 eu5 national health and wellness survey (nhws), Volume 21, Pages :S149-S150.
7. Ratziu1, A. Geier2, M. Balp3, S.J. Mckenna4, R. Przybysz5, J. Cai5, C. Brass5, T. Howe6, M. Gavaghan7, D. Rosen7, A. Knight8, V.C. Vazquez7, M. Rinella9, PGI49 - humanistic burden of non-alcoholic steatohepatitis (nash) in the first real-world cross-sectional study, symptomatic nash patients report worse quality of life, Volume 21, Page no: S150.
8. Kristin David, MPH1,2, Kris V. Kowdley, MD, FACP3, Aynur Unalp, MD, PhD4, Fasiha, Kanwal, MD5, Elizabeth M. Brunt, MD6, and Jeffrey B. Schwimmer, MD1, NIH Public Access, Vol no: 49, ISSN No: 6, Page no: 1904–1912.
9. Mehmet Sayiner,1 Maria Stepanova,2 Huong Pham,1 Bashir Noor,1 Mercedes Walters,2 Zobair M Younossi1,2, Assessment of health utilities and quality of life in patients with non-alcoholic fatty liver disease, BMJ Open Gastroenterology, page no: 1-5.
10. Zobair M. Younossi, Maria Stepanova, Linda henry, Brian lam, Huong T, Issah Younossi, Andrei Racila, A disease-specific quality of life instrument for non-alcoholic fatty liver disease and non-alcoholic steatohepatitis, CLDQ-NAFLD, Volume: 37, Issue no: 8, Pages 1209-1218.
11. Vernon, G., Baranova, A, Younossi, Z. M. (2011), Systematic review: The epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults, Aliment Pharmacol Ther, Vol no: 34, page no: 274–285.
12. Lopez-Velazquez, J. A., Silva-Vidal, K. V., Ponciano-Rodriguez, G., Chávez- Tapia, N. C., Arrese, M., Uribe, M., & Méndez-Sánchez, N. (2014), The prevalence of nonalcoholic fatty liver disease in the Americas, Ann Hepatol, vol no:13, page no: 166– 178.
13. Bugianesi, E., Leone, N., Vanni, E., Marchesini, G., Brunello, F., Carucci, P., Musso, A., De Paolis, P., Capussotti, L., Salizzoni, M., & Rizzetto, M, (2002, Expanding the natural history of nonalcoholic steatohepatitis: From cryptogenic cirrhosis to hepatocellular carcinoma, Gastroenterology, vol no: 123, page no: 134–140.
14. Wong, R. J., Aguilar, M., Cheung, R., Perumpail, R. B., Harrison, S. A., Younossi, Z. M., & Ahmed, A, (2015), Nonalcoholic steatohepatitis is the second leading etiology of liver disease among adults awaiting liver transplantation in the United States. Gastroenterology, vol no:148, page no: 547–555.
15. Younossi, Z. M., Koenig, A. B., Abdelatif, D, Fazel, Y., Henry, L., & Wymer, M. (2016), Global epidemiology of nonalcoholic fatty liver disease-meta-analytic assessment of prevalence, incidence, and outcomes, Hepatology, vol no: 64, page no: 73–84.