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A study on clinical profile of patients with non-alcoholic steatohepatitis

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Abstract
Background and Objectives: Non-alcoholic fatty liver disease (NAFLD) is the accumulation of lipid, primarily in the form of triacylglycerol's in individuals who do not consume significant amounts of alcohol and other known causes of steatosis, such as certain drugs and toxins, have been excluded. The rising incidence of obesity is associated with health complications. The non-alcoholic fatty liver disease is increasingly being recognized as a major cause of liver-related morbidity and mortality among 15-40% of the general population. Currently, a liver biopsy is the gold standard method for diagnosing NAFLD. Ultrasonography is relatively inexpensive and widely available in clinical settings. NAFLD is considered to be an integral part of the metabolic syndrome. The present study is designed to study the clinical profile of patients with NAFLD with varying degrees of severity as diagnosed by Ultrasonography and evaluate the relationship between the non-alcoholic fatty liver disease and the metabolic syndrome along with its individual components, as defined by the modified NCEP ATP III criteria. Presently there are no lab markers nor imaging modalities which can be relied upon for making the diagnosis. Similarly no clinical signs or symptoms can be relied upon as most of the pts are asymptomatic or may have vague and constitutional symptoms. This study is to analyze the presence of non-alcoholic Steato Hepatitis (NASH) by performing liver biopsy in non-alcoholic adults with evidence of fatty liver on abdominal ultrasonography and to study the association of NASH with other co-morbid conditions.
Methods: The study was conducted on 100 adult patients attending Dept. of Internal Medicine, Al-Ameen Medical College and District Hospital Bijapur with fatty liver on abdominal USG. Inclusion and exclusion criteria's were applied upon. Detailed history and clinical examination was done. Liver biopsy and other relevant investigations were done.
Results: NASH was found in 16% of the patients with mean age of 48.38 years. Majority of patients with NASH were female and all the patients had BMI >25kg/m^2. Diabetes mellitus was seen in 50% of NASH patients. 90% had increased serum triglycerides, all with severe NASH were diabetic and hypertensive. AST: ALT ratio was more than 1 as the disease progressed and both the enzymes were elevated in all the patients with NASH irrespective of severity. Hyperbilirubinemia and decreased platelet count was seen in severe forms.
Conclusion: NASH represents a severe form in spectrum of NAFLD, common in 5^{th} decade and mostly asymptomatic with obesity, DM, hypertriglyceridemia as risk factors. Distinction between NASH and steatosis cannot be made reliably on clinical grounds or imaging. Diagnosis can be made with certainty only by examination of liver histology and is a diagnosis of exclusion.

Keywords: NASH, body mass index, diabetes mellitus, hypertriglyceridemia, liver enzymes

Introduction
Non-alcoholic fatty liver disease (NAFLD) is defined as the accumulation of lipid, primarily in the form of triacylglycerol's in individuals who do not consume significant amounts of alcohol (<20 gethanol/d) [1]. The rising incidence of obesity in today's environment is associated with many obesity-related health complications, including cardiovascular disease, diabetes, hyperlipidemia, hypertension, and nonalcoholic fatty liver disease [2]. This combination is also recognized as the metabolic syndrome and is characterized by underlying insulin resistance [3]. Non-alcoholic fatty liver disease is increasingly being recognized as a major cause of liver-related morbidity and mortality among 15-40% of the general population [4].
The causes of fatty liver are obesity, Insulin resistance, high intake of refined carbohydrates, impaired gut health.

Symptoms may include fatigue and weakness, elevated levels of liver enzymes, elevated insulin and triglyceride levels. Excess alcohol consumption results in alcoholic fatty liver / simple steatosis. Steatosis in early stages is reversible with weight loss, cessation of alcohol consumption, Steatohepatitis may progress to liver fibrosis and cirrhosis can result in liver morbidity and mortality. Treatment mostly includes lifestyle changes to reverse fat accumulation i.e. exercise and gluten free diet in NAFLD patients and in AFD patients abstaining alcohol is must.

NASH has been shown to progress to cirrhosis overtime and also been associated with Hepatocellular Carcinoma. It is now also recognized as a major contributor to cryptogenic cirrhosis. Hence NASH left without any intervention can lead to potentially serious consequences. A disease of 'obscure cause' has now become a significant entity.

Hence in population with demographic risk factors, a routine, screening by a simple abdominal sonography would be helpful. However it is difficult differentiate between potentially benign steatosis and apparently more serious NASH on ultrasound which makes biopsy necessary. This study is to analyze presence of non-alcoholic Steato-Hepatitis by performing liver biopsy in non-alcoholic adults with evidence of fatty liver on abdominal ultrasonography and to study the association of NASH with other co-morbid conditions.

Aims of the study

1. To study the presence of Non-Alcoholic Steato Hepatitis (NASH) by performing liver biopsy in non-alcoholic adults with evidence of fatty liver on abdominal ultrasonography.
2. To Study the association of NASH with other co-morbid conditions.

Material and methods

Source of Data

Population: The study was conducted on 100 patients with fatty liver diagnosed on abdominal ultrasonography attending the Department of Internal Medicine at Shadan Institute of Medical Sciences, Hyderabad, Telangana, India.

Period of the Study: August 2015 to August 2016.

Type of Study: Sample study method of collection of data

Inclusion Criteria

- Patients with fatty liver disease on abdominal ultrasonography.
- Patients of either sex.
- Age > 18 years.
- Patients who were non alcoholic.

Exclusion Criteria

- Patients with other liver diseases based on history and / or investigations
  - HBs Ag/Anti HCV positive.
  - ANA positive.
  - K.F. ring / S. ceruplasmin.
  - USG – suggestive of extrahepatic liver disease.
  - Presence of clinical jaundice.
  - Evidence of cirrhosis – ascitis, splenomegaly, jaundice, hepatic, encephalopathy, spider nevi etc.
- History of bleeding tendency grossly deranged BT/CT/PT.
- History of alcohol abuse.
- Other serious illness or comorbid states.

Statistical analysis

The information collected regarding all the selected cases was recorded in a master chart. Data analysis was done with the help of computer using epidemiological information package (EPI 2002). Using this software, frequencies, percentage, mean, standard deviation, x^2 and 'p' were calculated.

Investigations required for the study

- Blood Sugar Level — Fasting / post parandial
- Lipid profile — S. Triglycerides; Total Cholestrol; S. HDL; S. VLDL; S. LDL
- Liver function tests — SGOT (AST); SGPT (ALT); SGOT / SGPT Ratio; S Bilirubin-Total/Direct/Indirect; S Alakaline Phosphates; S Proteins-Total/Albumin/ Globulin; S. GGT
- HBsAG / Anti HCV / HIV.
- ANA – TO rule out autoimmune hepatitis.
- Slit lamp examination to exclude K. F. rings (Wilsons Disease).
- HbA1c in Diabetics.
- BT / CT / PT / APTT to rule out bleeding tendency.
- Absolute platelet count.

USG – abdomen to confirm fatty liver and to determine the grading was repeated.

100 patients satisfying the above mentioned criteria's with fatty liver on USG consented to undergo liver biopsy. The pathologic diagnosis of NASH was confirmed in 8 patients and these patients were further analyzed. Preliminary data based on age/name/sex/ address was entered.

Evaluation of each patient included a proper history - present, past and family. Detail general and systemic examination and evaluation through necessary investigation.

The history included symptoms suggestive of NASH - fatigue, malaise, fullness of abdomen, right upper quadrant pain. No forthcoming history or asymptomatic were noted.

In addition to above symptoms, details to try and find out possible risk factors was undertaken. The history of associated illnesses and drug intake was noted, with emphasis on drugs associated with NASH.

In patients with history of type II diabetes mellitus a relevant history was elicited, that is the duration of illness and the drug history. The duration and dosage of these drugs was also noted.

A family history of cryptogenic cirrhosis was enquired about in other members of the family. History of similar symptoms in other family members was asked for.

In general examination in addition to vital parameters, icterus / clubbing / pallor were looked for.

By standard means the weight in KGS and height in meter of all the patients was measured. Body Mass Index was calculated by the formula as per Quetelet Index.

B.M.I = Weight in Kg./(height in meters)^2

Waist circumference was also recorded

Systemic Examination of Respiratory, Cardiovascular, Gastro intestinal and Central Nervous System was carried outs. The findings were recorded. Detailed per abdominal examination for palpability of liver and spleen, their size and consistency was made. Confirmation for absence of tenderness of liver and absence of free fluid was carried out. The patients were then subjected to necessary investigations. (All the 50 cases were subjected to liver biopsy with proper consent and due precautions. Biopsy specimens were collected in Bouin's fluid or formalin. Biopsies were then processed in our histopathology department. Slides were stained with Hematoxylin and eosin and examined.)

Grading and staging the histopathology lesions of NASH[97]

Grade 1, Mild

- Steatosis: predominantly macro vesicular, involves <33 up to 66% of the lobules.
- Ballooning: occasionally observed; zone 3 hepatocytes.
- Lobular inflammation: scattered and mild acute (polymorphs) inflammation and occasional chronic inflammation (mononuclear cells).
- Portal inflammation: none or mild.

Grade 2, Moderate

- Steatosis: any degree and usually mixed macro vesicular and micro vesicular.
- Ballooning: obvious and present in zone 3.
- Lobular inflammation: polymorphs may be noted associated with ballooned hepatocytes, per cellular fibrosis; mild chronic inflammation may be seen.
- Portal inflammation: mild to moderate.

Grade 3, Severe

- Steatosis: typically>66% (panacinar); commonly mixed steatosis Ballooning: predominantly zone 3; marked.
- Lobular inflammation: scattered acute and chronic inflammation; polymorphs may appear concentrated in zone 3 areas of ballooning and per sinusoidal fibrosis.
- Portal inflammation: mild or moderate.
  Steatosis: grade 1) 0–33%, 2) 33%–66%, 3) >66%
  Ballooning: zonal location noted and severity (mild or marked) recorded according to estimate of numbers of hepatocytes involved.
  Lobular inflammation: 0–3 based on observations of foci per 20_field; 1;1–2 foci, 2 up to 4 foci, 3;>4 foci. In addition, cell types (acute or chronic) and location were noted.
  Portal inflammation: 0–3, 1 mild, 2 moderate, 3 severe Staging fibrosis in NASH.
- Stage 1: Zone 3 perivenular per sinusoidal/per cellular fibrosis, focal or extensive.
- Stage 2: As above with focal or extensive per portal fibrosis.
- Stage 3: Bridging fibrosis, focal or extensive.
- Stage 4: Cirrhosis.

Results

Table 1 (a): Body Mass Index (BMI)

NASH			
BMI	**Mild**	**Moderate**	**Sever**
25-28 KG/M2	100.0%	100.0%	.0%
> 28KG/M22	.0%	.0%	100.0

Table 1 (b): BMI

BMI	No of patients	Percent
25-28 KG/M2	10	62.5
>28KG/ 2	6	37.5
Total	16	100.0

Table 2: Gender

Male	Female
6	10

Table 3: NASH severity in Gender

Gender	Mild	Moderate	Severe
Male	50%	33.3%	33.3%
Female	50%	66.7%	66.7%
Total	100%	100%	100%

Table 4: Age Distribution of Patients

Age	No. of Patients	Percentage
31-40	2	12.5
41-50	10	62.5
51-60	4	25.0
Total	16	100.0

Table 5 (a): Clinical Features (CF)

NASH			
CF	**Mild**	**Moderate**	**Se ere**
Present	.0%	.0%	100.0%
Absent	100.0%	100.0%	.0%

Table 5 (b): Presence of clinical features among NASH patient

Sl. No	Clinical features	No of patient	Percent
1	Present	6	37.5
2	Absent	10	62.5
	Total	16	100.0

Table 6: Diabetes Mellitus (DM)

	No. of patients	Percent
Present	4	50.0
Absent	4	50.0
Total	8	100.0

Table 7 (a): AST - ALT Ratio

No of Patients	Frequency	Percent
>1	4	25
<1	12	75
Total	16	100.0

Table 8: Alkaline Phosphatase (ALP)

ALP	Frequency	Percent
>92	12	75.0
<92	4	25.0
Total	16	100.0

Table 9: Albumin: Globulin Ratio

AG Ratio	Frequency	Percent
>1	12	75.0
<1	4	25.0
Total	16	100.0

Table 10 (a): Total Bilirubin (TBI)

TBI	Frequency	Percent
> 1.3 mg/dl	4	25
<1.3 mg/dl	12	75
Total	16	100.0

Table 11 (a): Platelet Count (PLT/mm^3)

PLT	Frequency	Percent
>150000	12	75.0
<150000	4	25.0
Total	16	100.0

Table 12 (a): Prothrombin Time (PT)

PT	Frequency	Percent
> 15SEC	4	25
<15SEC	12	75
Total	16	100.0

Table 13 (a): Waist Circumference (WC) in Males

WC	Frequency	Percent
>102	4	66.7
<102	2	33.3
Total	6	100.0

Table 13 (b): Waist Circumference (WC) in males

WC	Nash		
	Mild	Moderate	Sev r
>102cm	.0%	100.0%	100. %
<102cm	100.0%	.0%	.0

Table 13 (c): Waist Circumference (WC) in Females

WC	Frequency	Percent
>88cm	3	60.0
<88cm	2	40.0
Total	5	100.0

Table 13 (d): Waist Circumference (WC) in Females

Nash			
WC	Mild	Moderate	Sever
>88cm	.0%	50.0%	100.0%
<88cm	100.0%	50.0%	.0%

Table 14 (a): High Density Lipoproteins (HDL) Gender = Male

HDL	Frequency	Percent
<40	4	66.7
>40	2	33.3
Total	6	100.0

Table 14 (b): HDL Levels

Nash				
		Mild	Moderate	Severe
HDL	<40	0	1	1
		.0%	100.0%	100.0%
	>40	1	0	0
		100.0%	.0%	.0%
Total		1	1	1
		100.0%	100.0%	100.0%

Table 14 (c): Diabetes Mellitus

DM	NASH		
	Mild	Moderate	Sever
Present	.0%	33.3%	100.0%
Absent	100.0%	66.7%	.0%

Table 15: Serum Cholesterol

	Frequency	Percent
>200	6	37.5
<200	10	62.5
Total	16	100.0

Table 16 (a): High Density Lipoprotiens (HDL) Gender = Male

HDL	Frequency	Percent
<40	4	66.7
>40	2	33.3
Total	6	100.0

Table 16 (b): HDL Levels

		NASH		
	¿	Mild	Moderate	Severe
HDL	< 0	0	1	1
		.0%	100.0%	100.0%
	> 0	1	0	0
		100.0%	.0%	.0%
Total		1	1	1
		100.0%	100.0%	100.0%

Table 16 (c): HDL levels

NASH				
		Mild	Moderate	Sever
HDL	>50	0	2	0
		.0%	100.0%	.0%
	<50	1	0	2
		100.0%	.0%	100.0

Table 17: Serum Triglyceride

	Triglyceride
> 150	14
< 150	2

Discussion

Nonalcoholic steatohepastitis (NASH) represents the progressive form of Nonalcoholic fatty liver disease. To identify the patients at risk for NASH, 50 patients with fatty liver on USG with exclusion of other liver disorders were studied.

Prevalence of Nash: 16% of patients diagnosed NASH on liver biopsy in our study which is similar to the prevalence shown by other studies [6].

Gender: Majority of the NASH patients i.e. 62.5% were females, and the female to male ratio was almost 2:1.

According to publications by Ludwig in his Mayo clinic study [1] in 1980 and Angulo, *et al.* in 1999 on NASH, a female preponderance with 65% & 67% respectively was found.

In our study also there is a female preponderance with 62.5% i.e. 5 out of 8 NASH patient being females.

65% of female NASH patients as compared to 35% of males NASH patients showed moderate steatohepatitis. Similarly 66.67% of females as compared to 33.33% of males showed

severe steatohepatitis. Thus our study shows that female gender is associated with severe steatohepatitis.
According to a study conducted by Uslusoy HS, *et al.* [159] in August 2011 female gender had severe steatohepatitis.
Singh, *et al.* [152] signified that female gender is an independent predictor of liver damages in patients with NASH. In our study 20%, 40% and 40% of the affected female patients had mild, moderate and severe NASH as compared to 33%, 33%, 33% affected males in mild, moderate and severe NASH respectively.

Age: The youngest NASH patient in our study was 38 years and the oldest NASH patient in our study was 58years. 62.5% of the NASH patients were between the age group of 41-50 yrs. Thus in our study majority of the NASH patients were in 5th decade.
In a study conducted by Andy S. Emmet B, *et al.* [7] NASH was commonest in the 5th decade of life. Mild steatohepatitis was seen in two patients.
The average age in our study was 48.39 ±6.08 years. In a study conducted by Uslusoy HS, *et al.*, the average age was 47.9±8.74 yrs. Shimada, *et al.* [8] in 2002 and Daryani, *et al.* [156] in 2010 found that females over 55yrs had a correlation with advanced fibrosis.
In our study 2 females over 55yrs had severe NASH. Harrison, *et al.* [160] in 2008 said that advanced age was related to severe necroinflammation and advanced fibrosis.
In our study advanced age was associated with moderate to severe NASH.
In a study conducted by Daryani, *et al.* [9] in 2010 pointed towards the influence of age in the severity of NASH and its use as a predictor of NASH. Thus age is a predictor of NASH.

Diabetes Mellitus (DM): 4 out of 8 NASH patients in our study had Type II DM. i.e. 50% patients were Type II DM.
In a study conducted by Ludwing, *et al.* [1] in 1980 and Diehl, *et al.* [22] in 1988, the percentage of Type II DM was 50% & 55% respectively.
In our study none of the non-diabetics had severe steatohepatitis.
In a study conducted by Selim Giray, Macit Gulten and H.S. Uslusoy [10] in 2011, 14.2% of diabetic patients had severe NASH.
Pagano, *et al.* [163] defined the prevalence of metabolic syndrome as 47% in NASH cases. Diabetes is strongly associated with NASH [157].
Similarly, in our study all patients with severe NASH had diabetes mellitus.
This shows that diabetes increases the risk for severe necroinflammation.

Clinical features: In our study 75% of NASH patients were asymptomatic. In a study conducted by Angulo P and Lindor KD [9] most patients were asymptomatic.
In a study conducted by Ebrahimi Daryani in 2003, on Iranian patients 79.2% patients were asymptomatic.

Triglyceride Levels: 7 out of 8 NASH patients i.e. 87.5% patients in our study had serum triglyceride levels >150 mg/dl.
In a study by Matteoni, *et al.* [11] in 1999, 92% patients had hypertriglyceridemia. This shows that increase triglyceride levels correlates with NASH.

AST, ALT: In our study all the NASH patients had elevated liver amino transaminases.
A study conducted by Hossein Bahrani, Nasser Ebrahimi daryani in Iranian patients in 2003, patients were included on the basis of elevated liver amino transaminases levels.
The mean ALT levels of NASH patients in our study was 82.26±29.15 U/L. The mean AST of NASH patient's levels was 72.64±26.95 U/L. Similarly, the mean ALT and AST levels were 80.9±32.0 U/L & 69.8±28.9 U/L respectively in the above Iranian study.
The mean AST: ALT ratio in our study was 0.89±0.5. The mean AST: ALT ratio in Iranian study was 0.9±0.4.
In our study of NASH patients this ratio was below 1 in 62.5% patients and all the patients (100%) had ratio below 2. This ratio was below 1 in 65.3% patients & below 2 in 96.2% in the above Iranian study.
In a study by Agarwal S.R, *et al.* [12] published in the Indian Journal of Gestroenterology 2001, Bacon, *et al.* [28] AST: ALT ratio below 1 was characteristic of NASH, in contrast to ASH (Alcoholic steatohepatitis) where AST: ALT ratio is more than 1. Nevertheless the ratio becomes more than 1 as NASH progresses to cirrhosis. In our study 2 patients had AST: ALT ratio >1. Two patients had evidence of cirrhosis on histology. This explains that AST: ALT ratio which is <1 in NASH is reversed as NASH progresses towards cirrhosis. Thus AST: ALT ratio >1 is a predictor of advanced fibrosis & cirrhosis.
This shows that as the severity of NASH increased, the AST & ALT levels increases. Thus elevated transaminase levels correlated with NASH. Rodriguez – Hernandez, *et al.* [161] stressed that ALT was correlated with necroinflammation. Our study shows that ALT levels are increased as the severity of NASH increase.
Thus this shows than ALT is an independent predictor of steatohepatitis.

BMI: In 8 out of 8 NASH patients i.e. 100% patients the BMI was more than 25 kg/m^2.
In a study by Angulo, *et al.* [9] in 1999, 60% patients had BMI more than 28 kg/m^2.
In our study of NASH patients mean weight was 78.63±8.53 kg, mean height was 164.88±7.53cm, mean BMI was 28.98 ± 3.02 kg/m^2.
Obesity is the condition most often associated with NASH. As in most studies 69-100% patients with NASH were also obese. Steatosis is the common observation in the obesity and may be associated with inflammatory signs of non-specific hepatitis.
In our study 62.5% patients with NASH had BMI between 25-28kg/m^2 and 37.5% patients had BMI more than 28 kg/m^2.
Thus 100% of patients were overweight with NASH. Singh, *et al.* 13 in 2008 signified that BMI is an independent predictor of liver damage in patients with NASH.
In our study 3 patients out of 8 patients with NASH ad severe steatohepatitis with BMI more than 28 kglm^2 none of the patients with BMI less than 28kglm^2 had severe steatohepatitis. Thus BMI can be used as an independent predictor of severity of NASH.

Waist Circumference (WC): Mean waist circumference of the patients with NASH was 92.64cm±10.22 cm in our study.

Mean waist circumference in males was 100.66cm and in females was 87.8 cm in NASH patients.
3 out of 5 females with NASH i.e. 60% females had WC > 88cm and 2 out of 3 male patients with NASH i.e., 66.7% males had WC > 102 cm.
Visceral obesity is one of the most important risk factors for NASH, which is usually associated with impaired insulin activity, overflow of portal triglycerides and overproduction of inflammatory cytokines. Even though many surrogate parameters have been proposed as markers of visceral adiposity, WC remains the simplest and most widely used. In this direction, Singh, *et al.* [14] identified WC as an independent predictor of the degree of liver necroinflammation. 2 out of 5 females with WC > 88 cm had severe NASH and none of the females with WC < 88 cm. had severe NASH.
1 out of 3 males with WC >102cm had severe NASH and none of the males with WC < 102cm had severe NASH.
Thus it shows that WC is an independent predictor of degree of necroinflammation.

Lipid profile
6 out of16 patients with NASH, i.e. 37.5% had S. cholesterol levels ≥ 200 mg/dl, 2 out of 6 male patients with NASH, i.e. 33.33% HDL cholesterol ≥ 40 mg/dl, 4 out of 10 female patients with NASH, i.e. 40% HDL cholesterol ≥ 50 mg/dl, 14 out of 16 patients with NASH, i.e. 87.5% Tirglyceride ≥150 mg/dl, None of the patients had LDL cholesterol less than 160 mg/dl, Previous studies reported by Bacon B, *et al.* [28], Ludwig, *et al.* [1], Diehl AM [2], showed prevalence of dyslipidemia from 20 to 80%.

Hypertension (HTN): In our study, 4 out of 8 patients with NASH, i.e. 50% were hypertensive. Dixon, *et al.* [15] reported that arterial hypertensive was independent predictor for NASH. In our study 2 out of 3 patients i.e. 66.7% with moderate NASH were hypertensive. 3 out of 3 patients i.e. 100% with sever NASH were hypertensive. Thus hypertension can be used as an independent predictor for severity of NASH.

Alkaline phosphatase (ALP): In our study 3 out of 8 patients with NASH i.e. 37.5% showed elevated alkaline phosphatase.
It has been stated that alkaline phosphatase levels, may variably be elevated in patients of NASH as studies in journal published by American Gastroenterology Association technical review on non-alcoholic fatty liver disease Gastroenterology 2002.

Cirrhosis: As expected, measures of hepatic functional capacity do not become abnormal until cirrhosis and liver failure set in. The serum albumin level and prothrombin time become abnormal before the serum bilirubin levels does [1].
Hematologic parameters are usually normal unless cirrhosis & portal hypertension leads to hypersplenism. In our study out of 50 liver biopsies done, severe necroinflammatory activity was seen in 2 patients and none of the patients in stages 0, 1, 2 or 3 showed severe necroinflammatory activity. 2 patients in our study had hypoalbuminemia, reversal of A:G ratio, hyperbilirubinemia, thrombocytopenia and abnormal prothrombin time. Thus these lab parameters correlated with the histologic findings of cirrhosis.
According to Shimada, *et al.* [154] low platelet count was proposed to be a marker of fibrosis.
In our study 2 patients with NASH had a low platelet count and were having stage 4 fibrosis (cirrhosis).
NASH can cause fibrosis & progressed to cirrhosis. It has been shown that this progress is seen in 8.26% of patient [16].
In our study 4 patients out of 16 with NASH i.e. 12% had cirrhosis.
Studies showed by Patel T & Lee J.G. in 2001 about 30% of cases developed complications including vertical bleeding, ascites, encephalopathy & liver failure. Patients with cirrhosis are at increased risk of developing the above mentioned complications in the future. This shows that cirrhosis is a poor prognostic indicator.
Hence confirmation of diagnosis of our cases by liver biopsy and their histological staging & grading is critical.

BAAT Score: Ratziu, *et al.* [17] identified 4 independent variables predictive of septal fibrosis, hence cirrhosis. i.e. BMI≥28kglm^2, age ≥ 50yrs, ALT twice the normal, serum triglycerides ≥ 150 mg/dl. Each clinical variable was given a score of 0 or1 with total scores ranging from 0-4. An overall score of 0 or 1 was associated with a sensitivity and specificity of 100% and 47% respectively for the absence of septal fibrosis.
When all 4 variables are present (score of 4) specificity increased to 100% for the detection of septal fibrosis or cirrhosis, but the sensitivity decreased to 14%.
Accordingly to Ratziu, *et al.* [156], A BAAT score 0 or 1 excludes septal fibrosis or cirrhosis.
In our study 2 patients with cirrhosis had BAAT score of 4.
This confirms that BAAT score of 4 is highly specific for detection of cirrhosis.

Statistical Analysis and limitations in our study
As chi square calculations are only valid when all expected values are greater than 1 and at least 80% of the expected values are greater than 5. There conditions have not been set and thus the chi square calculations are not valid in our study.
Statistical significance was not reached due to small number of patients studied. Hence, patient's features were evaluated according to their percentage values.
In a study conducted by Uslusoy HS, *et al.* [18] in 2011, published in the world journal of Hepatology, statistical significance was not reached and p values were not available and percentage values were used for evaluation.
The study should be ongoing and a larger sample size would be desirable.

Conclusions
1. NASH represents a part of a wide spectrum of NAFLD. It could be one of the common causes of cryptogenic cirrhosis.
2. The occurrence of NASH is more in the 5th decade.
3. Patient with NASH are typically asymptomatic unless cirrhosis develops.
4. Hypertriglyceridemia is found in 89% of NASH.
5. Risk factors associated with NASH include obesity, type II DM and hypertriglyceridemia.
6. Age, gender, waist circumference, BMI, ALT, AST:ALT ratio, serum triglyceride levels, HTN & BAAT score are independent predictors of NASH.

7. Distinction between NASH and steatosis cannot be made reliably on clinical grounds or imaging. Diagnosis can be made with certainty only by examination of liver histology. Characteristic features include fatty change, inflammation, hepatocellular injury with ballooning degeneration and mallory bodies and/or fibrosis.
8. NASH is a diagnosis of exclusion and requires careful consideration of diagnosis.

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Conflict of Interest: None

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