



Research Paper

The Clinical , Biochemical , Serological And Radiological Profile Of Fatty Liver Disease

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ABSTRACT:

Back ground: Fatty liver disease has a rapidly increasing incidence worldwide due to multiple genetic and socio-economic factors, affecting people from all age groups. Initially thought to be a disease of only the obese, fatty liver is now known to be prevalent in lean individuals too. It is a disorder which goes undiagnosed for a very long time and its presence increases the risk of chronic liver disease.

Methods: A total number of 96 patients diagnosed as fatty liver on ultrasound, irrespective of the presenting complaint were enrolled for the study. A detailed analysis of the clinical, biochemical, serological and radiological profile including liver elastography was done for all the patients and the data was analysed with the help of SPSS.

Results: Fatty liver was found to be more common in males as compared to females. Non-alcoholic fatty liver disease [NAFLD] was found to be the most common cause of fatty liver followed by alcoholic fatty liver disease, Hepatitis B and Hepatitis C. Diabetes Mellitus and Metabolic syndrome were present in almost half of the total fatty liver cases. Liver enzymes were deranged in majority of the patients. Raised triglycerides were seen in majority of the patients. The agreement between ultrasound and elastography for grading of fatty liver was low at 55%.

Conclusion: All patients diagnosed to have fatty liver must be investigated extensively for the underlying etiology. As fatty liver represents the reversible stage in the pathogenesis of chronic liver disease, timely intervention can successfully prevent progression of disease into liver cirrhosis. Liver Elastography is preferable to ultrasonography for grading of fatty liver.

KEYWORDS: Fatty liver, Lipid profile, Liver elastography

I. INTRODUCTION

Fatty liver is a disorder of the liver characterized typically by the excessive accumulation of fat in the liver. Globally, about 25%-50% people have a fatty liver depending upon various factors namely age, race, lifestyle, ethnicity, dietary habits, physical exercise, alcohol intake, genetic susceptibility, insulin resistance, etc [1]. Historically, the prevalence of fatty liver has been higher in western [developed] countries as compared to their eastern [developing] counterparts but with time this disorder has spread its presence all over the world with the incidence rising steadily over the years owing to rising influence of western culture and lifestyle on the rest of the world. Lifestyle changes coupled with rising prevalence of other diseases [like diabetes, hypertension] have had a profound effect on the hepatic physiology of populations steering a progressive growth of the at-risk population for fatty liver [2].

Fatty liver has been studied extensively in the west where gender differences have been noted, the disorder afflicting more women than men. Asian studies into this disorder have only picked up pace in the last one and a half decade [3]. Indian and Asian studies have reported fatty liver to be more common amongst males as compared to females. This relationship held good for both alcohol induced fatty liver disease as well as “non alcoholic fatty liver disease”. Clinically, fatty liver has been found to be commonly asymptomatic though other features such as vague or non specific right upper quadrant pain, nausea, fatigue may also be common presenting features. Fatty liver is usually diagnosed incidentally on ultrasonography which is usually the accepted first line investigation for fatty liver screening. A good number of such patients may be obese, which usually indicates altered fat metabolism and excess fat deposition. History of alcohol consumption [for alcoholic fatty liver] is of great importance. Although alcohol consumption is usually reported to be higher in Western nations, the changing cultural habits and increasing western influence has increased the prevalence of alcoholism in India [4].

Investigations for a case of fatty liver usually report deranged liver function tests, where the spectrum usually ranges from mild to moderate derangement. Liver enzymes are often elevated in most patients of fatty liver but are usually less than 4 times the upper limit of normal. The AST:ALT ratio is usually 2:1 or more in cases of “alcoholic liver disease” and the ratio reverses in patients of NAFLD. A fair number of patients may present with absolutely normal liver function tests, marking the other end of the spectrum. Alteration of lipid profile is commonly observed due to a dysregulation of fat metabolism. Triglyceride, total cholesterol, LDL, VLDL elevation and decreased HDL are usually reported [5]. Serologically, investigation for hepatitis B virus and hepatitis C virus are warranted in patients with fatty liver as recent evidence suggests that both these viruses may have some association with fatty liver [3].

Ultrasonography has been the investigation of choice for fatty liver screening all over the world. It is quick, painless, relatively cheap. Other imaging modalities that have been tried include Liver Elastography [Fibroscan], Computed Tomography and Magnetic Resonance Imaging [3]. Of these, liver elastography has gained particular interest for its high sensitivity and specificity and ability to grade the fibrosis. The gold standard however, to grade fatty liver is the liver biopsy. The liver biopsy is also the only investigation which can reliably diagnose non alcoholic steatohepatitis. The liver biopsy has several limitations such as risk of complications like bleeding, perforation, organ injury, infection. Therefore liver biopsy is not a routinely performed investigation for evaluation of fatty liver [4].

A fatty liver represents an early stage of liver disease which later is at risk of proceeding to cirrhosis. Considering the worldwide rising incidence of fatty liver, it is imperative that all cases of fatty liver be investigated judiciously so as to delineate and modify the risk factors and underlying etiologies [5].

II . MATERIALS AND METHODS

Ethics statement: A written detailed informed consent was obtained from all patients recruited for the study.

Study design: The study was conducted in the Department of Medicine, Himalayan Institute of Medical Sciences, Swami Ram Nagar, Dehradun over a period of 12 months.

Type of study: Observational and cross sectional study.

Sample size : 96 patients with fatty liver diagnosed on ultrasonography

Selection of subjects : All patients with ultrasonography reported as fatty liver, irrespective of presenting complaint, were recruited for the study and investigated further.

Study protocol: A general physical examination, anthropometry measurements [height, weight, BMI] were done for all patients. Laboratory investigations included complete hemogram, hepatitis B antigen, Hepatitis C serology, liver function test, lipid profile, fasting blood sugar, glycosylated hemoglobin. Liver elastography was done for all patients.

Data Management and Statistical Analysis: The data was collected and entered in MS Excel 2010. Statistical Analysis was performed using SPSS software version 22. Normally distributed data was analysed using a general linear model analysis of variance [ANOVA]. The categorical data was analysed using the Chi square test. The level of significance usually denoted as α has the following criterion as: if $p < 0.05$ then hypothesis is said to be significant.

III. RESULTS

Table 1 : Age and gender wise distribution

Age group [years]	Male		Female	
	No.	Percentage	No.	Percentage
18- 30	10	10.41%	4	4.16%
31-40	26	27.08%	5	5.20%
41-50	19	20%	6	6.25%
51-60	8	8.33%	8	8.33%
61-70	7	7.29%	1	1.04%
>70	2	2%	0	0
Total	72	74.90%	24	24.98%
Mean age	43.53 ±13.14			

Table 1 - Out of total 96 patients , 72 [74.9%] were males and 24[24.98%] were females. The maximum number of males[n = 26 , 27.08%] belonged to the 31- 40 year age group and the maximum number of females [n=8,8.33%] belonged to the 51-60 year age groups.

Table 2 : Etiology of fatty liver

Etiology	No. Of Patients	Percentage
NAFLD	44	45.83%
AFLD	39	40.60%
HEPATITIS B	4	4.16%
HEPATITIS C	9	9.30%
HEPATITIS B + ALCOHOL	2	2.08%
HEPATITIS C + ALCOHOL	1	1.04%

Table 2 – Maximum [45.83%] cases belonged to the NAFLD group followed by alcoholic liver disease [40.60%], [4.16%] had Hepatitis B , [2.08%] had Hepatitis B and Alcohol use present, 9 [9.30%] had Hepatitis C and[1.04%] had Hepatitis C and Alcohol use.

Table 3 : Associations of fatty liver

Associated Conditions	No. of Patients	Percentage
DM	41	42.70%
HTN	35	36.45%
METABOLIC SYNDROME	46	47.91%
ALCOHOL	40	41.66%
SMOKING	36	37.50%

Table 3- [42.70%] had Diabetes Mellitus,[36.45%] had hypertension, [47.91%] had Metabolic Syndrome,[41.66%] had alcohol use,[37.50%] had smoking present.

Table 4: BMI groups in NAFLD patients

BMI GROUP [kg/m ²]	NAFLD [No. of Patients]	
	ABSENT	PRESENT
18-22.9 [normal]	17[32.7%]	13[29.5%]
23-24.9[overweight]	16[30.8%]	18[40.9%]
>=25 [obese]	19[36.5%]	13[29.5%]
TOTAL	52[54.16%]	44[45.83%]

Table 4 - NAFLD was present in total 44 [45.83%] subjects. 13[29.5%] subjects belonged to the normal BMI group, 18[40.9%] subjects belonged to the overweight group and 13 [29.5%] belonged to the obese group.NAFLD was absent in 52[54.16%] of the subjects.

Table 5 :Symptom wise distribution of patients

SYMPTOMS	No. Of Patients	Percentage
ASYMPTOMATIC	58	60.40%
FATIGUE	23	23.90%
ABDOMINAL PAIN	22	22.90%
NAUSEA	6	6.25%

Table 5 - [60.40%] were asymptomatic, [23.90%] had fatigue ,22[22.9%] had abdominal pain and [6.25%] had nausea.

Table 6: Liver Function Tests

	Ultrasound Grade	Mean
TOTAL BILIRUBIN [mg/dl]	Grade 1	1.30
	Grade 2	1.08
	Grade 3	4.61
AST [IU/L]	Grade 1	59.43
	Grade 2	79.71
	Grade 3	65.40
ALT [IU/L]	Grade 1	63.31
	Grade 2	80.10
	Grade 3	85.20
ALP [IU/L]	Grade 1	121.56
	Grade 2	110.33
	Grade 3	190.00

Table 6 – Total bilirubin was within normal limits for majority of the patients . Liver enzymes were mildly elevated in all ultrasound based severity groups[elevation was less than 4 times the upper limit of normal].

Table 7 : Lipid profile

	Ultrasound Grade	Mean
TG[mg/dl]	Grade 1	195.79
	Grade 2	188.10
	Grade 3	274.00
CHOLESTEROL [mg/dl]	Grade 1	185.707
	Grade 2	195.33
	Grade 3	174.60
HDL[mg/dl]	Grade 1	40.35
	Grade 2	41.57
	Grade 3	28.40
LDL[mg/dl]	Grade 1	104.56
	Grade 2	111.70
	Grade 3	91.40
VLDL[mg/dl]	Grade 1	39.16
	Grade 2	37.62
	Grade 3	54.80

Table 7 – The triglyceride levels were raised but the levels of total cholesterol, LDL, HDL and VLDL were within normal limits for majority of the patients.

Table 8 : USG grade vs Elastography grade

USG GRADE	ELASTOGRAPHY GRADE			AGGREEMENT
	METAVIR F1	METAVIR F2	METAVIR F3	
GRADE 1	56	14	0	0.551
	91.80%	45.20%	0.00%	
GRADE 2	5	16	0	
	8.20%	51.60%	0.00%	
GRADE 3	0	1	4	
	0.00%	3.20%	100.00%	
TOTAL	61[63.54%]	31[32.29%]	4[4.16%]	

Table 8 – The comparison between the grading of fatty liver on ultrasound as compared with grading on liver elastography shows an agreement of only 55% between the two investigations.

IV. DISCUSSION

On analysis of the population of fatty liver patients under study it was observed that [75%] patients were males and [25%] patients were females. Indian studies as well as other similar studies in the Asian subcontinent have revealed similar findings showing male predominance for fatty which is in contrast with the western world which shows female predominance. Genetic influences are believed to be the major reason for this variable gender distribution across populations [2,6]. Our study reports maximum[45.83%] cases belonging to the NAFLD group followed by alcoholic liver disease [40.60%], then hepatitis B [4.16%], Hepatitis B and alcohol [2.08%], Hepatitis C [9.30%], Hepatitis C and alcohol [1.04%]. Recent studies have shown that NAFLD has taken over Alcoholic fatty liver as the most common cause of fatty liver disease worldwide. Both hepatitis B and hepatitis C have been individually found to be responsible for fatty liver in numerous studies[6].

Analysis of our study population revealed that [42.70%] had Diabetes Mellitus, [36.45%] had hypertension, [47.91%] had Metabolic Syndrome, [41.66%] had alcohol use. Multiple studies have reported a close link between fatty liver and Diabetes, hypertension, metabolic syndrome and alcohol use. Each of these factors is independently responsible for playing a role in the pathogenesis of fatty liver[7]. Of all the NAFLD patients in our study population most [40.9%] patients belonged to the overweight category whereas a fair number [29.5%] belonged to the normal and lean category each when classified on basis of BMI. Numerous studies have revealed and supported the rising incidence of fatty liver in individuals with normal BMI as well as lean individuals. Chronic inflammation, mitochondrial dysfunction, metabolic and genetic factors have been postulated to be responsible[7].

In our study group, majority [60.40%] patients were asymptomatic while [23.90%] had fatigue, [22.9%] had abdominal pain and [6.25%] had nausea. Worldwide, the most common presentation of fatty liver across all the various etiologies is “asymptomatic”[8]. Few patients may report fatigue, abdominal pain and nausea. The asymptomatic nature of the illness masks the disease and delays the presentation of the patient to the health care system. Most cases are therefore identified incidentally while performing routine tests. The altered liver function explains the occasional symptoms of fatigue, abdominal pain and nausea. We also found that most of our patients had only mild [less than 4 times the upper limit of normal] elevation of liver function tests. We also observed that in our study group, the triglyceride levels were raised but the levels of total cholesterol, LDL, HDL and VLDL were within normal limits for majority of the patients. Although the underlying process of development of fatty liver is one which involves abnormal liver function, altered fat metabolism, it is not the sole mechanism responsible for the pathogenesis of fatty liver disease[9]. Therefore it is common to have a near normal liver function tests and lipid profile in patients with fatty liver. Both ultrasound and liver elastography are imaging techniques which can be used for grading the severity of fatty liver. Liver elastography has better sensitivity and specificity than conventional ultrasound when evaluating patients with lower fat [less than 20%] deposition. For higher [more than 20%] fat deposition, both have similar sensitivity [87.5% - 96.2%] and specificity [78.4% - 92.2%][10]. Our study showed the

agreement [using kappa statistics] between between the grading with ultrasound as compared to grading with elastography was low [55%]. Therefore liver elastography is still preferable for grading of fatty liver.

V. LIMITATIONS

Liver biopsy is the gold standard for grading of fatty liver but was not done due to risk of complications like infection, life threatening bleeding and organ perforation.

VI. RECOMMENDATIONS

All patients of fatty liver should be thoroughly investigated for underlying etiology as fatty liver represents the reversible stage in the pathogenesis of chronic liver disease. Grading of fatty liver should be preferably done with elastography.

VII. REFERENCES

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