

Study of Sonographically Diagnosed Non-Alcoholic Fatty Liver Disease and Association with its Risk Factors in Nepal Police Hospital

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ARTICLE HISTORY

Received : May 11, 2022

Accepted: Aug 21, 2022

ACCESS THE ARTICLE ONLINE



DOI: <https://doi.org/10.37080/nmj.150>

ISSN : 2645-8438

KEYWORDS

BMI, FLD, LFT, Lipid profile, NAFLD

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CONFLICT OF INTEREST : None

ABSTRACT

Introduction: Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in the West, and it is increasing alarmingly in the South-Asia as well the main cause is likely modern lifestyle and diets. The aim of the study is to find an association of different risk factors with sonographically detected and graded fatty liver disease in hospital-based Nepalese police personnel.

Methods: A cross-sectional prospective study was done, and 125 cases were included after fulfilling the inclusion criteria. Fatty Liver Disease (FLD) was sonographically diagnosed and graded. Association between graded NAFLD and risk factor was made using the Chi-square test keeping the inference <0.05. ANOVA analysis was done wherever applicable keeping inference < 0.05.

Results: Mean age with NAFLD was 42.9±12.2 with age group 40-49 mostly involved 43(34.4%). The male gender has more prevalence of 82(65.6%). Most of the NAFLD Body Mass Index (BMI) were overweight 77(61.6%). There was a significant association of graded NAFLD with BMI (Chi Square P <0.05) and a significant difference between Grade I and Grade II BMI (ANOVA < 0.05 and Post Hoc (Tukey)<0.05). Also, a significant association of graded NAFLD was seen with Total Cholesterol (TC), serum glutamic-pyruvic transaminase (SGPT), serum glutamic-oxaloacetic transaminase (SGOT) and Chronic diseases (Diabetes mellitus and hypertension).

Conclusions: Graded NAFLD is found to be strongly associated with BMI, TC, SGPT, SGOT, Diabetes mellitus and hypertension. Furthermore, the prevalence was found more in the middle age group, male gender and overweight person.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is characterized as fat accumulation in the liver that is greater than 5% to 10% by weight in the absence of persistent alcohol usage.¹⁻² NAFLD is the most frequent cause of chronic liver disease in the globe.³ Likewise, it is also the most common chronic liver disease in the West, and it is increasing alarmingly in South Asia, having reached a 30% epidemic rate in recent decades.⁴ Nepal is not so far from this prevalence and is reported to be around 17%.⁵ Although most NAFLD cases are mild

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How to cite (Vancouver Style)

Khadgi K, Singh TB. Study of Sonographically Diagnosed Non-Alcoholic Fatty Liver Disease and Association with its Risk Factors in Nepal Police Hospital. Nepal Med Jor. 2022;5(2):30-37.

with good prognosis however it can even lead to fibrosis, cirrhosis, liver failure, and hepatocellular carcinoma and therefore, it is the condition of the major concerned.⁶

Fatty liver can be detected by ultrasonography (USG), computed tomography (CT), and magnetic resonance imaging (MRI). Moreover, CT has shown limited sensitivity compared to USG. In addition, CT scans can be affected by other factors such as iron deposition and fibrosis. It has also been shown to be less accurate in detecting mild steatosis compared with more advanced steatosis. Also, CT scan has the risk of radiation hazard. However, MRI on the other hand has been proven to detect fat accurately.⁷ However, we are more concerned with incidental findings while performing abdominal routine or other symptomatic examinations and for which USG is the measure ahead of the other two. Furthermore, it is very sensitive and is currently the most preferred method regardless of several limitations.⁸ If there are appropriate clinical risk factors and fat deposition in the liver accounts for more than 33%, ultrasound can reliably detect NAFLD. Bright liver echoes, increased hepatorenal echoes, and vascular blurring in the portal or hepatic veins have been classified as special ultrasound features of NAFLD.⁹

The number of NAFLD patients has been steadily increasing because of modern lifestyles and diets. More sedentary lifestyles and adaptation to modern diets have also led to different disorders like obesity, dyslipidemia, Diabetes mellitus, hypertension, etc.¹⁰⁻¹² It has been documented the association of NAFLD with BMI, Dyslipidemia, Liver function, Diabetes Mellitus, and hypertension in previous studies.^{1,13} The aim of this study is also to find the association of these risk factors, however, with sonographically detected and graded fatty liver disease in a hospital-based cohort of Nepalese police personnel.

METHODS

1. Subjects

A descriptive cross-sectional prospective study was carried out between December 2021 and March 2022 in a Nepal Police Hospital (NPH), Kathmandu, and included all 125 police personnel fulfilling the inclusion criteria during the mentioned time period. We excluded the patients under the following criteria: (a) Alcohol consumption >140g/week for men and >70g/week for women as this is considered significant alcohol consumption¹⁴ (b) Subjects with hepatitis B or C viruses, liver insults, and surgery, and those

who had taken lipid-lowering medications. We included all those ultrasonographical diagnosed FLD patients after not meeting the exclusion criteria.

2. Ultrasound Screening of Fatty Liver Disease

We have used Toshiba Aplio 400 and Samsung RS 85 Ultrasound machine equipped with a curvilinear 3.5 MHz probe for screening the subject and making the diagnosis. Diagnosis of Fatty Liver Disease (FLD) was made and graded after fulfilling any of the following conditions under ultrasonography: Grade I: increasing liver echogenicity (bright liver) as compared with the right renal cortex and spleen (Figure 2), Grade II: Grade I with loss visualization of intrahepatic vascular walls (Figure 3) and Grade III: Grade II with impaired visualization of the diaphragm and posterior portion of the right liver lobe (Figure 4) (15, 16).

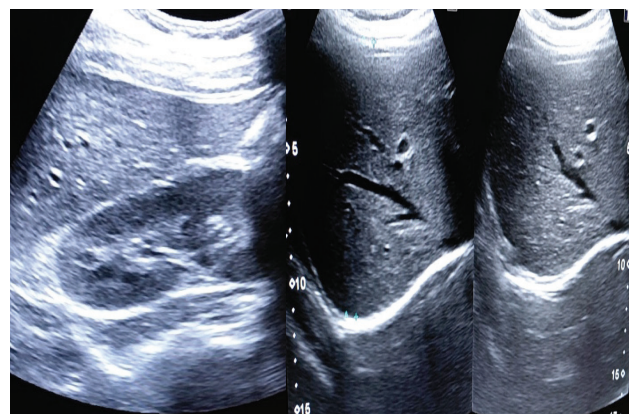


Figure 1: a,b shows the normal liver without fatty changes. Echogenicity of liver and renal parenchyma looks almost similar. Periportal echogenicity and diaphragm echogenicity is preserved

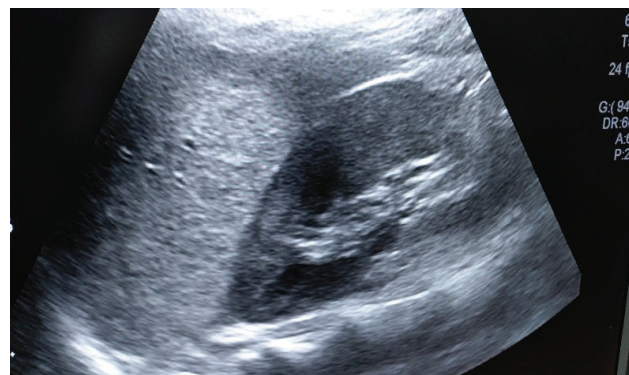


Figure 2: Grade I fatty changes in Liver. Hepatic parenchymal echogenicity is homogeneously increased compared to renal parenchyma however Periportal echogenicity and Diaphragm echogenicity is preserved.

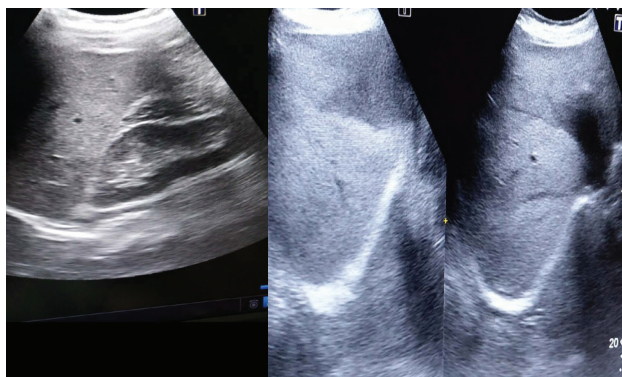


Figure 3: Grade II fatty changes in Liver. Hepatic parenchymal echogenicity is homogeneously increased compared to renal parenchyma and Periportal echogenicity is lost however diaphragm echogenicity is preserved.

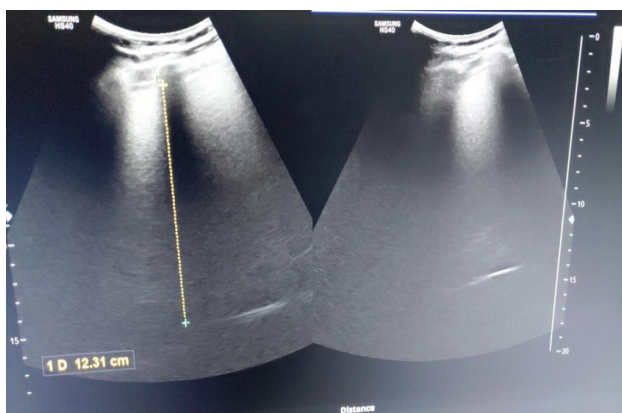


Figure 4: Grade III fatty changes in Liver. Periportal echogenicity and Diaphragm echogenicity is almost non visualized.

3. Biochemical and anthropometric risk factors

The patient's age, gender, medical history, history of diagnosed diabetes mellitus (DM) and hypertension (HTN), patient height and weight and resultant calculated body mass index (BMI) were recorded. After a diagnosis of NAFLD, the patient was sent for a lipid profile test and liver function test and the resultant total cholesterol (TC), triglyceride level (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), alkaline phosphatase (ALP), serum glutamic pyruvic transaminase (SGPT) and serum glutamic oxaloacetic transaminase (SGOT) was recorded in the predesigned form.

BMI was considered underweight if $< 18.5 \text{ kg/m}^2$, normal if between 18.5 to $< 25 \text{ kg/m}^2$, overweight if between 25.0 to $< 30 \text{ kg/m}^2$ and obese if $\geq 30.0 \text{ kg/m}^2$ or higher.¹⁷ Lipid profile was considered abnormal if either TC $> 200 \text{ mg/dl}$,

TG $> 150 \text{ mg/dl}$, LDL $> 129 \text{ mg/dl}$, or HDL $> 40 \text{ mg/dl}$ ¹⁸ and the Liver function test was considered normal if ALP between 30 to 120, SGPT if between 0 to 45 IU/L and SGOT if between 0 to 35 IU/L and abnormal if not within normal range.¹⁹

4. Statistical Analysis

Data were analyzed with Statistical Package for the Social Sciences program (SPSS) version 16.0 and 24.0. The characteristics of different risk factors were expressed in occurrence number (percentile), and normality was checked and expressed in Mean \pm SD wherever applicable and if not applicable; Mode (Interquartile range) was used. Association between different grades of FLD with risk factors was observed using the Chi-square test keeping the inference level < 0.05 . For the applicable risk factors, ANOVA analysis between the grades of fatty liver disease was done keeping inference level < 0.05 and if significant Post Hoc (Tukey) was done.

This study was approved by the Institutional Review Committee (IRC) of Nepal police hospital, Kathmandu. The IRC number of the study is 02/2078. Informed consent was obtained from each patient.

RESULTS

A total of 125 ultrasonographically diagnosed non-alcoholic fatty liver disease cases were included where the mean age was 42.9 ± 12.2 ranging between 18-85 years old (Table 1). Most cases were in the age group 40-49 years, consisting of 43(34.4%), and the least number in the age group 10-19 which was only 1(0.8%). Males constituted the major population of the cases 82(65.6%). Regarding BMI, most cases were overweight 77 (61.6%). The characteristic of lipid profile expressed in mean \pm SD and mode (Inter quartile range) was: TC: 170.8 ± 43.3 , 168(60.5); Serum TG: 149(144.5); HDL-C: 111(36) and LDL-C: 110.8 ± 30 , 40(13.5). Similarly, the characteristic of the Liver function test as expressed in mode (Inter quartile range) was; ALP: 86(39.5), SGPT: 35(36), and SGOT: 28(16.5). Diabetes Mellitus was seen only in 19(15.2%) cases and Hypertension was seen only in 27 (21.6%) cases. Tables 2 and 3 show most included cases were having Grade I FLD 94(75.2%) and a very small number in Grade III 2(16%).

Table 1: The Descriptive Analysis of Variables (risk factors)

Variables		N (%)	Mean \pm SD	Mode (IQR)	Skewness (S)and Kurtosis (K)
Age			42.9 \pm 12.2		S:0.85; K:1.0
	10-19 years	1(0.8%)			
	20-29 years	13(10.4%)			
	30-39 years	37(29.6%)			
	40-49 years	43(34.4%)			
	50-59 years	20(16%)			
	\geq 60 years	11(8.8%)			
Gender					
	Male	82(65.6%)			
	Female	43(34.4%)			
BMI			27.1 \pm 3.1		S: 0.55; K: 1.48
	Normal (18.5 to <25 kg/ m ²)	28(22.4%)			
	Overweight (25to <30 Kg/ m ²)	77(61.6%)			
	Obese (30 and above Kg/m ²)	20(16%)			
Lipid Profile					
	TC		170.8 \pm 43.3	168(60.5)	S: 0.2; K: -0.2
	Serum TG		N/A	149(144.5)	S: 3.4; K:17.7
	HDL-C		N/A	111(36)	S: 1.4; K: 4.2
	LDL-C		110.8 \pm 30.0	40(13.5)	S: -0.01; K: -0.5
Liver Function Test					
	ALP		N/A	86(39.5)	S: 1.4; K: 2.7
	SGPT		N/A	35(36)	S: 3.4; K: 16.1
	SGOT		N/A	28(16.5)	S: 58; K: 36.8
DM					
	Present	19(15.2%)			
	Absent	106(84.8%)			
HTN					
	Present	27(21.6%)			
	Absent	98(78.4%)			

BMI=body mass index, DM=diabetes mellitus, HDL-C=high-density lipoprotein-cholesterol, LDL-C=low-density lipoprotein cholesterol, NAFLD=nonalcoholic fatty liver disease, SD=standard deviation, TC=total cholesterol, TG=triglyceride, ALP=Alkaline Phosphatase, SGPT= serum glutamic pyruvic transaminase, SGOT= serum glutamic oxaloacetic transaminase, IQR=Inter Quartile Range, S=Skewness, K=Kurtosis

Table 2 shows there is no association between grades of fatty liver disease with the age group (chi-square $P>0.05$). Furthermore, there is no significant difference between the grades as well (ANOVA $P>0.05$) (Table 5).

Table 2: Age Group Vs Grade

Age Group (In years)	Grade I	Grade II	Grade III	Total	P value (Chi Square)
10-19	1 (1%)	0	0	1 (0.8%)	P= 0.602 ($P>0.05$)
20-29	12 (12.7%)	1 (3.4%)	0	13 (10.4%)	
30-39	31 (32.9%)	6 (20.68%)	0	37 (29.6%)	
40-49	28 (29.78%)	14 (48.27%)	1 (50%)	43 (34.4%)	
50-59	14 (14.89%)	5 (17.24%)	1 (50%)	20 (16%)	
≥ 60	8 (8.5%)	3 (10.34%)	0	11 (8.8%)	
Total	94 (75.2%)	29 (23.2%)	2 (1.6%)	125 (100%)	

Table 3 shows there is no association between grades of fatty liver disease with the age group (chi-square $P>0.05$).

Table 3: Gender Vs Grade

Gender	Grade I	Grade II	Grade III	Total	P value (Chi Square)
Male	60 (48%)	20 (16%)	2 (1.6%)	82 (65.6%)	P=0.51 ($P>0.05$)
Female	34 (27.2%)	9 (7.2%)	0	43 (34.4%)	
Total	94 (75.2%)	29 (23.2%)	2 (1.6%)	125 (100%)	

Table 4 shows BMI and Grades of fatty liver disease were significantly associated (chi-square $P<0.05$). Furthermore, there is a significant difference between the grades as well (ANOVA $P<0.05$) (Table 6). On Post Hoc analysis, Grade I and Grade II were observed significantly different.

Table 4: Body Mass Index(BMI) Vs Grade

BMI	Grade I	Grade II	Grade III	Total	P value (Chi Square)
Normal	24 (19.2%)	4 (3.2%)	0	28 (22.4%)	P=0.001*
Overweight	61 (48.8%)	16 (12.8%)	0	77 (61.6%)	
Obese	9 (7.2%)	9 (7.2%)	2 (1.6%)	20 (16.0%)	
Total	94 (75.2%)	29 (23.2%)	2 (1.6%)	125 (100%)	

BMI=body mass index, * represents $P<0.05$

Table 5 shows TC has a significant association (Chi Square $P<0.05$) with different grades of FLD in a non-alcoholic patient while other components of the lipid profile are not significantly associated. Furthermore, There was a significant difference between the grades of TC as well (ANOVA $P<0.05$) (Table 6). Also, Table 5 shows SGPT and SGOT component of LFT is significantly related to the grades of NAFLD, Likewise is Diabetes mellitus and hypertension (Chi-square $P<0.05$)

Table 5: Lipid Profile, LFT, DM, HTN Vs Grade

Variable		Grade I		Grade II		Grade III		Overall		P value (Chi Square)
		Normal	Abnormal	Normal	Abnormal	Normal	Abnormal	Normal	Abnormal	
Lipid Profile	TC	74(59.2%)	20(16%)	19(15.2%)	10(8%)	0	2(1.6%)	93(74.4%)	32(25.6%)	P=0.01*
	TG	53(42.4%)	41(32.8%)	11(8.8%)	18(14.4%)	0	2(1.6%)	64(51.2%)	61(48.8%)	P=0.07
	LDL-C	35(28%)	59(47.2%)	11(8.8%)	18(14.4%)	0	2(1.6%)	46(36.8%)	79(63.2%)	P=0.5
	HDL-C	86(68.8%)	8(6.4%)	27(21.6%)	2(1.6%)	2(1.6%)	0	115(92%)	10(8%)	P=0.88
LFT	ALP	85(68%)	9(7.2%)	25(20%)	4(3.2%)	1(0.8%)	1(0.8%)	111(88.8%)	14(11.2%)	P=0.17
	SGPT	63(50.4%)	31(24.8%)	12(9.6%)	17(13.6%)	1(0.8%)	1(0.8%)	76(60.8%)	49(39.2%)	P=0.045*
	SGOT	69(55.2%)	25(20%)	13(10.4%)	16(12.8%)	1(0.8%)	1(0.8%)	83(66.4%)	42(33.6%)	P=0.015*
Chronic Disease	DM	84(67.2%)	10(8%)	21(16.8%)	8(6.4%)	1(0.8%)	1(0.8%)	106(84.8%)	19(15.2%)	P=0.03*
	HTN	80(64%)	14(11.2%)	16(12.8%)	13(10.4%)	2(1.6%)	0	98(78.4%)	27(21.6%)	P=0.002*

DM=diabetes mellitus, HTN= Hypertension, HDL-C=high-density lipoprotein-cholesterol, LDL-C=low-density lipoprotein cholesterol, NAFLD=nonalcoholic

fatty liver disease, SD=standard deviation, TC=total cholesterol, TG=triglyceride, ALP=Alkaline Phosphatase, SGPT= serum glutamic pyruvic transaminase,

SGOT= serum glutamic oxaloacetic transaminase, *= P < 0.05

Table 6: Variables and their mean value wherever applicable according to grade

Variables	Grade I (Mean ±SD)	Grade II (Mean ±SD)	Grade III (Mean ±SD)	P-Value (ANOVA)	Post Hoc (Tukey)
Age	41.89±12.82	46.2±10.18	45.5±7.77	0.25	
BMI	26.67±2.74	28.35±4.05	31.22±0.00	0.001*	Grade I vs Grade II (P= 0.03*) Grade II vs Grade III (P=0.1) Grade III vs Grade I (P= 0.41)
TC	165.75±39.45	183.44±51.01	229.5±41.71	0.02*	Grade I vs Grade II (P= 0.12) Grade II vs Grade III (P= 0.3) Grade III vs Grade I (P=0.09)
LDL-C	109.71±27.23	111.58±36.81	154±36.76	0.1179	

BMI=body mass index, LDL-C=low-density lipoprotein cholesterol, SD=standard deviation, TC=total cholesterol, ANOVA = Analysis of Variance

*= P < 0.05

DISCUSSIONS

NAFLD is rising in Nepal as the traditional lifestyle is being replaced by a more sedentary life style and fast, fatty, and spicy food eating habits. Moreover, south asians are more likely to have NAFLD as these ethnic groups have a low muscle mass, high percentage of visceral body fat, hyperinsulinemia, insulin resistance and abdominal obesity(20). In this study, we have tried to find out the possible relationship between NAFLD with anthropometric data, Lipid profile, Liver Function Test, BMI, DM and HTN.

NAFLD mainly affects middle-aged and elderly people. Older patients show more risk factors, more serious laboratory abnormalities, and

histological changes with cirrhosis.²¹ For older, it is a common and benign finding and moreover not associated with metabolic syndrome.²² Here, we found mostly affected cases in the age group 40-49 and 30-39. The least affected were the younger group 10-19 and 20-29 (Table 1,2). These findings are consistent with previous studies. However, our study showed the percentage of the older age group affected is lesser than the middle age group, but the literature says with advancing age chance of getting NAFLD is more likely.²³ This is probably defined by the limitation of this study. Most recruited cases in this study constitute middle-aged patients (n=80 for 30-49 age group) than the older group (n= 31 for 50 and more age group). Also, we found age groups

were not associated with grades of NAFLD which is different from the previous study.¹⁶

The prevalence and severity of NAFLD are higher in men than in women of childbearing age. However, postmenopausal NAFLD is more common in women, suggesting that estrogen is protective. Therefore, gender differences is also the main risk factors for NAFLD.²⁴ In our study, we found the male population contributed significant cases of NAFLD ($n=82$, 65.6% for males and $n=43$, 34.4% for females). Only a few cases in our study surpass the childbearing age contributing very less incidence for that age group. We also found a non-association of different grades of NAFLD with gender.

BMI is one of the most classic epidemiological indicators for evaluating obesity and is associated with fatty liver risk. Compared with normal BMI, the risk of an obese liver is about 4.1 to 14 times more with a higher BMI (25). Mostly, NAFLD patients in our study possessed BMI overweight (61.6%) followed by obese (16%) (Table 1). Mean BMI showed an increasing trend from Grade I to Grade III and BMI was associated with grades of NAFLD as well there was a significant difference in BMI between the Grades (Table 4,6). Our finding is consistent with the study made by Afshin et al,²⁶ who also found significant differences between the grades. Tang et. al in their study has said that NAFLD people are more likely to have higher BMI and are not affected by age and sex.²⁷

Lipid profiles include TC, TG, HDL-C and LDL-C. Cholesterol is an indispensable lipophilic molecule in human life. Cholesterol is an important component of cell membranes. It contributes to the structural composition of the membrane and its fluidity. Cholesterol is used in the synthesis of vitamin D, steroid hormones (such as cortisol and aldosterone and adrenal androgens) and sex hormones (such as testosterone, estrogen and progesterone). Cholesterol is also a component of bile salts which is required to digest fat-soluble vitamins A, D, E and K. Red meat, Sheep and cattle and dairy products are considered to be the main source of cholesterol. HDL-C is considered good cholesterol and LDL-C is termed as bad cholesterol.¹⁶⁻²⁸ Patients with NAFLD diagnosed by ultrasound in previous studies had mixed findings, some showed raised TC, TG, LDL and decrease HDL, and some showed NAFLD relation only with increased TC and decrease HDL.^{6,16,29} However, our findings in this study have showed graded NAFLD is significantly associated with TC only and not with other components.

NAFLD is the commonest cause of abnormal liver function tests (LFT). Basically, we have considered LFT, SGPT and SGOT components of LFT in this study. Moreover, a previous study has agreed with elevated LFT in NAFLD.³⁰ Mostly it is incidentally raised LFT. In our study, in grade-wise comparison, ALP was increasing from Grade I to Grade III and is consistent with previous studies but SGPT and SGOT were increasing from Grade I to Grade II but small decrement from Grade II to Grade III and this can be because serum level of Transaminases is neither sensitive nor specific enough to screen for NAFLD(1). Furthermore, very few cases occurred in grade III in our study which can build controversy and limitations to this study. Meanwhile, SGPT and SGOT components of LFT are significantly related to the graded NAFLD (Table 5).

The liver plays an important role in the pathophysiology of T2DM because this organ greatly promotes the development of insulin resistance and is a risk factor even in patients with normal serum ALT levels.³¹ DM can be the cause of NAFLD and in contrast, NAFLD patient has more chance of developing DM.³² Our study showed the occurrence of DM only in 15.2% (Table 1). There is an increased risk of NAFLD among patients with type 2 diabetes and the pathogenesis of NAFLD is not fully understood.³³ Moreover, most of the cases in our study belong to the young and middle age group but diabetes is the disease of aging although it can occur as early as late teenage. Furthermore, only 20% of old people have DM, and a similar proportion has undiagnosed DM.³⁴ Table 4 shows DM is associated with the graded NAFLD as well.

Hypertension patients have a higher prevalence of NAFLD. Studies have reported a strong relationship between NAFLD and hypertension.^{35,36} Our study showed the presence of hypertension only in 21.6% (Table 1). In general, NAFLD is prevalent in middle-aged and elderly people with abnormal blood lipids, abnormal liver function tests, and a high prevalence of type 2 diabetes.³⁷ So, it is not necessary for NAFLD patients to have HTN as other comorbid factors can be the cause for HTN however HTN can be associated with NAFLD and our study has shown the association of HTN with graded NAFLD.

We have tried to make this study as robust as it can be however, we cannot deny that it still contains several limitations. First, Ultrasonography is observer-dependent and cannot quantify the fat in the liver like CT or MRI does. Second, our study contained a smaller number of patients with Grade III fatty liver as this grade is very

uncommon to rest two. Third, the population included was only from the single hospital in a city in the country.

CONCLUSIONS

NAFLD is a common disorder in Nepal. Nepal police personnel are expected to be more fit and healthy because of their daily physical activities, however, we found a good number (125 cases) in the span of four months of study. The prevalence of overweight police personnel was the most likely contributing factor to more NAFLD. Furthermore, the prevalence was found more in the middle age group and the male gender. Graded NAFLD was found to be significantly associated with Body Mass Index, Total Cholesterol, SGPT (serum glutamic-pyruvic transaminase) and SGOT (serum glutamic-oxaloacetic transaminase) and Chronic diseases (Diabetes mellitus and hypertension).

ACKNOWLEDGMENT

The authors acknowledge the pathology department of Nepal Police Hospital for providing needed laboratory investigation to the patients included in the study.

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