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Original Research Paper

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PREVALENCE OF NON ALCOHOLIC STEATO HEPATITIS IN PATIENTS WITH ISCHAEMIC HEART DISEASE AND HYPERTENSION

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ABSTRACT Non alcoholic steatohepatitis (NASH) which lies in the spectrum of the broader entity Non alcoholic fatty liver disease (NAFLD) is emerging as a common cause of chronic liver disease.All the patients with NASH have elevated liver enzymes (almost two to three times the normal upper limit) and all of them have sonological abnormality (hepatomegaly and /or fatty infiltration). Aim of this study was to measure prevalence of Non Alcoholic Steatohepatitis (NASH) in patients of ischaemic heart disease and hypertension. So, study was conducted in General Medicine Dept until sample size of 75 was reached. All necessary laboratory investigations and clinical parameters were checked. Prevalence of NASH in total study population with history of IHD and or HYPERTENSION is 12%.Conclusion we can say that, prevalence of NON ALCOHOLIC STEATO HEPATITIS (NASH), in patients with ischaemic heart disease and hypertension is low, but there is strong association of metabolic syndrome, with patients having NASH.

KEYWORDS : NASH, non alcoholic steato hepatitis, Hepatitis, Ischaemic heart disease ,hypertension

INTRODUCTION

Non Alcoholic Steatohepatitis (NASH) is a type of chronic hepatitis having histologic features of alcohol induced liver disease that occurs in individuals who do not consume significant amounts of alcohol. Hepatic steatosis "describes the accumulation of fat, mostly as triglyceride, cholesterol and phospholipids, in excess of 5 – 10% of liver weight. For many years, the discovery of fatty liver during a routine evaluation was not thought to have clinical significance. However, it was known that obese and diabetic patients could develop histological steatohepatitis similar to that seen with alcohol - induced liver disease. A number of retrospective studies have suggested that this is an uncommon disorder that occurs most often in middle-aged, obese women.[1-3]Like patients with other types of chronic Liver Disease, most patients with NASH are asymptomatic. Hence NASH is often diagnosed after abnormalities are noted during routine laboratory testing. Usually Fatigue, malaise, and vague right upper quadrant abdominal discomfort bring some patients with NASH to medical attention. Nonalcoholic steatohepatitis (NASH) is included in a broader entity called Non Alcoholic Fatty Liver disease (NAFLD) which has a spectrum ranging from fatty liver alone to steato-necrosis, which tends to be stable over time, to steatohepatitis, which may progress to cirrhosis.[4,5,6] Most common risk factors associated with NAFLD or NASH include obesity, type II Diabetes Mellitus, hyperlipidemia, jejuno ilial bypass and medications. In India, the prevalence of NASH in the general population has not been defined. Among patients who have had liver biopsy, the prevalence is approximately 7% to 9% in Western countries, and 1.2% in Japan. Data from patients who have had liver biopsies show that alcoholic hepatitis is 10-15 times more common than NASH. Although NASH has been reported in persons in the second decade of life.[7,8] Most cases occurs in persons in the fifth and sixth decades of life.[4,5,9,10,11] Cases occur more frequently in women (65% to 83%) [4,5,10,12], although Bacon and colleagues[11] recently found a high prevalence of NASH in men. The prevalence of the disease is expected to increase worldwide, as we are encountering the global obesity epidemic and the trend in developing countries toward the western lifestyles .There is no clear cut data of clinical and histopathological profile of NASH in the Indian population except few scattered studies done by researchers like by SK Sarin et al in New Delhi [13].

So, Aim of this was to measure prevalence of Non Alcoholic Steatohepatitis (NASH) in patients of ischaemic heart disease and hypertension and to check clinical and biochemical profile of the patients with NASH.

MATERIALS AND METHODS

This Study was conducted in Department of General Medicine, Medical College and Hospital, Kolkata during time period of January 2018 to July 2019.Patients above the age of 18 who were suffering from IHD and/ or hypertension were selected. Inclusion criteria for patients were patients having BP >130/85 mm of Hg, hypertensive patients on any hypertensive drugs, d iagnosed ischaemic heart disease patient by ECG/ECHO, non-alcoholic (alcohol consumption of less than 20 g per day in the case of women and 30 g per day in case of men).

Exclusion criteria:

a. Hepatitis B/C positive patient
b. Previously diagnosed Wilsons disease
c. ICTC positive patients
d. Creatinine clearance <50 umol/1
e. Those who will refuse to give consent / acute illness /pregnant women were excluded. Samples were not collected after immediate surgery and / or exercise

Sample size was determined considering 95% confidence interval and 5% error than considering prevalence of NASH in INDIA as (p) 5%, our target sample size (n) came out to be 75. All the patients reporting to hospital based on inclusion criteria were taken until the sample size of 75 was obtained hence, this study is cross sectional study.

Following Laboratory investigation, Parameters and procedures were done for each participants

a. Clinical examinations
b. BP measurements
c. waist circumference measurements

d. blood for: FBS/PPBS/HBALC/LFT/lipid profile/UR;CR
e. ECG, 2D echocardiography

The history taking, clinical examination and biochemical investigations of cases in the present study were done according to the proforma given below.
A thorough history was taken with special emphasis to exclude history of significant alcohol intake which was defined as intake less than 20 gm per day (in females) and less than 40 gm /day (in males).

Systemic data collection were carried out by review of all medical records

Diabetes Mellitus was defined as presence of any of the following [14]
i) FBS 126 mg/dl.
ii) RBS 200mg/dl or higher.

Dyslipidemia and Insulin Resistance was defined according to ATP III guidelines [15]

Dyslipidemia was defined as presence of one of the following :
LDLc > 160 mg/dl.
Total Cholesterol > 200mg/dl.
Triglyceride > 150 mg/dl.
HDLc < 40 mg/dl.

Insulin resistance syndrome (IRS) was defined as presence of more than 3 of the following criteria.
1. Abdominal obesity, defined as a waist circumference > 102 cm (40in)in men and >88 cm (35in) in women.
2. Tryglyceride> 150 mg/dl.
3. HDL cholesterol< 40 mg/dl in men and < 50 mg/dl in women.
4. BP > 130 /> 85 mm Hg.
5. FBS > 110 mg/dl.

Statistical Analysis:
For statistical analysis data were entered into a Microsoft excel spreadsheet and then analysed by SPSS (version 25.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples.

RESULT :

Variable	NASH		
	ABSENT No.(%) n=66	PRESENT No.(%) n=9	TOTAL No(%) n=75
Age			
31-40years	16(24.2)	3(33.3)	19(25.3)
41-50years	21(31.8)	3(33.3)	24 (32.0)
Sex			
Male	38 (57.6)	3(33.3)	41(54.7)
Female	28(42.4)	6(66.6)	34(45.3)

Table no.1 : Distribution of mean Age, Sex : NASH

Prevalence of NASH in our study population is 9(12%). patients having NASH are mostly from 3rd,4th and 5th decades of life. Among patients with NASH ,3(33.3%) patients had 31-40 years of age, 3(33.3%) patients had 41-50 years of age, 1(11.1%) patients had 61-70 years of age and 2(22.2%) patients had 71-80 years of age. so, maximum patients(66.6%) are within the age group between (31-50) years. p-value is 0.1558.Among patients with NASH , 6(66.7%) patients was female and 3(33.3%) patients was male. In patients without NASH, 28(42.4%) patients was female and 38(57.6%) patients was male. Association of sex vs. NASH was not statistically significant (p=0.3107866874). (Table.1)

Parameters	NASH					
		Number	Mean	SD	Median	P-Value
SBP	Absent	66	140.03	15.9	28.60	<0.0001
	Present	9	143.1	11.6	33.20	
DBP	Absent	66	87.6	9.4	90.0	0.83
	Present	9	88.2	6.6	90.0	
FBS	Absent	66	124.0	30.9	122.0	0.02
	Present	9	149.9	30.4	142.0	
PPBS	Absent	66	153.1	47.1	140. 0	0.03
	Present	9	190.6	56.1	182.0	
Lipid profile (TG)	Absent	66	135.6	36.7	141.5	0.01
	Present	9	170.0	41.9	160	
TC	Absent	66	168.5	46.6	182.0	0.2
	Present	9	188.7	42.6	212.0	
HDL	Absent	66	45.7	11.4	42.0	0.04
	Present	9	37.6	6.6	38.0	
LDL	Absent	66	98.4	22.2	102.0	0.001
	Present	9	126.1	26.6	122.0	
Liver function test AST	Absent	66	38.9	5.5	38.0	<0.0001
	Present	9	103.5	24.5	110.0	
ALT	Absent	66	30.1	5.5	29	<0.0001
	Present	9	145.4	29.9	155	
ALT/AST	Absent	66	0.77	0.10	0.78	<0.0001
	Present	9	1.4	0.2	1.4	

Table no.2: Association of lab parameters with NASH

In NASH patient, the mean SBP (mean± s.d.) of patients was 143.1111 ± 11.5806 mmHg.

In patients without NASH, the mean SBP (mean± s.d.) of patients was 140.0303 ± 15.8172 mmHg. Distribution of mean SBP vs. NASH was not statistically significant (p=0.5754). In NASH patient, the mean DBP (mean± s.d.) of patients was 88.2222 ± 6.6667 mmHg Distribution of mean DBP vs. NASH was not statistically significant (p=0.8393). (Table.2)

In our study we found that patients with NASH, having deranged blood sugar level, as NASH is closely related to insulin resistance syndrome. In NASH patients, the mean FBS (mean± s. d.) of patients was 149.8889 ± 30.4197 In patients without NASH, the mean FBS (mean± s .d.) of patients was 124.0909 ± 30.8678.In NASH patients, the mean PPBS (mean± s .d.) of patients was 190.6667 ± 56.1716, In patients without NASH, the mean PPBS (mean± s .d.) of patients was 153.1970 ± 47.1793. Distribution of mean PPBS vs. NASH was statistically significant (p=0.032). (Table.2)

In this study we found that patients with NASH have deranged lipid profile, the mean TG(169.7778 ± 41.9100) in patients with NASH was significantly higher than non NASH group (135.6061± 36.7741),and difference of mean TG vs. NASH was statistically significant (p=0.0121). the mean TC (188.7778 ± 42.6256) OF NASH group is higher than non NASH group(168.5455± 46.6378) . In patients without NASH, the mean HDL (45.7879 ±11.4764) was significantly higher than NASH group (37.6667 ±6.6708) and difference of mean HDL vs. NASH was statistically significant (p=0.0422). In NASH group the mean LDL(126.1111± 26.6760) was significantly higher than non NASH group (98.4091±22.2766)and difference of mean LDL vs. NASH was statistically significant (p=0.0010). patients with NASH having high AST and ALT value.,it is two to four times higher than their upper normal limit and in NASH patients ALT/AST ratio is more than 1. the mean AST (103.5556± 24.5770) was significantly higher than non NASH group(38.9091± 5.5712)and difference of mean

AST vs. NASH was statistically significant (p<0.0001). In NASH, the mean ALT(145.4444± 29.9003) was significantly higher than non NASH group(30.1061± 5.5640) and difference of mean ALT vs. NASH was statistically significant (p<0.0001). (Table.2)

Co-morbidity	NASH	TOTAL	P Value	
	ABSENT n=66 No.(%)	PRESENT n=9 No.(%)	n=75 No(%)	0.3
Hypertension				
Yes	54 (81.8)	9(100)	63(84)	
No	12(18.8)	0(0)	12(16)	
H/o Ischemic Heart Disease				
Yes	25 (37.9)	4 (44.4)	29(38.7)	0.1
No	41 (62.1)	5 (55.6)	46 (61.3)	
Fatty Liver				
Grade =1	20 (30.3)	5(55.6)	25(33.3)	<0.0001
Grade =2	1(1.5)	4 (44.4)	5 (6.7)	
Normal	45 (68.2)	0(0)	45 (60)	

Table.3 - Association of co-morbidities with NASH

Among patients with h/o hypertension, 9(100%) have NASH and there are no patient of NASH found in non-hypertensive group. In patients without NASH, 54(81.8%) patients had H/O HTN and in patient with NASH, 9(100.0%) patients had H/O HTN. Association of H/O HTN vs. NASH was not statistically significant (p=0.3622438945). H/o HTN or both among patients having h/o IHD, 4(13.8%) having NASH, and patients without h/o IHD,5(10.9%) having NASH. In patients without NASH, 25(37.9%) patients had H/O IHD in NASH, patients 4(44.4%) patients had H/O IHD. Association of H/O IHD vs. NASH was not statistically significant (p=0.9883567320.)We have studied 75 patients with h/o IHD and HTN or both Among 75 patients 30(40%) have fatty liver, among which 25(83.3%) patients have grade 1 and 5 (16.66%) patients have grade 2 fatty liver. In patients without NASH, 20(30.3%) patients had fatty liver grade 1, 1(1.5%) patient had fatty liver grade 2 and 45(68.2%) patients had normal liver. Among NASH patient, 5(55.6%) patients had fatty liver grade 1 and 4(44.4%) patients had fatty liver grade 2. (Table 3.)

Marker	NASH			
	ABSENT n=66 No (%)	Present n=9	Total n=75 No(%)	P value
ECG				
Abnormal	43 (65.2)	8 (88.9)	51 (68)	0.3
Normal	23(34.8)	1(11.1)	24(32)	
ECHO				
Abnormal	45 (68.2)	9(100)	54(72)	0.10
Normal	21 (31.8)	0(0)	21(28)	
LVDD				
Abnormal	30 (45.5)	7(77.8)	37(49.3)	0.14
Normal	36(54.5)	2(22.2)	38(50.7)	
RWMA				
NEGATIVE	46 (69.7)	7(77.8)	53(70.5)	0.9
POSITIVE	20(30.3)	2 (22.2)	22(29.3)	

Table.4 - Association of cardiovascular markers with NASH

ECG abnormalities are good predictor of cardiovascular involvement of NASH patients, we found 88.9% abnormal ECG in NASH patients. In patients without having NASH, 23(34.8%) patients had normal ECG. In NASH patients, 1(11.1%) patients had normal ECG. So, majority of NASH patients (88.9%) have abnormal ECG. In our study we found significant echo changes in NASH patients. In NASH patients 9(100.0%) patients had abnormal ECHO. In patients without NASH, 21(31.8%) patients had normal ECHO. p-value: 0.143. In NASH patients 2(22.2%) patients had normal LVDD. In patients without NASH, 36(54.5%) patients had normal LVDD and Association of LVDD group vs. NASH was not statistically significant (p=0.1431653341). In patients without NASH, 20(30.3%) patients had RWMA positive. In NASH patients, 2(22.2%) patients had RWMA positive. Association of RWMA group vs. NASH was not statistically significant (p=0.912). (Table 4.)

DISCUSSION:

Non-alcoholic steatohepatitis (NASH) which lies in the spectrum of the broader entity Non-alcoholic fatty liver disease (NAFLD) is emerging as common cause of chronic liver disease which in our study had prevalence of 12% approximately. Although there are only few studies regarding the prevalence of NASH in India, some studies have shown that the prevalence of NASH in the general population is 3% where as that of NAFLD is up to 30%.In a recent study done in Japan the prevalence of NAFLD was found to be 14%.[16] The patients in our study were mostly in their 3 rd., 4th and 5th decade of life and mean age of patients in our study was 51.11 ± 15.81 years. According to studies done by Ludwig J et al, [1] Nonomura et al, [9] Lee Rg et al, [17] most of the patient with NASH are in their 5th and 6th decade., although it has been reported in persons in the 2nd decade of life by Bacon and colleagues[11]. In our study, among NASH patients, the FBS, PPBS was statistically significant (p=0.0321). DM(Type II) and elevated Blood glucose levels are noted in 34%-75% of patients with NASH in studies done by Ludwig J et al,[1] Powell EE et al, [12] Lee RG,[17] Diel M et al [18]and Itoh S et al [10]. In our study, patients with NASH has mean TG, HDL, LDL, levels were significantly higher than patients without NASH group and difference of mean of these factors vs. NASH was statistically significant. Ludwig et al,[5]Powell et al,[12]Lee RG et al,[17] Itoh S et al,[10] in their studies have showed that dyslipidaemia is a common abnormality and has been reported in 2%-81% of patients with NASH. In our study patient present with NASH the mean AST,ALT was significantly higher than non-NASH group and difference of mean AST,ALT vs. NASH was statistically significant (p<0.0001).Also the ratio of the mean ALT/AST was significantly higher than non-NASH group and difference of mean ALT/AST vs. NASH was statistically significant (p<0.0001). In our patients with NASH, the AST and ALT levels are 2 to 3 times the upper limit of normal (ULN). Adler et al (1979)[19], Ludwig et al (1980)(n=20).[1] Itoh et al(1987)(n=16),[10]Diehl et al (1988)(n=39)[18]have shown almost similar reflections in the AST and ALT values and their ratio of AST to ALT was less than 1. In our study, prevalence of non-alcoholic fatty liver (NAFLD) is 30(40%) among total study population, among which 25(83.3%) have grade 1 fatty liver and 5 (16.66) have grade 2 fatty liver. So, prevalence of NASH in NAFLD patients is (30%). Association of fatty liver group vs. NASH was statistically significant (p<0.0001). Ahmed MH et al [20] found that non alcoholic fatty liver disease (NAFLD) is prevalent in people with the metabolic syndrome and type 2 diabetes and is present in up to one-third of the general population. Evidence is now accumulating that NAFLD is associated with obesity and diabetes and may serve as a predictor of cardiovascular disease (CVD). Yajima et al[21] indicated that combination of liver-kidney contrast with vascular blurring and deep attenuation can be used for semi-quantitative assessment of liver steatosis, When fatty change is over 30% in the hepatic lobule, using both liver-kidney contrast and vascular blurring will provide sensitivity of 83%, specificity of 100%, and an accuracy of 96% for diagnosis of fatty liver disease. Similarly some other authors suggested that ultrasound can be used with good results for diagnosis of hepatic steatosis. Though association of H/O HTN vs. NASH was not statistically significant (p=0.3622). But in our study, all NASH patients are found to had h/o hypertension. In patients without NASH, the mean SBP (mean± s.d.) of patients was 140.0303 ± 15.8172 mmHg .In NASH patient, the mean SBP (mean± s.d.) of patients was 143.1111 ± 11.5806 mmHg. In patients without having NASH, 23(34.8%) patients had normal ECG. In NASH patients, 1(11.1%) patients had normal ECG.

So, majority of NASH patients (88.9%) have abnormal ecg among abnormal ECGs, following are present , LVH(33.3%), STT changes(44.4%) ,POOR WAVEPROGRESSION with STT changes(11.1%) In patients without NASH, 21(31.8%) patients had normal ECHO. In NASH patients 9(100.0%) patients had abnormal ECHO. Association of RWMA, LVDD group vs. NASH was not statistically significant (p=0.9129931338). Oikonomou D et al[22] found that non alcoholic fatty liver disease (NAFLD) and hypertension (HT) independent of other components of metabolic syndrome. They searched the literature through Medline and the Cochrane Library for studies evaluating the relationship between hypertension and fatty liver disease. Studies testing this association are limited, but agree that HT and fatty liver disease are inter-related independent of other components of the metabolic syndrome such as obesity and diabetes mellitus. Clinical evidence shows that NAFLD is associated with new-onset HT, whereas increased blood pressure is related to the development of fatty liver disease and the possible subsequent progression to liver fibrosis. Insulin resistance and activation of the renin–angiotensin–aldosterone system (RAAS) might provide potential pathophysiologic links between these clinical entities. Assyn et al stated[23] that development of coronary artery atherosclerosis in patients with NAFLD/NASH is independent of traditional risk factors for CAD, though concomitant presence of these risk factors and metabolic syndrome components potentiates pathogenesis of NAFLD/NASH. There are also evidences indicating that NAFLD/NASH can cause endothelial dysfunction, elevate biomarkers of inflammation and result in subclinical atherosclerosis in carotid artery.

CONCLUSION:

Earlier day's fatty liver was considered insignificant finding, But, now a days we understand the association of metabolic syndrome with NAFLD/NASH, and its relationship with IHD and HTN. Though there is low prevalence of NASH in patients with ischaemic heart disease and hypertension ,but, prevalence of NAFLD among hypertensive and/or IHD patients is high, and as NASH and NAFLD both fall in same spectrum of disease group, thus, if we do early screening of all patients of IHD and HYPERTENSION for fatty liver, and start appropriate treatment (dietary changes ,life style modification ,pharmacological therapies) we can prevent occurrence of NASH and can prevent progression to cirrhosis, or hepatocellular carcinoma and can prevent this disease related morbidity and mortality.

So, as a conclusion we can say that, prevalence of NON ALCOHOLIC STEATO HEPATITIS (NASH), in patients with ischaemic heart disease and hypertension is low, but there is strong association of metabolic syndrome, with patients having NASH .

REFERENCES:

1. Ludwig J, Viggiano RT. Mc Gill DB,et al Non alcoholic steatohepatitis. Mayo clinic experiences with a hitherto unnamed disease. Mayo clinic Proc 1980; 55: 342-348.
2. Torsis JD, Barwick KW, Miller JD et al. Non alcoholic Laennec's. clinical characteristics and long term follow up. Hepatology :1985; 237-241.
3. Wanless IR, Lentz JS. Fatty liver hepatitis (steolohepatitis) and obesity. An autopsy study with analysis of risk factors. Hepatology 1990; 12 :1106-1110.
4. Diehl AM. Non alcoholic steatohepatitis. Seminar in liver disease 1999; 19: 221-228.
5. Schaffner F, Thaher H. Non alcoholic fatty liver disease. Prog liver disease 1986; 8: 283-298.
6. Younossi ZM, Gramlich T, LinYC, Matteoni C. Petrelli M, Gold Blum J, Rybicki L, Mc Cullough AJ, . Non alcoholic liver disease assessment of variability in pathologic interpretations. Med Pathol: 1989; 11: 560-565.
7. Baldridge AD, Perez- Atayde AR, Graeme-Cook, F Higgin L, Lavine JE, Idiopathic steatohepatitis in childhood: a multicentric retrospective study. J Pediatrics: 1995; 127: 700-4.
8. Moran JR, Grisham FK, Halter SA, Greave HL Steatohepatitis in children a cause of chronic liver dysfunction: AMJ Gastroenterial 1983; 78: 374-7.
9. Nonomura A, Mizukami Y, Unoura M, Kobayashi K, Takeda Y Takeda R. Clinico pathologic study of alcoholic liver disease in nonalcoholics:nonalcoholic steato hepatitis and fibrosis. Gastroenterol Jpn: 1992; 27: 521-5.
10. Itoh S, Yougel T, Kawagae K, Comparison between non alcoholic steatohepatitis and alcoholic hepatitis. AMJ Gasteroenterol 1987; 82: 650-4.
11. Bacon BR, Farahvash MJ, Janey CG, Neurchwonder Tetai BA, Non alcoholic Hepatitis, An expanded clinical entity. Gastroenterology 1994; 107: 1103-9.
12. Powell EE, Cooksky WG, Hanson R, Searle J, Halliday JW, Powell LW. The natural history of nonalcoholic steatohepatitis: a follow-up study of forty-two patients for up to 21 years. Hepatology. 1990;11:74-80.
13. Agarwal SR, Malhotra V, Sakhuja P, Sarin SK.:Clinical,biochemical and histologicalprofile of nonalcoholic steatohepatitis. Indian J Gastroenterol. 2001 Sep-Oct;20(5):183-6.
14. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 1997;20:1183-97.
15. National Cholesterol Education Program: Executive summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001; 285: 2486-97.
16. Nomura H, Kashiwagi S, Hayashi J et al: Prevalence of fatty liver in a general population of Okinawa, Japan: Jpn J Med: 1988; 27: 142.
17. Lee RG. Non Alcoholic steatohepatitis. A study of 49 patients. Hum Pathol 1989; 20: 594-599.
18. Diel AM. Goodman Z, Ishak KG. Alcohol- like liver disease in nonalcoholics. A clinical and histopathological comparison with alcohol- induced liver injury. Gastroenterology 1989; 95: 1056-1060.
19. Adler m, schaffner f, fatty liver hepatitis and cirrhosis in obese patients. am j med 1979; 67: 811-816.
20. Ahmed MH, Barakat S, Almobarak AO. Nonalcoholic fatty liver disease and cardiovascular disease: has the time come for cardiologists to be hepatologists?. Journal of obesity. 2012 Dec 23;2012
21. Yajima Y, Ohta K, Narui T, Abe R, Suzuki H, Ohtsuki Ultrasonographical diagnosis of fattyliver: significance of the liver-kidney contrast. Tohoku J Exp Med. 1983;139(1):43–50
22. Oikonomou D, Georgiopoulos G, Katsi V, Kourek C, Tsioufis C, Alexopoulou A, Koutli E, Tousoulis D. Non-alcoholic fatty liver disease and hypertension: coprevalent or correlated?. European journal of gastroenterology & hepatology. 2018 Sep 1;30(9):979-85
23. Assy N, Djibre A, Farah R, Grosovski M, Marmor A. Presence of coronary plaques in patients withnonalcoholic fatty liver disease. Radiology. 2010;254(2):393–400.