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Alcoholic Liver Disease and Non-Alcoholic Steatohepatitis: A Comparative Study

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Abstract: ***ALD and NASH are significant forms of liver disease and may progress to end-stage liver disease, cirrhosis, and its attendant physiologic, metabolic, and potentially malignant complications.The most difficult aspect of establishing a diagnosis of NASH is distinguishing it from ALD.A detailed history of alcohol should be obtained from patient, family members and the primary care provider.Our study is to assess the utility of clinical and biochemical parameters to differentiate ALD from NASH.***

Keywords: ALD, NASH, comparative study

1. Introduction

Alcoholic liver disease occurs due to excessive alcohol consumption with alcohol acting as a direct hepatotoxin. Globally 5 million people die per year due to alcohol related problems.[1] Seventy percent of deaths are due to liver related disease. Half of all cirrhosis in the world are alcohol induced and about 10–20 % of all alcoholics are cirrhotic. In 1980, Ludwig et al[2] described an alcoholic hepatitis-like pattern of injury in the liver of non-alcoholic patients. They introduced the term 'non-alcoholic steatohepatitis' (NASH) to describe this disease entity.

Non-alcoholic fatty liver disease (NAFLD), is now considered to be the commonest liver problem in the western world affecting 15-40% of the general population.[3] Non-alcoholic fatty liver disease is increasingly being recognised as a major cause of liver-related morbidity and mortality.[4,5] Because of its potential to progress to cirrhosis and liver failure, interest in this disease is increasing among researchers and clinicians in the relevant basic and clinical science fields. The pathologic picture of non-alcoholic fatty liver disease, ranging from simple steatosis to steatohepatitis, advanced fibrosis, and cirrhosis, resembles that of alcohol induced liver disease. . The third report of the national cholesterol education programme expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III [ATP III]) recommended the use of 5 variables for diagnosing the metabolic syndrome, namely waist circumference, serum triglyceride level, serum high-density lipoprotein (HDL) cholesterol level, blood pressure and fasting plasma glucose level.[6]

Both ALD and NASH are significant forms of liver disease and may progress to end-stage liver disease, cirrhosis, and its attendant physiologic, metabolic, and potentially malignant complications. Hepatocellular carcinoma is a recognized complication of both entities. Both diseases may necessitate liver transplantation, and have been reported to recur in the allograft Livers. The most difficult aspect of establishing a diagnosis of NASH is distinguishing it from ALD. In alcoholic hepatitis AST/ALT ratio may be >1[7,8].AST/ALT ratio is typically <1 in other causes of fatty liver[9,10,11]. When AST/ALT ratio is >1.5, it is considered as highly suggestive that alcohol is the cause of liver injury[12]. Patients with alcoholic hepatitis often demonstrate an AST to ALT ratio of >2 with absolute aminotransferase levels of >300 IU/l.Slight to moderate increases in ALP occur in many patients with liver disorders such as hepatitis and cirrhosis [13,14].Striking increase in ALP (10 times) occur more consistently with extra hepatic biliary tract obstruction or with intra hepatic cholestasis. Measurement of gamma glutamyltransferase (GGT)activity in serum has been found useful in screening alcohol abuse.

Our study is to assess the utility of clinical and biochemical parameters to differentiate ALD from NASH.

2. Study

The present study was conducted in a tertiary care hospital.This is a two year cross-sectional Comparative study between Alcoholic Liver Disease and Non-alcoholic Steatohepatitis patients.

Patients admitted in medicine ward of tertiary care hospital who satisfy the inclusion criteria were enrolled in the study.Total 100 patients were included in the study. (50 for each group).

Inclusion criteria:

1) Those who gave consent for the study.
2) For NASH group: Non-alcoholics or those who consume <20gm/day, elevated serum transaminases, presence of fatty liver or hepatomegaly on USG.
3) For ALD group: All the alcoholics will be included who consume > 20gm-40gm/day for last 5 years , elevated serum transaminases, with or without clinical evidence of alcoholic liver disease.

Exclusion criteria:

1) Those who will not give consent.
2) Concurrent viral infection,
3) Concurrent medications such as high dose estrogenic, corticosteroids and amiodarone, anti TB drugs , ART drugs etc.

Total 100 patient presenting with elevated liver enzymes were divided in two groups. In this study we saw the clinical and biochemical differences between alcoholic liver disease and non-alcoholic steato-hepatitis. We diagnosed patients on the basis of history and clinical and biochemical and ultra-sonographic approach.USG has sensitivity of 89% and specificity of 93%in detecting steatosis.

Liver biopsy is preferred method for establishing diagnosis of NASH. However, due to high prevalence of NAFLD in the general population and the associated low but real complication rate of this procedure, it appears to us to be unreasonable to refer every patient for liver biopsy. We followed the World Gastroenterology Organisation guidelines provided resource sensitive approach[15]. First group consisting of alcoholic patient and second group consisting of non-alcoholic. Both groups compared on the basis of clinical findings and biochemical findings.

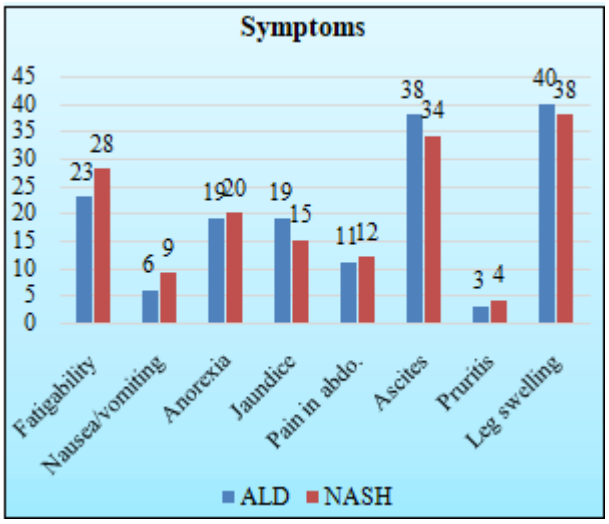

Chart No.3: Symptom wise Distribution

3. Results

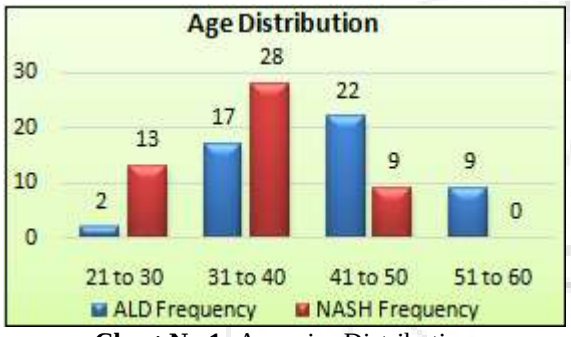

Chart No.1: Age wise Distribution

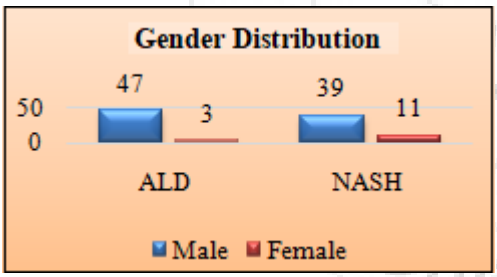

Chart No.2: Gender wise Distribution

Table 1: Symptom wise Distribution

Sr. No.	Symptoms	ALD Frequency (%)	NASH Frequency (%)	P value
1	Fatigability	23 (46)	28 (56)	>0.05
2	Nausea/vomiting	06 (12)	09 (18)	
3	Anorexia	19 (38)	20 (40)	
4	Jaundice	19 (38)	15 (30)	
5	Pain in abdo.	11 (22)	12 (24)	
6	Ascites	38 (76)	34 (68)	
7	Pruritis	03 (6)	04 (8)	
8	Leg swelling	40 (80)	38 (76)	

Table 2: Body Mass Index Wise Distribution

Sr. No.	BMI	ALD Frequency (%)	NASH Frequency (%)	Total (%)
1	Underweight	00 (00)	00 (00)	00 (00)
2	Normal	49 (98)	22 (44)	71 (71)
3	Pre-obese	01 (02)	28 (56)	29 (29)
4	Obese	00 (00)	00 (00)	00 (00)
	Total	50 (100)	50 (100)	100 (100)

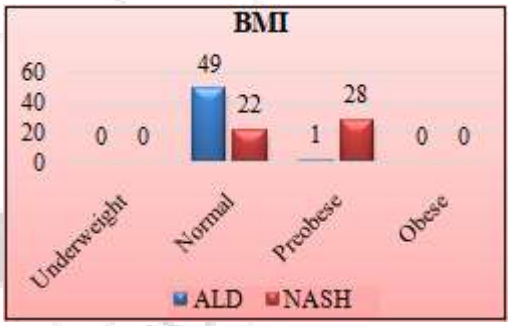

Chart No.4: Body Mass Index Wise Distribution

Table 3: Occupation wise Distribution

Sr. No.	Occupation	ALD (%)	NASH (%)	Total
1	Professional	01 (02)	08 (16)	09 (09)
2	Semi-Professional	02 (04)	20 (40)	22 (22)
3	Clerical, Shop Owner, Farmer	10 (20)	15 (30)	25 (25)
4	Skilled Worker	05 (10)	02 (04)	07 (07)
5	Semi-Skilled Worker	05 (10)	02 (04)	07 (07)
6	Unskilled Worker	25 (50)	02 (04)	27 (27)
7	Unemployed	02 (04)	01 (02)	03 (03)
	Total	50 (100)	50 (100)	100 (100)

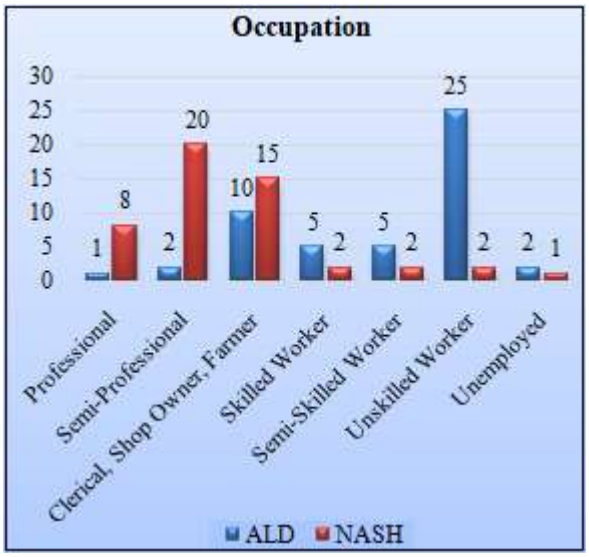

Chart No.5: Occupation wise Distribution

Table 4: Socio-economic Status wise Distribution (B G Prasad Classification)

Sr. No.	Socio Economic Status	ALD (%)	NASH (%)	Total
1	High	02 (04)	25 (50)	27
2	Upper Middle	08 (16)	12 (24)	20
3	Lower Middle	12 (24)	08 (16)	20
4	Poor	28 (56)	05 (10)	33
	Total	50 (100)	50 (100)	100 (100)

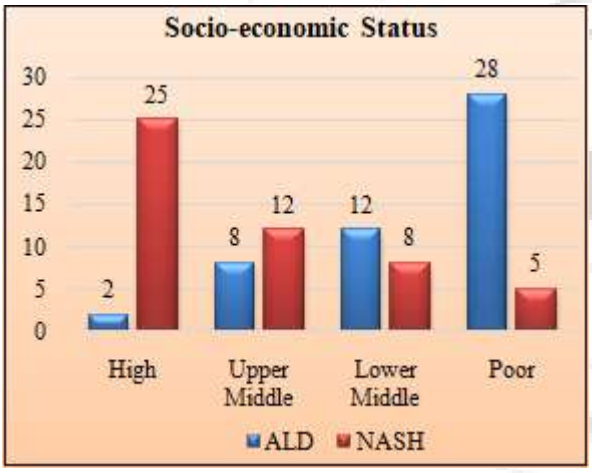

Chart 6: Socio-economic Status wise Distribution (B G Prasad Classification)

Table 5: Comparison of Clinical Parameters

Sr. No.	Clinical Parameters	ALD (Mean±SD)	NASH (Mean±SD)	P value
1	Age	43.10±7.28	34.56±4.84	0.001
2	Sex (F:M)	0.06	0.28	0.01
3	BMI	23.25±0.85	25.03±1.91	0.01

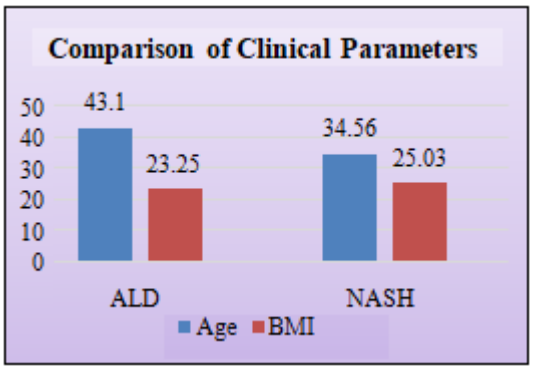

Chart No.7: Comparison of Clinical Parameters

Table 6: Comparison of Biochemical Parameters

Sr. No.	Biochemical Parameters	ALD (Mean±SD)	NASH (Mean±SD)	P value
1	AST	91.48±16.27	71.93±25.1	0.06
2	ALT	82.51±24.29	99.15±29.15	0.01
3	AST/ALT	1.28±0.77	0.802±.301	0.02
4	SAP	109.70±25.60	205.97±47.43	0.001
5	Bilirubin	8.37±2.24	1.49±0.46	0.02.

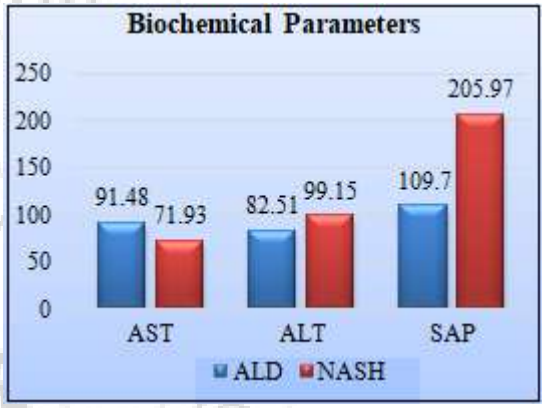

Chart No.8A: Comparison of Biochemical Parameters

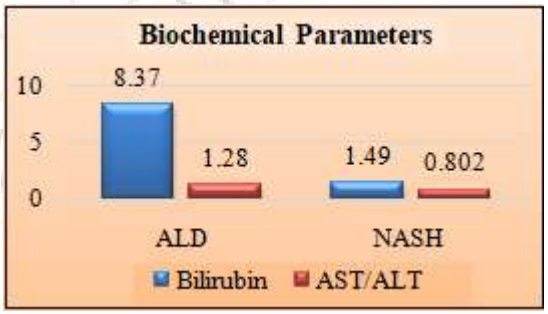

Chart No.8B: Comparison of Biochemical Parameters

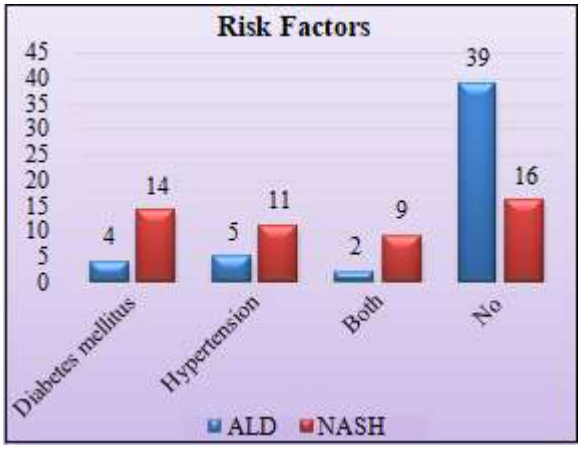

Chart No.9: Comparison of Risk Factors

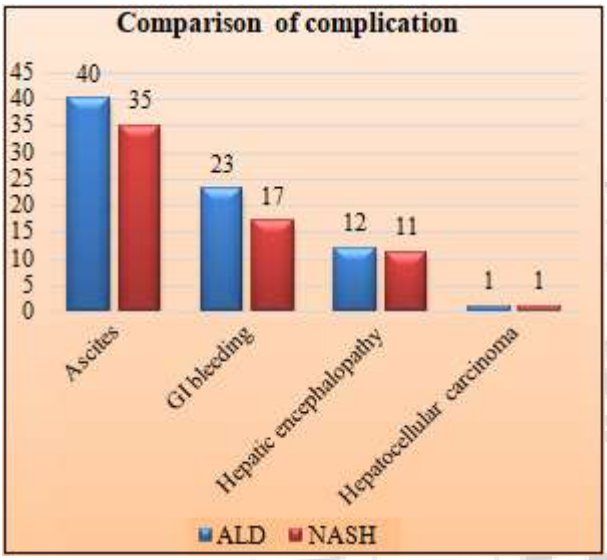

Chart 10: Comparison of complication

4. Discussion

Alcoholic liver disease is liver injury attributed to alcohol abuse. Research suggests, however, that liver disease may begin to develop after a "threshold" dose of alcohol has been consumed—generally assumed to be four drinks a day (four 12 ounces beers, four glasses of wine, or four ounces of hard liquor) for men, and one half that quantity for women. Alcohol consumption accounts for approximately 3.8% of all global deaths and 4.6% of global disability-adjusted life-years[16]. In India, this problem seems to be particularly relevant, with 6.5% of all deaths attributable to alcohol[17]. Taking into account the variability across Europe and figures extracted from the World Health Organization (WHO) mortality database,[18] one can estimate that 60% to 80% of liver-related mortality is due to excessive drinking[19]. 90–95% of heavy alcohol drinkers develop macrovesicularsteatosis in the centrilobulararea[20]. 10–35% of heavy drinkers develop necroinflammation along with steatosis, known as steatohepatitisoralcoholic hepatitis[21]. 8–20% of chronic alcoholics develop micronodular or Laennec's cirrhosis [22]. Alcohol is metabolised to acetaldehyde by both alcohol dehydrogenase (at low alcohol concentrations) and CYP2E1 (at higher concentrations, >10 mm), which is further metabolised by aldehyde dehydrogenase to acetate. Acetaldehyde forms protein adducts which causes hepatocyte injury directly or by autoimmune reaction[23]. A Maddrey's modified discriminant function (Mdf) = 4.6 × prothrombin time [PT] − control value [seconds]) + serum bilirubin [mg/dL]).value of >32 (which indicates severe alcoholic hepatitis and warrants corticosteroid treatment) and/ or hepatic encephalopathy in patients without treatment has a 28-day survival rate of 65%[24].

Non-alcoholic Fatty Liver Disease (NAFLD) encompasses the entire spectrum of fatty liver disease in individuals without significant alcohol consumption, ranging from fatty liver to steatohepatitis and cirrhosis. Non-alcoholic Fatty Liver (NAFL) presence of hepaticsteatosis with no evidence of hepatocellular injury in the form of ballooning of the hepatocytes or no evidence of fibrosis. The risk of progression to cirrhosis and liver failure is minimal. Non-alcoholic steatohepatitis (NASH) presence of hepaticsteatosis and inflammation with hepatocyte injury (ballooning) with or without fibrosis. This can progress to cirrhosis, liver failure and rarely liver cancer[25]. NAFLD is characterized by the accumulation of triglycerides, which are formed from the esterification of FFA and glycerol within the hepatocyte. The diagnosis of NAFLD and NASH should be strongly suspected in the presence of features such as obesity, diabetes and obstructive sleep apnoea (OSA); however, other causes should always be considered before attributing abnormal liver function tests (LFTs) to NAFLD/NASH alone. ALT is usually greater than aspartate aminotransferase (AST), and rarely more than three times the upper limit of normal.

Non-alcoholic steatohepatitis (NASH) is a condition in which severe fatty infiltration leads to hepatomegaly[26].Hepatomegaly and inhomogeneous patchy or diffuse increased echogenicity are common in chronic hepatitis and are related to the amount of fatty infiltration and fibrosis present[27].The World Gastroenterology Organisation guidelines provide a resource sensitive approach[15].Distinguishing ALD from non-alcoholic steatohepatitis is difficult as patient may deny alcohol abuse. Clinical examination, histology and serology may not differentiate these conditions. Accurate diagnosis is important as management of ALD differs from NASH patients.

Deepak Kumar Singh[28] et al in 2015 on Compaison of clinical, biochemical and histological features of alcoholic steatohepatitis and non-alcoholic steatohepatitis in Asian Indian patients concluded that older age, male sex, larger derangement of serum biochemistry, high serum bilirubin, AST/ALT > 1, more ballooning degeneration, portal inflammation, Mallory's hyaline, hepatocytic and ductular cholestasis, ductular proliferation and higher stage of fibrosis favours a diagnosis of ASH. Younger age, high ALT, AST/ALT < 1, higher grade of steatosis and absence of extensive neutrophilic portal inflammation favours a diagnosis of NASH.

Prasad P.[29] et al in their study in 2013 on Biochemical Evaluation of Patients of Alcoholic Liver Disease and Non-alcoholic Liver Disease concluded that There is significant difference in AST/ALT ratio, serum GGT and ALP in ALD group compared to that in NASH and acute viral hepatitis .

This study suggests that DeRitis ratio ≥2 in ALD patients may be due to alcohol induced hepatic mitochondrial injury and pyridoxine deficiency.

Sorbi [30] et al who concluded that AST/ALT ratio is a useful index for distinguishing ASH from NASH. Values < 1 suggest NASH and values ≥ 2 strongly suggest ASH.

In our study, ALD group has maximum number of study cases from age group 41 to 50 yrs (44%) in number followed by 31 to 40 yrs(34%), In NASH group maximum number of cases were from 31 to 40yrs in age group(56%) followed by 21 to 30 yrs. Mean age was 43.10±7.28years for alcoholic liver disease (ALD) group and 34.56±4.84for non-alcoholic steatohepatitis (NASH) group.

In our study, NASH group had more number of Pre-obese cases than ALD group which is a risk factor for the NASH. Mean BMI was 23.25±0.85 for alcoholic liver disease (ALD) group and 25.03±1.91 for non-alcoholic steatohepatitis (NASH) group. The difference was statistically significant.

In our study, in biochemical comparison we compared the AST, ALT, AST/ALT ratio. Bilirubin, SAP. The mean ALT and SAP was higher in NASH patients. Serum bilirubin and AST/ALT ratio was higher in ALD patients.. The mean ALT and SAP was higher in NASH patients (NASH vs. ALD; ALT - 99.15±29.15 IU/mL vs. 82.51±24.29, P = 0.014; SAP--205.97±47.43IU/mL vs. 109.70±25.60, P = 0.001). Serum bilirubin and AST/ALT ratio was higher in ALD patients (NASH vs. ALD; Bilirubin - 1.49±.46 mg% vs. 8.37±2.24 mg%, P = 0.02; AST/ALT - 0.802±.301vs. 1.28±0.77, P = 0.02) table no.8. The difference was statistically significant. (<0.05).

In our study there was a significant difference in AST/ALT ratio in ALD and NASH cases with ALD cases having a higher ratio. This was also reported by Sorbi et al who concluded that AST/ALT ratio is a useful index for distinguishing ASH from NASH.

Common complications were Ascites, GI bleeding, Hepatic encephalopathy, Hepatocellular carcinoma. There was no significant difference between the groups. Similar results were found in study conducted by Mallika Bhattacharyya.[31]

5. Conclusion

NASH group had more number of pre-obese (56%) cases than ALD group. The mean ALT and SAP were higher in NASH patients. Serum bilirubin and AST/ALT ratio was higher in ALD patients. Risk factors like DM, HTN were more in NASH then ALD patients. Common complications were Ascites, GI bleeding, Hepatic encephalopathy, Hepatocellular carcinoma in both groups. Therefore it is important to distinguish NASH from ALD.

References

[1] Shah SN. Alcoholic liver disease. In: API textbook of medicine. 7th ed. New Delhi: Jaypee Brothers Medical Publishers; 2003. p. 606–15.
[2] Ludwig J, Viggiano TR, Mc Gill DB, Oh BJ. Nonalcoholic steatohepatitis. Mayo ClinProc 1980;55:434-8.
[3] Farrell GC, Larter CZ. Nonalcoholic Fatty Liver Disease: from Steatosis to cirrhosis. Hepatology 2006;43:S00-S112.
[4] Angulo P. Nonalcoholic fatty liver disease. N Engl J Med 2002;346:1221-31.
[5] Neuschwander-Tetri BA, Caldwell SH. Non-alcoholic steatohepatitis: summary of an AASLD Single Topic Conference. Hepatology 2003;37: 1202-19.
[6] Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. 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.
[7] Wong F, Blendis L. Alcoholic liver disease. In: Thomson ABR, Shaffer EA, editors. First principles of gastroenterology: the basis of disease and an approach to management. 3rd ed. Edmonton: Canadian Association of Gastroenterology; 1997. p. 502–6
[8] Arthi M, Niranjan G, Hanifah M, Srinivasan AR. Efficacy of De Ritis ration in diagnosing liver diseases in Puducherry population. Adv Lab Med Int. 2011;1(4):61–8.
[9] Bain VG, Ma M. Chronic hepatitis. In: Thomson ABR, Shaffer EA, editors. First principles of gastroenterology: the basis of disease and an approach to management. 3rd ed. Edmonton: Canadian Association of Gastroenterology; 1997. p. 492–501.
[10] Laffaine MG, Mauricio LM. Non-alcoholic fatty liver disease. Ann Hepatol. 2004;3(3):93–9.
[11] Obika M, Noguchi H. Diagnosis and evaluation of non-alcoholic fatty liver disease. Exp Diabetes Res. 2012; 2012:12:article ID 145754.
[12] Correia JP, Alves PS, Camilo EA. SGOT–SGPT ratios. Dig Dis Sci. 1981;26(3):284.
[13] Heathcote J. Cirrhosis of liver. In: Thomson ABR, Shaffer EA, editors. First principles of gastroenterology: the basis of disease and an approach to management. 3rd ed. Edmonton: Canadian Association of Gastroenterology; 1997. p. 520–4.
[14] Dowman JK, Tomlinson JW, Newsome PN. Systematic review: the diagnosis and staging of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis. Aliment PharmacolTher. 2011;33(5): 525–40
[15] LaBrecque et al World Gastroenterology Organisation Global Guideline Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis, J ClinGastroenterol Volume 48, Number 6, July 2014
[16] Rehm J, Mathers C, Popova S, Thavorncharoensap M, Teerawattananon Y, Patra J. Global burden of disease and injury and economic cost attributable to alcohol use and alcohol-use disorders. Lancet 2009;373:2223-2233.

[17] World Health Organization. European status report on alcohol and health 2010. Copenhagen: WHO Regional Office for Europe, 2010.
[18] World Health Organization. WHO mortality database: raw data files. Geneva: World Health Organization, 2015.
[19] Sheron N. Alcohol and liver disease in Europe: simple measures have the potential to prevent tens of thousands of premature deaths. J Hepatol 2016;64:957-967.
[20] Gao B, Bataller R. Alcoholic liver disease: pathogenesis and new therapeutic targets. Gastroenterol. 2011;141(5):1572-85.
[21] Mathurin P et al. Fibrosis progression occurs in a subgroup of heavy drinkers with typical histological features. Aliment PharmacolTher. 2007;25(9):1047-54.
[22] Bruha R, Dvorak K, Petrtyl J. Alcoholic liver disease. World J Hepatol. 2012;4(3):81–90.
[23] Carithers RL, McClain C. "Alcoholic liver disease". Feldman M et al. (eds), Sleisinger&Fordtran's Gastrointestinal and Liver Disease 10th ed (2010), Philadelphia, PA: Elsevier Saunders; 2016, pp.1409-27.
[24] Mathurin P et al. Corticosteroids improve short term survival in patients with severe alcoholic hepatitis (AH): individual data analysis of the last three randomized placebo controlled double blind trials of corticosteroids in severe AH. J Hepatol. 2002;36(4):480-7.
[25] Naga Chalasani, The Diagnosis and Management of Non-Alcoholic Fatty Liver Disease: Practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association, HEPATOLOGY, Vol. 55, No. 6, 2012, 2005-2022.
[26] HishamTchelepi, MD, Philip W. Ralls, MD, Randall Radin, MD, Edward Grant, MD J Ultrasound Med 21:1023–1032, 2002
[27] Reid AE. Nonalcoholic steatohepatitis. Gastroenterology 2001; 121:710–723.
[28] Deepak Kumar Singh, ArchanaRastogi, Puja Sakhuja, RanjanaGondal, Shiv Kumar Sarin, Comparison of clinical, biochemical and histological features of alcoholic steatohepatitis and non-alcoholic steatohepatitis in Asian Indian patients, www.ijpmonline.org.
[29] Prasad P. Torkadi, I. C. Apte, A. K. Bhute, Biochemical Evaluation of Patients of Alcoholic Liver Disease and Non-alcoholic Liver Disease, Ind J ClinBiochem (Jan-Mar 2014) 29(1):79–83.
[30] Sorbi D, Boynton J, Lindor KD. The ratio of aspartate aminotransferase to alanine aminotransferase: potential value in differentiating non-alcoholic steatohepatitis from alcoholic liver disease. Am J Gastroenterol 1999;94:1018-22.
[31] Mallika Bhattacharyya, NarendraNath Barman, BhabadevGoswami, Clinical profile of cirrhosis of liver in a tertiary care hospital of Assam, North East India, Journal of Dental and Medical Sciences (IOSR-JDMS) e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 15, Issue 1 Ver. X (Jan. 2016), PP 21-27.