HEPATIC STEATOSIS: AN AETIOHISTOPATHOLOGICAL STUDY

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ABSTRACT

BACKGROUND

Fatty liver disease, i.e. hepatic steatosis defined as hepatic lipid accumulation greater than 5-10% of liver weight.[1-3] has become a common health problem in both developed and developing countries. Morphologically fatty liver is of two types: microvesicular and macrovesicular. Macrovesicular steatosis is a chronic condition associated with various risk factors like alcoholism, diabetes mellitus, obesity, etc. The aim of present study was to analyse various aetiological factors associated with macrovesicular hepatic steatosis and find its correlation with the grade of steatosis.

METHODOLOGY

This retrospective and prospective study was conducted in histopathology laboratory of a tertiary health care centre in Mangalore, Karnataka, from 2009 to 2014; 120 cases of liver biopsies and autopsy liver tissue of adults (≥18 years) showing histologically confirmed macrovesicular steatosis in >10% hepatocytes were analysed for aetiology and grade of steatosis.

RESULT

Hepatic steatosis was observed mainly in middle aged (31-50 years) males. ALD and non-alcoholic steatohepatitis (NASH) were most common causes followed by infections like TB, HCV, HBV, HIV and other causes like CPC (Chronic Passive Congestion) liver and drugs. Spearmen's correlation coefficient was used to analyse correlation between aetiology and grade of steatosis. ALD and NASH were most common causes for severe steatosis. ALD and NASH were also common causes for mild-to-moderate grade of steatosis. Mainly moderate-to-severe steatosis was found in association with TB, HCV, HBV, HIV. CPC cases predominantly showed moderate steatosis. The correlation between aetiology and grade of steatosis was found to be statistically significant. Drug induced steatosis was mostly severe grade, but the number of cases were too less to consider it statistically significant.

CONCLUSION

Various causes like ALD, NASH, TB, HCV, HBV and HIV infections, CPC and rarely drugs should be considered in cases of macrovesicular hepatic steatosis and histopathological sections of liver tissue should be studied extensively to rule out higher grades of steatosis.

KEYWORDS

Fatty Liver, Alcoholic Liver Disease, NASH.

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INTRODUCTION

Fatty liver, i.e. hepatic steatosis is the most common finding in liver biopsies. Fatty liver disease is defined as hepatic fat accumulation more than 5-10% of liver weight.[1-3] This condition which is common in both developed as well as developing countries like India is associated with various aetiological factors, which differ according to the type of steatosis. Hepatic steatosis is mainly divided into two types – microvesicular and macrovesicular. In micro-vesicular steatosis, numerous small lipid vesicles accumulate in hepatocytes, which leave the nucleus at centre. It is seen in conditions like acute fatty liver of pregnancy and Reye's syndrome.[4] It is associated with severe and acute form of liver injury. In contrast macrovesicular steatosis is a chronic condition, wherein large single lipid droplet accumulates in the hepatocyte pushing nucleus to the periphery.

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Causative factors for macrovesicular steatosis are broadly divided into Alcoholic Liver Disease (ALD) and Non-Alcoholic Fatty Liver Disease (NAFLD). In the present study, we have analysed the frequency of different aetiological factors in macrovesicular steatosis in adult population and its correlation with the grade of steatosis.

METHODOLOGY

This is a retrospective as well as prospective histopathological study done in histopathology laboratory of AJ Institute of Medical Sciences and Research Centre, Mangalore, Karnataka, from 2009 to 2014 (5 years).

Inclusion Criteria

Total 120 cases of liver biopsy and autopsy liver tissue of adults ≥18 years of age showing macrovesicular steatosis in more than 10% hepatocytes were included in the study.

Exclusion Criteria

Cases in which histopathology sections were showing mainly microvesicular steatosis and those cases where aetiology of steatosis could not be confirmed were excluded from the study.

All 120 cases were studied for aetiology and grading of macrovesicular steatosis and their correlation with each

other. Grading of steatosis was done using guidelines of Brunt et al[5] (With modification) and Mofrad et al.[6] H and E stained sections of liver tissue were observed under scanner view (40x) and grading of macrovesicular steatosis was done as follows:

- Grade 1 (Mild): Seen in ≥10%, but ≤30% hepatocytes.
- Grade 2 (Moderate): Seen in >30%, but ≤60% hepatocytes.
- Grade 3 (Severe): Seen in >60% hepatocytes.

STATISTICS

Data was analysed using Spearman's correlation coefficient to evaluate the correlation between aetiology and grade of hepatic steatosis; < 0.05 was set as the level of significance.

RESULT

We found that out of total 120 cases, 84 (70%) were males and 36 (30%) were females. Main clustering of cases was seen in the age group of 31-50 years (78 cases, i.e. 65%). Thus, abnormal findings were more commonly seen in middle aged males.

Age Group (Years)	Males (%)	Females (%)	Total (%)
18-20	2	1	3
21-30	11	3	14
31-40	25	16	41
41-50	27	10	37
51-60	16	2	18
61-70	2	3	5
71-80	1	1	2
Total	**84 (70%)**	**36 (30%)**	**120**

Table 1: Demographic Profile of Patients (N=120)

As shown in Table 2, Alcoholic liver disease was the most common aetiological factor (30.8% cases) in our study. NASH was the second most common cause accounting for 23.3% cases. Amongst infectious causes, TB was most common.

Sr. No.	Aetiology of Hepatic Steatosis	Number of Cases	Percentage
1.	Alcoholic liver disease	37	30.8
2.	Non-alcoholic steato-hepatitis	28	23.3
3.	TB	15	12.5
4.	HCV	12	10
5.	HBV	11	9.1
6.	HIV	10	8.3
7.	CPC	5	4.1
8.	Drugs	2	1.6
	Total	**120**	**100**

Table 2: Aetiology of Hepatic Steatosis

Sr. No.	Cause of Hepatic Steatosis	Grade of Steatosis			Total
		Mild (Grade1)	Moderate (Grade 2)	Severe (Grade 3)	
1.	ALD	9	9	19 (51.3%)	37
2.	NASH	6	14 (50%)	8	28
3.	TB	2	4	9	15
4.	HCV	2	7	3	12
5.	HBV	6	4	1	11
6.	HIV	2	5	3	10
7.	CPC	1	3	1	5
8.	Drugs	0	1	1	2
	Total	**28**	**47 (39.1%)**	**45 37.5%)**	**120**

Table 3: Grade of Hepatic Steatosis in Various Aetiologies

As shown in Table 3, moderate grade (Grade 2) of steatosis was most commonly seen (39.1% cases) followed by severe grade (37.5% cases). Most common cause of moderate steatosis was NASH, whereas ALD was most common cause of severe steatosis. Most common grade of steatosis seen in ALD was grade 3, i.e. severe steatosis (51.3%), whereas amongst NASH cases moderate grade of steatosis was most common (50%). Most common grade of steatosis in TB was grade 3. Amongst hepatotropic virus infections, HCV showed moderate grade of steatosis most commonly, whereas in HBV infected cases mild steatosis was most common. CPC cases showed moderate steatosis mostly. Drug induced steatosis cases showed moderate and severe grade of steatosis with equal frequency. Spearmen's correlation coefficient was utilized to analyse correlation between various aetiological factors and grade of steatosis considering <0.05 as level of significance. It was found that the correlation between above mentioned aetiological factors and grade of steatosis was statistically significant in all aetiologies except drug-induced steatosis. The number of cases of drug-induced steatosis were too less to consider statistically significant.

DISCUSSION

The demographic profile of our study showed clustering of cases in middle aged males (31 to 50 years). Richard Guerrero et al[7] and Hideyuki Kojima et al[8] found similar results. Amongst Indian population, Singh DK et al[9] found male**:**female ratio of 3.1**:**1 among 71 NASH cases.

The most common risk factor for hepatic steatosis in our cases was alcoholic liver disease and non-alcoholic steatohepatitis. Various past and recent studies done on western as well as Indian population have well established that the chronic alcoholism and NASH are the two most common causes of fatty liver disease.[8,10-12,13] Leevy CM.[14] analysed risk factors for fatty liver in 270 patients and found alcoholism to be the most common cause 43.3% followed by diabetes 6.3%. NASH is increasingly becoming causative factor for fatty liver disease because of increased incidence of obesity and diabetes mellitus. Association between TB and fatty liver is well established.[15] TB can cause fatty liver due to malnutrition, anoxia, starvation and tuberculous toxicity itself. Frequency of fatty change in pulmonary and extra-pulmonary TB in various studies ranges from 20-44%.[16-19] In our study, HCV and HBV were responsible for hepatic steatosis in 812 (10%) and 11 (9.1%) cases each. Macrovesicular hepatic steatosis is a common histological finding in patients with hepatitis C infection and known to be associated with progression of fibrosis independently in the absence of risk factors like alcohol and obesity.[20,21] The worldwide frequency of steatosis in HCV is 31-72%.[20-25,26] Hepatic steatosis is not commonly seen in hepatitis B infection; however, 10-20% patients of hepatitis B can have steatosis possibly due to overlap with metabolic syndrome as shown by Rozario et al[27]; 31–72% frequency of HBV associated steatosis is seen in various studies.[20-23] HIV was responsible for 10 (8.3%) of our cases. Steatosis in HIV can be because of malnutrition or therapy related.[28] It can be associated with HCV–HBV co-infection. CPC (In right-sided heart failure) was responsible for 5 cases (4.1%) in our study. Sung KC et al[29] have shown association between cardiovascular disease and fatty liver disease. Drug-induced steatosis was found in only 2 cases.

Drugs responsible were methotrexate and warfarin in 1 case each. These drugs are known to cause hepatic steatosis.[30] Elizabeth B et al[5] found grades of steatosis in ALD and HCV cases comparable to our study. Naga Chalasani et al[31] found mild, moderate and severe steatosis in 44%, 31% and 25% of biopsies, respectively. Thus mild steatosis was most common among their patients. However, moderate steatosis was also seen in significant number of cases 31%. Gordon et al[32] found grades of steatosis in HCV and HBV cases similar to our findings. Grades of hepatic steatosis seen in other aetiologies, i.e. TB, HIV, CPC drugs were comparable with other studies.[14,33,34]

CONCLUSION

Aetiologies like ALD, NASH, TB, HCV, HBV, HIV, CPC and drugs should be evaluated while analysing macrovesicular hepatic steatosis. Also the histopathological sections should be studied extensively to find out the grade and severity of steatosis.

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