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Research Article

INVESTIGATION OF EPIDEMIOLOGY AND ETIOLOGY OF LIVER DISEASES AND CHARACTERIZATION OF ITS ASSOCIATION WITH VARIOUS FACTORS

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ABSTRACT

Objective: The population of Gujarat is at higher risk of facing non-alcoholic liver diseases therefore it becomes important to examine etiology and epidemiology of liver diseases and to characterize its association to various risk factors.

Methods: Patient details such as socioeconomic background, demography, family history, medical history were collected at tertiary care trust hospital in Vadodara district, Gujarat. Causes of disease and various complications associated with the disease were investigated. The reports of various liver function tests were clinically co-related with patient conditions.

Results: Out of 137 patients of liver diseases, prevalence of alcoholic patients was 25%. Prevalence of viral infection was found to be 20%. Among all 78% were male and 22% were female and 80% patients were above 40 years of age. Urban population were found to be more susceptible to liver diseases. It was observed that 33% patients were of liver cirrhosis. Diabetes and cardiovascular disorders were most prevalent co-morbidities with 24% and 19.3% respectively. Gamma glutamyl transferase levels were significantly high ($p<0.001$) in alcoholics while alkaline phosphatase levels were significantly high ($p<0.001$) in viral manifestations. Hematocrit values also correlate well with the severity of liver diseases.

Conclusion: Thus, the present study concludes that gender, age, urbanization, comorbid conditions are risk factors associated with high prevalence of liver disease.

Keywords: Alcoholic liver disease, Fatty liver disease, Hepatitis, Liver disease, Non-alcoholic fatty liver disease.

INTRODUCTION

The liver is a vital organ and has a very wide range of functions such as detoxification, protein synthesis, and production of biochemical, glycogen storage, decomposition of red blood cells and hormone production. Because of its strategic location and multidimensional functions, the liver is also prone to many diseases. There are over 100 known forms of liver disease caused by a variety of factors. The major liver diseases that are responsible for the most morbidity and mortality are viral hepatitis (hepatitis B and C), alcoholic liver disease (ALD), non-alcoholic fatty liver disease (FLD), cirrhosis and hepatocellular cancer [1,2].

The present study aims to examine the etiology and epidemiology of liver diseases and to characterize its association with various risk factors. In Gujarat there is a higher risk of facing non-ALDs. Therefore, the objective of the present study was to know the exact scenario and burden of liver disease in the population and also to find out its association with various risk factors in the population of Gujarat.

METHODS

Patients from tertiary care trust hospital were enrolled in this study. The present study is a descriptive observational and patients selected for this study were of various age groups from 40 years, 40-60 years to >60 years.

The socio economic status of this patients were divided into four categories such as urban, semi-urban, semi-rural, and rural. Protocol was reviewed and approved by Institutional Ethical Committee. Permission to access case reports of all the patients admitted for gastrointestinal (GI) problems in the hospital was taken. Case record form and questionnaire was prepared for the collection of data. Patient privacy and confidentiality were maintained at all levels for this study.

Parameters which were included in case record form were age, gender, demography, socioeconomic status, family history, disease like hepatic, non-hepatic, associated complications, medications, biochemical estimation was carried out for aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), hematocrit (HCT).

RESULTS

In the present study, the data shows that, the prevalence of liver diseases is significantly high in the city, out of 200 GI patients 137 patients were of liver diseases. The prevalence of non-ALDs observed was 75% while ALD comprising of only 25% of prevalence. Around 20% of all cases are due to viral infection. The finding shows that the majority of patients were male having prevalence of 77.77% while females had only 22.23% prevalence. 80% of patients were above the age of 40 and 50% were belonging to age group of 40-60 years. There was no significant difference in mean age group of both liver and GI patient (Table 1). Urban population were found to be more susceptible to liver disease (Fig. 1).

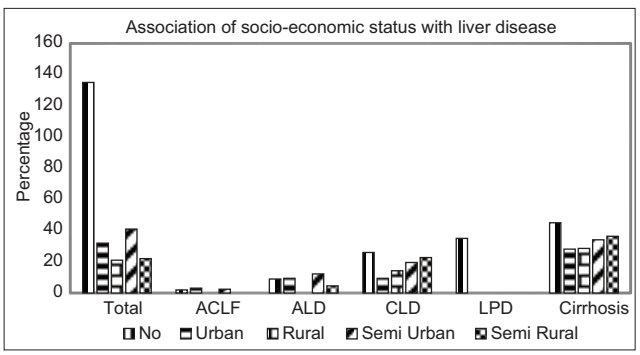

Fig. 1: Association of socio-economic status with liver disease

Disease wise classification

A disease wise demographic classification of patients was carried out. The patients were classified into various disease like acute chronic liver failure, liver parenchymal disease (LPD), ALD, chronic liver disease (CLD) and liver cirrhosis, it was observed that 45 patients admitted during the period were having liver cirrhosis, 35 patients had LPDs which includes ALD and CLD. It was found that males were having more prevalence of cirrhosis, ALD, and CLD. The mean ages were lowest for ALD. Cirrhosis and LPD have the highest prevalence above the age of 60. It was also observed that 10 out of 45 patients of cirrhosis are due to viral infection (Table 2).

Association of various co-morbidities to liver diseases

Diabetes and cardiovascular (CVS) disorders are common comorbidities associated with liver disease having prevalence of 32 and 26 cases respectively. Majority of co-morbidities observed were over the age of 40. There was no gender difference was observed for the association of these co-morbidities with liver disease. However, the mean age co-morbidities was observed very high (64.89 years). Carcinoma was also found to have mean 49.7 years and is not having any significant difference in males and females. Infection and sepsis were also associated comorbidities in patients of liver disease with lower age. CVS is co-morbidity in patients of liver disease at the mean age of 62 years, whereas diabetes mellitus (DM) is comorbidity associated with liver disease having age below 60. Females are more associated with CVS co-morbidities (Fig. 2).

Seasonal variation in liver disease

In liver disease, correlation with seasonal variation was not observed significantly. However, monsoon is related to higher incidences of viral diseases. Higher rate of hepatitis E was observed in the monsoon season. A rise in liver diseases was observed in starting of winter.

Complications associated with liver diseases

Varices, ascites, and encephalopathy are major complications of liver diseases. It was observed that 55 patients had ascites, 31 patients had varices and 13 patients were suffering from encephalopathy (Table 3).

Table 1: Distribution of patient by demographic characteristics

Number of patient	Male	Female	Below 40 years	40-60 years	Above 60 years
135	105	30	26	69	40

Table 2: Disease wise classification of patients suffering from liver disease

Disease	Total	ACLF (%)	ALD (%)	CLD (%)	LPD (%)	Cirrhosis (%)
Total	135	1.48	6.66	19.25	33.33	25.92
Male	105	0	8.57	21.90	27.61	35.23
Female	30	6.66	0	10	20	26.66
Below 40 years	26	0	19.23	11.53	34.61	26.92
40-60 years	69	1.44	5.79	20.28	28.98	31.88
Above 60 years	40	2.5	0	17.5	50	55

ACLF: Acute chronic liver failure, ALD: Alcoholic liver disease, CLD: Chronic liver disease, LPD: Liver parenchymal disease

Correlation to biochemical parameters with liver disease

The parameters which were found increase in liver diseases include ALT, AST, ALP, GGT, bilirubin levels. It was found that all these parameters were abnormal in patients of liver disease.

In patients of alcoholic history, it was observed that GGT levels were significantly increased with the highest value as high as 611 U/L.

High values of GGT were observed indicates high alcohol intake. The levels of GGT was observed more than 180 U/L indicates ALD. The mean GGT values of ALD was 223.05. The ALP levels were found higher in alcoholics and mean value was significantly higher as compared to viral infection in liver disease. On contrary, viral infection in liver disease ALP values are significantly high (242.32) as compared to GGT.

The ALT and AST levels were significantly high in alcoholic and non-alcoholic (Table 4). These levels were at least two-folds higher in viral diseases. In ALD and CLD, the values were found to be higher in CLD as compared to acute onset ALD. The values were also significantly increased in patients of hepatitis.

The mean value of total bilirubin was found to be 15.89 and 12.89 for direct bilirubin, in patients of hepatitis. In viral infections and alcoholic patient, the bilirubin levels were significantly high. The basic difference, however, lies in that the proportion of direct bilirubin is much more elevated in viral diseases as compared to alcoholic disease.

In obstruction diseases like gallbladder calculi, common bile duct stones, other blockage increased pressure the bilirubin levels were found to be higher, thus making direct bilirubin a major marker for obstructions in the hepatic system.

The parameters that seemed to associate quite well to the deterioration of the liver functions was HCT levels. In the present study, the HCT levels were found to be decreased in most liver disorders and increased with progression of disease. The levels were significantly decreased in cirrhosis and viral infections (Table 5).

DISCUSSION

The present study is aimed at examining etiology and epidemiology of liver diseases at a tertiary care trust hospital in Vadodara district and to characterize its association to various factors so as to lay the founding

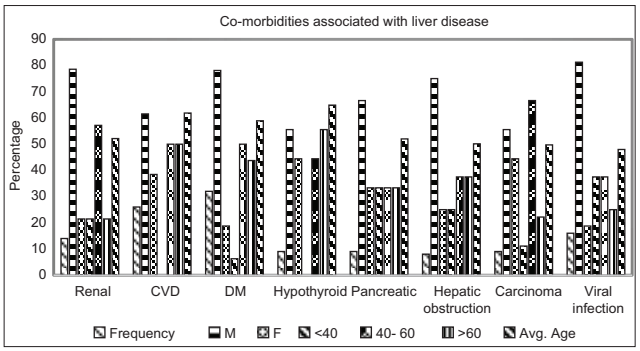

Fig. 2: Distribution of co-morbidities among various patients suffering from liver diseases

Table 3: Complications associated with patients suffering from liver disease

Complications	No.	M %	F %	<40 years %	40-60 years %	>60 years %
Ascites	55	78.18	21.81	20	56.36	23.63
Varices	31	87.09	12.90	25.80	54.83	19.35
Ascites+Varices	15	80	20	26.66	66.66	6.66
Encephalopathy	13	69.23	30.76	7.69	61.53	30.76

M: Male, F: Female

Table 4: Correlation of liver disease with liver function test

Parameters	Mean (SEM) U/L					
	Total billirubin	**Direct billirubin**	**ALT**	**AST**	**ALP**	**GGT**
Total hepatic	6.82 (0.91)	4.98 (0.75)	107.73 (17.52)	156.4 (20.11)	177.3 (14.69)	106.84 (15.46)
Alcoholic	8.43 (1.62)	6.15 (1.37)	111.96 (23.90)	196.45 (15.27)	187.79 (24.65)	181.7 (47.42)
Viral history	8.07 (2.46)	6.33 (2.46)	285.73 (2.05)	205.93 (16.71)	242.316 (26.87)	98.79 (26.49)
Cirrhosis	5.43 (1.27)	3.29 (0.82)	56.39 (7.92)	84.98 (11.77)	122.604 (11.79)	90.47 (34.91)
Hepatitis	15.89 (2.61)	12.89 (1.80)	89.6 (58.87)	139.13 (28.36)	284.6 (26.25)	126.8 (31.90)
Obstruction	2.3 (1.31)	2.125 (1.30)	58.6 (20.58)	35 (9.66)	197 (42.67)	37.33 (7.08)
ALD	11.195 (2.75)	8.36 (2.08)	46.7 (100.11)	126.1 (31.27)	168.85 (38.29)	223.05 (51.50)
CLD	4.55 (1.51)	3.49 (0.96)	86.29 (6.02)	86.9 (19.52)	213.2 (47.02)	120.9 (10.58)
LPD	6.08 (1.34)	4.14 (1.07)	70.96 (5.74)	86.55 (15.59)	195.2 (38.48)	119.3 (27.40)
Fatty liver	0.45 (0.25)	0.25 (0.05)	58.5 (22.50)	29 (14.0)	114.5 (1.50)	78 (3.00)

AST: Aspartate transaminase, ALT: Alanine transaminase, ALP: Alkaline phosphatase, GGT: Gamma-glutamyl transpeptidase, SEM: Standard error mean, ALD: Alcohol liver disease, CLD: Chronic liver disease, LPD: Liver parenchymal disease

5: Correlation of liver diseases to other biochemical parameters

Parameters	HCT (mean)
Total hepatic	30.9 (1.38)
Alcoholics	34.3 (4.09)
Viral history	29.8 (1.82)
Cirrhosis	29.23 (3.74)
Hepatitis	34.4 (1.87)
H. obstruction	33.5 (1.17)
ALD	30.96 (1.40)
CLD	31.7 (2.08)
LPD	33.52 (1.36)
Fatty liver	38.6 (3.75)

HCT: Hematocrit, ALD: Alcohol liver disease, CLD: Chronic liver disease, LPD: Liver parenchymal disease

brick to its better management and alleviation. In the present study, we observed that 75% of cases were not due to alcohol consumption.

The population of India is genetically pre-disposed to liver diseases this is due to the presence of a gene called APOC3 [3]. Study reveals that around 20% of all cases are due to viral infection. A study carried out in the south - Gujarat showed a high prevalence of hepatitis infection and co-infection in the state [4] which further contributes to liver disease. It is observed that the risk of a liver disease increases with age, especially above the age of 40 till the age of 60. From the study done in China and India, it is found that males are more susceptible to liver disease than females [5-8]. The prevalence of FLD in males increased stably with age, and steadily from 50 to 60 years of age in females. The peak prevalence was observed in females in the age group of 55 and above, which was about 7 years later than that in males, which might be due to the menopausal status and lack of physical exercise in this period of time [5]. Findings of the present study correlate to a study performed in china, among patients diagnosed having FLD (18.0% males, 16.7% female, p>0.05), a significantly large data set. The prevalence rate was significantly higher in urban population than in rural areas. The prevalence rate was higher in men than in women under the age of 50 years. All results correlate well with the study performed herewith. However, the opposite phenomenon was found over the age of 50 years [6].

Bedogni *et al*. found that the prevalence of non-alcoholic FLD (NAFLD) increases with age in both genders and then significantly decreases over 66 years of age. This variations may be due to the social, environmental and cultural background among the subjects [9].

In this we found that the prevalence of liver disease is more in urban population. The study indicates that urban residency, low education are the risk factors for FLD. The diagnosis rate generally tends to be low in a rural population. The high prevalence can be attributed by altered lifestyle, poor dietary habits, pollution, Type 2 DM, obesity and smoking that show high association with liver diseases. Genetic predisposal is also the factor contributing to liver disease. Higher number of cases during the festive season can be attributed to poor dietary habits, junk consumption and increased alcohol consumption during festivals and celebrations.

In the present study, it was found that liver diseases are correlated to various comorbidities like DM and CVS disease with most co-morbidities occurring over the age of 40. Multiple organ failure and metabolic disorders lead to increased mortality and morbidity and decreased life expectancy by adding an extra burden to the liver. Liver diseases also correlate most to diabetes and CVS disorders. However, it is unclear that DM precedes the risk of liver disease. Patients with NAFLD are at high risk for coronary atherosclerosis regardless of classical CVS risk factors, especially visceral adiposity. Many theories are suggested for the same, but no definitive mechanism is proven to explain the phenomenon [5,10]. Various studies have different outcomes regarding association of thyroid disorders to liver diseases [11-13]. An association was also found in our study. However, no strong argument is available. The results from the various study compared to the present study establishes the association of NAFLD with dyslipidemia, hypertension, and obesity among all age groups.

Varices, ascites and encephalopathy are major complications of liver diseases. More than half the admitted patients have either one or the other of these complications. These complications are markers of disease progression and depict diseases severity in its respective order. Alcohol consumption is related to decrease in mean age of onset of these complications.

In the present study, the overall mean for AST and ALT levels were significantly higher as compared to normal value which is in coordination with earlier reported studies [5-8]. The ALP and GGT values are also significantly high. In general, ALP levels and AST levels show more significant correlation with the severity, morbidity and prognosis of liver diseases. Patients with alcoholic history, the GGT levels were significantly increases having highest value (611 U/L). GGT is a non-specific marker for liver damage, but it has been reported that alcohol produces hepatocyte damage which causes an increase in GGT levels. Thus increased levels of GGT (>180 U/L) would indicate ALD. The ALT and AST are significant biomarkers for liver inflammation.

The bilirubin levels are significantly increased for alcoholics, in patients of non-chronic ALD.

As an outcome of the study, we have observed change in HCT which relates well to severity of liver diseases. This may be due to altered hematopoiesis [14,15].

NAFLD has been increasingly recognized as the most common liver disease globally. The prevalent data obtained from clinical series and

autopsy studies suggest that 20-30% of individuals have FLD. While the general trend in outcome is the same, variations amongst prevalence, distribution, and related outcomes have been observed among studies performed in same and different geographical regions. The discrepancy between these studies may probably be due to the difference in methods of sample selection, modalities used for diagnosis and diversity of life styles and dietary habits in different areas.

CONCLUSION

Liver diseases have more association with gender, age, socioeconomic status comorbid conditions. The pattern of change in liver function tests is characteristic for various diseases and can be instrumental in the identification and differential diagnosis of liver diseases. Prognosis in most of these cases is poor. A descriptive study has been therefore performed at length to assess the current situation, associated risk factors.

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