A Study of Clinicopathological Association in Chronic Liver Disease - A Cross Sectional Study from a Tertiary Referral Hospital of South India

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ABSTRACT

BACKGROUND

Chronic liver disease is a liver disorder of varying causes and severity with variable clinical, biochemical and histological findings with severity lasting for 6 months or more. The spectrum of chronic inflammatory diseases of the liver extends from acute hepatitis to chronic hepatitis and finally to cirrhosis. Whatever the aetiology, the same basic underlying histological changes may be seen in the liver. The objective of the study was to see the association of clinical diagnosis with the histopathological diagnosis among chronic liver disease patients.

METHODS

It is a cross-sectional study that included analysis of clinicopathological data of 40 patients with clinically suspected chronic liver disease who were admitted to the medical wards of government general hospital, Kakinada between March 2003 and May 2005.

RESULTS

Total number of patients (N = 40) of suspected chronic liver disease were included in the study in which 25 were males (62.5 %) and 15 were females (37.5 %). Most of the cases (36) were found in the age group of 30 - 69 years, a majority of 12 was in the age group of 50 - 59 years. The most common symptoms in this study were abdominal distension and loss of appetite in 28 (70 %) patients, followed by pain in abdomen 22 (55 %), jaundice 17 (42.5 %), loss of weight 16 (40 %), pedal oedema 11 (27.5 %). A total of 7 cases (41.7 %) of cirrhosis were seen in the age group of 40 - 49 years, 5 cases (45.45 %) with chronic hepatitis were in the age group of 50 - 59 years, 5 (45.45 %) hepatocellular carcinoma cases were in the age group of 60 - 69 years, hepatoblastoma was seen in a 60-year-old female. Clinical diagnosis was strongly associated with histopathology (Pearson chi-square value = 19.583, P = 0.021) and also showed fair agreement between clinical diagnosis and histopathology (P = 0.002).

CONCLUSIONS

Chronic liver disease is more in males, most commonly seen in the age group of 30 - 69 years and the majority of them are in the age group of 50 - 59 years. Cirrhosis is the most common chronic liver disease seen in North and Coastal Andhra, part of South India, followed by chronic hepatitis, hepatocellular carcinoma. The most common etiological factor is alcoholic abuse (35 %) followed by HBsAg positivity (15 %), native medicine in 5 % and unknown in 45 %. Clinical diagnosis of chronic liver disease should be confirmed with histopathological examination. In appropriate clinical settings, the clinical diagnosis of chronic liver disease made by experts is fairly associated with histopathological diagnosis.

KEY WORDS

Chronic Liver Disease, Clinical Diagnosis of Liver Disease, Histopathological Association

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BACKGROUND

Chronic liver disease is a liver disorder of varying causes and severity with variable clinical, biochemical and histological findings with severity lasting for 6 months or more.[1,2,3,4]

The spectrum of chronic inflammatory diseases of the liver extends from acute hepatitis to chronic hepatitis and finally to cirrhosis. Whatever the aetiology, the same basic underlying histological changes may be seen in the liver. The spectrum of chronic liver disease includes chronic inflammatory diseases like chronic hepatitis of various aetiologies including viral, drugs or toxins, autoimmune hepatitis, alcoholic liver disease, non-alcoholic fatty liver diseases including non-alcoholic steatohepatitis (NASH), tumours of the liver including primary benign, malignant tumours or secondaries[5,6,7,8] rare congenital diseases like Wilson's disease, hemochromatosis, and metabolic storage diseases like Glycogen storage disease, Gaucher's disease etc. and infiltrative diseases like amyloidosis, sarcoidosis, and granulomatous infiltrations.

Many patients are asymptomatic and in others, symptoms may be mild or intermittent. In some patients, symptoms do not develop and the diagnosis is not made until the disease progresses to cirrhosis.

Timely and correct diagnosis is very important in the treatment and thereby improving the morbidity and mortality in chronic liver diseases. Registry and robust data for chronic liver disease are also lacking in India.

Histopathological examination is the single most important diagnostic tool in accurately diagnosing various chronic liver diseases, despite the availability of advanced imaging techniques and serological investigations.

We wanted to see the association of clinical diagnosis with the histopathological diagnosis among chronic liver disease patients.

METHODS

The present study was a cross-sectional study that included analysis of clinicopathological data of 40 patients with clinically suspected chronic liver disease who were admitted to the medical wards of government general hospital, Kakinada between March 2003 and May 2005. A convenient sample of 40 was taken according to the total number of patients admitted to the medical wards. Adults above 15 years old with symptoms for more than 6 weeks duration with predisposing and precipitating factors, symptoms of liver disease of fewer than 6 weeks duration with significant history, and who were suspected with malignancies were included in this study.

Patients below 15 years, with bleeding diathesis, acute fulminant liver failure, acute massive upper GI bleed, acute hepatitis, grossly anaemic patients, with tense ascites, hepatic encephalopathy, comatose, and patients with psychosis were excluded.

The history details were noted including the nature of the symptoms, duration, progression and detailed history, detailed clinical findings, which were recorded after meticulous examination, complete blood serum including complete liver function tests, and virology, ascitic fluid and radiological investigations and histopathological findings, and the details of other relevant investigations. And also, the details of the complications of the liver biopsy were noted.

Statistical Analysis

Complete data were analysed. Statistical analysis was done using SPSS-16 and MS Excel-2017 software. Chi-square test was used to test the association of categorical data, standard error of proportions to compare proportions and kappa statistics to see the percent of agreement.

RESULTS

Total number of patients (N = 40) of suspected chronic liver disease were included in the study in which 25 were males (62.5 %) and 15 were females (37.5 %), mean age was 48.48 years with a standard deviation of 11.03 years ranging from 26 - 70 years. Most of them (36 cases) were found in the age group of 30 - 69 years, majority of them (12) were in the age group of 50 - 59 years.

Most common symptoms in this study were abdominal distension and loss of appetite in 28 (70 %) patients, followed by pain abdomen 22 (55 %), jaundice 17 (42.5 %), loss of weight 16 (40 %), pedal oedema 11 (27.5 %), fever 10 (25 %) and oliguria 8 (20 %) and sleep disturbances 4 (10 %). Ascites was the most common 26 (65 %) clinical finding followed by hepatomegaly 24 (60 %), icterus 19 (47.5 %), pedal oedema 17 (42.5 %), splenomegaly 14 (35 %), engorged veins over abdomen in 8 (20) %.

	Initial Complaints	No. of Cases (%)	Clinical Signs	No. of Cases (%)
1	Abdominal distension	28 (70)	Ascites	26 (65)
2	Loss of appetite	28 (70)	Hepatomegaly	24 (60)
3	Pain abdomen	22 (55)	Icterus	19 (47.5)
4	Jaundice	17 (42.5)	Pedal oedema	17 (42.5)
5	Loss of weight	16 (40)	Splenomegaly	14 (35)
6	Swelling of feet	11 (27.5)	Engorged veins over abdomen	8 (20)
7	Fever	10 (25)	Scanty body hair	2 (5)
8	Decreased urine output	8 (20)	White nails	2 (5)
9	Sleep disturbances	4 (10)	Scratch marks	2 (5)
10	Melena	3 (7.5)	Clubbing	1 (2.5)
11	Pale coloured stools	3 (7.5)	Palmar erythema	1 (2.5)
12	Vomiting	2 (5)	Spider naevi	1 (2.5)
13	Hematemesis	2 (5)	-	-
14	Pruritis	1 (2.5)	-	-

Table 1. Presenting Symptoms and Signs

Age distribution of different chronic liver diseases: Most of them 17 (40.5 %) were cirrhosis, 11 (27.5 %) were chronic hepatitis, 5 were (12.5 %) hepato-cellular carcinoma, hepatoblastoma, adenocarcinoma, fatty liver, liver abscess was found (2.5 %) in each patient.

Age distribution of different chronic liver diseases. A maximum number of cases of cirrhosis (7 cases (41.7 %) were seen in the age group 40 - 49 years, most of the chronic hepatitis cases [5 cases (45.45 %)] were in the age group of 50 - 59 years, most of the hepato-cellular carcinoma cases [5 cases (45.45 %)] were in the age group of 60 - 69 years, hepatoblastoma was seen in a 60-year-old female.

Among 40 clinically suspected cases of chronic liver disease, histopathology was confirmed in 38 patients, suspected diseases were confirmed in 22 (55 %) cases, and altered clinical impression in 16 (40 %) cases and the

specimen was inadequate in 2 (5 %) cases, this may be due to small and fibrotic liver and massive ascites.

13 (N = 40) patients were suspected with malignancy either primary or secondary of which 7 (53.84 %) were confirmed with malignancy [hepatocellular carcinoma in 5 (38.46 %), hepatoblastoma in 1 (7.69 %) and adenocarcinoma in 1 (7.69 %)]. Of these 13 patients, 2 were suspected with secondaries of which one patient had periampullary growth and evidence of secondaries in CT scan but histologically not confirmed.

Clinical Diagnosis	No of Cases Suspected	Histological Diagnosis Confirmed
Cirrhosis	20	14
HCC	9	5
Chronic Hepatitis	6	3
Hepatoma	2	0
Secondaries	2	0
Chronic Liver Abscess	1	0
Total Number of Cases	40	22

Table 2. Clinical Diagnosis and Histopathology Confirmation

Note: HCC: Hepatocellular carcinoma

		Histopathology				
		Cirrhosis	Noncirrhotic Liver Disease	Others	Tumours	Total
Clinical Diagnosis	Cirrhosis	11	6	1	1	19
	Noncirrhotic Liver Disease	4	4	1	0	9
	Others	1	0	1	1	3
	Tumours	1	1	2	5	9
Total		**17**	**11**	**5**	**7**	**40**

Table 3. Clinical Diagnosis-Histopathology Cross Tabulation Count

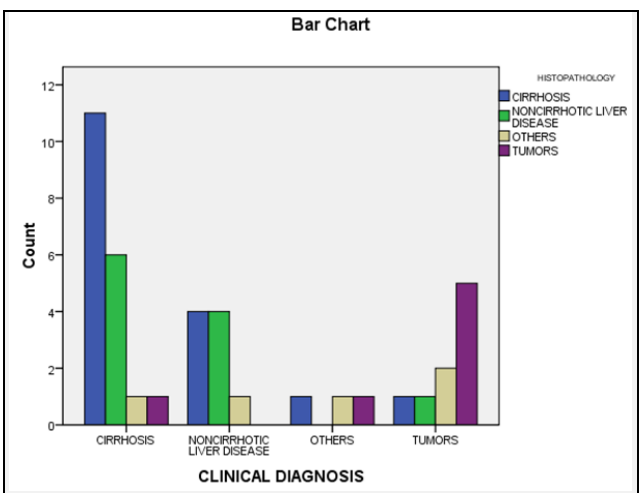

Chart 1. Bar Chart Showing Histopathology-Clinical Diagnosis Correlation

Clinical diagnosis was strongly associated with histopathology (Pearson chi-square value = 19.583, P = .021, P = 0.016 with Fisher's correction) and also showed a fair agreement between clinical diagnosis and histopathology (Measure of Agreement Kappa = .309, P = 0.002).

DISCUSSION

The correct diagnosis of chronic liver disease is very important for the planning of treatment and the prognosis. Histopathology is the most important aid in accurately diagnosing various chronic liver diseases, and assessing the progress and severity of the disease and also the response to therapy.

In this study of 40 patients with clinically diagnosed chronic liver disease, among which 17 (40.5 %) were cirrhotic, 11 (27.5 %) were chronic hepatitis, 5 (12.5 %) were hepatocellular carcinoma, and adenocarcinoma in 1 (2.5 %), fatty liver in 1 (2.5 %) and liver abscess in 1 (2.5 %) case, hepatoblastoma seen in a (2.5 %) 60-year-old female, which is the most common primary malignancy of liver in paediatric age and rare to occur in adults.[9,10,11]

Six (15 %) were HBsAg positive, alcoholic abuse seen in 14 (35 %), consumption of native medicine in 2 (5 %), aetiology could not be found in 18 (45 %) cases. HDV and workup for autoimmune causes were not available in all patients. These results were very low when compared to the findings of AC Anand et al.[12] (JAPI 2004, VOL 52; 78 - 787) of which among 187 patients of chronic liver disease, HBV infection was attributed in 91 (48.7 %) which was higher (P = 0.001) and cryptogenic in 24 (12.8 %) which was lower than P = < 0.001) the present study (2003 - 2005). HBV was the most frequent among infectious causes of CLD, found in the present study which was similar to many Indian studies,[12,13] HBV infection in the present study population was significantly lower in proportion than in patients of AC Anand et al.[12] (P = 0.001) study.

In the present study (N - 40), alcoholic abuse was seen in 14 (35 %) patients of which 8 (61.5 %) had cirrhosis, six patients (42.85 %) had non-cirrhotic liver disease and one patient was diagnosed with HCC (7.1 %). The age range of cirrhosis in the present study was 30 - 69 years.

The proportion of alcohol abuse was higher (35 %) in the present study population, in patients with cirrhosis 8 (61.5 %) and patients with non-cirrhotic liver disease (42.85 %), contrary to patients in Mukherjee PS et al. (2017)[4] study. A study by Mukherjee PS et al. (2017)[4] highlighted evolving risk factors for CLD as alcoholism and diabetes in India, like in other studies.[13,14,15] Alcohol was the most common cause of cirrhosis in this study, similar to our present study (2003 - 2005).

Comparison with trends of chronic liver disease in Gautam Ray (2014)[13] study is shown. Increasing trends of alcohol-related disease from 2003 - 2011, and cryptogenic liver disease was also similar to this study[13] from the year 2003 - 2007.

Results of recent data from a study from India (Mukherjee PS et al. (2017)[4] of 13014 patients with chronic liver disease is shown, 4413 were cirrhosis, 8163 patients had non-cirrhotic liver disease, 438 patients had hepatocellular carcinoma. In this study, 4336 (33.3 %) were hepatitis B virus infection related, 2806 (21.6 %) were hepatitis C virus related, 2253 (17.3 %) were alcohol-related, 1664 (12.8 %) were fatty liver and 2021 (15.5 %) were diagnosed with other diagnoses.

Proportion of cirrhosis in our present study (2003 - 2005) was similar to all regions patients' group of Mukherjee PS et al. (2017),[4] but HCC (hepatocellular carcinoma), alcohol-related diseases were significantly higher in proportions in the present study (2003 - 2005). Hepatitis B virus infection, fatty liver disease and miscellaneous conditions were significantly lower than in all regions patients' group of Mukherjee PS et al. (2017).[4]

Proportion of hepatocellular carcinoma was significantly higher in the present study (2003 - 2005) than in all regions

patients' group and north Indian patients of Mukherjee PS et al. (2017)[4] study.

	Patients with Cirrhosis (%)	HCC (%)	HBV Related (%)	Alcohol Related (%)	Fatty Liver (%)
Present Study 20032005(N = 40)	42.5	12.5	15	35	2.5
All Regions Patient Group (Mukherjee PS et al. (2017) N = 13014)	33.9 (P = 0.22)	3.4 (P = 0.001)	33.3 (P = 0.01)	17.3 (P = 0.002)	12.8 (P = 0.06)
North Indian Patient Group (Mukherjee PS et al. (2017) (N = 4342)	26.7 (P = 0.02)	5 (P = 0.04)	27.8 (P = 0.08)	10.9 (P = 0.01)	6.9 (P = 0.3)
South Indian Patient Group (Mukherjee PS et al. (2017) (N = 1854)	34.5 (P = 0.2)	1.4 (P = < 0.001)	40.5 (P = 0.001)	30.4 (P = 0.49)	3.1 (P = 0.82)

Table 4. Comparison with South Indian, North Indian and All Region Patient Groups of Mukherjee PS et al. (2017)[4]

HBV infection in our present study (2003 - 2005) was significantly lower and the hepatocellular carcinoma proportion in the present study was significantly higher in the south Indian population in Mukherjee PS et al.[4] (2017) study. But proportions of cirrhosis, alcohol-related disease, fatty liver were similar in South Indians from both the studies and alcohol-related disease was similar to the increasing trend shown in other studies.[14,16,17]

Cirrhosis was confirmed in 17 (40.5 %) cases and all were in the age group of 30 - 69 years with mean age: 45.11 ± 8.35 years, 11 (64.7 %) were males, 6 (35.29 %) were females, 8 (47 %) were with history of alcoholic abuse, and 3 (17.64 %) were positive for HBsAg. Although the number of cirrhotic patients was smaller in our study, these results were comparable to the larger number of patients in a study by Mukherjee PS et al. (2017)[4] from India.

In the present study, primary hepatic lesions (53.8 %) were more common when compared to the metastatic lesion which was seen in 1 patient (7.69 %). The alcohol abuse was a recognized aetiology in (20 %) of hepatocellular carcinoma patients in the present study (2003 - 2005), in contrast to higher proportions of HBV was HCV infections found in other Indian studies and studies from other countries.[13,16,18]

In the present study, the most common cause of chronic liver disease was cirrhosis of liver (40.47 %) followed by chronic hepatitis (27.5 %), followed by hepatocellular carcinoma (12.5 %).

Adequate tissue could not be yielded for histopathology in 2 cases (5 %). Biopsy related complications were observed as follows: mild post-procedure pain in all patients, pleurisy in one, pleural effusion in 2 patients and minimal bleeding from puncture site was observed in 4 cases. No other major complications and mortality were reported.

CONCLUSIONS

Chronic liver disease was more in males found in 25 (62.5 %) patients N=40, most commonly seen in [36 (90 %)] the age group of 30 - 69 years and the majority (30 %) of them in the age group of 50 - 59 years.

Cirrhosis is the most common chronic liver disease seen in North and Coastal Andhra, part of South India, followed by chronic hepatitis and hepatocellular carcinoma.

Most common etiological factor was found to be alcohol abuse (35 %) in this part of South India followed by HBsAg positivity (15 %), native medicine in 5 % and unknown in 45 %.

In patients with chronic liver disease, the most common presentations were abdominal distension and loss of appetite and the most frequent clinical findings were ascites, hepatomegaly, pain abdomen and jaundice.

Clinical diagnosis of chronic liver disease should be confirmed with histopathological examination. In ssappropriate clinical settings, the clinical diagnosis of chronic liver disease made by experts is fairly associated with histopathological diagnosis. Liver biopsy is a safe procedure that aids in establishing the diagnosis and helps in the appropriate management of a chronic liver disease.

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