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Evaluation of Histopathological Spectrum of Hepatic Lesions in Liver Biopsies: A Two Years Prospective Study

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Abstract

Introduction: Liver biopsy is an important diagnostic tool that assists determination of specific diagnoses and directs therapeutic decisions in patients with acute and chronic liver diseases. It can also be used to estimate the degree of liver damage to grade and stage hepatitis B and C, and to determine the best treatment for the damage or disease.

Material and Method: A two year prospective study was conducted on 78 liver biopsies in the Department of Pathology, M.S. Ramaiah Medical College and Hospital from January 2018 to January 2020. The sections were examined and the histopathological findings were recorded. Immunohistochemistry (IHC) was performed by using markerssuch as CK7, CK20, CDX2, CEA, Hep par 1, TTF-1, synaptophysin, chromogranin and AFP for increased diagnostic accuracy.

Results: In this study, age ranged from 3 months to 80 years. Mean age was 42.5 years. Out of 78 cases, 51 cases were males, 27 were females. Liver biopsy revealed that chronic hepatitis and metastasis were the commonest findings constituting 14.1% each. Hepatocellular carcinoma (HCC) and cirrhosis constituted 11.53% and 10.25% of total cases, respectively.

Conclusion: Liver biopsy continues to play an important role in modern clinical practice and remains the gold standard for the diagnosis of majority of the hepatic diseases. Histopathological examination of liver biopsy specimen is an essential, safe and reliable tool for the diagnosis, accurate assessment of severity and follow up of the various hepatic lesions.

Keywords: Histomorphological analysis; Hepatic lesions; Liver biopsy.

Introduction

Liver is the principle site of many metabolic activities and hence exposed to various metabolic, toxic, infectious and neoplastic insults. It is affected by a wide spectrum of primary and secondary diseases.[1] The common primary liver diseases are hepatitis, non-alcoholic fatty liver disease (NAFLD) and Hepatocellular carcinoma (HCC). Secondary hepatic involvement can be due to alcoholism, extrahepatic infections or metastatic spread of various primary malignancies, etc.[2] Liver biopsy is an essential tool in the diagnosis and management of liver diseases as liver function tests (LFT) alone are not entirely diagnostically specific.

A liver biopsy can also be used to estimate the degree of liver damage, to grade and stage hepatitis B and C, and to determine the best treatment for the damage or disease. Evaluation of liver biopsy has major clinical significance. The liver is frequently affected by wide spectrum of neoplasms including benign tumours as well as primary malignancies.[3–5] In addition, due to the rich dual blood flow to liver, malignant tumours also often secondarily involve liver. At present, biopsy is the gold standard in oncology.[6] Liver biopsy continues to play an important role in modern clinical practice where any significantly abnormal LFT and/or radiological finding with clinical findings of anaemia, jaundice, hepatomegaly, ascites and splenomegaly warrants

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a liver biopsy. The ease as well as it being a relatively safe procedure has made it a method of choice for diagnosis and subsequent management of hepatic lesions. Thus, histopathological study of liver biopsy is frequently done for diagnosis of different hepatic lesions. These diseases can be diagnosed by correlation of clinical, biochemical or radiological examinations. The main purpose of this study was to analyse different patterns of liver changes in various hepatic lesions.

Materials and Methods

The study was conducted on 78 liver biopsies prospectively in the Department of Pathology, M.S. Ramaiah medical college and hospital over a period of two years from January 2018 to January 2020. The clinical and radiological findings with LFT results were noted in all the cases. Liver biopsies were fixed in 10% formalin and processed through the routine standard procedure which is followed for all histopathology specimens and stained with Hematoxylin and Eosin (H&E) and were examined under microscope. Special stains like Reticulin, Periodic acid Schiff, Masson Trichrome and Prussian blue were employed wherever required. Immunohistochemistry (IHC) was performed by using markers like CK7, CK20, CDX2, CEA, Hep Par 1, TTF-1, synaptophysin, chromogranin A and AFP for increased diagnostic accuracy. The findings were recorded and analysed.(Fig. 9)

Statistical analysis

Statistical analysis was done by using SPSS software (Version 21). All values were given in mean±SD.

Result

In this study, age ranged from 3 months to 80 years. Mean age was 42.5 years. Out of the total 78 liver biopsy specimens, 51 cases were males and 27 were females. Mean alanine aminotransferase (ALT) for the entire cohort was 84 IU/L, and mean aspartate aminotransferase (AST) was 87 IU/L. Serum ALT was abnormally elevated in 30 (38.46%) subjects.

Liver biopsies revealed 19.23% cases of chronic hepatitis which constituted the majority of the cases. 14.10% of metastasis, 11.53% and 10.25% of hepatocellular carcinoma (HCC) and cirrhosis, respectively. Fatty liver was seen in 6.41% cases and 5.12% cases showed biliary atresia. Two cases each of tuberculosis, hepatoblastoma and giant cell hepatitis were seen. One case each of Dubin Johnson syndrome and autoimmune hepatitis were reported. The histopathological diagnosis are shown in (Table 1, Fig. 1).

Table 1: Sex-Wise Distribution of Liver Biopsies.

Histopathological Diagnosis	Male	Female	Number of Cases
HepatocellularCarcinoma	5	4	9
Positive for Malignancy	4	–	4
Acute Hepatitis	2	–	2
Storage Disorders	1	–	1
Metastasis	10	1	11
Giant Cell Hepatitis	1	1	2
Portal Triaditis	2	1	3
Cholestatic Hepatitis	4	2	6
Chronic Hepatitis	6	5	11
Biliary Atresia	1	3	4
Fatty Liver	3	2	5
Granulomatous Inflammation	–	1	1
Autoimmune Hepatitis	–	1	1
Acute On Chronic Inflammation	4	–	4
Cirrhosis	5	3	8
Hepatoblastoma	2	–	2
Tuberculosis	1	–	1
Chronic Cholestasis Liver Disease	–	3	3
Total	51	27	78

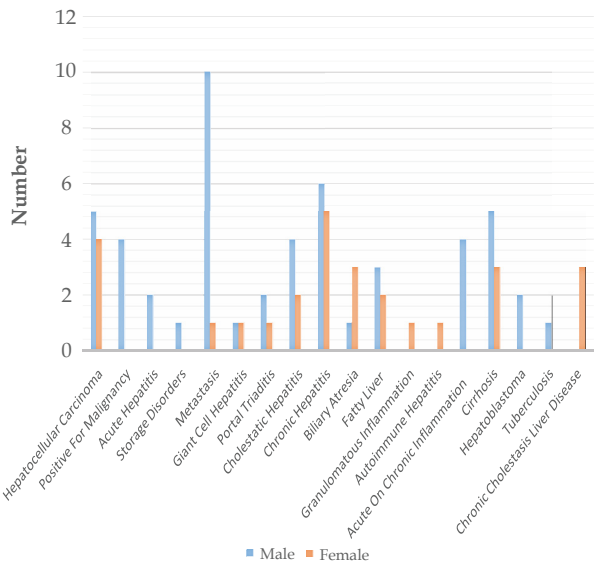


Fig. 1: Sex-Wise Distribution of Liver Biopsies.

Table 2: Age and Sex-Wise Distribution of Various Hepatic Lesions.

Age Group	Male	Female	No. of Cases	Percentage of Total Case
0–10	8	11	19	24.35
11–20	2	1	3	3.84
21–30	3	2	5	6.41
31–40	7	6	13	16.66

41–50	14	1	15	19.23
51–60	9	3	12	15.38
61–70	6	–	6	7.69
71–80	2	3	5	6.41
Total	51	27	78	100

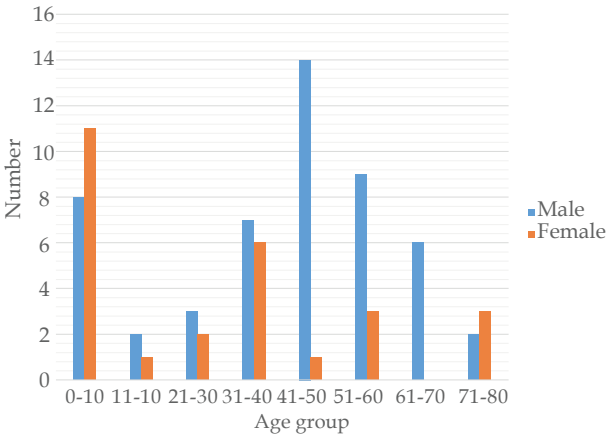


Fig. 2: Age and Sex-Wise Distribution of Various Hepatic Lesions.

Table 3: Spectrum of Various Histopathological Lesions.

Sr.No.	Histopathological Diagnosis	No. of Cases	% of Total Cases
1	Metastasis	11	14.10
2	Chronic Hepatitis	11	14.10
3	Hepatocellular Carcinoma	9	11.53
4	Cirrhosis	8	10.25
5	Cholestatic Hepatitis	6	7.69
6	Fatty Liver	5	6.41
7	Positive For Malignancy	4	5.12
8	Biliary Atresia	4	5.12
9	Acute On Chronic Inflammation	4	5.12
10	Portal Triaditis	3	3.84
11	Chronic Cholestatic Disease	3	3.84
12	Hepatoblastoma	2	2.56
13	Acute Hepatitis	2	2.56
14	Giant Cell Hepatitis	2	2.56
15	Storage Disorder	1	1.28
16	Granulomatous Inflammation	1	1.28
17	Autoimmune Hepatitis	1	1.28
18	Tuberculosis	1	1.28
	Total	78	100

Immunohistochemical analysis

Primary sites for metastatic tumors were from colorectal carcinoma in 2 cases, upper gastrointestinal tract (GI) tract in 1 case, pancreas in 2 cases and breast in 1 case. In cases of metastatic adenocarcinoma, primary malignancy being colorectal/ pancreatic ductal origin the tumor cells were diffusely and strongly positive for CK20 and focally positive for CDX2, CEA, AFP. Whereas in cases of metastatic adenocarcinoma with primary tumor in upper GI tract/ pancreas tumor cells were positive for CK7. In cases of HCC , the tumor cells were diffusely and strongly positive for Hep Par-1. (Fig. 4).

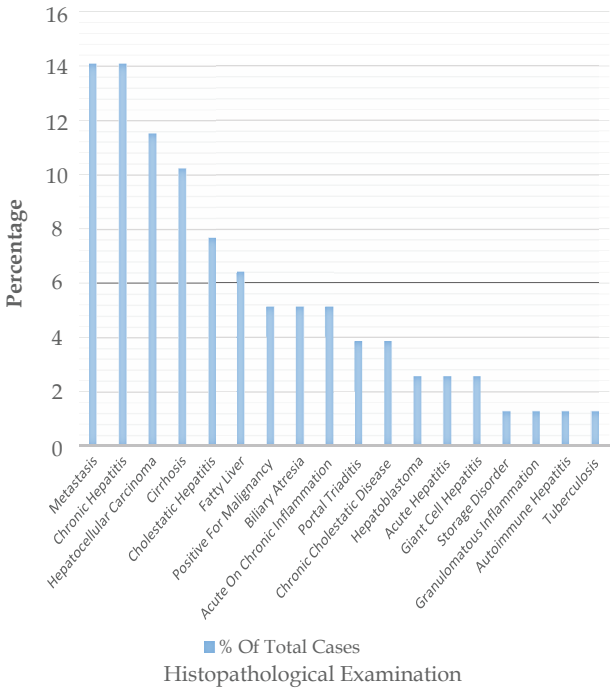


Fig. 3: Histopathological Examination of cases.

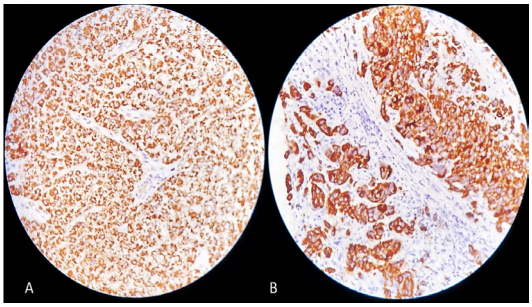


Fig. A showing Hep par-1 cytoplasmic staining and Fig. B showing CK20 membranous & cytoplasmic starining.

Fig. 4: IHC Hep Par-1 & CK20 (200x).

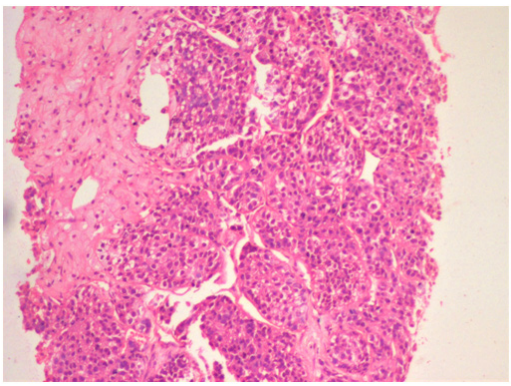


Fig. 5: H&E Hepatocellular carcinoma (HCC) (200x).

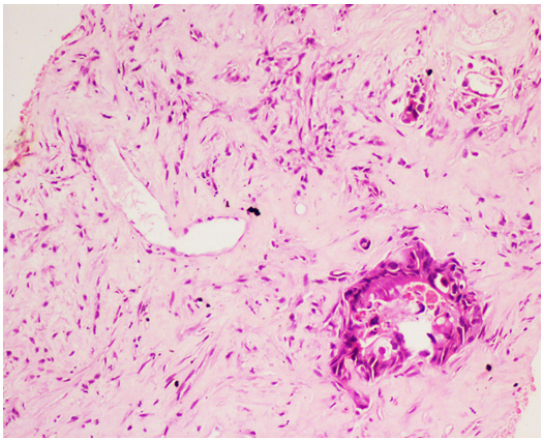


Fig. 6: H&E Adenocarcinoma (200x).

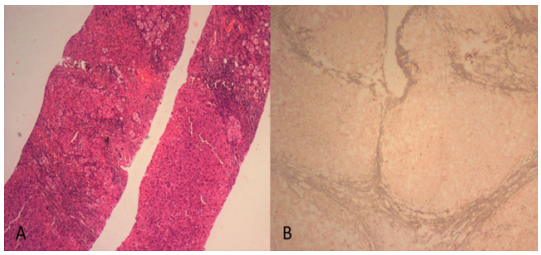
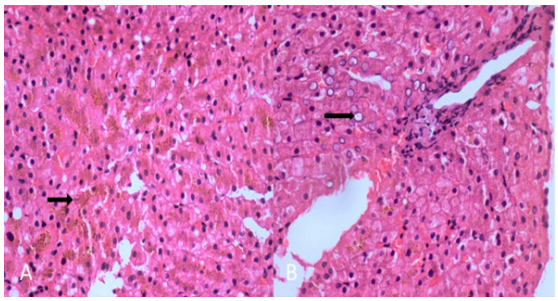


Fig. A shows Cirrhosis H&E (100x); Fig. B shows reticulin stain.

Fig. 7: H&E Cirrhosis with reticulin stain (200x).



Dubin Johnson syndrome. Fig. A showing diffuse deposition of coarse granular dark brown pigment in hepatocytes & Fig. B showing intranuclear cytoplasmic inclusions.

Fig. 8: H&E Dubin Johnson syndrome (200x).

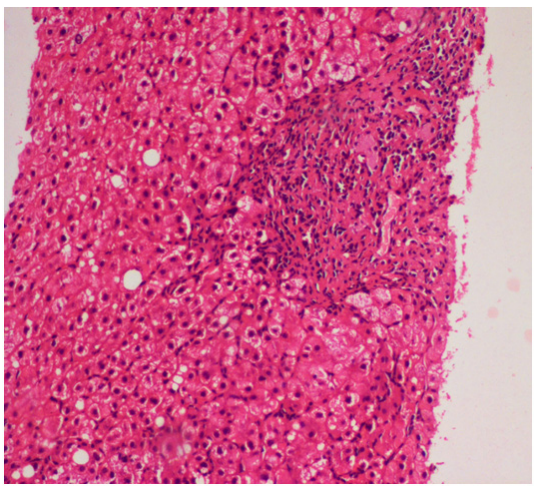


Fig. 9: H&E Chronic hepatitis (200x).

Majority of the lesions were in the age group of 41–50 years consisting of 15 total cases of which 14 were males and one case was female and majority of the lesions in this age group were cirrhosis and HCC. Most common histopathology finding in the age group 0–10 years was cholestatic hepatitis in females and extrahepatic biliary atresia and hepatoblastoma in males. Increased cases of malignancy were noted after the age of 50 years which included both HCC and metastatic tumors. Age and sex-wise distribution of various hepatic lesions are shown in (Table 2, Fig. 2). Spectrum of various histopathological lesions are shown in (Table 3, Fig. 3).

Discussion

Liver being affected by various primary and secondary diseases warrants an accurate diagnosis for patient management. Therefore, liver histopathology has become a most important diagnostic tool.[7] The spectrum of hepatic lesions varied from males to females as well as from infants to adults. In our study 25.31% of hepatic lesions were found in age group of 0–10 year.

In our study, the highest incidence of hepatic lesions were seen after age group of 30 years. This was probably due to increased alcohol intake, viral hepatic infections, obesity and other conditions during this period of life.[8,9]

In our study metastasis were found to be 14.10% the most commonly observed hepatic lesions were hepatic tumors and these results were in agreement with the other Indian study.[10] Hepatocellular carcinoma was found to be the most common hepatic lesion with the clinical features of abdominal pain, ascites, hepatomegaly. The common sites of primary tumours that frequently metastasizes to liver include lung, breast, gall bladder, stomach, pancreas, and large intestine.[11] Metastatic involvement of liver is more common than the primary hepatic tumours.[10] In present study the Hepatocellular carcinoma was the most common primary hepatic malignancy encountered in our study seen in 11.53% (n=9) cases (Fig. 5).

In our study, metastatic adenocarcinoma was the most frequent observation with primary tumours in gall bladder, stomach, pancreas, large bowel and breast. Adenocarcinoma shows irregular glandular pattern and surrounding desmoplasia in (Fig. 6).

The various etiological agents that cause cirrhosis include alcoholic liver disease, hepatitis B infection, hepatitis C infection, Wilson disease, malnutrition, Primary biliary cirrhosis, Secondary biliary

cirrhosis, and hemochromotosis. In present study the acute hepatitis was present in 2.56% of cases. Chronic hepatitis was present in 14.10% of cases. Our results were similar with the other studies.[10,12]

Cirrhosis was the third most common hepatic lesion seen in 10.25 % (n=8) cases. Gall et al has found the incidence of cirrhosis to be 6%.[13] Agarwal et al has found the incidence of cirrhosis were 12.3%.[12] The regenerative nodules of varying size from central to central portal of cirrhosis alongwith reticulin stain were shown in (Fig. 7).

Dubin-Johnson syndrome is caused by a mutation of ABCC2 encoding MRP2. Dubin-Johnson syndrome is characterized by conjugated hyperbilirubinemia without other serum enzyme abnormalities. One case of Dubin-Johnson syndrome was seen in 34 year old man. (Fig. 8).

The histologic findings are disease specific. However, in general, in hepatocellular causes of cholestasis, histology shows the presence of bile within hepatocytes and canaliculi spaces along with diffuse cholestatic injury pattern. While in the obstructive cholestatic pattern, histology shows bile plugging of interlobular bile ducts, portal expansion, and bile duct proliferation with mainly a centrilobular pattern of cholestatic injury. Retention of bilirubin (bilirubinostasis) can lead to stagnation of bile and bilirubin along cytoplasmic, canalicular, ductular or ductal regions, depending on the severity and duration of biliary obstruction.[14] In present study Cholestatic Hepatitis was seen in 6 (7.69%) of population. Bile duct changes are atypical of autoimmune hepatitis. Liver biopsy specimens were reviewed. Patients who satisfied international scoring criteria for autoimmune hepatitis, and the findings were correlated with clinical features and outcome.

In present study, four cases of extrahepatic biliary atresia were observed who presented with persistent jaundice. Similar cases (6.15%) were shown by Aggarwal et al.[12]

Conclusion

Liver biopsy is an essential, safe, reliable tool for the diagnosis, accurate assessment of severity and follow up of the various hepatic lesions. Liver biopsy continues to play an important role in modern clinical practice and remains the gold standard for the diagnosis of majority of the hepatic diseases. Microscopic examination of liver biopsy yields a diverse range of pathological findings. They are the most sensitive and specific means of evaluating the degree of liver cell injury and hepatic fibrosis. Liver biopsy provides information on the severity and distribution of lesions (codified in the staging and grading of chronic liver disease), the presence of confounding patterns of injury such as steatohepatitis coexisting with chronic viral hepatitis, and the presence of additional findings. It is most important investigation in reaching accurate diagnosis, detect cause and severity of liver diseases and in providing better treatment options. This information provides immense help in the diagnosis and prognostication of a variety of liver diseases. With careful selection of patients, and performance of the procedure appropriately, the complications become exceptionally rare in current clinical practice. Furthermore, the limitations of sampling error and inter-/ intra-observer variability may be avoided by obtaining adequate tissue specimen and having it reviewed by an experienced liver pathologist.

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