Original Article

Evaluating the Role of Liver Biopsy in Asymptomatic HBV Carrier

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Background: **The association between HBV asymptomatic carrier and liver histology is not well recognized. It is not uncommon to witness cirrhosis, hepatic decompensation and HCC in patients with HBV surface antigen (HBsAg) positive.**

Objective: **The main objective of this study is to determine the role of liver biopsy in asymptomatic HBV carrier to document the extent of liver damage.**

Place and Duration of Study: **The study was conducted at PIMS (Department of Gastroenterology) from august 2006 to august 2008.**

Materials and Methods: **It was a prospective study on outpatients with HBV asymptomatic carrier.The subjects with NASH/ NAFLD and history of treatment for CHB were excluded from study. All patients underwent liver biopsy using spinal needle 16Fr under local anaesthesia. Written informed consent was obtained.Prothrombin time and platelets counts were checked in every patient with in a week before procedure. Liver biopsy was done if baseline prothrombin time was no more than 3 seconds beyond control and platelets count was not less than 100x109/L.All patients were retained about 4 hours in hospital to observe any complication. The biopsies were scored using the modified HAI scoring system.**

Results: **The numbers of enrolled patients were 60 with (age ranging between 15-55 years). 44(73.3%) male and 16(26.6%) were females. Of 6(10%) patients with significant HAI-F≥2/ 6, 4 have stage HAI-F2 and 2 have HAI-F4 and all were male. Almost all patients 58/60 had some degree of HAI-NI on histology. We observed that ALT level and gender strongly affect histology but age had poor correlation with histology.**

Conclusion: **All patients with asymptomatic HBV carrier affected some degree of necroinflammation (HAI-NI) on histology significant number of patients also had advanced fibrosis. We recommend that assessment of liver biopsy specimens in a larger cohort of asymptomatic HBV carriers is necessary to establish management guidelines for such patients.**

Key Words: *HBV, Liver biopsy, carrier.*

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Introduction

Hepatitis B virus (HBV) infection and its sequelae are major global health problems.[1] It is estimated that 400 million people worldwide are HBV carriers.[2] Inactive carriers form the largest group in chronic HBV infected patients. Around 300 million people are inactive carrier.[5] The natural history of hepatitis B is complex and is influenced by many factors, including age at infection, viral factors(HBV genotype, viral mutations, level of HBV replication), host factors (gender, age, and immune status), and exogenous factors such as concurrent infection with other hepatotropic viruses or alcohol. The clinical spectrum of HBV infection ranges from subclinical to acute symptomatic hepatitis or, rarely, fulminant hepatitis during acute phase and from the inactive hepatitis B surface antigen (HBsAg) carrier state to chronic hepatitis, cirrhosis and its complications during the chronic phase.[3,4] The present study demonstrates the liver histology of asymptomatic HBV carrier.

Materials and Methods

This prospective study was conducted at PIMS (Department of Gastroenterology) from august 2006 to

august 2008. Outdoor patients with asymptomatic HBV carrier status were enrolled for study. We did not include patients with NASH/NAFLD and previously CHB treated patients. All patients were subjected to biochemical and radiological evaluation. Spinal needle was used for liver biopsy.

OPERATIONAL DEFINITIONS: Inactive HBV carrier: HBsAg+>6months, HBeAg-ve, anti-HBe+, HBV DNA<2,000IU/L, persistently normal ALT/AST levels and liver biopsy confirm absence of significant hepatitis. Chronic Hepatitis B: Chronic necroinflammatory disease of liver caused by persistent infection with HBV. HBsAg+> 6months, HBV DNA>20,000IU/L, 2,000-20,000 in HBeAg-ve, persistent/intermittent elevation in ALT/AST level and liver biopsy showing moderate/severe necroinflammation.

Results

Among 60 patients with asymptomatic HBV carrier status, 44 were male and 16 female (age 15-55 years).We diagnosed asymotomatic (inactive) HBV carrier on basis of HBsAg, HBeAg, anti HBe, HBV DNA level and ALT level. The approximate duration of these lab data were 1-3 years. Patient's characteristics are shown in table no I.

Table no I. Baselines characteristics

	Number	Variable	Number
Male	44	Female	16
Age Range	15-55 Years	Age	20-51 Years
ALT Range	20-30/30 30-40/14	ALT	18-28/12 30-40/4

The histological findings in female group revealed that 8/16 patients have HAI- F0 with minimal HAI- NI and 8/16 have HAI- F1 fibrosis with predominantly minimal HAI- NI as shown in figure no I. All female patients with HAI- F0 fibrosis have age < 30 years and ALT level <30 iu/l but patients with HAI- F1 fibrosis have age >35 years and 4/8 patients have ALT between 30-40iu/l.

All patients 6/60(10%) who have significant histology ≥HAI- F2 & HAI- NI mild were male. 4/6 patients with significant histology have age between 17-25 years and ALT level between 35-40iu/l. 2/6 patients with HAI- F4 and HAI- NI mild have age >50 years and ALT level between 35-40iu/l. 22/44 male patients with HAI- F0 have HAI- NI minimal. 16/44 male patients with HAI- F1 ,12/16 have minimal HAI- NI and 4/16 have mild NI. All male patients with HAI- F0/F1 fibrosis have age between 15-40 years as shown in figure II.

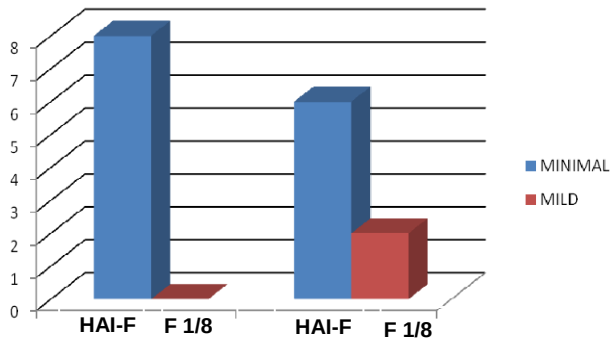

Figure I: Liver Biopsy and Histological Findings in Females

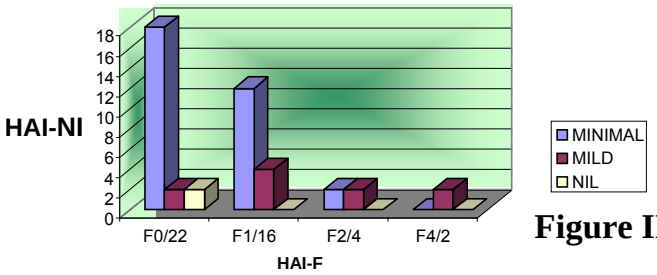

Figure II:

Figure II: Liver Biopsy and Histolgoical Findings in Male

Discussion

This study showed that liver biopsy in asymptomatic (inactive) HBV carrier, six patients revealed active disease but all were asymptomatic. In this study we used recent guidelines to define inactive HBV carrier.[5] Martinat-Peignoax et al found in their study that 98% patients with HBV carrier have mild degree of necroinflammation (HAI-NI).[6] We found in our study that almost all patients with HBV asymptomatic carrier have some degree of necroinflammation(NI).

We also found in our study that among males fluctuating level of ALT strongly correlate with activity of disease in asymptomatic HBV carrier but age has poor correlation with activity. Al-Mahtab M et al claimed that male sex and age older than 25 years correlated with disease activity[7]. Old age and alcohol intake are independent risk factor in inactive HBV carrier related deaths and HCC.[8] According to Villen et al long term follow up of HBV inactive carrier revealed low risk of HCC and cirrhosis.[9] Age and reactivation of inactive HBV carrier are two independent risk factors of cirrhosis in HBV carrier. [8, 10]

According to Kumar M et al 21% HBV inactive carrier have histological active disease (HAI>3&F>2).[11,15]

About 20% HBV carrier relapse in 25 years, relapse were frequent in earlier years of follow up. Male are more likely to relapse and less frequent below 30 years .[12]

Progression to cirrhosis in inactive HBV carrier is associated with sex, age and reactivation.[7,10]
Treatment of HBV asymptomatic (inactive) carrier is not recommended because available therapy does not affect HBsAg status.
Regular follow up 6 to12/months with ALT.[5,13]
If age>50 years and family history of HCC, AFP and ultrasound abdomin 6 to12/months.[14]

Universal precautions should be taken for pregnant women, vaccinate newborn with active and passive immunization and close monitoring if chemotherapy and immunosuppression required in HBV inactive carrier.

Limitations: Limitations of this study are that no local published data regarding liver biopsy in asymptomatic (inactive) HBV carrier is available and also limited international data were available.

Conclusion

The study demonstrates that features of liver damage were present in a considerable number of these patients. Assessment of liver biopsy specimens in a larger cohort of asymptomatic (inactive) HBV carriers is necessary to establish management guidelines for such patients.

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