Early diagnosis of Hepatitis B

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Abstract

Background

Chronic hepatitis B virus (HBV) infection affects about 296 million people worldwide and is the leading etiology of cirrhosis and liver cancer globally. Chronic hepatitis B has become a serious public health concern in China. Nonalcoholic fatty liver disease, or NAFLD, is one of the main causes of cirrhosis worldwide. The National Health and Nutrition Examination Survey found that advanced fibrosis was present in up to 10.3% of NAFLD patients. These results imply that considerable fibrosis, severe fibrosis, and cirrhosis can be evaluated using real-time shear wave elastography (SWE).

Objective

To determine the early diagnosis of hepatitis B virus

Methods

A cross-sectional study was conducted at Mardan Medical Complex, which was performed between January 2022 and october 2024, The total number of patients in our study was 100. In 100 consecutive patients who underwent Ultrasound (SWE) before their scheduled liver biopsy (48 men, 52 women). We used Michael Mindray ultrasound machine and its frequency was C6-1. The stages of liver fibrosis according to the METAVIR classification system. Data was analysed on SPSS version 27.

Results

According to our study total patients were 100, Distribution of patients according to gender was (48 were males and 52 were females). Distribution of patients according to mean age (out of 100 patients, 44.8983 were males and 48.9492 were females).

MEAN±SD of Alanine aminotransferase (ALT) was 91.6±113.14 u/L, MEAN±SD of Aspartate aminotransferase (AST) was 73.23±82.75 u/L, MEAN±SD of Alkaline phosphate (ALP) was 302.46±989.9 u/L, MEAN±SD of Total Bilirubin (TBIL) was 54.03±204.98 umol/L, MEAN±SD of bilirubin test (DBIL) was 7.18±21.3 umol/L, MEAN±SD of Gammaglutamyl transferase (GGT) was 162.80±711.1 u/L, MEAN±SD of Creatine kinase (CNE) was 4838.51±2187.2 u/L, MEAN±SD of Blood nitrogen urea (BUN) was 42.59±32.5 mmol/L, Distribution of patients on the basis of hepatitis B (n=100)

In male patients the frequency was 35 with a percentage 78.0 and in female it was 44 with a percentage of 84.7. Hepatitis B was not found in 13 male with a percentage of 22.0 and it was not found in eight female patient with a percentage 15.3.

P-value of stages of Liver fibrosis with respect to gender is 0.005.

Conclusion

Our result concluded that fibrosis stage F3 patients are more in our study (Heaptitis B). Liver fibrosis is more common in females as compared to males. According to the age males have higher risk as compared to females. Diagnosis of HBV infection on ultrasound is an important tool for determining acute, chronic hepatitis. Ultrasound is a straightforward, quick, and repeatable technique for noninvasively assessing Hepatitis B and liver fibrosis. Benefits include its low cost and global availability.

Keywords: Ultrasound (US), Liver fibrosis, Hepatitis B (HBV) and Fine needle biopsy.

Introduction

The Hepadnaviridae family includes the hepatitis B virus (HBV). It has a diameter of 30–42 nm and is made up of an icosahedral capsid core made of protein [1] and an outer lipid envelope that contains the hepatitis B surface antigen (HBsAg). The viral genome and reverse transcriptase-active DNA polymerase are found in the viral capsid. The circular, partially double-stranded DNA that makes up the HBV genome overlaps four open reading frames: Surface proteins (HBsAg) are encoded by (I) S; hepatitis B e antigen (HBeAg) and core protein (HBcAg) by (II) pre-C/C; polymerase, including reverse transcriptase, is encoded by (III) P; and a transcriptional transactivator factor (HBxAg) is encoded by (IV) X [2]. The transcriptional template of HBV is covalently closed circular DNA (cccDNA), which remains inside the hepatocyte nucleus as a miniature chromosome [3]. Similar to retroviruses and RNA viruses, the reverse transcriptase involved in HBV replication is prone to errors, which results in a high mutation rate [4,5].

The majority of chronic liver illnesses in the world are caused by HBV infection, which can spread vertically, sexually, and parenterally. About 240 million people have a chronic HBV infection, which increases their risk of developing hepatocellular carcinoma (HCC) and liver cirrhosis. HBV endemicity is classified as high, midrange, or low based on HBsAg prevalence. Because chronic HBV infection is documented in over 8% of the population, China, South East Asia, Indonesia, and sub-Saharan Africa are considered highly endemic regions [6]. South America, South West Asia, and Eastern and Southern Europe are examples of intermediate regions with chronic HBV infection rates ranging from

2% to 7% of the population. Low endemic zones include developed nations like Western Europe and North America, where HBV prevalence rates range from 0.5% to 2%.

The detection of acute, chronic, and occult HBV infection is an important way to reduce the burden of this disease in addition to aggressive anti-HBV vaccination. This article will examine the molecular and serological diagnosis of HBV.

MATERIALS AND METHODS

A cross-sectional study was conducted at Mardan Medical Complex, which was performed between January 2022 and october 2024, The total number of patients in our study was 100. In 100 consecutive patients who underwent Ultrasound (SWE) before their scheduled liver biopsy (48 men, 52 women). We used Michael Mindray ultrasound machine and its frequency was C6-1. The stages of liver fibrosis according to the METAVIR classification system. Data was analysed on SPSS version 27.

Inclusive criteria: Include all individuals who have Hepatitis B

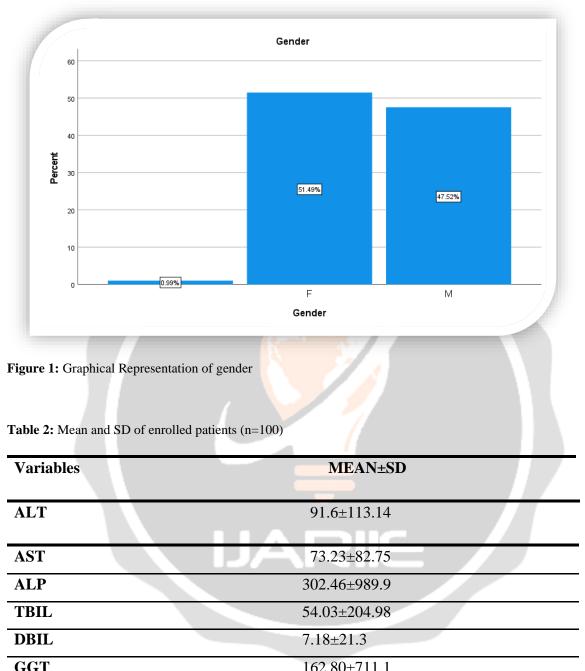
Exclusive Criteria: Exclude children and pregnant ladies

Results

Table 1: Distribution of patients according to gender and mean age (n=100)

Variable	Frequency	Percentage
Gender:		
Male	48	100.0
Female	52	100.0
Total	100	100%
	Mean	SD
Age		
Male	44.8983	12.16
Female	48.9492	16.92
Total Age	46.92	14.71

According to our study total patients were 100, Distribution of patients according to gender was (48 were males and 52 were females). Distribution of patients according to mean age (out of 100 patients, 44.8983 were males and 48.9492 were females). Distribution of patients according to mean age of standard deviation (12.16 were males and 16.92 were females). Graphical Representation of gender represent that both gender are same in number 48 were males and 52 were females.



001	102.00±/11.1
CNE	4838.51±2187.2
BUN	42.59±32.5

Mean and Standard Deviation (SD) of liver Function

MEAN±SD of Alanine aminotransferase (ALT) was 91.6±113.14 u/L, MEAN±SD of Aspartate aminotransferase (AST) was 73.23±82.75 u/L, MEAN±SD of Alkaline phosphate (ALP) was 302.46±989.9 u/L, MEAN±SD of Total

Bilirubin (TBIL) was 54.03±204.98 umol/L, MEAN±SD of bilirubin test (DBIL) was 7.18±21.3 umol/L, MEAN±SD of Gamma-glutamyl transferase (GGT) was 162.80±711.1 u/L, MEAN±SD of Creatine kinase (CNE) was 4838.51±2187.2 u/L, MEAN±SD of Blood nitrogen urea (BUN) was 42.59±32.5 mmol/L,

Table 3: The mean BMI of enrolled patients (n=100)

BMI	23.85±4.18

Table 4: The stages of fibrosis according to the METAVIR classification system (n=100)

Stages of fibrosis	Frequency	Percentage
F0	27	28.0
F1	4	4.2
F2	51	49.2
F3	10	11.6
F4	8	7.0
F0= no portal fibrosis;		

F1= perisinusoidal or portal/periportal fibrosis;

F2= both perisinusoidal and portal/periportal fibrosis;

F3= bridging fibrosis;

F4= cirrhosis.

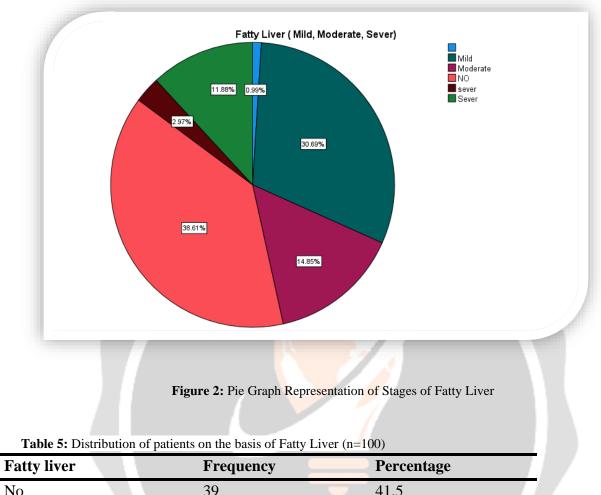
The stages of Liver fibrosis according to the METAVIR classification system (n=100),

The frequency of patients with F0 was 27 (28.0 %), The frequency of patients with F1 was 4 (4.2%)

The frequency of patients with F2 was 51 (49.2%), The frequency of patients with F3 was 10 (11.6%)

The frequency of patients with F4 was 8 (7.0%)

In the above pie graph F2: 49%, F0: 28%, F4: 11%, F3: 8% and F1: 4%.



-		_
No	39	41.5
Mild	31	33.1
Moderate	16	18.8
Severe	14	6.6
Total	100	100.0

Distribution of patients on the basis of Fatty Liver (n=100). Frequency of no fatty liver was 39 and its percentage was 41.5 %. Frequency of mild fatty liver was 31 and its percentage was 33.1 %. Frequency of moderate fatty liver was 16 and its percentage was 18.8 %. Frequency of sever fatty liver was 14 and its percentage was 6.6 %.

Table 6: Distribution of patients on the basis of Liver Fibrosis and Hep B (n=100)

Hepatitis	Frequency	Percentage	
Liver Fibrosis			
YES	86	81.4	
NO	14	18.6	

Hep B			
YES	64	77.3	
NO	36	23.7	

Hep= Hepatitis

The frequency of liver fibrosis was found in 86 patients and its percentage was 81 .4. The frequency of liver fibrosis was not found in 14 patients and its percentage is 18.6. The frequency of hepatitis B was found in sixty-four patients and its percentage was 77.3. The frequency of hepatitis B was not found in 36 patients and its percentage was 23.7.

	Liver Fibr	osis	
Gender	Frequency	Percentage	P-Value
MALE			
YES	51	98.3	_
NO	1	1.7	0.004
FEMALE			— 0.004 — Not
YES	47	98.3	significant
NO	1	1.7	
	Hepatitis B		
Male			
YES	35	78.0	0.002
NO	13	22.0	
Female			Not
YES	44	84.7	significant
NO	8	15.3	

Table 7: Distribution of patients on the basis of Liver Fibrosis and Hep B with respect to gender (n=100)

Distribution of patients on the basis of liver fibrosis (n=100)

The frequency of liver fibrosis in male patients was 51 with a percentage 98.3 and in female it was 47 with a percentage 98.3. It was not present in one male and one female with a percentage 1.7.

Distribution of patients on the basis of hepatitis B (n=100)

In male patients the frequency was 35 with a percentage 78.0 and in female it was 44 with a percentage of 84.7. Hepatitis B was not found in 13 male with a percentage of 22.0 and it was not found in eight female patient with a percentage 15.3.

Discussion

High serum aminotransferases, symptoms, and the presence of HBsAg are the clinical indicators of acute hepatitis B. Typically, HBV DNA is found along with anti-HBc IgM. Although it has no clinical significance, HBeAg can also be detected in the majority of acute infection phases. When HBsAg remains present for longer than six months, a chronic infection is diagnosed. It is more frequent to diagnose patients with persistent HBV infection by laboratory testing rather than clinical manifestations. The coexistence of IgG anti-HBc and anti-HBs indicates a history of HBV infection.

Low levels of intrahepatic HBV DNA that persist without detectable HBsAg are indicative of an occult HBV infection [7,8]. The existence of isolated anti-HBc and the lack of HBsAg and anti-HBs antibodies characterize this serological scenario [9,10]. Since cccDNA stays in the hepatocytes and HBV DNA is sometimes found in the liver but not in the serum, the gold standard of diagnosis for occult HBV infection is the detection of HBV DNA in the liver. However, because the process is invasive, obtaining hepatic HBV DNA in a clinical environment is challenging. HBV DNA testing is frequently used to diagnose occult HBV infection since real-time PCR for serum HBV DNA detection has been demonstrated to have sufficient sensitivity to identify occult HBV infection in many patients [8]. There is some clinical significance to occult HBV infection. Transfusion, solid organ transplantation, particularly orthotopic liver transplantation [11,12], or hemodialysis [13,14] are the first ways it can spread. Second, patients undergoing chemotherapy or in immunocompromised states may experience reactivation of their HBV infection [15–17]. Third, in patients with chronic liver illness, such as those with a chronic hepatitis C infection, it may hasten liver damage and cause hepatic fibrosis [18–20]. Furthermore, because of its carcinogenic impact and ability to cause persistent hepatic inflammation and fibrosis, it seems to be a risk factor for HCC [21-23].

Due to the potential for transmission, tests for occult HBV infection are taken into consideration in the following situations: patients with cryptogenic liver disease, particularly if their serum contains anti-HBc; patients contemplating immunosuppressive therapy or chemotherapy; and solid organ transplant donors [24].

The viral load, which indicates the virus's reproduction activity, can be directly measured using HBV DNA. It can be seen at the earliest stage of infection (one month after HBV infection), rises to a peak level (more than 108 copies/mL) about three months after HBV exposure, and then either steadily declines in chronic infections or vanishes throughout the healing process. HBV-DNA detection has gained significant attention in clinical medicine as the prevalence of serologically negative HBV infection (occult HBV infection and HbeAg-negative CHB) has grown [25]. Higher titers of HBV DNA are linked to a higher incidence of HCC and a faster rate of disease development, and their detection is a trustworthy indicator of replication activity [26]. Additionally, HBV DNA testing helps identify patients who require antiviral therapy and track them for appropriate treatment in a routine clinical environment [27].

Because HBV reproduces by a reverse transcriptase with inadequate proofreading abilities, it exhibits a significant genomic heterogeneity. Ten genotypes of HBV, designated A–J, may be distinguished based on sequence divergence; each has a unique geographic distribution [28]. While genotypes A and D are widespread but most prevalent in Africa and Europe, genotypes B and C are limited to Oceania and Asia [29]. While genotype J has been documented in Japan and Ryukyu, genotype I is uncommon and found in Vietnam, Laos, India, and China [30,31]. In Asia, other genotypes like E, F, G, and H are also sometimes observed.

CONCLUSION

Our result concluded that fibrosis stage F3 patients are more in our study (Heaptitis B). Liver fibrosis is more common in females as compared to males. According to the age males have higher risk as compared to females. Diagnosis of HBV infection on ultrasound is an important tool for determining acute, chronic hepatitis. Ultrasound is a straightforward, quick, and repeatable technique for noninvasively assessing Hepatitis B and liver fibrosis. Benefits include its low cost and global availability.

References:

[1] Takahashi T, Nakagawa S, Hashimoto T, et al. Large-scale isolation of Dane particles from plasma containing hepatitis B antigen and deomnstration of circular double-stranded DNA molecule extruding directly from their cores. J Immunol 1976;117:1392-7.

[2] Kramvis A. Genotypes and genetic variability of hepatitis B virus. Intervirology 2014;57:141-50. 10.1159/000360947

[3] Locarnini S, Zoulim F. Molecular genetics of HBV infection. Antivir Ther 2010;15 Suppl 3:3-14. 10.3851/IMP1619

[4] Ganem D, Schneider RJ. Hepadnaviridae: the viruses and their replication. Fields Virology 2001;2:2923-69.

[5] Simmonds P. Reconstructing the origins of human hepatitis viruses. Philos Trans R Soc Lond B Biol Sci 2001;356:1013-26. 10.1098/rstb.2001.0890

[6] Ott JJ, Stevens GA, Groeger J, et al. Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBsAg seroprevalence and endemicity. Vaccine 2012;30:2212-9. 10.1016/j.vaccine.2011.12.116

[7] Hollinger FB, Sood G. Occult hepatitis B virus infection: a covert operation. J Viral Hepat 2010;17:1-15. 10.1111/j.1365-2893.2009.01245.x

[8] Raimondo G, Allain JP, Brunetto MR, et al. Statements from the Taormina expert meeting on occult hepatitis B virus infection. J Hepatol 2008;49:652-7. 10.1016/j.jhep.2008.07.014

[9] Grob P, Jilg W, Bornhak H, et al. Serological pattern "anti-HBc alone": report on a workshop. J Med Virol 2000;62:450-5.

[10] Weber B, Melchior W, Gehrke R, et al. Hepatitis B virus markers in anti-HBc only positive individuals. J Med Virol 2001;64:312-9. 10.1002/jmv.1052

[11] Raimondo G, Caccamo G, Filomia R, et al. Occult HBV infection. Semin Immunopathol 2013;35:39-52. 10.1007/s00281-012-0327-7

[12] Mahboobi N, Tabatabaei SV, Blum HE, et al. Renal grafts from anti-hepatitis B core-positive donors: a quantitative review of the literature. Transpl Infect Dis 2012;14:445-51. 10.1111/j.1399-3062.2012.00782.x

[13] Minuk GY, Sun DF, Greenberg R, et al. Occult hepatitis B virus infection in a North American adult hemodialysis patient population. Hepatology 2004;40:1072-7. 10.1002/hep.20435

[14] Yoo JH, Hwang SG, Yang DH, et al. Prevalence of occult hepatitis B virus infection in hemodialysis patients. Korean J Gastroenterol 2013;61:209-14. 10.4166/kjg.2013.61.4.209

[15] Kusumoto S, Tanaka Y, Mizokami M, et al. Reactivation of hepatitis B virus following systemic chemotherapy for malignant lymphoma. Int J Hematol 2009;90:13-23. 10.1007/s12185-009-0359-5

[16] Onozawa M, Hashino S, Izumiyama K, et al. Progressive disappearance of anti-hepatitis B surface antigen antibody and reverse seroconversion after allogeneic hematopoietic stem cell transplantation in patients with previous hepatitis B virus infection. Transplantation 2005;79:616-9. 10.1097/01.TP.0000151661.52601.FB

[17] Yeo W, Johnson PJ. Diagnosis, prevention and management of hepatitis B virus reactivation during anticancer therapy. Hepatology 2006;43:209-20. 10.1002/hep.21051

[18] Squadrito G, Cacciola I, Alibrandi A, et al. Impact of occult hepatitis B virus infection on the outcome of chronic hepatitis C. J Hepatol 2013;59:696-700. 10.1016/j.jhep.2013.05.043

[19] Kannangai R, Vivekanandan P, Netski D, et al. Liver enzyme flares and occult hepatitis B in persons with chronic hepatitis C infection. J Clin Virol 2007;39:101-5. 10.1016/j.jcv.2007.03.006

[20] Covolo L, Pollicino T, Raimondo G, et al. Occult hepatitis B virus and the risk for chronic liver disease: a meta-analysis. Dig Liver Dis 2013;45:238-44. 10.1016/j.dld.2012.09.021

[21] Squadrito G, Pollicino T, Cacciola I, et al. Occult hepatitis B virus infection is associated with the development of hepatocellular carcinoma in chronic hepatitis C patients. Cancer 2006;106:1326-30. 10.1002/cncr.21702

[22] Obika M, Shinji T, Fujioka S, et al. Hepatitis B virus DNA in liver tissue and risk for hepatocarcinogenesis in patients with hepatitis C virus-related chronic liver disease. A prospective study. Intervirology 2008;51:59-68. 10.1159/000121363

[23] Shi Y, Wu YH, Wu W, et al. Association between occult hepatitis B infection and the risk of hepatocellular carcinoma: a meta-analysis. Liver Int 2012;32:231-40. 10.1111/j.1478-3231.2011.02481.x

[24] Valsamakis A. Molecular testing in the diagnosis and management of chronic hepatitis B. Clin Microbiol Rev 2007;20:426-39, table of contents. 10.1128/CMR.00009-07

[25] Datta S, Chatterjee S, Veer V. Recent advances in molecular diagnostics of hepatitis B virus. World J Gastroenterol 2014;20:14615-25. 10.3748/wjg.v20.i40.14615

[26] Chen CJ, Yang HI, Su J, et al. Risk of hepatocellular carcinoma across a biological gradient of serum hepatitis B virus DNA level. JAMA 2006;295:65-73. 10.1001/jama.295.1.65

[27] Chevaliez S, Pawlotsky JM. Diagnosis and management of chronic viral hepatitis: antigens, antibodies and viral genomes. Best Pract Res Clin Gastroenterol 2008;22:1031-48. 10.1016/j.bpg.2008.11.004

[28] Lin CL, Kao JH. The clinical implications of hepatitis B virus genotype: Recent advances. J Gastroenterol Hepatol 2011;26 Suppl 1:123-30. 10.1111/j.1440-1746.2010.06541.x

[29] Zehender G, Ebranati E, Gabanelli E, et al. Enigmatic origin of hepatitis B virus: an ancient travelling companion or a recent encounter? World J Gastroenterol 2014;20:7622-34. 10.3748/wjg.v20.i24.7622

[30] Li GJ, Hue S, Harrison TJ, et al. Hepatitis B virus candidate subgenotype I1 varies in distribution throughout Guangxi, China and may have originated in Long An county, Guangxi. J Med Virol 2013;85:799-807. 10.1002/jmv.23533

[31] Shi YH. Correlation between hepatitis B virus genotypes and clinical outcomes. Jpn J Infect Dis 2012;65:476-82. 10.7883/yoken.65.476.