A Descriptive Study of Iraqi Patients WithHBsAgSeropositivity Attending the Gastroenterology & Hepatology Teaching Hospital

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ABSTRACT

Background:Chronic infection with the hepatitis B virus (HBV) is endemic in Asian countries including Iraq. Few studies have analyzed the clinical and laboratory aspects of this disease in Iraq. **Objectives**:This study aims to define the demographic, clinical, virological, and biochemical features of Iraqi patients with chronic hepatitis B virus infection.**Methods**: in this retrospective study we took 219 patients referred from Baghdad and other governorates to the gastroenterology and Hepatology Teaching Hospital from 1/1/2011 to 30/12/2012 . History, clinical examination, biochemical, serological, and virological tests as well as abdominal ultrasound were available to all patients. Liver biopsy was performed in 52 (24%) patients as indicated by guidelines. **Results**:From a total of 219 patients, 141 (64.4%) patient were male and 78(35.6%)were female with a male to female ratio of (1.8:1). Median age was 35.8 ± 14.1 years. Twenty eight (13%) were HBeAg positive. Viral load was significantly higher in patients less than 40 years of age and those with HBeAg positivity. Positive family history reported in 20 (9%) cases, and symptoms were presented in 22 patients(13%). In patients who had a liver biopsy done, 36(16%) cases had significant fibrotic changes. **Conclusion**:Most of the HBsAg positive patients are asymptomatic at the time of referral. Household contacts are positive in many cases regardless of the mother HBsAg status. Significant hepatic fibrosis can be present despite young age and normal routine liver function tests.

Introduction:

In 1965, Blumberg et al reported the discovery of the hepatitis B surface antigen (HBsAg), also known as Australia antigen,Hepatitis B virus belongs to the family of hepadnaviruses,It is an extremely resistant strain capable of withstanding extreme temperatures and humidity, HBV can survive when stored for 15 years at 20°C, for 24 months at 80°C, for 6 months at room temperatures, and for 7 days at 44°C[1]. Hepatitis B is a worldwide healthcare problem, especially in developing areas. An estimated one third of the global population has been infected with the hepatitis B virus (HBV). Approximately 350 million people are lifelong carriers, and only 2% spontaneously seroconvert annually.Fulminant hepatic failure is unusual, occurring in approximately 0.1 to 0.5 percent of patients. Fulminant hepatitis B is believed to be due to massive immune-mediated lysis of infected hepatocytes. This explains why many patients with fulminant hepatitis B have no evidence of HBV replication at presentation [2]

The rate of progression from acute to chronic hepatitis B is determined primarily by the age at infection. The rate is approximately 90 percent for a perinatally acquired infection, 20 to 50 percent for Infections between the age of one and five years, and less than 5 percent for an adult-acquired infection[3,4]

Aim of the study

1-Illustrate the demographic, clinical, and laboratory parameters of Iraqi patients with chronic hepatitis B and correlate them to the findings on liver biopsy.

2-Compare the demographic and laboratory data of Iraqi patients with chronic hepatitis B to patients from other parts of the World.

Patients and Methods

In this retrospective study, Records of all patients presenting with positive HBsAg, whether symptomatic or asymptomatic, who attended the GIT hospital over a 2 year period (Jan 2011 to Dec 2012) were collected. All patients have at least 2 positive HBsAg tests more than 6 months apart. Aspects included in the study included the patient's demographics, clinical features, HBeAg status, viral load, aminotransferase levels at first presentation, as well as the result of histopathology report of liver biopsy when available.Patients with HCV coinfection and those with a well-established diagnosis of chronic liver disease unrelated to HBV as well as alcoholics, diabetics, and obese patients, were excluded even if they had a positive HBsAg test.

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Viral load was obtained using b-DNA technology assay and Liver biopsy was done by sterile reusable True Cut® needle according to the guidelines (AASLD/ American association for the study of liver disease).Histopathological changes on liver biopsy considered significant when fibrosis score (=2) according to ISHAK scoring system.

Results:

A total of 219 patients were included in the study, consisted of 141 males (64.4%) and 78 females (35.6%). The age ranging from 2 to 71 years and the mean age (±SD) was 35.8 ± 14.1 years. The mean age of male and female patients was the same (35.8 ± 14). Among the male patients, 79 (56%) were under age of 40 years, and 62 (44%) were more than 40. while female patients were 78(35.6%), 51(65%) were below 40, while 27 (35 %) were above 40.

Out of 219 patients, 170 (78%) were HBeAg negative and only twenty eight (13%)had HBeAg positive test.Features of Chronic liver disease were seen in 22(13%) patients,4 patients(2%) presented with stigmata of chronic liver disease, 3 patients(1%) presented with variceal bleeding, 1 patient(0.4%) has hepatocellular carcinoma, 14 patients(6%)presented with jaundice.Among those patients 15(63%) patients were below the age of 40. (table 1&2).

Among 170 (78%) negative HBeAg patients, 110 (65%) patients had VL >2000 IU/ml. while the 28(13%)HBeAg positive patients, 26 (93%) from them had VL >20000 IU/ml, 20 (72%) from them were under age of 40 (figure 1).

Viral load(VL) in HBeAg positive patients is heigher than HBeAg negative patients (P value < 0.001), and no significant difference between male and female (figure 3).Higher level of VL were seen in patients who are below 20 years (P value <0.05). (figure 2)Fifty two (24%) out of all study group (219) patients underwent liver biopsy: Of 52 patients underwent liver biopsy, 32(62%) were male patients, significant fibrosis was reported in 21(65%) cases. While female patients were 20(38%), significant fibrosis were reported in 15(75%).table 3.Figures (3) and (4) shows the correlation between the ALT value and the viral load in patients older and younger than 40 years of age, respectively.

P value was significant in those above 40 years (P= 0.001), no significant association in those below 40 (P<0.129)

Clinical feature	No. %
Chronic liver disease	**22(13%)**
Coarse texture liver, splenomegaly, esophageal varices ,ascites.	4 (2%)
GIT bleeding	3 (1%)
Hepatocellular carcinoma	1(0.4%)
Jaundice	14(6%)

Table 1: features of chronic liver disease.

No.(%)	age	No.	HBeAg +	
Male 14(63%)	<40 ..	9(36%) 5(23%)	1(0.04%) 2(0.08%)	9(36%) 3(0.12%)
Female 8(37%)	<40 e 40	6(27%) 2(9%)		6(27%) 2(9%)

Table2: clinical findings in relation to age and HBeAg status.

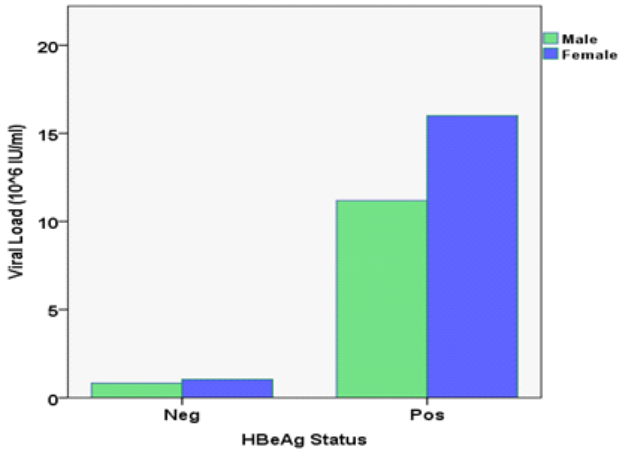

Figure 1 .
Viral load according to HBeAg status and gender

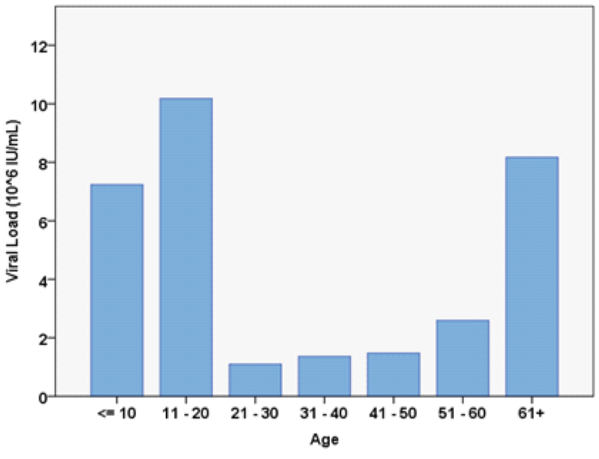

Figure 2.
Viral load according to the age

Gender	Age (years)	Necroinflammation* (0-18)		Significant* Fibrosis (e 2)	
		Minimal - Mild 0 - 8	Moderate - Severe 9 - 18	Male	Female
Males 32 patients	<40 17 (33%) e40 15 (28%)	17 15		**9** **12**	
Females 20 patients	<40 13 (25%) e40 7 (14%)	11 6	2 1	**2** **4**	**10** **5**
Total 52 patients		**49 (94%)**	**3 (6%)**	**21 (40%)**	**15 (28%)**

Table3 : liver biopsy result in relation to gender and age ,P value(0.17)

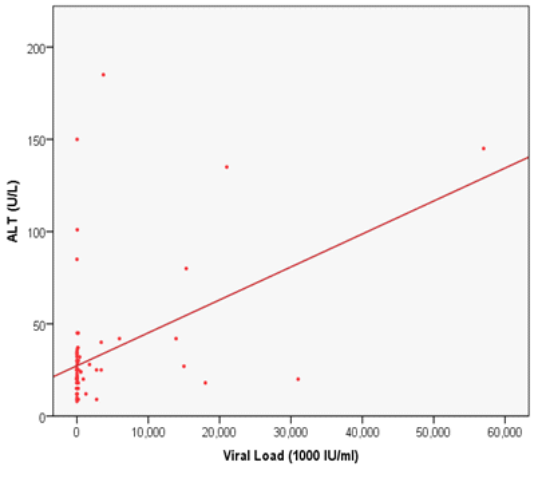

Figure 3.VL & ALT level in patients > 40
P value = 0.001

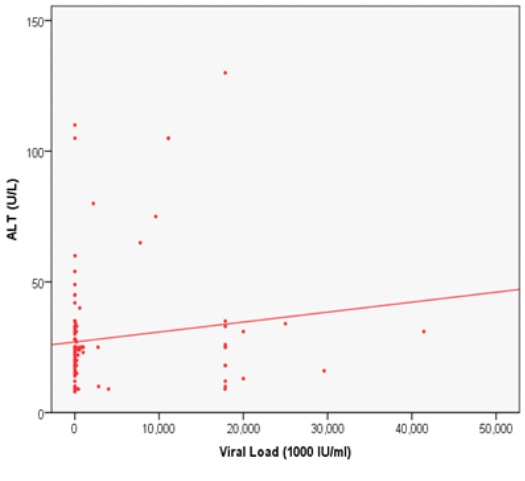

Figure 4.VL & ALT in patients < 40.
p value=0.12

Discussion :

From the total 219 patients enrolled in this study, we found that 141(64.4%) were males and 78 (35.6%) werefemales and this probably due to the higher exposure to occupationalHBV risk factors in males or else females clear the HBV more efficiently as compared to males. In our countrythe screening for hepatitis B in male is more than female due to blood donation, data from Iraqi national blood bank revealed that the HBsAgfemale to male ratio (blood donation) was ranged from 1:5 to 1:10, which was similar to a research done in our hospital at 1996[5].

Features of chronic liver disease were reported in 22 (13%) patients, The world data of symptomatic icteric disease is around 30% [6,7].

HBeAg negative in (170 (78%)) patients, and only 28 (13%) patients were HBeAg positive. In a study carried out in Iran the prevalence of HBeAg was (16.3%)[8].In a study carried out by Chia-Ming Chu et al; in Taiwan 19.6% of the patients were HBeAg+ve[9]. whether this is due to loss of HBeAg with age or precore mutation still needs further study, the HBeAg prevalence is highest among young age group[8, 10, 11].The patient's ALT values were significantly correlated to the viral load only in patients who are 40 years of age or older ($p<0.001$),Elevated ALT can reflect active necroinflammation but a normal ALT does not mean a normal histology[11].

Conclusion :

Most of the cases of hepatitis B referred to this hospital are males aged 20 to 50 years with asymptomatic HBeAg negative chronic hepatitis B.About one half of patients with significant fibrosis on liver biopsy are younger than 40 years of age. If this finding was confirmed in larger studies, this might lead to reconsideration of the age of 40 years as an approximate age after which immune tolerance gives way to active hepatitis.

Recommendations :

When we applied the American and European guidelines on Iraqi patients and we follow those patients, many of them came later with advance disease, and as mentioned before that Asian patients might differ from western patient in immune response, environmental factors, genetics, core and pre-core mutation, and different genotypes. So that we suggest to put a modified guidelines for the management of Iraqi patients.

References :

1. Blumberg BS. Australia antigen and the biology of hepatitis B. *Science*. Jul 1 1977;197(4298):17-25.
2. Wright TL. Mamish D. Combs, et al. Hepatitis B virus and apparent fulminant non- A, non-B hepatitis. Lancet 1992; 339:952.
3. Beasley RP, Hwang LY, L in CC, et al. Incidence of hepatitis B virus infections in preschool children in Taiwan.J Infect Dis 1982;146:198.
4. Coursaget P, Yvonnet B, Chotard J, et al. Age - and sex-related study of hepatitis B virus chronic carrier state in infants from an endemic area (Senegal).J Med Virol 1987;22:1.
5. JasimM.Ghadban Al-Maliki, prevalence of serological markers of hepatitis B surface antigen(HBsAg) and hepatitis c virus antibody(HCV Ab) among blood donors and certain risk groups(J.fac. Baghdad 2000, vol.42.1).
6. Chronic viral hepatitis; diagnosis and therapeutics;Raymond S. Koff,George Y. Wu,2002.
7. Liaw, YF, Tsai, SL, Sheen, IS, et al. Clinical and virological course of chronic hepatitis B virus infection with hepatitis C and D virus markers. Am J Gastroenterol 1998; 93:354.
8. *M.R. Fattahi, R. Keshavarz,* Hepatitis B "e" Antigen (HBeAg) Status and Its Relation to Transaminase Level in Patients Chronically Infected with Hepatitis B Surface Antigen (HBsAg) in Southwestern Iran (1999-2001), journal of medical research,2004,3:27-28
9. Chia-Ming Chu, I-Shyan Sheen, Shi-Ming Lin,et al. Sex Difference in Chronic Hepatitis B Virus Infection: Studies of Serum HBeAg and Alanine Aminotransferase Levels in 10,431 Asymptomatic Chinese HBsAgCarriers.Clinical Infectious Diseases 1993;16:709-13.
10. EASL clinical practice guidelines : management of chronic hepatitis B journal of hepatology 50(2009) 227-242.
11. Fujiwara A, Sakaguchi K, Fujioka S, Iwasaki Y, Senoh T, Nishimura M, *et al.* Fibrosis progression rates between chronic hepatitis B and C patients with elevated alanine aminotransferase levels. *J Gastroenterol*2008; Haresh Mani, David E. Kleiner[‡,*]Article first published online: 27 APR 2009 DOI: 10.1002/hep.22930 Copyright © 2009 American Association for the Study of Liver Diseases