A PRELIMINARY STUDY OF HEPATITIS B VIRUS GENOTYPES IN CHRONIC HEPATITIS B PATIENTS

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Abstract:
Aims: To study the prevalence of HBV genotypes in chronic hepatitis B patients and their relationship with some clinical and biochemical characteristics. **Methods:** 60 patients were enrolled in this study from 01/2009 to 06/2010. Clinical, laboratory data were collected at the hospitalized time. Sera were tested for HBeAg, HBV DNA quantitative. HBV genotyping was made by Real-time PCR. **Results:** Among the 60 patients, 38 patients (63.3%) had genotype B, 16 (26.7%) had genotype C and 6 have mixed genotype B-C (10%). Genotype B was predominant in group under 30 yrs (47.4%), but genotype C in group > 30-40 yrs (50%). 43.8% pts of genotype C had fatigue. About 50% of genotype C but only 31% of genotype B had ALT level higher than 5 times upper limit. In genotype C group, 41.7% patients had HBV DNA level higher than 10^7copies/ml. **Conclusions:** Most of the patients had genotypes B or C. In patients with CHB, patients of genotype C tended to have more severe necroinflammation and higher serological HBV DNA level than genotype B.

1. INTRODUCTION

Hepatitis B virus genotypes were first detected by Okamoto (Japan, 1988). Nowadays, there are 8 genotypes, designed from A to H. In the last two years, 2 new genotypes (I and J) were found in some other countries. Some studies showed HBV genotypes had relationships with prognosis and outcome of hepatitis B. HBV genotypes may be also the predictive factors of response to antiviral therapy of hepatitis B.

There are some studies about epidemiology and clinical significance of HBV in Vietnam. But there is no study about HBV genotypes in patients with chronic hepatitis B (CHB) in Central Vietnam.

Aims of study:

- To study prevalence of HBV genotypes in CHB patients in Central Vietnam.

- To study the relationship of HBV genotypes to some clinical, and biochemical characteristics.

2. PATIENTS AND METHODS

2.1. Patients

All the patients over 15 years old, admitted to Hue University Hospital with a diagnosis of chronic hepatitis B from Jan. 2009 to June 2010.

Inclusion criteria: history of HBV infection over 6 months, or HBsAg(+) và anti-HBc IgG(+), elevated transaminase over 2 times the upper limit.

2.2. Methods: Prospective analysis. HBV gentoype identified by Real-time PCR on Real-time PCR Stratagene Mx 3000, Department of Microbiology, Hue University Hospital.

3. RESULTS

There were 60 patients enrolled in this study (male 41, female 19). The average age was 32,43 ± 14,39.

3.1. HBV genotypes in CHB patients

Table 1. HBV genotypes in CHB patients

Genotype	n	%	p
B	38	63.3% (1)	$p^{(1)(2)}<0.0001$
C	16	26.7% (2)	
B-C	6	10%	

3.2. Relationship of HBV genotypes to some clinical, and biochemical characteristics

Table 2: Relationship of HBV genotypes to gender

Genotype	Male		Female		p
	n	%	n	%	
B	27	71.1%	11	28.9%	p< 0.0005
C	10	62.5%	6	37.5%	
B-C	4	66.7%	2	33.3%	

Table 3: Relationship of HBV genotypes to age

Genotype	15-30 yrs		>30-40 yrs		>40-50 yrs		>50 yrs	
	n	%	n	%	n	%	n	%
B	18	47.4%	11	28.9%	5	13.2%	4	10.5%
C	5	31.3%	8	50%	3	18.7%	0	0%
B-C	2	33.3%	3	50%	1	16.7%	0	0%

Table 4: Relationship of HBV genotypes to clinical characteristics

Charateristics	Genotype					
	B		C		B-C	
	n	%	n	%	n	%
Fatigue	10	26.3%	7	43.8%	2	33.3%
Anorexia	4	10.5%	3	18.7%	0	0%
Jaundice	3	7.9%	2	9.1%	1	16.7%
Hepatomegaly	10	26.3%	6	37.4%	1	16.7%

Table 5: Relationship of HBV genotypes to ALT level (tested in 46 patients)

ALT level	Genotype					
	B		C		B-C	
	n	%	n	%	n	%
≥ 2-5 times GTBT	20	69%	6	50%	4	80%
> 5 times GTBT	9	31%	6	50%	1	20%

Table 6: Relationship of HBV genotypes to viral load (HBV DNA) (tested in 46 patients)

HBV DNA (copies/ml)	Genotype					
	B		C		B-C	
	n	%	n	%	n	%
Low (< 10^5)	12	41.4%	3	25%	3	60%
Average (10^5 – 10^7)	11	37.9%	4	33.3%	2	40%
High (> 10^7)	6	20.7%	5	41.7%	0	0%

4. DISCUSSION

4.1. HBV genotypes in CHB patients

As per the results shown in table 1, genotype B was predominant in CHB patients (63.3%), genotype C in 26.7%, and mixed genotype B-C in only 10%. The other genotypes were not detected. This result was the same as the result of our other study in patients with acute hepatitis B, where the prevalence of genotypes B, C, B-C and A were 70.9%, 25.6%, 2.3% and 1.2% respectively [x].

The study of Nguyen C. Long et al (Bach Mai hospital, Hanoi) in CHB patients showed the prevalence of genotype B was 70.7%, and genotype C 29.3%. In the South, Dong T. H. An (Ho Chi Minh City) found a prevalence of genotype B of 77.8%, and genotype C of 21.3%. So in all of the studies, the majority of CHB patients in Vietnam had genotype B and C [1], [3].

Study of Yuen MF (Hong Kong) showed the prevalence of genotype B was only 32.5%, genotype C was very high (62.5%). The same situation was confirmed in Japan. Furusyo et al found 36.7% genotype B and 63.3% genotype C in CHB patients [5], [8].

4.2. The relationship of HBV genotypes to some clinical, and biochemical characteristics

Relationship with gender: Genotype B and mixed genotype B-C were found more commonly in male than in female patients. 71.1% and 66.7% of genotype B and B-C groups were male ($p<0.0005$). The male: female ratio in this study was 2.16:1.

Nguyen C. Long et al found male patients were predominant in both genotype B and C (82.9% and 92.2%). In a study by Dong T. H. An, the results were 70.2% and 69.6%. [1], [3]

Relationship with age: genotype B was predominant in < 30 years old (47.4%), genotype C was found mostly in 30-40 years group (50%). In Yuen's study, patients younger than 50 years had the prevalence of genotype B lower than patients over 50 yrs (32.5% vs 41%). Sumi (Japan) found that the genotype B group in CHB patients was older than the genotype C group ($p=0.018$) [7].

Fatigue was the most founded symptom in CHB patients, frequently in the genotype

C group (43.8%). But the majority of our patients were outpatients, so their clinical signs and symptoms were very rare.

As per the results shown in table 5, 50% of patients with genotype C had ALT levels over 5 times higher than the upper limit in comparison with only 31% in the genotype B group. The same result was shown in the study of Furusyo, where the ALT level in genotype C group was higher than in the genotype B group (84% vs 22.4%, $p < 0.05$) [5]. Sugauchi (Japan), found ALT levels, viral load and HBeAg (+) in genotype C higher than genotype B ($p < 0.05$). So in such studies, genotype C patients seemed to have more severe necroinflammation than genotype B patients.

Relationship with HBV DNA level: In our study, 58.6% of genotype B patients and 75% of genotype C patients had HBV DNA over 10^4 copies/ml. Especially 41.7% of genotype C patients had HBV DNA over 10^7 copies/ml. So patients with genotype C had a higher viral load. Nguyen C Long et al found HBV DNA levels were related to genotype C and more severe outcome for CHB patients. The genotype C patients had HBV DNA level significantly higher than genotype B patients ($6,6 \pm 2,2$ vs $4,9 \pm 2,0$ log copies/mL, $p<0.0001$) [3].

Yu et al (Taiwan) studied 4841 male CHB patients and concluded that genotype C was related to serum HBV DNA levels. This was also the conclusion of McMahon, Chu and A. Lok (USA) [4], [6]. High HBV DNA level may lead to severe outcomes for CHB patients.

5. CONCLUSIONS

Genotype B and C were predominant in our CHB patients (63.3% and 26.7%). Genotype C patients were older than genotype B. Genotype C patients seemed to have more severe necroinflammation and higher HBV DNA level than genotype B patients.

REFERENCES

1. Dong T. H. An, Pham T. T. Ha, Pham H. Phiet et al (2009), "Relationship of HBV genotypes to clinical forms of hepatis B", *Journal of Liver diseases*, Nr. 9, p.5-15.
2. Tran X. Chuong (2009), HBV genotypes and their clinical significance, Hue University Publisher.
3. Nguyen C. Long, Bui X. Truong, Nguyen K. Trach (2008), "High HBV-DNA level related to genotype C and severe liver disease in vietnamese CHB patients", *Journal of Vietnam Gastroenterology Association*, vol. 3, Nr. 11, p. 669-673.
4. Chu C, Anna SF Lok (2002), "Clinical significance of hepatitis B virus genotypes", *Hepatology*, 35, p. 1274-1276.
5. Furusyo N et al (2002), "Clinical outcomes of hepatitis B virus genotypes B and C in japanese patients with chronic HBV infection", *Am. J. Trop. Med. Hyg*., 67(2), p. 151-157.
6. McMahon B.J. (2009), "The influence of hepatitis B virus genotypes and subgenotypes on the natural history of chronic hepatitis B", *Hepatol Int.* 3: 334-342.
7. Sumi H et al (2003), "Influence of hepatitis B virus genotypes on the progression of chronic type B liver disease", *Hepatology*, 37, p.19-26.
8. Yuen MF et al (2004), "Epidemiological study of hepatitis B virus genotypes, core promoter and precore mutations of chronic hepatitis B infection in Hong Kong", *Journal of Hepatology*, 41, p.119-125.