Acute Hepatitis B Progression to Chronicity - A Prospective Study at Tertiary Care Centre of Northeren India

Parveen Malhotra*, Vani Malhotra, Yogesh Sanwariya, Isha Pahuja, Ajay Chugh and Akshay

Department of Medical Gastroenterology and Obstetrics & Gynecology, PGIMS, Rohtak, Haryana, India

Abstract: *Background:* There are limited number of studies providing information regarding the progression of acute hepatitis B virus (HBV) infection to chronic phase.

Aim: To determine the percentage of patients of acute hepatitis B who progressed to chronic hepatitis B stage.

Methods: It was a prospective study over a period of four years in which total 409 confirmed acute hepatitis B patients were enrolled but out of them only three hundred and four, (221 men and 83 women, 06–82 years old) were followed regularly for at least six months or more, thus data pertaining to them was analyzed.

Results: Out of total of 304 acute hepatitis B patients, 279 patients resolved and became Hepatitis B surface antigen (HbsAg) and Hepatitis B virus DNA negative whereas 25 patients went into chronic phase. No differences were found between groups with respect to age and sex. However, Serum Bilirubin, Serum amino transaminases, HbeAg and HBV DNA Quantitative levels were significantly lower in patients who progressed to chronic hepatitis stage.

Conclusions: Around 91.78% of acute hepatitis B patients resolved but 8.22% progressed to Chronic hepatitis B stage The twenty five patients who progressed to chronic infection had mild hepatitis on comparison to 279 patients who resolved, thus suggesting that patients with mild acute hepatitis B infection may have a higher risk of progressing to chronic infection.

Keywords: Hepatitis B, Acute hepatitis B, Chronic hepatitis B, Cirrhosis, HbsAg.

1. INTRODUCTION

Hepatitis B virus (HBV) is a DNA virus with 3200 base pairs and around 350–400 million people are chronically infected with HBV and more than 3 billion people have been exposed to HBV worldwide [1, 2]. HBV can impact liver in many ways, ranging from acute or fulminant hepatitis to liver cirrhosis and hepatocellular carcinoma. HBV infection is an important cause of liver cirrhosis and hepatocellular carcinoma and chronic carriers have an increased risk (15 to 40%) of developing cirrhosis, hepatic decompensation, and hepatocellular carcinoma, resulting in 1 million deaths each year [3, 4]. Acute hepatitis B is self-limited in most adult patients but 1-2% of patients progress to fulminant hepatic failure. The rate of progression from acute to chronic HBV infection is reported to be 90% in newborns and 5–10% in adults [5, 6]. HBV has 8 genotypes with a divergence of more than 8% of nucleotide sequences [7-9] and clinical presentation and routes of transmission vary between genotypes [10, 11]. The rate of chronicity of genotype A infections is reported to be higher than those of other genotypes [12-15]. It is important to understand the incidence, prevalence, and chronicity associated with HBV infection [16]. The present study was aimed to determine progression of acute hepatitis B infection into chronic phase.

MATERIAL AND METHODS

It was an epidemiology based, prospective study conducted at Medical Gastroenterology Department, PGIMS, Rohtak over a period of four years *i.e*. Ist April 2017 to 31st March,2021. Four hundred and nine (409) patients who were found to be having features of acute hepatitis and confirmed to be positive for HbsAg on Enzyme linked Immunoassay test (ELISA) and HBV DNA on PCR testing were enrolled in the study. Out of these 409 patients, 304 patients came on regular follow up and data pertaining to them was analyzed. The HbsAg, HbeAg, anti-HBe, IgM Anti-Hbc was assayed by chemiluminescence immunoassay and HBV-DNA level was assayed using polymerase chain reaction. The criteria of acute HBV infection were positive for IgM anti-Hbc and HbsAg in a previously HbsAg-negative patient. The criterion of progression to chronic infection was persistence of HbsAg from the onset of the disease for more than 6 months. The percentage and clinical features of subjects who progressed and did not progress to chronic infection were determined and analyzed.

*Address correspondence to this author at the Department of Medical Gastroenterology, Pt.B.D.S. Post Graduate Institute of Medical Sciences, 128/19, Civil Hospital Road, Rohtak – 124001, Haryana, India;
E-mail: drparveenmalhotra@yahoo.com

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Statistical Analysis

Statistical analyses were performed and tests as per need were applied.

Observations

Among three hundred and four (304 patients), only twenty five (8.22%) progressed to chronic infection while the other 279 (91.78%) did not. Out of these 304 patients, 221(72.69%) were males and 83 (27.30%) were females. On analysis of 221 males, 201 (90.95%) resolved and 20 (9.04%) developed chronic hepatitis B whereas out of 83 females, 78 (93.97%) resolved and 5 (6.02%) patients progressed to chronic hepatitis B stage. As there is separate pediatric department in our institute, hence number of patients below 14 years is less. The maximum number of patients were seen in younger age group of 20-50 yrs *i.e*. 215 patients (70.72%). The tendency of going in chronic phase decreased as age increased *i.e*. 66.66 % in 0-10 yrs of age group to 0% in above 70 yrs of age. On evaluation of risk factors, previous history of surgery, dental procedures and smoking was seen more in group of 25 patients who developed chronic hepatitis B whereas history of alcohol intake was more commonly seen in group of 279 patients who resolved. The history of tattooing and HCV co-infection was comparable in both the groups. All 304 subjects were HIV negative. On analysis of Aspartate and Alanine aminotransferase level, it was seen that levels of both of them were higher in resolved group of 279 patients in comparison to 25 patients who went into chronic phase of hepatitis B infection. In resolved group, AST and ALT level ranged from 139-3200 I.U. (mean of 1008 I.U.) and 194-4410 I.U. (mean of 1298 I.U.) respectively whereas in chronic phase group, AST and ALT level ranged from 113-2200 I.U. (mean of 765 I.U.) and 122-2300 I.U. (mean of 981 I.U.) respectively. In resolved group, serum Bilirubin level ranged from 1.8- 27.8 mg % (mean of 7.3 mg %) whereas in chronic phase group, serum Bilirubin level ranged from 1.2- 10.5 mg % (mean of 4.7 mg %). In resolved group, HBV DNA Quantitative level ranged from 10^3- 10^8 I.U. (mean of 10^5 I.U.) whereas in chronic phase group, HBV DNA

Table 1: Showing Total Number of Patients with Sex Distribution

Total (304)	Resolved (279 *i.e.* 91.78 %)	Chronic Phase (25 *i.e.* 8.22%)
Male (221 *i.e.* 72.69%)	201 (90.95%)	20 (9.04%)
Female (83 *i.e.* 27.30%)	78 (93.97%)	5 (6.02%)

Table 2: Showing Age Distribution in Different Group of Patients

Age Group	Total (304)		Resolved (279)	Chronic Phase (25)
0-10	3 (0.98%)		1 (33.33%)	2 (66.66%)
10-20	37 (12.17%)		32 (86.48%)	5 (13.52%)
20-30	108 (35.52%)		98 (90.74%)	10 (9.26%)
30-40	67 (22.03%)		64 (95.52%)	3 (4.48%)
40-50	40 (13.15%)		40 (100%)	0 (0%)
50-60	29 (9.53%)		28 (96.55%)	1 (3.46%)
60-70	18 (5.92%)		14 (77.77%)	4 (22.23%)
70-80	1 (0.32%)		1 (100%)	0 (0%)
80-90	1 (0.32%)		1 (100%)	0 (0%)

Quantitative level ranged from 10^2- 10^5 I.U. (mean of 10^4 I.U.). In resolved group of 279 patients, Hepatitis B antigen (HbeAg) was positive in 248 patients (88.88%) whereas in chronic phase group of 25 patients, Hepatitis B antigen (HbeAg) was positive only in 9 patients (36%).

Table 3: Showing Risk Factors Distribution

Risk Factors	Resolved (279)	Chronic Phase (25)
HCV	1 (0.35%)	1 (4%)
Alcohol	25 (8.96%)	1 (4%)
Smoke	31 (11.11%)	7 (28%)
Surgery	35 (12.54%)	6 (24%)
Dental Procedures	39 (13.97%)	6 (24%)
Tattoo	25 (8.96%)	2 (8%)

Table 4: Showing Distribution of Biochemical Parameters

Biochemical Parameters	Resolved (279)	Chronic Phase (25)
AST (I.U.)	139-3200 I.U. (mean 1008)	113-2200 I.U. (mean 765)
ALT (I.U.)	194-4410 I.U. (mean 1298)	122-2310 I.U. (mean 981)
S. Bilirubin (mg%)	1.8 -27.8mg% (mean 7.3 mg%)	1.2-10.5 mg% (mean 4.7 mg%)
HBV DNA (I.U.)	10^3- 10^8 I.U. (mean 10^5)	10^2- 10^5 I.U. (mean 10^4)
HbeAg Positive	248 patients (88.88%)	9 patients (36 %)
HbeAg Negative	31 patients (11.22%)	16 patients (64 %)

DISCUSSION

The present study was aimed at knowing the rate of chronicity in acutely HBV-infected patients and information collected in both the resolved as well as patients who progressed into chronic phase was analyzed. All 304 patients had no past record of HbsAg positivity but as acute hepatitis B can be asymptomatic in many cases, hence, the possibility of HBV reactivation from HbsAg-negative carrier or resolved hepatitis status in every patient cannot be ruled out. Many studies have been done in the past in which factors pertaining to the severity of acute hepatitis B infection and its clinical outcomes have been reported [17-19]. It is important to understand that both host and viral factors are suspected to affect the progression to chronic infection in acute hepatitis B infected patients [20-22] and rate of chronicity in immunocompromised conditions like HIV coinfection is high [23-24]. In the present study, 25 of 304 patients with acute HBV infection progressed to chronic infection. The Serum Bilirubin, ALT, AST levels, HbeAg positivity and HBV DNA Quantitative levels were significantly more in resolved group than those in developed chronic hepatitis B infection and differences were statistically significant *i.e*. p value <0.05. It is hypothesized that the progression from acute to chronic infection appears to represent a failure of immune clearance of virus-infected cells. The accompanying acute hepatitis is typically mild and subclinical with only modest serum ALT elevations and no jaundice in patients with acute hepatitis B who progressed to chronic infection [25]. Many published studies have shown chronicity of acute hepatitis B in patients up to 12% [26] but in our study, it was less *i.e*. 8.22%. Several factors are associated with the increased risk of chronic HBV infection, including male gender, various causes of immune deficiency, genome variations, and genetic, hormonal and nutritional factors [27]. Regarding gender, male patients were more likely to become chronic carriers, although this difference was not statistically significant. This result was in alignment with other studies, which have reported a higher evolution to chronicity in male individuals [28-30]. Only two patients in total pool of 304 acute hepatitis B were having HCV co-infection, one each in resolved and chronic phase group. The co-infection is due to common routes of transmission of these viruses *i.e*. sexual, Parenteral and vertical [31] and is associated with worse outcomes [32].

CONCLUSION

More researches dealing in depth analysis of factors leading to chronicity of acute hepatitis B infection is need of hour. The adult patients, especially males with mild or subclinical acute hepatitis B infection as evidenced by low serum transaminases and Bilirubin levels may have a higher possibility of progressing to chronic infection whereas those with high HBV DNA levels and Hepatitis B antigen positivity have high chances of resolution of disease. This highlights the importance of control measures, epidemiological assessments, appropriate follow-up of patients and

their contacts for decreasing morbidity and mortality associated with this deadly disease.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests regarding the publication of this paper.

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