

## Antiviral Treatment in Acute Hepatitis B

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## 1. Abstract

**1.1. Introduction:** Acute hepatitis B remains unrecognized in majority of cases as it usually presents as asymptomatic or mild disease. The usual symptom by which common man recognizes the disease is jaundice but it occurs only in 15-40% of cases of acute hepatitis B, thus leading to under reporting of it. Moreover, in 90-95% of adults, the disease never progresses into chronic phase and they become hepatitis B antigen negative (HbsAg) within six months, thus majority even does not know whether they got infected with acute hepatitis B. Only a subset of acute hepatitis B patients who develop severe disease require antiviral treatment.

**1.2. Aims and objectives:** The aim of study was to determine the percentage and Clinico-epidemiological profile of acute hepatitis B patients who needed antiviral treatment.

**1.3. Materials & Methods:** It was an epidemiology based, prospective study conducted at Medical Gastroenterology Department, PGIMS, Rohtak over a period of three years and eleven months. Four hundred and twenty five (425) 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 425 patients, the data of fifteen patients requiring antiviral treatment was analyzed.

**1.4. Results:** There is very less percentage of acute hepatitis B patients who need antiviral treatment but judicious and timely intervention can reduce morbidity and mortality associated with it.

## 2. Introduction

HBV infection is a pan global health and is present in significant proportion in India where Hepatitis B surface Antigen (HbsAg) positivity ranges between 2–4.7% [1,2]. Around 40 million people are chronically infected with Hepatitis B in India [3] but there is inadequate literature on acute hepatitis B. The well documented risk factors are multiple blood/ blood products transfusion, chronic renal failure patients on maintenance hemodialysis, intravenous drug abusers, males having sex with male, female sex workers, sexual partners and family members of infected people, prisoners etc. Hepatitis B can transit to chronic phase, thus may lead to cirrhosis of liver and hepatocellular carcinoma, hence early intervention is must for decreasing morbidity and mortality associated with it [4]. Acute hepatitis B can be prevented by widely available vaccine which is already proving beneficial in newborns and high risk group in most countries [5]. The majority of Hepatitis B infection are asymptomatic and may present only with mild elevation of transaminases and jaundice develops in about 14–30% of infected individuals [6-8]. The development of symptomatic disease following HBV infection is determined by the infectious dose within an inoculum [9], the pathogenicity of the infecting strain, and the immune response of the host. There are very few studies available on need of antiviral treatment in acute hepatitis B infection.

### 2.1. Aim and Objectives

The aim was to study to determine the percentage and Clinico-epidemiological factors of acute hepatitis B patients who needed antiviral treatment.

**Table 1:** Showing Age Distribution of Patients

Age Group	No. of Patients
0-20	1
20-40	7
40-60	5
60-80	2

**Table 2:** Showing Age Distribution of Patients

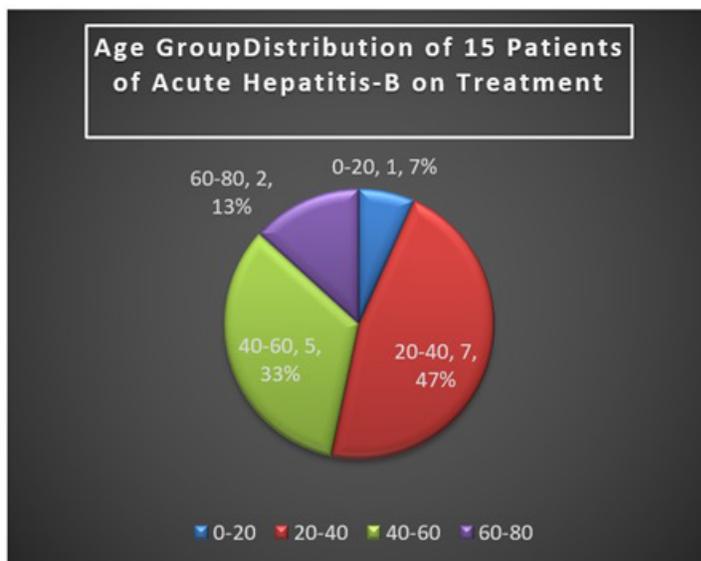
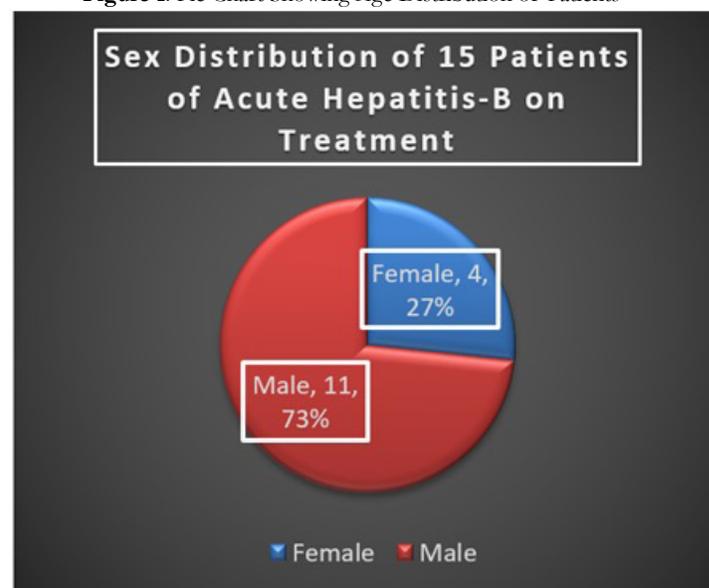
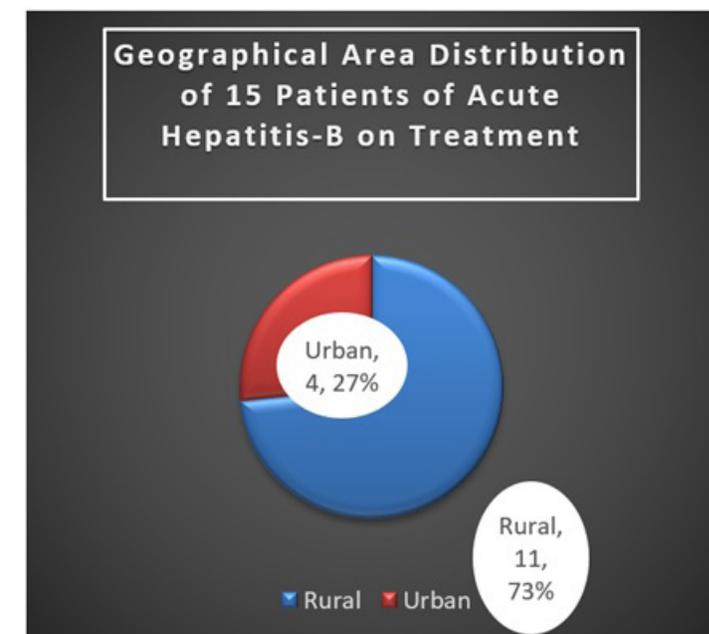
Sex	No. of Patients
Female	4
Male	11

**Table 3:** Showing Rural/Urban Distribution of Patients

Geographical Distribution	No. of Patients
Rural	11
Urban	4

### 3. Materials and Methods

The present study was a hospital based, prospective, observational study conducted at PGIMS, Rohtak from i.e. 1st April 2017 to 28th February 2021, for determining number and Clinico- epidemiological factors of acute hepatitis B patients who needed antiviral treatment. After proper informed consent, the enrolled patients detailed history and physical examination was carried out and samples were collected for every subject. The details of patients recorded included age, sex, rural or urban location, occupation, risk factors exposure especially in last six months like history of blood transfusion, tattooing, surgical or dental intervention, any hospitalization requiring injections or intravenous fluid requirement, intravenous drug abuse, history of jaundice in other family members or neighbourhood. An AVH case was defined as a person having an acute illness of <15 days duration with a discrete onset of any sign/symptom (e.g. Fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, and abdominal pain) and either a) jaundice or b) elevated serum Alanine Transferase (ALT) > 100IU/L documented at least twice at a 1 week interval without any history of pre-existing liver disease [10]. The patients having co-infection with hepatitis C & HIV, alcoholic, autoimmune, hemolytic, malarial, drug induced hepatitis, cholestatic jaundice, chronic liver disease or acute on chronic liver disease were not included in the study. Around 7ml of blood was drawn and serum was separated by centrifugation, aliquoted & stored at -20 degree, then complete set of investigations was done which included complete haemogram, liver & renal function test, ESR, INR, anti- HAV IgM ELISA, HbsAg ELISA, anti- HCV IgM ELISA, anti HEV IgM ELISA assay and ultrasound abdomen. Four hundred and twenty-five (425) patients having features of acute hepatitis and confirmed to be positive for HbsAg on Enzyme linked Immunoassay test (ELISA) and HBV DNA by polymerase chain reaction testing and were enrolled in the study. Out of these 425 patients, only fifteen [15] patients who needed antiviral treatment were analyzed.

**Figure 1:** Pie Chart Showing Age Distribution of Patients**Figure 2:** Pie Chart Showing Sex Distribution of Patients**Figure 3:** Pie Chart Showing Rural/Urban Distribution of Patients

### 3.1. Analysis of Data

All the relevant collected data was analyzed using SPSS (Statistical Package for Social Studies) and for differences between groups, Pearson's chi-square test was used. For calculating difference of means for quantitative variables, "t" test was used. The distributed data were presented as means and standard deviation, or 95% confidence intervals (CI), the p value of less than 0.05 was considered significant.

### 3.2. Observations and Results

In the present study, total 425 patients of acute hepatitis B were enrolled and data pertaining to fifteen patients who needed antiviral treatment as per scientific guidelines was analyzed. In this group of fifteen patients, there was male predominance i.e. 11 (73.33%) in comparison to females i.e. 4 patients (26.66%). There was rural or village predominance i.e. 11 (73.33%) and only 4 (26.66%) were having urban background. Out of total 15 patients, 12 patients (80%) were married and 3 patients (20%) were unmarried. The age group varied from 14yrs-65yrs of age but maximum number of patients belonged to 20 to 40 years age i.e. 7 patients (46.66%). Out of total fifteen patients, 7 (46.66%) & 3 (20%) had history of alcohol and smoking respectively. Four patients (26.66%) gave history of previous surgery. The history of intake of alternative medications was found in 4 (26.66%). The serum Bilirubin level varied from 10 mg%-28 mg% with mean of 16 mg%. The serum transaminases varied from 517- 3275 with mean of 826. The HBV DNA Quantitative level was significantly raised in all patients and ranged from 140000 I.U. to 200000000 I.U. with mean of 170000000 I.U. The Hepatitis B antigen (HbeAg) was positive in all patients and ranged from 1.58 to 1000 with mean of 578. The Internationalized ratio (INR) ranged from 1.30 to 1.80 with mean of 1.70.

### 4. Discussion

The more number of detection of acute hepatitis B cases is due to more frequent testing of HbsAg in patients of acute viral hepatitis, before surgery as Pre-anesthetic checkup, in pregnant females, in voluntary blood donors and screening camps for Hepatitis B [11]. There is no definitive explanation that why some patients progress towards chronicity, but it is likely related to the immune response being too weak compared to the required immune response. The low rate of chronicity in immunocompetent patients makes prevention of chronicity an unlikely indication of antiviral therapy in the setting of asymptomatic or mild acute hepatitis B [12]. However, a concept could be to initiate treatment for preventing chronicity in patients who show signs of failure to achieve spontaneous clearance, such as lack of HbsAg reduction by more than 50% within 4 weeks [13-15]. There are no well-established algorithms to predict severity of acute hepatitis B, but age has been reported to be relevant [16,17], with jaundice occurring more frequently among older individuals. In addition, factors associated with decreased or absent HbeAg expression might lead to more severe disease such as with viruses harboring basal core promotor and/or precore mutations [18]. For nonicteric

patients with mild acute hepatitis B, there seems to be no indication for antiviral therapy to ameliorate the course, as these patients are asymptomatic and amelioration would not be needed. In the absence of coagulopathy, antiviral therapy is currently not recommended in the AASLD or EASL guidelines outside of studies [19,20]. There have been cases series which indicated efficacy of antiviral therapy in patients with severe acute hepatitis B defined as fulfilling 2 of the following 3 criteria: hepatic encephalopathy, serum Bilirubin >10.0 mg/dl, and INR of coagulopathy >1.6 [21].

In our study group of fifteen patients, 73.33% were males and 73.33% belonged to rural or village background. Out of total 15 patients, 80% were married and maximum number of patients i.e. 7 (46.66%) belonged to younger age group of 20 to 40 years. The above highlighted epidemiological factors are totally in accordance with their representation in the overall pool of 425 patients of acute hepatitis B patients from which data of these fifteen patients of severe acute hepatitis B requiring antiviral treatment has been derived. The present study highlights more involvement of male gender in younger age group. The reason for very low percentage of cases in below ten years of age group can be due to effective implementation of hepatitis B National immunization program under which for last four years, majority of the newborns born in India are started on hepatitis B vaccination at the time of birth. The lesser involvement of older age group i.e. above 70yrs, can be attributed to lower exposure to risk factors, in view of remaining predominantly at home in safe surroundings. The reason for rural background predominance can be attributed mainly to unsafe needle practices due to lack of good healthcare infrastructure. One significant observation was history of alcohol intake was present in 7 (46.66%) patients and in a small study among American Indians, alcohol abuse and methamphetamine abuse was associated with worse outcome [22]. Four patients (26.66%) gave history of previous surgery which also is proven risk factor for contracting acute hepatitis B infection and the risk is more where proper sterilization techniques are not practiced. The history of intake of alternative medications was found in 4 (26.66%) and this is habit is very common in developing country like India where majority of patients of any kind of icteric illness, first use alternative medications. The two main reasons for it are illiteracy and poverty. As these patients were treated as per guidelines and only patients with severe acute hepatitis B were started on antiviral treatment, thus their serum Bilirubin level varied from 10 mg%- 28 mg% with mean of 16 mg%, serum transaminases varied from 517- 3275 with mean of 826 and International Normalized Ratio (INR) ranged from 1.30 to 1.80 with mean of 1.70. As all the fifteen patients were having acute severe hepatitis B, thus HBV DNA Quantitative level were significantly raised in all patients and ranged from 140000 I.U. to 200000000 I.U. with mean of 170000000 I.U. The Hepatitis B antigen (HbeAg) was also positive in all patients and ranged from 1.58 to 1000 with mean of 578.

## 5. Conclusion

The acute hepatitis B is becoming a significant health problem in certain hotspots, especially in young males of village background which can be due to unawareness, unhygienic practices and inadequate health care infrastructure. It is important to increase the awareness level for this disease both in society and health professionals. Acute hepatitis B has varied manifestation ranging from asymptomatic liver injury only identified by elevated liver transaminases to severe acute hepatitis and finally liver failure. Acute hepatitis B usually requires symptomatic treatment but in certain subset of patients where antiviral are used as per guidelines, then they can prove to be lifesaving.

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