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Importance of Hepatitis B Virus infection screening in Jharkhand: Hepatitis B positive asymptomatic patients are as iceberg in sea, threat to a sailing ship

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Abstract

Background: *Hepatitis B is a serious global public health problem affecting mankind. People infected with the hepatitis B virus (HBV) have variable manifestations: acute or chronic. In the acute stage, HBV infection can manifest as anicteric (viral hepatitis without jaundice: subclinical) hepatitis, icteric hepatitis, or, rarely, acute fulminant hepatitis. Chronic HBV infection can be asymptomatic (the HBV surface antigen carrier state), or it can be manifested by symptoms and signs of cirrhosis or hepatocellular carcinoma or both. Infants and young children as compared to adult infected at are at greatest risk of around 90% of developing chronic infection and are often asymptomatic and out of these individuals two-thirds of these develop chronic liver disease and approximately 15%–25% die prematurely from liver cancer cirrhosis.*
Objectives: *The study aimed to determine the number of asymptomatic and symptomatic cases of hepatitis B virus infections in Jharkhand. The study was conducted at Indian Council Medical Research Grade II Viral Diagnostic Laboratory, Department Of Microbiology, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand from May 2012 to Dec 2015, the study included patients attending the centre for diagnostic as well as screening purpose.*
Method: *Test methods employed were ELISA and chemiluminescence. Result Asymptomatic patient formed a larger proportion of total positive patients.*
Interpretation & Conclusion: *The alarming situation of HBV asymptomatic infection help in realizing that screening is necessary to avoid the transmission of blood-borne pathogens.*

Keywords: *Symptomatic, asymptomatic, icteric, chronic, Jharkhand*

INTRODUCTION

Hepatitis B is a serious global public health problem affecting mankind. People infected with the hepatitis B virus (HBV) have variable manifestations: acute or chronic.

In the acute stage, HBV infection can manifest as anicteric (viral hepatitis without jaundice. subclinical) hepatitis, icteric hepatitis, or, rarely, acute fulminant hepatitis. Chronic HBV infection can be asymptomatic (the HBV surface antigen carrier state), or it can be manifested by symptoms and signs of cirrhosis or hepatocellular carcinoma or both. Extra hepatic manifestations, including serum sickness, polyarteritis nodosa, essential mixed cryoglobulinemia, membranous glomerulonephritis, and aplastic anemia, have been reported in patients with HBV infection.(1). More than 350 million people infected chronically are at high risk of death from cirrhosis of the liver and liver cancer (2). HBV infection is highly prevalent in developing parts of world like Asia, sub-Saharan Africa, but less in the United States, except in Alaskan natives and immigrants from

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regions of high prevalence. Patients who are positive for the HBV surface antigen for more than 6 months are called chronic .It was estimated around 1.25 million chronically infected population live in the United States, and about half of them are Asian-American.[3,4] Other estimates increased the number up to 2 million, taking in account the prevalence of HBV immigrant populations also. India is also having a huge burden of this infection. In most of the adults who had acquired HBV infections (94%–98%) newly with normal immune status completely eliminates virus from the blood and produces neutralizing antibody that provides immunity from future infection but in case infants, young children, and immunosuppressed indivisuals it result in chronic infection.[5] Thus it is concluded that infants and young children infected at birth are at greatest risk of around 90% of developing chronic infection and are often asymptomatic and out of these individuals two-thirds of these develops chronic liver disease and approximately 15%–25% die prematurely from liver cancer cirrhosis. These persons often remain undetected since they are mostly asymptomatic chronic HBV infection and thus are a major reservoir for transmission of HBV infections. These undetected hepatitis B surface antigen (HBsAg) positive is potentially infectious to both household and sexual contacts so they are often detected in screening of blood donors, pregnant women, refugees, patients undergoing operation etc. A large number of symptomatic and asymptomatic carriers are present in our country. In developed countries, pre-operative screening for HBV and other blood borne infection is a standard laboratory investigation before any elective/ emergency surgical procedures so that further transmission of this infection can be interfered by adopting all possible precautionary measures. [6,7,8,9,10].

Screening identifies HBV carriers and also help in screening nearby contacts(family contacts and exposed sex partners) which aids in notifying of uninfected and get them vaccinated.[11] HBV vaccination is 90% effective in preventing HBV infection in healthy adults.[12,56] HBV screening is also important because CHB is now a treatable disease [13,14]. Studies have demonstrated that early diagnosis and effective antiviral treatment improves clinical outcomes by reducing progression of CHB to cirrhosis and the need for liver transplantation [15, 16.17.18.19.20.21.22.23.24.25.26].

In developing countries like India, pre-operative screening facilities for elective/ planned surgery for hepatitis B are not available generally at primary and secondary level but tertiary care facilities are available only in the large / teaching hospitals of the big cities. The present study was undertaken at tertiary care hospital Rajendra institute of Medical Sciences, Ranchi with the intent that it will provide a valuable insight into assessing the true nature of problem in the community, as patients from all districts and diverse backgrounds are received here, to assess the magnitude of asymptomatic HBV infection and aid in devising preventive measures. Patients from different departments medicine, surgery, ENT, obs and gynae, Eye, cardiology, ART, Neurosurgery etc.

MATERIALS AND METHODS

Study Area:

The study was carried out at Viral Diagnostic Laboratory, Department Of Microbiology, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand from May 2012 to Dec 2015. Jharkhand, a state in eastern India shares its border with the states of Bihar, Uttar Pradesh, Chhattisgarh, Odisha and West Bengal. It has an area of 30,778 sq mi (79,710 km2). Most of the patients attending the hospital came from the city and surrounding districts, belong to the lower socio-economic class.

Study Population:

Subjects included patients attending inpatient and outpatient facility at Rajendra Institute of Medical Sciences, Ranchi; Jharkhand for whom HBsAg detection was sought as diagnostic and screening purpose.

Ethical Issues:

The Institute Ethics Committee had granted permission for carrying out this research work.

Data Collection:

A questionnaire was framed to elicit demographic details of all patients who tested positive for hepatitis B which include hospital administration number, age, sex, district, occupation, history of jaundice, family history of Hepatitis B positivity, alcohol drinking habit, IVDU etc

Sample Collection & Processing:

Venous blood samples were collected aseptically. Around 5 ml whole blood was collected from each patient in a prelabelled sterile plain vacutainer using a disposable sterile needle and 5 ml syringe. Blood was allowed to clot for 30 minutes followed by centrifugation at 10000 RCF for 15 minutes. Serum was separated and stored at -20 °C.

Diagnostic Criteria:

The diagnostic parameters were clearly outlined as per the standard procedures and guidelines. Care has been taken to avoid any bias opinion or definition as per the literature. The details of the definition followed are as follows.

Hepatitis B surface Antigen Detection:

In the year 2012-2013 the samples were tested by ELISA and in the year 2014-2015 it was tested by Chemiluminescent Micro particle Immunoassay (CMIA)

An Enzyme Linked Immunoassay method was used for qualitative testing of the presence of HBsAg.ELISA Kit: Qualisa Microwell Enzyme immune assay which is an indirect sandwich ELISA was used for

the same. In this procedure the antigen is trapped between two layers of enzyme specific antibodies. The whole reaction is followed by a wash and enzyme activity of the bound material in each microtiter well is determined by adding the substrate of the enzyme.

Chemiluminescent Micro particle Immunoassay (CMIA) technology,is the serological diagnosis was based on a fully automated two-step immunoassay,with flexible assay protocols referred to as Chemiflex,(Abott Architect, spec) for the quantitative/qualitative determination of antigen /antibody in human serum and plasma. In the first step, sample and antigen/antibody coated paramagnetic micro particles are combined. Antigen/antibody present in the sample binds to the antigen/antibody coated micro particles. After washing, acridinium-labeled anti-body/antigen conjugate is added in the second step. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of antigen/antibody in the sample and the RLUs detected by the ARCHITECT i* optical system. The ARCHITECT software generate a calibration curve with the calibrators' provided by the company itself. The system has to be calibrated regularly as well the control which is also provided by the company is run in the machine before the sample is tested. If the control value lies in the acceptable range the test is preceded by the sample testing. It takes 20 minutes for each sample to be processed .This system marks the sample given a unique ID by the user as positive or negative. The presence or absence of Antigen/Antibody in the sample is determined by comparing the chemiluminescent signal in the reaction to the cut-off signal determined from an ARCHITECT calibration.

Symptomatic Hepatitis and Asymptomatic Hepatitis:

Asymptomatic Hepatitis is typically have subclinical or anicteric hepatitis..The onset of hepatitis B is typically insidious, with nonspecific symptoms of malaise, poor appetite, nausea and pain in the right upper quadrant. During the icteric phase, fatigue and anorexia usually worsen. Jaundice can last from a few days to several months, but usually 2–3 weeks. Itching and pale stools may occur. The convalescent phase begins with the resolution of jaundice. The physical signs of typical acute hepatitis B may include variable degrees of jaundice, mild and slightly tender hepatomegaly and mild enlargement of spleen and lymph nodes. In some cases are of fulminant hepatitis. These are symptomatic cases.Asymptomatic patients appears healthy in the society as they present no symptom of the infection but are suffering from the hepatitis B infection are asymptomatic cases. They are considered to be in immune tolerant phase.

RESULTS & DISCUSSION

In the year 2012 (May) , 2013, 2014 and 2015 out of 11786,15813,19607 and 19306 patients who visited the hospital for the diagnosis or testing of hepatitis b virus 2.56%. 2.58%, 2.45% (27) and 2.46% were found positive. In the year 2012-2015 11456 (97.21%), 15322 (96.89%), 19608 (97.25) and 18626 (96.47%) patients were not presenting any symptom of hepatitis were screened out of which 239 (2.08%), 317 (2.06%), 385 (2.01%) and 371 (1.99%) patients were found positive. In the year 2012-2015 63 (19.09%), 83 (16.90%), 96 (17.8%) and 113 (16.6%) were found positive out of symptomatic patients 330 (2.79%), 491 (3.10%), 539

Table-1. Total asymptomatic and symptomatic patients diagnosed attending RIMS

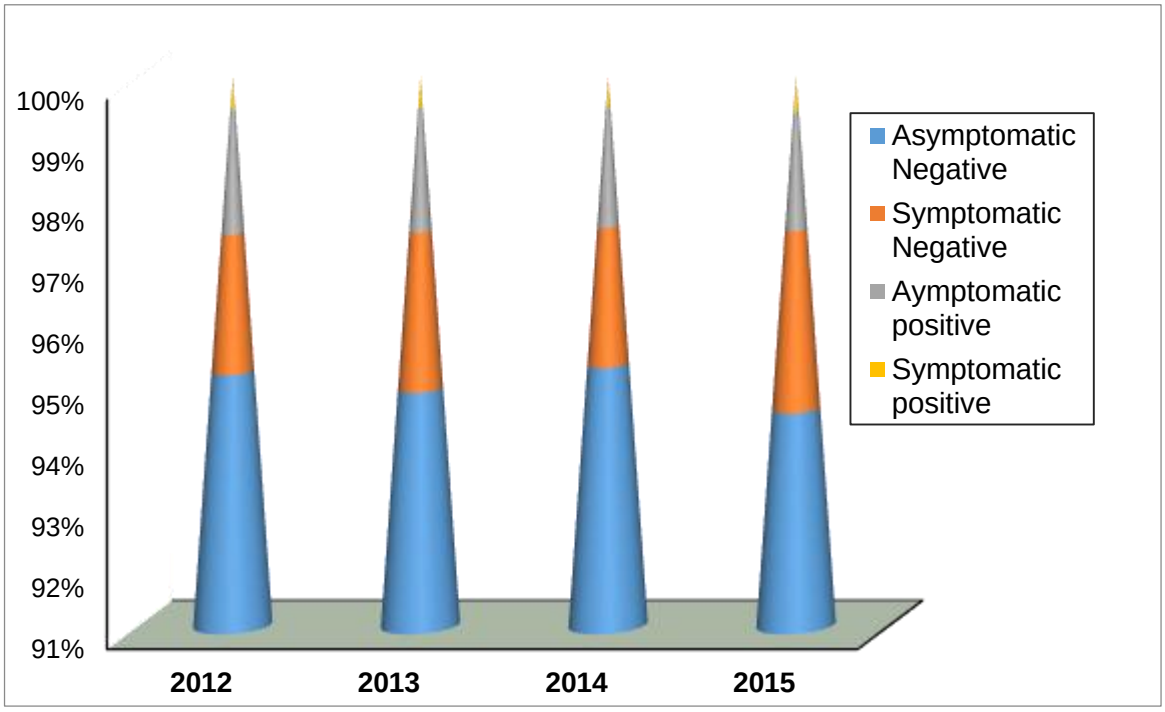
Year	2012		2013		2014		2015	
	N (%)	P (%)	N (%)	P (%)	N (%)	P (%)	N (%)	P (%)
Symptom-atic	267 (80.9 of 330) (2.32% of 11484	63 (19.09% of 330) (20.86% of 302)	408 (83.09 %of 491) (2.6% % of 15405)	83 (16.90 % of 491) (20.34% of 408)	443 (82.18% of 539) (2.31% of 19126)	96 (17.8% of 539) (19.95% of 481)	567 (83.38% of 680) (3.01% of 18822)	113 (16.6% of 680) (23.34% of 484)
Sub Total	330 (100) (2.79% of 11786)		491 (100) (3.10% of 15813)		539 (100) (2.74% Of 19607)		680 (100) (3.52% of 19306)	
Asymptom-atic	11217 (97.9% of 11456) (97.67 % of 11484)	239 (2.08 % of 11456) (79.14% of 302)	15005 (97.93% of 15322) (97.40% of 15405)	317 (2.06% of 15322) (77.69% of 408)	18683(97.9% of 19068)(97.68% 0f 19126)	385(2.01 % of 19068) (80.04% of 481)	18255(98% of 18626) (96.98% of 18822)	371(1.99 % of 19306) (76.65% 0f 484)
Sub Total	11456 (100) (97.21% of 11786)		15322(100) (96.89% of 15813)		19068(100) (97.25% of 19607)		18626 (96.47%of 19306)	
	11484	302	15405	408	19126	481	18822	484
Grand Total	11786 (100)		15813 (100)		19607 (100)		19306 (100)	

(2.74%), 680 (3.52%) respectively. Out of the total positives each year (2012-2015) 20.86% (63), 20.34% (83), 19.95% (96), 23.34% (113) were symptomatic positive and 79.14% (302) 77.69% (408), 80.04% (481) and 76.65% (484) were asymptomatic positives. (Table 1). Thus we find the asymptomatic positive patients are higher as compared to symptomatic patients in the total positive patients who were hidden as major part of icebergs in the sea which are threat to sailing ship similarly large number of hidden hepatitis positive patients are threat to other healthy population in the society. It is more clear by the graphical representation Figure 1 of the total population of patients attending the hospital. These asymptomatic patients were those who were detected during screening process. Screening is done to identify contacts of case-patients who require post exposure prophylaxis; detect outbreaks; identify infected persons who need counselling and referral for medical management; monitor disease incidence and prevalence; and determine the epidemiologic characteristics of infected persons, including the source of their infection, to assess and reduce missed opportunities for vaccination. To prevent chronic HBV infection is the primary goal of hepatitis B vaccination but since major proportion of persons are chronically infected are asymptomatic the affect are not seen for many years, thus to study direct impact of prevention programs on chronic infection prevalence is difficult.(28) .The positive asymptomatic patients are large in number thus these when undetected are source of reservoir of transmission of infection though they form a very small part of the total asymptomatic population as compared to the symptomatic positive population are forming larger part of symptomatic population which is very clear from the graph since the symptomatic patients once diagnosed after presenting the symptom the population nearby get alarmed and take the necessary actions for inhibiting any transmission but since asymptomatic are unidentified so no such actions are taken

In a study by Ashraf et al high prevalence of Hepatitis B was noted in the family members of Hepatitis B positive patients living in the same house. (29) More the prevalence of the disease more will be number of asymptomatic patients. Immunisation is the standard preventive strategy to overcome this problem as has occurred in many countries. (30) HBV screening is also important because CHB is now a treatable disease (31.32). Early diagnosis CHB aids in prescribing effective antiviral treatment which improves clinical outcomes by reducing progression of CHB to cirrhosis and the need for liver transplantation (33-44). HBV screening and vaccination have been demonstrated to be cost-effective public health measures (45-47). Vaccination of close contacts of infected persons is coined as ring vaccination. In 2005 CDC recommended routine HBV screening of individuals in countries with 8% HBV prevalence. (48) But later in late 2008 the guidelines was updated to screening to all individuals born in geographic regions with HBsAg prevalence 2% (49). It is now recommended that all foreign-born Asian Americans be screened for HBV infection. Counselling and referral for clinical evaluation and medical care should accompany HBV screening.

Thus screening programme should be enhanced. The most important barrier is the lack of knowledge about HBV transmission and its outcome especially in people with low socioeconomic background. People with educated background are mostly acquainted with the

Figure-1. Graphical representation of patients attending the hospital for HBV testing



same thus are self motivated and get themselves screened. Language is another important barrier to HBV screening since the individual cannot be communicated. Cultural values and beliefs is also important factor as many groups of people consider giving blood for testing as sin and even the young ones who want to indulge in such programmes are inhibited by the elder or old ones in the family. Other barriers to HBV screening include denial, social stigmata, concern about cost, and, if tested positive, the misconception that nothing can be done, These obstacles can be overcome when a family member, friend, or doctor recommends as well as motivates screening by conveying severe complications of CHB (i.e., cirrhosis or HCC), fear of transmitting the disease to a family member or peace of mind (49 -55). The knowledge that HBV-related disease is treatable and screening is very important for diagnosing and preventing the disease, after diagnosis if found positive they could lead a normal life with due respect as others will definitely motivate the person to go for screening.

Conclusion

The alarming situation of HBV infection requires that screening is necessary to avoid the transmission of blood-borne pathogens. The number of asymptomatic patients is much greater than the symptomatic positive cases. Patients should be encouraged to participate in routine and voluntary testing for blood-borne pathogens. This early detection due to screening of asymptomatic cases can help in better management of patients and reduction in transmission HBV infection .HBV is more efficiently transmitted than HCV or HIV, because of the high volume of Hepatitis B viruses in the blood of infected people compared to the lower viral load in people infected with HIV or Hepatitis C. Strict preventive measures and an intensive precautionary environment, promoting mandatory screening of preoperative patient for HBV viruses is essential to prevent the spread. It is important to educate the patients and to encourage them for screening or other medical treatments to ensure minimal risk of transmission, spread and onset of these diseases.

Competing interests

The authors have declared that no competing interests exist.

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