

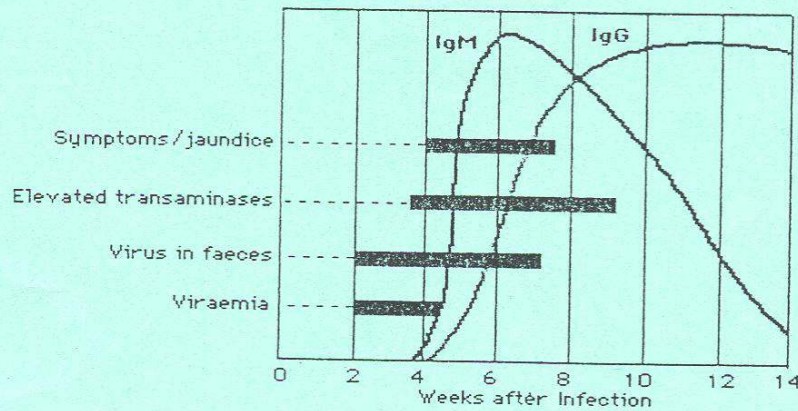


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A STUDY ON CORRELATION BETWEEN HEPATITIS B SURFACE ANTIGEN AND LIVER FUNCTION TEST AND THE POSSIBLE FACTORS RESPONSIBLE FOR HEPATITIS B AMONG THE PATIENTS ATTENDING TRIBHUVAN UNIVERSITY TEACHING HOSPITAL



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Abstract

The study of correlation between Hepatitis B Surface antigen (HBsAg) and liver function test and the possible factors responsible for hepatitis B among the patients attending TUTH was conducted in TUTH. Total 78 HBsAg reactive sera and patients along with 54 liver function elevated (both icteric and non icteric) were studied to explore the facts.

It was found that 20% of HBsAg reactive cases correlated with the liver function test indicating HBV a major threat of jaundice in our part. Amazingly of the total reactive case 14% were found to have decreased albumin concentration a state of clinical emergency.

Tracing the possible source of infection heterosexual activity was found most common (23%) but shockingly 6.4% of the patients were suspected to be transmitted from un hygienic surgical practice during vasectomy and only few (8%) were found to have knowledge regarding HBV transmission and Vaccination. Hence sterilization at any level of surgical practice and educational program is recommended to eventually stop the virus from transmission.

ACRONYMS

ALT:	Alanine Aminotransferase also known as SGPT
AST:	Aspartate Aminotransferase also known as SGOT
DNA:	Deoxyribonucleic Acid
HBV:	Hepatitis B Virus
HBsAg:	Hepatitis B Surface Antigen
HBeAg:	Hepatitis B e antigen
HBcAg:	Hepatitis B core antigen
HIV:	Human Immunodeficiency Virus
I V D A:	Intravenous Drug Abusers
LFT:	Liver Function Test
PLC:	Primary Liver Cancer
SGPT:	Serum Glutamyl Pyruvate Transferase also known as ALT
SGOT:	Serum Glutamyl Oxaloacetate Transferase also known as AST
TUTH:	Tribhuvan University Teaching Hospital
WHO:	World Health Organization

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1 INTRODUCTION

1.1 Introduction

HBV is a double-stranded DNA virus belonging to *Hepadnaviridae* family. It is the only hepadnavirus causing infection in humans and individuals incubating or suffering from acute or chronic hepatitis are highly infectious for at least as long as the HBsAg in the Blood⁵.

1.2 Statement of the problem

Hepatitis B is one of the major diseases of human and is a serious global public health problem. Hepatitis B also known as "Silent Killer" kills more than two million people throughout the world each year. Of the 2 billion people who have been infected with the hepatitis B virus (HBV), more than 350 million have chronic (lifelong) infections. These chronically infected persons are at high risk of death from cirrhosis of the liver and liver cancer¹. It is estimated that about one percent of total population of Nepal is infected by hepatitis B virus⁴. Although Nepal is low endemic area for hepatitis B it is responsible for significant cause of morbidity and mortality.

1.3 Rationale of the study

1. Hepatitis infection often leaves no visible symptoms such as jaundice and liver disease is often very subtle. The liver is a non-complaining organ so the disease is often advanced before symptoms occur. Chronic hepatitis B can lead to cirrhosis and liver cancer¹.
2. In chronic hepatitis B, the disease progresses with consistent cyclic hepatitis B virus (HBV) replication and host reaction to it with destruction of HBV-infected liver cells. In other words, serum GPT level repeatedly rises and falls with waving HBe antigen. It is known that occurrence of viral superinfection or alcoholic liver damage, if ever, during the course of chronic hepatitis B may lead to acute hepatic failure or to acute exacerbation (spontaneous reactivation) of the viral hepatitis with consequent hepatic failure due to so-called acute-on-chronic progression².
3. Patients receiving the drug must be followed by periodic liver function tests, for early detection of acute exacerbation of chronic hepatitis B and to avoid its progression into a severe illness. The drug should be discontinued immediately if exacerbation of hepatic function disorder or jaundice has appeared, contraindication, cautious administration and adverse reactions to warn about the potential for serious hepatic events².
4. The socio demographic factors responsible should be identified as a part of Hepatitis B eradication.

2 OBJECTIVE OF THE STUDY

2.1 General Objective:

To correlate between Hepatitis B Surface antigen (HBsAg) and Liver Function Test (GOT, GPT, Bilirubin) and to explore the possible factors responsible for Hepatitis B infection.

2.2 Specific Objectives:

1. To determine the presence of Hepatitis B Surface Antigen in the patients with elevated GOT, GPT and Bilirubin
2. To estimate the level of GOT, GPT, Bilirubin, Total Protein, and Albumin in the patients with Hepatitis B Surface Antigen.
3. To find out the possible factors responsible for Hepatitis B infection

3 LITERATURE REVIEW

Hepatitis B is One of the ten biggest killers in the world ¹¹. HBV causes acute and chronic hepatitis. Approximately one – third of the acute infection are completely asymptomatic in immunocompetent adult, one third present as flu like illness without jaundice that is rarely diagnosed as Hepatitis B (clinically unapparent) and one third present as full-blown viral hepatitis with typical signs and symptoms ⁷. These include jaundice, dark urine, extreme fatigue, anorexia, and right upper quadrant pain. Acute infection can sometimes lead to acute fulminant hepatitis (1%), which is always almost fatal. Of the total HBV infection cases 85% - 90% adult immunocompetent patients recover completely and develop life long immunity. The carrier state is defined as the presence of HBsAg in serum for 6 months or longer after initial detection. Only about 5% – 10% adults develop chronic hepatitis B⁴. Host factors predisposing to chronic HBV include infection in the neonatal period (90%), infection at children (50%) and infection in the presence of immunologic defects in the hosts. Infection during infancy and early childhood is usually asymptomatic. 25% chronic Hepatitis B carriers will die from cirrhosis or PLC.

The serum AST and ALT show a variable increase during the prodromal phase of acute viral hepatitis B ⁹. The ALT may exceed (>10 times) 400 U/L even before jaundice is the most striking abnormality of HBV infection⁸. When the jaundice is apparent the ALT level usually reached to peak (up to 4000 or more) and serum Bilirubin typically rises to levels ranging from 85 to 340 uol/l (5 – 20 mg/dl). In most instances total Bilirubin is equally divided between conjugated and unconjugated. Of the total acute cases 25–30% patients develop jaundice. In cases of icteric hepatitis along with the increase of aminotransferase mildly elevated conjugated Bilirubin may be found ⁹. In typical cases HBsAg becomes undetectable 1–2 months following the onset of jaundice and seroconversion of HBeAg to anti HBe coincides with the transient acute hepatic elevation including aminotransferase. ALT starts to drop at around the same time when e antigen is no longer detectable and became normal when anti – HBs appears. Alkaline Phosphatase level never exceed 250 U/L unless marked cholestasis develops⁸. Moderately elevated (100 –300) aminotransferase activity may be characteristic in chronic active hepatitis and Bilirubin may be mildly elevated. In chronic persistent hepatitis jaundice is a late event⁶.

Hepatitis B is primarily a disease of young adults most patients are between 20-35 years old. Prevalence varies among racial and ethnic groups. Most infection are linked with heterosexual activity. Intravenous drug abusers represent 12% of cases. 7%of the cases are attributed to other causes and about 26 % does not report any risk factors ¹⁰.

4 RESEARCH METHODOLOGY

4.1 Research design:

The design of the study is cross-sectional and conducted between the study period of July 4 to September 6 at TUTH

4.2 Sampling technique

The sampling technique is the Purposive sampling technique. From the requested HBsAg investigation samples from different wards and OPD, all the samples reactive to HBsAg ELISA during the study period at Tribhuvan University Teaching Hospital , Department of Microbiology, Virology and Immunology were selected. Interview from the patients with those reactive cases were also taken. And 54 LFT elevated samples were selected (both icteric and non icteric) to find out the presence of Hepatitis B surface antigen. While selecting the LFT elevated cases all those samples with elevated ALT along with any other (AST or Bilirubin or Both) were selected.

4.3 Sample size:

The sample size was the total number of hepatitis B surface antigen reactive cases (78) during the study period (July 4 to September 6) . The presence of Hepatitis B surface antigen was re confirmed by Enzyme Linked Immunosorbant Assay at TUTH , Department of Microbiology , Virology serology Laboratory. Also the 54 Liver function elevated cases were chosen (both icteric and non icteric) from TUTH, department of Biochemistry.

4.4 Study area:

- Department of Microbiology Tribhuvan University Teaching Hospital
- Department of Biochemistry Tribhuvan University Teaching Hospital

4.5 Data collection techniques:

Data collected by

1. Laboratory Findings
Liver function profile of all the reactive cases and hepatitis B surface antigen in all the LFT elevated cases.
2. Through poll interview.
Interview with the patients those were reactive to HBsAg by ELISA were taken.

4.7.3 Behavioral factors

- Alcoholic
- I V D A
- Sexual Behaviors

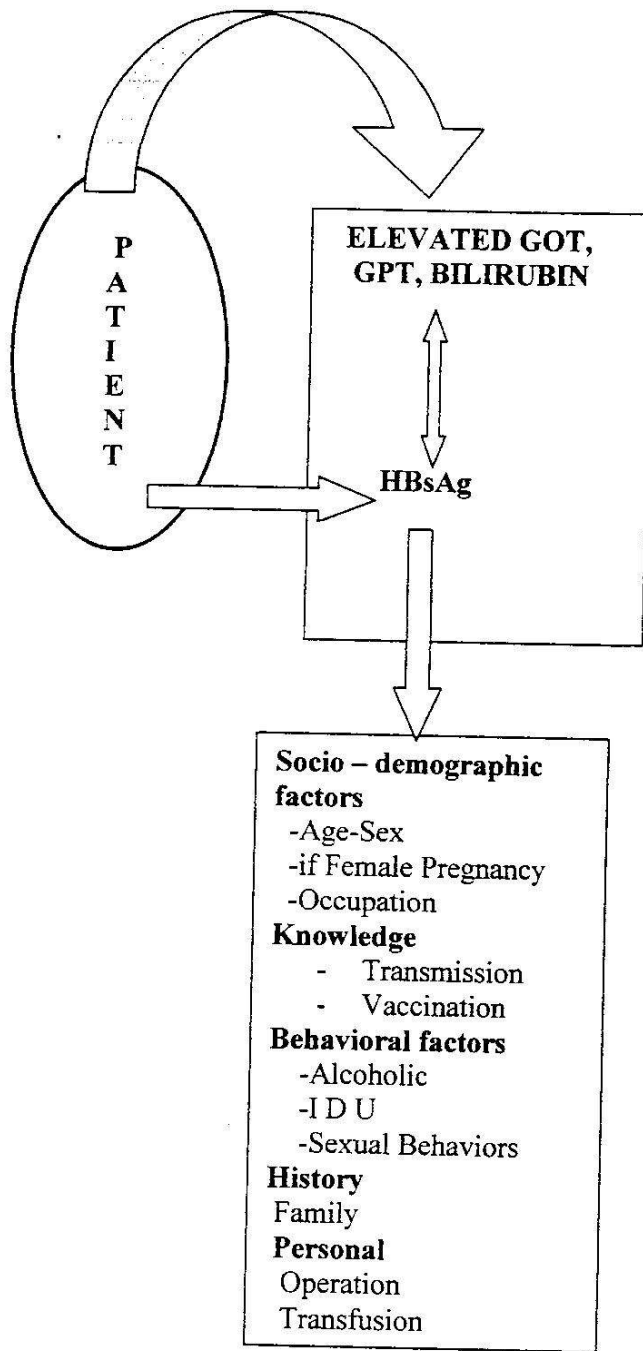
4.7.4 History

- Family
- Personal history of transfusion, jaundice

4.8 Limitations

The study has the limitation that HBsAg may be absent or present in very low titer in acute fulminant hepatitis cases and if the patients are recovering from the acute infection and developing anti – HBs antigen.

5. CONCEPTUAL FRAMEWORK OF THE STUDY



6.FINDINGS

6.1 Laboratory findings (LFT profile of HBsAg Reactive cases)

Of the total 78 HBsAg reactive cases 58 (74.3%) showed normal LFT and 18 (23%) showed moderately deviated LFT and 2 (2.5%) sera showed severely deviated LFT . The individual test profile can be seen in the below table.

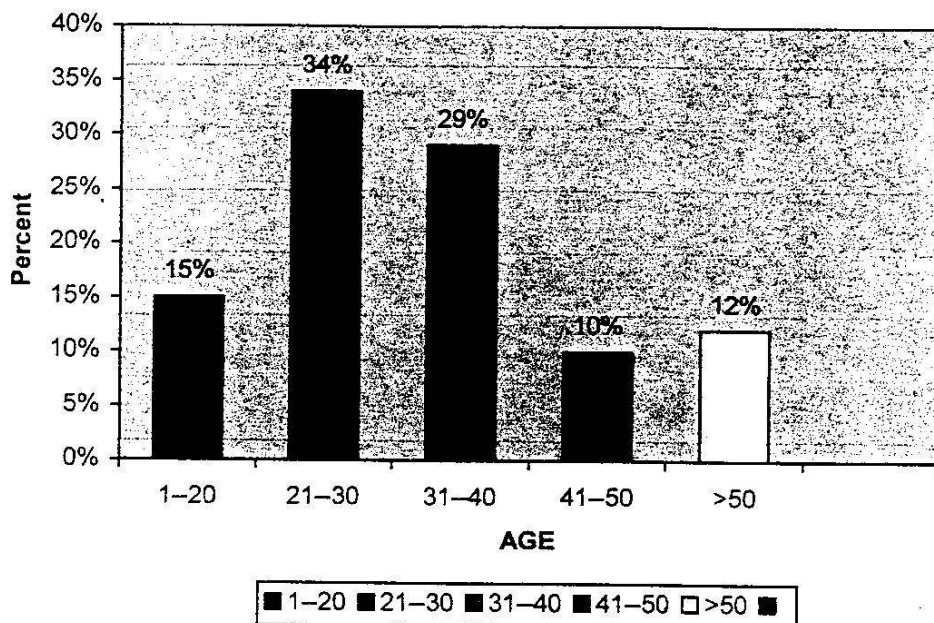
	ALT (SGPT)	AST (SGOT)	Bilirubin		Albumin	Protein	Alkaline Phosphatase
			T	D			
Normal	58	62	63	72	67	70	74
Moderate Deviation	18	14	13	4	4	6	4
Severe Deviation	2	2	2	2	7	2	0

6.2 Hepatitis B surface antigen in 54 LFT elevated samples

It was found that of the 54 LFT elevated cases 49 (91.8%) were non reactive to HBsAg and 5 (9.2%) were reactive to HBsAg. Of them 4 (8%) were icteric sera.

6.2 Socio Demographic Findings

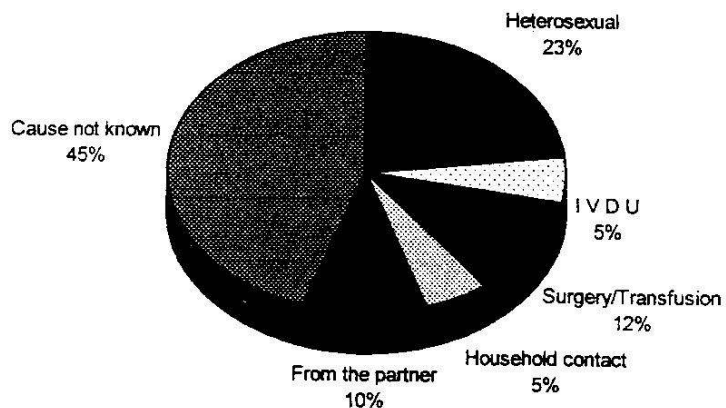
6.2.1 Age wise distribution in percent of the HBsAg reactive cases



Age Group 21 –30 uphold with 34% followed by 31-40 with 29%, 1-20 15%, >50 12% and 41 – 50 being the least with 10%

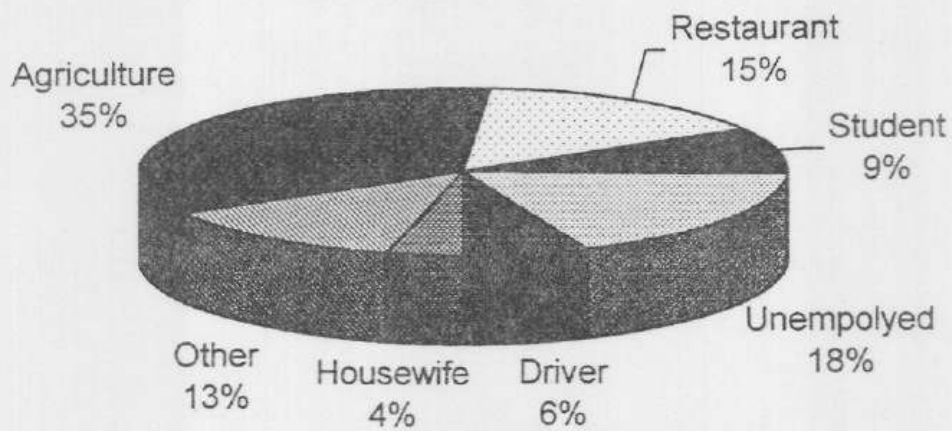
6.2.2 Route of transmission

Possible route of transmission as reported by the patients



The cause could not be traced in 45% of cases where the respondents do not present with any specific cause. The most common prevalence was found among the heterosexual 23% followed by surgery/transfusion 12%

6.2.3 Distribution by occupation



Profession by distribution of the reactive cases shows that Agriculture 35% was found most common followed by unemployed 18%, restaurant workers 15%, student 9%,

6.2.3 Other findings

- Only 8% respondents had knowledge regarding transmission and vaccination.
- 16% of the respondents present with their family history with HBV infection (present or past) of them 10% had their opposite partner infected.

7. DISCUSSIONS

7.1 Discussions

Among the 78 HBsAg reactive cases 58 (74.3%) of the patients showed normal liver function tests, 18 (23%) of the patients showed moderately elevated LFT (ALT not more than 2 fold) and 2 (2.5%) of the patients showed severely elevated LFT. The symptoms of jaundice could be either a de novo acute HBV infection or a spontaneous reactivation or seroconversion flare of chronic HBV⁵. 12% (9) of the patients were identified as chronic carriers (persisting HBsAg more than 6 months), and 4 (33%) of the chronic carriers were found deviation in their hepatic function hence identified as active chronic carriers. Amazingly 7+ 4 (14%) of the patients were found to have decreased albumin concentration, since albumin level generally remains unchanged in HBV infection and the decrease may indicate clinical emergency. It should be noted that serum albumin are influenced by a variety of non-hepatic factors most notably Nutritional status, hormonal factors and plasma oncotic pressure⁸. It was found from the history that 5 of the patients were found associated with other infectious diseases, 2 were pregnant mothers, 1 of them was a leukemia patient who died during study period. Alkaline Phosphatase was found normal in 74 (95%) of the patients and moderately elevated in 4 (5%). In HBV infection Alkaline Phosphatase level never exceed 250 U/L unless marked cholestatis develops⁸. Since these two subjects were chronic carriers of HBV from 20 years back, they might have developed cholestasis or other underlying diseases to cause moderately increased serum Alkaline Phosphatase. Our tool for the estimation of alkaline Phosphatase was not able to detect liver specific alkaline Phosphatase isoenzyme.

HBsAg was found most prevalent among the 21 –30 age group followed by 31-40, the most productive age group, if they became carriers the burden would definitely devastate the entire family and the whole community. It was found that Hepatitis B was most commonly found among the positive cases having multiple sexual relationships (heterosexual) 23% this results correlate with that of world's¹⁰. But significant numbers 5 (6.4%) of the respondents were found to have done their vasectomy in the last six months to one-year period. The possibility of transmission of Hepatitis B through the surgical instruments in the family planning clinic can be suspected because the virus is quite stable in room temperature up to one week⁷. Hence sterilization process can be questioned. Further researches should be performed to explore the facts that could relate unhygienic surgical practice to HBV infection. It is highly probable that HBV infection is through unsterilized or incompletely sterilized surgical instruments or unhygienic procedures.

It was found that only few respondents had knowledge regarding Hepatitis B transmission and vaccination (8%) indicating the need of educational program to eventually stop the virus from transmission in the scenario that HIV has remained frozen due to good education in many parts of the world.

Alcoholic behavior (occasionally, weakly, daily, and Heavily) was found in 37 (47%) cases. Among them 8 were heavy drunkards (> 2 times a day) the LFT profile was found abnormal in all the 8 cases.

Of the total cases identified, 35 per cent victims are farmers and amazingly it was found the prevalence of HBV was significantly found in higher rates among the restaurant workers 12 (15%) and drivers 5 (6%) and 10 (13%) respondents were involved in other various occupation (industry, carpentry teacher and security guard).

Among 8 of the female positive cases, 3 (4% of total) were housewives 3 (4%) were farmers 1 (1.2%) was a teacher and 1 (1.2%) not identified. Of the total females 2 were pregnant mothers.

7.2 Conclusion

It was found from the study that 20 % (18% + 2%) HBsAg reactive cases correlated with the LFT and 5 (9.2%) LFT elevated cases of which 4 (8%) were icteric correlated with HBsAg so it was shown that 8% acute icteric hepatitis in Nepal is due to HBV.

Tracing the possible factors responsible for such infection in Nepal heterosexual activity, unhygienic surgical practice, transfusion hepatitis B, infection to the partner, household contact were the responsible factors as reported by the victims and in the majority of the cases 45% the cause for the burden couldn't traced.

8. RECOMMENDATIONS

- It is recommended that each HBsAg elevated cases must be monitored with the liver function test and the possibility of Hepatitis B infection must be looked in each jaundice cases.
- Good education and improved information system can be major strides in preventing the disease through wide spread vaccination and screening.
- Proper hand washing, gloving appropriate decontamination and disposal of clinical waste is highly recommended to eliminate any risk of HBV transmission as a part of infection prevention program
- Every mother should be screen for HBV as a part of safe delivery and precaution could be taken to prevent the newborn baby from HBV infection
- Sterilization at any level of surgical procedure should be considered as an obligation.

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10 HEPATITIS B SURVEY QUESTIONNAIRES

Questionnaires

Name : _____ Age : _____ Sex: _____ Pregnancy(For f only) : _____

1. **Marital Status:** Married Unmarried

2. **Occupation**
Businessman Tourism Agriculture Industry
Student Unemployed Any Other _____

3. Knowledge

Do you know how is Hepatitis B transmitted ?

Right answer Wrong answer Don't know

Do you know that vaccine is available for the prevention of HBsAg ?

Know Don't know

If yes, Is any of your family member is vaccinated against Hepatitis B ?

Yes No Don't know

3. Family History

Is any member of your family is HBsAg Reactive ?

Yes No Don't know

If yes

Relation with the member

Father Mother Wife Child Other _____

4. Behavior

Intravenous drug user

Yes No

If yes

Is any of your friends HBsAg Reactive ?

Yes No Don't know

Have you any relationships (sexual) beside your husband /wife ?

Yes No

How often do you take alcohol ?

Never Rarely (Festival) weekly

Daily Heavily (2 times a day)

When did you came to know that you are HBsAg reactive ?

Have you taken any medication against HBsAg ?

Yes No

Have you ever had jaundice in the past few years?

Yes No

History of operation / transfusion

Yes No