

Biochemical and Serological Investigations in Incidentally Detected Asymptomatic HBsAg-Positive Subjects (IDAHS)

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Abstract

This cross-sectional, observational study was conducted among 50 incidentally detected asymptomatic HBsAg positive subjects (IDAHS) in the out-patient department (OPD) of the Department of Hepatology, Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh, between May and November of 2017. All demographic characters like age, sex, education level, occupation and socio-economic status as well as mode of detection and duration of HBsAg positivity and risk factors were documented in the data sheet. Serum bilirubin and alanine aminotransferase (ALT) were measured using auto analyzer in the biochemistry laboratory. Serum bilirubin ≤1.0 mg/dl and ALT levels ≤40 IU/L in males and ≤30 IU/L in females were set as normal. Serological tests were performed by using ELISA method, e.g., HBeAg and anti-HBeAg in the microbiology laboratory. The participants' age ranged between 21 and 57 years with a mean of 30.2±9.3 years. We found that 23(46%) subjects were detected HBsAg positive during routine checkup followed by blood donation 11(22%), antenatal check-up 7(14%), going abroad 4(8%), family screening 3(6%) and before vaccination in 2(4%) subjects respectively. Among risk factors, 18(36%) had family history of HBsAg and only 1(2%) subject had unsafe sexual exposure. In total, 17(34%) were found having elevated ALT levels and only 1(2%) had abnormal bilirubin level. In total, 38(76%) subjects were HBeAg negative, while 35(70%) were Anti-HBe positive. Most IDAHS subjects were negative to HBeAg, however, they need to be followed up at regular intervals so that appropriate measures can be taken in time.

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Introduction

The original recognition of a form of hepatitis, which was contagious through blood or blood products, was reported by Lurman in Germany in 1883. He reported that jaundice had developed in 15% of people who had received a vaccine prepared by human sera for smallpox. At some stage in World War II, a high incidence of jaundice was observed among soldiers who had received a yellow fever vaccine made from human serum. In late 1960s, a unique antigen

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was identified in the serum of an Australian aborigine patient with acute leukemia. Afterward this antigen, named 'Australia antigen', was documented as hepatitis B surface antigen (HBsAg) protein and initiate to occur most commonly in patients who had received several blood transfusions.¹ More than 2 billion people worldwide have been exposed to the hepatitis B virus (HBV), and an estimated 50 million new cases are diagnosed with 5-10% of adults and up

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to 90% of infants being chronically infected each year. Worldwide, there are 350 million such cases and 75% are found in Asia. The term 'healthy carriers' is now obsolete as such individuals still harbor the risk of developing chronic liver disease, including hepatocellular carcinoma (HCC), and 'chronic hepatitis B virus infection without liver disease' is the preferred description. Hepatitis B virus is the leading cause of chronic hepatitis in Asia-Pacific countries and up to 25% of these patients will eventually die of liver cirrhosis and its complications, including HCC, because the relative risks of death due to cirrhosis and HCC are higher in individuals who are positive for hepatitis B surface antigen (HBsAg) compared with the normal population.² Risk of developing chronic HBV following acute infection depends on the age at which the infection is acquired and the immune condition of the host.³ Hepatitis B surface antigen (HBsAg) is the hallmark of HBV infection which has been reported to be the foremost serological marker in acute hepatitis B, and persistence of HBsAg for more than 6 months suggests the commencement of chronic HBV infection.⁴ The course of chronic HBV infection is now considered to consist of 4 phases: immune tolerance, immune clearance (HBeAg-positive chronic hepatitis), inactive carrier and reactivation (HBeAg-negative chronic hepatitis), although not all patients go through every phase.⁵ Today with growing and substantial data it is obvious that a good portion of this people are virologically and histologically active and are at risk of developing decompensated liver disease and HCC. To avoid ambiguity related with the previous designations used for describing such people a new term was coined in early 1990's and 2000 as incidentally detected asymptomatic HBsAg positive subjects

(IDAHS) which looks more precise. The definition includes a heterogeneous group of patients who are asymptomatic for liver disease and have been found to be positive for HBsAg in their serum during workup for unrelated symptoms or during usual check-up. Heterogeneous for the reason that it includes patients who have active as well as inactive HBV infection, early as well as advanced liver disease, and patients with low as well as high viral load.^{6,7} The global picture of IDAHS shows that around 20-70% are 'e' antigen positive and 60-70% of them have elevated liver enzymes.⁶ We proposed this study to observe the biochemical and serological profile of IDAHS in an outdoor setting of a tertiary level hospital in Dhaka, Bangladesh.

Methods

This cross-sectional, observational study was conducted among 50 incidentally detected asymptomatic HBsAg positive subjects (IDAHS) in the out-patient department (OPD) of the Department of Hepatology, Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh, between May and November of 2017. All demographic characters like age, sex, address, education level, occupation and socio-economic status were documented in a structured form after patient's registration. Mode of detection and duration of HBsAg positivity were recorded as per statement of the subjects and relevant documents. Risk factors like family history, blood transfusion, surgery, any unsafe sexual exposure and IV drug abuse were documented in the data sheet. Findings of observation were recorded on prescribed data collection form and study subjects were prepared for laboratory investigations. Serum bilirubin and alanine aminotransferase (ALT) were measured using

Beckman system autoanalyzer in the biochemistry laboratory. Serum ALT levels above 40 IU/L in males and above 30 IU/L in females were taken as significant⁶, while serum bilirubin ≤1.0 mg/dl was set as normal. Serological tests were performed by using ELISA method; HSsAg was detected using kits provided by Beijing Wantai Biologicals Ltd. from China, while HBeAg and antibody response were detected using kits from Dia Pro-Diagnostics Ltd. from Italy. All the tests were run in presence of internal and external quality control samples to ensure validity.

After collection, data editing and clearing was done manually and then prepared for data entry and analysis. Statistical Package for Social Sciences (SPSS) version 18.0 for windows was used for data analysis. Values were presented as frequency and percentage as well as mean±SD where applicable. The study was approved by the Ethical Review Committee of Shaheed Suhrawardy Medical College, Dhaka. Bangladesh.

Results

Table-I shows the socio-demographic characteristics of the study subjects. Out of 50 incidentally detected asymptomatic HBSAg positive subjects (IDAHS), most of them were in the age group \leq 40 years, followed by >40 years age group. Among study subjects the age range was between 21 and 57 years. The mean age of the study subjects was 30.2±9.3 years. Among them, 28(56%) were males and 22(44%) females. Table-II shows that the majority of the subjects were detected during routine checkup 23(46%), followed by blood donation 11(22%), antenatal check-up 7(14%), going abroad 4(8%), family screening 3(6%) and before vaccination 2(4%)

respectively.

Table-I: Socio-demographic characteristics of thestudy subjects participated in the study (n=50)

Variables	Socio- demographic characteristics	Frequency	Percentage
	≤40	41	82.0
Age (years)	>40	9	18.0
	Mean ± SD	30.2 ± 9.3 years	
Sex	Male	28	56.0
	Female	22	44.0
Educational status	None	8	16.0
	Below 5	0	0.0
	Primary	15	30.0
	Secondary	7	14.0
	Higher Secondary	11	22.0
	Graduate and above	9	18.0
	Business	2	4.0
	Service	15	30.0
Occupation	Day labor	2	4.0
	Student	12	24.0
	Housewife	15	30.0
	Others	rs 4	
Socio-	Upper class	1	2.0
economic	Middle class	30	60.0
status	Lower class	19	38.0

Table-II: Distribution of study HBsAg positive subjects by mode of detection (n=50)

Mode of Detection	Frequency	Percentage
Blood donation	11	22.0
Going abroad	4	8.0
Routine medical check- up	23	46.0
Before vaccination	2	4.0
Family screening	3	6.0
Antenatal check-up (ANC)	7	14.0
Total	50	100

Table-III shows that out of 50 subjects, 18(36%) had HBsAg positive family history, while only 1(2%) subject had history of extramarital exposure. In the remaining 31(62%) subjects no risk factor was found.

Table-III: Distribution of incidentally detectedHBsAg positive subjects by risk factors (n=50)

Risk Factors	Frequency	Percentage
Family history	18	36.0
History of blood transfusion	0	0.0
History of surgery	0	0.0
History of unsafe sex exposure	1	2.0
None	31	62.0
Total	50	100

Table-IV shows that among male subjects, 12(24%) were found having elevated ALT levels. On the other hand, among female subjects, only 1(2%) had abnormal bilirubin level and 5(10%) had increased ALT levels. In total, ALT was found elevated in 17(34%) subjects.

Table-IV: Number of abnormal levels of biochemical parameters in study subjects (n=50)

Parameter	Sex	Total Subjects Frequency (Percentage)	Mean±SD	Abnormal values detected Frequency (Percentage)
Serum bilirubin (mg/dl)	Male	28 (56.0)	0.8±0.1	-
	Female	22 (44.0)	0.9±0.2	1 (2.0)
Total		50 (100)		1 (2.0)
ALT (U/L)	Male	28 (56.0)	45.4±31.4	12 (24.0)
	Female	22 (44.0)	32.0±24.6	5 (10.0)
Total		50 (100)		17 (34.0)

Table-V indicates that out of 41 HBsAg positive subjects, in \leq 40 years and 9 HBsAg positive in >40 years age group, 24.4% and 22.2% were HBeAg positive respectively. On the contrary, 68.3% and 77.8% were anti-HBe positive among age group \leq 40 and >40 years respectively. In total, 38(76%) subjects were HBeAg negative, while 35(70%) were Anti-HBe positive.

 Table-V:
 Age
 distribution
 of
 study
 subjects

 according to their profile (n=50)

Age group (years)	HBsAg positive Frequency	HBeAg positive Frequency (Percentage)	HBeAg Negative Frequency (Percentage)	Anti-HBe positive Frequency (Percentage)	Anti-HBe Negative Frequency (Percentage)
≤40	41	10 (24.4)	31 (75.6)	28 (68.3)	13 (31.7)
>40	9	2 (22.2)	7 (77.8)	7 (77.8)	2 (22.2)
Total	50	12	38	35	15

Discussion

In the present study, the population age ranged between 21 and 57 years (mean age was 30.2 ± 9.3 years). The mean age is almost similar to a study done by Malik *et al.* as reported study subjects were between 30 and 57 years.⁷ Our study also revealed that among 50 IDAHS, 41 were within the <40 years age group and 9 were in >40 years age group. Most of them were males (56%) and females were 44%. There was male predominance, with a male to female ratio of 1.27:1 and it is almost similar to the findings of the study done by Fatima & Anjum, which was 1.29:1.⁶

In addition, in our study, we found that 23(46%) subjects were detected HBsAg positive during routine checkup followed by blood donation

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11(22%), antenatal check-up 7(14%), going abroad 4(8%), family screening 3(6%) and before vaccination in 2(4%) subjects respectively. In majority of subjects no risk factor was found to be HBsAg positive. However, 18(36%) had positive family history of HBsAg and only 1(2%) subject gave history of extramarital sexual exposure. Previous studies reported that the most common intramuscular risk factors were frequent injections, dental procedure and previous surgery.⁶⁻¹² Study done by reported that surgery and injections together as the most common risk factor in his study as 13.5%.7 Khokhar & Gill reported that 32.1% of those subjects got through injections, while 25% infected during surgery and 6.3% through dental procedures.¹⁰

In the present study, in total, 38(76%) subjects were found HBeAg negative, while 35(70%) were Anti-HBe positive. HBeAg was non-reactive in about 85% subjects as reported in similar studies done among incidentally detected HBsAg positive subjects.^{7,13,14} In such studies, age of subject is important because when infection is acquired, it markedly influences the course of disease. The chance of developing chronic infection is 90% or even more among neonates infected with HBV through perinatal transmission. Besides, inactive exposure during adolescence or young adulthood is associated with a 95% or greater possibility that the disease will be self-limiting.¹⁵⁻¹⁷ However, in the present study, the higher percentages (56%) in ≤40 yrs age group of anti-HBe positive subjects were likely to be chronic carriers. Limitations of our study include a small sample size and a short study period.

Conclusion

Incidentally detected asymptomatic HBsAg positive subjects (IDAHS) seeks medical

attention when HBsAg is found during routine check-up, blood donation, family monitoring of connections with HBV-related CLD patients or a routine examination showing abnormal ALT levels. Most IDAHS subjects are negative to HBeAg; however, they should be considered as patients. They need to be under observation and followed up at regular intervals so that appropriate measures can be taken in time, whether or not HBV DNA is detected or undetected. Prevention and control program for hepatitis B needs to be intensified and strengthened by vaccinating infants, children, adults and high-risk groups with complete dose coverage.

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