

Original Research Article

Hepatitis B virus total core antibody status in unvaccinated general population in a community of Bangladesh

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ABSTRACT

Background: Hepatitis B virus (HBV) infection poses a significant health challenge in Bangladesh, with the hepatitis B core antibody (anti-HBc) being a crucial marker due to its lifelong presence in the bloodstream. This study aimed to evaluate the prevalence of anti-HBc (total) positivity among unvaccinated adults in Northeastern Bangladesh.

Methods: This cross-sectional observational study was conducted in the Sobhanighat area of Sylhet, Bangladesh, in collaboration with the department of gastroenterology, Sylhet MAG Osmani Medical College, from November 2022 to August 2023. A total of 216 participants were selected using consecutive sampling. HBsAg, anti-HBs, and anti-HBc (total) were tested for all subjects, and data were collected using a pre-formed questionnaire and analyzed using statistical package for the social sciences (SPSS) version 24.

Results: Among the participants, 16 (7.4%) tested positive for anti-HBc (total), while HBsAg was positive in 6 (2.77%) individuals. Anti-HBs was detectable in 23 (10.6%) participants, with 3 (1.38%) showing isolated anti-HBc positivity. Notably, 20% of HBsAg-positive cases exhibited heterotypic anti-HBs. Moreover, 56.25% of respondents with anti-HBc (total) positivity had detectable anti-HBs ($p < 0.001$). Gender did not show significant associations with HBsAg, anti-HBc (total), anti-HBs, or isolated anti-HBc ($p > 0.05$).

Conclusions: The study underscores a notable prevalence of anti-HBc (total) positivity among unvaccinated individuals in Bangladesh, indicative of past HBV exposure. It underscores the necessity for enhanced vaccination coverage and robust infection control measures to mitigate HBV transmission in this demographic.

Keywords: Hepatitis B virus, Seropositive, Antibody, Vaccination

INTRODUCTION

Hepatitis B virus (HBV) is a 42-nm hepadna virus with a partially double-stranded DNA genome, inner core protein (hepatitis B core antigen, HBcAg), and outer surface coat (hepatitis B surface antigen, HBsAg). After a person is

infected with HBV, the first virologic marker detectable in serum within 1–12 weeks is HBsAg. Anti-HBc develops in response to the HBV infection and typically persists for life, regardless of whether the infection resolves or remains chronic.¹ Anti-HBc is found in different phases of HBV infection: acute, chronic, resolved HBV infection,

occult HBV infection (OBI), and false positive cases. Anti-HBc positive with HBsAg positive indicates ongoing infection. IgM anti-HBc predominates during the first 6 months after acute infection. IgG anti-HBc is the predominant class of anti-HBc beyond 6 months. Patients with current or recent acute hepatitis B have IgM anti-HBc in their serum. HBsAg negative and anti-HBc positive indicate previous infection or resolved HBV infection. HBsAg negative, Anti-HBc positive, and anti HBs positive person is immune due to previous natural HBV infection. HBsAg-negative, anti-HBc positive patients, and anti HBs-negative can occur in certain conditions; previous exposure to HBV, it is the most common reason for anti-HBc positivity; false positive: less commonly anti-HBc may be a false-positive test result, particularly in low prevalence areas; window phase; and false negative HBsAg: in case of HBsAg mutations that lead to false-negative HBsAg with ongoing HBV infection.^{2,3} Occult HBV infection (OBI) OBI refers to the presence of HBV DNA in the absence of detectable hepatitis B surface antigen.⁴ In occult HBV infection, low viremia is detected by HBV DNA in serum or liver. Persons recovering from acute HBV in the past and anti HBs has waned to undetectable level, but some had been chronically infected with HBV for decades (with DNA 20-200 IU/ml) before clearing HBsAg. Anti-HBc is found positive. They are still at minor risk of developing HCC like inactive chronic HBV with undetectable DNA.^{5,6} When isolated anti-HBc occurs in the rare patient with chronic hepatitis B whose HBsAg level is below the sensitivity threshold of contemporary immunoassays (a low-level carrier), anti-HBc is of the IgG class. Generally, in persons who have recovered from hepatitis B, anti-HBs and anti-HBc persist indefinitely. There are few studies on anti-HBc antigens in Bangladesh and India. It showed prevalence of anti-HBc among HBsAg negative was 14.6%.⁷ The incidence of anti-HBc antibody among HBsAg-negative healthy blood donors was 11.7% and the prevalence of the hepatitis B core antibody was 10.01% among voluntary blood donors in Chennai, India.^{8,9} Among the blood donors in Bangladesh anti-HBc was detected in 20.6%.¹⁰ In Bangladesh, there is no study on anti-HBc (total) in the general population. One study in the Kalyanpur slum at Dhaka showed that the prevalence of anti-HBc total was 47.6%.¹¹ In South East part of Bangladesh (Sylhet) there is no such data. This study estimated the total core antibody status in the unvaccinated general population in a community in north eastern part of Bangladesh.

METHODS

This cross-sectional observational study was conducted in the Sobhanighat area of Sylhet, Bangladesh, in collaboration with the Department of Gastroenterology, Sylhet MAG Osmani Medical College, spanning from November 2022 to August 2023. The study population consisted of individuals aged >18 years old, with a total of 216 patients selected as study subjects using a consecutive sampling technique adhering to specific inclusion and exclusion criteria. Inclusion criteria comprised individuals

aged >18 years old, both males and females, who were willing to provide consent, while exclusion criteria included patients with known chronic liver disease, severe co-morbidities, chronic kidney disease (CKD) on dialysis, a history of HBV vaccination or infection, and those who declined to participate. Patients underwent comprehensive history taking and clinical examination, with HBsAg tested using the chemiluminescence immunoassay method, anti-HBs titer measured through enhanced chemiluminescence immunoassay, and anti-HBc total antibody evaluated using the same method. HBsAg (ELISA) positive patients and anti-HBc (total) positive individuals had their samples tested for HBV DNA by real-time quantitative micro-PCR. Data collection utilized a pre-formed questionnaire and was managed, edited, and analyzed using statistical package of social sciences (SPSS) version 24, with statistical significance set at a 95% confidence level. Continuous data were expressed as mean and standard deviation, while categorical data were presented as frequency and percentage. The association between categorical variables was determined through the Chi-square test and Fisher exact test, where applicable, and the difference between the previous prevalence rate and the study prevalence was assessed via a one-sample t-test. Results were subsequently presented in tables and charts. Ethical clearance was obtained from the ethical committee of MAG Osmani Medical College, Sylhet, and informed written consent was acquired from all participants.

RESULTS

The mean age of the respondents was 31.69±11.23 years, while most of the respondents were in the 18-29 years age group (48.6%). Maximum respondents were married (70.4%) and the majority of them were housewives (31.9%). The monthly family income of most of the respondents was 15000-30000 BDT (41.2%) (Table 1).

As a risk factor for hepatitis B infection, most commonly found ear-nose-body piercing (25.5%), then sharing of blade, razor (11.6%), circumcision by hajam (9.2%) and needle prick injury (2.3%) in whole life (Table 2).

Complete EPI vaccination (without hepatitis B vaccination) was found in 89.4% of respondents. Among 216 respondents, 6 (2.77%) had positive HBsAg. 216 respondents 23 (10.6 %) were detected for anti-HBs and the rest were not detectable. 16 (7.4%) had positive anti-HBc (total) (Table 3).

Out of 216 respondents, only 2 (0.9%) respondents had positive HBV DNA (>55.92 IU/ml). Other 14 (6.5%) were undetected and 200 (92.6%) were not advised for HBV DNA detection (Figure 1).

Among 216 respondents 3 (1.4%) respondents had positively isolated anti-HBcAb (HBsAg-, anti-HBs AB-) (Figure 2).

Table 1: Distribution of socio-demographic status (n=216).

Variables	N	%
Age (in years)		
18-29	104	48.6
30-39	73	33.7
40-59	21	9.7
50-59	8	3.7
>60	10	4.1
Sex		
Male	115	53.2
Female	101	46.8
Marital status		
Married	152	70.4
Unmarried	64	29.6
Occupation		
Hospital personal	11	5
Businessman	43	19.9
Housewife	69	31.9
Student	27	12.5
Private job	26	12
Driver	13	6
Teacher	2	0.9
Govt. job	3	1.38
Day laborer	6	2.7
Others	18	8.3
Monthly family income (BDT)		
<15000	24	4.1
15000-30000	89	41.2
30000-50000	69	31.9
>50000	34	15.8

Table 2: Risk factors of hepatitis B infection in whole life (n=216).

Risk factor	N	%
Needle prick injury	5	2.3
Blood transfusion history	2	0.9
Dental procedure history	4	1.8
Sharing of blade, razor	25	11.6
Circumcision by Hajam	20	9.2
Injectable drug user	1	0.4
Ear-nose-body piercing	55	25.5
Sexual exposure (unsafe)	4	1.8

Table 4: Investigation of hepatitis B infection among respondents (n=216).

Investigation	Total (%) n=216	Male (%) n=115	Female (%) n=101	P value
HBsAg positive	6 (2.77)	3 (2.6)	3 (2.97)	0.981*
Positive anti-HBs Ab	23 (10.6)	11 (10.5)	12 (11.7)	0.787*
Anti HBc Ab	16 (7.4)	9 (8.6)	7 (6.8)	0.631**
HBV DNA (≥ 55.92 IU/ml)	2 (0.9)	0	2 (1.98)	0.122*
Isolated anti-HBc Ab	3 (1.38)	2 (1.74)	1 (0.99)	0.572*

*Fisher's exact test and **Chi-square test were done

Table 3: Clinical characteristics among the respondents (n=216).

Variables	N	%
Past vaccination history (EPI vaccine)		
Complete	193	89.4
Not given	23	10.6
HBsAg		
Positive	6	2.78
Negative	210	97.2
Anti-HBs		
Detectable	23	10.6
Not detectable	193	89.4
Positive	16	7.4

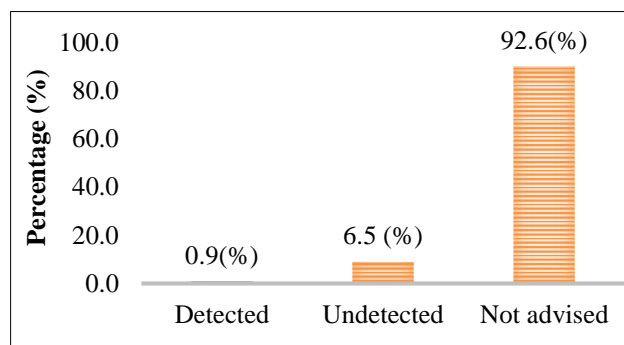


Figure 1: Frequency of positive HBV DNA among respondents (n=200).

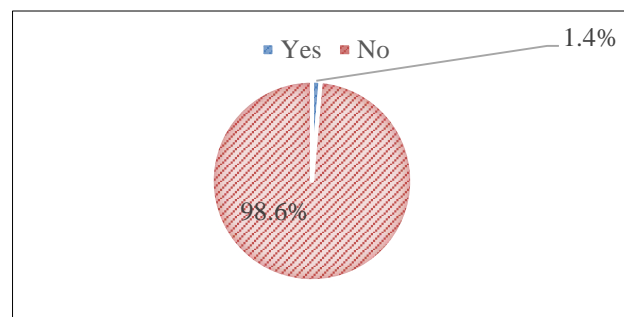


Figure 2: Frequency of isolated anti-HBcAb among respondents (n=216).

There was no significant association of male and female gender with HBsAg, anti-HBcAb, anti-HBs Ab, HBV DNA (>55.92 IU/ml), and isolated anti-HBc Ab (Table 4).

The majority of the respondents were found uninfected and not immune 185 (85.6%). However, 4 (1.85%) respondents had chronic hepatitis B infection and one (0.46%) had chronic hepatitis B infection with heterotypic anti-HBs Ab. Also, 12 (5.5%) respondents were found with past HBV infection, resolved or false-positive. Nevertheless, 14 (6.48%) respondents were immune (Figure 3).

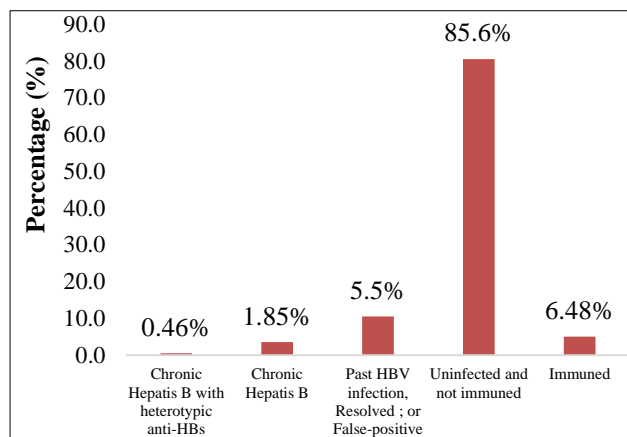


Figure 3: Distribution of diagnosis among respondents (n=216).

75% of past HBV infections (resolved) were found among positive anti-HBc (total) respondents. While 100% of respondents with negative anti-HBc (total) had no past HBV infection (Table 5).

Table 5: Association between past HBV infection, resolved or false-positive cases with anti-HBc (total) (n=216).

Past HBV infection (resolved)	Anti- HBc (total)		P value*
	Positive (%), n=16	Negative (%), n=200	
Yes	12 (75)	0	<0.001
No	4 (25)	200 (100)	

*A Chi-square test was done

Among positive anti-HBc antibodies, 43.7% had 0-9 mIU/ml of anti-HBs antibody titre. However, ≥51 mIU/ml was found in 25% (Table 6).

Table 6: Association between level of anti-HBs antibody with anti-HBc Ab positivity among respondents (n=216).

Anti-HBs antibody titer (mIU/ml)	Anti-HBcAb		P value*
	Positive (%), n=16	Negative (%), n=200	
0-9	7 (43.7)	186 (93)	<0.001
10-12	1 (6.25)	0	
13-50	4 (25)	6 (3)	
≥51	4 (25)	8 (4)	

*Fisher's Exact test was done

DISCUSSION

In this study, most of the respondents were in the 18-29 years age group (48.6%) with the mean age of 31.56±11.12 years, which was similar to other studies.^{8,12} The present study documented high numbers of Ear-Nose-body piercings (25.5%), sharing blade and razor (11.6%), circumcision by hajam (9.2%), and needle prick injury (2.3%) among respondents. Other risk factors were injectable drug users (0.4%), and unsafe sexual exposure (1.8%) in this study. Another study revealed HBsAg prevalence in injection drug users was 19.1% and a higher risk of contracting sexually transmitted infections due to comparatively unsafe sex lives.¹⁴ Also, hazardous use of medical equipment, including syringes, are major risk factor for hepatitis B transmission in Bangladesh and 7.2% of the health workers were found to have needle sticks or sharp injuries.^{15,16} Bangladeshi children are now 95% vaccinated with hepatitis B vaccine through EPI.¹⁷ In this study, out of 216 respondents, 6 (2.77%) had positive HBsAg. A study in the general population of Bangladesh showed the prevalence of HBV infection at 4.0%.¹⁸ In this study, out of 216 respondents, 16 (7.4%) had positive total anti-HBc. A study in Poland shows the seroprevalence of anti-HBc was 12.1%.¹⁹ In a study of Bangabandhu Sheikh Mujib Medical University, Dhaka, the incidence of anti-HBc antibodies among apparently healthy blood donors was found 11.7%.⁸ In a tertiary care hospital in Chittagong, Bangladesh, among HCWs, the seroprevalence of anti-HBc was 48.7% and in the current study, 6 persons out of 11 (54.54%) hospital staff were anti-HBc (total) positive.²⁰ Besides, 23 (10.6%) respondents were detected for anti-HBs in this study. In a similar study, overall seroprevalence of anti-HBs was 30.1%.²⁰ HBsAg and anti-HBs coexistence among chronic hepatitis B virus infections found in one out of five (20%) cases in this study. In a study concurrence of HBsAg and anti-HBs was found in 26.1%.²¹ Only 2 (0.9%) respondents had positive HBV DNA and 13.5% of respondents had undetected HBV DNA. Prevalence of HBV DNA among anti-HBc (total) positive was 12.5% (2/16). The overall prevalence of HBV DNA among the anti-HBc seropositive was 2.2% in a similar study.⁷

The majority of the respondents were found uninfected and non-immune (85.6%), which meant negative for HBsAg, anti-HBs Ab, and anti-HBc Ab. However, 1.85% of respondents had chronic hepatitis B infection and 0.46% had chronic hepatitis B infection with heterotypic anti-HBs. Total chronic hepatitis B was 2.31%. These findings were similar to another study an intermediate prevalence of HBV infection (4%).¹⁸ Though this study was conducted in an unvaccinated population, 5.5% of respondents were found with past HBV infection, resolved or false-positive, and 6.48% of respondents were found immune from HBV infection or those responders forgot vaccine history. In this study, those who were previously infected with hepatitis B virus, 75% had resolved hepatitis B virus infection.

Limitations

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community. Moreover, liver biopsy was not included in the study to confirm the serology and incidence of OBI. We could not determine HBV DNA less than 55.92 IU/ml by PCR machine in Sylhet.

CONCLUSION

The study highlights a significant prevalence of hepatitis B virus total core antibody (anti-HBc) positivity among respondents, indicating past exposure to HBV within the unvaccinated population in Bangladesh. The findings emphasize the importance of continued efforts to improve vaccination coverage and implement stringent infection control measures to reduce the burden of HBV transmission in this context.

Recommendations

HbsAg, anti-HBs, and anti HBc (total) should be tested before HBV vaccination of an adult person and HBsAg and anti-HBc (total) should be advised to donor before blood donation. Organ transplant recipients, before starting biologic agents for IBD patients and before immunosuppressive drugs, persons should be screened with HBsAg, anti-HBs, and anti HBc (total) to assess the risk of reactivation of HBV infection. Moreover, a community-based larger population study is recommended to use this finding.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

- Hollinger FB. Hepatitis B virus infection and transfusion medicine: science and the occult. *Transfusion*. 2008;48(5):1001-26.
- McMahon BJ, Parkinson AJ, Helminiak C, Wainwright RB, Bulkow L, Kellerman-Douglas A, et al. Response to hepatitis B vaccine of persons positive for antibody to hepatitis B core antigen. *Gastroenterology*. 1992;103(2):590-4.
- Raimondo G, Pollicino T, Cacciola I, Squadrito G. Occult hepatitis B virus infection. *J Hepatol*. 2007;46(1):160-70.
- Kwak MS, Kim YJ. Occult hepatitis B virus infection. *World J Hepatol*. 2014;6(12):860-9.
- Gounder PP, Bulkow LR, McMahon BJ. hepatitis B surface seroclearance does reduce the risk of hepatocellular carcinoma—authors reply. *Aliment Pharmacol Ther*. 2016;44(6):650-1.
- Nathanson MH, Terrault N. Hepatitis B surface antigen loss: not all that we hoped it would be. *Hepatology*. 2016;64(2):328-9.
- Madhavan A, Sachu A, Balakrishnan AK, Balakrishnan S, Vasudevapanicker J. Prevalence of Anti-HBc Antibodies among HBsAg Negative Individuals and Its Association with Occult Hepatitis B. *J Lab Physicians*. 2021;13(01):1-5.
- Shil N, Biswas J, Khatun A, Rahman A, Sultana N, Easmin F, et al. Incidence of anti-HBc antibody (IgG and IgM) among HBsAg negative healthy blood donors. *Bangabandhu Sheikh Mujib Med Univ J*. 2016;9(4):201-4.
- Maheswari KS, Arun R, Arumugam P. The prevalence of the hepatitis B core antibody and the occult hepatitis B infection among voluntary blood donors in Chennai, India. *J Clin Diagnostic Res JCDR*. 2012;6(10):1710.
- Jahan M, Islam MA, Akbar SM, Takahashi K, Tabassum S, Rahman A, et al. Anti-HBc screening of blood donors in Bangladesh: relevance to containment of HBV propagation. *J Clin Exp Hepatol*. 2016;6(2):115-8.
- Ghosh DK, Ghosh CK, Nath M, Safwath SA, Saha SK, Rowshon AH. Prevalence of anti-HBc total positivity in an impoverished Urban Community in Bangladesh. *Bangladesh Med Res Counc Bull*. 2017;43(2):63-70.
- Harun MG, Sumon SA, Mohona TM, Rahman A, Abdullah SA, Islam MS, et al. Hepatitis B Vaccination Coverage among Bangladeshi Healthcare Workers: Findings from Tertiary Care Hospitals. *Vaccines*. 2023;11(1):1-10.
- Uz-Zaman MH, Rahman A, Yasmin M. Epidemiology of Hepatitis B Virus Infection in Bangladesh: Prevalence among General Population, Risk Groups, and Genotype Distribution. *Genes (Basel)*. 2018;9(541).
- Kayesh ME, Kohara M, Tsukiyama-Kohara K. Epidemiology and Risk Factors for Acute Viral Hepatitis in Bangladesh: An Overview. *Microorganisms*. 2022;10(11):1-11.
- Uddin MS, Islam MN, Khan ME, Yeasmin S, Ahmed F, Amiruzzaman M. Frequency of Hepatitis B and C Viral Infection among the Medical Waste Handlers. *Bangladesh J Infect Dis*. 2018;4(1):3-9.
- Mustafa MG, Alam MS, Azam MG, Alam MM, Islam MS, Khan M. Eliminating Hepatitis B from Bangladesh by the Year 2030. *J Bangladesh Coll Physicians Surg*. 2020;38(3):145-9.
- Banik S, Datta A, Ghosh A, Ghosh KY, Debi H. The prevalence of hepatitis B virus infection in Bangladesh: a systematic review and meta-analysis. *Epidemiol Infect*. 2022;150(47):1-8.
- Roy Biswas R, Karim M, Bhattacharjee B. Hepatitis B virus infection and vaccination status among health care workers of a tertiary care hospital in Bangladesh. *J Sci Soc*. 2015;42(3):176-9.
- Hayashi J, Noguchi A, Nakashima K, Morofuji M, Kashiwagi S. Frequency of concurrence of hepatitis B surface antigen and antibody in a large number of carriers in Okinawa, Japan. *Gastroenterol Jpn*. 1990;25(5):593-7.

20. Mwangi IA, Wesongah JO, Musyoki VM, Omosa-Manyonyi GS, Farah B, Edalia LG, et al. Assessment of hepatitis B vaccination status and hepatitis B surface antibody titers among health care workers in selected public health hospitals in Kenya. *PLOS Glob Public Health.* 2023;3(4):1-10.
21. Gheorghe L, Csiki IE, Iacob S, Gheorghe C. The prevalence and risk factors of hepatitis B virus infection in an adult population in Romania: A nationwide survey. *Eur J Gastroenterol Hepatol.* 2013;25(1):56-64.

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