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**Original Research Article**

# Impact of transfusion history on hepatitis B virus seropositivity among thalassemic and hemophilic patients

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## ABSTRACT

**Background:** Patients with thalassemia and hemophilia require repeated blood transfusions, which increase the risk of transfusion-transmitted infections, including hepatitis B virus (HBV). Despite routine donor screening, previous exposure to HBV may still occur, particularly in multi-transfused populations. To assess the impact of transfusion history on hepatitis B virus seropositivity among thalassemic and hemophilic patients.
**Methods:** This cross-sectional analytical study was conducted at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from March 2021 to August 2023. A total of 50 multi-transfused patients (25 thalassemia and 25 hemophilia) were enrolled. HBsAg and Anti-HBc were tested and transfusion history, demographics and vaccination status were analyzed using SPSS.
**Results:** All participants were negative for HBsAg. Anti-HBc (total) positivity was detected in 22.0% of patients, including 24.0% of hemophilia patients and 20.0% of thalassemia patients. Demographic factors, transfusion burden, transfusion interval, type of blood component and hepatitis B vaccination history showed no statistically significant association with Anti-HBc positivity ($p>0.05$). However, a significant association was observed between Anti-HBc positivity and a history of receiving transfusions from multiple centers ($p=0.001$).
**Conclusions:** Although active HBV infection was not detected, a substantial proportion of multi-transfused patients had evidence of previous HBV exposure. Receiving transfusions from multiple centers was the most important risk factor for HBV seropositivity, highlighting the need for standardized and high-quality transfusion practices across all centers.

**Keywords:** Anti-HBc, Blood transfusion, Hemophilia, Hepatitis B virus, Thalassemia

## INTRODUCTION

Patients with β-thalassemia and hemophilia frequently depend on repeated transfusions of red cell concentrates and/or plasma products to prevent severe anemia, bleeding complications and long-term disability. While transfusion therapy is lifesaving, it also increases cumulative exposure to transfusion-transmitted infections (TTIs) particularly in settings where donor selection, screening platforms and hemovigilance systems vary across facilities.[1-3] HBV remains a key concern because it is efficiently transmitted through blood, can persist as chronic infection and contributes substantially to cirrhosis and hepatocellular carcinoma worldwide.[4]

In 2022, global estimates continued to indicate a very large chronic HBV burden and major ongoing incidence, reinforcing HBV as a sustained public-health threat despite vaccine availability.[5] Blood safety programs have reduced HBV transmission risk by implementing mandatory screening of donated blood, commonly including hepatitis B surface antigen (HBsAg) testing and additional assays depending on national policy and resources.

The World Health Organization (WHO) has long emphasized that screening of every donation using quality-assured methods is essential to prevent TTIs and it provides practical recommendations for strengthening screening systems in low- and middle-income countries (LMICs). Nevertheless, reliance on HBsAg alone may miss certain infections, especially during the window period and in occult hepatitis B infection (OBI), where HBV DNA may be present despite negative HBsAg. This residual risk is particularly relevant for multi-transfused patients who accumulate exposure over time, making even low per-unit risks clinically meaningful.[6]

Beyond routine donor screening, another challenge is that transfusion recipients may receive blood from multiple centers with heterogeneous screening quality, differing test kits and variable adherence to standard operating procedures.[7] In Bangladesh, regulatory frameworks such as the safe blood transfusion policy environment have aimed to ensure screening for major TTIs, yet real-world implementation can still differ across public and private sectors and across regions, affecting recipient risk. These realities make "transfusion history" (e.g., number of transfusions, duration of transfusion dependence and whether transfusions occurred at multiple facilities) an important epidemiologic variable when studying HBV exposure among chronically transfused populations.[8]

Serologic assessment of HBV exposure in transfusion-dependent patients often includes HBsAg (suggesting current infection) and total antibody to hepatitis B core antigen (anti-HBc) (suggesting prior exposure to HBV). Anti-HBc is valuable because it can identify previous or ongoing infection even when HBsAg is negative, including scenarios compatible with OBI or resolved infection. In thalassemia cohorts, studies from different regions have documented measurable rates of anti-HBc and/or HBV markers despite improvements in screening and vaccination coverage, reflecting ongoing exposure risk over years of transfusion care.[9] A large body of literature also shows that TTIs remain a continuing challenge in hemophilia and other heavily transfused groups, with HBV prevalence varying by country, era of blood safety measures and product types used (whole blood components vs. virally inactivated factor concentrates).[10] Vaccination is central to HBV prevention and is recommended for high-risk groups, including transfusion-dependent patients. However, vaccine response can be incomplete in some individuals and may wane without monitoring and patients may still have exposure risk prior to full immunization or booster coverage. Evidence from thalassemia populations suggests generally good vaccine immunogenicity, but anti-HBc positivity can still be detected in a minority, underscoring that vaccination alone cannot fully substitute for strong transfusion safety systems.[11]

Given these considerations, examining the impact of transfusion history on HBV seropositivity among thalassemic and hemophilic patients is important for several reasons. First, it helps quantify the cumulative risk associated with multi-center transfusion pathways.

Second, it can inform targeted interventions such as strengthening centralized transfusion services, improving quality assurance across sites and considering enhanced screening strategies where feasible. Finally, identifying associations between transfusion patterns and markers like anti-HBc (with or without HBsAg positivity) can guide clinicians toward appropriate follow-up testing and counselling, especially in settings where chronic transfusion programs are expanding and patient survival is improving.

### *Objectives*

The main objective was to assess the impact of transfusion history on hepatitis B virus seropositivity among thalassemic and hemophilic patients.

## METHODS

This cross-sectional study was conducted in the Department of Transfusion Medicine at Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, over a period from March 2021 to August 2023. The study included patients diagnosed with thalassemia or hemophilia as confirmed by clinical records, irrespective of age and sex, who had a history of receiving at least one blood or blood component transfusion and provided informed written consent (or assent with guardian consent in the case of minors).

Patients with known chronic liver disease unrelated to transfusion, those with documented HBV infection prior to

initiation of transfusion therapy, critically ill patients unable to participate and those unwilling to provide consent were excluded from the study. A total of 50 participants were enrolled using a purposive sampling technique based on availability and fulfilment of the inclusion criteria. Among them 25 hemophilia and rest 25 thalassemia participant.

After obtaining informed written consent (or guardian consent for minors), data were collected through face-to-face interviews and review of medical records using a predesigned structured data collection sheet. Information on sociodemographic characteristics, clinical diagnosis, duration and frequency of transfusions, history of receiving transfusions from single or multiple centers, type of blood components received and hepatitis B vaccination status was recorded.

For laboratory assessment, 3–5 ml of venous blood was collected aseptically from each participant. Serum was separated and tested for hepatitis B surface antigen (HBsAg) and total antibody to hepatitis B core antigen (anti-HBc total) using immunochromatographic test (ICT) kits according to the manufacturer's instructions and standard laboratory protocols.

HBV seropositivity was defined as the presence of anti-HBc (total) with or without HBsAg positivity. Written informed consent was obtained from all patients after proper explanation of the study. Ethical approval was obtained from the Ethical Review Committee of Bangabandhu Sheikh Mujib Medical University. Patient confidentiality was strictly maintained throughout the study.

### *Statistical analysis*

All data were recorded systematically in preformed data collection form and quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Statistical analysis was carried out by using Statistical analysis was done by using SPSS (Statistical Package for Social Science) Version 22. Confidentially was strictly maintained.

## RESULTS

Figure 1 shows age distribution of the patients. The majority of the study participants were aged ≤10 years (38.0%), followed by those aged 11–15 years (18.0%) and 16–20 years (16.0%). Smaller proportions of participants were in the age groups 21–25 years (10.0%), 26–30 years (6.0%) and 31–35 years (4.0%), while 8.0% were older than 35 years.

Figure 2 shows gender distribution of the study patient. The majority of the study participants were male, accounting for 40 (80.0%) cases, while females comprised 10 (20.0%) of the total study population.

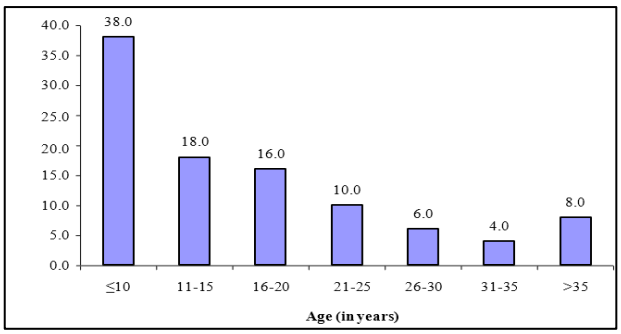


**Figure 1: Distribution of the study patient age.**

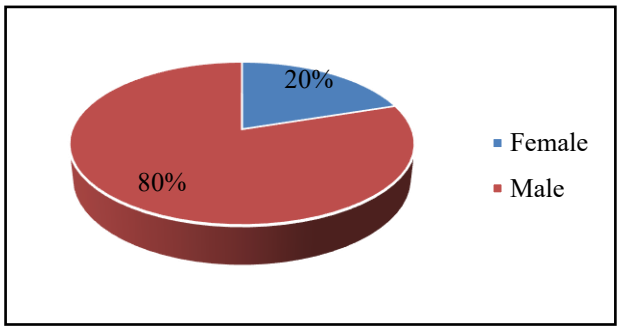


**Figure 2: Distribution of the study patient gender.**

Table 1 shows the distribution of study participants according to hepatitis B seropositivity. All hemophilia and thalassemia patients were negative for HBsAg. Anti-HBc (total) positivity was detected in 6 (24.0%) hemophilia patients and 5 (20.0%) thalassemia patients. Table 2 shows the association between demographic characteristics and anti-HBc (total) status. Although the mean age was lower in the Anti-HBc–positive group compared to the negative group, the difference was not statistically significant ($p>0.05$). Most participants were male, with no significant difference in gender distribution between the two groups. Similarly, there were no statistically significant differences in socio-economic status or place of residence between Anti-HBc–positive and anti-HBc–negative participants ($p>0.05$).

Table 3 shows association of transfusion burden and timing with anti-HBc (total) status. There was no statistically significant association between transfusion burden or timing and anti-HBc (total) status. Although anti-HBc–positive patients had a lower mean age at first transfusion and received a higher number of transfused units, these differences were not significant. The usual transfusion interval also did not differ significantly between anti-HBc–positive and anti-HBc–negative groups ($p>0.05$). Table 4 demonstrates that the type of blood component transfused and history of hepatitis B immunization were not significantly associated with anti-HBc (total) status ($p>0.05$). In contrast, a statistically significant association was observed between history of receiving transfusions from multiple centers and anti-HBc (total) positivity ($p=0.001$), with all anti-HBc–positive patients having a history of multi-center transfusion.

**Table 1: Hepatitis B virus serological status among thalassemic and hemophilic patients (n=50).**

| Serological marker | Hemophilia (n=25) | | Thalassemia (n=25) | |
|---|---|---|---|---|
| | N | % | N | % |
| **HBsAg** | | | | |
| Positive | 0 | 0.0 | 0 | 0.0 |
| Negative | 25 | 100.0 | 25 | 100.0 |
| **Anti-HBc (total)** | | | | |
| Positive | 6 | 24.0 | 5 | 20.0 |
| Negative | 19 | 76.0 | 20 | 80.0 |

**Table 2: Association between demographic characteristics and anti-HBc (total) status (n=50).**

| Characteristics | Anti-HBc positive (n=11) | Anti-HBc negative (n=39) | P value |
|---|---|---|---|
| **Mean age (in years)** | 15.4±5.3 | 17.0±10.8 | 0.631$^{ns}$ |
| **Gender** | | | |
| Male | 9 (81.8%) | 31 (79.5%) | 0.618$^{ns}$ |
| Female | 2 (18.2%) | 8 (20.5%) | |
| **Socio-economic condition** | | | |
| Middle | 2 (18.2%) | 10 (25.6%) | 0.472$^{ns}$ |
| Poor | 9 (81.8%) | 29 (74.4%) | |
| **Residence** | | | |
| Urban | 3 (27.3%) | 18 (46.2%) | 0.221$^{ns}$ |
| Rural | 8 (72.7%) | 21 (53.8%) | |

ns=not significant, p value reached from Fisher's exact test.

**Table 3: Association of transfusion burden and timing with anti-HBc (total) status (n=50).**

| Transfusion variables | Anti-HBc positive (n=11) | Anti-HBc negative (n=39) | P value |
|---|---|---|---|
| **Age at first transfusion (in years)** | 1.67±1.80 | 2.82±2.94 | 0.225$^{ns}$ |
| **Total units of transfusion** | 27.36±19.12 | 23.82±18.77 | 0.584$^{ns}$ |
| **Usual transfusion interval** | | | |
| ≤1 month | 9 (81.8%) | 29 (74.4%) | 0.965$^{ns}$ |
| >1 month | 2 (18.2%) | 10 (25.6%) | |

ns=not significant, p value reached from Fisher's exact test.

**Table 4: Association of transfusion source, blood component type and HBV immunization with anti-HBc (total) status (n=50).**

| Variable | Anti-HBc positive | Anti-HBc negative | P value |
|---|---|---|---|
| **Type of blood component** | | | |
| FFP (Hemophilia) | 6 (24.0%) | 19 (76.0%) | 0.733$^{ns}$ |
| RCC (Thalassemia) | 5 (20.0%) | 20 (80.0%) | |
| **History of transfusion from multiple centers** | | | |
| Yes | 11 (100.0%) | 10 (25.6%) | 0.001$^{s}$ |
| No | 0 (0.0%) | 29 (74.4%) | |
| **History of HBV immunization** | | | |
| Yes | 6 (17.1%) | 29 (82.9%) | 0.205$^{ns}$ |
| No | 5 (33.3%) | 10 (66.7%) | |

s=significant, ns=not significant, p value reached from Fisher's exact test.

## DISCUSSION

This study was conducted to evaluate the impact of transfusion history on HBV seropositivity among multi-transfused thalassemic and hemophilic patients attending BSMMU. Despite the implementation of stringent donor screening and infection control protocols at BSMMU, a proportion of patients demonstrated serological evidence of previous HBV exposure, as indicated by anti-HBc (total) positivity. This observation raises important concerns regarding the residual risk of transfusion-transmitted HBV infection even in well-regulated transfusion settings. One of the key explanations for this phenomenon is the limitation of routine serological screening, particularly the inability of HBsAg-based testing to detect infections during the immunological window period and occult hepatitis B infection. Occult HBV infection is characterized by the absence of detectable HBsAg with persistence of HBV DNA in liver tissue and, in some cases, serum. Such infections may

escape detection by conventional ICT kits commonly used in blood banks.[12] In addition, studies have demonstrated that ICT-based rapid tests have limited sensitivity for certain HBV serotypes, increasing the likelihood of false-negative results.[13] These findings support the recommendation for nucleic acid testing (NAT), which significantly shortens the window period and improves detection of low-level viremia.[14] In the present study, all thalassemic and hemophilic patients were negative for HBsAg, reflecting the effectiveness of routine donor screening practices. Similar findings have been reported by Sherief et al and Mirzaei et al who also observed an absence of HBsAg positivity among multi-transfused patients.[15,16] However, anti-HBc (total) positivity was detected in 22.0% of the study population, indicating previous HBV exposure. Comparable anti-HBc prevalence has been reported in other regional and international studies, although wide variation exists depending on geographic location, screening methods and transfusion practices.[17,18] Demographic characteristics such as age, gender, socio-economic status and place of residence were not significantly associated with anti-HBc (total) positivity in this study. Although anti-HBc-positive patients were slightly younger than anti-HBc-negative patients, the difference was not statistically significant. Similar observations have been reported by Tognon et al who found age-related trends without consistent statistical significance. The predominance of male participants, particularly among hemophilia patients, reflects the genetic nature of the disease and is consistent with previous studies.[19] Transfusion burden and timing, including age at first transfusion, total number of transfused units and usual transfusion interval, were not significantly associated with anti-HBc (total) positivity.

While anti-HBc-positive patients tended to receive transfusions at an earlier age and had a higher cumulative transfusion load, these differences did not reach statistical significance. Other studies have reported conflicting results; some suggest that early and frequent transfusions increase HBV exposure risk, while others, similar to the present study, did not demonstrate a significant association, possibly due to improved screening and limited sample size.[20,21] The most important and statistically significant finding of this study was the strong association between anti-HBc (total) positivity and a history of receiving transfusions from multiple centers. All anti-HBc-positive patients had received transfusions from centers other than BSMMU, whereas the majority of anti-HBc-negative patients had received transfusions exclusively from BSMMU. This finding strongly suggests that variability in screening quality, donor selection and laboratory facilities across different centers plays a critical role in HBV exposure. Similar associations have been reported in studies from low- and middle-income countries, where decentralized transfusion services are linked to higher residual risks of transfusion-transmitted infections.[19] No significant association was found between the type of blood component transfused (RCC or FFP) and anti-HBc (total) positivity. This suggests that, when appropriate screening is applied, the type of blood component alone does not significantly influence HBV exposure risk. Likewise, hepatitis B vaccination history was not significantly associated with Anti-HBc positivity. This may reflect HBV exposure prior to complete immunization, waning immunity or immune dysregulation related to iron overload and repeated antigenic stimulation in multi-transfused patients.[22] Similar findings have been reported by Mirzaei et al although other studies have demonstrated improved seroprotection following vaccination. Overall, the findings of this study indicate that although current transfusion practices have effectively prevented active HBV infection, previous HBV exposure remains a significant concern among thalassemic and hemophilic patients. The strong association between multi-center transfusion history and anti-HBc positivity highlights the need for standardized nationwide transfusion protocols, enhanced screening strategies including NAT and routine monitoring of HBV serological markers. Strengthening transfusion safety measures is essential to further reduce HBV exposure and improve long-term outcomes in transfusion-dependent populations.

The study was conducted at a single center with a relatively small sample size, which may limit the generalizability of the findings. Its cross-sectional design does not allow causal inference. HBV status was assessed using serological markers only, without nucleic acid testing, so occult HBV infection could not be confirmed. Additionally, reliance on patient records and recall for transfusion history may have introduced information bias.

## CONCLUSION

This study demonstrates that although active hepatitis B infection was not detected among multi-transfused thalassemic and hemophilic patients, a considerable proportion showed anti-HBc (total) positivity, indicating previous exposure to HBV. Transfusion burden and timing were not significantly associated with HBV seropositivity; however, a history of receiving transfusions from multiple centers showed a significant association with anti-HBc positivity. These findings highlight the importance of standardized and high-quality blood screening practices across all transfusion centers. Strengthening centralized transfusion services, ensuring strict donor screening and considering the incorporation of more sensitive testing methods may further reduce the risk of transfusion-related HBV exposure in transfusion-dependent patients.

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