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Research Article

Haemostatic Disorder and Thrombotic Risk in Chronic Hepatitis B Patients at UNIOSUN Teaching Hospital, Osogbo

***Rofiah Busayo OLAYINKA and Adesina Beatrice EBUN**

Department of Medical Laboratory Science, Faculty of Basic Medical and Health Sciences, Lead City University, Ibadan, Nigeria

****Corresponding Author's email*:** olayinkarofiah@gmail.com

ABSTRACT

Hepatitis B virus (HBV) infection is a significant global health burden, causing liver damage and throws off haemostatic balance, putting patients at risk for thrombosis and bleeding. A total of 120 study subjects between the ages of 18-64 years old, comprised of 80 confirmed chronic HBV patients and 40 healthy individuals (as control) attending UNIOSUN Teaching Hospital, Osogbo were enrolled into this study. Prothrombin time (PT), activated partial thromboplastin time (aPTT), international normalized ratio (INR), and platelet indices (PLT, MPV, PDW, PCT) were measured using Mindray BC-5000 analyzer following established protocols. Data obtained from the patients were subjected to statistical analysis using IBM SPSS Version 26. Parameters with $P \leq 0.05$ were considered statistically significant. HBV patients had substantially longer PT (15.1 ± 0.9 s vs. 13.4 ± 5.2 s, $p \leq 0.001$) and higher INR (1.22 ± 0.09 vs. 1.01 ± 0.07, $p \leq 0.001$), and slightly greater MPV, PDW, and PCT but lower PLT counts. There was no significant difference in aPTT. 18.5% of patients experienced abnormal bleeding, which was associated with greater PT and INR ($p \leq 0.05$). Disease duration had an unfavourable relationship with PLT ($r = -0.32$) and a weak positive correlation with PT ($r = 0.28$). Prolonged PT/INR, thrombocytopaenia, and elevated platelet activation indices are signs of a complicated haemostatic imbalance initiated by chronic HBV infection. This is known as "rebalanced haemostasis," and it is accompanied by bleeding and thrombotic risk. To enhance results, HBV management strategies should incorporate routine coagulation monitoring.

Keywords: Chronic hepatitis B; Coagulation disorder; Hemostasis; Nigeria; Platelet indices; Thrombosis

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INTRODUCTION

An estimated 296 million people globally are thought to be infected with the hepatitis B virus (HBV), with sub-Saharan Africa having one of the largest endemic regions (prevalence > 8%) (Ajuwon *et al.,* 2021; Al-Busafi *et al.*, 2024; Akabuike *et al.*, 2024; WHO, 2025). Hepatocellular carcinoma, cirrhosis, and chronic liver disease are all heavily impacted by HBV in Nigeria (Terrault *et al*., 2018)

Infection with HBV affects extrahepatic functions in addition to hepatic dysfunction, particularly haemostasis, which is a closely controlled interaction between the procoagulant, anticoagulant, and fibrinolytic systems (Lisman *et al.,* 2021; Roberts *et al.,* 2021; Northup *et al,* 2013). Hepatocellular damage causes both quantitative and qualitative alterations in clotting factors, platelet kinetics, and endothelial function since the liver produces the majority of coagulation and anticoagulant factors (Lisman *et al.*, 2010; Northup *et al.*, 2013; Lisman, 2021; Roberts *et al.*, 2021)

A "rebalanced haemostatic" model, in which reductions in both pro- and anti-coagulant components coexist, has replaced the traditional notion of "hypocoagulability" (Lisman *et al.,* 2021; Roberts, 2021; Lisman & Porte, 2010). Patients are simultaneously at risk for bleeding and thrombosis due to this delicate imbalance, which is impacted by inflammatory stresses, fibrosis stage, and infection activity (Lisman *et al.,* 2021; Roberts *et al.,* 2021; Northup *et al,* 2013).

The purpose of this study was to describe thrombotic risk and haemostatic abnormalities among long-term HBV patients at University of Osun (UNIOSUN) Teaching Hospital in Osogbo.

MATERIALS AND METHOD

Study design and setting

This was a cross-sectional analytical study carried out between January to June 2025 at University of Osun (UNIOSUN) Teaching Hospital, Osogbo, Osun State, Nigeria.

Participant

A total of 120 adults (18–65 years) were enrolled: 80 confirmed chronic HBV patients (HBsAg Positive > 6 months) and 40 healthy HBsAg-negative controls.

Inclusion criteria: Patient with confirmed chronic HBV infection, who are not on any concurrent antiviral therapy, and gave informed consent were included in the study.

Exclusion criteria: Patients with HCV/HIV coinfection, history of coagulopathy, pregnancy, anticoagulant medication use, or other chronic illnesses were excluded in the study.

Data collection and laboratory analysis

Structured questionnaires were used to gather clinical and socio-demographic data from the study subject. Aseptic venous blood sample was collected and placed in EDTA tubes for platelet indices and sodium citrate tubes for coagulation tests. PT and aPTT were measured using clotology reagents while the platelet indices were determined using MINDRAY BC-5000 (Xiang *et al.,* 2015)

Data analysis

IBM SPSS v26 was used to analyze the data. Frequencies (%) were used for categorical variables and mean ± SD for continuous variables. Analysis of variance (ANOVA) or independent t-test were employed for between-group comparisons. The relationship between haemostatic measures and the duration of the disease was evaluated using Pearson correlation. The threshold for significance was fixed at $p \leq 0.05$.

RESULTS

Demographic and Clinical Characteristics of Participants

The average age of HBV patients was 30.2 ± 7.8 years, which was similar to the control group's age of 32.1 ± 9.4 years ($p = 0.28$). Males made up 52% of the controls and 55% of the HBV group. Among HBV patients, the average length of infection was 4.2 ± 2.5 years. 15 (18.5%) HBV patients experienced abnormal bleeding symptoms, such as epistaxis, gum bleeding, or easy bruising, but none were seen in the control group (SPSS Sig. = 0.000; $p < 0.001$).

Comparison of Haemostatic Parameters Between Groups

When compared to healthy controls, chronic HBV patients showed notable changes in haemostatic indices, as Table 2 illustrates. The international normalized ratio (INR) was considerably higher in HBV patients (1.22 ± 0.09 vs. 1.01 ± 0.07; $p < 0.001$), and the mean prothrombin time (PT) was 15.1 ± 0.9 s in HBV patients compared to 13.4 ± 5.2 s in controls ($p < 0.001$). There was no significant difference in the groups activated partial thromboplastin time (aPTT) ($p = 0.227$). In comparison to controls, HBV patients exhibited significantly reduced platelet counts (PLT) but increased mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT), indicating platelet activation and a compensatory megakaryocytic response.

Bleeding Manifestation and Haemostatic Patterns

Abnormal bleeding events were recorded by 18.5% (15/80) of the 80 HBV patients. Compared to individuals without bleeding (PT = 15.0 ± 0.9 s; INR = 1.21 ± 0.09; $p < 0.05$), these patients had substantially longer PT (15.6 ± 0.8 s) and higher INR (1.26 ± 0.07). The prevalence of haemostatic abnormalities was higher in females (31.6%) than in males (19.0%) when stratified by sex, although this difference was not statistically significant ($p = 0.301$).

Correlation between Haemostatic Parameters and Disease Duration

Significant correlations between coagulation measures and platelet indices were found by correlation analysis among HBV patients (Table 3). Longer coagulation times are linked to

thrombocytopenia, as shown by the negative correlations between PT and INR and platelet count (r = –0.32 and –0.41, respectively; p < 0.01). The length of the infection was positively correlated with PT (r = 0.28; p = 0.013) and negatively correlated with platelet count (r = –0.32; p = 0.005), indicating a continuous decline in haemostatic function.

Table 1: Demographic and clinical characteristics of participants

Variable	HBV Patients (n = 80)	Controls (n = 40)	P - value
Mean age (years)	30.2 ± 7.8	32.1 ± 9.4	0.28
Male, n (%)	44 (55.0)	21 (52.5)	0.76
Female, n (%)	36 (45.0)	19 (47.5)	—
Mean disease duration (years)	4.2 ± 2.5	—	—
Participants with abnormal bleeding, (%)	15 (18.5)	0 (0.0)	<0.001

Table 2: C**omparison of haemostatic parameters between HBV patients and healthy controls**

Parameter	HBV (Mean ±SD)	Control (Mean ± SD)	p-value	Significance
PT (s)	15.1 ± 0.9	13.4 ± 5.2	<0.001	Significant
aPTT (s)	33.1 ± 3.2	32.7 ± 1.7	0.227	Not significant
INR	1.22 ± 0.09	1.01 ± 0.07	<0.001	Significant
PLT (×10^3/µL)	184.6 ± 47.9	238.5 ± 128.7	<0.001	Significant
MPV (fL)	10.4 ± 1.2	9.8 ± 1.1	0.008	Significant
PDW (%)	14.2 ± 3.5	13.1 ± 3.1	0.038	Marginally significant
PCT (%)	0.29 ± 0.09	0.23 ± 0.08	<0.001	Significant

Table 3: Correlation between haemostatic parameters and disease duration among HBV patients

Correlated parameters	r (rho)	p-value	Interpretation
PT vs PLT	–0.32	0.004	Moderate inverse correlation
INR vs PLT	–0.41	<0.001	Strong inverse correlation
Disease duration vs PT	0.28	0.013	Positive correlation
Disease Duration vs PLT	–0.32	0.005	Negative correlation

DISCUSSION

The results show that prolonged prothrombin time (PT), elevated international normalized ratio (INR), thrombocytopaenia, and increased platelet activation indices (MPV, PDW, and PCT) are indicative of severe disruptions in coagulation and platelet function linked to chronic HBV infection. The idea of "rebalanced hemostasis" in chronic liver illness, which is defined by concurrent impairment of procoagulant and anticoagulant pathways, is supported by these findings taken together (Lisman *et al.,* 2021; Roberts, 2021; Lisman & Porte, 2010).

As hepatocellular function deteriorates, prolonged PT and high INR seen in HBV patients are indicative of reduced hepatic production of vitamin K-dependent coagulation components (II, VII, IX, and X). This result is consistent with earlier research in people with viral hepatitis and chronic liver disease (Northup *et al,*2013; Hu *et al*., 2014; Pan *et al.,*2016; Roudsari *et al*., 2025. Because of its crucial role in haemostasis, the liver is especially susceptible to the effects of HBV-induced necroinflammatory damage, which reduces the synthesis of clotting factors and interferes with fibrinolytic regulation (Lisman *et al.,* 2021; Roberts *et al.,* 2021; Northup *et al,* 2013).

It's interesting to note that there was no significant difference in activated partial thromboplastin time (aPTT) between HBV patients and control group. This suggests that the intrinsic coagulation system may be largely unaffected at the chronic stage this study looked at. This trend is in line with studies showing intrinsic factors (VIII, IX, XI, and XII) are impacted later in the disease continuum, while early HBV infection selectively reduces extrinsic pathway factors (Roberts *et al.,* 2021; Northup *et al,* 2013).

The dual pattern of thrombocytopenia with high MPV, PDW, and PCT, which indicates both quantitative and qualitative platelet abnormalities, is a noteworthy discovery. HBV thrombocytopenia is a complex condition that results from immune-

mediated platelet destruction, bone marrow suppression, and splenic sequestration brought on by portal hypertension (Hu *et al*., 2014; Roudsari *et al*., 2025; Emenike *et al*., 2022).

On the other hand, larger, younger, and more metabolically active platelets are indicators of platelet activation and turnover are indicated by higher MPV and PDW (Pan *et al.,*2016; Roudsari *et al*., 2025). These indices are easily accessible indicators of endothelial dysfunction and inflammation. According to Lisman and colleagues' rebalanced hemostasis model, the co-occurrence of thrombocytopenia and platelet activation points to a compensatory mechanism to preserve haemostatic equilibrium in the face of chronic liver injury (Lisman *et al.,* 2021; Lisman & Porte, 2010).

Studies from China, Iran, and Nigeria have shown similar results ((Hu *et al*., 2014; Emenike *et al*., 2022; Olley *et al.,* 2023), confirming that platelet index abnormalities are common in all HBV-infected populations. This study's increase in plateletcrit (PCT) further implies that, in response to proinflammatory stimuli, total platelet biomass and activation potential stay elevated while platelet count decreases, increasing the risk of thrombotic consequences.

Abnormal bleeding was observed by about 18.5% of HBV patients, and it was strongly associated with both increased INR and extended PT. This finding emphasizes that bleeding in chronic HBV is a reflection of a wider dysfunction encompassing endothelial instability, platelet dysfunction, and inadequate coagulation factor production rather than only thrombocytopenia (Emenike *et al*., 2022; Guo et al., 2020). However, the concurrent rise in platelet activation markers suggests that HBV's haemostatic imbalance is more than just hypocoagulable. Instead, it is a dynamic equilibrium in which the risk of thrombosis and bleeding coexist and change based on the severity of the illness, inflammation, and triggering events such as immobility, infection, or exposure to hormones (Lisman *et al.,* 2021; Roberts *et al.,* 2021; Northup *et al,* 2013).

Clinically, this mechanism explains why, despite test evidence of coagulopathy, HBV patients may experience both spontaneous bleeding episodes and paradoxical thrombotic events including deep vein thrombosis or portal vein thrombosis (Roberts *et al.,* 2021; Northup *et al,* 2013; Lisman & Porte, 2010).

Prolonged PT and decreased platelet count have been found to be correlated with the length of the disease, indicating that haemostatic dysfunction deteriorates over time due to hepatic fibrosis and decreased synthetic function. This temporal correlation is consistent with previous longitudinal findings that viral persistence and histological liver damage are correlated with haemostatic disruption (Pan *et al.,*2016; Roudsari *et al*., 2025).

Chronic inflammation and fibrotic remodeling may eventually increase platelet turnover and endothelial activation, maintaining a prothrombotic milieu even when thrombocytopenia is present (Roberts *et al.,* 2021; Pan *et al.,*2016). These results emphasize the therapeutic necessity of regular coagulation parameter monitoring as part of long-term HBV treatment in order to identify changing haemostatic imbalance prior to clinical decompensation.

CONCLUSION

The need for thorough coagulation monitoring beyond conventional testing is highlighted by the conjunction of increased platelet indices and extended PT/INR in chronic HBV infection. Platelet indices (MPV, PDW, PCT) reveal information on platelet activation, inflammation, and thrombosis risk, whereas PT and INR show hepatic synthetic capability.

Risk stratification for bleeding and thrombotic events could be improved by incorporating these parameters into HBV patient follow-up, especially prior to invasive procedures or the start of antiviral therapy. Furthermore, in low-resource environments without access to sophisticated biomarkers (such as thrombin production tests or ROTEM), tracking platelet indices may be a low-cost supplement for evaluating hepatic inflammation.

Standard coagulation tests should be interpreted by clinicians in the context of rebalanced hemostasis, understanding that low platelet counts or prolonged PT do not always indicate a clinical risk of bleeding. Instead, for the best management, a customized evaluation that incorporates imaging, clinical, and laboratory data is crucial.

This study shows that persistent HBV infection significantly impairs haemostatic balance among infected individuals. The idea of a rebalanced but unstable haemostatic condition is supported by the pattern of prolonged PT, raised INR,

thrombocytopaenia, and increased platelet activation indices (MPV, PDW, PCT). These suggest that patients with HBV are at two-fold risk of having thrombotic problems due to increased platelet activation and endothelial dysfunction, as well as bleeding tendencies from decreased coagulation factor synthesis. The association between the length of the illness and haemostatic abnormalities highlights the gradual of liver stages of damage and the cumulative risk of coagulopathy over time. This study highlighted the necessity of extending routine HBV management to include systematic haemostatic monitoring, assuring early detection and prevention of bleeding or thrombotic consequences in settings with limited resources, by presenting context-specific data from a Nigerian cohort.

Temporal interpretation and causal inference are restricted by the cross-sectional design. Inflammatory cytokines, viral load, and the stage of liver fibrosis were not examined, which could have improved mechanistic understanding. The small cohort size and single-center sample may restrict generalizability. To better connect haemostatic characteristics with disease progression, future research should use prospective longitudinal designs with larger multicenter cohorts and incorporate liver stiffness and HBV DNA measurement.

In clinical practice, I recommend Routine coagulation screening**,** prior to invasive procedures or the start of antiviral therapy, utilizing haemostatic profiles to identify patients who are more likely to experience bleeding or thrombosis. interpret findings in the context of rebalanced hemostasis and ensure personalized clinical decisions are guided by multidisciplinary care involving medical laboratory scientists, hepatologists, and haematologists.

In Research, future studies should monitor dynamic changes in haemostatic measures during antiviral medication or illness development. Extend studies in Nigerian and sub-Saharan populations to investigate geographical and genetic factors influencing haemostatic dysfunction in HBV infection and integrate haemostatic testing into HBV care protocols.

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