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ORIGINAL ARTICLE

Utility of a High-Sensitivity HBV RNA Assay for Monitoring HBV Carriers Receiving Nucleos(t)ide Analogue Therapy

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SUMMARY

Background: **Chronic hepatitis B virus (HBV) infection is a dynamic condition with distinct phases, and accurate monitoring is essential for optimal disease management. Although conventional HBV biomarkers in serum such as HBV DNA, HBsAg, and HBcrAg are widely used, these markers have limitations in fully capturing viral activity, especially during nucleos(t)ide analogue (NA) therapy. Recently, HBV RNA has emerged as a novel biomarker reflecting the transcriptional activity of covalently closed circular DNA (cccDNA), yet its clinical relevance remains underexplored.**

Methods: **This study analyzed 168 serum samples collected from 124 patients with chronic HBV infection who were undergoing nucleos(t)ide analogue (NA) therapy. Serum HBV RNA levels were quantified using the high-sensitivity cobas® HBV RNA assay. The relationship between HBV RNA and other viral markers (HBV DNA, HBsAg, and HBcrAg) was evaluated. In addition, we assessed the potential of HBV RNA as a criterion for NA discontinuation by applying the Japan Society of Hepatology (JSH) scoring system for NA cessation.**

Results: **A strong correlation was found between HBV RNA and HBcrAg (r = 0.84), suggesting that HBV RNA may reflect intrahepatic cccDNA activity. HBV RNA levels declined earlier than HBsAg and HBcrAg during NA treatment. Notably, HBcrAg remained ≥ 3.0 log U/mL in many patients even when HBV RNA was undetectable. In the scoring analysis, all patients with HBV RNA levels ≥ 1.0 log copies/mL were assigned to higher-risk groups for virological relapse, indicating the need to continue NA therapy in these individuals. Importantly, undetectable HBV RNA alone did not consistently correlate with a low risk of relapse.**

Conclusions: **HBV RNA is a promising marker for detecting early suppression of viral replication during NA therapy. However, HBV RNA undetectability alone may not be sufficient to guide NA discontinuation.**

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KEYWORDS

cccDNA, HBV RNA, HBcrAg (HBc-related antigen), nucleos(t)ide analogue (NA) therapy, therapy discontinuation criteria

INTRODUCTION

Chronic infection with the hepatitis B virus (HBV) is closely associated with the development of cirrhosis and hepatocellular carcinoma [1,2], affecting an estimated 296 million people worldwide [3]. Current treatment options for chronic HBV infection include interferons

and nucleos(t)ide analogues (NAs) [4]. Continuous NA treatment can effectively suppress HBV replication and reduce serum HBV DNA to levels below the limit of detection. However, HBV remains in the liver even after HBV DNA is undetectable in serum. Therefore, discontinuing NA treatment frequently leads to virological relapse [5].

As covalently closed circular DNA (cccDNA) in HBV-infected hepatocytes is associated with HBV replication activity, the measurement of intrahepatic cccDNA can be a valuable marker to determine patients for discontinuation of NA treatment. HBc-related antigen (HBcrAg) is a well-recognized serum biomarker of transcriptional activity of cccDNA within the liver. Several guidelines for treatment of HBV state that NA treatment can be discontinued in HBeAg-negative patients who received NA therapy for 2 - 3 years and have achieved HBsAg levels below 80 - 100 IU/mL. In the Japan Society of Hepatology guidelines for the management of HBV infection, HBsAg and HBcrAg are used to predict the risk of relapse by scores of their antigen levels after NA discontinuation [6].

While HBcrAg is a surrogate marker of cccDNA transcriptional activity, serum HBV RNA has recently emerged as a potential biomarker of intrahepatic pregenomic (pg) RNA [7]. Since pgRNA (3.5 kB) is transcribed from cccDNA, serum HBV RNA reflects cccDNA transcriptional activity and is used for infection diagnosis, treatment monitoring, and viral risk assessment [8]. Recently, a highly sensitive HBV RNA assay has been developed [8]. Although HBV RNA may play an important role in predicting relapse after NA discontinuation [9], its clinical utility remains to be fully established.

While HBcrAg is widely used as a surrogate marker for the transcriptional activity of intrahepatic cccDNA, serum HBV RNA has recently emerged as a promising biomarker reflecting a different stage of the HBV life cycle. Therefore, the presence of HBV RNA in serum is considered a direct indicator of active HBV replication. In contrast, HBcrAg consists of core-related proteins including HBcAg, HBeAg, and p22cr, which all are derived from transcripts of the precore/core region of cccDNA and represent a reliable surrogate marker of overall cccDNA transcriptional activity. Because these two biomarkers reflect different complementary aspects of HBV biology - pgRNA representing replicative activity and HBcrAg representing transcriptional output - their combined evaluation may enhance clinical decision-making, especially in assessing relapse risk following nucleos(t)ide analogue (NA) cessation [9].

In the present study, serum HBV RNA in chronic hepatitis B patients receiving NA treatment was quantified using the newly developed high sensitivity cobas® HBV RNA assay. The associations of HBV RNA with conventional biomarkers including HBV DNA, HBsAg, and HBcrAg, which have been used as indicators of NA discontinuation, were analyzed. Furthermore, the potential of HBV RNA as a determinant of NA cessation was evaluated by comparing it with the criteria of NA discontinuation in the Japan Society of Hepatology guidelines for the management of HBV infection.

MATERIALS AND METHODS

Sample collection

The study included residual serum samples (n = 168) collected from 124 HBV carriers undergoing nucleos(t)ide analogue (NA) therapy. The minimal duration of NA therapy prior to sample collection was 6 months, and the average duration was 7.9 ± 4.5 years. Among the patients, 93 were treated with tenofovir alafenamide, 25 with entecavir, 5 with tenofovir disoproxil fumarate, and 2 with lamivudine. The samples were collected at the Central Clinical Laboratory of Kindai University Hospital over a four-month period in 2023.

These patients were confirmed to have been HBs antigen-positive and HBV DNA-positive at some point and had measurements taken of HBeAg, antiHBe, HBcrAg, and ALT.

Patients were classified into three groups based on their serological and biochemical status during NA therapy:

1) HBeAg(+) CH group (n = 30): HBeAg ≥ 1.0 S/CO, antiHBe < 50.0 S/CO, and ALT ≥ 31 U/L

2) HBeAg(-) CH group (n = 31): HBeAg < 1.0 S/CO, antiHBe < 50.0 S/CO, and ALT ≥ 31 U/L

3) antiHBe(+) CH group (n = 107): HBeAg < 1.0 S/CO, antiHBe ≥ 50.0 S/CO, and ALT ≥ 31 U/L.

Blood samples

All samples were collected in tubes containing thrombin. The blood collection tubes [10], blood collection procedure [11], and mixing procedure were according to the methods described by CLSI. The following occurrences were excluded from sample selection: Failure to adhere to the study-specific procedure; instrument, operator-related, or sample-related failure; and a data-invalidating flag as described in the operating instructions for each instrument.

Statistical analysis

Statistical analysis was performed with the following software: Excel 2016 (Microsoft); StatFlex ver.7 (Artech). Correlation coefficients were calculated by the least-square method and the intercept, the slope was done by Passing-Bablok regression. For statistical analysis, values below the lower limit of quantification (LLOQ) were substituted with LLOQ/2 for HBV RNA, HBcrAg, HBV DNA, and HBsAg. This allowed the calculation of means and standard deviations, including samples with undetectable values.

Measurement method

Cobas5800 system

The cobas 5800 System (cobas 5800) (Roche Holding AG, Basel, Switzerland) is a new low- to mid-throughput system for PCR-based nucleic acid testing. The co-

bas 5800 is designed to process up to six different assays within a run and complete up to 144 tests per 8-hour shift in a fully automated workflow that includes primary tube handling, nucleic acid extraction, real-time PCR amplification/detection, and data analysis, integrated into a single instrument. Despite its smaller footprint, it shares numerous design elements, technical characteristics, and key processes with the cobas 6800/8800 Systems, including test menu, reagents, consumables, and workflow [12,13]. The quantification range of the cobas® HBV RNA assay on the cobas® 5800 system is 10 to 10^7 copies/mL. Values below the lower limit of quantification (LLOQ) were categorized as "titer min" or "not detected," depending on the assay output. The cobas® HBV RNA assay selectively amplifies highly conserved regions of HBV pregenomic RNA (pgRNA) using organism-specific primers and does not detect precore RNA or mRNAs encoding preS/S regions. A minimum sample volume of 375 μL of serum is required for analysis.

Determination of HBV DNA and serological HBV markers

HBeAg and antiHBe levels were measured using the ARCHITECT® i2000SR (Abbott Laboratories, Illinois, United States). HBsAg was quantified with the Roche Cobas 801 system (Roche Holding AG, Basel, Switzerland). Serum HBV DNA levels were determined by RT-PCR using the Cobas TaqMan system (Roche Holding AG, Basel, Switzerland). HBcrAg levels were assessed using the LUMIPULSE L2400 platform (Fujirebio Diagnostics, Inc., Tokyo, Japan). The measurement ranges of the serum markers used in this study were 1.3 to 8.2 log IU/mL for HBV DNA, 0.05 to 250 IU/mL for HBsAg, and 2.1 to 6.8 log U/mL for HBcrAg; values below the lower limit of quantification were considered non-quantifiable. Samples with HBsAg levels exceeding the upper limit of quantification (250 IU/mL) were diluted using a dedicated diluent (Dil HepB; Roche Diagnostics) according to the manufacturer's instructions prior to measurement.

Comparability

Comparison between HBV RNA and serological HBV markers

For method comparison between the HBV RNA and the serological HBV markers, test data were measured using 168 samples.

Comparison between HBV RNA and serological HBV markers in the HBeAg(+) CH, HBeAg(-) CH, and antiHBe(+) CH groups

In each group, the values of HBV RNA (log copies/mL), HBcrAg (log U/mL), HBV DNA (log IU/mL), and HBsAg (IU/mL) were compared.

Evaluation of the relationship between HBV RNA and HBcrAg in the HBeAg(+) CH, HBeAg(-) CH, and antiHBe(+) CH groups

The HBV RNA and HBcrAg values were stratified, and the number of cases in the HBeAg(+) CH, HBeAg(-) CH, and antiHBe(+) CH groups were compared.

Evaluation of the relationship between HBV RNA and HBsAg in the HBeAg(+) CH, HBeAg(-) CH, and antiHBe(+) CH groups.

The HBV RNA and HBsAg values were stratified, and the number of cases in the HBeAg(+) CH, HBeAg(-) CH, and antiHBe(+) CH groups were compared.

Evaluation of the relationship between the NA discontinuation criteria score from the Japan Society of Hepatology and HBV RNA [6].

Based on the NA discontinuation criteria established by the Japan Society of Hepatology (JSH), which includes HBsAg and HBcrAg levels, we calculated the score for each of the 168 samples. The scoring criteria are summarized in Supplementary Table S1, adapted from the JSH guidelines [6].

RESULTS

Comparison between HBV RNA and serological HBV markers

The comparison between HBV RNA and serological HBV markers is shown in Figure 1. The correlation coefficients (r) between HBV RNA and HBcrAg, HBV DNA, and HBsAg were 0.84, 0.54, and 0.32, respectively.

Comparison between HBV RNA and serological HBV markers in the HBeAg(+), HBeAg(-), and antiHBe(+) CH groups

The values of HBV RNA, HBcrAg, HBV DNA, and HBsAg in the HBeAg(+) CH, HBeAg(-) CH, and antiHBe(+) CH groups are shown in Figure 2. In the HBeAg(+) CH group, the values were as follows: HBV RNA: 3.21 ± 1.74, HBcrAg: 5.99 ± 0.95, HBV DNA: 1.53 ± 1.18, and HBsAg: 2,930 ± 3,365.

In the HBeAg(-) CH group, the values were: HBV RNA: 1.02 ± 0.63, HBcrAg: 4.00 ± 0.53, HBV DNA: 0.86 ± 0.50, and HBsAg: 2,200 ± 3,881. In the antiHBe(+) CH group, the values were: HBV RNA: 0.69 ± 0.62, HBcrAg: 3.09 ± 0.43, HBV DNA: 0.86 ± 0.49, and HBsAg: 1,428 ± 2,681. In comparison of serological HBV markers among the HBeAg(+) CH, HBeAg(-) CH, and antiHBe(+) CH groups, HBV RNA levels were lower in the HBeAg(-) CH group compared to the HBeAg(+) CH group ($p < 0.01$), but no significant difference was observed between the HBeAg(-) CH and antiHBe(+) CH groups. In contrast, HBcrAg levels were lower in the HBeAg(-) CH group compared to the HBeAg(+) CH group ($p < 0.01$) and further decreased in the antiHBe(+) CH group compared to the HBeAg(-) CH group ($p < 0.01$). However, there were no significant differences in HBsAg levels among the three groups.

Table 1. Relationship between HBV RNA and HBcrAg in the HBeAg(+), HBeAg(-), and antiHBe(+) groups.

HBeAg(+) (n = 30)											
				HBV RNA (log copies/mL)							
				N.D.	1.0	1.1-	2.0-	3.0-	4.0-	5.0-	6.0-
HBcrAg (log U/mL)	6.8	≥		1	0	0	0	0	5	2	2
	6.0	-	6.7	0	0	0	0	2	0	1	0
	5.0	-	5.9	1	0	3	9	0	1	0	0
	4.0	-	4.9	1	0	1	1	0	0	0	0
	3.0	-	3.9	0	0	0	0	0	0	0	0
		<	3.0	0	0	0	0	0	0	0	0
HBeAg(-) (n = 31)											
				HBV RNA (log copies/mL)							
				N.D.	1.0	1.1-	2.0-	3.0-	4.0-	5.0-	6.0-
HBcrAg (log U/mL)	6.8	≥		0	0	0	0	0	0	0	0
	6.0	-	6.7	0	0	0	0	0	0	0	0
	5.0	-	5.9	0	0	0	0	0	0	0	0
	4.0	-	4.9	6	6	4	2	0	0	0	0
	3.0	-	3.9	7	1	3	1	0	0	0	0
		<	3.0	1	0	0	0	0	0	0	0
antiHBe(+) (n = 107)											
				HBV RNA (log copies/mL)							
				N.D.	1.0	1.1-	2.0-	3.0-	4.0-	5.0-	6.0-
HBcrAg (log U/mL)	6.8	≥		0	0	0	0	0	0	0	0
	6.0	-	6.7	0	0	0	0	0	0	0	0
	5.0	-	5.9	0	0	0	1	0	0	0	0
	4.0	-	4.9	1	3	3	2	0	0	0	0
	3.0	-	3.9	15	2	0	0	0	0	0	0
		<	3.0	66	11	3	0	0	0	0	0

Group classification was based on HBeAg, antiHBe, and ALT values during NA therapy.
For detailed criteria, see the Section "Sample collection" in the Methods.

Evaluation of the relationship between HBV RNA and HBcrAg in the HBeAg(+) CH, HBeAg(-) CH, and antiHBe(+) CH groups

The relationship between HBV RNA and HBcrAg in the HBeAg(+) CH, HBeAg(-) CH, and antiHBe(+) CH groups is shown in Table 1. In the HBeAg(+) CH group, there were 3 cases where HBcrAg was above 3.0 despite undetectable HBV RNA (N.D.).

In the HBeAg(-) CH group, 13 out of 14 cases had HBcrAg levels above 3.0 even when HBV RNA was undetectable. Additionally, no cases were found where HBV RNA titer was above the minimum (1.0) while HBcrAg was below 3.0. In the antiHBe(+) CH group, 16 out of 82 cases had HBcrAg levels above 3.0 despite undetectable HBV RNA. Furthermore, 14 cases were observed where HBV RNA titer was above the minimum while HBcrAg levels were below 3.0.

Evaluation of the relationship between HBV RNA and HBsAg in the HBeAg(+) CH, HBeAg(-) CH, and antiHBe(+) CH groups

The relationship between HBV RNA and HBsAg in the HBeAg(+) CH, HBeAg(-) CH, and antiHBe(+) CH groups is shown in Table 2. In the HBeAg(+) CH group, there were 2 cases where HBsAg was above 100 IU/mL, but HBV RNA was undetectable (N.D.). Additionally, no cases were found where HBV RNA titer was above the minimum (Titer min) while HBsAg was below 100 IU/mL. In the HBeAg(-) CH group, 9 cases had undetectable HBV RNA with HBsAg levels above 100 IU/mL. Furthermore, 2 cases were observed where HBV RNA titer was above the minimum and HBsAg levels were below 100 IU/mL. In the antiHBe(+) CH group, 57 cases had undetectable HBV RNA with HBsAg levels above 100 IU/mL. Additionally, 4 cases

Table 2. Relationship between HBV RNA and HBsAg in the HBeAg(+), HBeAg(-), and antiHBe(+) groups.

HBeAg(+) (n = 30)									
			HBV RNA (log copies/mL)						
			N.D.	1.0	1.1-	2.0-	3.0-	4.0-	5.0-	6.0-
HBsAg (IU/mL)	10,000	-	1	0	0	0	0	0	0	0
	2,000	-	0	0	1	2	1	5	3	2
	1,000	-	0	0	0	3	0	1	0	0
	500	-	1	0	0	4	0	0	0	0
	100	-	0	0	3	1	1	0	0	0
	< 100		1	0	0	0	0	0	0	0
HBeAg(-) (n = 31)									
			HBV RNA (log copies/mL)						
			N.D.	1.0	1.1-	2.0-	3.0-	4.0-	5.0-	6.0-
HBsAg (IU/mL)	10,000	-	2	0	0	0	0	0	0	0
	2,000	-	2	3	1	0	0	0	0	0
	1,000	-	1	1	0	0	0	0	0	0
	500	-	0	0	1	0	0	0	0	0
	100	-	4	2	5	2	0	0	0	0
	< 100		5	1	0	1	0	0	0	0
antiHBe(+) (n = 107)									
			HBV RNA (log copies/mL)						
			N.D.	1.0	1.1-	2.0-	3.0-	4.0-	5.0-	6.0-
HBsAg (IU/mL)	10,000	-	2	1	0	0	0	0	0	0
	2,000	-	8	3	2	0	0	0	0	0
	1,000	-	15	4	4	3	0	0	0	0
	500	-	9	1	0	0	0	0	0	0
	100	-	23	3	0	0	0	0	0	0
	< 100		25	4	0	0	0	0	0	0

Group classification was based on HBeAg, antiHBe, and ALT values during NA therapy.
For detailed criteria, see the Section "Sample collection" in the Methods.

Table 3. Relationship between HBV RNA and score to predict the risk of relapse after NA discontinuation in the Japan Society of Hepatology Guidelines for the management of HBV infection.

HBsAg (IU/mL)			HBcrAg (log U/mL)			score	HBV RNA (log copies/mL)		
							N.D.	< Titer min	1.0 ≥
	<	80		<	3.0	0	21	4	0
80	-	800		<	3.0	1	25	3	0
	>	800		<	3.0	2	21	4	3
	<	80	3.0	-	4.0	1	6	1	0
80	-	800	3.0	-	4.0	2	7	0	4
	>	800	3.0	-	4.0	3	9	2	0
	<	80		≥	4.0	2	3	0	0
80	-	800		≥	4.0	3	1	3	12
	>	800		≥	4.0	4	6	6	27

Scores were calculated based on HBsAg and HBcrAg levels in the criteria of the Japan Society of Hepatology guidelines.

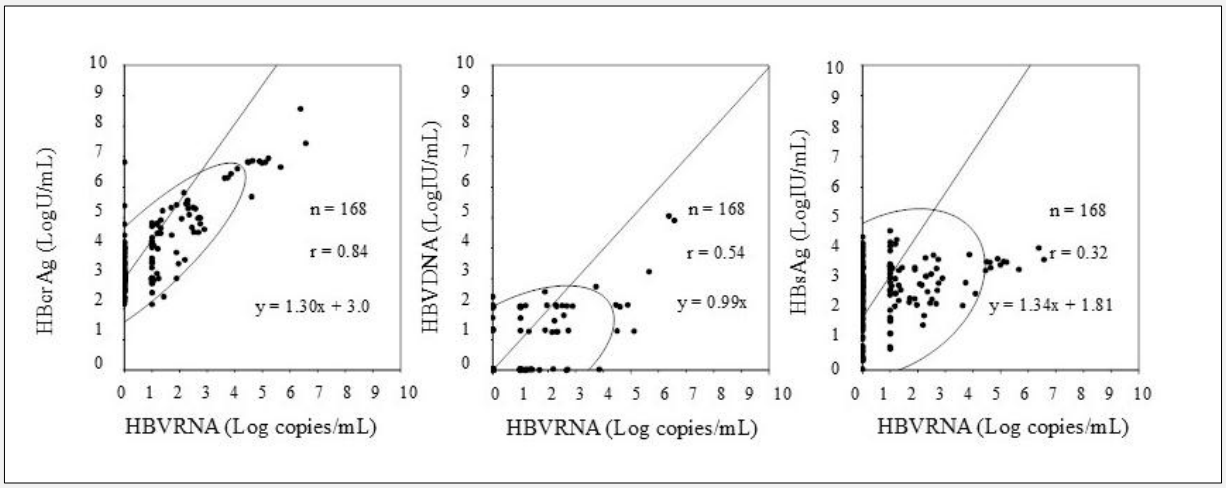

Figure 1. Correlations of HBV RNA with HBcrAg, HBV DNA, and HBsAg.

The figure illustrates positive correlations of HBV RNA with other serological HBV markers including HBcrAg, HBV DNA, and HBsAg.

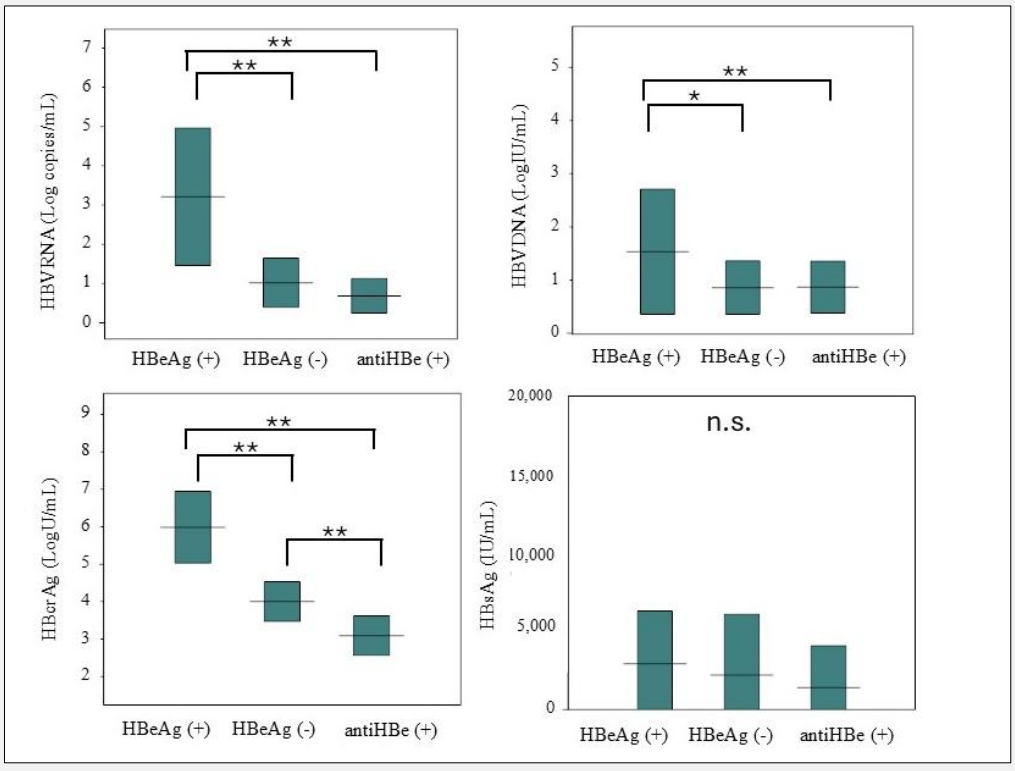

Figure 2. Comparison of individual serological HBV markers among HBeAg(+) CH, HBeAg(-) CH, and antiHBe(+) CH groups.

Serological markers including HBV RNA, HBcrAg, HBV DNA, and HBsAg are compared in the HBeAg(+) CH, HBeAg(-) CH, and antiHBe(+) CH groups.

were found where HBV RNA titer was above the minimum while HBsAg levels were below 100 IU/mL.

Evaluation of the relationship between the NA discontinuation criteria score from the Japan Society of Hepatology and HBV RNA

The results evaluated using HBV RNA values showed the following distribution: Score 0 had 25 cases (N.D.: 21 cases, Titer min: 4 cases, ≥ 1: 0 cases), Score 1 had 35 cases (N.D.: 31 cases, Titer min: 4 cases, ≥ 1: 0 cases), Score 2 had 42 cases (N.D.: 31 cases, Titer min: 4 cases, ≥ 1: 7 cases), Score 3 had 27 cases (N.D.: 10 cases, Titer min: 5 cases, ≥ 1: 12 cases), and Score 4 had 39 cases (N.D.: 6 cases, Titer min: 6 cases, ≥ 1: 27 cases) (Table 3).

DISCUSSION

In the present study, serum HBV RNA in patients with chronic hepatitis B undergoing NA therapy was determined using a newly developed high sensitivity cobas® HBV RNA assay to examine the relationship between HBV RNA and other viral markers including HBV DNA, HBsAg, and HBcrAg, which have been used as indicators for NA therapy discontinuation.

A strong correlation was observed between serum HBV RNA quantified by the cobas® HBV RNA assay and HBcrAg levels. HBcrAg comprises three separate proteins, HBcAg, HBeAg, and p22cr encoded by the precore/core region of the HBV genome, which all share a common 149-amino acid sequence and are derived from cccDNA [14,15]. HBcrAg was found to be more accurate than HBsAg in reflecting cccDNA transcriptional activity [15]. This study found that HBV RNA levels highly correlated with HBcrAg. Taken together, the result suggests that HBV RNA is a useful marker for assessing intrahepatic cccDNA levels. Furthermore, this finding is consistent with previous reports and confirms that the cobas® HBV RNA assay shows comparable performance to other commercially available assays [16].

The dynamic changes in HBV viral markers during NA treatment were evaluated among the HBeAg(+) CH, HBeAg(-) CH, and antiHBe(+) CH groups. As shown in Figure 1, HBV RNA levels showed a strong correlation with HBcrAg ($r = 0.84$), a moderate correlation with HBV DNA ($r = 0.54$), and a weak correlation with HBsAg ($r = 0.32$). These differences in correlation coefficients may reflect the different biological origins of each marker. The differential patterns of decline in serum levels of HBV markers are demonstrated in Figure 2. Given the consistent decline in serum HBcrAg levels over the course of treatment, HBcrAg may be a marker for monitoring sustained suppression of viral replication and cccDNA activity (Figure 2). In contrast, given the rapid early decline in serum HBV RNA in HBeAg-negative patients, HBV RNA may be a potential marker for determining the effect of suppression of viral replication in the early phase after initiation of treatment (Figure 2). Serum HBsAg levels showed little decline even in antiHBe-positive patients during NA treatment, which is in agreement with previous reports [17,18]. This finding indicates that HBsAg responds to NA treatment poorly, probably because HBsAg is persistently produced within the hepatocyte while NA treatment does not directly inhibit cccDNA transcriptional activity (Figure 2).

When the relationship between HBV RNA and HBcrAg levels was evaluated among the HBeAg(+) CH, HBeAg(-) CH, and antiHBe(+) CH groups, some patients had discrepant results between HBV RNA and HBcrAg levels. Numerous patients had HBcrAg levels ≥ 3.0 log U/mL even though HBV RNA was not detected, particularly in the HBeAg(-) CH group, while this trend decreased in the antiHBe(+) CH group. These findings suggest that HBV RNA may be a more sensitive marker than HBcrAg for detecting early effects of NA therapy. It should be noted that HBcrAg is composed of three core-related proteins - HBcAg, HBeAg, and p22cr - all sharing a common 149-amino acid sequence. In HBeAg-negative patients, the HBcrAg signal predominantly reflects HBcAg and p22cr. However, no study has quantitatively defined how many HBV core particles are represented by 1 U of HBcrAg. Therefore, HBcrAg levels should be interpreted with caution, especially in the absence of HBeAg in serum.

The different associations of HBV RNA with other biomarkers including HBcrAg and HBsAg are shown in Tables 2 and 3. In the antiHBe(+) CH group, even though HBV RNA was undetectable in serum, 57/82 (69.5%) patients had HBsAg levels ≥ 100 IU/mL (Table 2), whereas only 16/82 (19.5%) patients had HBcrAg levels ≥ 3.0 log U/mL (Table 1). Consistent with the results in Figure 2, these findings also suggest that HBsAg levels decline more slowly compared to HBV RNA and HBcrAg levels.

Quantitative HBsAg levels are widely used in various guidelines as one of the indicators to decide NA treatment discontinuation. Serum HBcrAg levels have been shown to predict viral relapse after treatment discontinuation [19,20]. In the present study, the utility of HBV RNA was evaluated by using scoring system for cessation of NA therapy in the Japan Society of Hepatology guidelines for the management of HBV infection. The results in this study demonstrated that HBV RNA levels increased with higher scores, which was calculated using the criteria for cessation of NA therapy. Even though HBV RNA was undetectable, only 21/99 (21.2%) patients had a score of 0 (Table 3), suggesting that HBV RNA undetectability alone may be insufficient as a determinant for therapy discontinuation. Conversely, all 46/46 (100%) patients with HBV RNA levels ≥ 1.0 log copies/mL had a score of ≥ 2 (Table 3). Therefore, NA should be continued if HBV RNA remains quantitatively detectable.

CONCLUSION

In the present study, HBV RNA levels were quantified by the cobas® HBV RNA assay. The results demonstrated that HBV RNA was characterized as a marker for detecting earlier effects of suppression of viral replication after initiation of nucleos(t)ide analogue (NA) therapy, compared to other viral markers HBcrAg and HBsAg. Furthermore, this study found that NA therapy should not be stopped in patients with HBV RNA levels of ≥ 1.0 log copies/mL.

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Declaration of Interest:
The authors declare no conflicts of interest.

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