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LETTER TO THE EDITOR

Comparative Performance of Three Rapid HBsAg Assays for Detection of HBs Diagnostic Escape Mutants in Clinical Samples

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The development of rapid tests (RTs) for hepatitis B surface antigen (HBsAg) detection is expanding, especially for point-of-care (POC) testing. As mutations in the a determinant of HBsAg have been associated with failures to detect HBsAg by using some traditional HBsAg assays, this study aimed to evaluate the performance of three RTs (VIKIA HBsAg [bioMérieux, Marcy l'Etoile, France], Alere Determine HBsAg [Inverness Medical, Japan], and the DRW-HBsAg v2 assay [Diagnostics for the Real World, Ltd., United States]) for detection of HBsAg diagnostic escape variants.

The limit of detection of the assays studied with serial dilutions of the WHO 2nd standard, HBsAg 00/588, subtype adw2 genotype A (gtA; National Institute for Biological Standards and Control, United Kingdom) between 5 and 0.05 IU/ml, was found to be between 0.05 and 0.5 IU/ml for DRW, between 0.5 and 1 IU/ml for VIKIA, and between 1 and 2 IU/ml for Determine. Only DRW met the European requirement for HBsAg analytical sensitivity (i.e., 0.13 IU/ml).

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TABLE 1 HBsAg and polymerase mutants included in the evaluation described in this report

Change	Amino acid position(s)[a]	No. of samples[b] with HBV genotype:					Total no. of samples
		A	B	C	D	E	
HBsAg mutation	s116	2					2
	s120	1 + 1 rcb			1		3
	s123				1		1
	s124			1			1
	s126		2	2	1		5
	s129		2		2		4
	s130	2			2		4
	s131				1		1
	s133	3			2 + 1 rcb	2	8
	s134				1	1	2
	s141					1 rcb[c]	1
	s143	2	1		2 + 1 rcb[c]	1	7
	s144		1		1	1 + 1 rcb	4
	s145				1 rcb[d]	2	3
Insertion	s114	1					1
	s115	1					1
	s116	1					1
Deletion	s112–115				1 rcb		1
HBsAg multiple (2 or 3) mutations		4	1	1	6		12
Polymerase mutation	rtL80V + rtI233V				1		1
	rtI169IT				1		1
	rtV173L					1	1
	rtA181T					1	1
	rtA194S				1		1
	rtI233V (+ sP120S)				1		1
Total no. of samples		18	7	4	28	11	68

[a] The abbreviations s and rt indicate HBsAg and polymerase (reverse transcriptase domain) mutations, respectively.
[b] rcb, recombinant HBsAg mutant.
[c] Negative by Determine.
[d] Negative by DRW.

Clinical sensitivity was evaluated by testing 61 clinical samples distributed into 55 specimens harboring HBsAg mutations associated with reduced sensitivity for HBsAg detection and obtained by direct sequencing of PCR fragments of the S gene (1) with concentrations (Architect HBsAg QT assay; Abbott Diagnostics, Rungis, France) that ranged from 3.4 to 71,700 IU/ml and 6 samples with polymerase-resistant viral variants and HBsAg titers of 7.3 to 12,800 IU/ml (Table 1). Seven previously described (2) calibrated recombinant HBsAg variants (7.3 to 26.3 IU/ml) were also tested.

The overall sensitivity was 100% for VIKIA and 98.5% for DRW and Determine.

The three RTs showed 100% sensitivity in the detection of clinical samples. However, slight differences in reactions were observed for six samples. Three were gtD samples weakly positive with VIKIA and Determine although unambiguously positive with DRW. The first sample had two combined mutations (M133I and Y134H) and a 3.4-IU/ml HBsAg concentration, and the other two samples had polymerase mutations (rtA194S and rtI169IT) and 9.7- and 7.3-IU/ml HBsAg concentrations, respectively. The remaining three samples (gtD, HBsAg titers of 51, 13.2, and 11.6 IU/ml, respectively) had G130R and multiple mutations (sT131I/sY134N/sS143L and sP120S/rtI233V) and were weakly positive by VIKIA.

The seven recombinant samples were positive by VIKIA, whereas DRW and Determine missed one sample (gtD, G145R, 7.3-IU/ml HBsAg concentration) and two samples (gtE, K141E, 6.3-IU/ml HBsAg concentration; gtD S143L, 10.7-IU/ml HBsAg concentration), respectively.

Our findings indicate that HBsAg mutations do not significantly affect the sensitivity of the RTs evaluated, at least in plasma samples, despite slightly reduced performance in detecting some samples, probably in relation to their low HBsAg concentrations. These high performance levels are in line with other studies performed with a variety of HBV genotypes (2–6). These three rapid HBsAg assays can be considered promising alternatives to traditional immunoassays with the potential for use in POC testing of whole blood.

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