Performance of rapid tests for detection of HBsAg and anti-HBsAb in a large cohort, France

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Background & Aims: The systematic use of rapid tests performed at points-of-care may facilitate hepatitis B virus (HBV) screening and substantially increase HBV infection awareness. The aim of this study was to evaluate the effectiveness of such tests for HBsAg and anti-HBsAb detection among individuals visiting a variety of healthcare centers located in a low HBV-prevalent area.

Methods: Three rapid tests for hepatitis B surface antigen (HBsAg) detection (VIKIA®, Determine™ and Quick Profile™) and one test for anti-hepatitis B surface antibody (anti-HBsAb) detection (Quick Profile™) were evaluated in comparison to ELISA serology. Sensitivity (Se), specificity (Sp), positive and negative predictive values (PPV and NPV, respectively) and area under the ROC curve were used to estimate test performance. Non-inferiority criteria of the joint Se and Sp were set at 0.80, 0.95.

Results: Among the 3956 subjects screened, 85 (2.1%) were HBsAg-positive and 2225 (56.5%) had a protective anti-HBsAb titer. Test Se and Sp (lower bound of 97.5% CI) were as follows: 96.5% (89.0%), 99.9% (99.8%) for Vikia®; 93.6% (80.7%), 100.0% (99.8%) for Determine™; and 90.5% (80.8%), 99.7% (99.5%) for Quick Profile™; with all three tests achieving minimal non-inferiority criteria. False negatives were typically observed in inactive HBsAg carriers. The anti-HBsAb Quick Profile™ test had excellent specificity (97.8%) and PPV (97.8%) albeit low sensitivity (58.3%), thus failing to establish non-inferiority.

Conclusions: All three HBsAg rapid tests could be considered ideal for HBV screening in low HBV-prevalent countries, given the ease of use, rapidity, and high classification probabilities. The anti-HBsAb Quick Profile™ could be considered reliable only for positive tests.

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Introduction

According to recent estimations, France has a low prevalence of chronic hepatitis B virus infection (CHB) as roughly 0.65% of those cases with health insurance are estimated to be infected [1,2]. Although the social security system provides a wide range of services targeted towards prevention and effective care, more than 280,000 people continue to live with chronic hepatitis B virus infection, of whom over 55% are unaware of their infection-status [1]. CHB diagnosis is therefore severely delayed in this group and often occurs when severe clinical repercussions, such as advanced stages of cirrhosis and/or hepatocellular carcinoma, are already present. As a result, it is estimated that over 1300 deaths per year are directly attributable to hepatitis B virus (HBV) in France [3].

Unawareness of HBV infection status could be explained by both the lack of knowledge among those at risk (i.e., subjects born in geographic regions with hepatitis B surface antigen (HBsAg) prevalence >2%, household contacts, sexual partners of subjects with CHB or intravenous drug users [4]) and the lack of recognition concerning the seriousness of its public health impact among general practitioners. Furthermore, the absence of national guidelines related to screening practices leads to further confusion, with highly variable screening protocols between healthcare...
centers. In order to remedy this inadequacy, the “National Hepatitis Plan, 2009–2012” [5] recommended increasing HBV screening and improving consistent reporting. One public health tool that could potentially drive such an increase is the use of rapid tests, which may facilitate access to screening services.

Until recently (2012), no HBV rapid test has been approved for use by European or North American regulatory agencies. Moreover, there have been very few studies validating their use in low HBV-prevalent countries, apart from those given by the tests’ manufacturers, in which their performance has been mainly evaluated on serum samples rather than on whole blood specimens. We then aimed at conducting a multicenter, cross-sectional, single-arm evaluation of several rapid tests that could be used to identify the presence of serological markers typically used in screening for CHB infection.

Patients and methods

Study participants

From September 2010 to August 2011, 4000 subjects were recruited from ten Paris-based healthcare centers whose aims involved screening, prevention and/or vaccination of diverse populations. Inclusion criteria for the present study were as follows: agreement to be screened for HBV, 18 years of age or older, and availability for a subsequent follow-up questionnaire via telephone. Participants without health coverage were also included [5]. All participants provided written informed consent and the protocol was approved by the Hôtel-Dieu Hospital Ethics Committee (Paris, France) in accordance with the Helsinki Declaration.

Rapid test comparisons and gold standard

Approximately 10 ml of whole blood was collected into a tube without any additive from each participant. Before the blood had yet to coagulate, a few drops were immediately removed from the sample and used for each rapid test according to manufacturers’ instructions. Anticoagulant was not added to the sample because only serum was required for subsequent study procedures. Three tests for HBsAg detection (VIKIA® Biomerieux, Marcy-l’Étoile, France; Determine™, Inverness Biomedical Innovations, Köln, Germany; Quick Profile™, Lumiquick, Santa Clara, CA, USA) and one test for anti-HBs antibody (anti-HBsAb) detection (Quick Profile™, Lumiquick) were evaluated (Fig 1). These qualitative tests are based on the principle of immunochromatography, in which membrane chromatography is used to determine the presence of polyclonal antibodies specific for HBsAg or anti-HBs antibody within a test region. In order to determine participants’ “true” HBV status, serum was processed from whole blood and tested using a commercially-available enzyme-linked immunoassay (ELISA) (MONOLISA AgHBs Ultra, anti-HBs plus, anti-hepatitis B core antibody-anti-HBc-plus, BIO-RAD, Hercules, USA). Only results of this testing were relayed to participants and their general practitioner. All participants found to have active HBV infection were asked if they would like to schedule a medical visit, during which a complete evaluation would be performed at a specialized clinic and therapy options would be discussed, if necessary. Additionally, all HBsAg-positive specimens had HBsAg quantification done using the ARCHITECT HBsAg enzyme-linked immunoassay (Abbott Laboratories, Rungis, France), and HBV DNA quantification, using the commercial quantitative polymerase chain reaction assay COBAS Taqman 48 HBV (Roche Diagnostic Systems, Meylan, France). For one specimen, HBV sequencing was performed on the pol/S region, as previously described [6]. The sequence was analyzed with the “HBV tool” accessible online at http://www.hiv-grade.de/cms/grade/hbv-tool.html.

Quality control of rapid tests

Rapid tests were performed immediately after the participant’s sample was taken and in the same room as where blood collection occurred. Staff noted the date and time at which all tests were performed. Each rapid test had a control indicating whether the sample sufficiently migrated along the membrane (i.e., the test was performed correctly). In the event of an invalid test, two other attempts were made at most in order to achieve a valid result. Valid test results were then read within 30 min by two independent, previously-trained staff members (for a total number of 5 clinic research associates). Only results that the two readers agreed upon were included. However, if one reading was indeterminate while the other was definitive, the definitive reading was taken as the final result.

Statistical analysis

Rapid tests were compared to ELISA, which served as the gold standard. Sensitivity (Se), specificity (Sp), positive and negative predictive value (PPV and NPV, respectively), positive and negative likelihood ratio (LR+ and LR−, respectively) were estimated. Area under the ROC curves (AUROC) were also calculated and compared between rapid tests using a test of equality of ROC areas. Inter-rater agreement was determined using the Kappa statistic, without taking into account indeterminate results. Using a previously described method [7], we powered the study in order to test desirable levels of the pair [false positive fraction (FPF), true positive fraction (TPF)] at (0.02, 0.95). Non-inferiority criteria were then selected with minimally acceptable (FPF, TPF) at (0.05, 0.80), reflecting the importance of decreasing the number of false positives while increasing the number of cases identified [8]. We aimed at testing a one-sided, null hypothesis assuming a joint power of 0.90 and type I error (α) of 0.05. After accounting for an estimated prevalence of 2.0% from previous population-based studies within Paris [1] and correcting for a difference in sample collection, we report the sensitivity (TPF) and specificity (1-FPF). Statistical analyses were performed using STATATA® (v11.2, College Station, TX, USA) statistical software.

Results

Study participants

At the end of the study, a total of 3956 subjects had at least one HBV rapid test with ELISA results and were hence included in the analysis. As discordant inter-rater results were excluded and the HBsAg Determine™ test was not available at the beginning of the study, but rather six months later, the number of participants varied among rapid tests (VIKIA®, N = 3928; Quick Profile™ HBsAg test, N = 3922, anti-HBsAb test, N = 3739; Determine™, N = 2472).

HBsAg rapid tests

Operator success and indeterminate results

Successful results were obtained on first attempt for the majority of rapid tests (Vikia®: 99.8%; Determine™: 100%; Quick Profile™:...
Inter-rater discrepancies
Overall, between-rater agreement was high for the Vikia\(\textregistered\), Determine\(\textsuperscript{\textregistered}\), and Quick Profile\(\textsuperscript{\textregistered}\) HBsAg tests (\(k = 1.00, 0.95, 0.98\), respectively). There were no inter-rater disagreements using the Vikia\(\textregistered\) test. A total of 4 inter-rater disagreements were observed with the Determine\(\textsuperscript{\textregistered}\) test, of which 3 were found in non-immunized participants and one in a person with resolved HBV infection. Finally, 3 inter-rater disagreements were found with the Quick Profile\(\textsuperscript{\textregistered}\) test, of which 2 were among vaccinated participants and 1 in a non-immunized person.

Diagnostic accuracy
As shown in Table 1, every rapid test had excellent specificity for HBsAg detection, all with values above 99.0%. Sensitivity ranged between 90.5% for the Quick Profile\(\textsuperscript{\textregistered}\) and 96.5% for the Vikia\(\textregistered\) tests. All three tests had achieved minimal non-inferiority criteria, with the lower 97.5% confidence interval of Se and Sp, respectively, as follows: 89.0% and 99.8% for the Vikia\(\textregistered\) test; 80.7% and 99.8% for the Determine\(\textsuperscript{\textregistered}\) test; 80.8% and 99.5% for the Quick Profile\(\textsuperscript{\textregistered}\) test. Only the AUROC for the Quick Profile\(\textsuperscript{\textregistered}\) test was significantly different (\(p = 0.002\)) when compared to the gold standard (AUROC = 1.0) (\(p = 0.08\) for both the Vikia\(\textregistered\) and Determine\(\textsuperscript{\textregistered}\) tests). Furthermore, there was a significant difference in AUROC when comparing the Vikia\(\textregistered\) and Quick Profile\(\textsuperscript{\textregistered}\) rapid tests (\(p = 0.02\)), but not between Vikia\(\textregistered\) and Determine\(\textsuperscript{\textregistered}\) (\(p = 0.3\)) or Quick Profile\(\textsuperscript{\textregistered}\) and Determine\(\textsuperscript{\textregistered}\), (\(p = 0.2\)).

Discordant results
There were a total of 14 false negative results: 3 with Vikia\(\textregistered\), 3 with Determine\(\textsuperscript{\textregistered}\), and 8 with the Quick Profile\(\textsuperscript{\textregistered}\) test. Details on rapid test results along with full ELISA battery, HBsAg quantification, HBV-DNA viral load, and HBV-related clinical status are given for all false negative tests in Table 2. Median HBsAg levels were significantly lower in patients with false negative versus true positive tests (19.5 vs. 2351.0 IU/ml, \(p = 0.0001\)) and only 4 false negative tests had HBsAg >10 IU/ml (Determine\(\textsuperscript{\textregistered}\), \(n = 1\); Quick Profile\(\textsuperscript{\textregistered}\), \(n = 3\)). Likewise, HBV-DNA levels were almost all below 200 IU/ml, with the exception of one patient, with a false negative Quick Profile\(\textsuperscript{\textregistered}\), who had a HBV viral load at 884 IU/ml, and one patient with a false negative Determine\(\textsuperscript{\textregistered}\) test, with a HBV viral load at 1.02 \(\times\) 10\(^6\) IU/ml, and three positive serological markers (HBsAg+, anti-HBcAb, anti-HBsAb = 43 IU/l). HBV from this last specimen was sequenced in the HBV S gene and displayed the typical G145R immune escape mutation. Interestingly, only two participants had false negative results for all three rapid tests (although patient number I-2-124, who had two false negative rapid tests, did not have an available Determine\(\textsuperscript{\textregistered}\) test). Two subjects had false positive tests (\(n = 2\), non-immunized) with the Vikia\(\textregistered\) and 10 subjects (vaccinated, \(n = 7\); non-immunized, \(n = 2\); resolved HBV infection with anti-HBsAb titer at 51 IU/l, \(n = 1\)) with the Quick Profile\(\textsuperscript{\textregistered}\) test. No false positive tests were observed using the Determine\(\textsuperscript{\textregistered}\) test (Table 1).

Anti-HBsAb rapid test

Operator success and indeterminate tests
Reliable results were obtained for 97.6% of the anti-HBsAb Quick Profile\(\textsuperscript{\textregistered}\) tests on first attempt. A total of 278 final results were given by a mix of one indeterminate reading and one definitive reading (one concomitant anti-HBsAb positive reading, \(n = 115\); one concomitant anti-HBsAg negative reading, \(n = 163\)).

Inter-rater discrepancies
Between-rater agreement of the anti-HBsAb Quick Profile\(\textsuperscript{\textregistered}\) test had low sensitivity (58.3%), but high specificity (97.8%). As shown in Table 3, predictive values were very different, with high PPV and low NPV. Non-inferiority could not be ascertained as the null hypothesis could not be rejected for the anti-HBsAb Quick Profile\(\textsuperscript{\textregistered}\) test, with lower 97.5% CI of sensitivity and specificity at 55.8% and 96.9%, respectively. Furthermore, the AUROC curve.

Table 1. Classification probabilities comparing rapid HBsAg tests compared to ELISA.

<table>
<thead>
<tr>
<th>HBsAg serology ELISA</th>
<th>AUC (95% CI)</th>
<th>Se</th>
<th>Sp</th>
<th>PPV</th>
<th>NPV</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vikia(\textregistered), n = 85</td>
<td>(n = 3843)</td>
<td>0.982 (0.962-1.000)</td>
<td>96.5</td>
<td>99.9</td>
<td>97.6</td>
<td>99.9</td>
<td>1854</td>
</tr>
<tr>
<td>Positive</td>
<td>82</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>3</td>
<td>3841</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Determine(\textsuperscript{\textregistered}), n = 47</td>
<td>(n = 2425)</td>
<td>0.968 (0.933-1.000)</td>
<td>93.6</td>
<td>100.0</td>
<td>100.0</td>
<td>99.9</td>
<td>∞</td>
</tr>
<tr>
<td>Positive</td>
<td>44</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>3</td>
<td>2425</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quick Profile(\textsuperscript{\textregistered}), n = 84</td>
<td>(n = 3838)</td>
<td>0.951 (0.919-0.983)</td>
<td>90.5</td>
<td>99.7</td>
<td>88.4</td>
<td>99.8</td>
<td>347</td>
</tr>
<tr>
<td>Positive</td>
<td>76</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>8</td>
<td>3828</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HBsAg, hepatitis B surface antigen; ELISA, enzyme-linked immuno-assay; AUC, area under the curve; Se, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR-, negative likelihood ratio.
was significantly lower when compared to the gold standard ($p < 0.0001$).

**Discordant results**

A total of 36 (1.0%) false positive and 872 (23.3%) false negative tests were identified with the anti-HBsAb Quick Profile™. Median anti-HBsAb titer of those with a false negative anti-HBsAb Quick Profile™ test was 58 IU/l (IQR: 24-157, min 10, max 1000). Furthermore, 69.6% of participants with false negative tests had been previously vaccinated.

**Discussion**

While many HBV rapid tests are distributed worldwide, very few are available in Europe. After an extensive search of companies allowing Phase IV evaluation of their rapid tests, three were finally included in our study. All three HBsAg rapid tests, Vikia®, Determine™, and Quick Profile™, met non-inferiority criteria and were highly accurate in predicting HBsAg status as determined by ELISA. On the contrary, the anti-HBsAb test by Quick Profile™ would require further refinement in its sensitivity, albeit specificity was rather high.

In comparison with previous evaluations of HBV rapid tests, this study presents several advantages. First, unlike the study populations from most previous research, our catchment area was established in a low HBV-prevalent country, while including a large sample, representative of those likely to be screened. Second, test effectiveness was the major focus in the sense that rapid tests were carried out in settings outside of a specialized laboratory, using whole blood specimens that were immediately assayed after participants’ blood draw. Finally, since most HBsAg-positive patients were followed at one specialized center, the clinical features of those with false negative rapid tests could be clarified in full detail.

Notwithstanding these differences, we observed similar classification probabilities compared to previous reports mainly from the Determine™ rapid test. All of these studies were conducted in high HBsAg-prevalent countries (sensitivity between 94.4% and 98.9% and specificity between 99.4% and 100%) [9–11]. Only one previous study has evaluated the effectiveness of the Vikia® anti-HBsAb Quick Profile™.

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Table 2. Participants with false negative results (between HBsAg rapid tests and ELISA).

<table>
<thead>
<tr>
<th>Participant</th>
<th>ELISA HBsAg</th>
<th>HBsAg rapid test</th>
<th>HBsAg titer (IU/ml)</th>
<th>HBsAb titer (IU/ml)</th>
<th>HBV viral load (IU/ml)</th>
<th>Hepatitis B clinical status*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Reader 1 Reader 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VIKIA®</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I-2-124</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>5 &lt;8 &lt;12 Inactive carrier</td>
</tr>
<tr>
<td>I-2-309</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>2.3 &lt;8 143 Lost to follow-up</td>
</tr>
<tr>
<td>I-8-272</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>5 &lt;8 62 Inactive carrier</td>
</tr>
<tr>
<td>DETERMINE™</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I-2-309</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>2.3 &lt;8 143 Lost to follow-up</td>
</tr>
<tr>
<td>I-7-14</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>?</td>
<td>-</td>
<td>90 43 &gt;10 Active hepatitis B</td>
</tr>
<tr>
<td>I-8-272</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>5 &lt;8 62 Inactive carrier</td>
</tr>
<tr>
<td>QUICK PROFILE™</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I-2-124</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>5 &lt;8 &lt;12 Inactive carrier</td>
</tr>
<tr>
<td>I-2-245</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>50 &lt;8 137 Inactive carrier</td>
</tr>
<tr>
<td>I-2-309</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>2.3 &lt;8 143 Lost to follow-up</td>
</tr>
<tr>
<td>I-2-315</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>5226 &lt;8 18 Inactive carrier</td>
</tr>
<tr>
<td>I-2-514</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>4.7 &lt;8 48 Inactive carrier</td>
</tr>
<tr>
<td>I-6-36</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>7.4 &lt;8 &lt;12 Inactive hepatitis B with advanced fibrosis</td>
</tr>
<tr>
<td>I-8-272</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>5 &lt;8 62 Inactive carrier</td>
</tr>
<tr>
<td>I-8-368</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>304.7 &lt;8 884 Inactive carrier; resolved HCV co-infection</td>
</tr>
</tbody>
</table>

Table 3. Classification probabilities comparing the rapid anti-HBs antibody test compared to ELISA.

<table>
<thead>
<tr>
<th>Anti-HBsAb serology</th>
<th>AUC (95% CI)</th>
<th>Se</th>
<th>Sp</th>
<th>PPV</th>
<th>NPV</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>QUICK PROFILE™</td>
<td>(n = 2091)</td>
<td>(n = 1648)</td>
<td>0.781 (0.769-0.792)</td>
<td>58.3</td>
<td>97.8</td>
<td>97.1</td>
<td>64.9</td>
</tr>
<tr>
<td>Positive</td>
<td>1219</td>
<td>36</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>872</td>
<td>1612</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Anti-HBsAb, anti-hepatitis B surface antibodies; ELISA, enzyme-linked immuno-assay; AUC, area under the curve; Se, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR-, negative likelihood ratio.
rapid test in Ghana among HIV-infected patients, giving a dramatically lower sensitivity (70.7%) but high specificity (100%) [12]. For the moment, it is unclear why such a large gap in sensitivity was observed, considering that most HBsAg-positive study participants originated from a country of high HBV endemicity. It should be noted that the Determine™ test also had very low sensitivity in this study (69.3%). Finally, no previous study, aside from the one reported by the manufacturer, has been documented for the Quick Profile™ test. Taken together, we consider our results as providing the most conclusive information to date regarding the effectiveness of these rapid tests for use in low-prevalent countries.

False negative results were very low across all three HBsAg rapid tests. With the VIKIA test, false negatives were only observed among inactive carriers, as defined by the European Association for the Study of the Liver (EASL) [13]; whereas all patients with active CHB requiring monitoring and/or treatment were accurately detected. The same was true for both Determine™ and Quick Profile™ tests, however certain exceptions were certainly noted. Using the Quick Profile test, one HBsAg-positive patient with advanced fibrosis and another with high levels of quantified HBsAg levels were incorrectly classified as HBsAg-negative. Even though both these patients were clinically inactive carriers, some research has suggested these additional characteristics may qualify them as having active chronic HBV [14,15]. Since inactive carriers continue to be at risk of developing hepatocellular carcinoma [16], other ways of ensuring their correct detection may need further investigation.

The Determine™ test failed to detect one HBsAg-positive patient (1-7-14) with high HBV viral load and an uncommon serological profile (positive for HBsAg, anti-HBsAb and anti-HBCAb). Interestingly, this patient was infected with an immune escape variant of HBV, with the G145R mutation in the S gene sequence. This variant has been associated with both concomitant positivity for HBsAg and anti-HBsAb [17] and reduction of antigenicity and immunogenicity (inability to recognize HBsAg by some diagnostic tests) [18–20]. Without knowing the individual components of each test, it cannot be clearly established why the VIKIA and Quick Profile™ tests were positive for this particular patient.

Unfortunately, we could not obtain HBV genetic information on the other false negative HBsAg-positive participants, mainly because they were either non-replicative or had very low viral loads (Table 2). This information would have allowed us to determine if some of these false negative results were also due to amino acid variability on the HBsAg “a” antigenic region. However, all but one of these patients (1-2-315) had very low levels of serum HBsAg, strongly suggesting that relative lack of rapid test sensitivity at low HBsAg levels was the main reason for false negatives rather than from mutations on the HBs “a” epitope.

Regarding rapid anti-HBs Ab detection, this is the first study evaluating the performance of such test to our knowledge. We observed a low sensitivity (regardless of anti-HBsAb titers) but excellent specificity, while at the same time NPV was poor and PPV very good. Therefore, it would be recommended that HBsAb Quick Profile™ results were considered reliable only in cases where the test is positive.

One limitation of our study was that we counted test results with one determinate and one indeterminate reading as confirmatory. This phenomenon was rarely observed and, when so, occurred predominately among HBsAg-negative patients. In contrast, 2.5% of the anti-HBsAb rapid tests had this result pattern. A systematic double reading procedure is probably not required for any of the rapid tests presented in our study.

To overcome this issue, it would be recommended that another trained reader blindly confirmed indeterminate results.

In conclusion, given the ease of use, rapidity, and high classification probabilities, the HBsAg tests evaluated in this study should be considered ideal for HBV screening, particularly among institutions in which patients are frequently lost to follow-up or where testing via ELISA is not readily available. Although a positive anti-HBsAb test would be reliable, it would be difficult to determine if an individual was previously exposed to HBV or vaccinated with a negative result. As was the case for HIV [21,22], these tests could allow accurate and potentially increased awareness of HBV status in a variety of settings, such as persons in socially-marginalized situations. More data on the medical-economic impact of including rapid tests is needed, especially in low-prevalent countries with abundant financial resources but limited systematic screening.

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Conflict of interest

The authors who have taken part in this study declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

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Addendum

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