Comparison of High-Throughput Fully Automated Immunoanalyzers for Detecting Hepatitis B Virus Infection

Dongju Won, MD; Younhee Park, MD, PhD; Dasom Choi, MT; Hyon-Suk Kim, MD, PhD

Context.—High-throughput automated immunoanalyzers for hepatitis B virus serologic markers have been introduced but have not been compared to existing systems.

Objective.—To compare hepatitis B surface antigen, hepatitis B surface antibody, and total hepatitis B core antibody analyses between our Architect i2000 platform and newer high-throughput fully automated immunoanalyzers.

Design.—From May to June 2018, a total of 932, 914, and 1055 samples tested for hepatitis B surface antigen, hepatitis B surface antibody, and total hepatitis B core antibody, respectively, with the Architect i2000 system for routine testing in our center were tested again with Alinity i, Atellica IM, and Cobas e801 systems.

Results.—Total concordance rates among the systems were 98.0%, 89.5%, and 93.0% for hepatitis B surface antigen, hepatitis B surface antibody, and total hepatitis B core antibody, respectively. Cohen’s \( \kappa \) values exceeded 0.8. The correlations between serum hepatitis B surface antibody levels quantified by all 4 systems were high (\( r > 0.85 \)). The hepatitis B surface antibody averages were greater for the Alinity i, Atellica IM, and Cobas e801 than for the Architect i2000 (\( P < .001 \)).

Conclusions.—Alinity i, Atellica IM, and Cobas e801 automated immunoanalyzers performed well when compared with the existing Architect i2000 system with regard to detection of hepatitis B viral infection. However, the new systems have higher titer and positivity rates for hepatitis B surface antibody and are more sensitive. Notably, the Atellica IM has a lower positive rate for total hepatitis B core antibody than does the Architect i2000.

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Hepatitis B virus (HBV) infection, the major cause of chronic hepatitis, cirrhosis, and hepatocellular carcinoma worldwide, is an important global health problem affecting human morbidity and mortality. Globally, more than 2 billion people have been or are currently infected with HBV, and more than 248 million people are currently positive for hepatitis B surface antigen (HBsAg).1,2 South Korea is an intermediate endemic area for HBV, with a prevalence between 2% and 7%.3

SeroLogic analysis, in combination with viral markers, plays an important role in HBV infection screening in HBV-endemic areas, disease progress monitoring in HBV carriers, treatment selection, and confirming response to therapy.4–10 SeroLogic methods include enzyme immunoassay, microparticle enzyme immunoassay, radioimmunoassay, and reverse passive hemagglutination, all of which are used to test for markers of HBV infection.11–14 However, since the introduction of the chemiluminescent immunoassay, analyses based on this principle have been used in many hospitals, with the Abbott Architect i2000 (Abbott Diagnostics, Abbott Park, Illinois) being the representative platform.15 In our facility, we plan to replace this system with a recently adopted high-throughput fully automated immunoanalyzer, as we intend to introduce total laboratory automation.

In this study, we therefore compared the results for HBsAg, anti–hepatitis B surface antibody (anti-HBs), and total anti–hepatitis B core antibody (anti-HBc), which are the major serologic markers for HBV infection, using our existing equipment, the Architect i2000, and recently adopted high-throughput fully automated immunoanalyzers: the Abbott Alinity i (Abbott Diagnostics), Siemens Atellica IM (Siemens Healthineers, Tarrytown, New York), and Roche Cobas e801 (Roche Diagnostics GmbH, Mannheim, Germany). A comparison of HBV serologic marker analyses using these systems has not previously been reported.

MATERIALS AND METHODS

Patients and Samples

Three serologic markers were selected for comparison: HBsAg, anti-HBs, and anti-HBc. These markers were selected because they are more often requested for evaluation than serologic markers for human immunodeficiency virus infection or hepatitis C virus infection. In total, 932, 914, and 1055 serum samples tested with

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the existing Architect i2000 system at Severance Hospital from May to June 2018 were submitted for HBsAg, anti-HBs, and anti-HBc and were retrospectively tested. These samples were residual specimens for which HBV clinical testing was requested. The specimens were stored at 4°C, and testing with the other devices was completed within a few days. Specimens were tested with Alinity i, Atellica IM, and Cobas e801 systems. At that time, the anti-HBe test with Cobas e801 was not approved and was thus excluded. The Alinity i is the next version of the Architect i2000 made by Abbott and measures serologic markers, using the same principle and kit as its predecessor. This study was approved by the Institutional Review Board of Yonsei University of Medicine (Seoul, Republic of Korea).

Assays and Methods

HBsAg, anti-HBs, and anti-HBc were qualified by using the Architect i2000, Alinity i, Atellica IM, and Cobas e801. Reagents for the Architect i2000 and Alinity i included the HBsAg Qualitative II, Anti-HBs Reagent Kit, and Anti-HBc II (all from Abbott Diagnostics). Reagents for the Alinity IM included the Hepatitis B surface Antigen II, Anti-Hepatitis B surface Antigen 2, and Anti-Hepatitis B core Total (all from Siemens Healthcare). For the Cobas e801 included the Elecsys HBsAg II, Elecsys Anti-HBs II, and Elecsys Anti-HBe II (all from Roche Diagnostics GmbH). The characteristics of each system are presented in Table 1. All 4 systems make use of chemiluminescence assays. However, in the Cobas e801, anti-HBe is assessed by using a competitive assay, while the other platforms use sandwich immunoassays. Furthermore, the Cobas e801 uses ruthenium as its chemiluminescent material, while the other systems use acridinium. The minimum sample volume is the smallest in the Cobas e801. Interpretation of anti-HBs results is done in the same way for all 4 machines but varies slightly for HBsAg and anti-HBe results. The number of testable samples per hour is the highest in the Atellica IM. Time to first result is 29 minutes for the Architect i2000 and Alinity i, 14 to 46 minutes for the Atellica IM, and 18 to 27 minutes for the Cobas e801. Reagent stability and specimen storage vary from system to system.

The Architect i2000 and Alinity i systems both use 2-step sandwich chemiluminescent microparticle immunoassay technology. Sample and acridinium-labeled conjugate are mixed with HBsAg, HBcAg, or anti-HBs coated with paramagnetic microparticles. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of analytes in the sample and the RLUs detected by the system optics. HBsAg and anti-HBc are determined qualitatively, while anti-HBs is determined quantitatively. In the former case, the systems calculate results by using the ratio of the sample RLU to the cutoff RLU (S/CO) for each specimen and control. Samples with a value of 1.0 or greater are considered reactive for HBsAg and anti-HBc. For anti-HBs, however, these systems use a 4-parameter logistic curve fit data analysis method for calibration and to generate results. Anti-HBs concentrations of 10 IU/L or greater are considered to be protective against HBV infection. The measuring interval for anti-HBs is 3.1 to 10,000.0 IU/L. Samples with an index value of at least 1.0 but lower than 50.0 are considered reactive for HBsAg, but the test must be repeated in duplicate. Samples with an initial value of at least 8.0 IU/L, but lower than 12.0 IU/L should be retested in duplicate for anti-HBs.

The Cobas e801 system uses electrochemiluminescence immunoassay technology. In this system, HBsAg and anti-HBs, and anti-HBc, are analyzed by using sandwich and competition immunoassays, respectively. The system uses the interaction of biotin and streptavidin with the ruthenium complex as chemiluminescent material. Application of a voltage to the instrument’s electrode induces a chemiluminescent emission, which is measured by a photomultiplier. The analysis results are determined automatically by the instrument software, which compares the electrochemiluminescence signal obtained from the product of sample reaction with the signal of the cutoff value obtained during calibration. For HBsAg, a cutoff index (COI) of 1.0 or greater is considered reactive, while values in the range of 0.9 to less than 1.0 are considered borderline. For anti-HBe, a COI value of 1.0 or less is considered reactive. For anti-HBs, results of 10 IU/L or greater can be automatically performed for HBsAg. For anti-HBe, retesting of samples with an initial COI of 0.90 or greater can be automatically performed for HBsAg. For anti-HBe, retesting of samples with an initial COI of 1.0 or less can be automatically performed.

Statistical Analysis

All statistical analyses were performed with Analyse-it Method Validation Edition, version 3.5 (Analyse-it Software, Leeds, England). We used concordance rates to establish the validity of recently adopted high-throughput fully automated immunoanalyzers for detecting HBV infection. The serologic tests for HBV infection are essentially qualitative. To test the reliability of concordance between the systems, the Cohen’s κ value was used. Anti-HBs titers between systems were compared by using the Pearson correlation coefficient, Passing-Bablok regression, and paired t tests. A P value of < .05 was considered statistically significant.

RESULTS

The positivity rates of HBsAg, anti-HBs, and anti-HBe for specimen analyses using the Architect i2000 were 21.0% (196 of 932), 55.7% (509 of 914), and 53.6% (565 of 1055), respectively. The total concordance rates among the 4 systems were 98.1% (914 of 932), 89.4% (817 of 914), and 93.0% (981 of 1055) for HBsAg, anti-HBs, and anti-HBc, respectively (Table 2). The 18 specimens with inconsistent HBsAg results were all negative in testing with Alinity i (Table 3). According to HBV DNA levels, aspartate aminotransferase/alanine aminotransferase levels, or follow-up HBsAg results after several months, all of these HBsAg results appeared to be negative. In addition, the patients had not recently been vaccinated and had a low HBsAg value of 0 to 10 units. Most false-positive results were observed with Alitella IM and Cobas e801. Most of the positive values of the samples showing discrepant results for anti-HBs were lower than 30 IU/L. Discrepancies in anti-HBc results were predominantly observed in specimens that were reactive in the Architect i2000 but negative in the Alitella IM (61 of 74, 82.4%). The median values of discrepant serologic markers related to HBV infection ranged from 0.19 to 1.10 for HBsAg, 5.84 to 13.90 for anti-HBs, and 0.27 to 1.66 for anti-HBe. The concordance rates between the respective systems all exceeded 90%, and Cohen’s κ values were also greater than 0.8 (Table 4). Of the 5 markers, HBsAg had the highest concordance rates, exceeding 98%. The correlations between the serum anti-
HBsAg: on board, system temperature, 28 d

Interference

Biotin, bilirubin, triglycerides, protein, hemoglobin

Abbreviations: Anti-HBc, hepatitis B core antibody; Anti-HBs, hepatitis B surface antibody; CLIA, chemiluminometric immunoassay; CMIA, chemiluminescent microparticle immunoassay; COI, cutoff index; ECLIA, electrochemiluminescence immunoassay; HBsAg, hepatitis B surface antigen; S/CO, sample relative light unit/cutoff relative light unit.

a Abbott Park, Illinois.
b Tarrytown, New York.
c Mannheim, Germany.

HBs levels measured quantitatively by the 4 systems were all high (r > 0.85) (Figure).

**DISCUSSION**

Despite advances in molecular genetic methods, serum HBV markers have retained their importance in the clinical screening and diagnosis of HBV infection in countries that do not have molecular genetic facilities. Currently, the chemiluminescent immunoassay method is the most widely used for serum HBV markers. Recently, high-throughput fully automated immunoanalyzers have been introduced for total laboratory automation. These are based on the

**Table 1. Characteristics of 4 Systems: Architect i2000, Alinity i, Atellica IM, and Cobas e801 Systems Measuring HBsAg, Anti-HBs, and Anti-HBc**

|                     | Architect i2000 (Abbott Diagnostics)a | Alinity i (Abbott Diagnostics)a | Atellica IM (Siemens Healthineers)b | Cobas e801 (Roche Diagnostics GmbH)c |
|---------------------|--------------------------------------|---------------------------------|------------------------------------|-------------------------------------|
| Principle           | CMA                                  | CMA                             | CLIA                               | ECLIA                               |
| HBsAg               | Sandwich                             | Sandwich                        | Sandwich                           | Sandwich                            |
| Anti-HBs            | Sandwich                             | Sandwich                        | Sandwich                           | Competition                         |
| Anti-HBc            | Sandwich                             | Sandwich                        | Sandwich                           | Ruthenium                           |
| Chemiluminescent    | Acridinium                           | Acridinium                      | Acridinium                         | Ruthenium                           |
| material            |                                      |                                 |                                    |                                     |
| Sample volume       |                                      |                                 |                                    |                                     |
| HBsAg               | 75 µL                                | 56 µL                           | 100 µL                             | 30 µL                               |
| Anti-HBs            | 75 µL                                | 75 µL                           | 100 µL                             | 24 µL                               |
| Anti-HBc            | 75 µL                                | 56 µL                           | 50 µL                              | 24 µL                               |
| Interpretation of   |                                      |                                 |                                    |                                     |
| result              |                                      |                                 |                                    |                                     |
| HBsAg               | S/CO                                 | S/CO                            | Index value                        | COI = Signal sample/cutoff          |
|                     | <1.0 Nonreactive                     | <1.0 Nonreactive                | <1.0 Reactive                      | <0.9 Nonreactive                    |
|                     | ≥1.0 Reactive                        | ≥1.0 Reactive                   | ≥1.0 Reactive                      | ≥1.0 Reactive                       |
| Anti-HBs            | Anti-HBs concentration, 1IU/L        | Anti-HBs concentration, 1IU/L   | Anti-HBs concentration, 1IU/L      | Anti-HBs concentration, 1IU/L       |
|                     | <10 Nonreactive                      | <10 Nonreactive                 | <10 Nonreactive                    | <10 Nonreactive                     |
|                     | ≥10 Reactive                         | ≥10 Reactive                    | ≥10 Reactive                       | ≥10 Reactive                        |
| Anti-HBc            | S/CO                                 | S/CO                            | Index value                        | COI = Signal sample/cutoff          |
|                     | <0.5 Reactive                        | <0.5 Reactive                   | <0.5 Reactive                      | ≥1.0 Reactive                       |
| No. of testable     | 200                                  | 200                             | 100                                | 300                                 |
| samples per hour    |                                      |                                 |                                    |                                     |
| Time to first result|                                      |                                 |                                    |                                     |
| HBsAg               | 29 min                               | 29 min                          | 26 min                             | 18 min                              |
| Anti-HBs            | 29 min                               | 29 min                          | 14 min                             | 18 min                              |
| Anti-HBc            | 29 min                               | 29 min                          | 46 min                             | 27 min                              |
| Reagent stability   |                                      |                                 |                                    |                                     |
| HBsAg               | Unopened, 2°C–8°C, until expiration  | Unopened, 2°C–8°C, until        | Unopened, 2°C–8°C, until expiration | Unopened, 2°C–8°C, until expiration |
|                     | date                                 | expiration date                 | date                               | date                               |
|                     | On board, system temperature, 30 d   | On board, system temperature,   | On board, system temperature,      | On board, system temperature,       |
|                     |                                      | 30 d                            | 60 d                               | 16 wk                              |
| Specimen storage    |                                      |                                 |                                    |                                     |
| HBsAg               | Room temperature (20°C–25°C), up to 6| Room temperature (20°C–25°C),    | Room temperature (20°C–25°C), up to | Room temperature (20°C–25°C), up to |
|                     | days                                | 6 d                             | 14 d                               | 14 d                               |
| Anti-HBs            | Room temperature (20°C–25°C), up to 6| Room temperature (20°C–25°C),    | Room temperature (20°C–25°C), up to | Room temperature (20°C–25°C), up to |
|                     | days                                | 6 d                             | 14 d                               | 14 d                               |
| Anti-HBc            | Room temperature (20°C–25°C), up to 3| Room temperature (20°C–25°C),    | Room temperature (20°C–25°C), up to | Room temperature (20°C–25°C), up to |
|                     | days                                | 3 d                             | 7 d                                | 7 d                                |
| Interference        | Biotin, bilirubin, triglycerides,    | protein, hemoglobin             |                                    |                                     |

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Table 2. Comparison of Serum Hepatitis B Virus Marker Results Among the Architect i2000, Alinity i, Atellica IM, and Cobas e801 Systems^a

| (A) HBsAg | (B) Anti-HBs | (C) Anti-HBc |
|-----------|--------------|--------------|
| Architect i2000 | Alinity i | Atellica IM | Cobas e801 | No. (%) | Architect i2000 | Alinity i | Atellica IM | Cobas e801 | No. (%) | Architect i2000 | Alinity i | Atellica IM | Cobas e801 | No. (%) |
| **Agreement** | | | | | | | | | |
| R | R | R | R | 194 (20.8) | R | R | R | R | 504 (55.1) | R | R | R | 981 (93.0) |
| N | N | N | N | 720 (77.3) | N | N | N | N | 313 (34.2) | N | N | N | 477 (45.2) |
| **Disagreement** | | | | | | | | | |
| R | R | N | R | 0 (0.8) | R | R | N | R | 1 (0.1) | R | N | R | 0 (0.0) |
| R | N | R | R | 2 (0.2) | R | N | R | R | 1 (0.1) | R | N | N | 60 (5.7) |
| R | N | R | N | 0 (0.0) | R | N | R | N | 3 (0.3) | R | N | R | 0 (0.1) |
| R | N | R | N | 0 (0.0) | R | N | R | N | 0 (0.0) | N | R | R | 0 (0.0) |
| R | N | N | R | 0 (0.0) | R | N | N | N | 0 (0.0) | N | N | R | 7 (0.7) |
| N | R | N | R | 0 (0.0) | N | R | R | R | 6 (0.7) | N | N | R | 2 (0.2) |
| N | N | R | R | 2 (0.2) | N | N | R | R | 22 (2.4) | N | N | R | 16 (1.8) |
| N | N | R | N | 7 (0.8) | N | N | N | N | 3 (0.3) | N | R | N | 6 (0.7) |
| N | N | N | R | 7 (0.8) | N | N | N | N | 30 (3.3) | N | N | N | 13 (1.3) |

**Total (N)** | 932 | 914 | 1055

Abbreviations: Anti-HBc, hepatitis B core antibody; Anti-HBs, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; N, negative; R, reactive.

^a Architect i2000 (Abbott Diagnostics, Abbott Park, Illinois), Alinity i (Abbott Diagnostics), Atellica IM (Siemens Healthineers, Tarrytown, New York), and Cobas e801 (Roche Diagnostics GmbH, Mannheim, Germany).
chemiluminescent immunoassay method but are more efficient than standard tests. In this study, we compared the results of HBsAg, anti-HBs, and anti-HBc analyses among 3 recently adopted high-throughput fully automated immunoanalyzers (Alinity i, Atellica IM, and Cobas e801) and our existing equipment (Architect i2000). A comparison of these new systems and the Architect i2000 has not been reported previously.

Reactive HBsAg results indicate HBV infection, which can be either acute or chronic. HBsAg is related to HBV DNA, and also to increased risk of liver cancer.16–18 Furthermore, it may be a predictor of treatment outcome.19 High concordance rates of greater than 98% were observed when all 4 systems were compared, simultaneously or in pairs, and were significantly higher than the rates of other markers (anti-HBs, anti-HBc). The antigen test appears to return more constant values, regardless of the system, than are seen with the antibody test.

Reactive anti-HBs results indicate that the testee has successfully responded to the hepatitis B vaccine, or has recovered from acute hepatitis B. This means that the patient will be immune to hepatitis B in the future. Anti-HBs with concentration values of 10 IU/L or greater are considered to be reactive and immune to hepatitis B.20 This test is necessary to check the effect of the vaccine, or to find subjects requiring booster injections because of decreases in anti-HBs levels over time.21 In HBsAg, high concordance rates of greater than 98% were observed when all 4 systems were compared, simultaneously or in pairs, and were significantly higher than the rates of other markers (anti-HBs, anti-HBc). The antigen test appears to return more constant values, regardless of the system, than are seen with the antibody test.

Table 3. Clinical Data of Patients With Discrepant HbsAg Results

| Diagnosis                                                                 | Real-time Quantitative PCR | Follow-up HBsAg | AST, ALT | Architect i2000* | Alinity i² | Atellica IM³ | Cobas e801⁴ |
|---------------------------------------------------------------------------|-----------------------------|----------------|----------|-----------------|-----------|-------------|-------------|
| P1  Hepatitis B, viral, chronic                                            Target not detected     | Negative                  | Normal range | 1.43    | R               | 0.97      | N           | 3.15        |
| P2  Hepatitis B, viral, chronic                                            Target not detected     | Negative                  | Normal range | 4.76    | R               | 0.89      | N           | 10.03       |
| P3  End-stage renal disease                                                Target not detected     | Negative                  | Normal range | 0.76    | N               | 0.71      | N           | 3.05        |
| P4  Coronary artery occlusive disease                                      Not tested                | Negative                  | Normal range | 0.19    | N               | 0.59      | N           | 1.21        |
| P5  Herniated cervical disc                                                Not tested                | Negative                  | Normal range | 0.15    | N               | 0.28      | N           | 4.43        |
| P6  Endometrial polyp                                                      Not tested                | Negative                  | Normal range | 0.20    | N               | 0.29      | N           | 5.46        |
| P7  Rheumatoid arthritis, seropositive                                     Not tested                | Negative                  | Normal range | 0.18    | N               | 0.36      | N           | 15.60       |
| P8  Acute rhinitis                                                         Not tested                | Negative                  | Normal range | 0.17    | N               | 0.28      | N           | 3.09        |
| P9  Physical examination                                                   Not tested                | Negative                  | Normal range | 0.14    | N               | 0.41      | N           | 2.34        |
| P10 Hepatocellular carcinoma (B-viral)                                     Not tested                | Negative                  | Normal range | 0.17    | N               | 0.29      | N           | 1.33        |
| P11 S/P kidney transplant                                                  Not tested                | Negative                  | Normal range | 0.19    | N               | 0.30      | N           | 1.49        |
| P12 Purpura, vasculitis                                                    Target not detected     | Negative                  | Normal range | 0.21    | N               | 0.29      | N           | 0.08        |
| P13 Proteinuria                                                            Not tested                | Negative                  | Normal range | 0.34    | N               | 0.44      | N           | 0.06        |
| P14 Rectal cancer                                                          Not tested                | Negative                  | Normal range | 0.19    | N               | 0.37      | N           | 0.13        |
| P15 Endometrial polyp                                                      Not tested                | Negative                  | Normal range | 0.17    | N               | 0.21      | N           | 0.15        |
| P16 Mature cystic teratoma of ovary                                        Not tested                | Negative                  | Normal range | 0.21    | N               | 0.32      | N           | 0.12        |
| P17 S/P kidney transplant                                                  Not tested                | Negative                  | Normal range | 0.15    | N               | 0.28      | N           | 0.29        |
| P18 S/P kidney transplant                                                  Not tested                | Negative                  | Normal range | 0.19    | N               | 0.23      | N           | 0.01        |

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; COI, cutoff index; HBsAg, hepatitis B surface antigen; N, negative; R, reactive; PCR, polymerase chain reaction; S/CO, sample relative light unit/cutoff relative light unit; S/P, status post.

a Abbott Diagnostics, Abbott Park, Illinois.

b Siemens Healthineers, Tarrytown, New York.

c Roche Diagnostics GmbH, Mannheim, Germany.
Comparison of hepatitis B surface antibody titers (IU/L) excluding the results above 1000 IU/L. A, Architect i2000 and Alinity i. B, Architect i2000 and Atellica IM. C, Architect i2000 and Cobas e801. D, Alinity i and Atellica IM. E, Alinity i and Cobas e801. F, Atellica IM and Cobas e801.

A: Architect i2000 (IU/L) vs. Alinity i
- y = 1.281x - 0.464
- r = 0.991, 95% CI: 0.990 to 0.992

B: Architect i2000 (IU/L) vs. Atellica IM
- y = 1.494x - 0.570
- r = 0.893, 95% CI: 0.881 to 0.904

C: Architect i2000 (IU/L) vs. Cobas e801
- y = 1.973x + 0.777
- r = 0.868, 95% CI: 0.851 to 0.882

D: Alinity i (IU/L) vs. Atellica IM
- y = 1.194x - 0.113
- r = 0.874, 95% CI: 0.858 to 0.889

E: Alinity i (IU/L) vs. Cobas e801
- y = 1.598x + 1.441
- r = 0.874, 95% CI: 0.858 to 0.889

F: Atellica IM (IU/L) vs. Cobas e801
- y = 1.312x + 1.646
- r = 0.851, 95% CI: 0.835 to 0.867
Abbreviations: Anti-HBc, hepatitis B core antibody; Anti-HBs, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; NA, not applicable.

* Architect i2000 (Abbott Diagnostics, Abbott Park, Illinois), Alinity I (Abbott Diagnostics), Atellica IM (Siemens Healthcare, Tarrytown, New York), and Cobas e801 (Roche Diagnostics GmbH, Mannheim, Germany).

greater in the Alinity i, Atellica IM, and Cobas e801 than in the Architect i2000 (P < .001). As shown in the Figure, the order of magnitude of the slopes of regression line was Cobas e801, Alinity I, Atellica IM, and Architect i2000, which should be considered when setting the desired concentration in each hospital. The new systems appear to be more sensitive toward anti-HBs than the existing equipment, which may be attributed to differences in the subtypes of HBV antigen in the reagents or in the method of antigen preparation. Considering the frequent migration of patients or clinicians between medical institutions, the comparison of these test methods may facilitate accurate determination and interpretation of the test results by analyzing qualitative agreement rates and discrepancies. Total anti-HBc appears at the onset of symptoms in acute HBV infection and persists for life. The presence of anti-HBc indicates previous hepatitis B antigen in the reagents or in the method of antigen preparation. Considering the frequent migration of patients or clinicians between medical institutions, the comparison of these test methods may facilitate accurate determination and interpretation of the test results by analyzing qualitative agreement rates and discrepancies. Total anti-HBc appears at the onset of symptoms in acute HBV infection and persists for life.

Table 4. Concordance Rates and Cohen’s κ Value Between 2 Analyzers Among the Architect i2000, Alinity I, Atellica IM, and Cobas e801 System

| Systems | Concordance Rates, % | Cohen’s κ Value |
|---------|----------------------|----------------|
| Architect i2000/Alinity I | | |
| HBsAg | 99.6 | 0.99 |
| Anti-HBs | 96.9 | 0.94 |
| Anti-HBc | 99.4 | 0.99 |
| Architect i2000/Atellica IM | | |
| HBsAg | 99.3 | 0.97 |
| Anti-HBs | 93.9 | 0.87 |
| Anti-HBc | 93.5 | 0.87 |
| Architect i2000/Cobas e801 | | |
| HBsAg | 99.0 | 0.97 |
| Anti-HBs | 92.4 | 0.84 |
| Anti-HBc | NA | NA |
| Alinity I/Atellica IM | | |
| HBsAg | 98.7 | 0.96 |
| Anti-HBs | 94.1 | 0.88 |
| Anti-HBc | 93.1 | 0.86 |
| Alinity I/Cobas e801 | | |
| HBsAg | 98.7 | 0.96 |
| Anti-HBs | 93.3 | 0.86 |
| Anti-HBc | NA | NA |
| Atellica IM/Cobas e801 | | |
| HBsAg | 98.6 | 0.95 |
| Anti-HBs | 94.3 | 0.87 |
| Anti-HBc | NA | NA |

References

1. MacLachlan JH, Cowie BC. Hepatitis B virus epidemiology. Cold Spring Harb Perspect Med. 2015;5(5):a021410.
2. Schweitzer A, Horn J, Mikołajczyk RT, Krause G, Ott J. Estimations of worldwide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013. Lancet. 2015;386(10003):1546–1555.
3. Pak SC, Alastal Y, Khan Z, Darr U. Viral hepatitis in South Korea. EuroJ Hepatogastroenterol. 2017;72(2):163–165.
4. Kao JH. Diagnosis of hepatitis B virus infection through serological and virological markers. Expert Rev Gastroenterol Hepatol. 2008;2(4):533–562.
5. Ponde RA. Hepatitis B virus infection or acute exacerbation of chronic hepatitis B infection: the differential serological diagnosis. Eur J Clin Microbiol Infect Dis. 2016;35(1):29–40.
6. Sundaram V, Knowles K. Management of chronic hepatitis B infection. BMJ. 2015;351:h4263.
7. Lubel JS, Angus PW. Hepatitis B reactivation in patients receiving cytotoxic chemotherapy: diagnosis and management. J Gastroenterol Hepatol. 2010;25(3):646–671.
8. Liang R. How I treat and monitor viral hepatitis B infection in patients receiving intense immunosuppressive therapies or undergoing hematopoietic stem cell transplantation. Blood. 2009;113(4):3147–3153.
9. Bonino F, Pitrone L, Brunetto MR, Liaw YM. Diagnostic markers of chronic hepatitis B infection and disease. Antivir Ther. 2010;15(suppl 3):35–44.
10. Chemin J, Jeantet D, Kay A, Trepo C. Role of silent hepatitis B virus in chronic hepatitis B surface antigen(-) liver disease. Antiviral Res. 2001;52(2):117–123.
11. Kimura T, Kurohara A, Sakamoto Y, et al. Sensitive enzyme immunoassay for hepatitis B virus core-related antigens and their correlation to virus load. J Clin Microbiol. 2002;40(2):439–445.
12. Barbara JA, Harrison PJ, Howell DR, et al. A sensitive single reverse passive haemagglutination test for detecting both HBsAg and anti-HBs. *J Clin Pathol*. 1979;32(11):1180–1183.

13. Seidl S, Ziegler GB. Detection of hepatitis B antigen in blood donors by radioimmunoassay and three reverse passive haemagglutination techniques. *Vox Sang*. 1976;31(2):81–86.

14. McCartney RA, Harbour J, Roome AP, Caul EO. Comparison of enhanced chemiluminescence and microparticle enzyme immunoassay for the measurement of hepatitis B surface antibody. *Vaccine*. 1993;11(9):941–945.

15. Ghosh M, Nandi S, Dutta S, Saha MK. Detection of hepatitis B virus infection: a systematic review. *World J Hepatol*. 2015;7(23):2482–2491.

16. Lee JH, Kim SJ, Ahn SH, Lee J, Park Y, Kim HS. Correlation between quantitative serum HBsAg and HBV DNA test in Korean patients who showed high level of HBsAg. *J Clin Pathol*. 2010;63(11):1027–1031.

17. Yang N, Feng J, Zhou T, et al. Relationship between serum quantitative HBsAg and HBV DNA levels in chronic hepatitis B patients. *J Med Virol*. 2018;90(7):1240–1245.

18. Yang Y, Gao J, Tan YT, et al. Individual and combined effects of hepatitis B surface antigen level and viral load on liver cancer risk. *J Gastroenterol Hepatol*. 2018;33(5):1131–1137.

19. Takkenberg RB, Jansen L, de Niet A, et al. Baseline hepatitis B surface antigen (HBsAg) as predictor of sustained HBsAg loss in chronic hepatitis B patients treated with pegylated interferon-alpha2a and adefovir. *Antivir Ther*. 2013;18(7):895–904.

20. Jack AD, Hall AJ, Maine N, Mendy M, Whittle HC. What level of hepatitis B antibody is protective? *J Infect Dis*. 1999;179(2):489–492.

21. Sahana HV, Sarala N, Prasad SR. Decrease in Anti-HBs antibodies over time in medical students and healthcare workers after hepatitis B vaccination. *Biomed Res Int*. 2017;2017:1327492.

22. Kim MH, Kang SY, Lee WI. Occult HBV among anti-HBc alone: mutation analysis of an HBV surface gene and pre-S gene. *Yonsei Med J*. 2017;58(3):557–563.