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

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• ***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 κ 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.**

(*Arch Pathol Lab Med.* 2020;144:612–619; doi: 10.5858/arpa.2019-0096-OA)

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 progression 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

Accepted for publication July 22, 2019.
Published online October 19, 2019.

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The authors have no relevant financial interest in the products or companies described in this article.

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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 analysis, respectively. 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-HBc 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 Reagent Kit, Anti-HBs Reagent Kit, and Anti-HBc II (all from Abbott Diagnostics). Reagents for the Atellica IM included the Hepatitis B surface Antigen II, Anti-Hepatitis B surface Antigen 2, and Anti-Hepatitis B core Total (all from Siemens Healthineers). Reagents for the Cobas e801 included the Elecsys HBsAg II, Elecsys Anti-HBs II, and Elecsys Anti-HBc 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-HBc 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-HBc 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 or anti-HBc. For anti-HBs, however, these systems use a 4-parameter logistic curve fit data reduction 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 2.00 to 1000.00 IU/L. If initial results indicate reactivity for HBsAg and anti-HBc, a retest in duplicate is needed. For HBsAg, repeatedly reactive specimens must be confirmed by using a neutralizing assay before disclosing the HBsAg status to the patient.

The Atellica IM system uses sandwich chemiluminometric immunoassay technology. Sample and streptavidin-coated paramagnetic microparticles are combined with biotinylated HBsAg and acridinium ester–labeled HBsAg, biotinylated HBcAg and acridinium ester–labeled HBcAg, or biotinylated anti-HBs and acridinium ester–labeled anti-HBs. A direct relationship exists between the amount of analytes present in the patient sample and the amount of RLUs detected by the system, and the result is determined according to the index value established with the calibrators. For HBsAg and anti-HBc samples with values of 1.0 and greater and values of 0.50 and greater, respectively, the indexes are considered reactive. Anti-HBs with concentration values of 10 IU/L or greater are considered to be reactive. The measuring interval for anti-HBs is 3.1 to 1000.0 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-HBc, a COI value of 1.0 or less is considered reactive. For anti-HBs, results of 10 IU/L or greater are considered positive. The measuring interval for anti-HBs is 2.0 to 1000.0 IU/L. Retesting of samples with an initial COI of 0.90 or greater can be automatically performed for HBsAg. For anti-HBc, 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-HBc 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 Atellica 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 Atellica 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-HBc. 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 3 markers, HBsAg had the highest concordance rates, exceeding 98%. The correlations between the serum anti-

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	CMIA	CMIA	CLIA	ECLIA
HBsAg	Sandwich	Sandwich	Sandwich	Sandwich
Anti-HBs	Sandwich	Sandwich	Sandwich	Sandwich
Anti-HBc	Sandwich	Sandwich	Sandwich	Competition
Chemiluminescent material	Acridinium	Acridinium	Acridinium	Ruthenium
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 <1.0 Nonreactive ≥1.0 Reactive	S/CO <1.0 Nonreactive ≥1.0 Reactive	Index value <1.0 Nonreactive ≥1.0 Reactive	COI = Signal sample/cutoff <0.9 Nonreactive ≥0.9 to 1.0 Borderline ≥1.0 Reactive
Anti-HBs	Anti-HBs concentration, IU/L <10 Nonreactive ≥10 Reactive	Anti-HBs concentration, IU/L <10 Nonreactive ≥10 Reactive	Anti-HBs concentration, IU/L <10 Nonreactive ≥10 Reactive	Anti-HBs concentration, IU/L <10 Nonreactive ≥10 Reactive
Anti-HBc	S/CO <1.0 Nonreactive ≥1.0 Reactive	S/CO <1.0 Nonreactive ≥1.0 Reactive	Index value <0.50 Nonreactive ≥0.50 Reactive	COI = Signal sample/cutoff >1.0 Nonreactive ≤1.0 Reactive
No. of testable samples per hour	200	200	400	300
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	Unopened, 2°C–8°C, until expiration date On board, system temperature, 30 d	Unopened, 2°C–8°C, until expiration date On board, system temperature, 30 d	Unopened, 2°C–8°C, until expiration date HBsAg: on board, system temperature, 60 d Anti-HBs: on board, system temperature, 90 d Anti-HBc: on board, system temperature, 28 d	Unopened, 2°C–8°C, until expiration date On board, system temperature, 16 wk
Specimen storage				
HBsAg	Room temperature (20°C–25°C), 24 h 2°C–8°C, up to 6 days	Room temperature (20°C–25°C), 24 h 2°C–8°C, up to 6 d	2°C–8°C, up to 7 d	Room temperature (20°C–25°C), up to 6 d 2°C–8°C, up to 14 d
Anti-HBs	Room temperature (20°C–25°C), 24 h 2°C–8°C, up to 14 days	Room temperature (20°C–25°C), 24 h 2°C–8°C, up to 14 d	2°C–8°C, up to 7 d	Room temperature (20°C–25°C), up to 3 d 2°C–8°C, up to 6 d
Anti-HBc	Room temperature (20°C–25°C), up to 3 d 2°C–8°C, up to 14 d	Room temperature (20°C–25°C), up to 3 d 2°C–8°C, up to 7 d	2°C–8°C, up to 7 d	Room temperature (20°C–25°C), up to 7 d 2°C–8°C, up to 14 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 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	No. (%)
Agreement				914 (98.1)					817 (89.4)				981 (93.0)
R	R	R	R	194 (20.8)	R	R	R	R	504 (55.1)	R	R	R	504 (47.8)
N	N	N	N	720 (77.3)	N	N	N	N	313 (34.2)	N	N	N	477 (45.2)
Disagreement				18 (1.9)					97 (10.6)				74 (7.0)
R	R	N	R	0 (0.0)	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	R	N	60 (5.7)
R	R	R	N	0 (0.0)	R	R	R	N	3 (0.3)	R	N	N	1 (0.1)
R	N	R	N	0 (0.0)	R	N	R	N	0 (0.0)	N	R	R	0 (0.0)
R	R	N	N	0 (0.0)	R	R	N	N	0 (0.0)	N	N	R	8 (0.8)
R	N	N	R	0 (0.0)	R	N	N	R	0 (0.0)	N	R	N	5 (0.5)
R	N	N	N	0 (0.0)	R	N	N	N	0 (0.0)				
N	R	R	R	0 (0.0)	N	R	R	R	13 (1.4)				
N	R	N	R	0 (0.0)	N	R	N	R	6 (0.7)				
N	N	R	R	2 (0.2)	N	N	R	R	22 (2.4)				
N	R	R	N	0 (0.0)	N	R	R	N	2 (0.2)				
N	N	R	N	7 (0.8)	N	N	R	N	16 (1.8)				
N	R	N	N	0 (0.0)	N	R	N	N	3 (0.3)				
N	N	N	R	7 (0.8)	N	N	N	R	30 (3.3)				
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).

Table 3. Clinical Data of Patients With Discrepant HbsAg Results

	Diagnosis	Real-time Quantitative PCR	Follow-up HBsAg	AST, ALT	Architect i2000[a]		Alinity i[a]		Atellica IM[b]		Cobas e801[c]	
					S/CO	Result	S/CO	Result	Index Value	Result	COI	Result
P1	Hepatitis B, viral, chronic	Target not detected	Negative	Normal range	1.43	R	0.97	N	3.15	R	1.24	R
P2	Hepatitis B, viral, chronic	Target not detected	Negative	Normal range	4.76	R	0.89	N	10.03	R	1.47	R
P3	End-stage renal disease	Target not detected	Negative	Normal range	0.76	N	0.71	N	3.05	R	1.64	R
P4	Coronary artery occlusive disease	Not tested	Negative	Normal range	0.19	N	0.59	N	1.21	R	1.06	R
P5	Herniated cervical disc	Not tested	Negative	Normal range	0.15	N	0.28	N	4.43	R	0.41	N
P6	Endometrial polyp	Not tested	Negative	Normal range	0.20	N	0.29	N	5.46	R	0.40	N
P7	Rheumatoid arthritis, seropositive	Not tested	Negative	Normal range	0.18	N	0.36	N	15.60	R	0.43	N
P8	Acute rhinitis	Not tested	Negative	Normal range	0.17	N	0.28	N	3.09	R	0.46	N
P9	Physical examination	Not tested	Negative	Normal range	0.14	N	0.41	N	2.34	R	0.49	N
P10	Hepatocellular carcinoma (B-viral)	Not tested	Negative	Normal range	0.17	N	0.29	N	1.33	R	0.34	N
P11	S/P kidney transplant	Not tested	Negative	Normal range	0.19	N	0.30	N	1.49	R	0.33	N
P12	Purpura, vasculitis	Target not detected	Negative	Normal range	0.21	N	0.29	N	0.08	N	1.43	R
P13	Proteinuria	Not tested	Negative	Normal range	0.34	N	0.44	N	0.06	N	1.13	R
P14	Rectal cancer	Not tested	Negative	Normal range	0.19	N	0.37	N	0.13	N	9.00	R
P15	Endometrial polyp	Not tested	Negative	Normal range	0.17	N	0.21	N	0.15	N	1.69	R
P16	Mature cystic teratoma of ovary	Not tested	Negative	Normal range	0.21	N	0.32	N	0.12	N	1.13	R
P17	S/P kidney transplant	Not tested	Negative	Normal range	0.15	N	0.28	N	0.29	N	1.67	R
P18	S/P kidney transplant	Not tested	Negative	Normal range	0.19	N	0.23	N	0.01	N	1.07	R

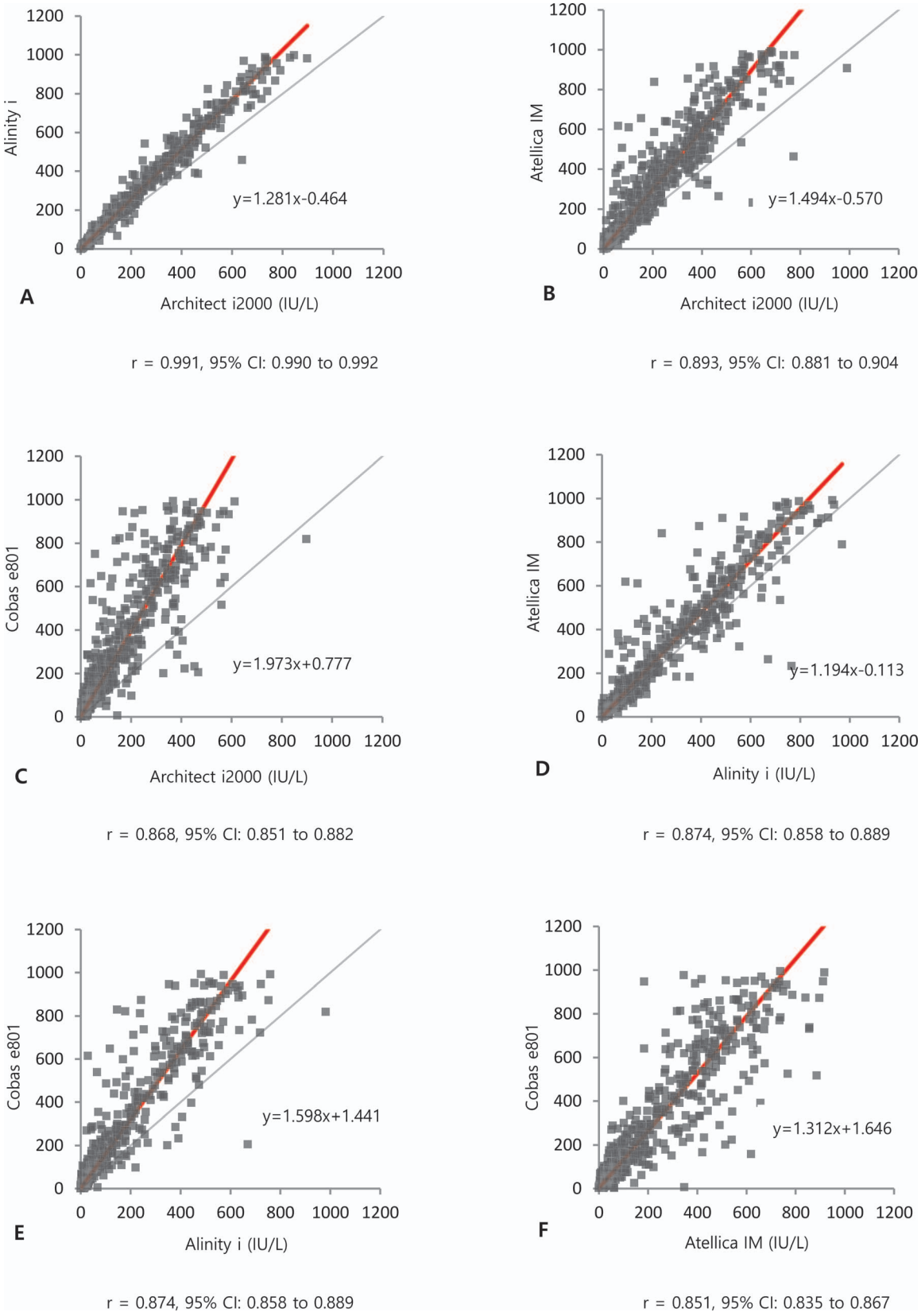
Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; COI; cutoff index; HBsAg, hepatitis B surface antigen; N, negative; R, reactive; PCR, polymerase chain reaction; S/CO, sample relative light unit/cutoff relative light unit; S/P, status post.

[a] Abbott Diagnostics, Abbott Park, Illinois.
[b] Siemens Healthineers, Tarrytown, New York.
[c] Roche Diagnostics GmbH, Mannheim, Germany.

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] 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.

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] Anti-HBs is the only quantitative measure. Concordance rates between the systems were greater than 90%, and the Cohen's κ values between systems were greater than 0.8 (Table 4). The results of the anti-HBs analyses were in very good agreement. In addition, the correlation coefficients of anti-HBs titers between the systems exceeded 0.85, indicating good correlations between the analyses. In the Architect i2000 system, however, negative anti-HBs results tended to be reactive in the new equipment (92 of 97, 94.8%), and the anti-HBs mean was



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.

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[a]	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	98.6	0.95
HBsAg	94.3	0.87
Anti-HBs	NA	NA
Anti-HBc	98.6	0.95

Abbreviations: Anti-HBc, hepatitis B core antibody; Anti-HBs, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; NA, not applicable.

[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).

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, Atellica IM, Alinity i, 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 or ongoing HBV infection in an undefined time frame. This marker can be used to determine whether positive anti-HBs reaction in a patient is due to vaccination or past infection. Indeed, occult HBV infection is known to be associated with "anti-HBc alone" subjects who are identified as positive for total anti-HBc, but negative for both HbsAg and anti-HBs.[22] The anti-HBc results in the Atellica IM (512 of 1055; 48.5%) were less positive than those in the Architect i2000 (565 of 1055; 53.6%) and Alinity i (569 of 1055; 53.9%), and tended to be in lesser agreement with results of the other systems. All 60 patients who were only anti-HBc negative according to Atellica IM were negative for HBsAg and had no history or remarkable clinical symptoms; therefore, these results were likely false positives, but this remains unknown because we have not evaluated any other tests.

The median discordant HBsAg values were 0.19 (0.14–4.76), 0.31 (0.21–0.97), 0.41 (0.01–10.03), and 1.10 (0.33–9.00), while the median discordant anti-HBs values were 5.84 (0.25–20.89), 7.53 (0.18–26.83), 10.51 (1.36–61.87), and 13.9 (2.00–107.00) for the Architect i2000, Alinity i, Atellica IM, and Cobas e801 platforms, respectively. Furthermore, the median discordant anti-HBc values were 1.66 (0.08–8.04), 1.81 (0.02–2.22), and 0.27 (0.13–9.05) for Architect i2000, Alinity i, and Atellica IM, respectively. The cutoff value for HBsAg in all 4 systems, and of anti-HBc in Architect i2000 and Alinity I, was 1.0; the cutoff value of anti-HBc in Atellica IM was 0.5; and the cutoff value for anti-HBs in all 4 systems was 10 IU/L. Therefore, the discordant values of serologic markers related to HBV infection were near the cutoff. Serologic results of HBV infection near the cutoff should be judged by re-examination and consideration of clinical signs or other markers.

The main limitation of this study was that the remainders of specimens used for other clinical tests were evaluated. Thus, the amount of the specimen was insufficient for retesting of specimens that showed inconsistent results.

In conclusion, the fully automated immunoanalyzers (Alinity i, Atellica IM, and Cobas e801) used to detect HBV infection performed well when compared with our existing Architect i2000 system. Because of the different sample volumes and throughput of each system, the choice of which to use depends on the hospital conditions; however, it should be noted that the new systems show higher titers and positivity rates for anti-HBs than the Architect i2000, and are also more sensitive. It should also be noted that the Atellica IM has a lower positive rate than does the Architect i2000. Because the results presented were from a single center, they should be confirmed by future studies using results from multiple centers.

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