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Mindray CL-900i assay: An effective assay for hepatitis B surface antigen screening with superior specificity

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ABSTRACT

Objectives: The chemiluminescence immunoassay automated Abbott ARCHITECT hepatitis B surface antigen (HBsAg) screening assay is globally recognized for its superior sensitivity but notably low specificity. This mandates positive results confirmation by another confirmatory assay, such as the widely used Abbott ARCHITECT HBsAg neutralizing assay. This study aimed to evaluate the performance of the new chemiluminescence immunoassay, Mindray CL-900i HBsAg screening assay in comparison to the ARCHITECT neutralizing/confirmatory assay.
Methods: A total of 200 archived HBsAg-positive and -negative samples by ARCHITECT screening were selected for this study. These samples were classified as follows: true positive (n = 39): positive by ARCHITECT screening and confirmatory assays, true negative (n = 144): negative by ARCHITECT screening and confirmatory assays, and false positive (n = 17): positive by ARCHITECT screening but negative by confirmatory assay. All samples were retested using the Mindray CL-900i HBsAg screening assay.
Results: Compared with ARCHITECT confirmatory assay, the Mindray HBsAg CL-900i demonstrated perfect agreement with the confirmatory assay, as indicated by a Cohen κ value of 0.98 (0.95-1.02). Mindray CL-900i exhibited a sensitivity of 97%, positive predictive value of 100%, and negative predictive value of 99%. The specificity was 100% because none of the true-negative and false-positive results were identified as positive.
Conclusions: Mindray CL-900i could offer a cost-effective alternative for HBsAg screening, boasting perfect specificity and overcoming the limitations of current automated assays.

Introduction

Hepatitis B affects around 296 million people worldwide, with approximately 600,000 deaths annually due to complications [1]. Although Qatar has a low hepatitis B prevalence (under 2%), the influx of diverse populations could increase this rate [2]. Early hepatitis B virus (HBV) diagnosis is crucial for reducing morbidity and guiding vaccination. The Medical Commission (MC) in Qatar uses the ARCHITECT hepatitis B surface antigen (HBsAg) screening assay, which is known for its high sensitivity, but this can sometimes reduce specificity, leading to false-positive results, as reported in studies on HBV and other viruses [3–7]. The Mindray CL-900i HBsAg chemiluminescence immunoassay has recently entered the market, promising better specificity. However, its sensitivity and specificity compared with neutralizing confirmatory assays remains to be validated. The aim of this study is to evaluate whether HBsAg Mindray CL-900i screening could offer a better alterna-

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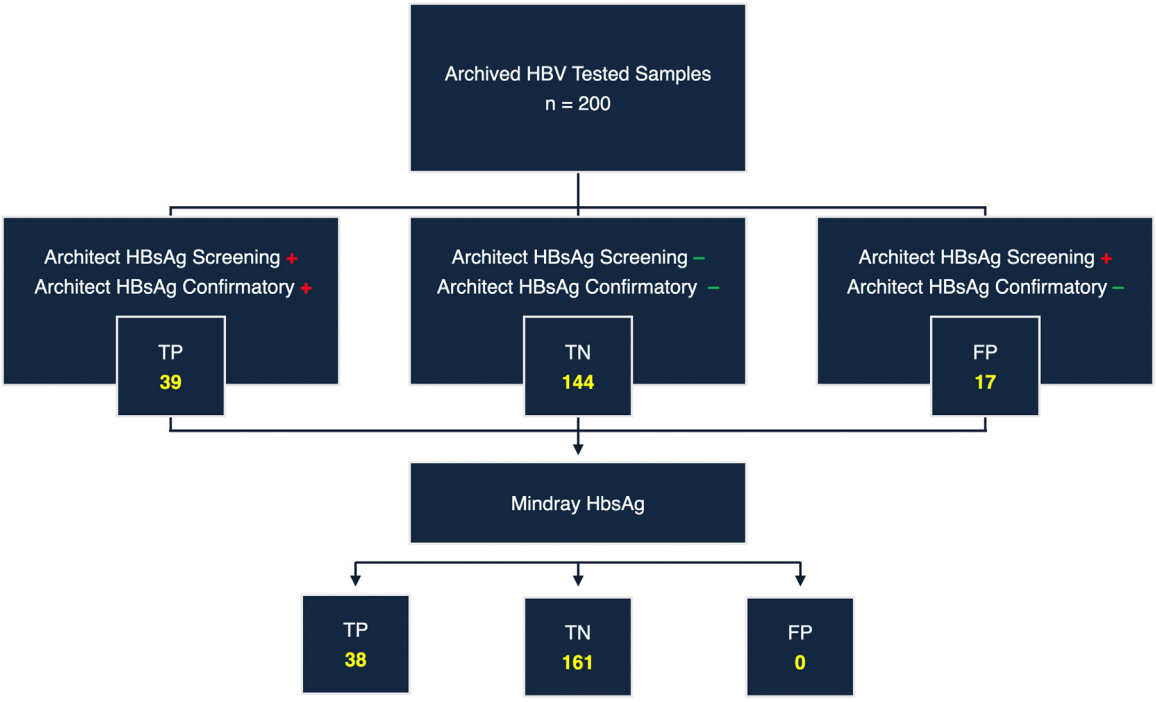

Figure 1. Flowchart depicting the sample selection process based on the results of HBV screening and confirmatory ARCHITECT HBsAg assays. The flowchart shows the distribution of HBV test results among selected samples, categorized into TP (n = 39), TN (n = 144), and FP (n = 17).
FP, false positive; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; TN, true negative; TP, true positive.

tive for HBsAg screening, boasting specificity and overcoming the limitations of current automated assays.

Materials and methods

Ethical approval

Ethical clearance was obtained from the institutional review board (IRB) at Qatar University, which authorized the project under reference QU-IRB 017/2024-E.

Study design

A total of 200 archived serum samples, HBsAg-positive and negative, were collected from the MC in Qatar, where routine screenings for infectious diseases are conducted for immigrants. HBV testing in MC is done by the ARCHITECT analyzer screening, followed by confirmation of the positive results by ARCHITECT neutralizing/confirmatory assay. These samples were classified as follows: true positive (n = 39): positive by ARCHITECT screening and confirmatory assays, true negative (n = 144): negative by ARCHITECT screening and confirmatory assays, and false positive (n = 17): positive by ARCHITECT screening but negative by confirmatory assay. All samples were retested using the Mindray CL-900i HBsAg assay (Figure 1).

Detection of HBV markers

Abbott ARCHITECT HBsAg and confirmatory HBsAg testing

Frozen archived samples from the MC in Qatar were initially screened for HBV using the Abbott ARCHITECT HBsAg (Abbott Diagnostics, USA). Positive samples were then confirmed with the Abbott ARCHITECT Confirmatory HBsAg assay, which uses chemiluminescent microparticle immunoassay (CMIA) technology. The Abbott ARCHITECT system is widely used across health care facilities in Qatar, with all analyses conducted according to the manufacturer's guidelines.

The Abbott ARCHITECT HBsAg Qualitative II assay detects HBsAg in human serum and plasma through a two-step CMIA process. In the first step, the sample, along with paramagnetic microparticles coated with anti-HBs and an anti-HBs conjugate labeled with acridinium, is incubated. The resulting reaction mixture is washed and processed further with additional wash buffers and pre-trigger and trigger solutions. The chemiluminescent reaction is measured in relative light units (RLUs), which correlate with the HBsAg concentration in the sample. If the RLUs exceed a predetermined cutoff, the sample is considered reactive for HBsAg.

The Abbott ARCHITECT HBsAg Confirmatory V.1 (Abbott Diagnostics, USA) assay confirms the presence of HBsAg using a two-step pretreatment CMIA method. It neutralizes HBsAg with pretreatment 1 and binds non-neutralized HBsAg with anti-HB–coated microparticles. After a second incubation with an acridinium-labeled anti-HB conjugate, the chemiluminescent reaction is measured. A sample is confirmed positive if the non-neutralized RLUs exceed the cutoff and decrease by at least 50% after neutralization, ensuring accurate HBsAg detection and minimizing false positives. The technical specifications of the analyzer can be found in Table S1. The assay was performed according the manufacturer's instruction as described in [8].

Mindray HBsAg

Serum samples previously screened and confirmed by Abbott ARCHITECT were evaluated for HBsAg assay (Abbott Diagnostics, USA) using the chemiluminescence immunoassay Mindray CL-900i (Mindray Bio-Medical Electronics, Shenzhen, China) at Qatar University, as previously described [8]. The samples were assessed for HBsAg. Testing followed the manufacturer's protocols, and positive results were cross-referenced with MC records and Abbott ARCHITECT screening and confirmatory outcomes for validation. The Mindray assay uses a two-site

Table 1
Comparative diagnostic performance analysis of HBsAg assays in hepatitis B virus detection.

				Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Concordance (%)	Cohen κ (%)
	[a]Architect HBsAg confirmatory +	[a]Architect HBsAg confirmatory −	Total	97 (87-100)	100 (98-100)	100 (91-100)	99 (97-100)	100 (97-100)	0.98 (0.95-1.02)
Mindray HBsAg +	38	0	38						
Mindray HBsAg−	1	161	162						
Total	39	161	200						

HBsAg, hepatitis B surface antigen.
Comparative diagnostic performance analysis of HBsAg assays in hepatitis B virus detection.
[a] Denotes that the indicated test was used as a reference in that specific scenario for the calculations of sensitivity, specificity, positive predictive value, negative predictive value, concordance, and Cohen κ.

sandwich method with paramagnetic microparticles and biotin-labeled anti-HB antibodies.

Abbott ARCHITECT anti-Hbc

The Abbott ARCHITECT Anti-HBc Core (Abbott Diagnostics, USA) is a chemiluminescent immunoassay for detection of antibody to hepatitis B core antigen (anti-HBc) in human serum and plasma. Testing was done according to the manufacturer's standard. Anti-HBc determinations can be used as an indicator of current or past HBV infection. Anti-HBc is found in serum shortly after the appearance of HBsAg in acute HBV infections. It will persist after the disappearance of HBsAg and before the appearance of detectable antibody to HBsAg. The presence or absence of anti-HBc in the specimen is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from an active calibration. If the chemiluminescent signal in the reaction is greater than or equal to the cutoff signal, the specimen is considered reactive for anti-HBc.

Statistical analysis

Statistical analysis was performed using GraphPad Prism 10.0.2 to evaluate the diagnostic performance metrics, including sensitivity, specificity, positive predictive value, negative predictive value, concordance, and Cohen κ. Cohen κ values range from 0 (no agreement) to 1.0 (almost perfect agreement). All tests were conducted using GraphPad Prism 9.

Results

Data from 200 samples from the MC were analyzed for HBsAg. The results are summarized in Table 1.

Comparative evaluation of Mindray HBsAg performance against Abbott ARCHITECT HBsAg confirmatory test

The Mindray HBsAg assay demonstrated 97% sensitivity, correctly identifying 38 of 39 true-positive samples, with only one false negative. It exhibited 100% specificity, with a positive predictive value of 100% and a negative predictive value of 99%. The assay showed perfect concordance with the Abbott ARCHITECT tests, achieving a Cohen κ of 0.98, indicating strong agreement and reliability.

Comprehensive analysis of HBsAg and anti-HBc results

The comprehensive analysis of HBsAg and anti-HBc results is summarized in Table 2, providing a detailed comparison of individual sample outcomes and highlighting key observations. Sample 38 (Table 2) represents the only false-negative result for HBsAg detection by the Mindray CL-900i assay. Although the ARCHITECT confirmatory test detected HBsAg in this sample, the Mindray platform did not. However, ARCHITECT anti-HBc assays returned positive result (Table 2).

A subset of 17 samples was flagged as false positives by the ARCHITECT screening assay. These samples tested positive for HBsAg according to the ARCHITECT screening assay but were negative upon confirmatory testing using the ARCHITECT confirmatory assay. The Mindray CL-900i assay accurately classified all 17 samples as HBsAg-negative, demonstrating complete concordance with the ARCHITECT confirmatory test. Among the 17 false-positive samples from the ARCHITECT screening assay, two samples (No. 40 and 41 in Table 2) exhibited positive results for anti-HBc when tested using the ARCHITECT platform (Table 2).

Discussion

Accurate HBV diagnosis is essential for curbing the spread and initiating timely therapy. Although many HBsAg assays prioritize sensitivity, they often result in high false-positive rates [3,4]. This study aimed to critically assess the performance of the Mindray CL-900i HBV assay as a potential alternative to the well-established ARCHITECT assay for HBV screening. This study evaluated the Mindray CL-900i's performance using 200 archived samples, revealing its strong reliability and potential as an alternative to the ARCHITECT assay for HBV screening.

The study confirmed the strong performance of the Mindray CL-900i in detecting HBsAg, with a sensitivity of 97% (Table 1). This high sensitivity is crucial for early HBV detection. However, one false-negative result was observed, highlighting the need for careful interpretation of diagnostic results. The false-negative sample in this study was later confirmed to be a chronic hepatitis B case. This sample exhibited the lowest HBsAg value (IU/ml) among all tested samples, consistent with cases in which patients with chronic HBV infections exhibit fluctuating or persistently low antigen levels. Such low levels may fall below the sensitivity threshold of certain immunoassays, as demonstrated by the Mindray CL-900i in this case. In addition, anti-Hbc testing confirmed the infection status of this sample. Variability in patient samples, such as the presence of HBsAg mutants or fluctuating antigen levels, may contribute to occasional false-negative results [9]. This finding underscores the diagnostic challenge of detecting low-value (IU/ml) samples or mutant strains, which are found in approximately 6-12% of chronic HBV cases [10]. These limitations necessitate a comprehensive diagnostic approach, incorporating additional markers such as core antigen or HBV DNA testing, particularly, in cases with strong clinical suspicion of HBV infection but negative HBsAg results.

The Mindray CL-900i demonstrated high specificity by correctly identifying 17 cases as HBsAg-negative, which the Abbott ARCHITECT screening assay had falsely marked as positive. This suggests that the Mindray test has a lower false-positive rate, making it highly valuable in large-scale screening programs. Its accuracy reduces unnecessary follow-up testing, alleviates patient anxiety, and potentially lowers health care costs. Among these samples, two cases (samples No. 40 and 41, Table 2) presented unique challenges. These samples were flagged as false positives by the ARCHITECT HBsAg assay due to negative results

Table 2
Comprehensive analysis of HBsAg and anti-HBc results.

Sample No	Architect HBsAg	Architect HBsAg range (IU/ml)	Architect neutralization confirmatory test HBsAg	Mindray HBsAg	HBsAg Mindray range (IU/ml)	Architect anti-HBc
1	Positive	3518	Positive	Positive	>250	Positive
2	Positive	4978	Positive	Positive	>250	Positive
3	Positive	3531	Positive	Positive	>250	Positive
4	Positive	2795	Positive	Positive	>250	Positive
5	Positive	82	Positive	Positive	3.09	Positive
6	Positive	4519	Positive	Positive	>250	Positive
7	Positive	3205	Positive	Positive	>250	Positive
8	Positive	3485	Positive	Positive	228.03	Positive
9	Positive	502	Positive	Positive	>250	Positive
10	Positive	4567	Positive	Positive	>250	Positive
11	Positive	1025	Positive	Positive	>250	Positive
12	Positive	3769	Positive	Positive	>250	Positive
13	Positive	4834	Positive	Positive	>250	Positive
14	Positive	2392	Positive	Positive	>250	Positive
15	Positive	756	Positive	Positive	>250	Positive
16	Positive	4984	Positive	Positive	>250	Positive
17	Positive	3619	Positive	Positive	>250	Positive
18	Positive	5391	Positive	Positive	>250	Positive
19	Positive	4341	Positive	Positive	>250	Positive
20	Positive	4504	Positive	Positive	>250	Positive
21	Positive	3488	Positive	Positive	218.74	Positive
22	Positive	5192	Positive	Positive	>250	Positive
23	Positive	3699	Positive	Positive	>250	Positive
24	Positive	20	Positive	Positive	1.38	Positive
25	Positive	4026	Positive	Positive	>250	Positive
26	Positive	4045	Positive	Positive	>250	Positive
27	Positive	4474	Positive	Positive	>250	Positive
28	Positive	1923	Positive	Positive	>250	Positive
29	Positive	5184	Positive	Positive	>250	Positive
30	Positive	5029	Positive	Positive	>250	Positive
31	Positive	4345	Positive	Positive	>250	Positive
32	Positive	2320	Positive	Positive	109.66	Positive
33	Positive	4166	Positive	Positive	>250	Positive
34	Positive	4357	Positive	Positive	>250	Positive
35	Positive	3904	Positive	Positive	>250	Positive
36	Positive	4886	Positive	Positive	>250	Positive
37	Positive	3745	Positive	Positive	>250	Positive
38	**Positive**	**6**	**Positive**	**Negative**	**<0.05**	**Positive**
39	Positive	1371	Positive	Positive	73.04	Negative
40	Positive	1.0751	Negative	Negative	<0.05	Positive
41	Positive	1.0507	Negative	Negative	<0.05	Positive
49	Positive	2.6418	Negative	Negative	<0.05	Negative
50	Positive	3.4104	Negative	Negative	<0.05	Negative
51	Positive	1.0197	Negative	Negative	<0.05	Negative
52	Positive	2.1031	Negative	Negative	<0.05	Negative
53	Positive	2.5672	Negative	Negative	<0.05	Negative
54	Positive	2.0949	Negative	Negative	<0.05	Negative
55	Positive	2.4592	Negative	Negative	<0.05	Negative
56	Positive	1.2231	Negative	Negative	<0.05	Negative
57	Positive	4.3634	Negative	Negative	<0.05	Negative
58	Positive	1.2097	Negative	Negative	<0.05	Negative
59	Positive	1.0629	Negative	Negative	<0.05	Negative
60	Positive	1.1297	Negative	Negative	<0.05	Negative
61	Positive	6.1157	Negative	Negative	<0.05	Negative
62	Positive	1.1206	Negative	Negative	<0.05	Negative
63	Positive	2.161	Negative	Negative	<0.05	Negative

This table provides a comprehensive comparison of hepatitis B surface antigen (HBsAg) and hepatitis B core antibody (anti-HBc) results for all 200 samples analyzed. Sample 38, marked in bold within the table represents the only false negative result for HBsAg, detection by the Mindray CL-900i assay. This sample was confirmed as HBsAg positive using the ARCHITECT confirmatory assay and demonstrated positive anti-HBc result. The HbsAg level for this samples was the lowest IU/ml value among all tested samples, consistent with a chronic hepatitis B infection.

in the HBsAg neutralization test, yet both tested positive for anti-HBc using the ARCHITECT platform. These findings raise important clinical and technical considerations. One plausible interpretation is that these individuals may have chronic HBV infection. The positive anti-HBc results detected by ARCHITECT strongly support this possibility because chronic HBV cases are often associated with detectable anti-HBc antibodies, even when HBsAg levels are low [11,12]. The low HBsAg values for these samples (Table 2) may explain the negative neutralization test results because false negatives in neutralization assays have been reported in cases with low antigen levels. An alternative explanation could be resolved or past HBV infection with residual anti-HBc positivity. However, the lack of HBsAg detection by Mindray and the neutralization test adds complexity to this interpretation, necessitating further investigation. To clarify these discrepancies, reviewing historical data from the MC laboratory database is crucial. Comparing baseline results with current findings could provide additional insights into the serological status of these individuals. Unfortunately, due to insufficient sample volume, further testing, such as HBV DNA or HBeAg (hepatitis B

e-antigen) assays, could not be performed, limiting the ability to confirm chronic HBV infection definitively. These limitations highlight the importance of incorporating additional diagnostic markers in cases where serological results are inconclusive.

To the best of our knowledge, this study provides the first comprehensive comparison of the Mindray CL-900i with the ARCHITECT confirmatory assay for HBsAg detection, as opposed to previous studies that only compared it with the ARCHITECT screening assay. However, the study has certain limitations, including the absence of confirmatory polymerase chain reaction testing due to the small sample volume, the subjectivity in sample selection based on ARCHITECT classification, and the relatively small sample size, which is attributable to the low prevalence of hepatitis B in Qatar. These limitations underscore the need for further research with larger, more diverse populations to ensure broader validation.

Conclusion

In conclusion, our study sheds light on the diagnostic potential of the Mindray CL-900i for HBV detection. With high sensitivity and zero false-positive rates, the Mindray CL-900i emerges as a cost-effective, accurate HBV screening alternative, addressing the limitations of current automated assays. Notably, the Mindray system accurately identified HBsAg-negative cases that were incorrectly flagged as positive by the Abbott ARCHITECT screening assay. This underscores the reliability and efficiency of the Mindray CL-900i in enhancing HBV diagnostic accuracy.

Declarations of competing interest

All the kits used were provided free of charge to support this study from Shenzhen Mindray Biomedical Electronic Co (CL-9000i kits) and the Abbot distributor in Qatar, Khalid Scientific Co. (Architect kits).

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Author contributions

Conceptualization, G.K.N and A.I.; methodology, G.K.N.; software, G.K.N.; validation, G.K.N., S.Y., and A.I.; formal analysis, S.Y. and Z.L.; investigation, N.Y., P.B.N., M.A.A., and K.N.M.; D.E.C.; resources, G.K.N. and A.I.; data curation, S.Y.; writing—original draft preparation, G.K.N. and S.Y.; writing—review and editing, G.K.N., S.Y., N.Y., P.B.N., M.A.A., K.N.M.; D.E.C., P.A., L.J.A-R.; Z.L., A.I.; visualization, S.Y.; supervision, G.K.N. and A.I.; project administration, G.K.N and A.I.; funding acquisition. All authors have read and agreed to the published version of the manuscript.

Institutional review board statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the IRB (or ethics committee) of Qatar University, which authorized the project under reference QU-IRB 017/2024-E. It is important to note that the samples used in this study were archived samples and this study did not involve recruiting patients or applicants, and there was no direct or indirect interaction with human subjects. Therefore, informed consent was not required as per QU-IRB.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2024.100561.

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