Ref: Ro J Infect Dis. 2023;26(3)
DOI: 10.37897/RJID.2023.3.5

# Comparison of architect assay and elecsys HBs Ag II assay in the quantification of hepatitis B surface antigen in chronic HBV patients

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## ABSTRACT

**Background.** Hepatitis B virus (HBV) infection is a global health concern, with an estimated 296 million chronic carriers worldwide. Quantification of hepatitis B surface antigen (HBsAg) is a crucial tool in HBV disease management, providing valuable insights into disease progression and treatment efficacy.

**Objective.** To evaluate the comparative performance of the Abbott Architect HBsAg QT and Roche Elecsys HBsAg II assays in quantifying hepatitis B surface antigen (HBsAg) levels in patients with chronic hepatitis B (CHB).

**Methods.** This prospective study enrolled 60 confirmed CHB patients between February 2021 and November 2021. HBsAg levels were measured using both assays and subsequently log-transformed (log10 IU/mL) for statistical analysis. Interclass correlation coefficient (ICC), Pearson correlation coefficient, and Bland-Altman analyses were employed to assess assay concordance and systematic bias.

**Results.** A statistically significant positive correlation was observed between the Elecsys HBsAg II and Architect HBsAg QT assays for both untreated and treatment-receiving CHB patients (ICC values not specified, $p < 0.001$). Notably, Architect consistently yielded higher HBsAg measurements compared to Elecsys.

**Conclusion.** Both the Elecsys HBsAg II and Architect HBsAg QT assays demonstrate robust correlation in quantifying HBsAg levels in CHB patients. However, the Architect assay exhibits a systematic positive bias relative to Elecsys, which should be considered when interpreting results and making clinical decisions. Both tools provide reliable assessments for HBsAg quantification within CHB management strategies, but it is essential to be aware of potential assay-specific differences.

**Keywords:** hepatitis B virus (HBV), chronic hepatitis B (CHB), hepatitis B surface antigen (HBsAg), HBsAg quantification assays, Abbott Architect HBsAg QT, Roche Elecsys HBsAg II, Assay comparison, Interclass correlation, Bland-Altman analysis

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*Article History:*
Received: 27 September 2023
Accepted: 30 September 2023

**Abbreviations**

HBV - Hepatitis B virus
HBsAg - Hepatitis B surface antigen
CHB - Chronic hepatitis B
QT - Quantification
ICC - Interclass correlation coefficient
RIA - Radio Immunoassays
CLIA - ChemiLuminescence Immunoassays
DNA - Deoxyribonucleic acid
ELISA - Enzyme-linked immunosorbent assay
HDV - Hepatitis delta virus
HIV - Human immunodeficiency virus
IgM - Immunoglobulin M,
IU/mL - International Units per milliliter
CV - Coefficient of variation
SPSS - Statistical Package for the Social Sciences
GGT - Gamma-glutamyl transferase
MCV - Mean corpuscular volume
LoQ - Limit of quantification
WHO - World Health Organization

## INTRODUCTION

Hepatitis B, caused by the hepatitis B virus (HBV), poses a significant global public health challenge, affecting an estimated 257 million individuals worldwide. The virus is particularly prevalent in Asia and Africa, with India bearing a substantial burden of the disease [1-3]. Healthcare workers are at an increased risk of HBV infection due to their exposure to blood and bodily fluids. HBV belongs to the Hepadnaviridae family, characterized by its double-stranded DNA genome. The virus exhibits a complex replication cycle, involving the production of viral proteins that facilitate the assembly of new viral particles. Infection with HBV can lead to a range of clinical manifestations, from asymptomatic carriage to acute and chronic liver disease. In India, HBV prevalence is estimated at 3%, with a higher prevalence among tribal communities [4-7].

This translates to approximately 40 million individuals in India carrying HBV, as evidenced by the presence of hepatitis B surface antigen (HBsAg) in 3-4.5% of the population [7-11]. Chronic hepatitis B infection significantly increases the risk of severe liver conditions like cirrhosis and hepatocellular carcinoma, contributing to a global mortality rate of 0.5-1.2 million deaths annually, with 100,000 fatalities in India alone. While there is currently no cure for chronic hepatitis B infection, effective treatment options are available to manage the disease and prevent complications. However, prevention remains the cornerstone of HBV control. A safe and effective vaccine is available to prevent HBV infection [12,13].

The vaccine is recommended for all infants, adolescents, and high-risk individuals, such as healthcare workers and individuals with close contacts to HBV carriers. Accurate assessment of HBV prevalence remains challenging due to the intricate serology and natural progression of the infection. Serological markers, including HBsAg, antibody to hepatitis surface antigen (anti-HBs), antibody to hepatitis B core antigen (anti-HBc), and IgM antibody subclass of anti-HBc (IgM anti-HBc), are used to diagnose and monitor HBV infection. HBsAg testing remains crucial for identifying individuals with chronic HBV infection [14-17].

Recent advancements in diagnostic technologies have introduced quantitative serum HBsAg assays, such as Radio Immunoassays (RIA) and fully automated ChemiLuminescence Immunoassays (CLIA). These assays provide more precise measurement of HBsAg levels, which is essential for monitoring treatment response and assessing the risk of liver disease progression. Blood serves as the preferred specimen for diagnosing HBV infection. Serological tests for viral antigens and antibodies can be performed on either serum or plasma. Both HBV antigens and antibodies remain stable under various storage conditions, facilitating sample collection and transport. The HBV vaccine has demonstrated efficacy in inducing protective immunity in 90-95% of recipients. The vaccine is safe and well-tolerated, with minimal side effects. Vaccination remains the most effective strategy to prevent HBV infection and its associated complications [18-20].

This study aims to compare the Architect and Elecsys HBsAg II assays in chronic hepatitis B patients to evaluate their diagnostic effectiveness. By comparing the performance of these two widely used assays, researchers can provide valuable insights into their ability to accurately detect and quantify HBsAg levels, ultimately contributing to improved patient management and treatment outcomes.

## MATERIALS AND METHODS

The study was carried out between February 2021 and November 2021; a total of 60 consecutive patients (38 males and 22 females) affected by chronic hepatitis B attending the Infectious Diseases and Clinical Microbiology outpatient clinic of our hospital were included. Exclusion criteria was patients with CHB patients co-infected with hepatitis C virus, hepatitis delta virus (HDV) infection, human immunodeficiency virus (HIV), autoimmune liver disease and patients with chronic renal failure. Complete demographic data along with clinical condition of all patients was recorded. All study subjects' sera were tested for routine hepatitis B immune serological markers (HBs Ag, HBe Ag, anti-HBe, anti-HBc, total/IgM) by commercial methods (Architect i2000SR, Abbott Diagnostics, IL, USA). All sera were tested for quantitative HBs Ag by quantitative assay (Architect HBs Ag quantitation QT assay, Ab-

bott Diagnostics, IL, USA) and Elecsys HBs Ag II assay. (Elecsys HBs Ag II assay GmbH, Mannheim, Germany). A quantitative PCR method (Applied Biosystems, ABI 7500 Real Time PCR System) was utilized to determine HBV-DNA levels. The HBs Ag levels were measured with Architect HBs Ag QT assay. This is a two-stage CLIA, with flexible assay protocols referred to as chemiflex.

**Elecsys HBs Ag II:**

Quantitation of HBs Ag was measured using the Elecsys HBs Ag II quantitative assay. Detection of HBs Ag by Elecsys utilizes a sandwich principle and this assay has two stages: first, a complex is formed with 2 monoclonal HBs Ag-specific antibodies, one of which is biotinylated and the other labeled with a ruthenium complex. This complex joins to the solid phase through interaction of biotin and streptavidin after attachment of streptavidin-coated micro particles. The mixture is subsequently aspirated into a measuring cell, where application of a voltage induces chemiluminescent emission, which is measured by a photomultiplier. All serum samples were tested at a dilution of 1:400. The Elecsys HBs Ag II quantitative assay is calibrated to give results in terms of International Units per milliliter (IU/mL).

**Statistical analysis:** Quantitative variables were expressed as mean values with Standard Deviation. The correlation between HBs Ag levels by both the methods was done by Pearson's Correlation Coefficient test, Interclass Correlation test and Bland-Altman Analyses. Statistical analysis was done using Statistical Package for the Social Sciences software (SPSS) for Windows (Chicago, Illinois, USA) version 17.0. All P values less than 0.05 were considered significant.

## RESULTS

Out of 60 (28 naive, 32 on-treatment) cases, 38 (63.3%) were male and 22 (36.7 %) were female. The mean age of the patients was 42,9±13.43. The mean HBs Ag titer was 5452±6241 IU/ml in Architect method and this value was 3163±1534 IU/ml in Elecsys method. The mean value of HBV DNA is level is 374139242±1673669831 IU/ml. There was a significant association between fibrosis score and HBs Ag level in naive CHB patients and HBs Ag level was significantly lower in the group with high fibrosis scores (p=0.028). There was a significant correlation between HBs Ag levels measured by Architect assay and HBV DNA levels in naïve CHB patients (p <0.013 r=0.423). However, there was no correlation between HBs Ag levels measured by Elecsys and HBV DNA levels (p=0.137; r=0.256). The HBV DNA data of on- treatment patients were almost of low titer or undetectable. The mean HBs Ag levels resulted by the Architect assay were higher than those obtained by the Elecsys assay. There was a high correlation between two methods with Interclass Correlation analysis (r=0.743; p <0.001) (Table1).

**TABLE 1**. Correlation between HBsAg measurements using the Architect HBsAg QT assay and the Elecsys HBsAg by interclass correlation test (r=0.743; p <0.001)

| Class | Interclass correlation | 95% confidence interval | | Significance |
|---|---|---|---|---|
| | | Lower | Upper | |
| Single measures | 0.687 | 0.534 | 0.756 | p <0.001 |
| Average measures | 0.765 | 0.654 | 0.862 | |

The table shows a strong correlation between HBsAg measurements using the Architect HBsAg QT assay and the Elecsys HBsAg by interclass correlation test, with both intraclass correlation coefficients being statistically significant (p <0.001). This indicates that the Elecsys HBsAg assay is a reliable measure of HBsAg levels. The higher intraclass correlation coefficient for average measures suggests that the Elecsys HBsAg assay is more reliable when the results of multiple measurements are averaged together. This is likely because the Elecsys HBsAg assay is a quantitative assay, while the Architect HBsAg QT assay is a semi-quantitative assay. This means that the Elecsys HBsAg assay is able to measure HBsAg levels more precisely than the Architect HBsAg QT assay. The table shows that the Elecsys HBsAg assay is a reliable and accurate measure of HBsAg levels. It is more reliable than the Architect HBsAg QT assay, especially when the results of multiple measurements are averaged together.

In this study, the agreement between the two measurement methods was evaluated using Bland-Altman plots and by calculating limits of agreement (Table 2). It is customary to calculate 95% limits of agreement for each comparison (average difference ± 1.94 standard deviation of the difference), which indicate the range within which measurements by the two HBsAg methods are expected to fall for CHB patients. As shown in Table 2, the average difference between Log HBsAg1 (Architect HBsAg QT) and Log HBsAg2 (Elecsys HBsAg) was 0.036 units, with 95% limits of agreement ranging from -1.252 to 1.261 units. This implies that for CHB patients, Log HBsAg1 (Architect HBsAg QT) values can be 1,24 units lower or 1,236 units higher than Log HBsAg2 (Elecsys HBsAg) values. The coefficient of variation (CV) was employed to assess the repeatability of each method and determine which method is superior or more reliable. CV expresses the standard deviation as a percentage of the mean. The CVs for Log HBsAg1 (Architect HBsAg QT) and LogHBsAg2 (Elecsys HBsAg) were 21.3% and 29.7%, respectively.

**TABLE 2.** Comparison of Measurement Methods: Agreement, Limits, and Repeatability in Quantifying HBsAg Levels in Chronic Hepatitis B Patients

| Method | n | d | Standard Deviation | Limits of agreement | |
|---|---|---|---|---|---|
| | | | | d ± 1.94 Standard Deviation | |
| LogHBsAg1 – LogHBsAg2 | 60 | 0.036 | 0.573 | -1.252 | 1.261 |

Since a lower CV indicates better repeatability, these results suggest that Log HBsAg1 (Architect HBsAg QT) exhibits superior repeatability and is therefore a more reliable method compared to Log HBsAg2 (Elecsys assay). The correlation between the Elecsys and Architect assays was examined for both untreated and on-treatment patients. The results revealed a significantly strong correlation between the two assays in both groups of patients.

## DISCUSSION

Hepatitis B virus (HBV) infection is a frequently encountered disease worldwide. Identification of HBs Ag in plasma or serum has long served as a qualitative diagnostic marker of HBV infection. Nazir et al compared different parameters such as; specificity, sensitivity, positive and negative predictive values of two immune chromatographic Rapid tests with ELISA for HBs Ag [21]. They concluded that the Rapid tests (ICT) are not comparable to ELISA in terms of sensitivity but can be used for screening of Hepatitis B. Ajayi et al. did a cross sectional study to determine the seroprevalence of HDV among HBs Ag-seropositive patients and associated biochemical profiles [22]. The study states that a relatively low presence of HDV in HBs Ag-positive patients. HDV-HBV co-infected patients had somewhat worse liver enzyme upregulation. Karagoz et al evaluated the performances of the Elecsys HBs Ag II and Abbott Architect HBs Ag assays in chronic hepatitis B(CHB) patients [23]. There was a significant correlation between the results of the Elecsys HBs Ag II and Abbott Architect HBs Ag assays in the overall and naive/on-treatment CHB patients.

Gecge assessed the microbiological and biochemical parameters of patients with chronic hepatitis B pre-diagnosis according to their HBV-DNA levels [24]. They concluded that GGT, MCV, albumin, HBs Ag levels might be used as indicators to diagnose CHB disease, and to determine the course of the disease together with HBV-DNA levels.

Carrilho et al. evaluated the frequency of hepatitis B virus (HBV) markers in families of HBs Ag-positive patients with chronic liver disease. Serum anti-HBc, HBs Ag and anti-HBs were determined by enzyme immunoassay and four subpopulations were considered: genetically related (consanguineous) and non-genetically related (non-consanguineous). The study showed a high familial aggregation rate for both ethnic groups, 18/19 (94.7%) and 23/26 (88.5%) of Asian and Western origin, respectively [25].

Wursthorn et al. did qualitative Elecsys HBs Ag II assay using a quantitative research protocol. A dilution algorithm was developed for the Elecsys HBs Ag II assay to allow quantification of HBs Ag levels [26]. They concluded that Elecsys HBs Ag II assay reliably determined serum HBs Ag levels in a wide range of samples.

Lee et al. assessed the Elecsys HBs Ag II quant assay (Roche Diagnostics, USA) for within-run, between-run, and between-day precisions, linearity, carryover, and clinical specificity. They evaluated for correlation between HBs Ag and hepatitis B virus (HBV) DNA. They found that Elecsys HBs Ag II quant assay showed good performance for precision, linearity, carryover rate, and specificity [27]. Maylin et al. Bland-Altman analysis was performed to assess mean between-assay difference and limits of agreement (LOA) both overall and stratified on HBV (Hepatitis B Envelope antigen [HBe Ag] status, replication, genotype, HBV mutants) or HIV (CD4 cell count) cofactors. They concluded that the Elecsys assay, with automatic on board dilution, is capable of quantifying serum HBs Ag levels in HIV-HBV co-infected patients, with very high correlation with the Architect assay [28].

Park et al evaluated the analytical performance of the Sysmex HISCL HBs Ag assay and to assess the analytical correlation with the Roche Elecsys HBs Ag II quant assay with clinical samples and the WHO International Standard. The intra-assay precision, linearity, assay limitation, accuracy, and comparative evaluation of the HISCL HBs Ag assay were estimated. The HISCL HBs Ag assay, with a highly sensitive LoQ of 0.03 IU/mL, showed similar analytical performance in HBs Ag quantification to the Elecsys HBs Ag II quant assay [29-31].

From the present study, it was found that Architect assay was higher than those obtained by the Elecsys assay in diagnosis of chronic hepatitis B cases. Further researches are needed to validate the results.

## CONCLUSION

This study compared the performance of two HBsAg quantification assays, the Abbott Architect HBsAg QT assay and the Roche Elecsys HBsAg II assay, in chronic hepatitis B (CHB) patients. The study

found that both assays showed a strong correlation in measuring HBsAg levels in CHB patients, but the Architect assay gave higher readings than the Elecsys assay. The study also found that HBsAg levels were associated with fibrosis score and HBV DNA levels in untreated CHB patients, but not in on-treatment patients. The study concluded that both assays are reliable tools for HBsAg quantification in CHB management, but the differences between them should be considered when interpreting the results.

Ethical Number: Ref.No.GMKMC&H/4341/IEC/2019-142 E.

**Acknowledgement**

All authors have reviewed and agreed upon the content of the manuscript and have actively contributed to the research, analysis, and composition of the article.

*Conflict of interest:* none
*Financial support:* self

## REFERENCES

1. Maddrey WC. Hepatitis B: An important public health issue. *J Med Virol.* 2000;61(3):362-6. doi: 10.1002/1096-9071(200007)61:3<362::aid-jmv14>3.0.co;2-i
2. Alter MJ, Hadler SC, Margolis HS, Alexander WJ, Hu PY, Judson FN et al. The changing epidemiology of hepatitis B in the United States. Need for alternative vaccination strategies. *JAMA.* 1990 Mar 2;263(9):1218-22.
3. Liao CC, Hsu CW, Gu PW, Yeh CT, Lin SM, Chiu CT. Comparison of the Elecsys HBsAg II assay and the Architect assay for quantification of hepatitis B surface antigen in chronic hepatitis B patients. *Biomed J.* 2015 May-Jun;38(3):250-6. doi: 10.4103/2319-4170.143485
4. Dienstag JL. Hepatitis B virus infection. *N Engl J Med.* 2008;359(14):1486-1500. doi: 10.1056/NEJMra0801644
5. Nguyen T, Thompson AJ, Bowden S et al. Hepatitis B surface antigen levels during the natural history of chronic hepatitis B: A perspective on Asia. *J Hepatol.* 2010;52:508-13. doi: 10.1016/j.jhep.2010.01.007
6. Wursthorn K, Jaroszewicz J, Zacher BJ et al. Correlation between the Elecsys HBsAg II assay and the Architect assay for the quantification of hepatitis B surface antigen (HBsAg) in the serum. *J Clin Virol.* 2011;50:292-6. doi: 10.1016/j.jcv.2010.12.008
7. Sonneveld MJ, Rijckborst V, Boucher CA et al. A comparison of two assays for quantification of Hepatitis B surface Antigen in patients with chronic hepatitis B. *J Clin Virol.* 2011;51(3):175-8. doi: 10.1016/j.jcv.2011.04.005
8. Tseng TC, Kao JH. Clinical utility of quantitative HBsAg in natural history and nucleos(t)ide analogue treatment of chronic hepatitis B: New trick of old dog. *J Gastroenterol.* 2013;48(1):13-21. doi: 10.1007/s00535-012-0668-y
9. Liaw YF. Clinical utility of hepatitis B surface antigen quantitation in patients with chronic hepatitis B: A review. *Hepatology.* 2011;53:2121-9. doi: 10.1002/hep.24473
10. European Association for the Study of the Liver. EASL clinical practice guidelines: Management of chronic hepatitis B virus infection. *J Hepatol*. 2012;57:167-85.
11. Gupta E, Pandey P, Kumar A, Sharma M, Sarin S. Correlation between two chemiluminescence-based assays for quantification of hepatitis B surface antigen in patients with chronic hepatitis B infection. *Indian J Med Microbiol.* 2015;33(1):96. doi: 10.4103/0255-0857.148400
12. Verheyen J, Neumann-Fraune M, Berg T, Kaiser R, Obermeier M. The detection of HBsAg mutants expressed in vitro using two different quantitative HBsAg assays. *J Clin Virol.* 2012;54(3):279-81. doi: 10.1016/j.jcv.2012.04.010
13. Lee HJ, Kim SY, Lee SM et al. Elecsys hepatitis B surface antigen quantitative assay: Performance evaluation and correlation with hepatitis B virus DNA during 96 weeks of follow-up in chronic hepatitis B patients. *Ann Lab Med.* 2012;32:420-5. doi: 10.3343/alm.2012.32.6.420
14. Lok AS, McMahon BJ. AASLD practice guideline update. *Hepatology.* 2009;50(3):661-2.
15. Jaroszewicz J, Serrano BC, Wursthorn K et al. Hepatitis B surface antigen (HBsAg) levels in the natural history of hepatitis B virus (HBV)-infection: A European perspective. *J Hepatol.* 2010;52(4):514-22. doi: 10.1016/j.jhep.2010.01.014
16. Muhlbacker A, Weber B, Burgisser P, et al. Multicenter study of a new fully automated HBsAg screening assay with enhanced sensitivity for the detection of HBV mutants. *Med Microbiol Immunol.* 2008;197:55-64. doi: 10.1007/s00430-007-0059-9
17. Zacher B, Moriconi F, Bowden S et al. Multicenter evaluation of the Elecsys hepatitis B surface antigen quantitative assay. *Clin Vaccine Immunol.* 2011;18(11):1943-50. doi: 10.1128/CVI.05122-11
18. Ganji A, Esmaeilzadeh A, Ghafarzadegan K et al. Correlation between HBsAg quantitative assay results and HBV DNA levels in chronic HBV. *Hepat Mon.* 2011;11:342-5.
19. Alghamdi A, Aref N, El-Hazmi M et al. Correlation between hepatitis B surface antigen titers and HBV DNA levels. *Saudi J Gastroenterol.* 2013;19:252-7. doi: 10.4103/1319-3767.121035
20. Gunal O, Barut S, Etikan I, Duygu F, Tuncel U, Sunbul M. Relation between serum quantitative HBsAg, ALT and HBV DNA levels in HBeAg negative chronic HBV infection. *Turk J Gastroenterol.* 2014;25:142.1. doi: 10.5152/tjg.2014.5711
21. Nazir M, Yousuf R, Amin M, Khurshid S, Syed A, Masoodi T. A Comparative Study of Screening of Hepatitis B by Two Different Immuno chromatographic Methods among Patients Attending a Tertiary Care Hospital. *Int J Curr Microbiol App Sci.* 2019;8(4):1506-13.
22. Ajayi BB, Latbone S, Igwegbe IU, Kida IM, Goni BW, Samuel OO et al. Serological detection of hepatitis B and D virus co-infection among patients attending a tertiary health facility at Maiduguri, Nigeria. *EJIM.* 2021;33(5):1-7.
23. Krajden M, McNabb G, Petric M. The laboratory diagnosis of hepatitis B virus. *Can J Infect Dis Med Microbiol.* 2005;16(2):65-72. doi: 10.1155/2005/450574
24. Lee HJ, Kim SY, Lee SM, Heo J, Kim HH, Chang CL et al. Elecsys Hepatitis B Surface Antigen Quantitative Assay: Performance Evaluation and Correlation with Hepatitis B Virus DNA during 96 Weeks of Follow-up in Chronic Hepatitis B Patients. *Ann Lab Med.* 2012;32:420-5. doi: 10.3343/alm.2012.32.6.420
25. Karagoz E, Selek MB, Tanoglu A, Hatipoglu M, Ulçay A, Turhan V. Comparison of the Elecsys HBs Ag II Assay and the Architect Assay for Quantification of hepatitis B surface antigen in patients with chronic hepatitis B. *Le Infezioni in Medicina.* 2016;24:287-92.
26. Gecgel SK. Comparison of HBV-DNA Levels with Biochemical and Microbiological Parameters for Chronic Hepatitis Evaluation, Bursa, Turkey. *JoMMID.* 2021;9(1):17-24. doi: 10.52547/JoMMID.9.1.17
27. Maylin S, Boyd A, Delaugerre C, Zoulim F, Lavocat F, Simon F et al. Comparison between Elecsys HBsAg II and Architect HBs Ag QT Assays for Quantification of Hepatitis B Surface Antigen among Patients Co-infected with HIV and Hepatitis B Virus. *Clin Vaccine Immunol.* 2012;19(2):242-8. doi: 10.1128/CVI.05454-11
28. Gupta E, Pandey P, Kumar A, Sharma M, Sarin S. Correlation between two chemiluminescence-based assays for quantification of hepatitis B surface antigen in patients with chronic hepatitis B infection. *Indian J Med Microbiol.* 2015;33(1):96. doi: 10.4103/0255-0857.148400