J Immunol Clin Microbiol
Available online at: https://dergipark.org.tr/tr/pub/jicm
DOI: 10.58854/jicm.1512343

CASE REPORT/OLGU SUNUMU

Case report: Example of the impact of laboratory processes on patient safety: Reflection of 'HBsAg' test results on analytical and post-analytical process management

Laboratuvar süreçlerinin hasta güvenliğine etkisine örnek: 'HBsAg' test sonuçlarının analitik ve post-analitik süreç yönetimine yansıması

Erdoğan YAYLA[1]

[1] Medical Microbiology, Central Laboratory, Karacabey State Hospital, Bursa, Türkiye

Geliş: 08.07.2024, Kabul: 13.12.2024

Abstract

Hepatitis B virus (HBV) infections are a group of infections that primarily affect the liver and cause inflammatory hepatitis. This group of infections; In Turkey, it develops as acute hepatitis at a rate of 2% to 10%, and 4% to 6% of these cases later develop as chronic hepatitis. 10% of chronic hepatitis cases face the risk of developing hepatocellular carcinoma (HCC) in the future. Various methods are used in the diagnosis of HBV infections. The most commonly used method in diagnosis is the screening of serological indicators (ELISA tests: HBsAg, Anti-HBs, Anti-HBc IgM and Anti-HBc IgG) in serum. Among these indicators, the 'HBsAg' test is the first test used for screening purposes for HBV infection and in the study and interpretation of test results; the evaluation is made by taking into account various factors related to the patient, employee and test procedure. Accuracy and reliability of laboratory test results; it is a very important parameter in terms of both patient safety and control of laboratory test processes. In our case; based on the 'HBsAg' test result of one patient, our studies and recommendations regarding the false positive HBsAg test results detected in a total of three patients are included. In the root cause analysis studies conducted on the process of 3 patients with unusual 'HBsAg' positivity; lack of training among the relevant personnel, lack of awareness, failure to carry out device technical service maintenance checks on time, and deficiencies in communication with clinicians came to the fore. As a result of our work on these inappropriate test results; Regular service maintenance and checks of ELISA devices, follow-up and traceability of quality-control studies, and effective communication between the patient's physician and the patient's clinic will prevent the development of situations that may jeopardize patient safety on a laboratory basis.

Keywords: Patient safety, Hepatitis B virus (HBV), Test result

Corresponding Author: Erdoğan Yayla, Medical Microbiology, Central Laboratory, Karacabey State Hospital, Bursa, Türkiye, E mail: erdoganyayla2005@gmail.com

How to Cite: Yayla E. Case report: Example of the impact of laboratory processes on patient safety: Reflection of 'HBsAg' test results on analytical and post-analytical process management. *Journal of Immunology and Clinical Microbiology* 2024;9(4):148-152

Öz

Hepatit B virüs (HBV) enfeksiyonları, öncelikle karaciğeri etkileyen ve inflamatuvar hepatite neden olan bir grup enfeksiyondur. Bu grup enfeksiyonlar; Türkiye'de %2 ila %10 oranında akut hepatit olarak gelişmekte ve bu vakaların %4 ila %6'sı daha sonra kronik hepatit olarak gelişmektedir. Kronik hepatit vakalarının %10'u ileride hepatosellüler karsinom (HCC) gelişme riski ile karşı karşıyadır. HBV enfeksiyonlarının tanısında çeşitli yöntemler kullanılmaktadır. Tanıda en sık kullanılan yöntem serumda serolojik göstergelerin (ELISA testleri: HBsAg, Anti-HBs, Anti-HBc IgM ve Anti-HBc IgG) taranmasıdır. Bu göstergeler arasında 'HBsAg' testi HBV enfeksiyonu için tarama amaçlı kullanılan ilk testtir ve test sonuçlarının incelenmesi ve yorumlanmasında; hasta, çalışan ve test prosedürü ile ilgili çeşitli faktörler göz önünde bulundurularak değerlendirme yapılır. Laboratuvar test sonuçlarının doğruluğu ve güvenilirliği; hem hasta güvenliği hem de laboratuvar test süreçlerinin kontrolü açısından çok önemli bir parametredir. Olgumuzda; bir hastanın 'HBsAg' test sonucundan yola çıkarak toplam üç hastada tespit edilen yanlış pozitif HBsAg test sonuçlarına ilişkin çalışmalarımız ve önerilerimiz yer almaktadır. Olağandışı 'HBsAg' pozitifliği tespit edilen 3 hastanın sürecine ilişkin yapılan kök neden analizi çalışmalarında; ilgili personelin eğitim eksikliği, farkındalık eksikliği, cihaz teknik servis bakım kontrollerinin zamanında yapılmaması ve klinisyenlerle iletişimdeki eksiklikler ön plana çıkmıştır. Bu uygunsuz test sonuçları üzerine yaptığımız çalışma sonucunda; ELISA cihazlarının düzenli servis bakım ve kontrollerinin yapılması, kalite-kontrol çalışmalarının takibi ve izlenebilirliği, hastanın hekimi ve hastanın kliniği arasında etkin iletişimin sağlanması laboratuvar bazında hasta güvenliğini tehlikeye atabilecek durumların gelişmesini engelleyecektir.

Anahtar Kelimeler: Hasta güvenliği, Hepatit B virüsü (HBV), Test sonucu

INTRODUCTION

People can grouped who may be in the risk group in screening tests for HBV infections; healthcare workers, born in, living in, and migrating from medium-high endemicity regions (prevalence >2), living with HBV-infected people and with a history of sexual contact, IV (Intravenous) drug addicts and who constantly receive blood products, homosexuals, polygamists, heterosexuals and HIV(+) patient groups, with chronic liver disease (infected with HIV/HCV), hemodialysis patients, receiving immunosuppressive treatment, pregnant women and babies born to HBV-infected mothers (1).

Evaluation of 'HBsAg' tests and possible interference situations

Nowadays, for HBsAg tests, either manual (Immunochromatographic-Card test) or Enzyme immunoassay (EIA) methods are generally used. There are situations where both methods used have advantages and disadvantages compared to each other. In a study; while the sensitivity of the card test is low (93%) and the specificity rate is 100%; In EIA tests, the sensitivity rate was found to be high (100%) and the specificity rate was found to be 100% (2).

When evaluating HBsAg screening test results, there are various factors that may cause misinterpretation of the test results. Especially in cases where isolated HBsAg positivity is detected; the patient being in the initial (incubation) period of acute HBV, a history of blood transfusion from an HBsAg positive person, the presence of chronic HBV infection that does not develop an anti-HBc response, the use of test kits and the presence of problems related to the test device, sample-related contamination, antigenemia cases after high-dose hepatitis vaccine in young children and the presence

of HBV-S mutants should be evaluated (3).

Features of the 'HBsAg' kit that is used in the ELISA device in the laboratory

The test kit used for HBsAg screening is used in our laboratory with a single device and a single test kit; It is the Architect HBsAg Qualitative II test kit from Abbott company and performs the test procedure with chemiluminescent microparticle immunoassay technology. The HBsAg antigen detection range of the test (measurable range) is defined as ≥1 (Sample/Cut-off: S/CO), and in the kit package insert the this test kit specificity is stated as 99.91% and the sensitivity is 99.09%. In the kit package insert; The issues that need to be taken into consideration in the selection of test samples, storage of test kits and use of test reagents during the testing stages are also emphasized (Abbott, Architect system, HBsAg II Qualitative test prospectus) (4).

CASE PRESENTATION

As of September 18, 2023; since we have never encountered this situation before, in order to interpret it in line with the information request of the relevant patient and to examine this situation we decided to make an evaluation about 'HBsAg' test result approved on 'August 21, 2023' . On this date (August 21, 2023); The HBsAg test result of the patient (49 years old, female) was measured as 53.75 S/CO (positive) on the Abbott Architect device and was approved by us. The patient's biochemistry test results were normal and there were no abnormal laboratory findings. The same patient had the HBsAg test done again in Izmir, 1 week after August 21, 2023 (29.08.2023), and this time the test result was measured as '0.18' S/CO (negative). Upon this result, the patient said; She reported his complaint to the patient rights unit of our hospital, saying "They diagnosed me with Hepatitis B" and requested information from the laboratory. Upon this request, we examined the package insert of the HBsAg test kit used in the laboratory and conducted a literature search to examine the situations that may cause HBsAg cross-reactions (false positive results). At the end of both source research; we told to the patient rights unit to write an answer, explaining that may be cross-positive results due to situations which is arising from the patient status (hunger-satiety, vaccination history, non-HBV viral and bacterial hepatitis, autoimmune disease, immunosuppressive treatment, etc.) or test kit (thermostability of the kit, interaction due to serum content, gray zone due to test sensitivity). 2 days after September 18, 2023, on September 20, 2023, the HBsAg test result of another patient (70 years old, M) diagnosed with vitamin D deficiency, who entered the infection clinic, was 73.95 S/CO (positive) with the same device and kit. The test has been concluded and the test result has been approved by us. The next day (21.09.2023), the infectious disease doctor called laboratory and said that the patient did not have a risky condition in terms of HBV, that there could be that she would request a blood test for HBsAg from the same patient again. We suggested working with patient serum that gives results that was tested the day before and tested positive. As of September 21, 2023; with the same device and the same kit, the serum that gave a positive result the day before was '0.24' S/CO (negative) on the second day, and the test result of the patient's blood on the second day was '0.25' S/CO (negative). In a short period of time; Considering these results, it was thought that the situation was caused by the test or device, not the patient, and examinations related to the device and test kit were carried out to perform root-cause analysis.

The results of the calibration and internal quality and external quality control studies performed on the device on the days when the tests of the relevant patients were studied were appropriate and approved by us. For the ELISA device, which was installed in April 2023, the technical service has come for routine maintenance for the ELISA device several times since the device installation time (about 6 months), only for technical equipment repair and several times for %CV (consecutive work-test for analytical measurement error analysis-study on the

coefficient of variation) was carried out and there were records associated with regarding this, but there was no record regarding detailed (comprehensive) technical service, control and maintenance. There upon, a interwiewed was held with the relevant company officials on September 22, 2023, and they came from the relevant company technical service for detailed maintenance of the device on September 27, 2023. On the same day (September 27, 2023); Before the technical service maintenance work, the HBsAg test result of another 60-year-old male patient, who was referred to the laboratory from the internal medicine outpatient clinic with the diagnosis of 'vitamin D deficiency', was measured as '101.25' S/CO (positive) even though his other laboratory tests were normal. It was not approved, the physician who requested the tests was contacted, the patient's risk status in terms of HBV was questioned, and it was learned that there was no risky situation for the patient. After technical service control and maintenance; In this serum put back into the device; The result, which was previously measured as '101.25' S/CO, was this time measured as '0.19' (negative) S/CO, and it was stated to the relevant physician that such a result was encountered due to a problem related to the device and kit (Table 1).

Table 1. Evaluation of patients' HBsAg test results

Patients	1st test result (S/CO) and date	2nd test result (S/CO) and date	Comment
Patient 1	53,75 (21.08.2023)	0,18 (29.08.2023)	False positive result
Patient 2	73,95 (20.09.2023)	0,24 (21.09.2023)	False positive result
Patient 3	101,25 (27.09.2023)	0,19 (27.09.2023)	False positive result

CONCLUSION AND RECOMMENDATİONS

Medical microbiology laboratory processes consist of 5 parts; pre-preanalytical process, pre-analytical process, analytic process, post-analytical process and post-postanalytical process. Pre-preanalytical process; It covers processes such as informing physicians about the test guide, making test orders in accordance with the indications, applying decision-support systems, and designing test panels and test order forms. Pre-analytical process; It includes the processes of preparing the patient for sample collection, sample collection, sample transfer, acceptance of the sample to the laboratory and preparation for analysis. Analytical process; It is a process that includes the control of materials, devices and equipment used in performing tests in the laboratory, the competence of the personnel, device/ test quality control studies and validation studies, and consists of measurable and controllable parameters. Post-analytical process; It includes processes related to determining test result delivery times and informing the target audience about these times, arrangements for patient result reports and the design of the minimum information that should be included in these reports, and archiving of patient test results and related reports. Post-analytical process; It is the process that includes effective notification of test results (panic/ critical value) that will affect the safety of the patient to the relevant physician, information and guidance support for the interpretation of test results, and practices to encourage rational antibiotic use (5).

In order to avoid such risky situations or to minimize the possibility of encountering them, laboratory analytical and post-analytical process controls must be managed effectively and accurately. In the root cause analysis studies conducted on the process of 3 patients with unusual 'HBsAg' positivity; Lack of training among

the relevant personnel, lack of awareness, failure to carry out device technical service maintenance checks on time, and deficiencies in communication with clinicians came to the fore. In the improvement works for this; Training was provided to relevant personnel and awareness was raised. In consultation with the technical service, periodic device service maintenance was planned to be carried out regularly. Clinicians were informed to contact the laboratory in cases similar to the specific situations described in this case. In our case, the 'false positive' HBsAg test results of the 3 patients mentioned were recorded as a random error. Our work towards this end: Carrying out detailed device control-maintenance works by the technical service and organizing plans for the sustainability of these works, cleaning of the device equipment (technical parts and pipetting equipment), device calibration studies, delivery of the reworked internal quality control study results to us and control of all these works are to be recorded by us. In addition, it was planned to conduct sequential (consecutive) studies (%CV) for HBsAg testing on 10 serum samples selected from among the serum samples whose ELISA tests were performed, once a month, within our laboratory. However, when a suspicious positive test result was encountered in HBsAg tests (as in HCV and HIV antibody screening tests), it was decided to create a procedure to evaluate the accuracy of the result by either centrifuging the serum sample again or waiting for at least two hours and then re-running it.

In the non-laboratory process; since it is a process that affects patient safety, activities were organized to inform the quality management unit and evaluate it in the patient safety committee by notifying the adverse event reporting system. Via the hospital information-management system; Informational messages were sent to all users and they were advised to contact the laboratory if the patient's diagnosis, clinic and test results were suspicious, as in this case.

ACKNOWLEDGEMENT

Conflict of Interest: The author(s) declare that there is no conflict of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

Authorship Contributions: Concept – E.Y.; Design – E.Y.; Supervision – E.Y.; Funding – E.Y.; Materials – E.Y.; Data collection &/or processing – E.Y.; Analysis and/or interpretation – E.Y.; Literature search – E.Y.; Writing – E.Y.; Critical review – E.Y.

REFERENCES

1. Weinbaum CM, et al. MMWR Recomm Rep. 2008;57(RR-8):1-20. Lok AS, et al. Hepatology. 2009;50:661-662
2. Samal J, Soni A, Pandey A, Chooramani G, Gupta E. Performance Evaluation of Determine HBsAg 2 Rapid Card Test for the Detection of Hepatitis B Surface Antigen in Clinical Samples. Euroasian J Hepatogastroenterol. 2024 Jan-Jun;14(1):9-11. doi: 10.5005/jp-journals-10018-1403. PMID: 39022211; PMCID: PMC11249907.
3. Kumar M, Pahuja S, Khare P, Kumar A. Current Challenges and Future Perspectives of Diagnosis of Hepatitis B Virus. Diagnostics (Basel). 2023 Jan 19;13(3):368. doi: 10.3390/diagnostics13030368. PMID: 36766473; PMCID: PMC9914745.
4. Ndiaye AJS, Diop-Ndiaye H, Lo G, Dia A, Diakhaby MEHB, Sow A, Dieng A, Mboup S, Boye CSB, Kane CT. Detection and quantitation of hepatitis B surface antigen (HBsAg) on dried blood spots: a solution for easy access for hepatitis B diagnosis and elimination in remote areas. Pan Afr Med J. 2022 Jun 7;42:100. doi: 10.11604/pamj.2022.42.100.30531. PMID: 36034040; PMCID: PMC9379421.
5. Hawkins R. Managing the pre- and post-analytical phases of the total testing process. Ann Lab Med. 2012 Jan;32(1):5-16. doi: 10.3343/alm.2012.32.1.5. Epub 2011 Dec 20. PMID: 22259773; PMCID: PMC3255486.