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Comparison of 2 different antibody assay methods, Elecsys Anti-HCVII (Roche) and Vidas Anti-HCV (Biomerieux), for the detection of antibody to hepatitis C virus in Egypt

Ahmed Mohammed Gaballah, Marwa Mohammed Esawy *

Department of Clinical Pathology, Faculty of Medicine, Zagazig University, Egypt

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ABSTRACT

The measurement of antibodies against hepatitis C virus (HCV) is important to screen HCV infection. The aim of this study is to investigate the reliability of 2 commercially available anti-HCV antibody kits used in routine laboratory testing in Egypt. One thousand nine hundred and thirty-one serum samples were analyzed using 2 anti-HCV test systems: Cobas e 411® Elecsys Anti-HCVII and Vidas® Anti-HCV Biomerieux. Discrepant samples were tested using the recombinant immunoblot assay Innogenetics® INNO-LIA HCV Score. Overall agreement of the 2 tests was 94%. Following discrepant sample testing by LIA, sensitivity and specificity using Vidas were 94% and 99%, respectively, while those for Cobas were 97% and 96%, respectively. This study demonstrates superior specificity by Vidas and higher sensitivity by Cobas. Both methods are suitable for laboratory and/or blood screening programs. The concomitant use of a supplementary or confirmatory assay is necessary to compare the accuracy of HCV serological assays.

1. Introduction

Hepatitis C virus (HCV) is a single-stranded RNA virus with an organization most closely resembling that of the Flaviviridae. HCV infection is considered one of the major causes of death related to liver cirrhosis and hepatocellular carcinoma (Choo et al., 1991).

Hepatitis C is a worldwide disease with 177.5 million infected adults, representing 2.5% of the global population (Petruzziello et al., 2016). HCV is endemic in developing countries, and the largest numbers of HCV infected individuals are in Asia (representing nearly 3.6% of the world population), followed by Africa (3.2% of the global population) and Latin America (1.4% of the global population) (Daw et al., 2016). The lowest prevalence of HCV has been reported from the United Kingdom and Scandinavia (0.01%–0.1%) (Alter, 2007). Egypt has the highest HCV world prevalence, with a 2008 estimation of 14.7% among 15–59-year-old age group (El-Zanaty and Way, 2009), representing a national epidemic (Mohamoud et al., 2013).

The diagnosis and monitoring of HCV infection are based on 2 types of tests: a serological test that detects HCV antigen-specific antibodies and tests that detect viral RNA or HCV core antigens (Berger et al., 2008). However, serological tests make no distinction between active infections and resolved ones. In addition, false-negative results are frequent due to a long window period, the time period from initial infection to seroconversion, which lasts between 45 and 68 days (Morota et al., 2009). False-positive results from serological test may occur due to interfering factors, including high gamma globulin levels, nephritic syndrome, pregnancy, autoimmune diseases, or viral or parasitic infections (Zachary et al., 2005).

The objective of this study is to investigate the reliability of 2 commercially available anti-HCV antibody kits used in routine laboratory testing in Egypt: the electrochemiluminescence immunoassay (ECLIA) (Cobas e 411® Elecsys Anti-HCVII) and the Enzyme Linked Fluorescent Assay (ELFA) (Vidas® Anti-HCV Biomerieux).

2. Subjects and methods

2.1. Subjects samples

The study protocol was approved by the Ethical Committee of the Faculty of Medicine, Zagazig University. One thousand nine hundred and thirty-one study subjects were enrolled, including 1431 hospital outpatients and 500 blood bank donors. Study subjects were referred to Zagazig University Hospitals Laboratories (Sharkia, Egypt). A written informed consent was obtained from all participants. Samples were collected over a period of 1 month (October 2015). Venous blood samples were collected from study subjects for serum separation. The same protocol of sample collection was used in both outpatients and blood bank donors. Study subjects' whole blood, obtained by venipuncture, was collected in 4 mL BD Vacutainer® Plus Plastic Serum Tubes (Becton,

Abbreviations: ECLIA, electrochemiluminescence immunoassay; ELFA, enzyme-linked fluorescent assay; HCV, hepatitis C virus; LiRAS, Line reader and analysis software; NS, nonstructural protein; OPA, overall percent agreement.

* Corresponding author. Tel./fax: +20-1066343326; +20-1013981211.
E-mail addresses: agaballaa2011@yahoo.com (A.M. Gaballah), dr.marwaesawy@ymail.com. (M.M. Esawy).

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Dickinson and Company, Franklin Lakes, NJ). Samples were allowed to clot for 30 min at room temperature, followed by centrifugation at 1200×*g* for 10 min. Using a disposable transfer pipet, aliquots of 1 mL serum were transferred to 1.5-mL sterile microcentrifuge tubes (GOMAC, Egypt) and analyzed sequentially on Cobas and then on Vidas within 6 h after centrifugation. Excess serum aliquots were transferred to −80°C for LIA testing. Samples were stored for no longer than 30 days prior to LIA analyses.

2.2. Methods and analyses

All serum samples were tested using 2 different anti-HCV antibody assays. The characteristics of the anti-HCV antibody assays are shown in Table 1. Samples with discrepant results between the 2 screening assays were tested with recombinant immunoblot assay Fujirebio INNO-LIA HCV Score assay (Ghent, Belgium). All assays were performed according to the manufacturers' instructions.

2.2.1. Cobas e 411® Elecsys Anti-HCVII (Roche Diagnostics, Mannheim, Germany)

Cobas e 411 is a third-generation immunoassay analyzer. ECLIA is intended for use on Cobas. The Elecsys Anti-HCV II assay reagent uses peptides and recombinant antigens representing core, NS3, and NS4 proteins to determine anti-HCV antibodies. PreciControl Anti-HCV was utilized in parallel with each run.

2.2.2. Vidas® Anti-HCV (Biomerieux, Chemin de l'Orme, France)

Vidas is a third-generation immunoassay analyzer. ELFA is intended for use on Vidas. The Anti-HCV assay uses antigens representing core, NS3, and NS4 proteins to determine anti-HCV antibodies. One positive control and 1 negative control were used in each run. These controls are included in each Vidas Anti-HCV kit.

2.2.3. INNO-LIA HCV Score assay (Ghent, Belgium)

INNO-LIA HCV Score is a third-generation line immunoassay which incorporates HCV antigens derived from the core region; the E2-hypervariable region; the NS3 helicase region; and the NS4A, the NS4B, and the NS5A regions. The intensity of the reaction was evaluated visually and densitometrically, followed by software evaluation with Line Reader and Analysis Software (LiRAS)™ (Belgium).

2.3. Statistical analysis

Statistical analysis was carried out using Excel® 2007 (Microsoft Co., Redmond, WA). Quantitative variables were expressed as mean ± standard deviation, and qualitative variables were expressed in terms of absolute and relative frequencies. The study results were analyzed as all equivocal ones had been considered negative.

Table 1
Tests characteristics.

Assays	Principle	Sample volume (μL)	Reaction time (min)	Interpretation
Cobas	ECLIA	50	18	Cutoff index: • <0.9 Negative • ≥0.9 and <1.0 borderline • ≥1.0 Positive
Vidas	ELFA	100	40	Test value: • <1.00 Negative • ≥1.00 Positive

ECLIA = electrochemiluminescence immune-assay; ELFA = enzyme-linked fluorescent immunoassay.

3. Results

Demographic characteristics of study subjects showed that the mean age ± standard deviation of the hospital outpatients and blood bank donors was 42.69 ± 20.24 and 29.92 ± 6.55 years, respectively. Regarding study subject gender, hospital outpatients included 959 males and 472 females, while blood bank donors included 478 males and 22 females.

The clinical profile of the hospital outpatients included 974 subjects (68.06%) with preoperative screening, 203 subjects (14.19%) with no liver-related symptoms, 171 subjects (11.95%) with liver-related symptoms, 40 subjects (2.80%) with prehemodialysis screening, 29 subjects (2.03%) with a routine checkup, and 14 subjects (0.98%) who were relatives of patients with HCV infection. In addition, the prevalence of diabetes was 11.32%, history of cancer was 6.57%, and chemotherapy was 5.5%. Clinical evaluation of the blood donors denoted they are apparently healthy subjects.

Total anti-HCV seropositivity rates for the 1931 serum samples were 24.7% ($n = 477$) by Cobas and 21.7% ($n = 419$) by Vidas. Total anti-HCV seronegativity rates were 74.9% ($n = 1447$) by Cobas and 78.3% ($n = 1512$) by Vidas. Cobas had a borderline rate of 0.4% ($n = 7$).

Distribution of index values [signal/cutoff values] showed that 95% of the concordant negative samples had index values less than 0.6 for both assays. Concordant positive samples showed a different distribution of index values, where 95% exceeded 20 and 2 for Cobas and Vidas, respectively. Eighty-six percent of Vidas-positive samples exhibited an index value exceeding 5 (Fig. 1).

Regarding the index values distribution in the discrepant samples, all Cobas-negative samples had an index of less than 0.2, while Vidas-negative samples showed dispersed values. Ninety-three percent of Vidas-positive samples had an index of less than 5. Eighty percent of Cobas-positive samples were less than 20, while the remaining 20% was scattered over a more extended range (20–120) (Fig. 2).

Of the 1931 samples analyzed, 73.6% ($n = 1421$) exhibited negative results, and 20.4% ($n = 393$) were positive in the 2 assays. Sensitivity, specificity, and overall percentages of agreement (OPAs) of both assays are illustrated in Table 2.

A comparison of INNO-LIA interpretation methods disclosed that LIRAS detected more indeterminate results. The agreement between assays and INNO-LIA regarding samples with discrepant screening results is shown in Table 3. For samples with discrepant screening results, Vidas results had a higher percentage of agreement with INNO-LIA results (~70%). The sensitivity, specificity, and agreement for merged results following discrepant sample testing by INNO-LIA (visually and LIRAS) are presented in Table 4. Concerning these merged results, Vidas had a higher percentage of agreement (~98%) compared to Cobas (~96%).

4. Discussion

HCV infection has an asymptomatic presentation; therefore, accurate anti-HCV assays are essential. For HCV screening in blood donation, the most sensitive test should be used to avoid false-negative results. On the other hand, for the screening of patients, false-positive results should be avoided (Kim et al., 2008). Recently, various anti-HCV assays have been developed, which offer improved precision, reliability, turnaround time, and throughput rate.

To the best of our knowledge, this is the first study evaluating the performance of Cobas e 411® Elecsys Anti-HCVII and Vidas® Anti-HCV in Egypt. While this study shows an Egyptian HCV prevalence of 21–24%, this percentage is representative only of the cohorts studied and is not a survey study. Regarding the distribution of the index values, further research is needed to define country-specific cutoff values and ranges for indeterminate results.

The performance agreement of Vidas and Cobas was approximately 94%. Concerning discrepant samples, the performance agreement of

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