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Diagnostic accuracy evaluation of the ImmunoFlow HCV rapid immunochromatographic test for the detection of hepatitis C antibodies

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A B S T R A C T

2% of the world's population lives with a hepatitis C virus (HCV) infection with highest rates in developing countries. The most common mode of transmission takes place via unsafe blood transfusions and unsafe therapeutic injections.

Thus, screening potential blood donors for hepatitis C infection is a must to ensure safe blood transfusions. Rapid immunochromatographic tests are the best suitable test format to be used for screening for blood donors in resource-limited settings.

The ImmunoFlow HCV from Core Diagnostics was evaluated at the Paul-Ehrlich-Institute, Germany for its test accuracy on three seropanels. Panel 1 consisted of 26 HCV positive and 55 negative samples, panel 2 of 193 HCV positive samples. Panel 3 contained 116 samples of 10 patients during seroconversion period. 39 of these 116 samples were characterized as HCV positive.

The HCV ImmunoFlow had a sensitivity of 100% (95% CI: 93.5–100) and a specificity of 100% (95% CI: 86.8–100) when samples of panel 1 were tested.

191 samples of the 193 samples in panel 2 were correctly by the HCV Immunoflow, resulting in a sensitivity of 99.0%.

9 of 10 HCV infections were detected by the HCV ImmunoFlow when panel 3 was used.

This evaluation revealed good sensitivity of the HCV ImmunoFlow test from and compares favorably with the results from the WHO evaluation and a systematic review conducted of field evaluations of Hepatitis C rapid diagnostic and other point of care tests.

1. Introduction

Hepatitis C virus (HCV) is a single stranded RNA virus of the Flaviviridae family. Globally, approximately 150 million people are infected chronically with hepatitis C and at risk of developing liver cirrhosis and/or liver cancer (WHO, 2013a). Further estimates indicate that three to four million persons are newly infected each year (Perz et al., 2006; WHO, 2013a). However, infection rates differ greatly by country and region (Madhava et al., 2002; Shepard et al., 2005; Alter, 2007; Kershenobich et al., 2011; Sievert et al., 2011; Cornberg et al., 2011; Qureshi et al., 2010; Averhoff et al., 2012; WHO, 2013b). A concentrated epidemic can be found in Eastern Europe and Asia in high-risk groups and a generalized epidemic in high prevalent countries (Qureshi et al., 2010; Cornberg et al., 2011). However, in many countries, no reliable epidemiological data is available, and so the extent of the HCV epidemic remains unknown (MSF, 2013; WHO, 2013b).

The transmission of HCV infection occurs via blood-to-blood contact. Most frequently, transmission occurs from the transfusion of unscreened blood or by sharing contaminated needles or other drug injection equipment (Gibb et al., 2000; Candotti et al., 2001; Madhava et al., 2002; Shan et al., 2002; Busch et al., 2003; Hauri et al., 2004; Prati, 2006; Aceijas and Rhodes, 2007; Nelson et al., 2011; MSF, 2013). Less commonly, HCV is transmitted by sexual contact with an infected person or at birth via mother to child transmission (Yeung et al., 2001; Dal Molin et al., 2002; Ferrero et al., 2003; Shepard et al., 2005; World Hepatitis Alliance, 2011).

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Globally, only 30% of the world's population has access to hepatitis C diagnosis free-of-charge. Altogether, 54% of people, ranging from 3% of the population of high income countries to 82% of that in low income countries, live in areas without any provision for free testing (Centers for Disease Control and Prevention, 2013).

To screen for HCV infection a screening test to detect antibodies against the virus either by lateral flow immunoassay (LFI) or by enzyme-linked immunosorbent assay (ELISA) is carried out. Screening test results reactive initially should be confirmed by a supplemental recombinant immunoblot assay or HCV nucleic acid testing (NAT) for RNA to confirm the presence of HCV specific antibodies and activity of infection (Alter et al., 2003; Shivkumar et al., 2012). This algorithm detects effectively active infection, however, ELISA and NAT tests are expensive, have long turnaround times, and require well-trained staff and a well-equipped laboratory (Kamili et al., 2012). Convenient, quality-assured, antibody-based rapid diagnostic tests and point-of-care tests could facilitate preliminary screening, although they cannot differentiate between acute and chronic infections (Kamili et al., 2012).

In addition to screening patients for diagnosis, HCV testing is also needed to test potential blood donors for infection (WHO, 2010; Operskalski and Kovacs, 2011; O'Connell et al., 2013). Screening of potential blood donors is currently the main use of HCV LFIs at Médecins sans Frontières, a non-governmental, medical humanitarian organization. Thus, requirements for this HCV test are different from diagnostic tests: in order to be able to exclude HCV infected blood donors, a high sensitivity and a high negative predictive value are required, while the specificity and positive predictive value of the test does not need necessarily to match highest performance criteria.

However, interagency discussions on HIV-infected patients where HCV/HIV-co-infected patient may in the future be initiated on anti-retroviral-therapy regardless of their CD4 count are ongoing (England et al., 2009; WHO, 2013c), similarly to patients who are HBV/HIV co-infected (WHO, 2013c). If this policy becomes practice the above named requirements for a screening test may change again, meaning that the specificity and positive predictive value of an HCV screening test also need to be of highest performance criteria in addition to the sensitivity and negative predictive value.

Hepatitis C rapid tests to be used for screening for infection, should ideally have a sensitivity close to 100% and be able to detect HCV infection as early as ELISA tests used commonly. In addition, the test should be simple in its procedure, free of cold chain requirements and be of low cost, thus fulfill the ASSURED criteria (Peeling and Mabey, 2010).

Another aspect not to be overlooked is the quality of the manufacturing, to ensure tests are produced with consistent quality. The minimum criterion is that the manufacturer follows the international standards for good manufacturing practice. Additional quality requirements include the Conformité Européenne (CE) marking from a stringent notified body, the approval from stringent regulatory authorities and the WHO pre-qualification (Médecins sans Frontières – Access Campaign, 2013).

The ImmunoFlow HCV test from Core Diagnostics meets many of the above operational named requirements but there is only little knowledge on its performance (Health Protection Agency, 2007). It was neither included on the systematic review (Shivkumar et al., 2012) nor was it included in the hepatitis C assays evaluation in 2001 (WHO, 2001a,b). Thus, MSF decided to commission this evaluation to the Testing Laboratory for In Vitro Diagnostic Medical Devices at the Paul-Ehrlich Institute, Langen, Germany, in order to gather independent performance data.

2. Materials and methods

2.1. Investigation procedures

The evaluation of the ImmunoFlow HCV test from Core Diagnostics was conducted from September to October 2011 on three serum panels at the Paul-Ehrlich-Institute, Langen, Germany.

Serum samples of all three serum panels were thawed and centrifuged before use.

The results were read by two independent laboratory technicians 15 and 30 min after application of the sample. The technicians were blinded to each other's readings as well as to the result of the reference testing. In case of disagreement between the readers, the positive result was evaluated in favor for the ImmunoFlow HCV test.

2.2. Serum panel description

The ImmunoFlow HCV test was tested on three panels procured and differentiated by the Paul-Ehrlich Institute, Langen, Germany.

The first panel ($n = 82$) was procured from ZeptoMetrix, New York, USA and consisted of samples collected from intravenous drug users bearing a high risk for HCV infection. All samples have been screened with the Architect® Anti-HCV test (product number: 6C37; Abbott, USA), the AxSYM® Anti-HCV version 3 (product number: 3B44-20; Abbott, USA), the Innotest™ HCV Ab IV (product number: 80068; Innogenetics, Gent, Belgium) and the Ortho® HCV 3.0 Enhanced Save ELISA (product number: 930820; Ortho Clinical Diagnostics, USA).

All positive and discrepant samples have been characterized using a supplemental test: the Chiron RIBA HCV 3.0 SIA (product number: 930600 and 930790; Novartis Vaccines and Diagnostics, Emeryville, USA).

A positive status was defined as (i) reactive screening test(s) and positive supplemental test, (ii) positive result in several anti-HCV screening tests, negative result in one screening test only and positive supplemental test. An indeterminate status was defined as reactive screening test(s) and indeterminate supplemental test. A discrepant result was defined as discrepant anti-HCV screening results and negative supplemental test result. A negative status was defined as a negative screening tests and/or negative supplemental test.

55 samples of this first panel were HCV positive and 26 HCV negative and 1 indeterminate.

The second panel ($n = 199$) originated from the University of Frankfurt, Germany and had been stored at the Paul Ehrlich Institute.

The samples have been screened with at least one of the following screening tests: the Architect® Anti-HCV test (product number: 6C37; Abbott, Green Oaks, USA), the Ortho® HCV 3.0 Enhanced Save ELISA (product number: 930820; Ortho Clinical Diagnostics, Raritan, USA), the ADVIA Centaur HCV (product number: 3438099; Siemens, Tarrytown, USA) and the Murex anti-HCV Version 4 (7F51) (product number: VK47/48; DiaSorin, South Africa), In addition, most samples (121/199) have been characterized using the Chiron RIBA HCV 3.0 SIA (product number: 930600 and 930790; Novartis Vaccines and Diagnostics, Emeryville, USA) as supplemental test.

A positive status was defined as (i) reactive screening test(s) and positive supplemental test, (ii) reactive screening test(s) where no supplemental test result was available. An indeterminate status was defined as (i) reactive screening test(s) and indeterminate supplemental test, (ii) indeterminate screening test and indeterminate supplemental test, (iii) indeterminate screening test and positive supplemental test.