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Performance of a new rapid diagnostic test for the detection of antibodies to hepatitis C virus

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ABSTRACT

Rapid diagnostic tests (RDTs) represent an attractive alternative to conventional diagnostic methods for hepatitis C virus (HCV) infection.

The aim of the present study was to assess the clinical performance of the new CE-marked Advanced Quality™ Rapid Anti-HCV Test for the detection of HCV antibodies in various patient populations.

A total of 396 individuals, including 178 patients with chronic HCV infection, 26 patients with resolved HCV infection, and 192 subjects not infected with HCV, were studied.

The clinical sensitivity and specificity in serum samples of the Advanced Quality™ Rapid Anti-HCV Test were both 99%.

The new CE-marked RDT Advanced Quality™ Rapid Anti-HCV Test fulfills the World Health Organization recommendations acceptance criteria for serological assays in terms of sensitivity and specificity and can thus be confidently used for the screening of HCV antibodies.

Hepatitis C virus (HCV) infection is a major cause of chronic liver disease worldwide, resulting in an estimated 700,000 deaths per year (Mortality and Causes of Death, 2015). The most recent modeling suggests that 71 million individuals are chronically infected with HCV worldwide (Polaris Observatory, 2017). Over 80% of infected people are unaware of their infection (Papatheodoridis et al., 2016). The World Health Organization (WHO) recommends that individuals who are part of a population with a high seroprevalence or have a history of risk exposure or behavior should be tested for HCV (Anon., 2017). Thus, new assays that facilitate easy and affordable access to care are needed.

Rapid diagnostic tests (RDTs) using serum, plasma, capillary whole blood or oral fluid as matrices can be used instead of classical enzyme immunoassays to facilitate HCV antibody screening and improve access to care, as recommended by recent international scientific society and WHO guidelines (European Association for the Study of the Liver et al., 2018; Hellard et al., 2017; Panel, 2015). WHO recommends using RDTs in settings where there is limited access to laboratory infrastructure and testing, and/or in populations where access to rapid testing would facilitate linkage to care and treatment (Hellard et al., 2017).

The aim of the present study was to assess the clinical performance of the new CE-marked Advanced Quality™ Rapid Anti-HCV Test (InTec Products, Inc., Xiamen, China) for the detection of HCV antibodies in various patient populations. The performance of the new CE-marked RDT has been assessed in serum samples from 396 individuals recruited in the Department of Hepatology of the Henri Mondor Hospital between September 2012 and November 2013 and at the Muhimbili National Hospital OST clinic in Dar-es-Salaam. One hundred and seventy-eight patients with chronic HCV infection (defined by the presence of both HCV antibodies and detectable HCV RNA), 26 individuals with resolved HCV infection (characterized by the presence of HCV antibodies and negative HCV RNA detection), and 192 individuals who were HCV-negative (without detectable HCV antibodies and HCV RNA) (Table 1) were included. Patients with chronic HCV infection were infected with HCV genotype 1 in 88 cases (41 with subtype 1a, 40 with subtype 1b and 7 with another genotype 1 subtype), 10 were infected with genotype 2, 31 with genotype 3a, 40 with genotype 4 (18 with subtype 4a, 5 with 4d, 6 with 4f, 3 with 4r and 8 with another genotype 4 subtype), 2 with genotype 5a and 1 with genotype 6q. The HCV genotype could not be determined by phylogenetic analysis of a portion of the NS5B gene (i.e, the reference method) in 6 patients due to a low HCV RNA level

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Table 1
Demographic and virological characteristics of the study population, including patients with chronic HCV infection, subjects with resolved infection, and subjects seronegative for HCV.

	Patients with chronic infection (n = 178)	Patients with resolved infection (n = 26)	Seronegative subjects (n = 192)
Age, median (year, range)	60 (33-91)	65.5 (32-72)	45 (22-84)
Male gender, n (%)	116 (62.5)	10 (38.5)	77 (40.1)
Treatment-naïve, n (%)	158 (88.8)	13 (50)	NA
Anti-HCV signal/cutoff (mean ± SD)	26.9 ± 4.3	24.6 ± 8.2	0.06 ± 0.1
Signal/cutoff < 8.0, n (%)[1]	0 (0)	2 (7.7)	192 (100)
Signal/cutoff ≥ 8.0, n (%)[1]	178 (100)	24 (92.3)	0 (0)
HCV RNA level (Log IU/mL), median (IQR)	5.9 (5.4-6.3)	< 1.10	< 1.10
HCV RNA > 800,000 IU/mL, n (%)	86 (48.3)	0	0
HCV genotype, n (%)			
1	88 (51.2)	NA	NA
2	10 (5.8)	NA	NA
3a	31 (18.0)	NA	NA
4	40 (23.2)	NA	NA
5a	2 (1.2)	NA	NA
6	1 (0.6)	NA	NA
Coinfection, n (%)			
With HIV	1 (0.6)	1 (3.8)	3 (1.6)
With HBV	2 (1.2)	1 (3.8)	14 (7.3)

NA: not applicable.
[1] Specific ratio that predicts a true antibody-positive result more than 95% of time regardless of the anti-HCV prevalence or characteristics of the population being tested, according to CDC.

(range: 1.8–2.6 Log IU/mL). Serum samples were retrospectively tested with the Advanced Quality™ Rapid Anti-HCV Test and in parallel with another CE-marked RDT used as a comparator: Toyo® Anti-HCV Test (Türklab Medical Devices, Izmir, Turkey) (Chevaliez et al., 2016). The study followed the principles of good clinical practice and was approved by the ethics committee (Comité de Protection des Personnes - Ile-de-France IX, approval number: 12-006; Muhumibili University for Health and Allied 138 Sciences (MUHAS) and the Tanzanian National Institute for Medical Research 139 (NIMR) (NIMR/HQ/R8a/Vol.ix/2298) institutional review board panels) in accordance with the Helsinki Declaration. All individuals gave written informed consent to their inclusion.

The Advanced Quality™ Rapid Anti-HCV Test had a clinical sensitivity of 99% [95% confidence interval (CI): 96.5%–99.7%], as compared to third-generation EIA (aHCV VITROS ECi™; Ortho-Clinical Diagnostics, Raritan, NJ). This sensitivity was in the same order as that of Toyo® Anti-HCV Test (98.5%; 95%CI: 95.8%–99.5%), but the latter assay required a larger sample volume (60 µL *vs* 10 µL for the Advanced Quality™ Test). Table 2 shows the positive and negative likelihood ratios. Two and 3 samples tested negative in Advanced Quality™ Rapid Anti-HCV Test and Toyo® Anti-HCV Test, respectively, while HCV antibodies were detected in serum by EIA (Table 3). The 2 false negatives in Advanced Quality™ Rapid Anti-HCV Test were characterized by a low signal-to-cutoff value in two EIAs for HCV antibodies (aHCV VITROS ECi and HCV Ab PLUS Access EIA Test, Bio-Rad, Hercules, CA). One had a low HCV RNA level (2.6 Log IU/mL), whereas the other one had no detectable HCV RNA. Three samples were falsely negative with Toyo® Anti-HCV Test as compared to EIA: one displayed a high signal-to-cutoff value in both EIAs and a high HCV RNA level (6.4 Log IU/mL), whereas the remaining two were characterized by low signal-to-cutoff values in both EIAs and undetectable HCV RNA (Table 3).

Table 2
Performance of the two anti-HCV antibody RDTs tested in serum, using the EIA result as the reference.

Test	Specificity (95%CI)	Sensitivity (95%CI)	LR+	LR-
Advanced Quality™ Rapid Anti-HCV Test	99.0% (96.3%-99.7%)	99.0% (96.5%-99.7%)	95.059	0.010
Toyo® Anti-HCV Test	99.5% (97.3%-99.9%)	98.5% (95.8%-99.5%)	189.176	0.015

EIA: enzyme immunosorbent assay; LR+: positive likelihood ratio; LR-: negative likelihood ratio, 95%CI: 95% confidence interval.

Table 3
Virological characteristics of the samples with a false-negative result in one of the 2 RDTs in serum (HCV Ab Plus, was used in these cases to back up the results of aHCV Vitros ECi™).

Patient	Anti-HCV antibodies in serum by EIA (signal-to-cutoff)		HCV RNA level (Log IU/mL)	HCV genotype
	aHCV VITROS ECi™	HCV Ab PLUS Access®		
Advanced Quality™ Rapid Anti-HCV Test				
Pt-5	8.80	4.25	2.6	ND
Pt-92	1.80	1.30	< 1.1	NA
Toyo® Anti-HCV Test				
Pt-7	17.9	1.76	6.4	2l
Pt-92	1.80	1.30	< 1.1	NA
Pt-93	1.60	3.20	< 1.1	NA

ND: not determined due to a low HCV RNA level; NA: not applicable.

The Advanced Quality™ Rapid Anti-HCV Test had a high sensitivity (99.0%; CI95%: 96.5%–99.7%), in the same order as that of the comparator test (Table 2). Only two non-HCV-infected subjects tested anti-HCV-positive with Advanced Quality™ Rapid Anti-HCV Test, whereas one false-positive result was observed with the Toyo® Anti-HCV Test.

Classical virological tests require blood sampling by venous puncture, capacity for cold storage, specific infrastructure, equipment and personnel training. They may be unavailable and/or unaffordable in low- to middle-income settings. RDTs often overcome these issues. In addition, rapid tests enable the delivery of results at the time of testing, do not require a follow-up visit to receive the result, and may be combined with reflex testing for HCV RNA and linkage to care in case of seropositivity. Our study shows that the new CE-marked RDT Advanced Quality™ Rapid Anti-HCV Test fulfills the WHO recommendations acceptance criteria for serological assays in terms of sensitivity and specificity (recommended sensitivity > 98%, recommended specificity > 97%) (Guidelines, 2017).

Our study has limitations. First, it was performed with serum specimens. Whether similar performance can be obtained when testing capillary whole blood remains to be determined. Secondly, the performance of this assay in HIV-coinfected or immunosuppressed patients was not tested (only 2 patients were HIV-HCV coinfected). RDTs may indeed be less sensitive in such patients, as already suggested (Jewett et al., 2012; Larrat et al., 2012; Smith et al., 2011). The assay also suffers from the fact that its control line does not reflect the presence of a sufficient amount of immunoglobulins, but rather proper liquid migration through the strip.

In conclusion, our study shows that the new CE-marked RDT Advanced Quality™ Rapid Anti-HCV Test easily and reliably detects HCV antibodies in serum samples. This test uses only 10 µL of matrix liquid, including alternative matrices such as capillary whole blood, making it well-suited to remote settings. This RDT is both specific and sensitive for HCV antibody detection and thus represents a promising tool for broad-scale screening of HCV antibodies.

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