Hepatitis C Virus (HCV) Core Antigen Reliably Diagnoses HCV Infection in Injection and Non-injection Drug Users

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Abstract

Background and Aims: HCV RNA detection, the standard method to confirm hepatitis C virema, can be difficult to perform among transient populations such as individuals with substance use disorders and the homeless. HCV core antigen (Ag), with the advantages of relative ease of sample handling compared to RNA detection methods, reduced cost, and potential as a point-of-care test (POCT), could be an alternative method to diagnose chronic HCV infection. Since the test might have utility among difficult-to-engage populations, we sought to evaluate its performance in injection and non-injection drug users.

Methods: Levels of HCV core Ag (Abbott ARCHITECT) from 109 patients were compared to HCV RNA levels (Abbott Real-time M2000). Assay agreement and associations between baseline predictors were investigated using linear regression.

Results: Mean age was 53.8 ± 7.8 years, 59.6% were male, 68.8% African American, and 28.4% were Hispanic. A history of injection and non-injection drug use was reported by 60% and 94% of patients, respectively. Active (i.e. previous six months) injection and non-injection drug use was reported by 10% and 50% of patients, respectively. HCV RNA was detected in 44%, the majority (77%) infected with HCV genotype 1. Among HCV RNA positive patients, 29% (14/48) were HCV/HIV co-infected. HCV core Ag was detectable in 47 of 48 HCV RNA positive patients. Core Ag was not detected in any HCV RNA negative patients or in one patient with detectable but low level (less than 500 IU/ml) HCV RNA. In comparison with HCV RNA levels, HCV Core Ag had excellent performance with sensitivity = 97.9%, specificity = 100%, positive and negative predictive value = 100%. We found high correlation between HCV RNA and HCV core antigen assays with a correlation coefficient of 0.93 (95% CI 0.84; 0.97, p < 0.01). Conclusion: Among injection and non-injection drug users, the HCV core antigen has excellent performance for the diagnosis of active HCV infection. These data underscore its potential for development as a POCT for HCV diagnosis with applicability to difficult-to-engage populations, such as those with substance use disorders.

Background

- Two-thirds of US HCV-infected individuals unaware of infection status.
- Although persons with substance use disorders (PWSUD) have the highest HCV prevalence and incidence, many are medically disenfranchised and therefore remain with undiagnosed HCV infection.
- An additional obstacle is the frequent need for multiple, sequential diagnostic assays to determine active infection.
  - Most often, HCV RNA testing is required after detection of a positive HCV antibody (i.e. two separate medical appointments).
- HCV core antigen could be an alternative strategy to HCV RNA testing.
  - Core antigen is detectable in blood one to two days after HCV RNA becomes detectable.
  - Sample handling is easier than HCV RNA
  - It could be offered as a point-of-care test that could be used to diagnose active HCV infection.
  - Cost may be substantially reduced in comparison to HCV RNA testing, which could be useful in many resource limited settings that are now attempting to have large increases in the number of treated patients.

Objectives

The goal of this study was to evaluate the performance of the HCV core antigen in methadone-maintained injection and non-injection drug users.

Specific objectives are:

1) To evaluate the relationship between HCV core antigen (Abbott) and HCV RNA levels among PWSUD.
2) To determine factors that affect expression of HCV core antigen.

Patients and Methods

- All patients were recruited from a methadone maintenance program and were on stable methadone maintenance.
  - This project was part of a larger project assessing telemedicine-based treatment of HCV infection.
- After obtaining informed consent, blood was obtained for HCV RNA and HCV core antigen testing.
  - Two separate HCV RNA testing strategies were employed.
    - Roche COBAS Taqman performed by Labcorp
    - Abbott real-time m2000
  - HCV core antigen assay was performed on the ARCHITECT i2000SR platform.
  - Values were treated as follows:
    - < 3.00 fmol/L are considered nonreactive for HCV Ag.
    - ≥ 3.00 fmol/L are considered reactive for HCV Ag
    - ≥ 3.00 fmol/L to < 10.00 fmol/L were retested in duplicate
    - If both values were nonreactive, the specimen was considered nonreactive for HCV Ag.
    - If one or both duplicate testing is ≥ 3.00 fmol/L, the specimen was considered positive for HCV Ag.
- Demographic information and life-time drug use data were obtained from a survey completed at study entry as previously described (Zeremski et al, 2014). HCV and HIV antibody results were obtained from the medical record.
- Statistical analysis
  - Scatterplots and Spearman correlation to evaluate associations between continuous measurements (HCV RNA and HCV core antigen).
  - Bland-Altman Plot to assess agreement between each of the HCV RNA measurement types.
  - Linear regression to assess influence of demographic, infection and drug use variables on HCV core antigen.

Results

Variables (Log 10 transformed)	Correlation	95% Confidence Interval	P-value
HCV RNA (LabCorp) VS Core Ag	0.8775	(0.7559 0.9527)	< 0.001
HCV RNA (LabCorp) VS HCV RNA (Abbott)	0.9466	(0.8910, 0.9658)	< 0.001
HCV RNA (Abbott) VS Core Ag	0.9258	(0.8432 0.9687)	< 0.001

Patient Characteristics

Variable	Level	All patients		HCV positive	
		Count/Mean	%/SD	Count/Mean	%/SD
Age		53.8	7.80	56.7	8.30
Gender	Male	66	60.55	32	68.09
	Female	43	39.45	15	31.91
Race	White	5	4.59	3	6.38
	Black	75	68.81	30	63.83
	Mixed	2	1.83	13	27.66
	Other	27	24.77	1	2.13
Ethnicity	Latino	32	29.36	14	29.79
	Non-latino	77	70.64	33	70.21
Duration in MMTP		6	5.20	8.3	6.30
Hx IDU	Yes	65	59.63	39	82.98
	No	44	40.37	8	17.02
Hx Non-IDU	Yes	103	94.50	44	93.62
	No	6	5.50	3	6.38
IDU-past 6 mos	Yes	11	10.09	6	12.77
	No	98	89.91	41	87.23
Non-DU-past 6 mos	Yes	54	49.54	18	38.30
	No	53	48.62	28	59.57
	Missing	2	1.83	1	2.13

Abbreviations: SD, standard deviation: MMTP, methadone maintenance treatment program; IDU, injection drug use,

Linear Regression

Variable	Coefficient	SD	95% Confidence Interval		P-value
Intercept	-2.1809	0.2656	-2.7017	-1.6602	<0.001
HCV RNA (LabCorp) (log10)	0.9226	0.0423	0.8396	1.0055	<0.001

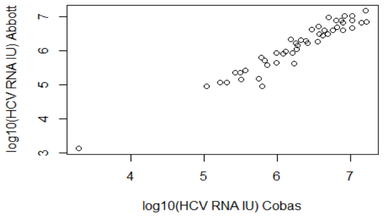
All predictors of core Ag negative except HCV RNA

Conclusions

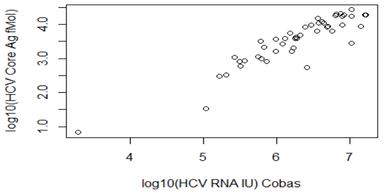
- HCV core Ag is highly correlated with HCV RNA when measured by either the Abbott real-time PCR assay or by Roche Cobas.
  - Association shown by correlation coefficient, linear regression, and graphically.
- None of the other factors significantly influenced the association between HCV RNA and HCV core antigen in this population of patients on opiate agonist therapy.
- These factors should promote development of the HCV core Ag test as a point-of-care test for medically disenfranchised individuals.

Scatterplots

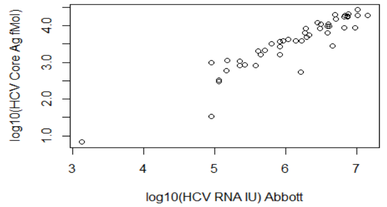
HCV RNA (Abbott) versus HCV RNA (Cobas)

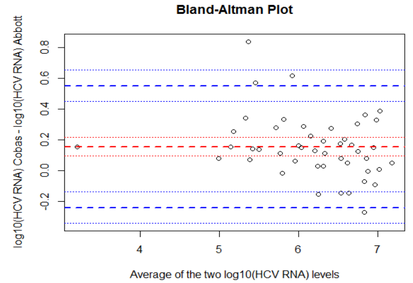


HCV core antigen versus HCV RNA (Cobas)



HCV core antigen versus HCV RNA (Abbott)





BA plot assessing agreement between HCV RNA measurements by Cobas and Abbott. Red line is mean difference between assays and blue line is limit of agreement. Methods generally agree with each other.