Prevalence of false-positive hepatitis C antibody results, National Health and Nutrition Examination Survey (NHANES), 2007-2012

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Abstract

Screening large numbers of persons in a population with low prevalence of a disease leads to many false-positives; we determined the percentage of true vs false-positive HCV antibody (anti-HCV) test results among 2007-2012 participants in the National Health and Nutrition Examination Study (NHANES), a nationally representative study with approximately 1% HCV infection prevalence, much lower than in groups typically recommended for HCV screening. Anti-HCV test confirmation was performed using a recombinant immunoblot assay (RIBA) test and follow-up HCV RNA testing. Overall, of 22,359 NHANES participants tested, 479 (2.1%) were anti-HCV screening reactive and were tested for RIBA; of these 323 (68%) confirmed as true positive and 105 (22%) were false-positives. Many others (49, 10.3%) were RIBA indeterminate and likely false-positive. Among all anti-HCV screening reactive cases tested for HCV RNA, 218 (51.4%) were HCV RNA positive representing current infection.

Introduction

Screening for HCV infection is recommended in the US for populations considered to be at risk for infection, such as persons who inject drugs (PWIDs) and persons with a higher prevalence of HCV infection than the general population, such as persons born between 1945 and 1965.

Anti-HCV- positive/HCV RNA negative results may indicate either a true past resolved HCV infection (as approximately 20% of all acute infections spontaneously resolve), or a false-positive screening test. The predictive value positive of laboratory tests is typically much reduced in populations with prevalence <10%. We sought to determine the prevalence of false-positive vs true-positive anti-HCV screening tests among participants in the 2007-2012 National Health and Nutrition Examination Survey (NHANES), a nationally representative sample of the US non-institutionalized civilian population (10).

Methods

During 2007-2012 the initial screening anti-HCV test was performed on all NHANES examinees aged 6 years or older. Testing for anti-HCV in serum or plasma was conducted using anti-HCV chemiluminescent assay (CIA) on VITROS automated immunodiagnostic platform (Ortho Clinical Diagnostics, Raritan, NJ). Signal to cut-off ratios ≥1.0 were considered to be anti-HCV reactive. Reactive specimens were then tested using a confirmatory recombinant immunoblot assay (RIBA) (Chiron RIBA HCV 3.0 Strip SIA), an in vitro qualitative immunoassay for the detection of anti-HCV in human serum or plasma. (Note that RIBA confirmatory test for HCV antibody assay positive samples no longer available.)

RIBA-positive samples were reported as positive for anti-HCV, RIBA-negative samples were reported as negative for anti-HCV, and RIBA-indeterminate results were reported as indeterminate. Serum samples that were confirmed positive or indeterminate for RIBA were further tested for HCV RNA using the COBAS AMPLICOR HCV Test, version 2.0 (Roche Diagnostics, Indianapolis, Indiana), on the COBAS AMPLICOR Analyzer (Roche Diagnostics).

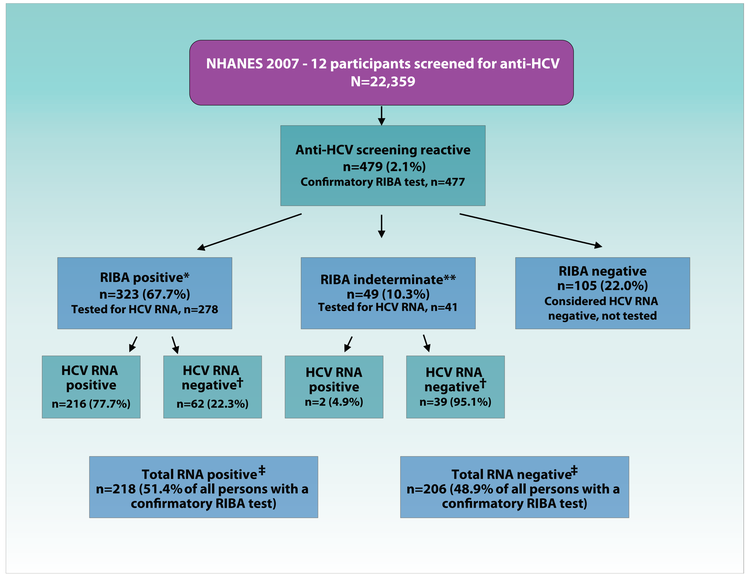
Case definitions

Persons testing anti-HCV reactive and RIBA positive were considered to have had a 'true-positive' anti-HCV test. Those testing anti-HCV reactive and RIBA indeterminate were categorized as having unknown anti-HCV status (although most commonly indeterminate results are associated with false-positive anti-HCV tests. Persons testing anti-HCV reactive and RIBA negative were considered to have had a 'false-positive' anti-HCV screening test.

Persons with a 'true-positive' anti-HCV test and a negative HCV RNA test were considered to have had past resolved infection. For those testing RIBA-indeterminate with a negative HCV RNA test result we were unable to differentiate between past resolved infection and a false-positive anti-HCV result with no prior infection.

All persons with a positive test for HCV RNA were considered to have current HCV infection; all those with a negative test for HCV RNA were considered to be currently uninfected.

Figure. Testing flow diagram



*Persons testing anti-HCV screening reactive and RIBA positive were considered to have had a 'true-positive' anti-HCV test.

**Persons testing anti-HCV screening reactive and RIBA indeterminate were of unknown anti-HCV confirmatory status.

¶ Persons testing anti-HCV screening reactive and RIBA negative were considered to have had a 'false-positive' anti-HCV test and to be HCV RNA negative13.

† The 62 persons with a 'true-positive' anti-HCV test and a negative HCV RNA test were considered to have had past resolved infection. For the 39 RIBA-indeterminate persons with a negative HCV RNA test we were unable to differentiate between past resolved infection and a false-positive anti-HCV result with no prior infection.

‡All persons with a positive test for HCV RNA were considered to have active chronic infection; all those with a negative test for HCV RNA were considered to be currently uninfected.

Results (Figure)

- Of 22,359 NHANES participants tested for anti-HCV by CIA during 2007-2012, 479 (2.1%) were anti-HCV reactive. Of these, 477 (99.6%) had a confirmatory RIBA test and were included in further analysis.
- Among the 424 anti-HCV positive participants with known HCV RNA status, 218 (51.4%) were HCV RNA positive indicating current infection and 206 (48.9%) were HCV RNA negative indicating no current infection. (Figure)
- Overall, of 22,359 NHANES participants tested, 479 (2.1%) were anti-HCV screening reactive and were tested for RIBA; of these 218 (51%) were current infections, and 105 (22%) were false-positives. Many others (49, 10.3%) were RIBA indeterminate and most were also likely false-positive; among these only 2 (4.9%) represented current infection.

Discussion

- Screening persons in a population with low prevalence of a disease leads to many false-positives that may in turn have health, economic and psychological impacts on patients, providers, and health systems.
- In this sample with 1% prevalence of HCV infection, about seven of every ten screening-reactive anti-HCV results (68%) were true-positives and two of ten (22%) false-positives.
- One in 10 (10%) was "indeterminate," of which most were also likely false-positive (12).
- Based on our overall HCV RNA prevalence, clinicians and health researchers might expect that only approximately half of persons testing anti-HCV reactive among a population with similar prevalence (approximately 1%) would have a positive HCV RNA result indicating current infection. All patients with a positive HCV RNA result should be evaluated by a practitioner with expertise in assessment of liver disease severity and treatment.

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