TECHNICAL SERIES

Hepatitis C Screening

Overcoming Challenges

...Setting trends

HEPATITIS C VIRUS (HCV)

Hepatitis C is an infectious disease caused by Hepatitis C Virus (HCV) which primarily affects the liver.
The Hepatitis C virus is the major cause of the disease formerly known as non-A non-B post transfusion hepatitis. The virus can cause both acute and chronic hepatitis, ranging in severity from a mild illness lasting a few weeks to a serious, lifelong illness.
HCV, a single stranded RNA virus, is a member of the family Flaviviridae. Six major genotypes (1-6) and a series of subtypes of HCV have been identified. Genotypes 1-3 show a worldwide distribution while genotypes 4 and 5 appear predominantly in Africa and genotype 6 in Asia.

GENOTYPES & SUBTYPES

In addition to the impressive heterogeneity that often exists amongst HCV sequences present within an infected individual, (quasispecies variation) there is also a remarkable genetic heterogeneity and divergence amongst the sequences that have been recovered from different individuals (strain and genotype variations). Based on HCV sequences recovered from multiple geographical regions of the world, there are at least six major genotypes of the HCV that have been identified, and many more are in the process of being characterised. At the second International Conference of HCV and related viruses, a consensus nomenclature system was proposed for the future studies of the HCV genotypes and subtypes.
According to this system the HCV is classified on the basis of their nucleotide sequence into major genetic groups designated as “genotypes” and are assigned a number (Arabic numerals) in the order of their discovery. The more closely related HCV strains within same genotypes are designated “subtypes” and are assigned lower case letters (in alphabetical order) in the order of their discovery. The complex of genetic variants found within an infected individual's isolate are termed as the “quasi species”. It is hypothesized that the distinct viral quasispecies play a role in the pathogenesis and progressive HCV infection. Due to the sequence variability of the quasispecies post infection, HCV is present in patients as a pool of viruses representing different epitopes. Modification of both B and T epitope patterns during HCV infection have been observed and clones contribute to HCV evasion from the immune system.

Terminology used in studies related to the HCV genomic heterogeneity

Terminology	Definition	% Nucleotide* similarity
Genotype	Genetic heterogeneity among different HCV Isolates	65.7-68.9
Subtype	Closely related isolates within each of the major genotypes	76.9 - 80.1
Quasispecies	Complex of genetic variants within individual isolates	90.8 -99.0
* % Nucleotide Similarity refers to the nucleotide sequence identities of the full - length sequences of the HCV genome.		

Comparative sequence analysis amongst HCV subtypes

Comparative sequence analysis among HCV subtypes of a 222-nucleotide segment derived from the viral NS5 region*											
	% Similarity to										
Subtype	**1a**	**1b**	**1c**	**2a**	**2b**	**2c**	**3a**	**3b**	**4a**	**5a**	**6a**
1a	100	81	85	65	66	63	67	66	68	69	64
1b		100	77	64	67	64	67	71	64	70	65
1c			100	68	70	67	65	70	64	61	61
2a				100	82	77	67	67	66	66	68
2b					100	81	64	69	65	67	66
2c						100	64	65	65	66	65
3a							100	79	65	67	64
3b								100	66	68	61
4a									100	66	66
5a										100	68
6a											100
*Nucleotide position 7975 to 8196 of the prototype virus.											

The phylogenetic grouping of HCV strain appears to be independent of the segment of genome that is analysed.
Substantial regional differences appear to exist in the distribution of HCV genotypes. Although genotypes 1, 2 and 3 appear to have a worldwide distribution, their relative prevalence varies from one geographical area to another.
HCV subtypes 1a and 1b are most common in USA and also predominant in Europe. Subtype 1b is responsible for upto 73% of the HCV infections in Japan. Subtype 2c is found commonly in north Italy whereas subtype 3a is particularly prevalent in IV drug users in Europe and North America. The genotype 4 is prevalent in North Africa and the Middle East and 5 and 6 seems to be confined to South Asia and Hong Kong respectively. Genotype 7, 8, 9 have been identified in Vietnamese patients and 10 and 11 have been identified in Indonesia.
In India, genotype 1 and 3 are common to all parts of India. Genotype 3 is predominant (63.85%) followed by Genotype 1 (25.72%). Genotype 3 is most common in northern, eastern & western parts. Genotype 1 is common in southern part. An increasing trend in prevalence of 4 & 6 Genotypes is observed in India. 4 is found in south India patients from Andhra Pradesh & Tamil Nadu & 6 is found in north eastern patients. Genotype 2 is rarely reported &Genotype 5 not yet reported in India.

The presence of numerous genotypes may provide clues about the historical origin of the HCV as well as proof that HCV has been endemic in these areas for a long time.

TRANSMISSION

HCV is a blood borne virus and the most common modes of infection are through exposure to small quantities of blood. This may happen through injection drug use, unsafe infection practises, unsafe health care, and the transfusion of unscreened bold and blood products.
Some modes of transmission of hepatitis C virus are well documented and widely accepted; others are less well defined and require further study. It is clear that HCV is most frequently transmitted through large or repeated direct percutaneous exposures to infected blood. The two most common exposures associated with transmission of HCV are blood transfusion and injection drug use.

- **Blood Transfusion / Receipt of Blood Products**
  Early case-control studies of patients with newly acquired, symptomatic non-A, non-B hepatitis found a significant association between disease acquisition and a history six months prior to illness of blood transfusions, injection drug use, health care employment with frequent exposure to blood, personal contact with others who had hepatitis, multiple sexual partners or low socioeconomic status.

- **Injection Drug Use**
  Injection drug use has been the principal mode of transmission of HCV since the 1970's. In comparison to other viral infections, HCV is more rapidly acquired after initiation of intravenous drug use. In addition, rates of HCV among young injecting drug-users are four times higher than HIV infection. Studies of injection drug users have demonstrated that the prevalence of HCV infection in them is extremely high, with up to 90% having been exposed. In addition, the incidence of new infections is also high, with seroconversion rates of 10-20 percent per year of injecting. Duration of injecting is the strongest single predictor of risk of HCV infection among injection drug users.

- **Sexual Transmission**
  The topic of sexual transmission of HCV has been controversial. It is believed that HCV can be transmitted sexually, but that it is inefficient -- meaning, it is not easy or likely to pass the virus during sex. On the other hand, HCV infection is very efficient when it is passed from the blood of one person to the blood of another person, such as when people share needles for drug use. The frequency of HCV transmission between monogamous sex partners is very low according to most studies. However, the likelihood of sexual transmission of HCV is increased under any of the following circumstances:
  - Having multiple lifetime sex partners.
  - Engaging in rough sex such as anal sex.
  - Having a history of a sexually transmitted disease.
  - Having HIV
  - Having sex with a prostitute or intravenous drug user
  - Having sex during menstruation or whenever blood is present

Other Modes of Transmission

- **Household Transmission**
  The prevalence of HCV among household contacts of people with HCV infection is low. Care providers need only advise patients to take "common sense" precautions such as not sharing items that may have blood on them (e.g., razorblades, toothbrushes) and properly covering open cuts or wounds.
  The study of HCV transmission among household contacts is complicated by the difficulty of ruling out other possible modes of acquisition.

- **Occupational Exposures**
  Health care workers who have exposure to blood are at risk of infection with HCV and other blood borne pathogens. The prevalence of HCV infection, however, is no greater in health care workers, including surgeons, than for the general population. According to the CDC, the average rate of anti-HCV seroconversion after unintentional needle sticks or sharps exposure from an HCV-positive source is 1.8% (range 0%-7%).

SYMPTOMS

Hepatitis C infection is mostly asymptomatic. Approximately 70%–80% of people with acute Hepatitis C do not have any symptoms. Some people, however, can have mild to severe symptoms soon after being infected, including:

- Fever
- Fatigue
- Loss of appetite
- Nausea
- Vomiting
- Abdominal pain
- Dark urine
- Clay-colored bowel movements
- Joint pain
- Jaundice (yellow colour in the skin or eyes)

SCREENING AND DIAGNOSIS OF HCV INFECTION

Due to the fact that acute HCV infection is usually asymptomatic, few people are diagnosed during the acute phase. In those people who go on to develop chronic HCV infection, the infection is also often undiagnosed because the infection remains asymptomatic until decades after infection when symptoms develop secondary to serious liver damage.

HCV infection is diagnosed in 2 steps:

- Screening for anti-HCV antibodies with a serological test identifies people who have been infected with the virus.
- If the test is positive for anti-HCV antibodies, a nucleic acid test for HCV ribonucleic acid (RNA) is needed to confirm chronic infection because about 30% of people infected with HCV spontaneously clear the infection by a strong immune response without the need for treatment. Although no longer infected, they will still test positive for anti-HCV antibodies.

After a person has been diagnosed with chronic hepatitis C infection, they should have an assessment of the degree of liver damage (fibrosis and cirrhosis). This can be done by liver biopsy or through a variety of non-invasive tests.

In addition, these people should have a laboratory test to identify the genotype of the hepatitis C strain. There are 6 genotypes of the HCV and they respond differently to treatment. Furthermore, it is possible for a person to be infected with more than 1 genotype. The degree of liver damage and virus genotype are used to guide treatment decisions and management of the disease.

LABORATORY ASPECTS OF HCV TESTING

The laboratory diagnosis of HCV infection is usually made on the basis of the detection of circulating antibodies. Serological tests for detecting antibodies to HCV are generally classified as screening tests or confirmatory tests. Screening tests provide the presumptive identification of antibody-positive specimens, while confirmatory tests are used to confirm that specimens found reactive with a particular screening test contain antibodies specific to HCV. Several screening tests may be used in a testing algorithm to determine a final sero-status. These second and/or third line tests are generally referred to as supplemental tests.

The most widely used anti-HCV screening tests are ELISAs as they are the most appropriate for screening large numbers of specimens on a daily basis, as is the case in blood transfusion services in industrialized countries. Currently, more sensitive tests such as Chemiluminescence are also developed which are able to detect the analyte at a very low concentration thereby further reducing the diagnostic window period and ensuring early diagnosis of HCV infection. However, many blood transfusion services in resource limited countries process only limited numbers of specimens. Hence, individual tests would be more appropriate.

Several simple, instrument and electricity-free screening tests have been developed including agglutination, immunofiltration (flow through) and immunochromatographic (lateral flow) membrane tests. A positive result is indicated by the appearance of a coloured dot or line, or the presence of an agglutination pattern. While most of these tests can be performed in less than 10 minutes, other simple tests are less rapid and their performance requires 30 minutes to 2 hours. The results are read visually. In general, these simple/rapid (S/R) tests are most suitable for use in laboratories that have limited facilities and/or process low numbers of specimens daily.

Confirmatory assays that are commercially available for the diagnosis of HCV include Molecular HCV RNA tests based on Nucleic Acid Amplification Technologies (NAT). This assays are available both as qualitative and quantitative test. The quantitative test are capable of detecting HCV RNA down to 100 copies/ml.

- **GENERATIONS OF HCV TEST**

  Following the discovery of HCV and the sequencing of its genome in 1989, the first generation of anti-HCV ELISAs was produced using, as antigens, recombinant proteins complementary to the NS4 region of the HCV genome. These assays showed limited sensitivity and specificity. Second generation tests, which included recombinant or synthetic antigens from the putative core and non-structural regions NS3 and NS4 resulted in a marked improvement in sensitivity and specificity. The third generation tests include antigens from the NS5 region of the genome, in addition to those used in second generation assays. Third generation tests have improved sensitivity, though this has been shown to be more likely due to the improvements to the core and NS3 antigens rather than the inclusion of the NS5 antigen. However, despite these improvements, the time between infection with HCV and the appearance of detectable antibodies (window period) is generally more than 40 days (Schreiber et al, 1996; Barrera et al, 1995). It is anticipated that test kits will undergo further improvement in the future.

  The term generation is used to show the development of the kits over time by the manufacturers in their effort to increase the specificity and sensitivity of the assays and each generation does not denote a specific format or configuration of the assay. Some manufacturers use the term generation in their kit title which does not mean a specific format but is indicative of further developments in their assay.

Scenario of HCV testing in India.

Hepatitis C virus (HCV) causes both acute and chronic infection. Acute HCV infection is usually asymptomatic, and is only very rarely (if ever) associated with life-threatening disease. About 15–45% of infected persons spontaneously clear the virus within 6 months of infection without any treatment. The remaining 60–80% of persons will develop chronic HCV infection. Of those with chronic HCV infection, the risk of cirrhosis of the liver is between 15–30% within 20 years.

The above clearly suggest that Hepatitis C infection is dangerous and could be life-threatening. Still HCV screening is not performed routinely in many laboratories as clinicians are not aware about the increasing prevalence of HCV infection in India.

Most of the laboratories perform HIV and HBsAg screening of all the patients as prescribed by the clinicians. Rural India remains unaware about the rising threat to Humanity. Due to this, the health care workers become vulnerable to HCV as they are in repeated contact with Human blood or blood products.

HCV screening is mostly performed in Dialysis centres. Even Blood banks have to test each blood component for HCV following the guidelines of Transfusion Transmitted Infections. (TTI).

Considering the rising cases of HCV infections in India, the need is to create awareness about HCV infection and incorporate HCV screening in routine profiles such as Antenatal Profile, Pre-operative cases, routine Health check-ups and also during admission of patients in the hospital.

Challenges in HCV testing

HCV screening (diagnosis) is associated with high number of false positivity in the areas with low prevalence of HCV infection. This means that out of the total number of samples which are reactive with antibody test, the probability of samples being true positives decreases. According to Centre for Disease Control & Prevention (CDC), the false positive results averages approximately 35-40 % in case of areas with low prevalence for HCV infection.

Currently, majority of laboratories report positive anti-HCV results based on a positive screening assay alone. When a single screening test is used for testing in a population with a very low prevalence of HCV infection, the probability that a person is infected when a reactive test result is obtained (i.e. the positive predictive value) is low, since the majority of people with reactive results are not infected (i.e. the positive results are false). This problem occurs even when a test of excellent quality and having high specificity is used.

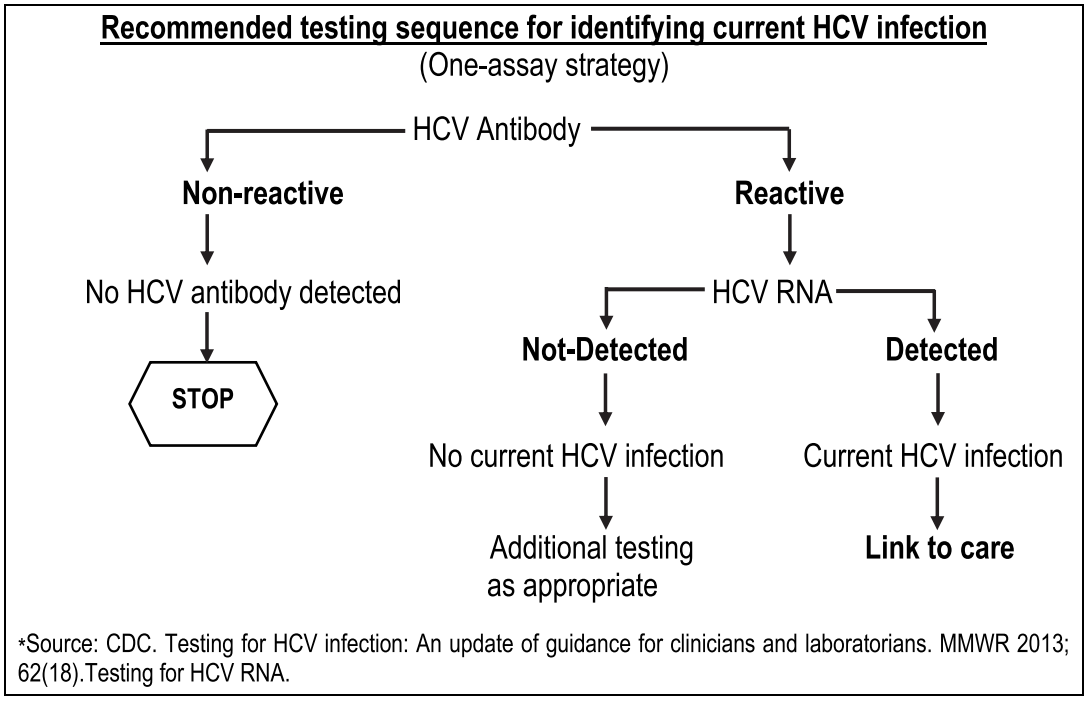
The current trends in testing also leads to lack of differentiation between current and resolved infection. This is important in HCV infection as 15-25% of new infections spontaneously resolve. Those who resolve the infection may still test positive in the antibody assays for many years following the clearance of the virus.

Accuracy can be improved if additional supplemental or confirmatory test(s), of equal or higher specificity, are used to retest all those samples found reactive by the screening test. Screening and supplemental tests, to be used in an HCV confirmatory strategy, must be selected carefully to ensure that common false reactivity between these assays does not occur.

The discontinuation of Immunoblot assays as supplemental / confirmatory tests has further increased the difficulties in HCV testing as majority of the people are not aware about the new testing algorithm. By creating the awareness and educating laboratories on the recommended HCV testing algorithm, laboratories will overcome the challenges faced in Hepatitis C testing.

RECOMMENDED HCV TESTING ALGORITHM

Testing for HCV infection begins with either a rapid or ELISA / CLIA assay for HCV antibody in serum or plasma. An FDA-approved test for HCV antibody should be used. In order to appropriately identify anyone with active HCV infection, two laboratory tests must be conducted. The first is a test that screens for HCV antibodies. If this initial HCV antibody test is reactive, it should be immediately followed with an HCV RNA test. If HCV RNA is detected in serum or plasma, active HCV infection is confirmed. (See HCV testing algorithm).



*Source: CDC. Testing for HCV infection: An update of guidance for clinicians and laboratorians. MMWR 2013; 62(18).Testing for HCV RNA.

- **Testing for HCV RNA.**

  An FDA-approved NAT assay intended for detection of HCV RNA in serum or plasma from blood of at-risk patients who test reactive for HCV antibody should be used. There are several possible operational steps toward NAT after initial testing for HCV antibody:

  1. Blood from a subsequent venepuncture is submitted for HCV NAT if the blood sample collected is reactive for HCV antibody during initial testing.
  2. From a single venepuncture, two specimens are collected in separate tubes: one tube for initial HCV antibody testing; and a second tube for HCV NAT if the HCV antibody test is reactive.
  3. The same sample of venepuncture blood used for initial HCV antibody testing, if reactive, is reflexed to HCV NAT without another blood draw for NAT.
  4. A separate venepuncture blood sample is submitted for HCV NAT HCV if the antibody test for initial testing of HCV antibody has used finger stick blood.

- **Interpretation of results of tests for hepatitis c virus (HCV) infection**

TABLE. Interpretation of results of tests for hepatitis c virus (HCV) infection and further actions.

Test Outcome	Interpretation	Further action
HCV antibody non-reactive	No HCV antibody detected	Sample can be reported a non-reactive. No further action required. If recent HCV exposure in person tested is suspected, test for HCV RNA.*
HCV antibody reactive	Presumptive HCV infection	A repeatedly reactive result is consistent with current HCV infection, or past HCV Infection that has resolved, or biologic false positivity for HCV antibody. Test for HCV RNA to identify current infection.
HCV antibody reactive HCV RNA detected	Current HCV infection	Provide person tested with appropriate counselling and link person tested to medical care and treatment. †
HCV antibody reactive HCV RNA not detected	No current HCV infection	No further action required in most cases. If distinction between true positivity and biologic false positivity for HCV antibody is desired, and if sample is repeatedly reactive in the initial test, test with another HCV antibody assay. In certain situations follow up with HCV RNA testing and appropriate counselling.§

* If HCV RNA testing is not feasible and person tested is not immunocompromised, do follow-up testing for HCV antibody to demonstrate seroconversion. If the person tested is immunocompromised, consider testing for HCV RNA.
† It is recommended before initiating antiviral therapy to retest for HCV RNA in a subsequent blood sample to confirm HCV RNA positivity.
§ If the person tested is suspected of having HCV exposure within the past 6 months, or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.

CDC has recommended that a person be considered to have serologic evidence of HCV infection only after an anti-HCV screening-test-positive result has been verified by a more specific serologic test or a Nucleic Acid Test (NAT). This more specific, supplemental testing is necessary, particularly in populations with a lower prevalence of disease, to identify and exclude false positive screening test results.

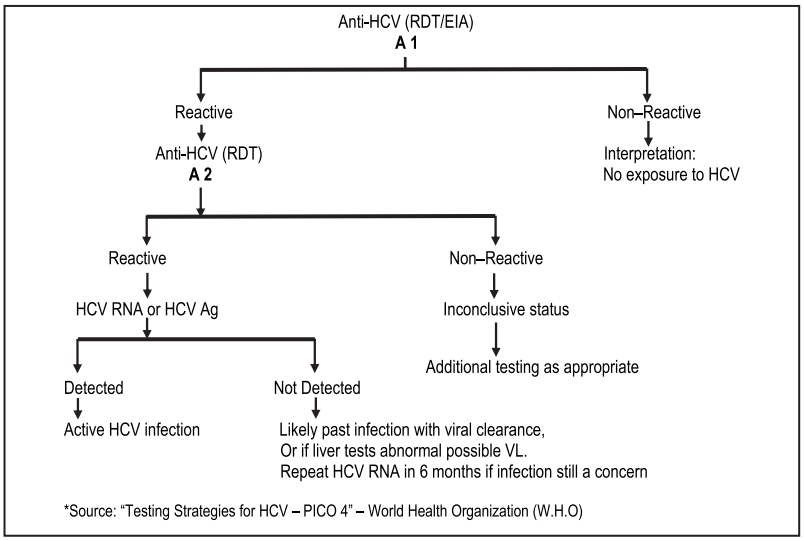
BIOCHEMICAL TEST PANEL FOR DIAGNOSING HCV IN CONJUGATION WITH IMMUNOASSAYS

Biochemical liver panel play an important role as a supplementary to Immunoassays for diagnosing HCV infection. These test measures the activity in the liver. During HCV infection, the levels of 2 enzymes i.e. Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) in the patient sample provides a useful insight on the condition of liver.
When HCV infects liver, the hepatocytes produces higher than normal ALT levels, indicating inflammation of liver. In acute phase, ALT may increase to 10 times the normal levels. When HCV becomes chronic, ALT drops to a relatively low level, but remains persistently high.
AST is also a liver enzyme, which is often elevated in chronic phase. AST levels are usually lower than ALT but during cirrhosis, AST levels may increase than ALT indicating worsening damage to the liver.

STANDARDISED TESTING STRATEGIES FOR HCV

Word Health Organization (W.H.O) recommends standardized testing strategies to maximize accuracy while minimizing cost and increasing simplicity. A testing strategy describes a testing sequence for a specific testing objective, taking into consideration the presumed prevalence of the analyte to be tested in the population. In both high and low prevalence settings, more than one serological assay may be required to establish exposure to HCV.
Antibody testing is an important first step, but antibody detection by using a single assay is not sufficient to identify someone with an active HCV infection. To ensure the complete and timely diagnosis of HCV, HCV reflex testing is recommended to ensure that the HCV RNA test is performed following all reactive HCV antibody screening assays.

- **Supplemental / Reflex testing**
  Reflex testing simply means a laboratory will automatically perform a second test, or refer the specimen for the second test. When the result of the first and second test meets specific criteria, then the laboratory will perform an HCV RNA test on the specimen as it is repeatedly reactive for HCV antibody.



Challenges in following the recommended HCV testing algorithm & strategies in India

The recommended testing algorithm will help in overcoming the challenges faced in HCV testing but the most critical issue is the accessibility and affordability to HCV RNA test. HCV RNA test are still not available in most parts of India. The laboratories situated in rural parts have to rely on reference centres which are mostly situated in cities. The financial resources of such laboratories are also limited. Moreover, it becomes difficult to appoint technicians who are skilled and technically sound to perform RNA testing. The accessibility to HCV RNA is limited also in urban areas.

Even the laboratories in interiors parts of India lack financial and other resources for upgraded / latest technologies such as ELISA or CLIA which are more sensitive screening tests. Unskilled workers

Follow-up testing is also a challenge in India. It becomes difficult to follow-up patients for requirement of repeat / fresh sampling, monitoring and post treatment follow-up due to lack of awareness and information about HCV infection amongst the people. Further testing an antibody positive patient with HCV RNA is generally not possible considering the paying capacity of the patients.

Moreover, the testing strategy designed by Word Health Organization (W.H.O) suggest of using two different assays. When the result of two assays are reactive, the sample is termed as reactive for HCV. But in case of discrepancy, wherein one assay is reactive and the other is non-reactive, it is suggested to report the status of the sample as inconclusive and recommends further testing, which is to test with HCV RNA.

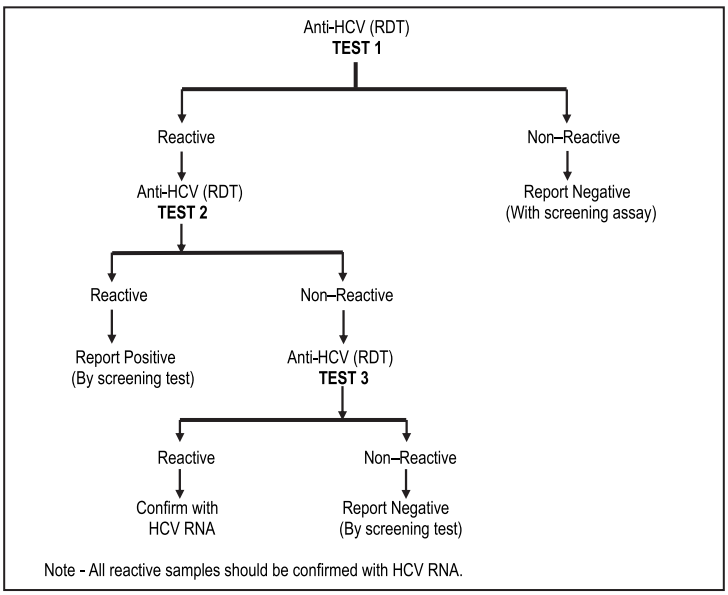
As the disease prevalence in India is low, the probability of producing inconclusive results is high. The inconclusive results will further add to the challenge of reporting and as mentioned earlier the availability of HCV RNA PCR is also subjective. To overcome such situation, a third alternate assay can be incorporated in the same strategy. The results of the third assay will help the laboratories in reporting the status of the patients and recommend them for further confirmatory testing.

ALTERNATE REFLEX TESTING

Considering the challenges faced by the laboratories in India, the following alternate reflex testing can be adopted to report the status of HCV infection of a patient and reduce the cost of HCV RNA testing for each antibody reactive sample.

- **Alternate Reflex testing**
  - A. Rapid assay reflex testing
  - B. ELISA / CLIA reflex testing

A. Rapid assay reflex testing



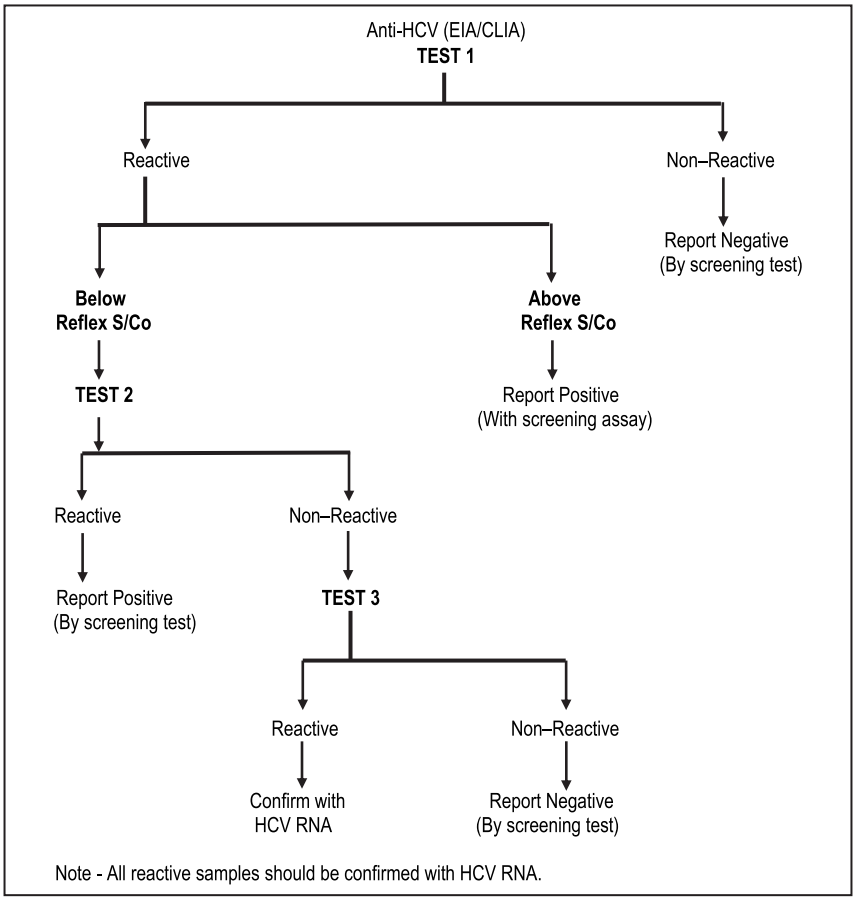
B. **ELISA / CLIA reflex testing**

Use of Signal-to-Cut–Off Ratio.

The recommended anti-HCV testing algorithm has been expanded to include an option that uses the signal-to-cut–off (s/co) ratios of screening-test--positive results. This can serve as an alternative to a supplemental test in some circumstances, minimizing the number of specimens that require supplemental testing and providing a result that has a high probability of reflecting the person's true antibody status.

Setup Reflex signal to Cut-off Ratio

(Specific S/Co ratio that would predict a true antibody positive result ≥ 95% time, through comparative testing on HCV RNA)



- **Establishing Reflex S/Co ratio**

  Signal-to-cut–off ratio is calculated by dividing the optical density (OD) value of the sample being tested by the OD value of the assay cut-off for that run. Analysis of enzyme immunoassay and Chemiluminescence assay data indicates that s/co ratios can be used to predict supplemental test-positive results. A specific s/co ratio can be identified for each test that would predict a true antibody-positive result (as defined by the results of supplemental testing) ≥95% of the time, regardless of the anti-HCV prevalence or characteristics of the population being tested).

  1. Select "N" number of samples repeatedly reactive with HCV antibody ELISA / CLIA screening test.
  2. Supplemental testing of these samples with HCV RNA/ Western Blot / RIBA.
  3. Analyse & compare the supplemental test results with S/Co ratio of ELISA /CLIA.
  4. Calculate the average S/Co ratio for – False positive results (ELISA/CLIA) and True Positive results (by Supplemental test)
  5. Determine the specific S/Co ratio that predicts a true antibody-positive result >95% of the time.
  6. Establish as Reflex S/Co ratio.

ROLE OF BIOCHEMICAL TEST PANEL

The liver panel test i.e. Alanine aminotransferase (ALT or SGPT) and Aspartate aminotransferase (AST or SGOPT) provide a useful insight and are important marker in conjugation with Immunoassays for the diagnosis of HCV infection.

Almost all laboratories today are equipped with biochemistry analysers which are semi-automated. These analysers are efficient to perform all type of biochemical tests and are open systems i.e. reagents from different manufacturer can be used.

Moreover, the biochemical tests are easy to perform and may not require skilled manpower. Also, factors such as availability, affordability of the laboratories and paying capacity of the patients are not limited.

The laboratories should consider these biochemical reactions in conjugation with Immunoassays before reporting the results of HCV status.

PREVENTION OF HCV INFECTION

The key to reducing the incidence of HCV is by decreasing exposure to contaminated blood and reducing post transfusion HCV infection rates. This can be achieved by screening all patients for HCV and utilizing high sensitivity screening test, as per World Health Organization (W.H.O) recommendation, which ensures early detection of HCV infection.

Nosocomial HCV transmission can be controlled through adherence to universal precautions and infection control protocols diligently.

TREATMENT

Hepatitis C does not always require treatment as the immune response in some people will clear the infection, and some people with chronic infection do not develop liver damage. When treatment is necessary, the goal of hepatitis C treatment is cure. The cure rate depends on several factors including the strain of the virus and the type of treatment given.

The standard of care for hepatitis C is changing rapidly. Sofosbuvir, daclatasvir and the sofosbuvir/ledipasvir combination are part of the preferred regimens in the WHO guidelines, and can achieve cure rates above 95%. These medicines are much more effective, safer and better-tolerated than the older therapies. Therapy with DAAs can cure most persons with HCV infection and treatment is shorter (usually 12 weeks). WHO is currently updating its treatment guidelines to include pan genotypic DAA regimens and simplified laboratory monitoring. Meanwhile, there remains a very limited role for PEGylated interferon and ribavirin in certain scenarios.

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