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Positive Malaysian Treatment Access & Advocacy Group

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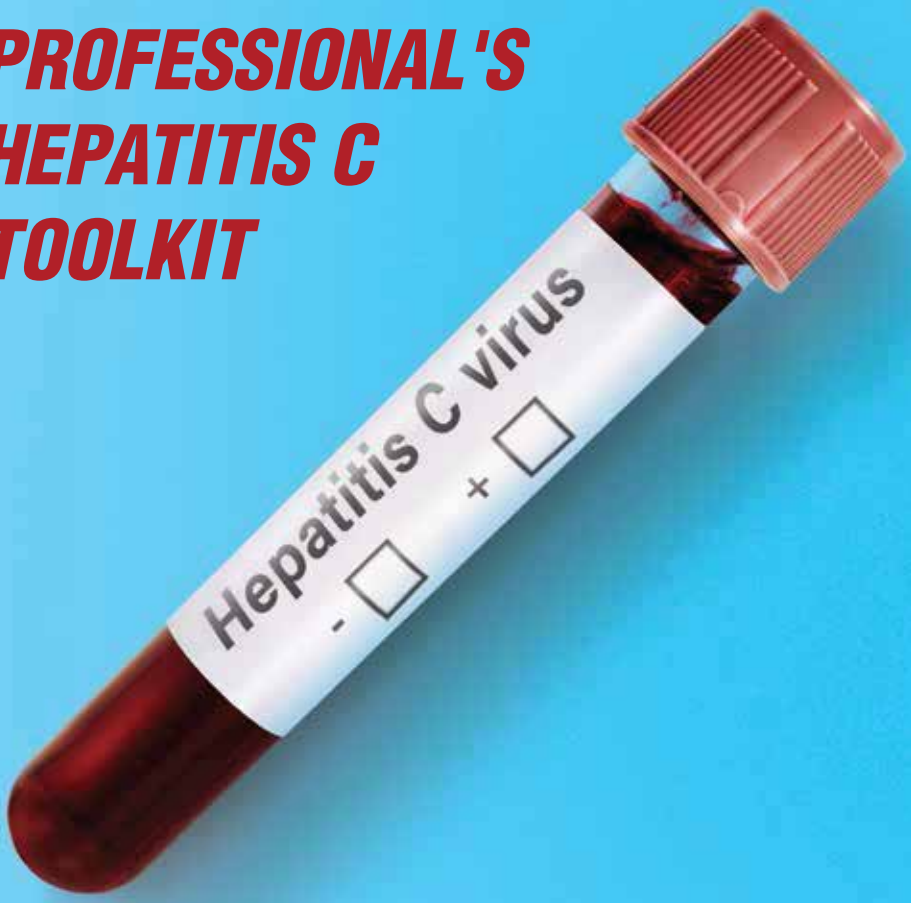
HEALTHCARE PROFESSIONAL'S HEPATITIS C TOOLKIT



95% of people living with Hepatitis C are UNAWARE that they are infected.

INTRODUCTION

World Health Organization (WHO) estimates that 71 million people are chronically infected with the hepatitis C virus (HCV), while the viremic prevalence among adults in Asia Pacific countries ranges from 0.4 to 1.1%. In Malaysia, total adult population size with chronic HCV infection was estimated at 380,000. Genotype 1 accounts for half of hepatitis C cases followed by genotype 3 worldwide. In Malaysia, the predominant HCV genotype is genotype 3 (63%) followed by genotype 1 (36%). Majority of patients contracted the infection through contaminated blood by sharing infected needles among intravenous drug users (IVDU) or receiving infected blood or blood products. Malay male-injecting drug user is the most high-risk population, which represented 59% of all HCV patients in Malaysia. The most common risk factor amongst women is blood transfusion which represented 63% of all women with the infection.

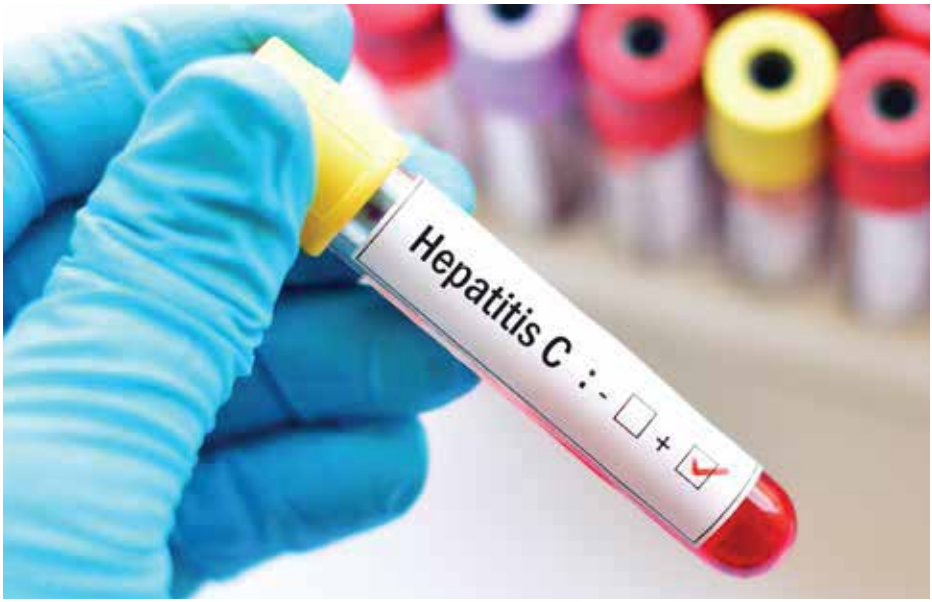
The major burden of hepatitis C disease comes from the complications following chronic infection. As many as 350,000 deaths happens per year as a results of cirrhosis and hepatocellular carcinoma due to HCV infection. The risk of progression to liver cirrhosis increases with increasing duration of infection, with 20% risk of cirrhosis within 20 to 30 years. Following development of cirrhosis, the annual risk of developing decompensated cirrhosis and hepatocellular carcinoma is approximately 6% and 5% respectively. With decompensated cirrhosis, the mortality risk in the following years is almost 20%. In Malaysia, it was projected that the disease burden related to Hepatitis C will rise steeply over the next few decades, with increasing deaths related to cirrhosis and its complications, particularly related to decompensated cirrhosis and hepatocellular carcinoma. To address the rising Hepatitis C disease burden, we need to strengthen preventive measures for Hepatitis C transmission, identify undiagnosed cases and increase access to affordable Hepatitis C treatment.

The asymptomatic presentation of early HCV infection often leads to many infected

individuals being unaware of their infection and leads to delayed diagnosis and initiation of treatment. WHO has established the Global Health Sector Strategy 2016-2021 on viral hepatitis, which recommended all countries to aim for the elimination of viral hepatitis by 2030. This target has provided individual countries with defined goals and visible landmarks, towards achieving HCV elimination through comprehensive screening and treatment program. In order to achieve the target, large proportion of individuals needs to be identified, diagnosed, linked to clinical care and started on treatment. It is crucial for Malaysia to "Find the Missing Thousands" and this initiative is to encourage the public, especially high-risk groups, to get tested for HCV and help to link affected patients to clinical care to receive treatment.

Recently, access to highly effective HCV treatment has been made available in public hospitals at affordable prices. To meet the 2030 targets treatment uptake scale-up would have to be steeper than currently considered viable, and depends on an enormous scale-up in screening/diagnosis and the provision of treatment and follow-up services. This highlights the urgent need for better HCV control measures, and for supportive policies that lead to improved case-finding and consequent referral to care for HCV treatment.

ABOUT HCV



What are the case definitions for HCV infections?

The specific viral cause of illness cannot be determined based solely on signs, symptoms, history, or current risk factors. It must be verified by specific serologic testing.

How is HCV transmitted?

HCV is transmitted primarily through parenteral exposures to infectious blood or body fluids that contain blood. Possible exposures include:

- Injection drug use
- Received donated blood, blood products, and organs prior to 1994
- Needle stick injuries in health care settings
- Birth to an HCV-infected mother
- Have body piercings or tattoos using unsterilised equipment

How soon after exposure to HCV do symptoms appear?

Most people with chronic HCV infection are asymptomatic or have non-specific symptoms such as chronic fatigue and depression. In those people who do develop symptoms, the average period from exposure to symptoms onset is 2–12 weeks (range: 2–26 weeks).

What are the signs and symptoms of chronic HCV infection?

Most people with chronic HCV infection are asymptomatic or have non-specific symptoms such as chronic fatigue and depression. Many eventually develop chronic liver disease, which can range from mild to severe, including cirrhosis and liver cancer.

Chronic liver disease in HCV-infected people is usually insidious, progressing slowly without any signs or symptoms for several decades. In fact, HCV infection is often not recognized until asymptomatic people are identified as HCV-positive when screened for blood donation or when elevated alanine aminotransferase (ALT, a liver enzyme) levels are detected during routine examinations.

What are the signs and symptoms of acute HCV infection?

People with newly acquired HCV infection usually are asymptomatic or have mild symptoms that are unlikely to prompt a visit to a healthcare professional. When symptoms do occur, they can include:

- Fever
- Fatigue
- Dark urine
- Abdominal pain
- Loss of appetite
- Nausea
- Vomiting
- Joint pain
- Jaundice

What percentage of those infected with HCV develop symptoms of acute illness?

Approximately 20–30% of those newly infected with HCV experience fatigue, abdominal pain, poor appetite, or jaundice.

Can a patient have normal liver enzyme (e.g. ALT) levels and still have chronic Hepatitis C?

Yes. It is common for patients with chronic Hepatitis C to have liver enzyme levels that go up and down, with periodic returns to normal or near normal levels. Liver enzyme levels can remain normal for over a year despite chronic liver disease.

How likely is HCV infection to become chronic?

HCV infection becomes chronic in approximately 75-85% of cases.

HIGH RISK GROUPS

HCV testing is recommended for those:

- Who have certain medical conditions, including persons:

Who have received blood transfusion, blood components, or an organ transplant before 1994.

Who are on hemodialysis.

With persistently abnormal ALT levels.

Who have HIV infection.

Who have injected drugs, including those who injected once or more, many years ago.

Who have body piercings or tattoos using unsterilised equipment.

From populations most affected by HCV infection[1] (i.e. who are either part of a population with high HCV seroprevalence or who have a history of exposure and/ or high-risk behaviours for HCV infection, including above, MSM, transgender, those who use intranasal medications)

With a clinical suspicion of chronic viral hepatitis[2] (i.e. symptoms, signs, laboratory markers). (Strong recommendation, low quality of evidence)

Note: Periodic retesting using HCV nucleic acid tests (NAT) should be considered for those with ongoing risk of acquisition or reinfection.

- HCV-testing based on a recognized exposure is recommended for:

Healthcare, emergency medical, and public safety workers after needle sticks, sharps, or mucosal exposures to HCV-positive blood.

Children born to HCV-positive women.

[1] Includes those who are either part of a population with higher seroprevalence (e.g. some mobile/ migrant populations from high/intermediate endemic countries, and certain indigenous populations) or who have a history of exposure or high-risk behaviours for HCV infection (e.g. PWID, people in prisons and other closed settings, men who have sex with men and sex workers, and HIV-infected persons, children of mothers with chronic HCV infection especially if HIV-coinfected).

[2] Features that may indicate underlying chronic HCV infection include clinical evidence of existing liver disease, such as cirrhosis or hepatocellular carcinoma (HCC), or where there is unexplained liver disease, including abnormal liver function tests or liver ultrasound.

HCV SCREENING & CONFIRMATION

How to test for chronic HCV infection and monitor treatment response?

1. Which serological assay to use?

To test for serological evidence of past or present infection in adults, adolescents and children (>18 months of age),[1] a HCV serological assay (antibody or antibody/antigen) using either a rapid diagnostic test (RDT) or laboratory-based immunoassay formats[2] that meet minimum safety, quality and performance standards[3] (with regard to both analytical and clinical sensitivity and specificity) is recommended.

- 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, RDTs are recommended.
  (Strong recommendation, low/moderate quality of evidence)

2. Serological testing strategies.

In adults and children older than 18 months, a single serological assay for initial detection of serological evidence of past or present infection is recommended prior to supplementary nucleic acid testing (NAT) for evidence of viraemic infection. (Conditional recommendation, low quality of evidence)

[1] This may include fourth-generation combined antibody/antigen assays.

[2] Includes those who are either part of a population with higher seroprevalence (e.g. some mobile/ migrant populations from high/ intermediate endemic countries, and certain indigenous populations) or who have a history of exposure or high-risk behaviours for HCV infection (e.g. PWID, people in prisons and other closed settings, men who have sex with men and sex workers, and HIV-infected persons, children of mothers with chronic HCV infection especially if HIV-coinfected).

[3] Features that may indicate underlying chronic HCV infection include clinical evidence of existing liver disease, such as cirrhosis or hepatocellular carcinoma (HCC), or where there is unexplained liver disease, including abnormal liver function tests or liver ultrasound.

Serological Assays

- Rapid diagnostic tests (RDTs) are single-use disposable assays that are provided in simple-to-use formats that generally require no additional reagents except those supplied in the test kit. They are read visually and can give a simple qualitative result in under 30 minutes.

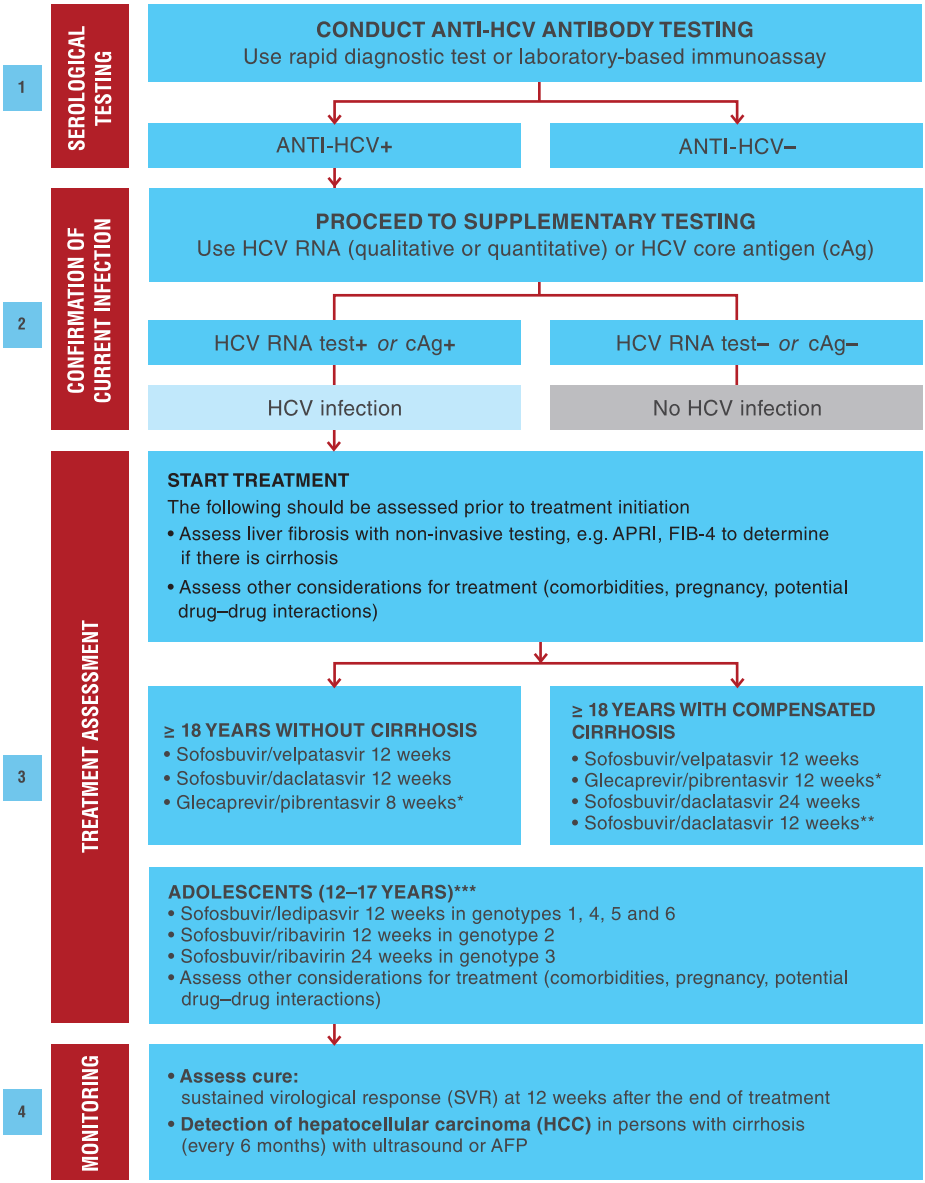
- Most laboratory-based serological immunoassays (EIAs, CLIAs and ECLs) detect antibodies, antigens, or a combination of both and differ only in the mode of detection of immune complexes formed:

  - HCV RNA Nucleic Acid Test (NAT) is useful in establishing the diagnosis of acute HCV infection, since RNA is detectable as early as one week after exposure and at least 4-6 weeks prior to seroconversion as demonstrated in a number of transmission setting.

  - HCV core Antigen (HCVcAg) test requires less technical expertise and is less expensive compared to molecular techniques. HCVcAg assay detects HCV infection as effective as NAT. Also, HCVcAg levels closely follow HCV RNA dynamics and allow clinical monitoring of a patient's therapy, independently of HCV genotype. Detection of HCVcAg, where the assay has comparable clinical sensitivity to NAT technologies, may be considered as an alternative.

WHO HCV GUIDELINES 2018

Summary algorithm for the diagnosis, treatment and monitoring of chronic HCV infection in adults and adolescents



* Persons with HCV genotype 3 infection who have received interferon and/or ribavirin in the past should be treated for 16 weeks.
** May be considered in countries where genotype distribution is known and genotype 3 prevalence is <5%.
*** Treatment in adolescents at this time still requires genotyping to identify the appropriate regimen.
AFP: alpha fetoprotein, APRI: aspartate-to-platelet ratio index, FIB-4: fibrosis stage

NON-INVASIVE TESTS

Transient Elastography (TE) Test/Fibroscan

The use of non-invasive tests to stage the severity of liver disease (ie. scarring) is now well established in the management of patients with chronic liver disease. This is because assessment of liver scarring provides prognostic information and assists in establishing treatment priorities.

Transient elastography (TE) is a simple, safe and efficient way to estimate liver scarring. When performed in the appropriate clinical setting, TE provides a reliable method of detecting cirrhosis and excluding significant fibrosis, particularly when the results are supported by clinical and laboratory data.

Liver hardness is evaluated by measuring the velocity of a vibration wave (also called a 'shear wave') generated on the skin. Shear wave velocity is determined by measuring the time the vibration wave takes to travel to a particular depth inside the liver. Because fibrous tissue is harder than normal liver, the degree of hepatic fibrosis can be inferred from the liver hardness.

Transient Elastography/FibroScan > 12.5 kPa = Cirrhosis

APRI Test

Liver biopsy is the recognised gold standard for liver fibrosis staging but it is expensive and invasive. The aspartate aminotransferase to platelet ratio index (APRI) has been proposed as a non-invasive and readily available tool for the assessment of liver fibrosis in chronic Hepatitis C (CHC).

APRI is a simple and cheap method to ascertain the ratio between aspartate aminotransferase (AST) and platelets and is easy to use in clinical practice. APRI is a serological marker that has satisfactory sensitivity and specificity together with a high predictive value and it can be useful either in the absence of a biopsy or to reduce the frequency with which biopsies need to be carried out to monitor the evolution of chronic Hepatitis C and the right moment for the treatment indication.

AST to Platelet Ratio Index (APRI) Calculator

$$\text{APRI} = \frac{\text{AST Level (IU/L)}}{\text{AST (Upper Limit of Normal) (IU/L)}} \times 100 = \frac{\text{AST Level (IU/L)}}{\text{Platelet Count } (10^9/\text{L})} \times 100 =$$

APRI > 2.0 = Cirrhosis

APRI < 0.5 Rule out significant fibrosis and cirrhosis

MANAGEMENT & TREATMENT

What is the treatment for chronic HCV?

Over 90% of HCV infected persons can be cured of HCV infection regardless of HCV genotype, with 8-12 weeks of oral therapy.

What is the treatment for acute HCV?

Patients may have another blood test after a few months to see if their bodies fight off the virus. If the infection continues for several months, treatment will usually be recommended.

What should be done for a patient with confirmed HCV infection?

HCV-positive patients should be evaluated including assessment of liver function tests, evaluation for severity of liver disease, assesment for HCV treatment, and determination of the need for Hepatitis A and Hepatitis B vaccination.

Is it necessary to do HCV genotyping when managing a person with chronic Hepatitis C?

In certain circumstances. Because there are seven distinct genotypes and more than 67 subtypes of HCV, genotype information may be helpful in making recommendations regarding appropriate treatment regimen.

How many different genotypes of HCV exist?

Seven distinct HCV genotypes and more than 67 subtypes have been identified. Genotype 3 is the most common HCV genotype in Malaysia.

AASLD/IDSA HCV GUIDELINES: RECOMMENDATIONS FOR FIRST-LINE HCV TREATMENT

HCV GT	Regimen	Duration, weeks	
		No Cirrhosis	Compensated Cirrhosis
1	GLE/PIB GZR/EBR* SOF/LDV SOF/VEL	8 12 8 or 12† 12	12 12 12 12
2 or 3	GLE/PIB SOF/VEL	8 12	12 12‡
4	GLE/PIB SOF/VEL GZR/EBR SOF/LDV	8 12 12 12	12 12 12 12
5 or 6	GLE/PIB SOF/LDV SOF/VEL	8 12 12	12 12 12

GLE/PIB:Glecaprevir/Pibrentasvir
GZR/EBR: Grazoprevir/Elbasvir
SOF/LDV: SOF/Ledipasvir
SOF/VEL: SOF/VELPATASVIR

*Only if no baseline NS5A RAS for GT 1a; if NS5A RAS present for GT 1a, EBR/GZR not recommended.

†8 wks of LDV/SOF only if non-black race, HIV-uninfected, and HCV RNA < 6 million IU/mL.

‡Only if no baseline Y93H for GT 3. If Y93H present for GT3, add RBV or choose alternative regimen (consider SOF/VEL/VOX).

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ABOUT MTAAG+:

Positive Malaysian Treatment Access & Advocacy Group (MTAAG+) is a group of local PLHIV was empowered during a ITPC Regional workshop held in Pattaya in September, 2004. They realized the need to form a strong poz-representative in Malaysia to speak out and be heard in international events. After several months of planning and execution, MTAAG+ was formed on the 21st, December, 2005.

MTAAG+'s mission is to develop a national network for better access to ARV treatment and common agenda for all PLHIV & Hep C groups in Malaysia.

www.mtaagplusmalaysia.wordpress.com

RESOURCES

For more information about Hepatitis C, here's a list of resources that you can refer to.

Alaska Native Tribal Health Consortium

World Health Organization (WHO)

World Hepatitis Alliance

European Association for the Study of the Liver (EASL)

Centers for Disease Control and Prevention (CDC)

Ministry of Health Malaysia (MOH)

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NOTES

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