STANDARD OPERATING PROCEDURE FOR

PREVENTION, SCREENING, DIAGNOSIS & TREATMENT OF HEPATITIS C IN MANIPUR

2019

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Langpoklakpam Jayantakumar Singh

Hon'ble Minister, Health &Family Welfare
Government of Manipur

MESSAGE

I am pleased to learn that a Standard Operating Procedure for the state of Manipur on Hepatitis C Prevention, Screening, Diagnosis and Treatment has been developed. This will ensure that the state has a clear defined procedure to follow for prevention, diagnosis and treatment of hepatitis C under the National Viral Hepatitis Control Program. This will also set a framework for physicians in the private sector, remote hill and valley districts and other healthcare workers to understand and follow public health procedures to address hepatitis C. It is also evident that hepatitis C virus infection has become a serious public health concern with, Globally, an estimated 71 million people infected, and if left untreated, it can have serious implications thereby leading to cirrhosis, and even cancer. Published materials on hepatitis C for Manipur are limited, although some studies have shown hepatitis C antibody prevalence of 74% among people who inject drugs. Much research work from different expertise and institutions are needed to understand not only the prevalence but also other social issues that hepatitis C is causing in Manipur.

In this context, the Standard Operating Procedure will contribute immensely towards public health responses to eliminate viral hepatitis by 2030 as mandated by the World Health Assembly.

Jayantaku Singh
23/7/2019

(Langpoklakpam Jayantakumar Singh)

V. Vumlunmang, IAS

Principal Secretary Health & FW
Government of Manipur

MESSAGE

Hepatitis C virus infection has become a serious Public Health concern. According to WHO report, globally an estimated 71 million people are infected, and if left untreated, it can have serious implications thereby leading to cirrhosis, and liver cancer. Published materials on hepatitis C for Manipur are limited, although some studies have shown high hepatitis C antibody prevalence among people who inject drugs. Overtime the various research works from different institutions would facilitate a better understanding of not only the prevalence but also other socio-cultural, customs that might cause hepatitis infection in the state of Manipur.

A Standard Operating Procedure (SOP) for the state of Manipur on Hepatitis C Prevention, Screening, Diagnosis and Treatment has been developedto assist in the prevention, testing, diagnosis and treatment of hepatitis C. This will form a guiding framework for physicians working in the Govt. and private sectorto address hepatitis Calongwith guidelines/SOP's issued by Ministry of health & Family Welfare.

This SOP has benefitted from technical inputs from variousphysicians and gastroenterologists of the stateas well as experts from WHO India through a number of formal meetings and discussions which took over a year to arrive at this level. The SOP also follows the processes of diagnosis and management as per the national guidelines. In addition, it has been developed to include details on hepatitis C prevention and to contextualize based on the need of the state. The SOP is aimed at bringing a consistent understanding of how to diagnose and manage hepatitis C fromPublic Health perspective, and allow physicians, nurses, para-medics to utilize it to supplement their knowledge in matters relating to understanding the infection, testing and treatment.

(V. Vumlunmang)

Dr. Soram Manikanta Singh

State Mission Director, NHM
Government of Manipur

PREFACE

This Standard Operating Procedure has been formulated to enable in having a consistent public health response towards viral hepatitis C in the state and follows the guidelines set out in the National Viral Hepatitis Control Program. This document also addresses the prevention, screening, diagnosis and treatment of hepatitis C as a public health response.

Best efforts from all stakeholders involved; including specialist in the state, registered medical practitioners, government departments and civil society groups have been put forth in developing and finalizing the document. We also anticipate and hope that this standard operating procedure will eventually enable decentralization and task sharing with physicians in remote hill and valley districts of the state, being trained using the procedures defined to prevent, diagnose and provide treatment for hepatitis C among the population they serve.

I am certain that thisstandard operating procedures will contribute immensely in enabling access to hepatitis C prevention, screening, diagnosis and treatment. It will also greatly contribute towards reducing morbidity and mortality attributed to hepatitis C and achieving elimination of hepatitis C by 2030.

(Dr. Soram Manikanta Singh)

Contents:

Abbreviations:

ALT:	Alanine aminotransferase
AST:	Aspartate aminotransferase
APRI:	Aspartate aminotransferase/platelet ratio index
ART:	Anti-retroviral therapy
CBC:	Complete Blood Count
CBOs:	Community Based Organisations
CrCL:	Creatinine Clearance
DAA:	Direct-acting antiviral
DCGI:	Drug Controller General of India
EASL:	European Association for the Study of the Liver
eGFR:	Estimated Glomerular Filtration Rate
Hb:	Hemoglobin
HBsAg:	Hepatitis B Surface Antigen
HBV:	Hepatitis B virus
HCC:	Hepatocellular Carcinoma
HCV:	Hepatitis C virus
HIV:	Human Immunodeficiency Virus
IA:	Immunoassay
LFT:	Liver Function Test
MTC	Model Treatment Centre
NASH:	Non-alcoholic Steatohepatitis
NAT:	Nucleic Acid Testing
NS5A:	Non-structural Protein 5A
NS5B:	Non-structural protein 5B (of HCV)
PCR:	Polymerase Chain Reaction
PegIFN:	Pegylated interferon
PI:	Protease Inhibitor
PWID:	People Who Inject Drugs
RBV:	Ribavirin
RDT:	Rapid Diagnostic Test
RNA:	Ribonucleic acid
SVR:	Sustained Viral Response
SOP:	Standard Operating Procedure
WHO:	World Health Organization

Introduction:

Hepatitis C virusis usually transmitted through sharing of infected needles and syringes among people who inject drugs (PWID), transfusion of infected blood and blood products and also using medical equipments which is not properly sterilized. Hepatitis C virus (HCV) can also be transmitted sexually and from an infected mother to her child. There is no vaccine against HCV, making prevention, testing, and treatment initiatives critically important. Globally, an estimated 71 million people are living with HCV.[1] If left untreated, HCV infection can cause chronic and debilitating liver diseases, namelycirrhosis and liver cancer. In 2015, HCV infection contributed to 30% of viral hepatitis related deaths and needlessly ~400,000 lives were lost.

Of the 36.7 million people living with HIV (PLHIV), the prevalence of those with evidence of prior HCV infection is 6.2%. HCV infection rates have been especially high among people who inject drugs (PWID) who are also HIV positive, with co infectionrates as high as 80%.[2]

In India, HCV prevalence is estimated at about 0.5–1.5%[3] but contributes a significant proportion of Global HCV burden because of its large population. In absolute terms, the country has approximately 12 to 18 million exposed to HCV[4] and approximately 8.7 million of themare living with the virus currently.[5]

There is paucity of population-based studies of HCV from India. With limited data available, blood donors show an anti-HCV prevalence of 0.29–1.85% in northern states, 0.08–1.4% in southern states, 0.27–1.17% in northeastern states, and 0.31–1.09% in eastern states and western Indian states show a lower prevalence of 0–0.9%.[6]

Limited studies among tribal population of India have shown higher level of anti-HCV positivity at 7.89% among Lisu community in Arunachal Pradesh and 2.02% in Lambada tribe in Andhra Pradesh.[7,8]The prevalence of HCV in high risk, including patients undergoing hemodialysis, repeated blood transfusions (e.g. thalassemia major), PWID, and health care workers (HCW's), is expected to be more to the general population. Overall, the availability and quality of epidemiological data from India is, however, not optimal.

In Manipur, published materials on HCV among different populations have been hard to find. However, some limited work has been done among PWID and shows anti-HCV prevalence of 74%.[9].

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[1]World Health Organization, Global Hepatitis Report, 2017

[2]World Health Organization, Global Hepatitis Report, 2017

[3]Puri.P, et al, Consensus Statement of HCV Task Force of the Indian National Association for Study of the Liver (INASL). Part I: Status Report of HCV Infection in India, Journal of Clinical and Experimental Hepatology, June 2014

[4]DhimanRk, Future of therapy for hepatitis C in India: A matter of accessibility and affordability?, Journal of Clinical and Experimental Hepatology, June 2014

[5]Puri. P, et al, Disease Burden of Chronic HCV in India, HCV Task Force, Indian National Association for Study of the Liver (INASL), 2014

[6]Puri.P, et al, Consensus Statement of HCV Task Force of the Indian National Association for Study of the Liver (INASL). Part I: Status Report of HCV Infection in India, Journal of Clinical and Experimental Hepatology, June 2014

[7]Phukan AC, et al, HCV activity in an isolated community in north east India, Indian Journal of Pathology and Microbiology, October 2001

[8] Chandra M, Prevalence, risk factors and genotype distribution of HCV and HBV infection in the tribal population: a community based study in south India, Tropical Gastroenterology, October 2003.

[9] Kermode M, et al, High burden of hepatitis C & HIV co-infection among people who inject drugs in Manipur, Northeast India, Indian Journal of Medical Research, March 2016.

Prevention and Transmission

Prevention:

Prevention is better than cure. However, there is currently no vaccine which can prevent HCV. Prevention of HCV is mostly done through reducing/avoiding the risk of exposure since no prophylactic vaccine is available currently. Prevention is quite challenging because of the varied routes of transmission.Treatment canprevent development of complications of infection, including cirrhosis and hepatocellular carcinoma and can reduce the risk of transmission by treating and curing the reservoir pool. Some of the strategies are cited below to promote preventiveefforts.

PreventionofHCVincommunitysettings[10]

Avoid unsafe practices bynon-medical andtraditional practitioners (unsafe tattoos, unsafe circumcision procedures, unnecessary injections, specially unsafe injection practices from informal health care providers)
Safe household practice (not sharing toothbrushes, razors, shaving blades and dental flosh)

Prevention of sexual transmissionofHCVinfection[11]

Avoid multiple partners, regular screening and treatment for STIs, Promotion of correctand consistent condom use
Routine screening of sex workers in high-prevalence settings
Integrated action to eliminate discrimination and gender violence and increased access to healthcareand social services for vulnerable persons

PreventionofHCVInfectioninHealth-careSettings[12,13]

Universal Precaution: Proper hand washing, use of gloves, sterilization of equipments etc.
Bio-medical waste management: Proper disposal of bio-medical waste by encouraging use of the colour coated bins.
100% donated blood units screened for HCV.
Improved access to safe blood
Capacity building of different cadres of health workers.

Prevention of HCV Infection among PWID[14]

Offer peer interventions to people who inject drugs to reduce the incidence of viral hepatitis
Offer Opioid substitution therapy to treat Opioid dependence, reduce HCV risk behavior and transmission through injecting drug use, and increase adherence to HCV treatment
Integrate Opioid substitution therapy and other drug-dependence treatment with health care services for hepatitisC
Targeted information, education and communication for people who inject drugs and their sexual partners

[10]World Health Organization, Prevention and treatment of HIV and other sexually transmitted infections for sex workers in low- and middle-income countries: recommendations for a public health approach, http://www.who.int/hiv/pub/guidelines/sex_worker/en/, December 2012

[11] World Health Organization, Prevention and treatment of HIV and other sexually transmitted infections among men who have sex with men and transgender people, http://www.who.int/hiv/pub/guidelines/msm_guidelines2011/en/ , June 2011

[12] World Health Organization, Guidelines on hand hygiene in health care, http://www.who.int/gpsc/5may/tools/9789241597906/en/, 2009

[13] World Health Organization, Universal access to safe blood transfusion, http://www.who.int/bloodsafety/publications/UniversalAccesstoSafeBT.pdf, 2008

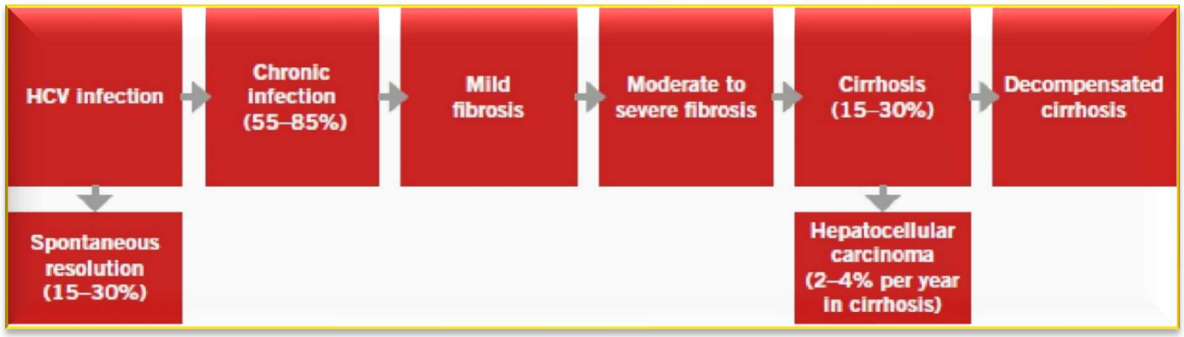
[14] World Health Organization, prevention of viral hepatitis Band C among people who inject drugs,http://www.who.int/hiv/pub/guidelines/hepatitis/en/

Injection safety:
Safe injection practice is very important for prevention of HCV specially at the health care settings/facilities. Injection associated transmission of blood borne diseases/injection can be prevented through the development of a strategy to reduce injection overuse and achieve injection safety.
The three elements of WHO strategy for the safe and appropriate use of injections are
(1) Behavior change among patients and health-care workers to decrease injection overuse and achieve injection safety;
(2) The availability of necessary equipment and supplies, namely a transition to the exclusive use of WHO prequalified Auto-disable/Re-Use prevention/Sharps injury prevention syringes for therapeutic injections;
(3) Proper management of sharps waste.[15]

Route of Transmission:
HCV is transmitted by exposure to infectious blood and blood products (e.g. transfusions of HCV-infected blood and blood products, contaminated syringes, needles and contaminated materials used during medical procedures). Transmission can also occur among people who inject drugs through the sharing of contaminated needles or syringes. HCV infection may be transmitted from mother to child (4%), HCV may be transmitted sexually but much more higher in patients who are co-infected with HIV and who have multiple sexual partners however, transmission may be higher if the mother is co-infected with HIV. It may also be transmitted through unsafe sex especially amongst the MSM and co-infected with HIV. It is also transmitted through procedures like tattooing, body piercing and circumcision.

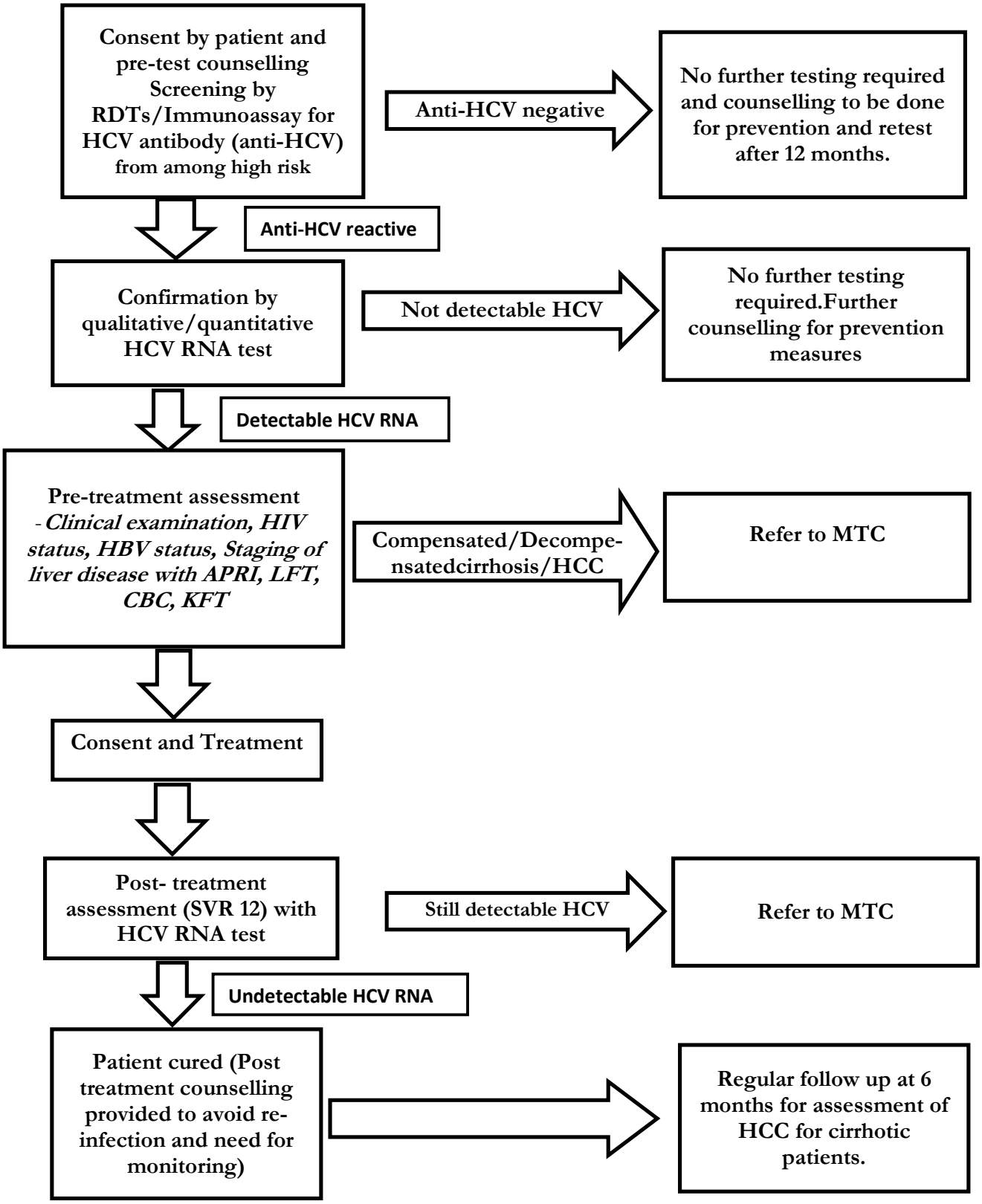
Natural history ofHCV

HCV infection is a slow progressive disease therefore, majority of people who are infected with HCV are unaware of their infection. They are at a high risk of developing chronic liver disease and it can be associated with complications like cirrhosis and hepatocellular carcinoma. HCV infection causes both acute and chronic hepatitis..Acute HCV infection is defined as the presence of HCV within six months of exposure to and infection with HCV. Among15-30% of infected individuals, spontaneous clearance of HCV will occur within first six months of infection without any treatment intervention. Almost all of the remaining 55-85 % will carry HCV for the rest of their lives (if not treated) and are considered to have chronic HCV infection. Anti-HCV antibodies develop as part of acute infection and remain through life. A confirmatory HCV RNA test is needed to detect the presence of the virus and confirm chronic infection.



[15] World Health Organization, Guidelines on drawing blood: best practices in phlebotomy,http://www.who.int/infection-prevention/publications/drawing_blood_best/en/, 2010

Testing and diagnostic algorithm:



Who shouldbeoffered testing?

Anti-HCV antibody test should be offered to hospital admitted patients with signs and symptoms of liver disease (e.g. jaundice, abdominal distention, and abnormal liver function tests etc.). Screening for HCV should be made available for all the pregnant women. Screening with anti-HCV should be offered to PLHIV, PWID, Men who have sex with men (MSM), Sex Workers (SW), repeated transfusion recipients, health care workers, and hemodialysis patients. Screening with anti-HCV should also be provided to people in institutional reform centers (e.g. Jails and drug treatment centers).

Testing strategy:
Testing should be done at the designated centres. However, under special situations, testing will be encouraged and conducted targeting high risk groups to ensure greater coverage in collaboration with community based organizations (CBOs), HIV program and relevant authorities or departments.

HIV and drugs programs: Testing and awareness camps can be organized in HIV treatment centers, targeted intervention programs covering high risk groups Viz. PWID, PLHIV, MSM, Sex workers and Transgender, drug treatment program centers, in collaboration with CBOs and HIV programs. This will include centers run by the Government and other NGOs.

Mobile testing programs: Decentralized mobile testing programs, in collaboration with CBOs, NGOs and HIV program will be conducted to ensure greater coverage. Existing infrastructure of the HIV program and other national health programs can be utilized to ensure availability of manpower and equipment needed.

Prison settings: Testing will be offered to inmates of prisons in collaboration with prison authorities and CBOs, NGOs working in the prison settings. This will allow tapping of the opportunity to cure a person during his/her stay in the jail settings and also serve prevention efforts through treatment.

Screening and diagnosis and interpretation of results:

Screening forAnti-HCVantibody
Screening for initial detection of exposure to HCV (anti-HCV Ab) should be done with a single serological test. The screening can either be done with a Rapid Diagnostic Test (RDT) or an Immunoassay (IA) with sensitivity and specificity of the test specified and approved by Drug Controller General of India (DCGI). The single initial screening test is recommended before confirmatory testing regardless of the prevalence level within the population. RDTs should be prioritized over immune assays in settings where they will increase access to testing. All antibody positive individuals should be confirmed by HCV RNA detection prior to offering initiation of anti-HCV treatment. Only patients diagnosed with viraemic current infection will benefit from treatment. Patients who have spontaneously resolved HCV infection (and who are thus anti-HCV positive, but confirmatory test negative) should not be treated. Patients with ongoing risks should be offered to be retested annually.

People Testing Anti-HCV Negative

All patients who are tested anti-HCV non-reactive should receive post-test counseling with the aim of reducing or eliminating risky behaviors which could lead to future transmission. The counseling session should include the following:

- Explanation of the results and implications: if the antibody test is nonreactive, no antibodies were found in the blood, and this usually means the patient doesn't have HCV. This does not mean patient is immune to the virus in the future. In HIV positive patients' antibody could be non-reactive if the CD4 is very low.
- If the patient has recent or ongoing risk, testing annuallyis recommended.
- General disease education, with emphasis on prevention and modes of transmission.
- Discussion of benefits of retesting in the future.
- Encourage the patient to make healthy choices and to get vaccinated against HBV if appropriate

People TestingAnti-HCVPositive

All patients who are tested reactive to an anti-HCV test should receive education and counseling about their HCV infection, care and treatment. The aim of the counseling is to encourage confirmatory testing and to prevent transmission before confirmatory testing. The counseling session should include the following:

- Explanation of the results and implications: Patient has been infected with the hepatitis C virus, but may or may not currently have hepatitis C as some people are able to clear the virus, although most do not. Patient will need to have another blood testfor HCVRNAto find out if the patient is currently infected with HCV.
- Emphasis on the need for confirmatory testing and assistance with determining next steps.
- General health educationabout HCV, with emphasis on prevention and modes of transmission.
- Until the confirmatory testsis done, adherence counseling on standard prevention practices to avoid transmission in case chronic infection exists.
- Provide information that this is curable infection and can be treated easily with newer oral drugs within 12 to 24 weeks with clear definition of need to do Sustained virological response or test for cure at 12 weeks after the end of treatment.

Interpretation of HCV antibody test result:

Antibody Test Result	HCVRNATest Result	Interpretation
Negative	Negative	No HCV exposure/ infection
Positive	Negative	Exposed to HCV.
Positive	Positive	HCV exposed &Current Infection

Confirmatory testing for chronic HCV infection with HCVRNAassays

NAT/PCR for HCV RNA (either qualitative or quantitative) should be performed sequentially following a positive HCV serological test to confirm current (active) chronic infection since 15-45% of patients will clear the virus naturally and thus will not need anti-HCV treatment. Only patients who are confirmatory test positive (either NAT qualitative or quantitative) should be assessed for treatment and offered treatment.

Patient with negative results on screening or HCV RNA confirmation, no further testing is required and the patient can be counseled for preventive measures.

People Confirmed withChronicHCV

All patients who receive a positive NAT PCR test and are confirmed positive for chronic hepatitis C should receive education and counseling about their HCV infection, care and treatment. The aim of the counseling should be to help the person reduce progression of liver disease and prevent him/her from transmitting HCV to others. The counseling session should include:

- Explanation of the results and implications: Patient has been infected with hepatitis C virus, and if the confirmatory test is positive, which means the patient has HCV infection, Emphasizing that many people with HCV infection remain healthy throughout their lives, and highly efficacious treatment optionsexist.
- Education on how to prevent transmission to others, especially in the case of PWID. The counseling should also include an explanation of how HCV is not transmitted (sneezing, coughing, sharing drinking glasses, utensils).
    - o Discussion on other measures that can be takento stay healthy: Alcohol and Liver Wellness: All patients should be counseled on the importance of abstaining from alcohol and if necessary support in identifying resources to support the cessation of alcohol consumption.
    - o Weight Management: HCV-infected people with a body mass index (BMI) of greater or equal to 25 kg/m^2should be counseled on how to reduceweightvia nutrition, exercise ormedicalintervention.
    - o Testing/Vaccinations: Consider hepatitis A and B vaccination if susceptible and if liver disease is present. Consider testingforHIV.
    - o Caution/Medications: Avoid new medicines, including over-the- counter and herbal agents without first checking with a healthcare provider. Connect patient with the necessary services if not available on-site.

People TestingRNANegative

All patients who are confirmed RNA negative should receive post-test counseling with the aim of assessing and then reducing or eliminating risky behaviors which could lead to future transmission. The counseling session should include:

- Explanation/interpretation of results: The patient isanti-HCV positive, but RNA negative, so the patient was infected with HCV, but then cleared the virus naturally. They do not have HCV infection.
- Education about HCVif patient has not received this education prior, highlighting that not having a current infection should not be confused with future immunity.
- If there is an ongoing risk to the patient, emphasize on disease transmission and prevention awareness.
- Emphasis the benefits of retesting in the future if exposed to risky behaviors.

Genotyping test

Genotyping of HCV can be used to select different combinations of DAA and decide on the duration of therapy. However, genotyping test is no longer mandatory with the introduction of pan-genotypic treatment regimen viz. Sofosbuvir + velpatasvir and sofosbuvir and daclatasvir. Nowadays, Pan-genotypic regimens for treatment are available and is effective for all genotypes of HCV. If genotype testing is affordable, available or the genotype is already known, the treatment regimen could be chosen based on the genotype. Additionally, in instances where patients fail their first treatment, genotyping can be considered to guide selection of appropriate second-line treatment, if accessible.

Pre-treatment assessments

All patients confirmed to have current active infection of HCV should be properly assessed before initiation of treatment. Some indicators could include:

1. Alcohol consumption
2. HIV status, current ART treatment regimen, HBV status
3. Pregnancy status-Contraception during treatment and 6 months after the treatment
4. Baseline biochemicaltests
   a. Liver Function Test (LFT)- ALT, AST, Alkaline Phosphate, Globulin Bilirubin, Albumin
   b. Renal Function Assessment - Urea & Creatinine(Cr)
   c. Complete Blood Count (CBC) to determine platelet count (Plt).and other indicators like Hb%
5. Exclusion of hepatocellular carcinoma (HCC) by USG if patient demonstrates signs of end stage liver disease
   a. Alphafeto protein(Optional)

   Of these tests, the minimum tests to be performed prior to initiating patients on all oral DAA therapy are:
   - AST, Platelet andCreatinine
6. The AST and Plateletwill be used to calculate the AST to Platelet Count Ratio Index (APRI) score to stage the patient and Creatinine will be used to determine renal function.
7. In addition to the above tests, a physical examination of the patient by a trained medical professional is necessary to determine whether the patient is suspected of having advanced liver disease (decompensated cirrhosis or HCC), in which case, they should be referred to Modal Treatment Centres.

Clinical signs of cirrhosis: Shrunken liver with firm and irregular margin and surface of the liver lowerborder, spider nevi, palmar erythema, white nail, gynecomastia, and wasting syndrome.

Clinical signs of decompensation: Jaundice, Ascites, distended abdominal veins and caput medusa, hepatic encephalopathy, haematemesis and malena, and coagulopathy.

Liver disease stagingoptions and scoring

Non-Invasive tests are the preferred method for staging. Liver biopsy is no longer recommended as a routine investigation for staging. Where available in public health settings, non-invasive processes like transient elastography can also be used to stage liver disease. Staging is important to identify patients with impaired liver function and advanced stages of the disease that should be prioritized for treatment. They may also need longer treatment durations, additional medications or require referral to specialists for clinical management in certain instances. The **Aminotransferase/Platelets Ratio Index (**APRI) score correlates with METAVIR scores to indicate the degree of liver fibrosis:

METAVIR Liver Biopsy Scoring System[16]

METAVIR STAGE	F0	F1	F2	F3	F4
Definition	Nofibrosis	Portal fibrosis Withoutsepta	Portal fibrosis with septa	Numerous septawithout cirrhosis	Cirrhosis

Aminotransferase/Platelets Ratio Index (APRI)

Non-invasive test	Components assessed	Lower cut off	Upper cut off	Fibrosis stage assessed
1. APRI	AST and platelet count	0.7	2. 0	F2 - F4

Formula: APRI = [{AST (IU/L)/ AST_ULN (IU/L)} xlOO]/platelet count (10^9/L)

APRI Score Interpretation

APRI score[17]	Interpretation
> 2	Cirrhosis
0.7 - 2	Fibrosis, risk of cirrhosis
< 0.7	No Fibrosis

An APRI score of greater than 2.0 has 91% specificity to rule in the presence of cirrhosis. An APRI score greater than 0.7 has 72% specificity and 77% sensitivity to diagnose the presence of significant fibrosis (F2), with the higher the APRI score indicating a greater likelihood of significant fibrosis. Patients who are HIV co-infected should be prioritized for treatment, as should cirrhotic patients (APRI >/ = 2.0)

Referraltospecialist

In Manipur could be a physician who has practiced or been trained in the field of gastroenterology and hepatology care. Patients with decompensated cirrhosis, irrespective of APRI score, should be referred to specialists for clinical management. The referral pathways in Manipur can be suggested a follows;

Patient has physical signs of decompensation +/- APRI > 2.0	→	Refer to Specialist (MTC)
Patient has APRI > 2.0 and no physical signs of decompensation {cirrhotic)	→	Refer to Specialist (MTC)
Patient has APRI <2.0 (non- cirrhotic)	→	Registered Medical Practitioner

[16] World Health Organization, Guidelines for the screening, care and treatment of persons with chronic hepatitis C infection, http://www.who.int/hepatitis/publications/hepatitis-c-guidelines-2016/en/ , 2016

[17]World Health organization, Guidelines for the care and treatment of persons diagnosed with hepatitis C virus infection, July 2018

Treatment

All HCV infected patient should be considered for treatment irrespective of prior treatment history, i.e. both treatment-naive and experienced patients.

Aim of treatment isto reduce morbidity,mortality, prevent further complications and reduce transmission of HCV.

Medications: Direct-ActingAntivirals

The treatment of chronic HCV infection has been transformed by the development of all oral DAAswhich have shortertreatment duration, are associated with fewer side effects, and significantly high SVR rates. However, there may be adverse drug interactions with certain drugs.

Recommended regimens

The WHO recommends pan-genotypic DAA regimens be used for the treatment of persons with hepatitis C infection.[18],[19]The recommended regimen for Manipur has been considered based on recommendations from WHO and the India National Guidelines for Diagnosis and Management of Viral hepatitis.

Regimen(s) for publichealthapproach: Non-Cirrhotic patients

Sofosbuvir and daclatasvir

- 12weeks(Allgenotypes)fornon-cirrhoticpatients(APRI<2.0)

Regimen(s) for public health approach: Compensated cirrhosis

Sofosbuvir +Velpatasvir

- 12weeks(All genotypes)forcirrhoticpatients(APRI>2.0)

Regimen(s) for public health approach: Decompensated cirrhosis

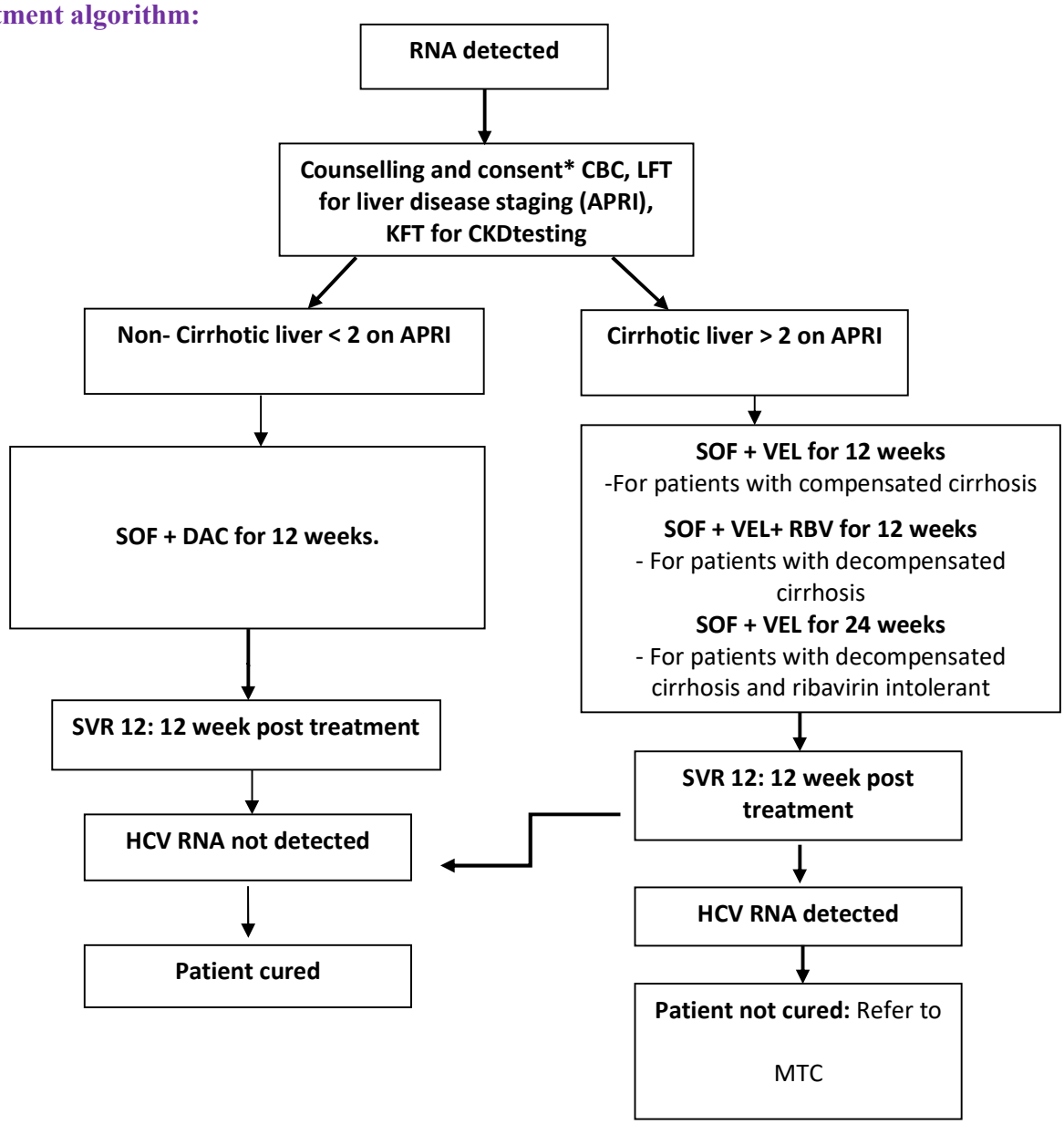
Sofosbuvir + VelpatasvirandRibavirin

- 12 weeks(All genotypes)for decompensated cirrhotic patients
- 24 weeks (All genotypes) for decompensated patients with ribavirin intolerance

[18]World Health Organization, Guidelines for the screening, care and treatment of persons with chronic hepatitis C infection, http://www.who.int/hepatitis/publications/hepatitis-c-guidelines-2018/en/, 2018

[19]National Guidelines for Diagnosis and Management of viral hepatitis, Ministry of Health and Family Welfare, Government of India, July 2018

Treatment algorithm:



*Please refer to Annexure 1 and 2 for consent forms for screening and treatment initiation.

** Please refer to HIV co-infection section for dose adjustment with HIV related anti-retroviral medicines

Dosing for HCVtreatmentregimen

Dosing for Recommended HCV Treatment Regimens

Regimen	Dosage per tablet	Dosing Frequency and Timing
Ribavirin	200 mg capsule or tablet	Body weight < 75 kg - 2 in the morning and 3 in the evening Body weight >75 kg - 3 in the morning and 3 in the evening
Sofosbuvir	400 mg tablet	Once daily
Daclatasvir	30 mg or 60 mg tablet (special considerations for ART patients)	Once daily
Velpatasvir+ sofosbuvir	100 mg +400 mg tablet (consider contraindications with ART)	Once daily

**Increase daclatasvir dosage to 90 mg per day when co-administered with efavirenz. Decrease daclatasvir dosage to 30 mg per day when co-administered with atazanavir/ritonavir. Daclatasvir should not be co-administered with velpatasvir.*

Treatment monitoring

Treatment week	DAA Alone			DAA+RBV		
	CBC, renal, liver function	Adherence, side effects	HCV RNA	CBC, renal, liver function	Adherence, side effects	HCV RNA
Baseline	✓		✓	✓		✓
Week 1				✓	✓	
Week 2				✓	✓	
Week 4	✓	✓		✓	✓	
Week 8				✓	✓	
Week 12				✓	✓	
Week 12 after end of treatment			✓	✓		✓

Community and civil society involvement in successful program implementation:

Civil society and key population groups have proven their important role in successful implementation and quality improvement or assurance of public health interventions. In the case of Tuberculosis, HIV and different key population related services for HIV, they have shown the role that peer interventions can play in ensuring linkages in the cascade from testing to treatment. To ensure successful quality implementation of the hepatitis C program, civil society and community groups can be engaged in several sphere viz. but not limited to;

a) Awareness generation and reaching the hard to reach population.
b) Encourage people to understand the infection and motivate to other testing and diagnosis.
c) Assist paramedics and physicians in building treatment education and preparedness of patients.
d) Undertake community led testing program in collaboration with relevant agencies.
e) Assist to ensure compliance to patient clinic visits and assist in lose to follow up.
f) Assist in ensuring treatment adherence of people who are on treatment
g) Be a part of key committees or working groups formed by the government under the program to ensure quality assurance and improvement.

Treatment considerations forspecialpopulations

HCV/HIVCo-infection

The WHO's 2016 guidelines for the treatment of HCV recommend that all persons with HIV/HCV co-infection be considered for HCV treatment as there is generally a more rapid progression of liver fibrosis in HIV/HCV co-infected persons, especially in patients with a CD4 count of 200 cells. In addition, the risk of hepatic decompensation remains higher in co-infected patients even if successful control of HIV infection has been achieved. Patients with HIV co-infection should be considered for stabilizing first of their HIV infection prior to initiating HCV treatment.

The choice of ART for persons with HIV/HCV co-infection is the same as for those with HCV alone, although drug-drug interactions and dose adjustments of DAA must be taken into account.

(*Special Considerations for patients on HIV treatment:* Increase daclatasvir dosage to 90mg per day when co-administered with efavirenz. Decrease daclatasvir dosage to 30 mg per day when co-administered with atazanavir/ritonavir. Nevirapine should not be co-administered with daclatasvir.) Velpatasvir should not be co-administered with efavirenz or nevirapine.

Pregnant women

Screening: Screening of pregnant women for HCV can identify women whose infants will need to be tracked postpartum. During pregnancy treatment is not recommended.

Care and Treatment: There are currently no treatments available that have been designated as safe during pregnancy. Women who are screened antibody-positive should be linked to MTC for further management support.

People whoinjectdrugs

Screening: PWID should be prioritized for screening due to their high rates of prevalence, morbidity and ongoing transmission in Manipur. Screening should be performed as part of the

harm reduction package annually among PWID, which also includes opioid substitution therapy, sterile injection equipment and counselling. For PWID who have successfully achieved SVR12 and are continuing to inject drugs, re-infection can occur so regular consolidated/intrinsic counseling session and, if possible, screening should be continued annually using HCV RNAtest.

Care and Treatment: HCV treatment has been proven effective in PWID, and may have a treatment as prevention effect if networks of drug users are treated. Multiple studies have demonstrated that there is no difference between SVR12 rates for PWID and non-PWID, even when PWID are active users. PWID who complete treatment must receive counseling on the possibilities of re-infection due to continuing risk behaviors such as sharing of needles and paraphernalia.

Decompensated cirrhosis

Decompensated cirrhosis is associated with ascites, esophageal and gastric varices, and can eventually progress to liver failure, renal failure and sepsis, all of which are life threatening. The diagnosis of decompensated liver disease is based on both laboratory and clinical assessment, and therefore a careful medical examination of patients must be made before starting treatment. While certain treatment regimens have been shown to be safe for use in patients with decompensated liver cirrhosis, close monitoring is required in these patients, and it is thus recommended that treatment for these patients be considered only under close supervision of specialist teams with experience in treating and managing complications.

Treatmentexperienced

Patients who have undergone treatment in the past using older drugs could pose certain challenges. All treatment experienced patients should be referred to MTC with experience in treating and managing complicated patients. It could also be advised to consult professional liver society viz. AASLD and EASL HCV Treatment Guidelines for guidance prior to treatment initiation.

Co-morbidities considerations

HCV/HBVinfection

Hepatitis C virus may suppress HBV replication in acutely or chronically infected patients with reduction of HBsAg serum titer observed in HCV/HBV co-infected patients.[20],[21]Some studies also demọnstrate mutual suppression of HCV and HBV, dual infection of both viruses may lead to increased hepatitis related morbidity. Additionally, during treatment with DAA medications and after HCV clearance, there is a risk of HBV reactivation and potentially fatal acute flares.

Given the risk of reactivation, **all HCV patients should be screened forevidence of current or prior HBV infection before initiating HCV therapy.** The US Federal Drug Administration (FDA) recommends screening all patients for evidence of current or prior HBV infection by measuring HBsAg and anti-HBc as cases have been reported in HBsAg negative patients and those with evidence of resolved infection (HBsAg negative and anti-HBc positive).Chronic HCV patients with evidence of active or resolved HBV infection should be treated by physicians with expertise in managing and monitoring hepatitis B and with consideration for HBV antiviral treatment in HBV/HCV co-infected patients. It has been recommended to start patients who

[20] Crespo J et.al, Viral replication in patients with concomitant hepatitis B and C virus infections, https://link.springer.com/article/10.1007/BF02471908, European Journal of Clinical Microbiology and infectious diseases, June 1997.
[21]Liaw Y.F et al, Displacement of hepatitis B virus by hepatitis C virus as the cause of continuing chronic hepatitis, https://www.ncbi.nlm.nih.gov/pubmed/8143971, Gastroenterology 1994

meet criteria for treatment of active HBV infection on therapy at the same time (or before HCV DAA therapy is started). Monitoring of patients with active or resolved HBV infection should include clinical and laboratory monitoring (i.e. HBsAg, HBV DNA, serum aminotransferase levels, bilirubin) of hepatitis flare or HBV reactivation during DAA treatment and post-treatment follow-up.

HCV/TBinfection

TB screening should be completed before consideration of HCV treatment, especially among those with advanced immune suppression. The absence of cough, fever, weight loss or night sweat is reasonable to excludeactive TB infection. Concurrent treatment of TB and HCV should be avoided secondary to interactions between HCV DAAs and TB medications. Specifically, anti-tuberculosis medicines such as rifampicin, rifapentin or rifabutin modulate the concentration of several HCV DAAs when given concurrently and should not be co-administered. HCV infected patients diagnosed with TB infection should complete TB treatment before starting HCV treatment, and should be referred to referred to specialist teams.

HCV andalcohol use

The consumption of alcohol, even in moderate amounts, in people with chronic HCV infection results in more rapid progression of advanced liver disease and HCC.[22]People diagnosed with chronic HCV should be counseled to limit or abstain from alcohol consumption and offered access to alcohol cessation services, where possible. For patients with alcohol disorders who are eligible for treatment, it is recommended that patients stop drinking prior to treatment due to its deleterious effects on adherence. For patients who continue drinking during treatment, clinicians should provide extra support to ensure adherence.

HCV/NASH

Non-alcoholic steatohepatitis is a liver disease characterized by a build-up of fat in the liver along with inflammation and damage. Like hepatitis C, NASH develops slowly over time and progresses to advanced liver disease. Chronic HCV patients with NASH are a recommended target population for treatment in order to halt progression of liver disease. Patients should be monitored carefully during treatment for any complications arising from more severe underlying liver disease.

HCV/Chronickidneydisease

Co-morbidity between HCV and renal impairment is common. Renal impairment patients have a high risk of morbidity, disease progression and mortality and are a priority group for treatment, where clinically safe to do so. However, limited treatment options for patients with advanced renal disease currently exist.

- Patients with eGFR rates above 30 ml/min/1.73 m^2can be treated with normal doses of DAAs, including sofosbuvir and daclatasvir.
- However, eGFR rates below 30 ml/min/1.73 $m^2$are currently contra- indicated for treatment with sofosbuvir as it is eliminated through the renal system. Limited clinical studies have been conducted in this population, and studies like the TARGET 2.0 real-world cohort study showed progressive deterioration of renal function among patients with advanced renal disease taking sofosbuvir- containing regimens.[23]

[22]Vandenbulcke, H. et al, Alcohol intake increases the risk of HCC in hepatitis C virus-related compensated cirrhosis: A prospective studyhttps://www.ncbi.nlm.nih.gov/pubmed/27180899, Journal of hepatology, September 2016

[23]Saxena V et al, Safety and efficacy of sofosbuvir-containing regimens in hepatitis C-infected patients with impaired renal function,https://www.ncbi.nlm.nih.gov/pubmed/26923436, Liver International, June 2016

- Inpatients with low eGFR rates, referral to a specialist is recommended.
- Patients with an eGFR<50 ml/min/I. 73 m^2should not be treated with ribavirin and those on dialysis must have the dose lowered to 200 mg per day or take it three times per week. Increased monitoring is required in this group.

ANNEXURE 1: Manipur State Health Mission

CONSENT TO ENROLL IN HEPATITIS C SCREENING AND DIAGNOSIS

Date: _____Treatment center/Hospital: _____

You are willingly and voluntary undergoing screening of hepatitis C (HCV) under the National Viral hepatitis control program implemented by Manipur State Health Mission under the Ministry of Health & Family Welfare, Government of India/ National Health Mission (NHM).

Before deciding whether you will undergo screening and diagnosis, please carefully read this document. It provides details of the process that will be undertaken. If at any time you have questions or concerns about the program or the process of screening and diagnosis, please feel free to discuss them with the counsellor. Before you decide to proceed with the screening or not, you can also take time to ask for advice from your family or friends. If you decide to go ahead with the screening, you can sign this form as consent to undergo the screening and complete the diagnosis process, if needed.

SCREENING and DIAGNOSIS PROCEDURES:

Screening step 1: HCV Antibody test
You will be asked to provide a blood sample to do an HCV antibody test. If this test is negative, then you have not been exposed to the virus and you do not need any further testing.
If the test is positive it will mean that you have been exposed to HCV. Further confirmatory test will be required to confirm whether you currently have HCV infection. This confirmatory test is described below in Screening Step 2.

Screening step 2 Confirmatory process: HCV RNA PCR test
You will be undergoing this step only if you have been tested reactive/positive to HCV antibody test above. This test is also known as HCV RNA PCR test or simply a HCV viral load test. If this test is positive, then it will be confirmed that you currently have infection with HCV and will be needing treatment.

CONFIDENTIALITY:

Your full confidentiality will be maintained and shall be kept under safe custody of the authority concerned.

POSSIBLE BENEFITS:

After confirming your viral status and clinical conditions you will be offered free medical support. This will make you get rid of the virus and will have physical and clinical improvement.

CONSENT

Participation in this process is voluntary. You have the right not toparticipate. By signing this document, you do not give up any of your rights as a patient.

By signing this form, you understand and agree as follows:

- I have asked all the questions I had, received appropriate answers and know whom to contact during the screening and diagnosis process.
- I agree to give 4-5 ml of blood sample to conduct my HCV antibody and further confirmatory test as needed and agree to cooperate with the doctor and with all the designated persons.
- I understand that any information collected from me will remain confidential, and that my identity will not be disclosed, unless disclosure is required by law.
- I agree that my medical records and other personal data collected and generated during the process may be examined by staff concerned.
- This content of the consent is fully explained to me in my own vernacular.
- I have been offered a signed copy of this form to take home with me.
- I, the undersigned, voluntarily give my detail information for future correspondence and to help in analyzing of screening data.
- I also voluntarily give my consent to take undergo screening for HCV antibody and HCV RNA PCR test, as needed.

Patient's Name: _____Contact no: _____

Patient's Address:_____

Patient'sSignature: _____Date: _____

Name of witness: _____

Signature of staff concerned: _____Date:_____

Annexure 2: Manipur State Health Mission

CONSENT TO ENROLL IN HEPATITIS C (HCV) TREATMENT

Date: _____Treatment Centre /Hospital: _____

You are willingly and voluntarily considering to undergo in the treatment of hepatitis C (HCV) program under the National Viral Hepatitis Control Program (NVHCP) implemented by the Manipur State Health Mission under the Ministry of Health & Family Welfare, Government of India/ National Health Mission (NHM).

Before deciding whether you will like to undergo treatment, please carefully read this document. It provides details of the process that will be undertaken. If at any time you have questions or concerns about the process of treatment, please feel free to discuss with the staff concerned. Before you decide to undergo treatment or not, you can also take time to ask for advice from your family or friends. If you decide to undergo treatment, you will be asked to sign this form as consent to undergo treatment.

TREATMENT & MONITORING PROCEDURES:

Enrollment /week 0 visit: The enrollment visit is the first visit when your antibody test was done.
Follow-up visits:
During the process of the treatment, you will need to attend the treatment centre/hospital depending on the advice of the treating physician as a part of regular follow-up visits. You may be under treatment for 12 or 24 weeks depending on the assessment of your liver staging. If the doctor determines that you only need 12 weeks of treatment, treatment will be stopped at that point and you will be asked to come back for another follow-up visit 12 weeks later. If your doctor determines that you need 24 weeks of treatment, you will continue treatment and you will be asked to come back for another follow-up visit 12 weeks later.

At the follow-up visit 12 weeks after you have completed HCV treatment, the doctor will repeat the HCV viral load test to see if you have been cured of the infection or not.

MEDICATIONS:

Depending on the condition of your liver, you will be prescribed with an all oral medicine using sofosbuvir and daclastavir OR sofosbuvir and velpatasvir. Adding on ribavirin (RBV) will be decided by the specialists in the model treatment center. RBV is an antiviral medicine that has activity against HCV. It comes as oral capsules that need to be taken twice a day. You will also be given written instructions on how to use RBV, if you would need to.

POSSIBLE RISKS AND DISCOMFORTS DURING THE TREATMENT:

Risks from blood draws

Some possible discomfort caused by the blood drawing include local pain, mild local bruising, fainting, and, rarely, infection at the site where the blood was taken. However, these things are uncommon or quickly resolve.

Risks associated with DAAs

No life threatening risk has been reported with the DAAs which are the medicines that will be given to you. However, fatigue, headache and tiredness have been reported. In case of co-administration with certain HIV medicines, dose adjustment is required. You should report your current HIV medications so that the doctor can advise the correct regimen and dosage. If you are using any other medicines, please report it to your doctor.

Specific risks of Ribavirin:

Pregnancy

RBV cannot be used by women who are pregnant or by male partners of women who are pregnant. Extreme care must be taken to avoid pregnancy during treatment and for six months after completing treatment in both female patients and in female partners of male patients. Female patients must agree to use reliable forms of birth control (including a barrier method, such as a condom) during treatment and for six months after treatment has been completed or stopped.

RBV may also cause mild to severe anemia, and can lead to worsening symptoms in persons who have heart disease (like chest pain or fainting due to troubles with for example the heart beats or low blood pressure). The information that you have received about the possible side effects and complications of HCV treatment is intended to help you to identify side effects or other treatment-related issue. It is important to notify the doctor of any side effects at each visit. If your side effects get worse, notify the doctor immediately.

UNKNOWN RISKS:

There might be side effects of the HCV treatment other than those already mentioned. For your own safety, please inform the staff concerned if you experience any unexpected symptoms. If you have any questions or concerns regarding the risks associated, please feel free to ask the staff concerned at any time.

POSSIBLE BENEFITS:

Starting treatment guarantees you a 95 to 100% possibility of getting cured from HCV. If you agree to accept the treatment, the medicines and the tests required will be provided at no cost to you.

CONFIDENTIALITY:

Your full confidentiality will be maintained and shall be kept under safe custody of the authority concerned.

YOUR RESPONSBILITY AS A PATIENT:

If you agree to participate in this program, the implementing authority would like to ask for your cooperation in order to achieve a successful program, and in particular that you:

- Provide details of your medical history and current medical information.
- Inform the physician of any problem or side effects that occur while you are taking part in the program.
- Inform the physician if you receive other medicines.

YOUR RIGHTS AS A PATIENT:

As a patient enrolled in this treatment program, you have the following rights:

1. To be well informed of the treatment
2. To receive clear explanations about the possible risks and discomforts of undergoing treatment
3. To receive clear explanations about possible benefits of receiving treatment
4. You have the opportunity to ask any question, at any time.
5. You will receive a copy of the signed and dated consent form.
6. You will have the opportunity to make free decision about whether or not you will participate in the program.

QUESTIONS:

If you have any questions about your treatment process, you may contact the below officials:

State Nodal Officer/Nodal Officer MTC/TC
State Viral Hepatitis Control Program

CONSENT:

Participation in the treatment process is voluntary. You have the right to decline treatment. By signing this document, you do not give up any of your rights as a patient.

By signing this form, you understand and agree as follows:

- I have asked all the questions I had about the treatment and have received appropriate answers.
- I have been given the name of a person to contact if I have any questions during the treatment process.
- I agree to cooperate with the doctor and with all the designated persons from his/her team. I will inform them immediately if I observe any abnormalities or have problems with my treatment.
- I understand that any information collected from me will remain confidential, and that my identity will not be disclosed, unless disclosure is required by law.
- I agree that my medical records and other personal data collected and generated during the project may be examined by staff concerned or other authorized people.
- I have read or have been read this consent form and I understand its contents.
- I have been offered a signed copy of this form to take home with me.
- I, the undersigned, voluntarily give my consent to undertake treatment as explained.

Signature of patient:_____Date: _____

Address of patient:_____

Patient's Name: _____ Contact no: _____

Code no: _____ (For official use only)

If the patient is illiterate, a witness must be present during the consent process. After the patient gives consent to undertake treatment by placing a mark in the place of his/her signature (e.g., with an X, thumb print, or other mark), the witness will write the name of the patient and the date in the above lines, then sign and date in the below lines.

Signature of **Witness**, for non-literate patient: _____

Witness's Name: _____ Date: _____

Signature of **treatment center staff:** _____ Date:_____

Annexure 3: Patient Testing & Treatment Card

PATIENT TESTING & TREATMENT CARD

Registration Details

Hospital ID Number

Patient ID under program

Date of starting DAA : ..../...../.....

Basic Demographic Information

Name : ..... Age : ..... Gender : M F TG

Address

Contact number

Aadhaar Number

Date of Anti-HCV testing Rapid ELISA Other

Date of HCV Viral Load Result

Previous Exposure to Hepatitis C Treatment Yes No

If yes, details

DAA Interferon

Details

Is there Cirrhosis at Registration No Compensated Decompensated

Criteria for evaluating cirrhosis (At least one)

Ultrasound .../...../..... :Date

Fibroscan ..... (LSM Value (in kPa .../...../..... :Date

APRI* .....Score ..... Platelet Count .....AST .../...../..... :Date

FIB-4* .....ALT ..... AST ..... Age/...../..... :Date

.....Score ..... Platelet Count

If Decompensated cirrhosis, select basis

CP Score Variceal Bleed Ascites Encephalopathy

Regimen Prescribed	Duration of Treatment	
	12 weeks	24 weeks

Patient not treated at this center but transferred to higher center

Date .....Place.....

*mandatory. The center must do both APRI and FIB-4 scoring.

Baseline and Follow Up Investigations										
S No	Date of Visit	Hemoglobin	Platelet Count	ALT	AST	S. Bilirubin	S Albumin	INR	HCV Viral Load	Other-1 (USGetc)
1										
2										
3										
4										
5										

Follow Up Visits									
Visit Number	Date of Visit	Pills Left	Any New Complaints or side effects	Any other medications	Any Remark	Next Follow up date	Signature of Doctor	Signature of Pharmacist	Patient's Signature/ Thumb Impression
1									
2									
3									
4									
5									

Treatment Outcomes						
SVR Achieved (Date)	Failure (write HCV RNA quantity)	Relapse		Lost to Follow up	Death	Other

Annexure 4: Hepatitis C Treatment Register

Month: **Year:**

	1	2	3	4	5			6	7	8		9	10	11	12 Follow up Date and status (Months)						13	14	15	16	17
S. No.	Registration Number	Name of Patient	Age	Sex M/F/ TG	Patient's address	District	Contact number	Guardian / Care Giver name and contact number, if any	Prior treatment history	Date of ANTI-HCV testing	Date of HCV RNA testing*	Pre Treatment HCV RNA Level	Regimen started * I, II, III	Date of start of treatment	1	2	3	4	5	6	Date of completion of Treatment	Due Date of SVR 12	SVR Done on	Result of SVR	Remarks, if any**
1									☐ Y ☐ N																
2									☐ Y ☐ N																
3									☐ Y ☐ N																

*HCV RNA is done only if ANTI-HCV is positive. In case HCV RNA is not detectable, please put a line across the rest of the fields from 10-16

** In the remarks, please mention the status of patient (died, lost to follow up, stop treatment due to medical reasons, transferred out, referred to higher center). For any of these, also mention date.

Annexure 5: Monthly reporting format

1.Name of Centre _____ 2. Code Number _____

3. Name of the District _____

4. Name of the State _____

5. Name of the Site Incharge _____

6. Report for the period _____ _____

month year

7. Number of Hepatitis C infected people seeking care at the treatment center (Registering in Care)	adult male	adult female	children <18 years	total
7.1 Cumulative number of persons registered in Hepatitis C care at the beginning of this month				
7.2 Number of new persons registered in during this month				
7.3 Cumulative number of persons registered at the end of this month = 7.1 + 7.2				
8. Initiation of Treatment	**adult male**	**adult female**	**children <18years**	**total**
8.1 Cumulative number of patients ever started on Treatment (Number at the beginning of this month)				
8.2 Number of new patients started on Treatment during this month				
8.3 Number of patients on Treatment "transferred in" during this month				
8.4 Cumulative number of patients ever received Treatment (Number at the end of this month) = 8.1+ 8.2 + 8.3				
9. Treatment status (at the end of the month) out of all patients ever started on treatment (8.4)	**adult male**	**adult female**	**children <18years**	**total**
9.1 Cumulative number of patients who have completed treatment				
9.2 Cumulative number of patients who are currently taking treatment (9.2=9.1-(9.3+9.4+9.5+9.7+9.8)				
9.3 Cumulative number of patients who "transferred out"				
9.4 The number of all patients whose treatment status in this month is "stopped treatment" due to medical reasons				
9.5 Cumulative Number of patients who are lost to follow-up (LFU)				
9.6 The number of patients who did not return to the (Defaulter) and missed their doses in this month				
9.7 Total number of patients Referred to Higher center for further management				
9.8 number of deaths reported				
10. Sustained Virologic Response	**adult male**	**adult female**	**children <14 years**	**total**
10.1 Cumulative number of patients who are eligible for SVR (i.e have completed 12 weeks after end of treatment)have completed 12 weeks treatment (Out of 9.1)				
10.2 Cumulative number of patients who have undergone SVR out of the eligible patient (out of 10.1)				
10.3 Cumulative number of undetectable HCV RNA (out of 10.2)				

11. REGIMENS AT THE END OF THE MONTH		
Regimen	**a) Number of ADULTS alive and on treatment**	**b) Number of CHILDREN alive and on treatment**
Others		
Total number of patients		

Addendum for Lost to Follow up		
S No	Reason for lost to follow up	Number of Patients
Total*		

*Total should match 9.5

Addendum for Deaths		
S No	Reason for Death	Number of Patients
1	Liver related causes	
2	Due to causes not related to liver disease	
Total*		

*Total should match 9.8

Acknowledgement:

Hoping that this Standard Operating Procedure contributes significantly in bridging any gap that may exist and facilitate easier access to hepatitis C prevention, diagnosis and treatment, we would like to extend our special thanks all the people involved from the development, reworking and finalization of this standard operating procedure.

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