Scope and Plan
3. SCOPE AND PLAN

Hepatitis C virus (HCV) is a recently discovered hepatitis virus, although extensive research has been carried out in other parts of the world, there are not many reports about this virus infection from the Indian subcontinent. The notable feature about this virus infection is that only 10% of the infected population are symptomatic, presenting an acute picture and majority of the cases go unnoticed until tested for HCV. Though HBV and HEV have been implicated in the etiology of fulminant and subacute hepatic failure, a similar role of HCV is still dubious. Another characteristic feature of HCV infection is that more than 50% of the infected cases go in for chronicity, a proportion of them subsequently developing hepatocellular carcinoma in 18-20 years and ultimately leading to death.

In the background of incomplete epidemiology of HCV in India, the first part of the study was planned to find out the prevalence pattern of HCV among the liver disease groups with the following objectives:

3.1 LIVER DISEASE GROUP

3.1.1 Acute Viral hepatitis (AVH)

* To study the prevalence of HCV among sporadic AVH cases.
* To analyse the impact of HCV in transfusion-associated AVH.
* To compare the biochemical and virological profile of sporadic AVH and TA-AVH.
3.1.2 Subacute hepatic failure (SAHF) and Fulminant hepatic failure (FHF)

* To screen for the role of HCV in Subacute hepatic failure.
* To study the role of HCV in fulminant hepatic failure.

3.1.3 Chronic liver diseases (CLD)

* To study the prevalence pattern of HCV in CLDs.
* To compare the clinical, biochemical and virological findings in HBV-positive, HCV-positive and NBNC cases.
* To study the prevalence of HCV among HCC cases.
* To compare the virological and biochemical profile between transfusion-associated CLDs and non-transfusion-associated CLDs.

3.2 HIGH-RISK GROUPS

As the transmission of HCV is through parenteral, sexual and vertical modes, the high risk groups comprise people exposed to blood and blood products, haemophiliacs, transplant recipients, patients undergoing haemodialysis, intravenous drug users, health care workers, etc. It has been seen that there is a marked decrease in the number of post-transfusion hepatitis cases since the mandatory screening for HBsAg and anti-HCV status of blood/organ donors.
In India the screening for anti-HCV in blood banks is still not mandatory and hence there are still a large number of PTH cases which are on the rise. Health care professionals are constantly at a risk for acquiring HBV or HCV as the screening measures are not adequate. Needle sharing among the injecting drug users is another prime factor involved in the transmission of these viruses. In order to get a clear picture of HCV prevalence among these high risk groups the next part of the study was designed with the following objectives:

3.2.1 Chronic Renal failure cases

* To study the prevalence of HCV in patients undergoing haemodialysis, transfusion and/or transplantation.
* To study the correlation between the number of haemodialysis/transfusion and viral transmission.
* To analyse the biochemical profile of the cases to correlate with the viral positivity.

3.2.2 Intravenous drug users

* To study the prevalence of HCV among IVDUs.
* To analyse the substance abuse practices and risk behaviours of the IVDUs.
* To study the biochemical profile of the IVDUs and to correlate with the viral positivity.
3.3.3 Health care workers

* To study the prevalence of HCV in health care workers like doctors, nurses, technicians, Lab.attenders and medical students.

3.3 HCV BASELINE DATA

The prevalence of hepatitis C among the general population is found to be varying between 0.6% in the United States to, as high as, 22% in Cameroon. The HCV data presently available in India is far inadequate to be considered as a baseline data for our country. Hence, to generate a baseline data, concerning the prevalence of HCV infection in apparently healthy population the next part of the study was:

* To study the prevalence of HCV in normal healthy population represented by voluntary blood donors.
* To analyze some of the factors involved in HCV transmission.

3.4 EVALUATION OF DIAGNOSTIC SYSTEMS

Currently there are an array of commercially available ELISAs for the detection of HBsAg and anti-HCV. All the diagnostic systems are not similar in performance. A comparative evaluation study could identify the test method which is best in terms of specificity and sensitivity. Currently the RIBA is a supplemental assay for anti-HCV. The RIBA pattern could indicate the possible genotype, the HCV-RNA status or an immunodeficient status in RIBA indeterminate cases. Antibody positivity necessarily doesn't mean HCV-RNA
positivity. In some studies, ALT levels and anti-HBc IgM positivity have been used as surrogate markers for HCV infection. Keeping all these facts as the basis, the next part of the study was attempted:

3.4.1 Evaluation of HBV diagnostics

* To evaluate the efficacy of commercially available ELISAs for the detection of HBsAg.

3.4.2 Evaluation of HCV diagnostics

* To comparatively evaluate the II and III generation ELISA, III generation RIBA 3.0 and RT-PCR for the diagnosis of HCV infection.
* To study the RIBA seroreactive pattern of all the anti-HCV positive cases and to correlate with the possible HCV genotype.
* To study the HCV-RNA status and anti-HIV status in the RIBA indeterminate cases.
* To study the usefulness of ALT levels and anti-HBcIgM positivity as surrogate markers for HCV infection.

3.5 HCV AND AUTOANTIBODIES

There have been many theories put forward regarding the mechanism of chronic liver diseases. Studies have been conducted to see whether there is a linkage between the autoimmune status and the hepatitis viral infection. Among the hepatitis viruses, HCV has been reported to be most commonly
associated with induction of autoantibodies. Hence the next part of the study was:

* To standardise an immunofluorescent assay for the detection of autoantibodies.
* To study the prevalence of autoantibodies like antinuclear antibodies (ANA), anti-mitochondrial antibodies (AMA) and anti-smooth muscle antibodies (ASMA) in HBV-positive, HCV-positive, NBNC-CLD cases.

3.6 PRELIMINARY FOLLOW-UP STUDIES

It is documented that most of acute HCV infections are anicteric and more than 50% of HCV infected cases slip on to chronic liver diseases. In order to assess the progression of HCV positive cases in comparison with HBV positive ones in South India, patients were followed up for a period of 6 months to 2 years with the following plan:

* To study the virological features associated with HBV-positive and HCV-positive liver disease cases in a prospective follow-up.