



## To Study the Clinical Profile and Viral Markers (Hepatitis B and C) In Acute and Chronic Liver Disease

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### Abstract

**Background and Objective:** *Hepatitis B and Hepatitis C virus are endemic in India and have an aetiological role in acute hepatitis, 50-70% of which end up with chronic liver disease. Hepatitis B is responsible for approximately 300 million cases of chronic liver disease worldwide and is the leading cause of chronic hepatitis, cirrhosis and hepatocellular carcinoma worldwide. Hepatitis C is the major cause of transfusion transmitted non-A and non-B hepatitis and continues to be a major cause of liver disease throughout the world. As there are limited numbers of studies regarding this, the present study is undertaken.*

**Methodology:** *50 patients selected using purposive sampling technique admitted in the Department of Medicine, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala from the period of July 2014 to September 2016*

**Results:** *Fifty patients with liver disease were studied. Majority of patients were in mean age group of 41-60 years. Male to female ratio was 4.5:1. Majority of patients presented with abdominal distension, anorexia and jaundice. Majority of patients had abnormal liver function test. 34% patients had viral markers in the form of HBs Ag in 26% and Anti HCV in 8% cases.*

**Interpretation and Conclusion:** *Hepatitis B and C are the major causes of chronic liver disease.*

**Keywords:** *Hepatitis B; Hepatitis C; Acute hepatitis; Chronic hepatitis; Liver Cirrhosis, Hepato cellular carcinoma.*

### INTRODUCTION

**LIVER** – one of the most vital organs of the body which happens to be the second largest organ in the body next to skin. Liver has the critical job of maintaining body's metabolic homeostasis which includes processing of dietary amino acids, carbohydrates, lipids and vitamins, removal of microbes and toxins from splanchnic blood, enrooted to systemic circulation, detoxification and excretion into bile of endogenous waste products.<sup>[1,2,3,4]</sup> The

diversity and complexity of hepatic function is such that, it exceeds brain in terms of biologic sophistication and no doubt liver is held in high esteem since ancient times. Enormous functional reserve of liver masks the clinical impact of early liver damage. However, with progression of diffuse disease the consequences of deranged liver function becomes life threatening.<sup>1,2,3</sup> Liver is vulnerable to wide variety of metabolic, toxic, microbial, circulatory and neoplastic insults.<sup>1,2,3,4,5</sup>

The dominant primary disease of liver are viral hepatitis, alcoholic liver disease and hepatocellular carcinoma. Infectious disorders of liver dominate the clinical practice of hepatology. Hepatology experienced an extraordinary boost when major viruses that affect the liver were identified.

Hepatitis virus A-G have been identified and studied as etiological agents for various liver disorders.<sup>1,2,3,4,5</sup> Hepatitis B and C virus are the major cause of CHRONIC LIVER DISEASE in India.<sup>1,2,3,4,5</sup> Hepatitis B is a common disease worldwide with an estimated global prevalence of over 350 million or approximately 5% of world's population.<sup>1,2,3,4,6</sup> Also 2/3rd of all cases of hepatocellular carcinoma is caused by hepatitis B virus.<sup>1,2,3,4,7,8</sup> Total hepatitis B virus occurrence in India is around 3-4%.<sup>9,10</sup> . The WHO places HBV in the top 10 causes of death world wide.<sup>11</sup> Chronic hepatitis B constitutes more than 50% of chronic hepatitis cases. In this context of large population and absence of a national immunization programme would mean a projected increasing burden of infection and liver disease due to HBV in India in the years to come. In this perspective, the HBV epidemiology in India becomes relevant not only nationally but also internationally, because of the possibility of India becoming THE LARGEST HBV infection pool in the world.<sup>9,12,13</sup> WHO estimates that 3% of world population is infected with HCV and around 170 million individuals are chronic carriers at risk of developing liver cirrhosis and hepatocellular carcinoma.<sup>1,2,3,4,14,15,16</sup>

Hepatitis B virus is a member of the Hepadna virus family.<sup>17</sup> The virus particle, called Dane particle<sup>18</sup> (virion), consists of an outer lipid envelope and an icosahedralnucleocapsid core composed of protein. The nucleocapsid encloses the viral DNA and a DNA polymerase that has reverse transcriptase activity similar to retroviruses.<sup>19</sup> The outer envelope contains embedded proteins which are involved in viral binding of, and entry into, susceptible cells. The virus is one of the smallest enveloped animal viruses with a virion diameter of 42 nm, but pleomorphic forms exist, including

filamentous and spherical bodies lacking a core. These particles are not infectious and are composed of the lipid and protein that forms part of the surface of the virion, which is called the surface antigen (HBsAg), and is produced in excess during the life cycle of the virus.<sup>20</sup>

The early evolution of the Hepatitis B, like that of all viruses, is difficult to establish. The divergence of orthohepadna virus and avihepadna virus occurred ~125,000 years ago (95% interval 78,297–313,500).<sup>21</sup> Both the Avihepadna virus and Orthohepadna viruses began to diversify about 25,000 years ago.<sup>22</sup> The branching at this time lead to the emergence of the Orthohepadna genotypes A–H. Human strains have a most recent common ancestor dating back to 7,000 (95% interval: 5,287–9,270) to 10,000 (95% interval: 6,305–16,681) years ago.

The Avihepadna virus lack a X protein but a vestigial X reading frame is present in the genome of duck hepadnavirus.<sup>23</sup> The X protein may have evolved from a DNA glycosylase.

The rate of non-synonymous mutations in this virus has been estimated to be about  $2 \times 10^{-5}$  amino acid replacements per site per year.<sup>24</sup> The mean number of nucleotide substitutions/site/year is  $\sim 7.9 \times 10^{-5}$ .

A second estimate of the origin of this virus suggests a most recent common ancestor of the human strains evolved ~1500 years ago.<sup>25</sup> The most recent common ancestor of the avian strains was placed at 6000 years ago. The mutation rate was estimated to be  $\sim 10^{-6}$  substitutions/site/year.

Another analysis with a larger data set suggests that Hepatitis B infected humans 33,600 years ago (95% higher posterior density 22,000–47,100 years ago).<sup>26</sup> The estimated substitution rate was  $2.2 \times 10^{-6}$  substitutions/site/year. A significant increase in the population was noted within the last 5,000 years. Cross species infection to orangutans and gibbons occurred within the last 6,100 years.

.The hepatitis C virus particle consists of a core of genetic material (RNA), surrounded by an icosahedral protective shell of protein, and further encased in a lipid (fatty) envelope of cellular

origin. Two viral envelope glycoproteins, E1 and E2, are embedded in the lipid envelope. Hepatitis C virus has a positive sense single-stranded RNA genome. The genome consists of a single open reading frame that is 9600 nucleotide bases long.<sup>27</sup> This single open reading frame is translated to produce a single protein product, which is then further processed to produce smaller active proteins.

At the 5' and 3' ends of the RNA are the UTR, that are not translated into proteins but are important to translation and replication of the viral RNA. The 5' UTR has a ribosome binding site<sup>17</sup> (IRES — Internal ribosome entry site) that starts the translation of a very long protein containing about 3,000 amino acids. The core domain of the hepatitis C virus (HCV) IRES contains a four-way helical junction that is integrated within a predicted pseudoknot.<sup>18</sup> The conformation of this core domain constrains the open reading frame's orientation for positioning on the 40S ribosomal subunit. The large pre-protein is later cut by cellular and viral proteases into the 10 smaller proteins that allow viral replication within the host cell, or assemble into the mature viral particles.<sup>19</sup> Structural proteins made by the hepatitis C virus include Core protein, E1 and E2; non-structural proteins include NS2, NS3, NS4A, NS4B, NS5A, and NS5B.

Identifying of the origin of this virus has been difficult but genotypes 1 and 4 appear to share a common origin.<sup>28</sup> A Bayesian analysis suggests that the major genotypes diverged about 300–400 years ago from the ancestor virus.<sup>29</sup> The minor genotypes diverged about 200 years ago from their major genotypes. All of the extant genotypes appear to have evolved from genotype 1 subtype 1b.

A study of genotype 6 strains suggests an earlier date of evolution: ~1,100 to 1,350 years before the present (95% credible region, 600 to >2,500 years ago).<sup>[28]</sup> The estimated rate of mutation was  $1.8 \times 10^{-4}$  (95% credible region  $0.9 \times 10^{-4}$  to  $2.9 \times 10^{-4}$ ). This genotype may be the ancestor of the other genotypes.<sup>28</sup>

A study of European, USA and Japanese isolates suggested that the date of origin of genotype 1b was ~1925.<sup>29</sup> The estimated dates of origin of types 2a and 3a were 1917 and 1943 respectively. The time of divergence of types 1a and 1b was estimated to be 200–300 years.

A study of genotype 1a and 1b estimated the dates of origin to be 1914–1930 (95% credible interval: 1802–1957) for type 1a and 1911–1944 (95% credible interval: 1806–1965) for type 1b.<sup>30</sup> Both types 1a and 1b underwent massive expansions in their effective population size between 1940 and 1960. The expansion of HCV subtype 1b preceded that of subtype 1a by at least 16 years (95% credible interval: 15–17 years). Both types appear to have spread from the developed world to the developing world.

The genotype 2 strains from Africa can be divided into four clades that correlate with their country of origin: (1) Cameroon and Central African Republic (2) Benin, Ghana and Burkina Faso (3) Gambia, Guinea, Guinea-Bissau and Senegal (4) Madagascar.<sup>31</sup> There is also strong evidence now for the dissemination of hepatitis C virus genotype 2 from West Africa to the Caribbean by the Trans-Atlantic slave trade.<sup>32</sup> Genotype 3 is thought to have its origin in South East Asia.<sup>33</sup>

Hepatitis B flare, defined as an event with abrupt rise of alanine aminotransferase (ALT) levels to >5 times the upper limit of normal during chronic hepatitis B virus (HBV) infection, is considered to be the result of a human leukocyte antigen-I restricted, cytotoxic T lymphocyte mediated immune response against HBV and its downstream mechanisms. It may occur spontaneously, during or after antiviral therapy and in the setting of immunosuppression and/or chemotherapy. The clinical spectrum of hepatitis B flares varies from asymptomatic to symptomatic and typical overt acute hepatitis, even with hepatic decompensation or failure. Flares may also occur in viraemic patients with cirrhosis with higher incidence of decompensation/mortality, hence requiring immediate antiviral therapy.<sup>35</sup>

Evidence has indicated several functional roles for the formation of these complexes, including co-opting of lipoprotein receptors for attachment and entry, concealing epitopes to facilitate immune escape, and hijacking host factors for HCV maturation and secretion. Here, we review the evidence surrounding pathogenesis of the hepatitis C infection regarding lipoprotein engagement, cholesterol and triglyceride regulation, and the molecular mechanisms underlying these effects.

Patients with dual HBV and HCV infection may also have higher rate of hepato cellular carcinoma than patients infected with either virus alone.<sup>6,17</sup> It is a paradox that such an important organ has little capacity to repair itself once it is damaged beyond a critical level. Damaged liver not only affects normal functioning of liver but also, will lead to derangement of function of other organs.

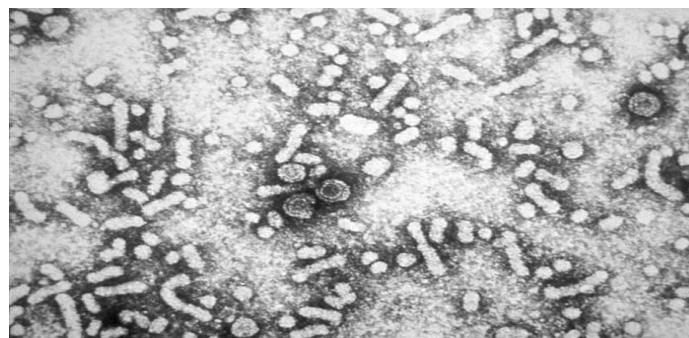
To cap it all there are no satisfactory specific treatment for LIVER DISEASE. Hence PREVENTION IS MORE IMPORTANT and more relevant. Early diagnosis may contribute to prevention of complications.

This study is undertaken in view of the common prevalence, huge magnitude, seriousness of the problem and not many studies are available in India.

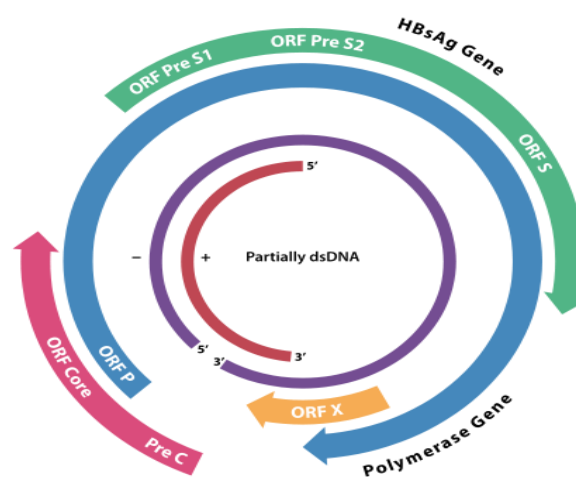
## REVIEW OF LITERATURE

Viral hepatitis is a systemic infection affecting predominantly the liver and causing its inflammation. It may be acute (recent infection, relatively rapid onset) or chronic. The most common clinical consequence of infection with HAV or HEV is an illness characterized by sudden onset of fever and systemic symptoms, which is followed a few days later by jaundice. Majority of people with acute viral hepatitis recover spontaneously within a few weeks, without any residual consequences. However in some persons, the illness is complicated by occurrence of a severe form of the disease, known as acute liver failure (ALF), which is characterized by altered sensorium and bleeding tendency (coagulopathy). Patients with ALF have a high case-fatality rate, in the

absence of liver transplantation, which is either inaccessible or non-affordable for a large majority of Indian population.<sup>33</sup>



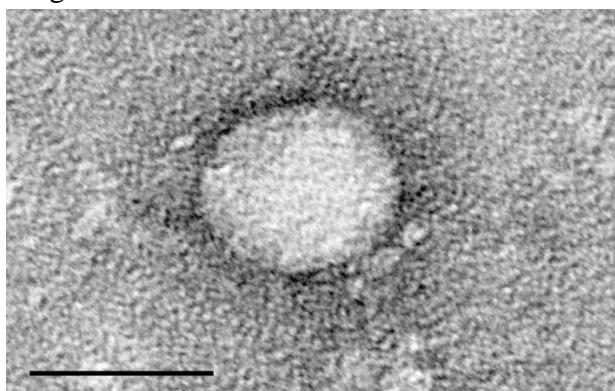
**Figure 1:** TEM micrograph showing hepatitis B viruses



**Figure 2:**

Extensive studies have focused on the natural history of HCV infection.<sup>34,35</sup> An early study indicated a poor prognosis of HCV cirrhosis.<sup>36</sup> However, subsequent large cohort studies showed that the long-term outcomes of HCV cirrhosis, although progressive, are more variable.<sup>37,38,39,40,41,42,43</sup> The knowledge about clinical profiles of CHC at the initial presentation and the factors which affect disease progression, especially from CHC to cirrhosis, remains limited. Data on these issues are particularly lacking in publicly-funded patients. However, such data are essential to provide these patients with improved quality and cost-effective care. It is well known that CHC is associated with a wide variation in ALT, from normal ALT to persistent elevation of ALT. Although studies have shown that patients with

persistently normal ALT usually have slower progression and lower prevalence of cirrhosis.<sup>41</sup> the clinical importance of dynamic ALT follow-up for the disease activity and predict disease progression remains to be defined. Occult or latent hepatitis B virus (HBV) infection is defined as the detect ability of HBV DNA in the absence of HBsAg. Recent studies have raised the concern that occult HBV infection may play a role in disease progression and treatment response of CHC.<sup>44</sup> However, the prevalence of occult HBV infection in these patients and its true role in HCV pathogenesis remains to be determined.<sup>45</sup>



**Figure 3:** Electron micrograph of hepatitis C virus from cell culture (scale = 50 nanometers)

The study by Irshad et al described the frequency of hepatitis viral markers in patients with uncomplicated acute viral hepatitis (AVH; n = 32) and in patients with severe liver diseases, including those with fulminant hepatic failure (FHF; n = 110), subacute hepatic failure (SAHF; n = 65), and chronic active hepatitis (CAH; n = 33). The results indicated that hepatitis A virus infection is quite rare, whereas hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are the predominant causes of acute and chronic liver failure in India. The incidence of HBV infection in AVH, FHF, SAHF, and CAH groups was recorded in 3.7, 19.1, 23.1, and 69.7% of the cases, respectively. Similarly, HCV infection in those four groups was noted in 12.5, 45, 44.6, and 48.5% of the cases, respectively. Further analysis of HCV infection demonstrated that it was as frequent as single infection in acute cases, but more commonly found in association with HBV infection in chronic liver

failure cases. Hepatitis D virus (HDV) infection, as indicated by the presence of IgM anti-HDV antibodies, was recorded in 7.3% of the cases with AVH, in 7.3% of the cases with FHF, in 9.2% of the cases with SAHF, and in 6.1% of the cases with CAH. HDV was associated with HBV both as super infection as well as co-infection. Interestingly, nearly 2-6% of the cases in each group showed the presence of simultaneous HBV, HCV, and HDV infection. 83.3% of the AVH, 42.1% of the FHF, 37.0% of the SAHF, and 15.1% of the CAH patients had unknown viral markers.<sup>46</sup>

Hu et al performed a study which was aimed to assess the clinical profiles of chronic hepatitis C (CHC) at first presentation and clinical implication of dynamic follow-up of ALT level in a county medical center setting. A total of 294 patients were selected from the population consecutively evaluated in the Hepatitis Clinic at Los Angeles County-USC Medical Center between Jan. 1990 and Dec. 1998. Ethnicity of the patients was Hispanics-49.0%, Caucasian- 28.6%, African American-13.6%, and Asian-8.8%. Risk factors were identifiable in 84.0% of patients, and injection drug use (IDU) represented the leading risk factor for HCV acquisition (47.4%). History of alcoholism was present in 39.1%. The initial clinical diagnoses were chronic hepatitis 76.9%; compensated cirrhosis 20.4%; and decompensated cirrhosis 2.7%. Elevation of ALT, alpha fetoprotein (AFP), ferritin, and anti-nuclear antibody (ANA) titer were seen in 219/294 (74.5%), 60/194 (30.9%), 20/83 (24.1%), and 35/97 (36.1%) patients, respectively. Anti-HBc (total) test was positive in 65/129 (50.5%) patients. The presence of cirrhosis was significantly associated with age greater than 55 years at entry, female gender, non-African American ethnicity, history of transfusion, lower level of albumin and elevated level of AFP. Longitudinal observation of ALT changes in 178 patients who had neither evidence of cirrhosis at entry nor received interferon treatment showed persistently normal, intermittently or persistently elevated ALT level in 15.2%, 38.3%, and 46.6% patients, respectively. The frequency of developing

clinical evidence of cirrhosis during follow-up was significantly higher in patients with persistently (16.0%) or intermittently (7.0%) elevated ALT than that in patients with persistently normal ALT (4.0%).<sup>47</sup>

Bhat et al performed a one year prospective cohort, of all the suspects of viral hepatitis enrolled from 01/08/2003 to 31/07/2004 involving all health facilities (a total of 18 health institutions) of Dakhliya region, Sultanate of Oman, was subjected to centralized laboratory confirmation. Notification of viral hepatitis confirmed cases was the tool for analysis. A subset of unconfirmed viral hepatitis cases that were admitted and discharged from the referral hospital were retrieved and analysed utilizing their computerized hospital records.

There was a shift of incidence of hepatitis B towards higher age groups (32.4 +/- 16.2 years) with only one case under 15 years of age ( $p < 0.0001$ ). While as under 15 year age group was less prone to hepatitis C ( $p < 0.05$ ), it had a high incidence for hepatitis A with mean age 11.4 +/- 13.9 years ( $p < 0.01$ ). Hepatitis E incidence had a higher mean age of 44.6 +/- 24.1 years with insignificant linear trend ( $p > 0.05$ ).<sup>48</sup>

Tawfiq et al performed a retrospective analysis of the reported cases of viral hepatitis was conducted from January 2000 to June 2005. A total of 1214 patients with viral hepatitis were identified during the study period. Of hepatitis A, B, and C, HBV was the most predominant type of hepatitis, accounting for 49.3% of the cases, followed by HCV (40.7%) and HAV (10%). Nine (0.7%) patients had both HBV and HCV. The male-to-female ratio was higher in HBV (1.8:1), whereas HAV and HCV showed no significant differences. HAV infection predominates in children (1-20 years), HBV in young adults (31-50 years), and HCV in older adults (51-70 years).<sup>49</sup>

Garg et al examined 91 patients; besides jaundice (median bilirubin 23.1 mg/dL) and coagulopathy, acute onset ascites with or without encephalopathy was the presenting symptom in 92%. In all patients a first diagnosis of chronic liver disease was made, mainly due to hepatitis B (37%) or alcohol (34%).

Reactivation of chronic hepatitis B and alcoholic hepatitis were the common acute insults. The 90-day mortality was 63%. On multivariate analysis, hepatic encephalopathy, low serum sodium, and high INR were found to be independent baseline predictors of mortality. Amongst all severity scores studied, MELD, SOFA and APACHE-II scores had AUROCs of  $> 0.8$  which was significantly higher than that of Child.<sup>50</sup>

The causes of acute injury in acute-on-chronic liver failure (ACLF) are variable. There may be simultaneous presence of more than one acute insult. We describe the clinical profile of ACLF and the effect of dual acute insult on the natural history. In a Study by Jha et al, Fifty-two patients with ACLF (mean age  $38.6 \pm 16.7$  years; M/F 41:11) were included. Hepatitis virus infection (46.1 %) and bacterial infection (36.5 %) were the most common acute insults. Hepatitis virus infections were the sole acute insult in 34.6 % and associated with another injury in 11.5 %. Bacterial infections were identified as acute insult in 19 patients (sole acute insult in 13). Drugs, autoimmune disease, surgery, malaria, and dengue were other acute injuries identified. The cause of acute decompensation was unknown in 11.5 %. Mortality (66.6 % vs. 51.1 %) was higher in patients with dual insult ( $n=9$ ) as compared with single/unknown insult ( $n=43$ ).<sup>51</sup>

Bjomsson Et al performed a cross-sectional study in which 40 cases who have non-alcoholic fatty liver based on ultrasound abdomen and 40 controls who do not have NAFLD on USG finding were recruited. Severity of NAFLD was measured based on USG abdomen finding. Routine investigations, lipid profile, fasting blood sugar, C-reactive protein, and S. ferritin were measured. BMI, waist circumference and BP were calculated. Results were analysed statistically. In that study it was found that NAFLD is more common in the age range 40 - 49 yr. Among the NAFLD group, various risk factors, i.e., BMI  $> 25$  was present in 85%, hypertension in 47.5%, DM in 67.5%, high triglyceride in 47.5%, low HDL in 57.5%, central obesity in 62.5%. Prevalence of persons with high

CRP and S. ferritin in NAFLD group was 67.5% and 40% respectively.<sup>52</sup>

The term non-alcoholic fatty liver disease (NAFLD) is used to describe a wide spectrum of fatty liver changes ranging from simple steatosis to steatohepatitis, even to cirrhosis.<sup>53</sup> Most of the patients are asymptomatic, detected on routine examination with other features of metabolic syndrome like, diabetes, hypertension, and obesity. The term NAFLD was first coined by Ludwig et al in 1980.<sup>54</sup> In many countries, more than 80% of NAFLD patients have an increased BMI and 30-40% are obese; approximately 50% show signs of insulin resistance, 20 - 30% have type 2 diabetes, 80% show hyperlipidaemia, and 30 - 60% have arterial hypertension. Using liver ultrasonography, a recent population-based cohort study performed in Italy found that one in four or five adults in that country suffer from NAFLD.<sup>55</sup> Liver biopsy remains the gold standard in diagnosis and prognosis of NAFLD, but being invasive has limitation for patient consent. Serum ferritin and C-reactive protein (CRP) are nonspecific inflammatory markers, but while it is not specific for diagnosis of NAFLD, once the diagnosis has been established, their level has been shown to be significantly more elevated in patients with NASH compared to with those with simple steatosis (SS).<sup>56</sup> Since NAFLD is an inflammatory condition of the liver, increased levels of S. ferritin and CRP may be expected.

Alcohol is most common substance abused. Alcoholic liver disease is a major health care problem in India. Alcohol consumption is directly associated with liver disease mortality and accounts for increased social and economic costs. Alcoholic liver disease may take the forms of acute involvement (alcoholic hepatitis) or chronic liver disease (steatosis, steatohepatitis, fibrosis and cirrhosis). The severity and prognosis of alcohol-induced liver disease depends on the amount, pattern and duration of alcohol consumption, as well as on the presence of liver inflammation, diet, nutritional status and genetic predisposition of an individual. While steatosis is complete benign

disease, liver cirrhosis is associated with marked morbidity, mortality and life expectancy shortening.

Hemang et al took a total of 50 patients, who were studied and their clinical profile, laboratory parameters and radiological investigations were taken.

Among 50 patients 58 % belonged to age group 40-49 years. 60 % of patients have chief complaint of abdominal distension and melena each. Jaundice (60%) and ascites (60%) were commonest finding. All patients had raised SGPT, SGOT, S.AIPO4 and S. bilirubin suggesting liver damage. Prolonged PT and reduced S. albumin suggested reduced protein synthesis because of liver disease. Alcoholic hepatitis was in 24% cases, while 40% had fatty liver and 36 % had alcoholic cirrhosis. Overall mortality rate was 20 % . , most common cause is encephalopathy (40%), coagulopathy leading to DIC (40%) and hepatorenal syndrome(20%).<sup>56</sup> Hepatic encephalopathy (HE) is an important neuropsychiatry complication of liver disease causing significant morbidity and mortality worldwide. Efforts at improving the outcome have resulted in development of new strategies in the management given the background of new insights in the pathogenesis of this disease entity. Understanding the disease profile including precipitants as well as prognostic factors will contribute in this regard as new strategies are yet to be widely applied. In a prospective study by Onyekwere, all patients managed for HE from January to December 2008 were recruited. A questionnaire was used to extract their basic demographics, clinical features noting any possible precipitants, complications, management protocol as well as outcome. A total of 21 subjects were seen during the period under review. (mean age 57.9±13). There was no significant difference in the mean ages of males and females. Two patients had acute encephalopathy, while others had acute-on chronic encephalopathy. The risk factors for liver disease included significant alcohol ingestion, hepatitis B virus infection, and previous jaundice, while other complications of liver disease noted

were deepening jaundice, ascites, bleeding tendencies, and renal failure. The identified precipitants for HE were sepsis 6 (29%), electrolyte imbalance 3 (14%), gastrointestinal bleed 5 (24%), drugs (5%), and possible malignant transformation 6 (29%). Focus of sepsis was bacterial peritonitis in two cases. Majority of our patients (61%) came during advanced stage of liver disease (Child-Pugh class C). Length of hospital stay ranged from 1 to 7 weeks and a mortality of 48% was observed. Predictors of mortality were a history of significant alcohol ingestion, previous blood transfusion, Hepatitis B and C infections, and severe liver dysfunction on presentation (Child-Pugh class C).<sup>57</sup>

Zeeba et al, included 117 patients with ages ranging between 1.5 months to 18 years. There was an obvious male preponderance, the male female ratio being 1.34:1. Loss of appetite was observed to be the predominant presenting feature (95.7% cases) and was followed by nausea and vomiting (90.6% cases), hepatomegaly (75.2% cases), icterus (53.9% cases), abdominal pain (51.3% cases), fever (45.3% cases), gastro-intestinal bleed (34.2% cases), ascites (24.8% cases), varices (24.8% cases), pruritus (15.4% cases), and altered sensorium (8.6% cases). Histopathological diagnosis of cases revealed Twenty four (20.5) cases had cirrhosis of liver with portal hypertension. Acute hepatitis was seen in 28 (23.9) cases. All patients of hepatitis had icterus and elevated transaminases. Serological evidence of hepatitis A infection was present in 10 (35.7%), hepatitis B in 6 (21.4%), hepatitis E in 3 (10.7%), hepatitis C in 2 (7.1%), and both hepatitis A and B in 2 (7.1%) patients with acute hepatitis. In the remaining 5 cases no viral marker was detected. Fifteen patients had hepatic failure (of whom 9 died). All these patients had icterus, 10 (66.7%) had encephalopathy, 6 (40.0%) had gastrointestinal hemorrhage, and 3 (20.0%) had ascites. Of the patients of hepatic failure, 3 (20.0%) had serological evidence of hepatitis B alone, 4 (26.7%) of hepatitis A, 3 (20.0%) of both hepatitis B and D, and 2 (13.3%) of hepatitis E. The

remaining 3 cases had no positive markers. Liver biopsy showed evidence of sub-massive to massive necrosis. Elevated bilirubin was seen in all these cases while elevation of transaminases was present in 10 (66.7%) cases. Chronic hepatitis was present in 11 patients, 4 (36.4%) of whom had icterus, 2 (18.2%) had ascites and 1 (9.1%) had gastrointestinal hemorrhage. Five (45.5%) of them tested positive for hepatitis B and 3 (27.3%) for hepatitis C. Six (54.6%) of these patients had elevated bilirubin while 8 (72.7%) had elevated transaminases. On the whole hepatotropic viruses were responsible for 43 (36.8%) cases, hepatitis B for 19 (16.2%) cases and hepatitis.<sup>58</sup>

Samanta et al performed a prospective study to estimate the prevalence of hepatotropic viruses in the causation of acute liver failure in children admitted to a tertiary hospital in Kolkata. Analysis of clinical and laboratory parameters (including viral markers) of children with acute liver failure with predesigned structure proforma. Admitted patients aged from 1 through 12 years who met the criteria of acute liver failure were included in the study. Of the 45 patients in that study, a majority was from the southern part of West Bengal. It was possible to determine the aetiology in 35 of the 45 patients (77.7%) admitted. Of these 35, a diagnosis of hepatitis due to hepatotropic viruses was made in 30 patients. The hepatitis A virus was responsible for 16 of the 30 cases (53.3%), 9 cases attributed to HAV only. Following this was the hepatitis E virus causing ALF in 14 cases (46.6%), 7 singularly so. Hepatitis B virus caused 8 cases (26.6%), 6 singly. The survival rate during hospital stay was 51.1%. Prodrome, decreased liver span, ascites, cerebral oedema, coagulopathy, renal failure, spontaneous bacterial peritonitis, signs and symptoms of clinical sepsis (corroborated by laboratory data), severe hypoalbuminaemia and electrolyte imbalance were significantly more in patients who died. The mean age, prothrombin time, serum bilirubin level and stage of encephalopathy differed significantly between survivors and non-survivors.<sup>59</sup>



Nikolaou performed a study to assess the prevalence of abnormal liver function tests (LFTs) and the associated clinical profile and outcome(s) in acute decompensated heart failure (ADHF) patients as Alteration in LFTs is a recognized feature of ADHF, but prevalence and outcomes data from a broad contemporary cohort of ADHF are scarce and the mechanism(s) of ADHF-induced cholestasis is unknown. They conducted a post hoc analysis of SURVIVE, a large clinical trial including ADHF patients treated with levosimendan or dobutamine. All LFTs were available in 1134 patients at baseline. Abnormal LFTs were seen in 46% of ADHF patients: isolated abnormal alkaline phosphatase (AP) was noted in 11%, isolated abnormal transaminases in 26%, and a combination of abnormal AP and transaminases in 9%. Abnormal AP was associated with marked signs of systemic congestion and elevated right-sided filling pressure. Abnormal AP had no relationship with 31-day mortality but was associated with worse 180-day mortality (23.5 vs. 34.9%,  $P = 0.001$  vs. patients with normal AP). Abnormal transaminases were associated with clinical signs of hypoperfusion and with greater 31-day and 180-day mortality compared with normal transaminase profiles (17.6 vs. 8.4% and 31.6 vs. 22.4%, respectively; both  $P < 0.001$ ). There was no additive value of abnormal AP plus abnormal transaminase on a long-term outcome. Abnormal LFTs were present in about a half of patients presenting with ADHF treated with inotropes. Abnormal AP and abnormal transaminases were associated with specific clinical, biological, and prognostic features, including a short-term mortality with increased transaminases but not with biological signs of cholestasis, in ADHF patients.<sup>60</sup>

Heart failure (HF) is a clinical syndrome associated with haemodynamic changes that may result in pressure-related damage to one or more organs.<sup>61,62</sup> Interactions between renal and cardiac dysfunction have been recently construed to be 'cardiorenal syndromes', including subtypes with specific pathophysiology, diagnostic and

prognostic values, and management strategies.<sup>63,64,65</sup> Liver involvement has been mostly described and investigated in patients with chronic HF.<sup>66,67</sup> Liver enzyme alterations are usually classified as relating predominantly to liver cell necrosis (signified by transaminase elevations) or predominantly to cholestasis signified by elevated alkaline phosphatase (AP) levels].<sup>68,69</sup> The prognostic importance of abnormalities in liver function tests (LFTs) has varied among published studies. The unfavourable predictive value of abnormal LFTs has been described in patients with chronic HF<sup>70</sup> or acute decompensated heart failure (ADHF).<sup>71</sup> Total bilirubin was among the most highly significant predictors of mortality in a post hoc analysis of a large cohort of chronic HF patients in a clinical trial.<sup>72</sup> However, a haemodynamic-independent prognostic value of liver function abnormalities was not found in a recent analysis of 323 patients with a history of HF.<sup>73</sup>

Amarapurkar et al conducted a retrospective analysis of 363 consecutive patients with chronic HBV infection was performed. All patients were HBsAg-positive. Tests for liver profile, HBeAg and anti-HBe antibody were performed in all patients. Serum HBV DNA was tested using branched DNA assay in 245 patients. The patients were classified into three groups: no cirrhosis with normal ALT levels, no cirrhosis with elevated ALT levels, and clinical or histological evidence of cirrhosis. Of 363 patients, 141 (39%) were HBeAg-positive and 222 (61%) HBe Ag-negative. Of HBeAg-negative patients, 120 (54%) had normal ALT, 45 (20%) had elevated ALT and 57 (26%) had evidence of cirrhosis; corresponding figures in the HBeAg-positive patients were 40 (28%), 66 (47%) and 35 (25%). HBV DNA was positive in 53 of 131 (40%) HBeAg-negative patients tested; of these 53 patients, 9 (17%) had normal ALT, 20 (38%) had elevated ALT and 24 (45%) had cirrhosis. Thus, 72% of HBeAg-positive and 46% of HBeAg-negative patients had elevated ALT and/or cirrhosis. Among the latter group, 83% of HBV DNA-positive patients had elevated

ALT and/or cirrhosis. Overall, 18% of HBsAg-positive patients had HBeAg-negative, HBV DNA-positive liver disease.<sup>74</sup>

Brunetto et al studied the influence of biochemical and virologic patterns and interferon on the outcome of anti-HBe positive chronic hepatitis B in 164 (103 treated) consecutive patients, followed-up prospectively for a mean of 6 years (21 months-12 years). Histology, biochemical and virologic profiles were characterized by monthly monitoring during the first 12 months of follow-up. Thereafter patients underwent blood and clinical controls every 4 and 6 months, respectively. Cirrhosis at follow-up histology or end stage complications of cirrhosis served as end points for the analysis of factors influencing disease progression in patients with baseline chronic hepatitis or cirrhosis, respectively. Disease progression was associated with older age ( $P < 0.001$ ), absence of previous HBeAg history ( $P = 0.017$ ) and higher serum HBV-DNA levels ( $P = 0.009$ ) (more frequently observed in unremitting disease profile,  $P = 0.012$ ) at multivariate analysis. Fluctuations of IgM anti-HBe levels (associated with disease exacerbations,  $P = 0.045$ ) correlated with end stage complications in cirrhotic ( $P = 0.011$ ). Disease improved in 14.6 and 1.6% of treated and untreated patients, respectively ( $P = 0.015$ ): interferon slowed disease progression ( $P < 0.001$ ). Conclusions: The outcome of anti-HBe positive chronic hepatitis B is worsened by older age and persistent viral replication or hepatitis exacerbations in chronic hepatitis or in cirrhotic patients, respectively.<sup>75</sup>

A paper by Tenney et al revealed that Entecavir (ETV) is a deoxyguanosine analogue approved for use for the treatment of chronic infection with wild-type and lamivudine-resistant (LVDr) hepatitis B virus (HBV). In LVD-refractory patients, 1.0 mg ETV suppressed HBV DNA levels to below the level of detection by PCR ( $<300$  copies/ml) in 21% and 34% of patients by Weeks 48 and 96, respectively. Prior studies showed that virologic rebound due to ETV resistance (ETVr) required pre-existing LVDr HBV reverse

transcriptase substitutions M204V and L180M plus additional changes at T184, S202, or M250. To monitor for resistance, available isolates from 192 ETV-treated patients were sequenced, with phenotyping performed for all isolates with all emerging substitutions, in addition to isolates from all patients experiencing virologic rebounds. The T184, S202, or M250 substitution was found in LVDr HBV at baseline in 6% of patients and emerged in isolates from another 11/187 (6%) and 12/151 (8%).<sup>76</sup>

ETV-treated patients by Weeks 48 and 96, respectively. However, use of a more sensitive PCR assay detected many of the emerging changes at baseline, suggesting that they originated during LVD therapy. Only a subset of the changes in ETVr isolates altered their susceptibilities, and virtually all isolates were significantly replication impaired in vitro. Consequently, only 2/187 (1%) patients experienced ETVr rebounds in year 1, with an additional 14/151 (9%) patients experiencing ETVr rebounds in year 2. Isolates from all 16 patients with rebounds were LVDr and harbored the T184 and/or S202 change. Seventeen other novel substitutions emerged during ETV therapy, but none reduced the susceptibility to ETV or resulted in a rebound. In summary, ETV was effective in LVD-refractory patients, with resistant sequences arising from a subset of patients harbouring pre-existing LVDr/ETVr variants and with approximately half of the patients experiencing a virologic rebound.<sup>76</sup>

A randomized, double-blind, vaccine/placebo trial of the Merck 20- $\mu$ g hepatitis B virus (HBV) vaccine was done among 1402 homosexual men attending venereal disease clinics in five American cities. Vaccination was followed by only minimal side effects. Two doses of vaccine induced antibody in 80% of vaccine recipients. A booster dose 6 months after the first dose induced antibody in 85% of recipients and markedly increased the proportion of recipients who produced high antibody titers. The incidence of HBV events was markedly less in the vaccine recipients compared to that in the placebo recipients ( $p = 0.0004$ ).

Between month 3 and 15 after the first dose, 56 more significant HBV events (hepatitis, or hepatitis B surface antigen positive, or both) occurred in the placebo group while only 11 occurred in the vaccine group. Ten of the 11 HBV events in the vaccine recipients occurred in hypo- or non-responders to the vaccine.<sup>77</sup>

The prevalence of HBV and HCV infection varies markedly in different populations. Both diseases are concentrated in certain subpopulations such as injecting drug users who have a prevalence rate ten times higher than the general population. The prevalence is also higher in men who have sex with men as compared with the heterosexual population. In 1999, WHO estimated the worldwide prevalence of HCV at 3%. Most affected areas are Africa (5%) and the Eastern Mediterranean region (4.6%), followed by the Western Pacific region (3.9%), and South-East Asia (2%). The Americas and Europe had the lowest prevalence estimates, 1.7% and 1%, respectively.<sup>78</sup> At the country level, the incidence of reported cases is variable, and abrupt changes in incidence can be seen. These trends probably reflect changes in surveillance systems or prevention activities rather than true changes in incidence.<sup>79</sup> According to national estimates, 8.8 million (1.3%) people are infected in 22 European countries.<sup>80</sup> In Europe, the prevalence of HCV can be roughly divided in three patterns: in Northern Europe, the epidemic is mainly transmitted by IDU, with overall prevalence rates between 0.1 and 1%. In Central Europe, the HCV prevalence is intermediate, ranging from 0.2% to 1.2%. In Southern Europe, the overall prevalence ranges between 2.5% and 3.5%

HBV can effectively be prevented by vaccination. The risk of developing a chronic form depends on age at infection: the younger the patient, the higher the risk of developing chronic hepatitis: chronic infection is seen in 90% of infants infected at birth, 30 to 50% of children infected between the age of one to four years, and 1 to 10% of those infected at older age or as adults. A safe and effective HBV vaccine has been available since the 1980s and can

prevent acute and chronic infection with an estimated effectivity of 95%. In 1992, the WHO recommended to implement universal vaccination against hepatitis B for newborns in all countries with an HBV prevalence rate higher than 5% in 1995. All other countries were recommended to implement universal vaccination in 1997. With regard to HCV, it has been estimated that 170 million persons have chronic infection and that three to four million new cases occur each year. Initial infection is frequently asymptomatic or mild (70%–90% of cases). Of those infected, 50–80% later develop chronic infection, and cirrhosis (up to 50%) and liver cancer (1%–5%) over a period of 20 to 30 years. Although other studies show a somewhat lower percentage of cirrhosis and liver cancer. There is no vaccine against HCV infection. HCV is a major public health problem. A person with HCV can infect others from one to several weeks before symptoms. In case of chronic infections, infectivity may persist indefinitely. Research is in progress but the high mutability of the HCV genome complicates vaccine development. The greatest impact on HCV disease burden will likely be achieved by focusing efforts on reducing the risk of HCV transmission from nosocomial exposures (e.g. screening of blood, rigorous implementation of infection control, reducing unsafe injection practices) and high risk behaviours (e.g. injection drug use). Relevant measures to reduce transmission are early diagnosis, effective prevention and screening programmes, as well as appropriate treatment. It is known that a large number of people carrying the HCV virus are not aware of being infected due to high proportion of asymptomatic infections.

In the HD setting, cross-contamination to patients via environmental surfaces, supplies, equipment, multiple-dose medication vials and staff members is mainly responsible for both HBV and HCV transmission. The incidence and prevalence of HBV in HD centers have dropped markedly as a result of isolation strategy for HBsAg positive patients, the implementation of infection control measures and the introduction of HBV vaccine.

The incidence and prevalence of HCV infection among HD patients remain higher than the corresponding general population. There is ongoing debate as to whether isolation of HCV infected patients is needed to combat high anti-HCV seroconversion rates. The current guidelines do not recommend isolation or the use of dedicated machines for HCV infected patients, and rely on strict adherence to infection control measures for the prevention of HCV transmission in the HD setting. Investigations of dialysis associated outbreaks of HCV infection indicate that transmission most likely occurs because of inadequate infection control practices. Routine screening of anti-HCV negative patients, with HCV-antibody testing, and monthly monitoring of ALT levels is recommended to monitor transmission within centers.

The Centers for Disease Control and Prevention (CDC) estimates that 5.6 million workers in the healthcare industry and related occupations are at risk of occupational exposure to blood borne pathogens, including human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), and others.<sup>81</sup> Although the focus on post-exposure management is on HIV, HBV, and HCV, more than 30 different pathogens have caused documented occupational infection following exposure to blood or body fluids in healthcare personnel (HCP) or hospital laboratory personnel.<sup>81</sup>

Hepatitis viruses B (HBV), D (HDV) and C (HCV), which predominantly transmit through the parenteral route, pose a serious “silent epidemic” challenge to India. Infected persons are unaware of their chronic carrier status, and continue to infect others for decades and eventually burden the society with loss of productive workforce, and the health care system with expenses of treating liver failures, chronic liver diseases, and cancers.

Disease burden and sero-prevalence. HBV and HCV together are estimated to have led to 500 million chronically infected persons and one million deaths annually (Figures 2 and 3 present global HBV endemicity and HCV endemicity,

respectively). In the South-East Asia region, the estimated burden of chronic HBV infection is 100 million and the estimated burden of chronic HCV infections in South Asia is 50 million. HBV is the second most common cause of acute viral hepatitis after HEV in India. With 3.7% point prevalence, that is, over 40 million HBV carriers, India is considered to have an intermediate level of HBV endemicity. Every year, one million Indians are at risk for HBV and about 100,000 die from HBV infection.

The population prevalence of HCV infection in India is 1%. HDV infection is not very common in India and is observed in 10% to 20% of HBV positive patients. Epidemics due to unsafe injection practices have been documented in India (hepatitis B carriage and C infection is 46% and 38%, respectively), such as among injecting drug users and healthcare workers caring for infected people. Transmission through unsafe sexual intercourse and transmission from mothers to infants is well-established, though less frequent for HCV infection. Perinatal transmission is about 10% if the mother is hepatitis B surface antigen (HBsAg) positive only and about 90% when the mother is positive for both HBsAg and hepatitis B e-antigen (HBeAg). HCV accounts for most of the post transfusion hepatitis cases.

Prevention and control can be achieved through safe and effective HBV vaccines. WHO recommends routine infant vaccination along with catch-up immunization for adolescents and high risk population. India introduced universal immunization against hepatitis B in 10 states in the year 2002, and in 2011, scaled up this operation countrywide. The HBV vaccine also protects from HDV infection. There is no vaccine against HCV. Screening and immunization of high-risk groups, such as those with history of exposure, risky practices, and occupational risk; specific measures for prevention of mother-to-child transmission and promoting safe blood supply, safe injections and safe sex are other recommended preventive measures.

All occupational exposure to blood and other potentially infectious material place HCP at risk for infection with blood borne pathogens. The Occupational Safety and Health Administration (OSHA) define blood to mean human blood, blood components, and products made from human blood<sup>82</sup>. Other potentially infectious material includes body fluids such as: semen, vaginal secretions, cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, amniotic fluid, saliva associated with dental procedures, and body fluid that is visibly contaminated with blood. All body fluids should be considered infectious in situations where it is difficult or impossible to differentiate between bloody fluids. Any unfixed tissues or organs (other than intact skin) from a human (living or dead) are also considered potentially infectious material. For laboratory personnel, other potentially infectious material includes HIV-containing cell or tissue cultures, organ cultures, HIV- or hepatitis virus-containing culture medium or other solutions, as well as blood, organs, or tissues from experimental animals infected with HIV, HBV, or HCV.

The main occupational risk for acquiring a blood borne pathogen is a percutaneous sharps injury with a contaminated object. Mucous membrane exposure to blood or other potentially infectious material can also transmit HIV, HBV, and HCV. Reports regarding the frequency of such occupational risks are as follows:

There are very few studies had been conducted in india hence we have taken this subject as our study to study the viral markers (hepatitis B and C) present in acute and chronic liver diseases and to study the clinical profile and the biochemical changes in acute and chronic liver diseases

#### **AIMS AND OBJECTIVES**

- To study the viral markers (hepatitis B and C) present in acute and chronic liver diseases.
- To study the clinical profile of patients with acute and chronic liver disease.
- To study the biochemical changes in acute and chronic liver diseases.

#### **MATERIALS AND METHODOLOGY**

##### **SOURCE OF DATA**

Patients fulfilling the inclusion and exclusion criteria attending either outpatient or in patients from department of Medicine in MMIMSR.

##### **METHOD OF COLLECTION OF DATA**

**Sample size:** 50 cases

**Sampling Method:** Simple random sampling

##### **INCLUSION CRITERIA**

- I. Clinical features suggestive of hepatitis and cirrhosis
- II. LFT and/or USG abdomen detected acute and chronic liver disease.
- III. Clinically suspected Hepatocellular carcinoma.

**EXCLUSION CRITERIA:** None

##### **PROTOCOL OF THE STUDY**

Data will be collected in a pre-tested proforma to fulfill the needs of the study. Detailed history, physical examination and necessary investigations are recorded. Purpose of the study will be carefully explained to patients and consent will be taken. Institutional Ethical Committee Clearance will be taken.

##### **INVESTIGATIONS**

- i. Haemoglobin
- ii. Total count
- iii. Differential count
- iv. ESR
- v. Random blood sugar
- vi. Blood urea
- vii. Serum creatinine
- viii. Urine analysis
- ix. USG abdomen
- x. Liver function test
- xi. HBsAg (HEPACARD)
- xii. Anti HCV (TRIDOT)
- xiii. Liver biopsy when indicated
- xiv. Reticulocyte count
- xv. Prothrombin time

**OBSERVATIONS AND RESULTS**

This cross sectional observational descriptive hospital based study was conducted in attending either outpatient or in patients from Department of Medicine in Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala.

This study was conducted over a period of more than 2 years (from July 2014 to September 2016). A total of 50 patients suffering Clinical features suggestive of hepatitis and cirrhosis with other relevant investigations were taken into the study.

**SOCIO DEMOGRAPHIC DETAILS OF THE PATIENTS**

**Table 1:** Mean age of patients

Variable	No. of patients	Minimum age	Maximum age	Mean age	Std. Deviation
Age	50	22	80	47.32	11.44

In our study mean age of hepatitis patients was 47.32 ± 11.44 years. The minimum age of the study participants was 22 years where as the

maximum age of the participants was 80 years. The range of the age for study participants was 58 years.

**Table 2:** Distribution of Hepatitis patients according to Age Group.

			Sex		Total
			Male	Female	
Age Group	20 to 39	N	9	1	10
		% within Sex	22.0%	11.1%	20.0%
	40 to 59 years	N	26	6	32
		% within Sex	63.4%	66.7%	64.0%
	=> 60 years	N	6	2	8
		% within Sex	14.6%	22.2%	16.0%
Total	N	41	9	50	
	% within Sex	100.0%	100.0%	100.0%	

Among male patients, majority i.e. 26(63.4%) were found in the age group of 40 to 59 years followed by 9 patients (22%) were found in the age group of 20 to 39 years. Minimum 6 patients among males were found in the age group of more than 60 years.

Among female patients, majority i.e. 6(66.7%) were found in the age group of 40 to 59 years followed by 2 patients (22.2%) were found in the age group of 20 to 39 years.

**Table 3:** Distribution of Hepatitis patients: Type of Hepatitis Versus Age Group

Type of Hepatitis	Statistics	Age Group			Total
		20 to 39	40 to 59 years	≥ 60 years	
Acute Hepatitis	N	2	4	3	9
	%	22.2%	44.4%	33.3%	100.0%
Liver Cirrhosis	N	7	27	4	38
	% within Age Group	33.3%	33.3%	33.3%	100.0%
Chronic Hepatitis	Count	1	1	1	3
	% within Age Group	20.0%	64.0%	16.0%	100.0%
Total	N	10	32	8	50
	% within Age Group	20.0%	64.0%	16.0%	100.0%

$\chi^2 = 4.58, P \text{ value} < 0.05$

Thirty eight patients are suffering from Liver Cirrhosis followed by 9 from Acute Hepatitis and 3 patients from Chronic hepatitis.

Among acute hepatitis patients, majority i.e. 4(44.4%) were found in the age group of 40 to 59 years followed by 3 patients (33.3%) were found in the age group of more than 60 years. Only 2(22.2%) patients among males were found in the age group of 20 to 39 years.

Among liver cirrhosis patients, majority i.e. 27(33.3%) were found in the age group of 40 to 59 years followed by 3 patients (33.3%) were found in the age group of more than 60 years. Only 2(22.2%) patients among males were found in the age group of 20 to 39 years. .Among chronic hepatitis patients, all age groups has one patient each.

**Table 4:** Sex Distribution among AgeGroup

Age Group Versus Type of Hepatitis Versus Sex									
Age Group		Diagnosis						Total	
		Acute Hepatitis		Liver Cirrhosis		Chronic Hepatitis			
		Sex		Sex		Sex		Sex	
		Male	Female	Male	Female	Male	Female	Male	Female
20 to 39	N	1	1	7	0	1	0	9	1
	% within Type of Hepatitis	20.0%	25.0%	20.6%	.0%	50.0%	.0%	22.0%	11.1%
40 to 59 years	Count	2	2	23	4	1	0	26	6
	% within Type of Hepatitis	40.0%	50.0%	67.6%	100.0%	50.0%	.0%	63.4%	66.7%
Above 60 years	N	2	1	4	0	0	1	6	2
	% within Type of Hepatitis	40.0%	25.0%	11.8%	.0%	.0%	100.0%	14.6%	22.2%
Total	N	5	4	34	4	2	1	41	9
	% within Type of Hepatitis	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

$\chi^2 = 4.02, P \text{ value} < 0.05$

The patients suffering from Acute Hepatitis is 5(100%) male and 4(100%) are female. The age bifurcation is one each in the age group 20 to 39, two each in the age group 40 to 59 and two male and one female in the age group greater than equal to 60 years. Similarly those suffering from Liver Cirrhosis are 34(100%) males and 4(100%) females distributed age wise are majority i.e.23(67.6%) males in the age group 40 to 59 and

4(100%) females in the same age group. Otherwise those who are suffering in Chronic Hepatitis are 2 males one each in age group 20 to 39 and 40 to 59 and one female in the age group greater than 60 years.

The association is statistically significant.

**Table 5:** Distribution of Patients according to symptoms

Diagnosis	Statistic	Anorexia	Nausea	Vomiting	Jaundice	Fever	Pain Abdomen	Abdominal Distension	Altered Behaviour	G.I. Bleeding	
										Hemat emesis	Malaena
Acute Hepatitis(N=9)	N	7	7	8	9	6	5	0	0	0	0
	%	77.8%	77.8%	88.9%	100.0%	66.7%	55.6%	.0%	.0%	.0%	.0%
Liver Cirrhosis(N=38)	N	24	13	6	19	1	6	35	4	4	11
	%	63.2%	34.2%	15.8%	50.0%	2.6%	15.8%	92.1%	10.5%	10.5%	28.9%
Chronic Hepatitis(N=3)	N	2	0	2	1	0	2	0	0	0	0
	%	66.7%	.0%	66.7%	33.3%	.0%	66.7%	.0%	.0%	.0%	.0%
Total	N	33	20	16	29	7	13	35	4	4	7
	%	66.0%	40.0%	32.0%	58.0%	14.0%	26.0%	70.0%	8.0%	8.0%	14.0%
Chi Square		0.69	7.88	19.63	8.26	25.30	8.72	36.84	1.37	4.45	
P Value		0.707	.019	0.00	0.016	0.00	0.013	0.00	0.50	0.35	

In acute hepatitis, most common presenting symptom was jaundice (100%) followed by vomiting (88.9%), anorexia and nausea (77.8%).

In chronic hepatitis, most common presenting symptom was anorexia (66.7%) and vomiting (66.7%).

In cirrhosis, majority of the patients presented with abdominal distension (92.1%), followed by anorexia (63.2%), jaundice (50%), 15 patients had GI bleeding– 11 had malena (28.9%) and 4 patients had haematensis (10.5%)

**Table 6:** Type of Hepatitis versus Past History

Diagnosis	Statistics	Past History				Total
		Tattooing	Diabetes Mellitus	Blood Transfusion	Non significant	
Acute Hepatitis	N	0	0	0	9	9
	%	.0%	.0%	.0%	100.0%	100.0%
Liver Cirrhosis	N	5	4	3	26	38
	%	13.2%	10.5%	7.9%	68.4%	100.0%
Chronic Hepatitis	N	0	0	0	3	3
	%	.0%	.0%	.0%	100.0%	100.0%
Total	N	5	4	3	38	50
	%	10.0%	8.0%	6.0%	76.0%	100.0%

Chi Square=4.98, P value=0.546

10% of the cases with acute and chronic liver disease had history of tattooing followed by 8%

patients had past history of Diabetes Mellitus and 6% patients with blood transfusion.

**Table 7:** Distribution of Patients according to Personal History

Diagnosis	Statistics	PersonalHistory		Total
		Alcohol Consumption	Non significant	
Acute Hepatitis	N	0	9	9
	%	.0%	100.0%	100.0%
Liver Cirrhosis	N	10	28	38
	%	26.3%	73.7%	100.0%
Chronic Hepatitis	N	0	3	3
	%	.0%	100.0%	100.0%
Total	N	10	40	50
	%	20.0%	80.0%	100.0%

Chi Square=3.95, P value=0.139



10 patients (26.3%) patients of liver cirrhosis had history of alcohol consumption while majority of

the patients were non-alcoholics.

**Table 8:** Distribution of Patients according to Physical Examination

Diagnosis	Statistic	Pallor	Icterus	Pedal Edema	Ascitis	Hepatomegaly	Splenomegaly	Dilated Veins	CNS involvement
Acute Hepatitis(N=9)	N	1	9	0	0	5	0	0	0
	%	11.1%	100.0%	.0%	.0%	55.6%	.0%	.0%	.0%
Liver Cirrhosis(N=38)	N	11	18	36	36	3	35	35	4
	%	28.9%	47.4%	94.7%	94.7%	7.9%	92.1%	92.1%	10.5%
Chronic Hepatitis(N=3)	N	2	0	0	0	0	0	0	0
	%	66.7%	.0%	.0%	.0%	.0%	.0%	.0%	.0%
Total	N	14	27	36	36	8	35	35	4
	%	28.0%	54.0%	72.0%	72.0%	16.0%	70.0%	70.0%	8.0%
Chi Square		3.51	11.86	40.60	40.60	12.91	36.84	36.84	1.37
P Value		0.17	0.003	0.00	0.00	0.002	0.007	0.002	0.50

Among Liver Cirrhosis patients, majority i.e. 11(28.9%) were having pallor followed by 2(66.7%) patients among Chronic Hepatitis who were having pallor present. Only 1(11.1%) Acute Hepatitis patient was having pallor.

Among Liver Cirrhosis patients, majority i.e. 18(47.4%) were having icterus followed by all patients of acute Hepatitis. No any Chronic Hepatitis patient was having icterus.

Among Liver Cirrhosis patients, majority i.e. 36(100%) were having Pedal Edema present. Both Acute Hepatitis and Chronic Hepatitis patient were having no Pedal Edema present.

Majority of Liver Cirrhosis i.e. 36(94.7%) patients were having ascitis present where as in both Acute Hepatitis and Chronic Hepatitis patients ascites was absent.

Majority i.e. 5(55.6%) Acute Hepatitis patient have hepatomegaly followed by 3(7.9%) Liver Cirrhosis patients.Chronic Hepatitis patient were having no hepatomegaly.

Among Liver Cirrhosis patients, majority i.e. 35(92.1%) were having splenomegaly present. Both Acute Hepatitis and Chronic Hepatitis patient were having no splenomegaly present.

Majority of Liver Cirrhosis patients i.e. 35(92.1%) were having dilated veins present. Both Acute Hepatitis and Chronic Hepatitis patient were having no dilated veins present.

Four patients of Liver Cirrhosis i.e. 4(10.5%) were having Hepatic encephalopathy. Both Acute Hepatitis and Chronic Hepatitis patient were having no hepatic encephalopathy.

**Table 9:** Distribution of Patients according tohaematological and biochemical parameters

Diagnosis	Mean values of haematological and biochemical parameters of patients			
	Haemoglobin (g/dl)	Bilirubin (mg/dL)	SGOT (IU/L)	SGPT (IU/L)
Acute Hepatitis	11.6	9.03	427.03	586.6
Liver Cirrhosis	9.1	4.1	118.4	127.05
Chronic Hepatitis	10.6	1.6	126.7	141.13

The mean haemoglobin value of Acute hepatitis patients was 11.6g/dL, Among Cirrhosis patients mean Hb was 9.1g/dL and mean Hb of chronic hepatitis was 10.6mg/dl.

Mean Bilirubin level among acute hepatitis, chronic hepatitis and liver cirrhosiswas 9.03mg/dL, 1.mg/dL and 4.1mg/dL respectively.

Mean SGOT in acute hepatitis was 427.03, 118.4 in iver cirrhosis and 126.7 among chronic hepatitis Mean SGOPT in acute hepatitis was 586.6, 127.05 in liver cirrhosis and 141.13 among chronic hepatitis.

**PROTHROMBIN TIME**

Prothrombin time prolongation was presented in 4 (44.4%) patients with acute hepatitis and 6

patients (15.7%) with liver cirrhosis and in 1 patient (33.3%) with chronic hepatitis.

**Table 10:** Distribution of Hepatitis patients:Type of Hepatitis Versus HbsAg

Diagnosis	Statistics	HbsAg		Total
		Positive	Negative	
Acute Hepatitis	N	4	5	9
	%	44.4%	55.6%	100.0%
Liver Cirrhosis	N	8	30	38
	%	21.1%	78.9%	100.0%
Chronic Hepatitis	N	1	2	3
	%	33.3%	66.7%	100.0%
Total	N	13	37	50
	%	26.0%	74.0%	100.0%

Chi square=4.34, p value=0.114

In this case majority i.e. 8(21.1%) Liver Cirrhosis patient were found having HbsAg positive followed by 4(44.4%) of Acute Hepatitis patient

and minimum i.e.1 (33.7%) Chronic Hepatitis patients was having HbsAg positive.

The association is statistically significant.

**Table 11:** Distribution of Hepatitis patients: Type of Hepatitis versus Anti HCV

Diagnosis	Statistics	AntiHCV		Total
		Positive	Negative	
Acute Hepatitis	N	0	9	9
	%	.0%	100.0%	100.0%
Liver Cirrhosis	n	3	35	38
	%	7.9%	92.1%	100.0%
Chronic Hepatitis	n	1	2	3
	%	33.3%	66.7%	100.0%
Total	n	4	46	50
	%	8.0%	92.0%	100.0%

Chi square=3.39, p value=0.183

Three.7.9%) Liver Cirrhosis patient, were having Anti-HCV positive followed by 1(33.3%) Chronic Hepatitis patient. No Acute Hepatitis patient were having Anti HCV positive. The association is statistically significant

**DISCUSSION****DEMOGRAPHIC PEOPLE****Age group**

In the present study, age group ranges from 22-80 years. In acute hepatitis 44.4% of patients were in

the age group of 40-60 years and 33.3% were above 60 years. Mean age in acute hepatitis was  $41.6 \pm 14.27$  years.

Ravinder Kaur<sup>83</sup> et al. study of 306 patients with acute hepatitis age group ranges from 1-68 years with mean age of  $26 \pm 2.5$  years. Estrada JY<sup>84</sup> et al. a study of clinical profile of acute hepatitis shows mean age of  $34.1 \pm 11.7$  in study of 203 patients.

In the present study, in chronic hepatitis patients were in all age groups without any clustering.

In cirrhosis 33.3% of patients were in the all age groups in the present study. Kumar T.<sup>85</sup> study of 80 cases with cirrhosis 46.83% patients were in the age group of 31-60 years.

#### Sex ratio

Out of 50 patients, 41 patients (82%) were males and 9 (18%) were females. Male: Female ratio of 4.5:1.

In acute hepatitis male: female was 1.25:1, chronic hepatitis 2:1, cirrhosis 8.5:1

Kaur H<sup>86</sup> et al. a study of spectrum of acute viral hepatitis in 101 patients showed male: female ratio of 1.65:1.

Golnaz Bahramedi<sup>87</sup> et al. a study of clinical, virologic and phylogenetic features of chronic hepatitis in Iranian patients had male: female ratio of 4:1.

Paul SB<sup>88</sup> et al. study of cirrhosis of liver in Indian patients showed male: female ratio of 6:1.

All studies show male preponderance of disease comparable with present study probably because of high risk behaviour in males.

**Table 12:** Comparison of symptoms and signs in acute hepatitis patients with other studies

	Kaur H et al. <sup>86</sup>	Holgado GM et al. <sup>89</sup>	Present study
Jaundice	93.06%	97.2%	100%
Anorexia	72.6%	61.1%	77.8%
Pain abdomen	-	75%	55.6%
Fever	-	55.5%	66.7%
Hepatomegaly	38.6%	63.9%	55.6%

In the present study, jaundice was the commonest clinical symptom and sign (100%) which were comparable to Kaur H et al.<sup>86</sup>(93.06%) and Holgado GM et al.<sup>89</sup>(97.2%).

Followed by Anorexia (77.8%), 72.6% in Kaur H et al.<sup>86</sup> and 61.1% in Holgado GM et al.<sup>89</sup>

Pain abdomen was present in 55.6% in the present study which was little lower comparable to Holgado GM et al.<sup>89</sup>

Fever was present in 66.7% of patients higher than Holgado et al.<sup>89</sup>(55.5%).

Hepatomegaly was present in 55.6% of patients comparable to Holgado GM et al.<sup>89</sup>63.9%, which was slightly higher than Kaur H et al.<sup>86</sup>38.6%.

**Table 13:** Comparison of symptoms and signs in chronic hepatitis patients with other studies

	Usha Arora et al. <sup>90</sup>	Present study
Jaundice	93.06%	33.3%
Anorexia	72.6%	66.7%
Pain abdomen	-	66.7%

In the present study, among patients with chronic hepatitis 33.3% had jaundice, 66.7% had anorexia and 66.7% had pain abdomen.

Usha Arora et al.<sup>90</sup> had higher incidence of jaundice 92.8%, followed by anorexia 45% and pain abdomen 35.71%.

However, these three symptoms were the commonest in both studies. The present study had only 3 patients with chronic hepatitis without cirrhosis, so there is difference in the incidence of jaundice and anorexia.

**Table 14:** Comparison of symptoms and signs in liver cirrhosis patients with other studies

	Sarin SK et al. <sup>91</sup>	Present study
Abdominal distension	93.4%	92.1%
Anorexia	74.2%	63.2%
Jaundice	31.7%	50.0%
GI bleeding	55%	39.4%
Nausea	-	34.2%
Pedal oedema	82.1%	94.7%
Hepatomegaly	7.5%	7.9%
Splenomegaly	87.5%	92.1%

In the present study, in patients with cirrhosis abdominal distension (92.1%) was the commonest presenting symptoms followed by anorexia (63.2%), jaundice (50%) and GI bleeding (39.4%). Commonest signs were pedal oedema (94.7%) followed by splenomegaly (92.1%).

The above symptoms and signs are comparable to Sarin SK et al.<sup>91</sup> where abdominal distension (93.4%), followed by anorexia (74.2%) and GI bleeding (55%) were commonest presenting

symptoms followed by signs pedal oedema (82.1%) and splenomegaly (67.5%).

**Table 15:** Comparison of alcohol consumption in liver disease with other studies

Saigal S. et al. <sup>92</sup>	Present Study
30.7%	10(20.0%)

In our study alcohol consumption was seen in 10 (20.0%) patients in comparison to Saigal S. et al.<sup>92</sup> 30.7% cases.

## LIVER FUNCTION TESTS

**Table 16:** Comparison of liver function tests in acute hepatitis patients with other studies

	Holgado GM et al. <sup>89</sup>	Present study
Bilirubin	10.6 +/- 7.9	9.03
AST	410.2 +/- 136	427.03
ALT	441.6 +/- 226	586.6

In the present study, mean bilirubin in acute hepatitis was 9.03, which was comparable to Holgado GM et al.<sup>89</sup> bilirubin (10.6 ± 7.9). AST and ALT were 427.03, 586.6 in the present study which was also comparable to Holgado GM et al.<sup>89</sup> AST (410.2 ± 136) and ALT (441.6 ± 226).

**Table 17:** Comparison of liver function tests in chronic hepatitis patients with other studies

	Alam et al. <sup>93</sup>	Present study
Bilirubin	5.1	1.67
AST	56.4 ± 36.3	126.67
ALT	170 ± 100.1	141.13

Mean bilirubin, AST and ALT in the present study, in patients with chronic hepatitis were 1.67, 141.13, 126.67, respectively comparable to Alam et al.<sup>93</sup> where bilirubin (5.1), AST (56.4 ± 36.3) and ALT (170 ± 100.1) respectively.

**Table 18:** Comparison of liver function tests liver cirrhosis patients with other studies

	Kumar T et al. <sup>85</sup>	Present study
Bilirubin	5.1 +/- 2.2	4.12
AST	106 +/- 8.6	118
ALT	186 +/- 2.6	127.05

Mean bilirubin, AST and ALT in patients with cirrhosis in the present study were 4.12, 118, 127.05 respectively comparable to Kumar T et al.<sup>85</sup> bilirubin 5.1 ± 2.2, AST 106 ± 8.6 and ALT 186 ± 26.

## Seroprevalence of HBV and HCV

**Table 19:** Comparison of seroprevalence of HBV and HCV in acute hepatitis patients with other studies

	Ayoola et al. <sup>94</sup>	Kaur H et al. <sup>86</sup>	Present study
HBV	35.6%	29.7%	44.4%
HCV	3.7%	-	-

Seroprevalence of hepatitis B virus in the present study was 44.4% which was comparable to Ayoola et al.<sup>94</sup> 35.6%, which was slightly lower in Kaur H et al.<sup>86</sup> 29.7%.

No patient with acute hepatitis was seropositive for HCV in the present study. However seroprevalence of acute hepatitis C ranged from 0-3.7% in comparative studies.

**Table 20:** Comparison of seroprevalence of HBV and HCV in chronic hepatitis patients with other studies

	Aminuddin et al. <sup>95</sup>	Present study
HBV	25.4%	33.3%
HCV	16.3%	33.3%

Seroprevalence of hepatitis B in chronic hepatitis was 25% which was comparable to Aminuddin et al.<sup>81</sup> 25.4%.

Seroprevalence of HCV in chronic hepatitis in the present study was 33.3%, higher compared to Aminuddin et al. 16.3%.

**Table 21:** Comparison of seroprevalence of HBV and HCV in liver cirrhosis patients with other studies

	Kumar T et al. <sup>85</sup>	Blankson A et al. <sup>96</sup>	Present study
HBV	24%	17.5%	21.1%
HCV	2.6%	7.1%	7.9%

Seroprevalence of hepatitis B virus in patients with cirrhosis was 21.1% in the present study.

Seroprevalence ranges from 17.5% (Kumar T et al.<sup>72</sup>) to 42.9% (Blankson A et al.<sup>96</sup>).

Seroprevalence of Hep C virus in the present study was 7.9% which was comparable to Blankson et al.<sup>96</sup> 7.1%.

**SUMMARY**

Fifty patients with liver diseases were studied among whom 9 patients (18%) had acute hepatitis, 3 patients (6%) had chronic hepatitis and 38 patients (76%) had cirrhosis of liver.

Males outnumbered females in all groups of liver disorders.

Presenting symptoms in the patients with acute hepatitis was jaundice and anorexia, while patients with chronic hepatitis experienced anorexia and in cirrhosis abdominal distension was most prevalent.

Among all the study cases 10% cases were having history of tattooing, 8 % cases were diabetic and 6% cases had history of blood transfusion.

In patients of liver cirrhosis, 26.7% cases were related to alcohol consumption.

In the present study, mean bilirubin in acute hepatitis was 9.0367mg/dL, mean AST and ALT were 427.03IU/L, 586.6IU/L respectively which was comparable to other studies.

Mean bilirubin, AST and ALT in patients with chronic hepatitis were 1.67mg/dL, 141.13 IU/L, 126.67 IU/L respectively comparable to other studies.

In patients with liver cirrhosis, Mean bilirubin, AST and ALT were 4.12mg/dL, 118IU/L, 127.05IU/L respectively comparable to other studies.

Prothrombin time prolongation was presented in 4 (44.4%) patients with acute hepatitis and 6 patients (15.7%) with liver cirrhosis and in 1 patient (33.3%) with chronic hepatitis.

In patients with acute hepatitis, 44.4% cases were due to HBV infection. No case of acute HCV infection was noted.

Out of 3 patients with chronic hepatitis, one had HBV and one patient had HCV infection.

In patients with cirrhosis high prevalence of HBV (21.1%) was noted.

No case of co-existent infection of both HBV and HCV was observed in the present study.

**CONCLUSIONS**

HBV and HCV infections are common among acute and chronic liver disease.

Prevention and control can be achieved through safe and effective HBV vaccines.

WHO recommends routine infant vaccination along with catch-up immunization for adolescents and high risk population.

India introduced universal immunization against Hepatitis B in 10 states in the year 2002, and in 2011, scaled up this operation countrywide.

The HBV vaccine also protects from HDV infection. There is no vaccine against HCV.

Screening and immunization of high-risk groups, such as those with history of exposure, risky practices, and occupational risk;

Specific measures for prevention of mother-to-child transmission and promoting safe blood supply, safe injections are other recommended preventive measures.

The HBV vaccine also protects from HDV infection. There is no vaccine against HCV.

Screening and immunization of high-risk groups, such as those with history of exposure, risky practices, and occupational risk.

Specific measures for prevention of mother-to-child transmission and promoting safe blood supply, safe injections and safe sex are other recommended preventive measures.

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## ANNEXURE 1

### PERFORMA

Name :

DOA:

Age:

DOD:

Sex:

IP No.:

Occupation:

Address:

Chief Complaints:

History of present illness

Past history :

Treatment history –

Family history:

Personal history:

Socio-economic status:

Vitals:

BP:

Pulse:

RR:

Temperature:

General examination: GCS:

Pallor:

Icterus:

Clubbing:

Cynosis:

Lymphadenopathy:

Edema:

Systemic Examination:

RESPIRATORY SYSTEM:

a) Inspection

- b) Palpation
- c) Percussion
- d) Auscultation

**CARDIOVASCULAR SYSTEM:**

- a) Inspection
- b) Palpation
- c) Percussion
- d) Auscultation

**PER ABDOMEN:**

- a) Inspection
- b) Palpation
- c) Percussion
- d) Auscultation

**CENTRAL NERVOUS SYSTEM:**

- a) Mini Mental Score Examination:
- b) Cranial Nerves
- c) Motor System
- d) Sensory System
- e) Cerebellar signs

**ANNEXURE 2****CONSENT FORM**

Patients consent:

I, \_\_\_\_\_ S/O, D/O, W/O \_\_\_\_\_ Aged \_\_\_\_\_ resident of \_\_\_\_\_ willingly give my full consent to DR.SHIVANI SAINI and other members of the Department of General Medicine of M.M Institute of Medical Sciences & Research, Mullana, Ambala, for his dissertation project on "TO STUDY THE CLINICAL PROFILE AND VIRAL MARKERS (HEPATITIS B AND C) IN ACUTE AND CHRONIC LIVER DISEASE". All details of my clinical problem and risk factors for test have been explained to me in my mother language and I have clearly understood all of them.

(Signature of PG Student with date)

(Signature of patient/ guardian)

(Name & Signature of Supervisor)

(Name & Signature of Co-Supervisor)