INTRODUCTION
Viral hepatitis can be caused by hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis delta virus (HDV) hepatitis E virus (HEV) and many other unrelated viruses yet to be identified. The mode of transmission of these viruses are either through the fecal-oral route or by the percutaneous route.

Hepatitis A virus which is transmitted by the fecal-oral route, is highly endemic throughout the developing world, and infects virtually 100% of the population by the age of 10 years. A vast majority of these infections are subclinical. Also HAV infections are not known to go to chronicity.

Another virus that is transmitted by the fecal-oral route is hepatitis E virus, which has been documented to cause extremely large epidemic outbreaks of viral hepatitis in areas with inadequate public sanitation or malnourished population. This form of hepatitis has been referred to as water - borne hepatitis, epidemic hepatitis or enterically transmitted non A - non B hepatitis. The unique properties of this pathogen include its associated mortality in pregnant women, which is as high as 20% in some studies. Acute form of the disease is self limiting and long term follow up have failed to demonstrate a chronic sequelae.

Hepatitis C virus falls in the category of viruses that are transmitted by the percutaneous route. HCV has been implicated in 60% of the post - transfusional hepatitis in
USA. Half of these infections result in chronic hepatitis and 20% of these chronic infections lead to cirrhosis of liver.

Hepatitis B virus is capable of causing a highly polymorphic form of liver disease ranging from an inapparent form to acute or fulminant hepatitis, chronic hepatitis and cirrhosis. Primary infection is usually self limiting, with clearance of viral antigens and infectivity from liver and blood and the development of lasting immunity to reinfection. However 5-10% of individuals do not resolve primary infection, and develop a persistent, usually lifelong, hepatic infection. As in primary infections, such individuals may be asymptomatic or experience varying grades of chronic liver injury. Chronic HBV carriers estimated to number over 300 million world wide, represent the reservoir from which infection is spread to other individuals either horizontally (through blood, blood products or sexual contact) or vertically (from carrier mothers to newborn). Severe chronic hepatitis frequently leads to premature death from liver failure.

Epidemiological data has shown an association of chronic HBV infection and primary hepatocellular carcinoma (PHC). The risk of PHC development in long term HBV carriers is over 100 fold more, than that of age matched non carriers.
HBV belongs to the hepadna viridae group of animal viruses. The other members of the group are the woodchuck hepatitis virus (WHV), the beechey ground squirrel hepatitis virus (GSHV) and the Pekin duck hepatitis B virus (DHBV). Apart from man the only other host for the human hepatitis B virus are chimpanzees. There is so far no available cell line that can be used for the culture of the virus in vitro.

The different serological markers used to monitor HBV infection are, presence of surface antigen (HBsAg), a marker of current HBV infection, the hepatitis B e antigen (HBeAg), a marker of HBV multiplication and antibodies to the core antigen (anti-HBcIgM) again a marker of ongoing infection, anti-HBcIgG and antibodies to the surface antigen (anti-HBs) both reflecting a past and resolved HBV infection.

The detection of HBV DNA sequences, is another marker of HBV infection which could have clinical implications in terms of detection of viremia and also to monitor effect antiviral therapy. The use of cloned HBV DNA sequences in the liver and serum has been well established. Presence of HBV DNA in some HBsAg negative sera, as well as in sera negative for HBeAg, suggests the need for use of HBV DNA probe as an essential diagnostic marker.

This technique also allows to distinguish the state of virus in hepatocytes, whether free or integrated into the
hepatocellular DNA, the latter being thought to be the primary event towards development of liver cancer.

The serological markers available for the detection of HBV do not identify all infected individuals as HBV DNA has been detected in some chronic patients of liver disease that were negative for all markers of HBV infection. HBV DNA has also been detected in patients, serologically immune to HBV infection. This suggests the existence of HBV mutants or variants, some of which have been characterized.

The work carried out for this thesis was aimed at:

1) irrefutably establishing the potential of HBV DNA probe as an essential diagnostic marker.

2) improving the sensitivity of the probe assay by employing the recently introduced technique of polymerase chain reaction.

3) identification and characterization of variants of HBV by the combined use of PCR and DNA probe.