I General Introduction
Hepatitis B virus (HBV) infection is one of the most common infectious diseases in the world. HBV infection is responsible for over 50% of the worldwide attributable risk of hepatocellular carcinoma (Pujol et al., 2009). An estimated 400 million people worldwide are chronically infected with hepatitis B virus, manifested by persistence of the virus and Hepatitis B surface antigen (HBsAg) in serum and production of viral antigens and HBV DNA in the liver (Schiff et al., 2006). Over a million individuals die annually of HBV related chronic liver disease, most of which occur in the developing world (Lavanchy et al., 2004). HBV infection causes a spectrum of liver diseases, including subclinical, acute self-limited and fulminant hepatitis, an asymptomatic carrier (ASC) state and chronic hepatitis progressing to cirrhosis and hepatocellular carcinoma (HCC). Cirrhosis, liver failure or hepatocellular carcinoma develops in 15–40% of individuals with chronic HBV infection (Lok et al., 2002; Bosch et al., 2005). Host and viral factors, as well as coinfection with other viruses, in particular hepatitis C virus (HCV), hepatitis D virus (HDV), or human immunodeficiency virus (HIV) together with other comorbidities including alcohol abuse and overweight, can affect the normal course of HBV infection as well as the efficacy of antiviral strategies.

HBV infection is an important health problem in developing countries like India, which is a vast country, comprised of multiracial communities with wide variations in ethnicity and cultural patterns, which is attributable to its geographical location, gene influx due to invasion and/or anthropological migrations in the past.

The prevalence of chronic HBV infection in India is in the intermediate range with an estimated 40 million subjects infected (Chaudhari et al., 2004). HBV is reported to be responsible for 70% of cases of chronic hepatitis and 80% of cases of cirrhosis of the liver (Thakur et al., 2000). About 80% of Indian patients with hepatocellular carcinoma have Hepatitis B virus associated liver disease (Dhir et al, 1997).
Based on >8% divergence in the complete nucleotide sequence, HBV strains are divided into eight different genotypes, namely A–H (Norder et al., 2004). Further, based on >4% (but <8%) divergence in the complete nucleotide sequence within a particular genotype, subgenotypes have been classified within genotypes A, B, C, D and F (Schaefer et al., 2005). The prevalence of different genotypes and subgenotypes vary geographically and is associated with ethnicity (Arauz-Ruiz et al., 2002). Recent studies clearly indicate that HBV genotypes and even the subgenotypes considerably differ in terms of emergence of mutations, replication, hepatitis B e antigen (HBeAg) status, disease severity (Franc et al., 2004; Wang et al., 2007), response to antiviral treatment (Yuen et al., 2004; Chan et al., 2005) and vaccination against the virus (Kramvis et al., 2005). There is a paucity of information on the genotype distribution of HBV in Kerala. The present study attempts to clarify the picture in Kerala, the southern most state of India.

The main objectives of the study are:

1. To elucidate and quantify the risk factors associated with chronic HBV infection in Kerala.
2. To study the dynamics of intrafamilial transmission from infected individuals and to analyze the risk factors.
3. Detailed histological analysis of liver biopsy tissue specimens to determine extent of steatosis, necroinflammatory grade and stage of liver disease.
4. Genotyping, subgenotyping and sequence analysis of the Basal Core Promoter and Precore region for mutations that may affect HBeAg expression and disease severity.