Virological characteristics of a large prospective cohort of patients with chronic hepatitis B newly seen in hepatology reference centers in France in 2008-2010

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Background: Chronic hepatitis B (CHB) is a major cause of morbidity and mortality, despite an effective vaccine and potent antiviral drugs. Approximately 15% to 25% of chronic HBV carriers may die prematurely of either end-stage liver disease or hepatocellular carcinoma. **Objective**: To assess the virological characteristics of HBsAg-positive patients newly referred to hepatology reference centers in France between January 2008 and January 2010, assess the relationship between HBsAg and HBV DNA levels according to the HBeAg status, and estimate the prevalence of primary resistance to nucleos(t)ide analogues (NA) in this large prospective cohort of patients. **Methods**: 480 consecutive patients with CHB referred for the first time to a hepatology reference center during the study period were included. Most of them (91.9%) were treatment-naïve and 86.0% of them were HBeAg-negative. HBsAg and HBV DNA levels were measured, the HBV genotype was determined, and the sequence of the reverse transcriptase domain of HBV polymerase was determined by means of ultra-deep pyrosequencing, a novel highly sensitive method for the detection of minority viral populations. **Results**: At baseline, the median HBsAg level was 3.65 Log_{10} IU/mL (range: <1-5.38), and the median HBV DNA level was 3.14 Log_{10} IU/mL (<1.2-8.5). 61.5% of patients were inactive carriers. The most prevalent genotypes were genotype D (35.5%), genotype E (26.6%) and genotype A (26.0%). HBsAg levels did not vary according to the HBV genotype, but positively correlated with HBV DNA levels (r=0.37, P<0.001) and were significantly related to the HBeAg status (r=0.33, P<0.001). The correlation between HBsAg and HBV DNA levels was stronger in HBeAg-positive than HBeAg-negative patients. Ultra-deep pyrosequencing data are under analysis and will be presented. **Conclusion**: In France, most patients newly seen for chronic hepatitis B in tertiary care centers are HBeAg-negative and inactive carriers. HBV genotypes A, E and D are the most prevalent genotypes. Although HBsAg production by infected hepatocytes does not depend solely on HBV replication, serum HBsAg levels are significantly related to HBV DNA levels, especially in HBeAg-positive patients. The prevalence of primary resistance to NAs by ultra-deep pyroquencing will be presented in this large cohort of patients.