

**CHRONIC HEPATITIS B CLINICAL OUTCOMES AND HEPATITIS B VIRUS MUTATIONS DURING PREGNANCY AND POST-PARTUM FOLLOW UP**

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**INTRODUCTION**

Chronic hepatitis B (CHB) is a dynamic disease, which may be affected by host immunological changes in pregnancy. Certain HBV genotypes (i.e., C vs B) and HBV core (C), basal core promoter (BCP) and surface (S) variants are associated with increased liver disease risk, and rarely linked to fulminant hepatitis in newborns due to transmission of the pre-core variant [1]. In highly viremic mothers guidelines recommend consideration of nucleos/tide analogs (NA) therapy targeting the HBV polymerase (P) to reduce MTCT risk [2].

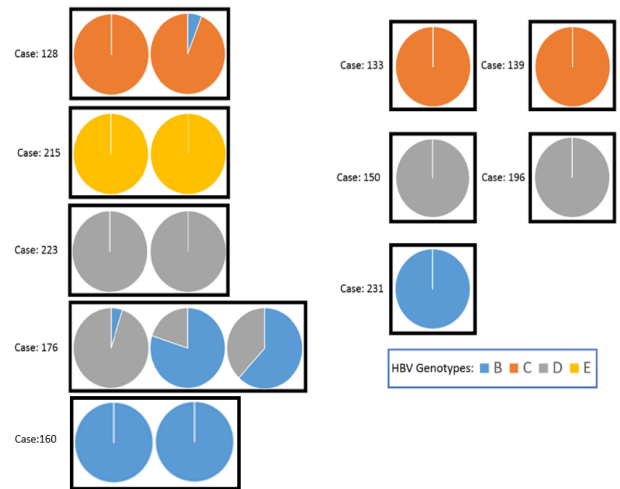
**METHODS**

HBV viral load, ALT levels, HBeAg and anti-HBeAg were assessed by chemiluminescent microparticle immunoassays. Serum viral loads were quantified by PCR. HBV genotype was determined by line probe assay. Live stiffness were measured by transient elastography or liver biopsy. 50mL of whole blood were collected from 44 pregnant patients during the 2<sup>nd</sup> trimester. Following blood isolation, the pre-C/C region was sequenced in the plasma samples using the clonal sequencing method.

**RESULTS**

*Clinical assessments*-The median age for the 21 patients is 31, the majority (72%) are Asian. ALT levels were normal. 33% of the patients have the mild hepatitis flare as their postpartum ALT level have doubled from the baseline value. The median HBV DNA level did not differ prepartum and postpartum, however there is a large range due to the different CHB phases. 23% patients were treated with Tenofovir. The majority of patients (44%) is in the inactive phase while 28% is in the reactivation phase, 24% is in the immune tolerant phase and 4% is in the active phase.

*Genotype analysis*-To date, genotype B, C, D and E were detected (Figure 1). Mixed genotype infection was detected in 2/10 patients. Genotype distribution in these patients also appeared to change overtime. *Pre-C/C analysis*-The pre-C variant was detected in 8/10 patients while the BCP variant was not detected in any patient to date.



**Figure 1.** Preliminary HBV genotype analysis of 10 patients sequenced to date. Patients on the left had both prepartum and postpartum samples. Case 176 had a second pregnancy. Patients on the right had prepartum sample only.

**DISCUSSION AND CONCLUSIONS**

Clinical assessments have shown that the pregnant patients do not have liver disease although some were detected with mild hepatitis flares. The cause of these hepatitis flares is currently unknown. Patients in the immune tolerant have high viral loads and are treated with Tenofovir to reduce MTCT risk. Surprisingly, majority of the patients are in the inactive phase. This was unexpected since pregnant patients are expected to be immune tolerant. Detecting the pre-C variant in these patients may increase their risk of CHB reactivation as well as severe liver disease in infants.

**REFERENCES**

1. Terazawa S, et al. *Pediatric Research*. **29**:5-9, 1991.
2. Coffin C, et al. *Can. J. Gastroenterol*. **26**:917-38, 2012.