Post-partum ALT increases are observed in 30% of HBsAg+ mothers and are also noticed in mothers administered nucleoside analogues (NA) to prevent mother-to-child transmission (MTCT). As such flares may be injurious we have studied the utility of novel and sensitive markers of cccDNA transcriptional activity [hepatitis B core-related antigen (HBcrAg) and pre-genomic (pg)RNA] to predict post-partum ALT flares in both NA treated and untreated HBsAg+ mothers.

We aimed to evaluate the role of serum levels of HBcrAg and pgRNA in pregnancy to predict post-delivery ALT flares, their severity and by inference, a preference to continue on NA.

**Methods** Plasma samples from 642 HBsAg-positive pregnant women were collected during 3rd trimester and at 6, 12, 24, 36 and 48 weeks post-partum. 103(16%) were HBeAg +; median age 31 years. Samples were tested for HBeAg, HBV DNA (Roche; IU/ml); quantitative HBsAg (Abbott Architect; log10IU/ml), HBcrAg levels (CLEIA Fujirebio; log10U/ml) and pgRNA concentrations (PCR assay Abbott Diagnostic; log10U/ml). 95/642(15%) mothers with HBV DNA concentrations >200,000 IU/ml started tenofovir prophylaxis from 28 weeks of gestation to prevent HBV MTCT. The ALT flares incidence and severe flares (defined as >10xULN) was correlated with HBcrAg and pgRNA in treated and untreated mothers.

**Results** Untreated cohort: 106/547(19%) of untreated mothers developed a post-delivery flare, but none was severe. Higher pre-delivery HBV DNA, HBcrAg and pgRNA concentrations were observed in untreated mothers with post-partum ALT flares vs. mothers without a flare. Pregnancy ALT and HBsAg concentrations were similar in flare vs. no flare patients.

NA treated cohort: Higher pre-delivery HBcrAg and pgRNA concentrations were observed in NA treated mothers with a post-partum flare. 80/95(84%) treated mothers stopped NA therapy post-partum (median 4 weeks). However no difference in flares incidence was observed in mothers discontinuing treatment vs. mothers who continued NA.

Seven HBeAg-negative treated patients who stopped NA developed a severe ALT flare within 12 weeks post-delivery. High pre-delivery levels of HBcrAg (>7 log10U/ml) and pgRNA (>4 log10U/ml) were associated in mothers with severe flare, but no flares were associated with hepatic synthetic dysfunction and resolved after re-starting NA. 13/103(13%) mothers lost HBeAg and 6 (1%) lost HBsAg spontaneously within 1 year post-delivery (all mild flares).

**Conclusion** Post-partum ALT flares are more common in pregnant women with higher pregnancy HBcrAg and pgRNA levels, in both NA treated and untreated mothers. High pre-delivery levels could suggest that NA therapy should be continued post-partum to avoid severe and injurious ALT flares.