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# Mother-to-infant transmission of hepatitis B virus infection: Significance of maternal viral load and strategies for intervention

*To the Editor:*

We read with great interest the paper by Wen *et al.* [1], prospectively evaluating hepatitis B viral load as a significant factor for immunoprophylaxis failure of infants born of hepatitis B surface antigen (HBsAg) positive mothers. The authors suggested that the risk of immunoprophylaxis failure increased with increasing viral load and that intervention, such as anti-viral therapy in mothers with high viral load, may be considered. We agreed with the authors that high maternal viral load correlated with an increased risk of vertical transmission, but the optimal cut-off was yet to be determined [2]. However, we believed that further clarification of the data would be needed before change in clinical practice can be recommended.

First of all, the timing of blood test on the viral load of the subjects was not clearly stated. The authors mentioned that it was checked in the third trimester or within 2 months after delivery. However, the viral load may vary throughout pregnancy and after delivery. In a retrospective study which evaluated the change of viral load in 33 HBsAg positive mothers, of whom 9 were hepatitis B e antigen (HBeAg) positive, it was found that viral load increased by a mean of 0.4 log in late pregnancy or early postpartum, of which four HBeAg negative mothers had >1 log change during pregnancy [3]. In another retrospective study, ter Borg *et al.* studied 38 HBsAg pregnancies of which 24 were HBeAg positive. Lamivudine was started in the third trimester to reduce the viral load in 13 pregnancies. The median viral load increased from 7.8 $\log_{10}$ copies/ml before, to 8.2 $\log_{10}$ copies/ml during pregnancy, and then decreased to 6.8 $\log_{10}$ copies/ml after delivery [4]. We were not told the reason why a proportion of the women's blood tests were collected after delivery for viral load testing and not before delivery, in this prospective study. Assuming the postpartum viral load to be similar to the antenatal level may give rise to a wrong conclusion. Therefore, it would be important for the authors to provide the median gestational weeks when the blood test was taken, and to clarify the proportion of mothers having postpartum test. Furthermore, as the authors also pointed out, the result would be more meaningful if the viral load levels were obtained before 28 weeks of gestation. Anti-viral therapy was started from 28 weeks of gestation in most of the trials evaluating the efficacy of anti-viral treatment to decrease the risk of immunoprophylaxis failure in women with high viral load [5]. Viral load quantification in the late third trimester, at delivery, or even after delivery, would be less useful clinically as intervention to alter outcome may not be possible. Caesarean delivery could not decrease the risk of immunoprophylaxis failure [2] and late viral load quantification would not allow adequate time for anti-viral treatment to decrease viral load.

Secondly, we also wondered if any subjects were receiving anti-viral therapy during the studied period. Anti-viral therapy initiated after the blood test before delivery, or *vice versa*, could affect the viral load level and subsequent correlation with risk of the immunoprophylaxis failure. Thirdly, horizontal transmission of hepatitis B virus was possible [6] in 17.5% of children who were tested for HBsAg at 1–3 years of age. The HBsAg positive status in this group could be due to horizontal infection rather than genuine immunoprophylaxis failure. Finally, we were interested in the high rate of invasive prenatal diagnostic test (amniocentesis/CVS) and first vaccine given beyond 24 hours in the ten infants who suffered from chronic hepatitis B infection. Could these be the potential factors that led to a higher rate of immunoprophylaxis failure? We hope the authors could provide more data on that.

## Conflict of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

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