Follow Up of Infants Born to Women with Hepatitis B in the National Maternity Hospital

Abstract:
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Abstract
Infants born to women with hepatitis B virus (HBV) are at risk of vertical transmission. This risk is significantly reduced with correct post-natal treatment. After initial perinatal management and neonatal treatment, these infants receive subsequent follow up HBV immunisations at two, four and six months. These infants then require post vaccination serological testing. This review was conducted to determine the number of infants born to mothers with HBV in the National Maternity Hospital who had appropriate post vaccination serological testing. There were seventy eight HBV infections identified antenatally in the years 2010 and 2011 resulting in seventy live born infants at our institution. Thirteen (18.6%) infants had evidence of post vaccination serological testing. This is below international rates of follow up. There is an urgent need for a centralised national programme to ensure adequate follow up and management of all infants born to women with HBV in Ireland.

Introduction
Infants born to women with acute hepatitis B infection or chronic carriers of hepatitis B virus are at risk of acquiring hepatitis B infection by vertical transmission. Without treatment, the risk of acquiring HBV perinatally is 70-90% in infants of women who are both hepatitis B surface antigen (HBsAg) positive and hepatitis B e antigen (HBeAg) positive. The risk of acquiring HBV infection is 5-20% in infants of women who are HBsAg positive but HBeAg negative. Infants infected with HBV have a 95% risk of developing chronic infection with a 15-25% risk for premature death from cirrhosis or cancer of the liver. It is estimated that between two and three hundred HBsAg positive women give birth in Ireland per year. There is currently no nationally agreed policy with regard to the management of these women and their infants. In the National Maternity Hospital (NMH) pregnant women are screened for hepatitis B infection as part of routine antenatal care. The risk of vertical transmission of HBV, is decreased through antenatal serological screening and subsequent treatment of infants postnatally. Perinatal transmission of HBV infection can be prevented in approximately 95% of infants with appropriate management. The infant exposure to maternal blood is avoided as far as possible e.g. by avoiding use of fetal scalp electrodes and fetal blood sampling. The newborn infant is then routinely bathed in the delivery room. Following careful disinfection of the skin with alcohol, babies born to mothers who are HBsAg positive receive Hepatitis B Immunoglobulin (HBIG) via intravenous injection and HBV vaccination via intramuscular injection to provide both passive and active immunity. This treatment should be provided within 12 hours of delivery. The practice in NMH is to provide treatment as soon as possible after delivery. All children then receive additional HBV vaccines at two, four and six months as part of the national immunisation schedule. Infants of mothers with hepatitis B require HBV serology at least 2 months after completion of this vaccination course to monitor response to treatment.

In the National Maternity Hospital, upon infant discharge, a letter is sent out to the registered GP requesting HBV serological testing at 8-10 months of age. Serum should be tested for HBsAg to exclude infection and anti-HBs to check for immunity. If HBsAg is positive it is recommended to refer the infant to a specialist hepatologist. If HBsAg is negative and anti-HBs is present, the infant is commenced on routine HBV vaccination as per standard infant vaccination schedules. If HBsAg is negative and anti-HBs is absent, the infant is considered HBsAg negative and requires no further management.

Methods
The National Maternity Hospital microbiology database was used to determine the number of HBV notifications in the years 2010 and 2011. The hospital patient administration system was then used to identify infants born to these women. At the National Virus Reference Laboratory (NVRL) each patient has been given a unique patient identification number. All following data, including demographic details are linked to this unique number and entered onto the laboratory information system (LIS). The LIS is computerised and allows for unique patient identification. Using specific patient search parameters to identify all laboratory records linked to this unique patient identification number, the number of infants born to mothers with active HBV infection are at increased risk of infection. It is recognized by the authors that international bodies including the Centers for Disease Control and Prevention (CDC) do not recommend a blood test for HBsAg in pregnant women. This is a more conservative approach than the practice used in NMH. HBsAg and Architect anti-HBc were utilized. When necessary, additional assays for anti-HBs and anti-HBc were used to confirm the presence of low levels of anti-HBs or anti-HBc. This study was approved by the National Maternity Hospital Ethics Committee.

Results
There were seventy-eight HBV notifications in NMH over the two year period. The seventy-eight HBsAg positive women delivered seventy live born infants at our institution. Thirteen (18.6%) infants had evidence of follow up samples from this patient cohort and the investigations performed. All following tests, including Architect HBsAg Qualitative II, the Architect anti-HBs and Architect anti-HBc were utilized. When necessary, additional assays for anti-HBs and anti-HBc were used to confirm the presence of low levels of anti-HBs or anti-HBc. This study was approved by the National Maternity Hospital Ethics Committee.

Discussion
There was no evidence of post vaccination serological follow up in the majority of infants delivered to mothers infected with HBV during this study period. If we include those women who had confirmed delivery of infants in NMH this shows that 13/70 (18.6%) had evidence of follow up. This is below international rates of follow up. The figure for post vaccination serological testing in the United States is over sixty three percent. In the Netherlands this figure is higher again at eighty percent of children followed up with testing. Post vaccination serological testing is important for guiding further management of infants born to mothers infected with Hepatitis B by allowing identification of infected or at risk infants. In total four out of the thirteen (30.8%) infants tested had the correct tests performed at the correct time. The recommended tests of HBsAg and Anti-HBs were carried out in eleven out of thirteen infants tested. One infant was tested for HBsAg while not being tested for
Anti-HBs. Another infant was tested for Anti-HBs but not for HBsAg.

Among those tested, one infant out of thirteen had evidence of low response, although this infant was considered immune. The median seroprotection following a completed vaccination schedule in infants born to mothers with HBV is as high as 98%. Eight infants were tested for anti-Hbc but this test is not considered a necessary part of follow up. This test usually reflects passive transplacentral transfer of maternal IgG anti-Hbc.

The age at which infants were tested although often exceeding the recommended time period on the standard letter sent to GPs of between eight and ten months, was still mostly within the time frame for testing according to the CDC of between 9 and 18 months. Eleven of the thirteen infants were tested between eight months and twelve and a half months. One infant was tested just before seven months of age. The CDC does not recommend testing within one month of the completion of the standard HBV vaccine series or completion of anti-HBs at the time of occurrence on account of the HBIG administered in the perinatal period. Testing at the recommended time improves the likelihood of detecting late HBV infection. One infant was tested before twelve months of age which is older than the recommended age and puts the infant at risk of either a delay in diagnosis of HBV infection or a delay in recognition of non-response to vaccination. It was noted that eight of the seventy eight women identified through antenatal screening were not delivered in NMH. It is unknown if any infants in another hospital inside or outside of Ireland. This may be an indication that the group of women identified through antenatal screening are from countries where HBV is endemic. This study was a single centre study with limited generalisability. As there is currently no unified approach to follow up of infants born to women with hepatitis B in Ireland, it is probable that the method of follow up of infants born in NMH is different from other units in the country who may have their own local policies.

There is a need for a centralised national programme to ensure adequate management and follow up of all infants born to mothers with HBV. Resource implications would include the employment of a full-time nurse to ensure follow up occurs as per the Immunisation Guidelines for Ireland. Quality improvement programs could include family reminders, education, provider reminders and community coordination. Accuracy and completeness of perinatal hepatitis B infection reporting can help progress to eliminate HBV transmission. Intensified follow up programs of at increased risk of acquiring hepatitis B infection in the future. Follow up of these infants has evolved on an ad hoc basis. The low level of serological testing of these infants identifies a gap in current system for follow up of these infants relying on primary care is not working. It must be noted that this is a single centre study with limited generalisability. As there is currently no unified approach to follow up of infants born to women with hepatitis B infection in Ireland, it is probable that the method of follow up of infants born in NMH is different from other units in the country who may have their own local policies.

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