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Immunization of babies born to HBsAg positive mothers: An audit on the delivery and completeness of follow up in Norfolk and Suffolk, United Kingdom

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Abbreviations: AHPT, Anglia Health Protection Team; anti-HBe, antibodies against hepatitis B 'e' antigen; CHIS, Child Health Information System; DBS, Dried Blood Spot; DNA, Deoxyribonucleic acid; GP, General Practitioner; HBeAg, Hepatitis B 'e' Antigen; HBIG, Hepatitis B Immunoglobulin; HBsAg, Hepatitis B surface Antigen; HepB, Hepatitis B; HBV, Hepatitis B Virus; NSC, Norfolk, Suffolk and Cambridgeshire; UK, United Kingdom

Perinatal transmission of hepatitis B infection has increased in the UK over the last decade. Routine antenatal screening of pregnant mothers (based on HBsAg) provides an effective means to identify 'at risk' babies. Follow up of babies born to infected mothers involves 4 doses of vaccination and/or a single dose of HBIG at birth. In this study we report the outcome of follow up of babies born to infected mothers over a 5 y period. One hundred sixty-three babies born to HBsAg positive mothers were followed up to ascertain the completeness for immunization and serological testing. Vaccination completion was 99.4% (162 of babies) at birth (1st dose), 95.6% (152 babies) for the second dose (at 1st month), 94.3 % (148 babies) for the 3rd dose (at 2nd month) and 83.4% (106 babies) for the 4th dose (at 12 months). Additionally, at 12 months 29.9% (38) of babies had their blood tested serologically to ascertain infection status; all babies receiving antigen testing were HBsAg negative. The overall vaccination coverage was good, although there is scope to improve the coverage of 4th dose. However, the proportion of children who were serologically tested for surface antigen at 12 months was considerably lower and there is a greater need to test babies concurrently at the time of giving the 4th dose. The proposed dried blood spot testing which will be rolled out from September 2014 should address this issue.

Introduction

Hepatitis B infection is a growing public health issue in the UK accounting for 25% of all liver disease.[1] When untreated, it is estimated that 15–40% of individuals with hepatitis B infection suffer serious liver damage, including cirrhosis, liver failure and hepatocellular carcinoma.[2] The risk of developing chronic hepatitis B infection is inversely associated with the age of acquisition with 90% of individuals infected perinatally developing persistent hepatitis B virus (HBV) infection and a 25% lifelong risk of developing serious liver disease and hepatocellular carcinoma.[3]

The likelihood of vertical transmission is dependent on the serological status of infected mothers. In babies born to high risk (see **Table 1** for classification) mothers (10–15% of infected women) the risk of transmission is 70–90% while the risk for babies born to low risk mothers is 10% (90% of infected women).[4-6]

Since 2000, UK national policy has been to routinely offer pregnant women screening for hepatitis B as part of the routine antenatal care and the provision of hepatitis B immunization to babies born to positive mothers. Babies born to healthy mothers in the UK do not receive immunization for hepatitis B. Based on UK national guidelines a full schedule of hepatitis B (HepB) immunization in the UK consists of hepatitis B immunoglobulin (HBIG) at birth for babies born to high risk mothers (a dose of 200IU per dose[7]), 4 doses of HepB vaccine (5μg or 10μg dependent on vaccine product[7]), with the first dose given at birth (within 24 hours) and 3 further doses by 12 months (the fourth dose should be given at least one month from 3rd), and a blood test at 12 months (to check infection status).[8] The immunization

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Table 1. Classification of mothers into high and low risk based on HBeAg and anti-HBe from serology

Hepatitis B status of mother	High or low risk	Babies should receive	
		Hepatitis B vaccine	HBIG
Mother is HBsAg positive and HBeAg positive	High	Yes	Yes
Mother is HBsAg positive, HBeAg negative and anti-HBe negative	High	Yes	Yes
Mother is HBsAg positive where e-markers have not been determined	High	Yes	Yes
Mother had acute hepatitis B during pregnancy	High	Yes	Yes
Mother is HBsAg positive and anti-HBe positive	Low	Yes	No

schedule is both highly clinically effective, preventing the development of persistent HBV infection in over 90% of cases[8] and highly cost-effective[10]

In the UK 2 different models of care for delivering post birth HepB vaccinations and 12 month blood tests have been outlined in national guidance [11] with one model centered on primary care and the other within the local pediatric service, **Table 2** outlines the 2 approaches.

With either model robust monitoring is needed to ensure vaccinations and blood tests are administered in a timely manner. National best practice guidance recommends that provider/commissioning immunization leads or local health protection services are best positioned to provide this role.[11]

In Norfolk and Suffolk (rural counties in the East of England) the Anglia Health Protection Team (AHPT), previously known as Norfolk, Suffolk and Cambridgeshire (NSC) health protection team took the responsibility for monitoring the completion of hepatitis B immunizations for at risk babies. Following notification of a case HBsAg-positive pregnant woman from an antenatal screen the details of the mother and her due date are recorded on a case management system called HPZone^{TM} and follow up is scheduled to ensure the baby receives the 4 HepB and/or HBIG and 12 month blood test. All babies in Norfolk and Suffolk are managed through the primary care model. Follow up with GP practices and child health information systems teams are undertaken by a dedicated health protection nurse within the AHPT for babies with incomplete immunization histories.

AHPT has been monitoring the follow up for over 6 y now and we felt it was the right time to evaluate this practice. Our principle aim was therefore to review the uptake of the national HepB immunization program for at risk babies born to HBsAg positive mothers in the rural counties of Norfolk and Suffolk. The study also discusses the use of the local health protection team for coordinating this service.

Method

We undertook a retrospective audit of vaccination coverage for babies born to HBsAg positive mothers between 1st January 2008 and the 31st December 2013 in Norfolk and Suffolk. Data on the infectivity status of mothers, neonatal immunization history (vaccinations and or hepatitis B immunoglobulin), 12 month blood test and reasons for incomplete vaccination history were extracted from 2 legacy hepatitis B antenatal databases for Norfolk and Suffolk and a new combined database for Norfolk and Suffolk. Duplicate records were identified and removed (cases in the new combined database overlapped with cases from the legacy databases). Cases with missing delivery dates or year of delivery were excluded from the analysis. The infectivity status (high or low) of mothers was already classified for Suffolk mothers and ascertained from serological markers for Norfolk cases. Vaccination completion rates were calculated based on eligible babies (babies with vaccination dates in the future were excluded from the denominator). All data were analyzed using Microsoft Excel^{TM} and results presented as proportions.

Results

A total of 163 pregnant women positive for HBsAg, delivered babies in Norfolk and Suffolk between 2008 and 2013. Twenty two mothers (13.5%) were classified as high risk, while the infectivity status was unknown for 28 (17.1%) mothers. In total 16 babies received HBIG at birth with 59.1% (13/22) of babies born to high risk mothers documented as receiving HBIG. When the data for years 2011–13 was examined the rate was 84.6% (11/13 babies).

Table 2. Outline of 2 models of care for delivering postnatal hepB vaccination

Pediatric/acute care model	Primary care model
In this model the hospital takes responsibility for the coordination and delivery of the immunization schedule. Babies are invited to attend hospital clinics to receive 2nd, 3rd and 4th hepatitis B vaccinations and blood serology testing.	Following immunization at birth by the hospital, the scheduling of the 2nd, 3rd and 4th hepatitis B immunization is managed through the Child Health Information System (CHIS); the system responsible for scheduling all childhood immunizations. Babies are invited to attend their local GP practice to receive all hepatitis B vaccinations and blood serology testing.

Table 3. No (%) uptake of hepatitis B vaccinations and serological testing at 12 months

Dose	Eligible babies	No (%)	Moved away	% excluding babies moved away
Birth	163	162 (99.4%)	0	99.4%
2nd	159	152 (95.6%)	1	96.2%
3rd	157	148 (94.3%)	1	94.9%
4th	127	106 (83.4%)	11	91.4%
12 month blood	127	38(29.9%)	11	32.8%

At birth 99.4% (162) of babies received a first HepB vaccine; the mother of 1 baby declined immunization. For the 2nd dose at 1 month, 95.6% of babies (152) received a vaccination, 1 baby moved from Norfolk and Suffolk before receiving the immunization. 94.3% of babies (148) received a 3rd immunization at month 2 and again 1 baby had moved away before completing the immunization. At 12 months 83.4% (106) of eligible babies received a 4th hepatitis b immunization with 11 babies moving from the area before the fourth dose. When these babies were excluded from the analysis 91.4% of babies received all 4 vaccinations. (**Table 3**)

Over the 6 y period 24 babies received incomplete immunization for their age with 11 babies moving away before completing the full set of vaccinations (5 left the country, 3 moved within England and the destination was unknown for 3 babies), 5 did not attend appointments, 1 declined all vaccination from birth and the reason for incomplete vaccination were unknown for 7 babies. Among the 24 babies 95.8% (23 babies) received a first dose of hepatitis B vaccination at birth, 70.8% (17) received a second dose at 1 month and 62.5% (15) received a third dose at 2 months of age.

At 12 months 29.9% (38 babies) of babies had their blood tested serologically to ascertain infection status; antibody testing was incorrectly requested for 3 babies. All babies receiving antigen testing were HBsAg negative. The serological status of 59.1% (75/127) of all eligible babies was not recorded.

Discussion

The retrospective audit identified 163 babies born in Norfolk and Suffolk between 2008 and 2013 to HBsAg positive mothers of which 83% of eligible babies (106) received the complete course of 4 vaccinations (91% if you exclude babies whom moved away during the period). It is not possible to compare these findings against national data due to limitations in the experimental national COVER program data which monitors uptake. A brief search of the literature identified 3 audits from the UK examining the coverage of hepatitis B vaccination to at risk babies. The coverage rate for the 4th vaccination was higher (83%) in Norfolk and Suffolk compared to the other studies (range 28% to 76%), it was also higher for the 3rd vaccination 94.3% (66% to 69%). Coverage of HBIG at birth and serology at 12 months were lower (**Table 4**). In previous studies the cohort of at risk babies was followed up by acute hospitals or a mixture of acute hospital and/or primary care. The current study adds to the literature by reviewing the coverage of HepB vaccinations for at risk babies followed up in primary care only. Further, the current study makes use of data collected proactively as part of the process for monitoring at risk babies, rather than as part of a retrospective audit.

The low level of recorded HBIG uptake at birth for high risk babies may reflect historic data recording issues. Examination of the most recent 3 years' worth of data showed HBIG uptake at a similar levels to the studies in **Table 4** (85%).

The low completion rate of 12 month blood test (only 30% of babies had an outcome recorded on the database) may reflect data recording issues, difficulties taking venous blood samples in primary care for young children[15] and the attitude of parents and professionals in requesting blood sample in a young child, who are perfectly well. Additionally, as viral hepatitis is a notifiable infection, all ante-natal HepB cases, by law, are notified to the health protection team. A dedicated nurse in the team follows up these cases working closely with the mid-wives in the hospital and community to ensure HBIG doses are stocked in the hospital near the estimated time of delivery. Further, follow up of vaccination of babies is also undertaken by the same nurse collecting data from GP practices and Child Health Informatics System. The same nurse have been doing this for the last 7 y and hence we believe there is no under-ascertainment of the follow up data.

The current method to test for evidence of infection in babies is by a serological test and most primary care practices are reluctant to do venepuncture on babies. Hence they are referred to the hospital for a further appointment just for the testing. This is resulting in a poor uptake of the testing. Further, the analysis shows that some practices were referring the babies for 'antibody'

Table 4. Hepatitis B immunization coverage reported in previous studies

Study	HBIG	Birth	2nd	3rd	4th	Blood
Wallis and Boxall 1999[12]	80% of babies born to e-antigen positive mothers	98%	78%	66%	28%	22%
Giraudon et al 2009[13]	20/28 71.4%	241/249 97%	—	172/249 69%	49% (95% CI 43–56)	33%
Dyson et al 2014[14]	15/15 100%	—	—	—	76%	55%

testing (i.e. evidence of immunity/vaccine effectiveness) which is against the national guidance. The proposed Dried Blood Spot (DBS) testing being rolled out nationally in the UK allows primary care practices to test for infection concurrently at the time of administering the 4th dose of the vaccine via a simple heel prick test rather than venous sample taking from the arm. The advantage being this can be performed locally at the GP surgery, community clinic or at the infant's home removing the need to travel to specialist pediatric phlebotomy clinics at acute hospitals.[15] The NSC area will be rolling this out in September 2014.

Given the increased risk of developing chronic hepatitis B from parenteral transmission and the long term health burden of chronic hepatitis B to both the individual and the health system it is essential that all babies at risk are fully immunised. Health Protection teams are ideally placed to monitor and coordinate the completion of vaccinations and blood tests as they are notified of all women testing positive for hepatitis B during pregnancy. Further they are well positioned to take an overview of the whole system and co-ordinate efficiently with the primary care (General Practice) and the Hospital Maternity units.

Conclusion

Although different models for delivering the hepatitis B immunization schedule may exist there is a clear need for a single organization to take oversight of uptake across the system and ensure no babies fall through the gap. The central coordinating role provided by the Anglia Health Protection Team helped ensure a high proportion of babies in Norfolk and Suffolk received 4 Hepatitis B vaccinations. Future implementation of the dried blood spot (DBS) should help increase the uptake of 12 month blood serology.

Recommendations

We recommend that the quality of data recording should be improved across the counties of Norfolk, Suffolk and Cambridgeshire particularly to ensure all the HepB markers including viral loads are completely recorded. We also recommend that all babies born to mothers who were HBV carriers must have 100% coverage for all 4 doses of HepB vaccine and for HBIG (for babies born to high risk mothers). The testing of infants at 12 months of age to ascertain infection status (rather than response to immunization) should also be 100%. Further we recommend that health protection teams are best placed to work closely with relevant stakeholders to ensure that the data collection, analysis and follow up is complete.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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