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Hepatitis B screening: outcomes and management of pregnant women and infants in the Cook Islands.

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ABSTRACT

Introduction

To describe current Cook Islands practice for screening and management of Hepatitis B (HB) in pregnant women and their newborns and to consider the implications of an updated screening and management strategy.

Methods

A retrospective study of pregnant women booked for antenatal care in the Cook Islands from January 2010 to December 2014 was conducted. Data were collected on maternal Hepatitis B serology status, timeliness of hepatitis B immune globulin given if indicated and the completion of hepatitis B immunisation for newborns who were due their vaccinations, special service referral and contact tracing from the electronic health information system. Simple descriptive statistics were used to report the data.

Findings

All women who attended the antenatal clinics accepted Hepatitis B screening in pregnancy. Data from 803 women were analysed. Hepatitis B surface antigen (HBsAg) was detected in 23 of 803 (2.9%) of women of which 21 were Antibody-HBs (Anti-HBs) positive and two were hepatitis B e antigen (HBeAg) positive. Hepatitis B DNA viral load was unable to be tested. Hepatitis B immune globulin was given to 21 of the 23 babies within one day, one was given on day 3 and one was missed. None of the 23 mothers and their babies had any ongoing follow up.

The first Hepatitis B vaccine, due within 24 hours of birth, was given within a day to 743 of the 803 (93%) of babies. The second, due at 6 weeks, was given by 8 weeks to 645 of the 778 babies due for their six week vaccination (83%). The third, due at 3 months, was given by 4 months to 648 of the 744 (87%). The fourth, due at 5 months was given by 6 months to 553 of the 712 (78%). Of the 712 babies over 6 months of age, 601 (84%) were recorded as having completed four HB vaccines at any time.

Conclusion

The hepatitis B screening and immunisation in the Cook Islands appears effective but this study indicates that the follow up of both the mother and their infants needs to be improved.

Key words: Hepatitis B, mother to child transmission, pregnancy, immunisation

INTRODUCTION

The Cook Islands consist of 15 islands and atolls spread over 2 million km² of the Pacific Ocean. The total resident population is 17,794 of which 8979 are females and 3655 of these women are in the reproductive age group (age 15 to 49 years).¹

Chronic hepatitis B virus (HB) infection remains endemic in many parts of the world and there are over 2 billion infected individuals worldwide.² The risk of chronicity of hepatitis B

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virus (HB) is inversely related to the age of acquisition of infection; vertical transmission (mother to child) is associated with a risk of chronicity of more than 80%.³ Infants with chronic infection have a 25% lifelong risk of developing cirrhosis and/or hepatocellular carcinoma.⁴ Screening of pregnant women for HB and managing infected women and their infants appropriately in order to interrupt vertical transmission is a very cost-effective health intervention.²

The risk of vertical transmission of HB is 70-90% when a woman is Hepatitis Be antigen (HBeAg) positive and around 40% when HBeAg is absent.⁵⁻⁸ The use of active or passive immunisation or both reduces the risk of vertical transmission by 90%.⁹ A high maternal viral load increases risk of transmission to the child,¹⁰ with babies born to women who are HBeAg positive with a high viral load (above 2×10^7 IU/ml or \log^8 copies/ml) having a transmission risk of at least 10% despite administering Hepatitis B immune globulin (HBiG) to the neonate.¹¹

Screening for HB has been recommended as a routine antenatal screening test in the Cook Islands since the 1980s. However, there is no specific guideline for the referral of HB positive mothers, contact tracing or a post-partum follow up pathway. Currently, after parental consent, all neonates are given HB vaccine (HBV1) at birth according to the Cook Islands Immunization policy. HBiG is also given to neonates of HBsAg positive mothers within 24 hours of birth.

A HB screening policy has been in place for over 30 years, but the uptake, prevalence, screening method (serology), and the effectiveness of follow up has never been evaluated. In addition the current guidelines do not consider a specialist referral service for mother or baby.

It is likely that the incidence of HB infection in the Cook Islands is changing due to changes in sexual practices, a more mobile population and high incidence of other sexually transmitted infections (especially Chlamydia) in the population¹² making a better understanding of issues concerning HB important. Our neighbouring countries are implementing an enhanced evidence based screening, follow up and referral program for both the mother and child which the Cook Islands needs to consider adopting. The aim of this study is to describe current Cook Islands practice for screening and management of HB in pregnant women and their newborns and to consider the implications of an updated screening and management strategy.

METHODS

The study population included all booked pregnant women in the Cook Islands, from January 2010 to December 2014 inclusive. Women who gave birth overseas were excluded as their data were not known. Women with twin pregnancies were included. For women who had more than one birth during the study period, or who had twins only the last born was counted.

Ethics approval was granted by the research committee of the Ministry of Health. Data on demographic, maternal HB status, serology and immunisation status of infants were collected retrospectively from the patient record shared in the electronic patient management system (Medtech32; www.medtech.co.nz) and the Rarotonga Hospital obstetric patient register. Data required for this study were extracted by midwives using predetermined Query Building templates.

Outcomes

Antenatal outcomes included the number of women screened at the clinics, the number of HBsAg positive women and their serology results. Postnatal outcomes included the proportion and timely immunisation with HBiG, the first HB vaccine (HBV1) for all neonates, and the completion of the HB immunization programme (HBV2, HBV3 & HBV4) as the vaccinations were due. Specialist referral of both the HB positive mothers and their babies were also studied.

Immunisation rate calculations

The Cook Island immunisation guidelines state when HB vaccines are due (at birth, 6 weeks, 3 months and 5 months). They do not state when a vaccination is considered late or overdue. Based on overseas recommendations, we assigned a 1-day period as acceptable for the first vaccine, after which it was considered overdue.¹³ We assigned a 2-week window as acceptable for the 6 week vaccine, calling it overdue after 8 weeks. Similarly we called the 3 month vaccine overdue if not given by 4 months, and the 5 month vaccine as overdue if not given by 6 months. We calculated rates based on the denominators of children who were within the window of acceptability for their due vaccination. Descriptive statistics were calculated in Microsoft® Excel Version 2010, and Stata version 12.1.

FINDINGS

A total of 1148 women were booked for the antenatal care between January 2010 and December 2014 inclusive. All these women were offered HB screening (100%). This analysis is based on data from 803 women and infants, being the last live-born baby from each woman who gave birth during study period. Women were excluded due to giving birth overseas (n=179), on an outer island (n= 67) or at home (n=1) or because they had a miscarriage, termination of pregnancy, intra-uterine death or perinatal death (n=27) (some women had more than one reason for exclusion). In addition, 81 women had more than one baby in the study period and only the last baby was included. **Table 1** shows the characteristics of women and prevalence of HBsAg seropositivity. Of the 803 women, 23 (2.9%) were HBsAg positive.

Table 1. Characteristics of women included in the study. N=803

Age (median, range)	30, 15 to 50
Gravida (median, range)	2, 1 to 13
Parity (median, range)	1, 0 to 12
HB screening offered and accepted	803 (100%)
HBsAg positive	23/803 (2.9%)

Table 2 describes the demographic and serologic characteristics of the 23 pregnant women with positive HBsAg serology. Only 2 women were tested for HBeAg and both were positive. Most of the 23 women were Cook Island Maori. Of the 23 neonates from HBsAg positive mothers; 22 received their HBiG within 24 hours and 1 after 24 hours. One neonate was not recorded as receiving HBiG.

Table 3 shows that 743 of the 803 newborns were given first dose of Hepatitis B according to the Cook Islands Immunization Guideline with all catch up doses for all 3 hepatitis B immunization in 89% range to 94%. Only 78 % of the infants completed the 4 doses of Hepatitis B immunization during the study period.

DISCUSSION

This is the first study in the Cook Islands of HB infection prevalence among pregnant women and the management of positive mothers and their newborns. The analysed data represent 70% of all births in the Cook Islands. There is a

high uptake of HB screening (100%) in the Cook Islands.

Table 2. Hepatitis B positive mothers (n=23), demographics, serology, HB immune globulin delivery to neonates.

Age (years)	32 (24-43)
Gravida	1 to 6
Parity	0 to 5
Ethnicity	
Cook Island Maori	20
Asian	1
Others	2
HB positive (new case)	7
HB positive (known case)	16
HBsAg positive in pregnancy	23
Anti-HBs (2 missing)	21 <10 IU/L
HBe-Ag positive (21 missing)	2
Anti-HBe positive (10 missing)	11
HB core IgM (13 missing)	10
Anti HB core positive (2 missing)	21
HBiG given to baby within 24 hours of birth	22 (one given on day 3)

Table 3. Hepatitis B vaccinations for 803 babies.

Vaccine	due	Given on time	Given any time
1	within 24 hours	By 1 day 743/803 (93%)	787/803 (98%)
2	6 weeks	By 8 weeks for babies 8 weeks or older 645/778 (83%)	751/803 (94%)
3	3 months	By 4 months for babies 4 months or older 648/744 (87%)	716/803 (89%)
4	5 months	By 6 months for babies 6 months or older 601/712 (84%)	629/803 (78%)

The prevalence of HB in the pregnant women in our study was 2.9%. The World Health Organisation (WHO) define the prevalence of chronic HB infection as high when ($\geq 8\%$), intermediate ($\geq 2-8\%$), and low ($< 2\%$).² In our

literature search HB infection among antenatal women in Tonga is 15%¹⁴ and Fiji 5% to 6%.¹⁵ Cook Islands can be regarded as intermediate in prevalence of chronic Hepatitis B in comparison to the other Pacific Island countries.

The 23 HB positive mothers, had a median age of 32 years. It is likely that Cook Islands HB chronic carrier population is relatively young and at increased risk of cirrhosis and hepatocellular carcinoma. This warrants the need to develop more robust pathways for follow up, referral to special services and to consider antiviral to reduce the premature deaths from complications of chronic HB infection.

In our study, only 2 out of the 23 women had their HBeAg status confirmed. Viral load was not tested for the HBeAg positive mothers; indicating the need for improvement in serological study of HB positive women. Updated international guidelines from WHO,² The Royal Australia and New Zealand College of Obstetrics and Gynaecology,¹⁷ The New Zealand Maternal Fetal Medicine Network¹⁸ and the UK Department of Health¹⁹ recommend HB DNA testing to determine the need for antiviral therapy. Antiviral therapy for HB positive pregnant mothers is now available. However, safety and efficacy data on use of antiviral for suppression of transmission purposes are not robust yet.

During the 4 years of the study period, 7 of the 23 (30.5%) HBsAg positive women were new cases. This confirms antenatal screening is an important opportunity for case detection and follow up. Referral of women with HB infection for specialist care was unsatisfactory as no referral was documented.

Cook Islands National Immunization guideline indicates that all babies born in country should be given a first dose of hepatitis B vaccination (HBV1) at birth or within 24 hours with HBiG for new born of HBsAg positive mother, concurrently. Our study confirms maternity ward staff were delivering HBV1 to 93% of all neonates within 24 hours as per guidelines with 98% at any time. HBiG was given at an appropriate time to 21 of the 23 (91%) babies of HB positive mothers on day 1, one baby on day three and one was missed. Delays in the delivery of HBV1 could have been due to paediatric indications but it is not possible for this study to confirm.

A total of 601 of 712 infants (85%) received four doses of HB vaccine during the study period. This seems to be lower than published the immunisation rate for Cook Islands (99%).^{12,20} HB vaccine 2, HB vaccine 3 and HB vaccine 4 are

given in the community and rates could be under recorded if caregivers have difficulty accessing our computerised or internet based records system. There is an opportunity to improve documentation and access to our medical records system for community and outer islands based medical and nursing staff.

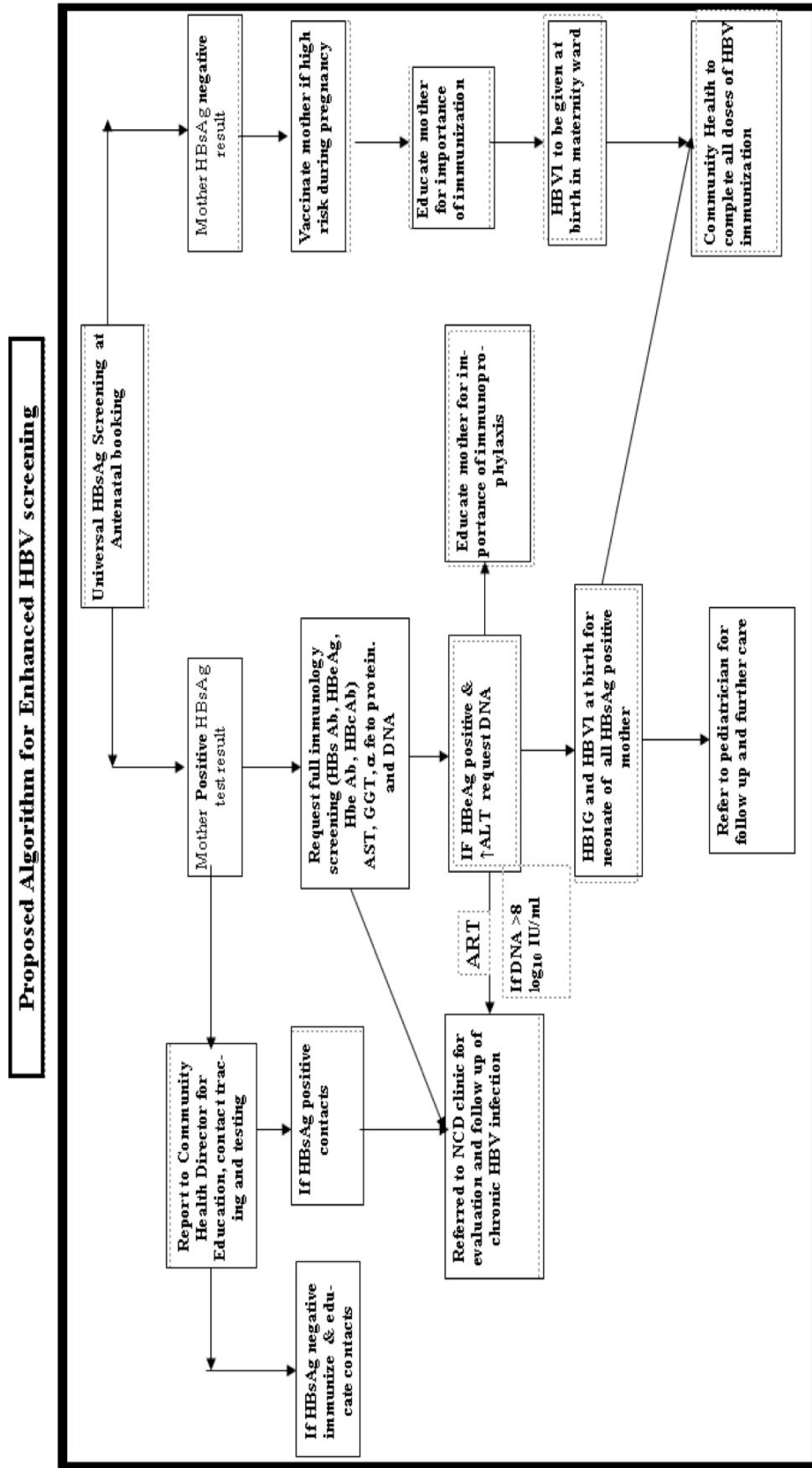
International guidelines on management of neonates of HB positive mothers recommend that the neonates of HB positive mother should be tested for HBsAg and anti HBs at age 9 to 12 months to confirm their immunity status after completing the HBiG at birth and 4 doses of HB immunisation.^{18, 21} HBsAg-negative infants with anti HBs levels greater than 100mIU/ml are considered protected and no further medical management is required.¹⁸ Those with anti HBs levels less than 100mIU/ml are not protected and should be revaccinated with a second three-dose series followed by retesting 1 to 2 months after the final dose. Passive immune prophylaxis with HBiG at birth followed by at least 3 doses of hepatitis B vaccine provides approximately 95% protection from perinatal infection, whereas the vaccine alone is approximately 75% protective¹⁸.

In our study, we found no evidence of follow up or referral to special services of the 23 neonates of HB positive mothers at age 9 to 12 months in the Cook Islands. There is a need to review the current management for infants of HB positive mothers by the paediatric team and community services.

There were several limitations to this study. A lack of data on immunisation of HBV1 for women who delivered overseas and incomplete documentation of immunisation status in the electronic patient record system hampers the evaluation of completeness of overall immunisation. We were also not able to analyse hand recorded immunisation records which might have reflected a better coverage than shown in this study. Nevertheless, our analysis represents 85% of the population.

Based on our review of HB infection screening and management, we recommend an enhanced screening program for pregnant women and new follow up and referral pathways for both mother and their babies. We believe this would be cost-effective in a Cook Island population and sustainable and culturally acceptable. **Figure 1** refers to the new enhanced program.

Figure 1: Proposed Algorithm for Enhanced HBV screening



CONCLUSION

National guidelines and standardisation of the pathway of management of women with hepatitis B and their infants is required to improve the care provided across the sector and to prevent the development of chronic cirrhosis and hepatocellular carcinoma. Rigorous auditing of the documentation of immunization records on the Medtech 32 electronic patient record system should be implemented. Newly detected maternal infections should be seized as an opportunity to provide appropriate care to the mother, her baby and extended family. As the management of these women and infants is complex, there is a need for the different teams within the Ministry of Health to work much more closely together to reduce the risk of women of high infectivity and the newborns being lost to follow up.

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