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Original Article

A Study on Prognosis of Acute Hepatitis B in Hepatitis B Vaccinated Cohort

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Abstract

Taiwan initiated the implementation of national neonatal hepatitis B vaccination program in July 1986. This retrospective study on the epidemiological characteristics and prognosis of acute hepatitis B in the hepatitis B vaccinated cohort aims to provide background for prospective hepatitis B prevention and control policy-making. Identified from the Taiwan Centers for Disease Control Notifiable Disease Surveillance System (NDSS) database, 75 acute hepatitis B patients, born after July 1, 1986 and diagnosed between January 1, 2008 and March 31, 2012, were approached. After voluntary recruitment, the participants underwent a hepatitis B serum marker test and completed a questionnaire. The participants' family members were also tested for hepatitis B carriage status. Thirty-seven eligible patients (37/75, 49.3%) consented to the study, among whom 81.1% (30/37) received at least three doses, while those who had incomplete vaccination series or no vaccination record were mostly born between 1987 and 1990. Nine participants (9/37, 24.3%) had a family history of hepatitis B carriage, while no one had hepatitis B carrier siblings. The most common age of disease onset was 15-24 (N=32), among whom six were married to/ in partnership with a hepatitis B carrier. Second most common age of disease onset was under 1 (N=3), of whom all were born to hepatitis B carrier mothers. Prognosis based on hepatitis B serum marker profiles showed that HBsAg disappeared and Anti-HBs appeared in 21 participants (21/37, 56.8%), HBsAg disappeared without Anti-HBs appeared in 12 participants (12/37, 32.4%), 3 participant became hepatitis B carriers (3/37, 8.1%) whose age of hepatitis B disease onset was 8 months, 6 years and 19 years old respectively, and 1 participant died of fulminant hepatic failure in acute hepatitis B. This survey shows that the prognosis of acute hepatitis B patients of the

hepatitis B vaccinated cohort is not always clearance of HBsAg in conjunction with appearance of Anti-HBs. Regarding the prevention and control of acute hepatitis B, except for certain reasons and mother-to-infant perinatal transmission which can not be fully prevented with vaccination, the disease risk is still present among the 15-24 age group. Therefore, work remains to be done on developing hepatitis prevention and control strategies for this group in order to achieve the target of hepatitis B elimination.

Keywords: acute hepatitis B, vaccinated cohort, prognosis

Introduction

Taiwan is the first country in the world to implement a massive neonatal hepatitis B vaccination program. The neonatal hepatitis B vaccination program started with infants born to HBV carrier mothers in July 1984 [1] and the coverage was extended to all new-borns in July 1986. The paediatric hepatitis B vaccination program has been in place for 29 years in Taiwan and proven successful. It marks indeed a significant achievement in the public health history in Taiwan. The program not only terminated the threatening "national epidemic" in benefit of the domestic public, but also has been followed by many countries as a global model of hepatitis B control. Previous studies showed that the mass hepatitis B immunisation program reduced effectively hepatitis B carriage rate in children by 78-87% [2], hepatocellular carcinoma incidence in children (aged between 6-9) by 75% [3], and mortality of fulminant hepatic failure related to hepatitis B in infants by 68% [4]. A study in 2009 also showed that since the implementation, the hepatitis B carriage rate has decreased remarkably from 10% to 0.9% among people under the age of 25 in Taiwan [5]. While the hepatitis B carriage rate is declining in Taiwan, the carriage rate in children born to HBeAg positive mothers remains as high as 9.3% after receiving a comprehensive hepatitis B immune globulin and hepatitis B vaccination [6]. In fact, hepatitis B vaccination does not provide permanent protection, and anti-HBV antibody vanished among 63%of HBV vaccinees after 12 to 18 years and they may be re-infected with HBV if exposed [7,8]. Hence there are still challenges to overcome after the implementation of vaccination policy in Taiwan.

Since the implementation of hepatitis B vaccination program, a number of studies have been conducted in HBV vaccinated cohort; but they were mainly focused on seroepidemiology, hepatitis B vaccination efficacy and protective effect of hepatitis B vaccine, while a relatively fewer number of studies explored the prognosis of acute hepatitis B cases in hepatitis B vaccinated cohort. Therefore, this study was set up specifically for acute hepatitis B patients, born after July 1, 1986 and diagnosed between January 1, 2008 and March 31, 2012. Blood samples were collected from the participants, their mothers and family members for serological tests (HBsAg, anti-HBs, anti-HBc, HBeAg and anti-HBe) and molecular biological assays. The participants also answered a questionnaire. Their vaccination record and their mother's prenatal screening results were obtained through National Immunization Information System (NIIS) database. These data allowed the

understanding of hepatitis B vaccination completion rates of the acute hepatitis B patients, exposure to risk factors of the hepatitis B infection, recovery rate of the hepatitis B infection, the correlation between HBV genotypes of the carrier participants and of their carrier mothers, relevance of acute hepatitis B surveillance and hepatitis B infection status of family members of the hepatitis B patients. The survey aims to provide background for prospective hepatitis B prevention and control policies. Additionally, upon confirmation of diagnostic testing, chronic hepatitis B carrier participants of the study will be provided follow-up and referral services to ensure their health.

Materials and Methods

1. Study participants

(1) Eligible participants were identified from CDC's infectious diseases reporting system. Inclusion criteria were acute hepatitis B confirmed cases from the vaccinated cohort, born after July 1986 and diagnosed between January 2008 and March 2012. Patients received explanation and clarification, either through telephone or fact sheet, on the methodology and purposes of study as well as the potential risks and benefits of participation. Participants' mothers and other family members were also surveyed in order to analyse the concordance of exposure to risk factors and infection status of their families. Participation in the study is voluntary and written informed consents were sought from patients and their family members who agreed to take part in the study.

(2) The project was reviewed and approved by Taiwan CDC's human and clinical research ethics committee.

2. Data collection

(1) Serum samples:

Serum samples were taken from the participants and their family members at least six months after the HBV disease onset. Blood samples of 34 cases were collected by the study group; sample of one fatal case, taken at the time of illness onset, was retrieved from the hospital; and blood samples of 2 cases were taken at hospital.

(2) Questionnaire:

Participants were required to complete a pre-structured questionnaire. Questions include whether the participant's mother is a chronic hepatitis B carrier, whether any of the family members has experienced acute hepatitis B infection or is a chronic hepatitis B carrier, as well as any exposure to risk factors in the three months prior to disease onset. (The incubation period ranges from 45 to 160 days, usually between 60-90 days.)

(3) Participants' basic information was extracted from Taiwan CDC's data warehousing system and linked with their vaccination records (including hepatitis B vaccine and HBIG) along with their mothers' prenatal screening data obtained from subsystems of the central database management of National Immunization Information System (NIIS). Participants' personal medical records were reviewed if necessary.

3. Laboratory tests

(1) Serologic tests: including HBsAg, anti-HBs, anti-HBc, HBeAg and anti-HBe assay (Abbott Laboratories, North Chicago, IL, USA).

(2) HBV DNA detection: Nested PCR (ABI7500) was used to detect HBV DNA in serum in order to determine whether the participant has occult HBV infection.

(3) HBV genotype and viral genetic sequencing analysis ('a' determinant region of hepatitis B surface antigen S gene): When both a participant and his/her mother or other family members were HBV carriers, PCR type-specific primer was used to carry out genotyping and genetic sequencing to provide data for vertical or intra-familial transmission correlation analysis.

4. Follow-up and referral of chronic hepatitis B carriers: Acute hepatitis B patients who became chronic hepatitis B carriers or family members who were confirmed as chronic hepatitis B carriers from the study were referred to a local public health bureau (or center) for health education on the necessity of 6-monthly routine follow-up at clinic/hospital. They were also recommended to seek medical treatment to reduce potential risk of developing liver cirrhosis or cancer. Assistance to arrange follow-up appointments or treatment at local hospital was also provided to protect participant's health.

Results

1. Participants

Identified from the Center for Disease Control's infectious diseases reporting system, 75 confirmed acute hepatitis B cases, born after July 1986 and diagnosed between January 2008 and March 2012, were approached through telephone interviews, written invitations and home visits conducted by local public health officers. Thirty-seven among them (49.3%, 37/75) voluntarily consented to the study. The age distribution of participants was: 3 cases aged under 1 year, 2 cases aged 1-14 years and 32 cases aged 15-24 years (Table 1). Response rate was about 50% across all age groups. Blood samples were taken from participants' family members, including: 29 mothers (in which one is a stepmother), 11 fathers, 14 siblings and 1 cohabitant girlfriend.

Table 1. Summary of age of disease onset, vaccination records, mother's hepatitis B serum marker profiles in prenatal screening results, and participants' hepatitis B serum marker profiles.

	Confirmed case (N)	Voluntary participant (N)	Received at least 3 doses of vaccine N (%)	Received HBIG	Mother's prenatal screening for HBsAg/HBeAg				Prognosis of participant (excluding one fatal case)			
									HBsAg(-)		HBsAg(+)	
					-/-	+/-	+/+	NA/NA	Anti-HBs (+)	Anti-HBs (-)	HBeAg (-)	HBeAg (+)
Aged under 1	5	3	2(66.7%)	1	0	2	1	0	2	0	0	1
Aged 1-14 years	4	2	2(100%)	1	1	0	1	0	0	1	0	1
Aged 15-24 years	66	32	26(81.3%)	2	16	2	2	12	19	11	1	0
Total	75	37	30(81.1%)	4	17	4	4	12	21	12	1	2

NA: No data available

2. Personal Hepatitis B Vaccination Records

Thirty patients (30/37, 81.1%) had a complete personal vaccination record (Table 1). Among them, 4 participants' mothers were highly infectious carriers (HBeAg positive or RPHA surface antigen titers ≥ 2560) according to their prenatal screening results, and at birth, the participants received one dose of HBIG and 3 doses of hepatitis B vaccine in compliance with the vaccination schedule. (4 doses of plasma vaccine were required from July 1984 to October 1992, while 3 doses of genetically engineered vaccine have been required since November 1992). The other 26 participants, whose mothers were not highly infectious carriers at the time, received 3-4 doses of hepatitis B vaccine at birth in accordance with regulations.

Four cases (4/37, 10.8%) had incomplete vaccination records, and 3 cases (3/37, 8.1%) had no vaccination record. Of the 4 cases with incomplete vaccination, one did not need to complete the series because the participant had disease onset at 2.5 months old after first 2 doses of vaccine and had developed antibodies. The other three cases were short of 1 - 2 dose(s) (having received 2 doses of vaccine) and were born in 1987, 1988 and 1990 respectively. As for the 3 cases without vaccination records, they were all born in 1989. In summary, the 6 cases with incomplete or no vaccination records were all born between 1987-1990.

3. Participants' Exposure to Risk Factors

The peak of acute hepatitis B infection was observed at the age group 15-24, accounting for 86.5% (32/37) of participants. Exposure to risk factors within 3 months prior to disease onset in this age group include: 59.4% (19/32) reported having sexual behavior, among whom 18.8% (6/32) had sexual contact with hepatitis B carriers, 18.8% (6/32) have had dental or surgical treatment, 15.6% (mother: 1; stepmother:1; father: 2; girlfriend: 1; 5/32 in total) had hepatitis B carrier in the family, 9.4% (3/32) have had transfusion, 9.4% (3/32) have had injections in a pharmacy, 9.4% (3/32) have had ear piercing (or tongue rings, nose rings, navel rings, tattoos, eyebrow tattoo and eye liner tattoo, etc.), 6.3% (2/32) have received alternative therapy such as acupuncture or cupping, and 25.0% (8/32) had been exposed to unidentified risk. The second peak of acute hepatitis B infection was the age group under 1 year, accounting for 8.1% (3/37) of cases. Being born to a hepatitis B carrier mother was the most important exposure to risk factors in this age group (3 / 3,100%). Finally, the age group 1-14 accounted for 5.4% (2/37) of all cases, among whom 50% (1/2) was born to a hepatitis B carrier mother.

4. Prognosis

Prognostic follow-up blood test (Table 1) showed that 21 participants (21/37, 56.8%) developed anti-HBV antibodies, 11 participants (11/37, 29.7%) didn't develop detectable specific antibodies and were non-carriers, 1 participant (1/37, 2.7%) had occult HBV infection, 3 participants (3/37, 8.4%) became carriers, and one (1/37, 2.7%) died. Among them, the occult HBV-infected participant was a 20 year-old male at the time of disease onset.

The blood sample was taken more than 3 years after the disease onset. Neither HBsAg nor anti-HBs were detected in the serum, yet HBV DNA (genotype C) still existed. As to the 3 participants who became carriers, their age of disease onset were 8 months, 6 years and 19 years respectively, and their hepatitis B serum marker profile were HBeAg positive, HBeAg positive and HBsAg single positive (HBeAg negative). The fatal case was 16 years old at the time of disease onset. The hospital reported the case (case A) on January 17, 2012, with a disease onset date of January 9, 2012. The patient's initial symptoms were vomiting, poor appetite and intermittent fever etc. The diagnosis was fulminant hepatitis leading to hepatic failure and hepatic encephalopathy (WBC: 6830/ul, Ammonia level: 254ug/dl, PT: 61.3 sec, GOT / GPT: 3179 mU / ml / 7356mU/ml, T / D Bilirubin: 11.46/6.54mg/dl, HBsAg: 0.02 IU / mL, IgM anti-HBc: 31.17 S / CO). Unfortunately the patient deceased on January 30, 2012. The patient's mother was carrier (HBsAg positive and HBeAg negative), so the patient received a complete 3-dose series of vaccine in compliance with the required vaccination schedule in infancy and early childhood. According to hepatitis B serum marker results in the patient's high school medical check record, he was non-carrier and had no anti-HBs. The patient's parents indicated that during incubation period, the patient had not been exposed to any risk factors, such as trauma, recreational drug injection, acupuncture, ear piercing, blood transfusions or surgical treatment. The risk factors of his infection remained unclear at this moment. Results from molecular biological assays showed that the patient and his mothers were both infected by HBV genotypes B, while there was an M1331 T mutation on ‘a’ determinant region of the mother's HBsAg gene and the patient's was wild-type (Table 2).

Table 2. The fatal case and his parents' serum marker profile, analysis on ‘a’ determinant region of HBV and genotype

Participant and Parents	Age of blood sampling	Gender	HBsAg	Anti-HBs	Anti-HBc	HBeAg	Anti-HBe	Point mutation (Amino Acid Position)	Genotype	Age of Onset
Case A	16	male	-	+	+	-	+	Wild Type	B	16
Case A biological mother	43	female	+	-	+	-	+	M133T	B	
Case B biological father	48	male	-	-	+	-				

5. HBV Genotypes and Serum Marker Profiles of Carrier Participants and Their Mother/ Stepmothers

Three participants became chronic carriers after acute hepatitis B. Among them, the ones who had disease onset at 8 months (case B) and 6 years (case C) old were infected and became carriers despite having received a complete vaccination series in compliance with required schedule (1 dose of HBIG and 3 doses of HBV vaccine). In both cases, the participants and

their mothers' hepatitis B serum marker profile were all HBeAg positive with HBV genotype C. As to the carrier participant who had disease onset at 19 years old (case D), he had an incomplete and untimely vaccination record. His biological mother's prenatal screening results showed that she was HBsAg negative at the time, while the participant and his stepmother had the same serum marker profile, i.e., HBsAg single positive with genotype B. The 2 mother-child pairs and the 1 stepmother-child pair were having the same serum marker profiles (2 HBeAg-positive pairs and 1 HBsAg single positive pair) and HBV genotype (2 genotype C pairs and 1 genotype B pair) (Table 3). Analysis on mutation in the 'a' determinant region of HBsAg gene showed that the wild type was common among the participants with the only exception of the participant who had disease onset at 6 (case C). In his case, there is a P142L +W156L point mutation in amino acid position.

Table 3. The 3 carrier participants and their mothers' hepatitis B serum marker profile

Participant & mother	Age of Onset	Gender	HBsAg	HBeAg	Anti-HBe	Point mutation (Amino Acid Position)	genotype	Mother's Prenatal Screening Results
Case B	8 months	female	+	+	-	Wild Type	C	HBsAg(+) & HBeAg(+)
Case B Biological Mother		female	+	+	-	Wild Type	C	
Case C	6	male	+	+	+	P142L+ W156L	C	HBsAg(+) & HBeAg(+)
Case C biological Mother		female	+	+	-	Wild Type	C	
Case C	19	male	+	-	-	Wild Type	B	Biological Mother HBsAg (-)
Case C Stepmother		female	+	-	+	Wild Type	B	

6. Infection Status of Participants' Family Members

Thirty-five blood samples were taken from participants' family members, of which 29 were from participants' mothers. Their blood test results showed that 6 mothers (20.7%) were carriers, 17 mothers (58.6%) had anti-HBs (2 were HBsAg positive and RPHA>2560 at the time of prenatal screening, but have developed antibodies at the time of study), 6 mothers (20.7%) were non-carriers without antibodies (among which 4 were anti-HBc negative).

Eleven blood samples were taken from participants' fathers, among whom 2 (18.2%) were carriers, 6 (54.5%) developed anti-HBs, and 3 (27.3%) were non-carriers without antibodies (they were all anti-HBc-positive, and one claimed to be former carrier.) Fourteen blood samples were taken from participants' siblings, among whom 9 (64.3%) had anti-HBs and 5 siblings (35.7%) were non-carriers without antibodies (all anti-HBc positive). One blood sample was taken from a participant's carrier girlfriend. In total, 9 carriers (6 mothers, 2 fathers and 1 cohabitant girlfriend) were identified among participants' family members. None of the siblings were carriers, and none had both parents being hepatitis B carriers.

7. Chronic hepatitis B carriers were provided follow-up and referral services to maintain their healthy status

This study identified 12 hepatitis B carriers (3 participants and 9 family members) and 1 hepatitis C infected participant. They were all offered health education by the local public health bureau/center, assistance for future health education as well as follow-up and referral services.

Discussion

In Taiwan, the neonatal hepatitis B vaccination program was initiated in July 1984 (for infants born to carrier mothers) and the coverage was extended to all new-borns in July 1986. The Department of Health statistics showed that the third dose vaccine coverage reached 96.7% for the birth cohort 2010, while coverage of at least 3 doses of vaccine was only 86.9 to 89.4% for the birth cohort 1986-1989. Vaccination coverage of the birth cohort 1987-1989 is indeed lower than that of other cohorts. The study identified 6 participants who received incomplete vaccination (excluding one who developed antibodies after infection and did not require further immunisation) or no vaccination, 5 of whom were born during the 1987-1989 period. Also, the number of participants born between1986-1989 account for 60% (22/37) of the total number of participants surveyed in this study. These findings correspond to the result of a domestic serological prevalence study which surveyed people under the age of 30 in Taiwan and found that anti-HBc positive has a higher prevalence in the vaccinated birth cohort 1986-1989.[11].

Limitations of the study include recall error, lack of control group for correlation between infection and risk factor exposure, and selection bias as asymptomatic or mild symptomatic acute hepatitis B patients may have not sought medical treatment and thus not been reported. The most common age of disease onset was 15-24 years old (86.5%), followed by under 1 year old (8.1%) and 1-14 years old (5.4%). As to exposure to risk factors in the age group 15-24, sexual contact (19/32, 59.4%) came on top and 31.6% (6/19) knew that their sexual partners were hepatitis B carriers. The result showed that sexual contact increases HBV exposure risk in this age group and for those who have received complete vaccination series, and the infection is related to diminishing anti-HBs [7,8]. A previous study found that the sexual contact is the major route of acute hepatitis B infection in Taiwanese adults [12]. Another research showed that acute hepatitis B is related to sexual behavior within 3 months prior to disease onset. Through molecular biological tests, the same research found that genetic sequence similarity between patients' HBV DNA and their sexual partners' was 100% [13], which provides evidence for identifying "hepatitis B carrier sex partners" as origin of infection. In the present study, "carrier mother" (4/5, 80%) is the major risk factor for age group under 1 year and age group 1-14. Infection occurred despite complete and timely vaccination series showed that vaccine did not provide full protection against mother-to-infant vertical transmission [11].

In regard to prognosis, 3 participants (8.1%) became carriers. According to previous studies, age of disease onset is an important factor in becoming a carrier. The probabilities of becoming a carrier after HBV infection in perinatal period, early childhood and adulthood are 90% [14], 23% [15] and 2.7% [16] respectively. In the present study, despite the fact that participants in the age group 15-24 accounted for as much as 86.5% (32/37), only one (1/32; carriage rate: 3%) became as a carrier. The carriage rate of age group 15-24 is much lower than that of the age group under 1 year and the age group 1-14. In terms of the age of disease onset, the probability of becoming a carrier after infection is relatively lower after early childhood.

Another study pointed out that more than 80% of those who became carriers despite vaccination were children of carrier mothers [5,6]. In the present study, the 2 carrier participants' mothers and one carrier participant's stepmother were all carriers. There seems to be a strong association between participant becoming a carrier and mother being a carrier. As to evidence of mother-to-infant vertical transmission, taken their HBV genotype, age of disease onset and risk factor exposure into account, the cases of 8 months and 6 years were more likely being infected by their mothers through perinatal transmission. As to the case of the 19 year-old who acquired HBV infection not from his biological mother at birth, because his biological mother's prenatal screening results showed that she was HBsAg negative at the time. Although his stepmother (39 years old) was a carrier (HBsAg concentration: 123.97 IU / mL), she had not been in contact with the participant until he was 8 years old. Little was known about their intra-familial contact in early years, and the relationships observed could just be a chance occurrence. In addition, the family reported that the participant had been physically weak and unhealthy since childhood, and thus he often received injections as medical treatment. They became aware of his hepatitis B infection when he was in junior high school. Therefore, exposure to risk factors might have come from outside family.

A Taiwanese domestic study also showed that hepatitis B carrier mothers with genotype C had higher prevalence of HBeAg positivity and higher viral load, which made them more likely to transmit the virus to their children. Vaccination failure rate was also higher among patients infected by HBV genotype C [17]. In the present study, the 2 mothers of carrier participants (8 months and 6 years) were both HBeAg positive with genotype C. It seems that such carrier mothers are more infectious and children born to them are more likely to become carriers in the future. HBV breakthrough infections due to maternal transmissions present yet another major threat to Taiwan public heath since the implementation of mass neonatal hepatitis B vaccination program.

One participant (2.7%) in the study had occult HBV infection, while occult HBV infection is 0.1% in healthy population of vaccinated cohort [5]. It has been reported HBV genotype C carriers are more likely to become occult HBV infection [17], and it is also genotype C in the occult HBV infection case in this study. As to the infectivity of occult

HBV infection, a study argued that as the subjects are still carrying HBV and the presence of HBV meant that, under certain circumstance, they were able to transmit the virus to others. Accordingly, when the majority of blood donors were born after the beginning of mass vaccination program, disqualifying those who had HBV infection (anti-HBc positive) from donating blood [5] will decrease the risk of occult HBV infection.

In this study, one participant (2.7%) died unfortunately of fulminant hepatitis B at the age of 16. According to his high school entrance physical examination report, the participant was cleared of anti-HBs. Although his mother was carrier and they both were infected with genotype B, there was an M1331T mutation on ‘a’ determinant region of the mother's HBsAg gene while the patient's was wild-type. This suggests that the participant's infection is not associated with his mother, and that the fatal infection might have been caused by another source of HBV virus exposure.

Are confirmed cases of acute hepatitis B indeed "acute hepatitis B" or "acute exacerbation of chronic hepatitis B" instead? Among the 37 participants surveyed in this study, 34 participants (91.9%) did not become carriers, i.e. not acute exacerbation of chronic hepatitis B case. As to the 3 chronic carrier participants (8.1%) whose age of disease onset was 8 months, 6 years and 19 years respectively, the one having disease onset at 8 months was perinatal acute hepatitis B, while the 6-year-old case (who might have been infected in perinatal period) and the 19-year-old case was acute exacerbation of chronic hepatitis B. In regard to relevance of current acute hepatitis B surveillance, the present study also assessed the accuracy of current surveillance system in positive case identification. The result showed that 95% of the cases (35/37) were indeed acute hepatitis B, indicating that the notification system has a 95% accuracy in identifying acute hepatitis B infection cases in vaccinated cohort.

Regarding infection situation within family, 9 participants (24.3%) had carrier family members (6 mothers, 2 fathers, 1 cohabitant girlfriend), the fatal case is the only participant whose parents had been both carriers at one time, and no one had carrier siblings. Identifying carriers or HBsAg negative and anti-HBs negative cases among carriers' family members should be a focus of hepatitis surveillance and control plan in the future. In addition, this study identified 2 mothers (according to NIIS prenatal screening record) and 1 father (self-reported, father of the fatal case) used to be carriers, but after 20 to 30 years, their serologic test results showed the mothers have both developed antibodies, and the father was non-carrier without anti-HBs. It indicates spontaneous seroconversion and virus clearance which happen in a hepatitis B carrier as part of natural course of disease.

Mother-to-infant transmission has been significantly improved in Taiwan since the implementation of mass paediatric hepatitis B vaccination program. Mother-to-infant transmission by highly infectious mothers, however, is not completely blocked. Further studies should continue to be conducted on risk reduction strategies against

mother-to-infant transmission by highly infectious mothers (HBeAg positive). Such studies include risk assessment of in utero HBV transmission and research on antiviral therapy for highly infectious pregnant women. In order to achieve the target of hepatitis B elimination, the high-risk population in vaccinated cohort who do not have antibodies should be informed and encouraged to receive a booster dose of hepatitis B vaccine at their own expense for adequate protection.

Recommendations

1. Neonates born to HBeAg positive mothers face a quite high probability of HBV breakthrough infection even after receiving complete vaccination series. In order to provide scientific evidence for prospective policy implementation, more support should be provided to domestic studies related to prevention of mother-to-infant transmission by highly infectious hepatitis B carrier mothers.
2. In hope to enhance protection for children with higher risks, the policy should be promoted and made known that infants born to highly infectious hepatitis B carrier mothers are suggested to have follow-up HBsAg and anti-HBs tests at the age of one, and those having neither HBsAg nor anti-HBs detected will have access to publicly funded booster dose. Follow-up and public education should continue to be provided for the small sub-group who become chronic hepatitis B carriers.
3. Health education should be strengthened on preventing horizontal hepatitis B transmission (e.g. sexual contact, needle sharing, piercing, etc.) by minimizing exposure to risk factors. People without detectable HBV antibodies should be encouraged to receive booster dose at their own expense to secure sufficient protection if they belong to high risk groups (hemodialysis patients, organ transplant patients, patients receiving blood product, immunodeficiency persons, people having multiple sexual partners, injecting drug users, people living with carriers or having carrier sexual partners, residents and workers of institutions for individuals with mental retardation or developmental disabilities, healthcare workers at risk of blood exposure, etc.).
4. The acute hepatitis B section in Taiwan CDC's Communicable Diseases Control Workbook should be amended to include the proactive interventions that a local public health bureau (center) should conduct on acute hepatitis B case follow-up such as:
   (1) Six months after the disease onset, the patient should visit clinic/hospital to take a follow-up test for prognostic assessment.
   (2) The patient's family members who have no anti-HBs are strongly recommended to get vaccinated to obtain protection at their own expense.
   (3) The patients who become chronic hepatitis B carriers should receive health education and be urged to take regular follow-up examinations. Those who meet clinical criteria will be referred and provided treatment to reduce risk of developing cirrhosis and hepatocellular carcinoma in the future.

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Epidemiological Analysis and the Prevention Policies for the 2010-2013 Epidemic of Acute Viral Hepatitis A in Taiwan

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Abstract

Since Taiwan revised the notification criteria of acute viral hepatitis A on February 4, 2010, the caseload of confirmed acute viral hepatitis A had been significantly reduced. Nevertheless, the number of confirmed cases has appeared an elevated trend since March 2013. To figure out the risk factors and the epidemiology of indigenous cases of acute viral hepatitis A in Taiwan, this study utilized the Notifiable Infectious Diseases Statistics System to analyze the data of indigenous confirmed cases of acute viral hepatitis A in Taiwan from 2010 to 2013. It revealed that the incidence of indigenous confirmed cases of acute viral hepatitis A was 0.3-0.4 per 100,000 population with a male to female sex ratio of 1.11-1.9. The dominant age group was the 20-44 year-old adults. Food stalls accounted for the highest rate of the eating places within the maximum incubation period, and 26% -42% was attributed to raw food consumption.

In order to enhance the efficacy on acute viral hepatitis A prevention, Taiwan CDC organized a task force in response to outbreaks of hepatitis A and held regular meetings for case investigation. Furthermore, test results of PCR and genotyping were also adopted which were helpful for clarifying the suspect spreading source in a short time to block the spreading and to reduce the risk of acute viral hepatitis A occurred in Taiwan.

Keywords: acute viral hepatitis A, indigenous confirmed cases, epidemiology

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