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Prevalence and Mother-to-newborn Transmission of Hepatitis B Virus in Tertiary Care Hospital in Nepal

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ABSTRACT

Background: The prevalence of hepatitis B infection is heterogeneous and ubiquitous. This study aimed to identify the prevalence of the infection among the pregnant women who attended in a tertiary care hospital, transmission of the infection in their newborn and associated risk factors.

Methods: A one year prospective study was conducted. Mother's venous blood was collected for the hepatitis B serological test during the antenatal care or before delivery; the newborn's cord blood was also collected for the HBsAg.

Results: A total 16400 pregnant women were tested; of them 53 were HBsAg positive. The total prevalence of the infection was 0.32% among the pregnant: 0.5% among the indigenous and 0.2% in other than indigenous. The infection was significantly high in the indigenous group compare to other than indigenous [2.596 (1.475-4.569), p=.001]. Thirty-two out of 53 hepatitis B positive pregnant were delivered in the hospital, of them 75% (n=24) were indigenous and 25% (n=8) were other than indigenous. Eight out of 32 were highly infectious (HBeAg+), of them majority (75%) were indigenous ethnicities. Twenty-one out of 32 were anti-HBe reactive, among which majority were indigenous ethnicities (76.2%). Six out of eight babies, born with HBeAg reactive mothers, were infected (75%), of which majority were indigenous ethnicities (67%). In total, one-fifth of the newborn delivered were HBsAg positive (18.8%).

Conclusions: The prevalence of hepatitis B infection among the total pregnant was low. The proportion of the infection in the indigenous ethnicity was significantly high compared to other ethnic group, which shows that the infection was clustered among the indigenous people.

Keywords: Hepatitis B; indigenous people; newborn transmission; Nepal.

INTRODUCTION

Hepatitis B infection is a global public health problem. An estimated 257 million people are living with Chronic Hepatitis B (CHB) infection that is 3.5% of the global population.[1] The prevalence of the infection is considered low (0.9 %) in Nepal.[2] A various studies have suggested that the infection is disproportionately high among the indigenous people ranging between 1 and 38 percentages.[2-4] With this consideration, the study has aimed to identify the prevalence, mother-to-newborn transmission and to explore the risk factors of the infection in the biggest tertiary care hospital.

METHODS

This is a nested prospective case study, conducted among pregnant mothers who had attended in the tertiary care Hospital, the Paropakar Maternity and Women's Hospital (PMWH), Nepal for the period of July 2015-Jun 2016. Ethical approval was taken from the Institutional Review Board, Institute of Medicine/Tribhuvan University and the PMWH. The participants were enrolled in the study from the hospital ANC clinic or labor room. As per the rule of the hospital, all pregnant mothers who attended the hospital were subjected to hepatitis B test, after 1st trimester of the pregnancy. All the mothers registered in the morbidity record with HBsAg reactive were requested to participate in the study. A written informed consent

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was obtained from the all the participants.

Venous blood (sample) was taken for hepatitis B biomarkers in the pregnant women as per the defined procedures and WHO guideline[5] during the first ANC visit or before the delivery if a pregnant woman attended hospital for only for delivery without any ANC visit. The markers include: hepatitis B surface antigen (HBsAg), antibody to hepatitis B surface antigen (anti-HBsAg), total antibody to hepatitis B core antigen (anti- HBc), hepatitis B e antigen (HBeAg) and antibody to hepatitis B e antigen (anti-HBeAg). The newborn cord blood was collected for the HBsAg by the hospital nurse. A sample was collected by a lab technician or nursing staff in the hospital who has knowledge and practice. The sample was carried out and tested in the National Public Health Laboratory (NPHL) with the Enzyme-linked immunosorbent assay.[6] Hepatitis B counseling service was provided for both HBsAg reactive and non-reactive participants.

Variables were operationalized with a specific definition and measurement (Table 1). The variables are; address, age, caste, heard hepatitis, hepatitis status, number of ANC visit, type of ANC services, knowledge on pregnancy danger signs, use of alcohol, hepatitis B risk exposure, immediate newborn care, mother and newborn's sero-prevalence. A survey questionnaire was administered to HbsAg positive pregnant during the ANC visit and within the 24 hours after delivery at the hospital. All the data was double entered in an electronic database and analyzed using the SPSS 20 version for windows.

The respondents who were not able to give blood sample due to severe illness/hemophilia, severe mental illness, and twin delivery were excluded. Those who were not delivered in the hospital or refused to participate in the study were also excluded. The pregnant women of aged 15-49 years as a new visit, after the 1st trimester of pregnancy and singleton visited at the PMWH were included in the study.

Table 1. Operationalization of the variables.

SN	Variable	Definition	Measurement
1	Age	Completed age of the pregnant women by recall	15-24 yrs , 25-34 yrs ; 35-44 yrs; 45 and above yrs
2	Sex	Sex of newborn	Male and Female
3	Ethnicity/caste	Caste/Ethnicities of the respondents	Indigenous, other than indigenous
4	Heard Hepatitis	Respondents who have heard of hepatitis B virus	Yes, No
5	Hepatitis test	Respondents tested for the HBV	Yes, No
6	Hepatitis status	Awareness of the test result of the HBV	Yes, No
7	ANC visit	Antenatal care (ANC) of the pregnant women	Yes, No
8	ANC number	Number of ANC visit(Less than 4 ANC visit=1, 4 or >4 ANC visit=2)	Yes, No
9	ANC services	ANC services taken during the pregnancy(Iron, TT, Hepatitis B vaccine)	Yes, No
10	Pregnancy danger signs	Danger signs during the pregnancy (Hypertension, Protein urea, Edema, Convulsion)	Yes, No
11	Use of Alcohol	Use of alcohol during the pregnancy	Yes, No
12	Hepatitis B risk	Risk behavior related to hepatitis B (Blood transfusion, exposure with non-sexual household members and sex partner, haemodialysis, injection without doctor's prescription, direct blood contact, Shared diabetic supplies, tattoo and piercing)	Yes, No
13	Immediate newborn care	Immediate newborn care (details below)	Yes, No
14	Mother's Sero-prevalence	Anti-HBc (antibody to hepatitis B core antigen); Anti-HBe (antibody to hepatitis b e antigen); Anti-HBs (antibody to hepatitis B surface antigen); HBeAg (hepatitis e antigen); and HBsAg (hepatitis B surface antigen)	Yes, No
15	Newborn sero-prevalence	HBsAg (hepatitis B surface antigen)	Yes, No

RESULTS

The total number (N=16400) of pregnant women with new visit attended to the hospital were tested for HBsAg for the one year period, among the total pregnant women, the sample proportion of the Indigenous and other than Indigenous was 40.2% (n=6586 and 59.8% (n=9814) respectively. Indigenous ethnicity was defined by the National Foundation for Development of Indigenous Nationalities (NFDIN) Act-2000.[7] The categories of the Indigenous and other than Indigenous were based on the definition of Central Bureau of Statistic (CBS) Nepal, where the national proportion of the Indigenous and other than Indigenous was 35.81% vs. 64.19%.

The total 53 participants were HBsAg positive, among them 75.5 % were Indigenous and 24.5% were other than Indigenous. The prevalence of the infection among the total pregnant women was 0.32 %. The prevalence of the infection among the Indigenous was 0.5% and other than Indigenous was 0.2%. The infection rate was significantly high among the Indigenous (Pearson Chi-Square 11.788, p=.001). The odds of the infection among the Indigenous with reference to other than Indigenous was 2.596 (1.475-4.569), p=.001.

Among the total 53, twenty-one HBsAg reactive women were dropout. Thirty-two out of 53 hepatitis B positive pregnant women were followed till the delivery to explore the mother-to-newborn transmission of the infection. The causes of non-response were not able to explore.

The mean and median ages of the respondent who delivered in the hospital were 24.38, and 23 years respectively, with range 23 from 17-40 years. The age group composition of the participants was as follows; 15-24 years (59.4 %), 25-34 years (34.4 %) and 35 and above(6.3 %). The majority of the participants were from Hindu religion (53. %) followed by Boudhist (40.5 %), Kristian (3.1 %) and Kirat (3.1 %). Participants were from 20 different districts among 75 districts. The majority were Indigenous ethnicity (75 %) followed by Brhamin/Chhetri (18.8 %) and others (6.3 %) (Table 2).

Table 2. Socio-demographic characteristics of the participants.

SN	Variables	Number (N=32)	Percent
A	Caste/Ethnicity		
1	Brhamin/Chhetri	6	18.8
2	Indigenous	24	75.0
3	Others	2	6.3
B	Age group		
1	15-24 years	19	59.4
2	25-34 years	11	34.4
3	35-44 years	2	6.3
C	Religion		
1	Hindu	17	53.1
2	Buddhist	13	40.6
3	Christian	1	3.1
4	Kirat	1	3.1
D	Literacy		
1	Illiterate	3	9.4
2	Literate	29	90.6

Table 3. Information related to awareness of hepatitis B, pregnancy, and risk behavior related to hepatitis B.

SN	Hepatitis B related information (N=32)	Yes(%)
1	Heard about Hepatitis B infection before this pregnancy	15.6
2	Had tested for Hepatitis B before this pregnancy	3.1
3	Had known the status of hepatitis B before pregnancy	3.1
4	Had known hepatitis B status of family members before pregnancy	6.3
Information related to pregnancy		
1	Antenatal care during the pregnancy	100.0
2	Antenatal care zero and less than 4 visit during pregnancy	21.9
3	Antenatal care 4 and more visit during pregnancy	78.1
4	Iron tablet taken during pregnancy	100.0
	less than 90 day	15.6
	90 days and above	84.4
5	TT vaccination during pregnancy	96.9
6	Ever received hepatitis B vaccination/ HBIG before the pregnancy	0
Risk behavior related to hepatitis B		
1	Exposure with the Blood or blood products [transfusion]	3.1
2	Exposure with the Hepatitis B positive Household Member (non-sexual)	12.5
3	Exposure with the Hepatitis B positive Sex Partner	-
4	Exposure with the Haemodialysis	-
5	Inject drugs not prescribed by Doctor	3.1
6	Direct blood contact	9.4
7	Shared diabetic supplies	0
8	Receive a tattoo	12.5
9	The piercing performed	81.3

The respondents were asked whether they had known the hepatitis B infection before the pregnancy or not: the overwhelming (84.4 %) number of participants were unaware of the infection, less than one-fifth (15.6 %) had heard of the infection, a very few were informed about their status (3.1 %) and their family status of the infection (6.3 %) (Table 3). A majority (78.1 %) of the respondents had attended 4 or more ANC visit during the pregnancy and had taken Iron tablet. TT vaccination coverage was almost universal; however, vaccination against hepatitis B before pregnancy was nil (Table 3).

One-fourth pregnant mothers had consumed drinks containing alcohol during the pregnancy. The commonest form of drinks was *Jad* and *Chhyang* (a locally fermented alcohol). Nearly one-tenth had taken the drinks every day or 2-3 times a week, and nearly 16 % had taken the drinks less than once week. The Overwhelming (84.4 %) numbers of participants had not heard about hepatitis B infection before the pregnancy and had not tested (96.9 %) and were not familiar with their own status (96.9 %) including families (93.8 %) (Table 3).

The piercing was very common (81.3 %) following by receiving tattoos and exposure to hepatitis B infected household members (12.5 %). Other risk practices were direct blood contact, blood transfusion (3.1 %) and injecting drugs not prescribed by a doctor (3.1 %) (Table 3). Only few women had symptoms of yellowish eye or skin (6.3 %) (Table 4). A majority (87.5 %) were delivered by normal vaginal delivery and one-eighths (12.5 %) were delivered by the caesarean section. Of the total caesarean delivery (n=4), 1 (25 %) baby was reactive. However, among the total vaginal delivery (n=28); 5 (17.9 %) babies were reactive. Among the total reactive babies (18.8 %); 3.1 % had fallen in caesarean and 15.6 % in vaginal delivery (data not shown).

Three-out of 32 pregnant were HBsAg and anti HBs positive. One-fourth of the total infected pregnant mothers (n=8) were highly infectious, i.e. HBeAg reactive (Table 5),of them majority of the pregnant women (six out of eight) were indigenous ethnicities. Similarly, nearly two-thirds of the total respondents were anti-HBe reactive that is suggestive of virulence in the past, among whom majority (sixteen out of twenty one) were indigenous ethnicities. Almost three fourth (six out of eight) babies who were born from the HBeAg reactive mothers were infected (HBsAg), of them majority (four out of six) were indigenous ethnicities (data not shown).

Nearly one-fifth (18.8 %) of the newborn was infected with the virus (HBsAg reactive). The newborns with indigenous background were infected more with the virus, i.e., the indigenous 12.5% and other than indigenous 6.2% among the total newborns. In absolute term, the newborns with indigenous background were infected overwhelmingly, i.e. 66.7% from the indigenous and 33.3% from other than indigenous background of the total reactive cord blood (Table 6).

Table 4. Information related to Symptoms of Jaundice during and before the pregnancy, and immediate newborn care.

SN	Information related to jaundice and newborn care	Yes, n (%)
1	Symptoms of Jaundice during the pregnancy	
	Abdominal Pain	9.4
	Arthalgia	3.1
	Clay Colored Stool	0
	Dark urine	6.3
	Diarrhea	0
	Fatigue	9.4
	Fever	6.3
	Loss of appetite	31.3
	Nausea	59.4
	Vomiting	43.8
2	Yellowish eye or ski before this pregnancy	15.5
3	Yellowish eye or skin before pregnancy (within one year)	6.3
4	Yellowish eye or ski before pregnancy (before one year)	9.4
5	Hospitalized for yellow eye or skin during the pregnancy	3.1
6	Immediate newborn care	
	Baby cry/breathe easily immediately after birth	90.6
	Help the baby cry or breathe at the time of birth (Rubbed/Massaged/Dried)	9.4
	Help the baby cry or breathe at the time of birth (suction)	6.3
	Help the baby cry or breathe at the time of birth (Resuscitation using bag and mask)	3.1

Table 5. Information related to mother's hepatitis B serology and its caste-wise distribution.

SN	Mother's hepatitis B serology (N=32)	Reactive, n (%)	Non-reactive,n(%)
1	Hepatitis B Virus Anti HBc	32(100)	-
2	Hepatitis B Virus Anti HBe	21(65.6)	11(34.4)
3	Hepatitis B Virus Anti HBs	3 (9.4)	29 (90.6)

4	Hepatitis B Virus e Antigen	8 (25.0)	24(75.0)
Caste-wise distribution of mother's hepatitis B serology			
1	Caste in two category (HBeAg), N=32	Reactive, n (% of total)	Nonreactive, n (% of total)
	Others	2(6.2)	6(18.8)
	Indigenous	6(18.8)	18(56.2)
2	Caste in two category (Anti-HBe)		
	Others	5(15.6)	6 (18.8)
	Indigenous	16(50.0)	8(25.0)

Table 6. Caste-wise distribution of hepatitis B virus sero-prevalence in baby cord blood.

Caste-wise distribution of hepatitis B virus sero-prevalence , N=32		Reactive	Non-reactive	Total
Indigenous	Count (n)	4	20	24
	Percentage within	16.7	83.3	100.0
	Percentage within total cord blood	66.7	76.9	75.0
	Percentage of Total	12.5	62.5	75.0
Other than indigenous	Count (N)	2	6	8
	Percentage within	25.0	75.0	100.0
	Percentage within total cord blood	33.3	23.1	25.0
	Percentage of Total	6.2	18.8	25.0
Total	Count (n)	6	26	32
	Percentage within all caste	18.8	81.2	100.0

DISCUSSION

The hepatitis B surface antigen (HBsAg) seroprevalenc of ≥8 % defines highly endemic areas, prevalence of 5 %-7 % defines high intermediate, 2% - 4 % defines low intermediate, <2 % defines low endemic areas[8,9] and the prevalence varies considerably among the countries and ethnic population.[1,10]

A national survey conducted in a pre- and post-vaccinated child in Nepal has revealed that the prevalence of the infection among the children was 0.3 and 0.1 % respectively.[11] But a number of small studies on sub-group/indigenous populations have shown that the prevalence of hepatitis B infection in indigenous communities have remained high ranging from 7 %-38 %.[2,4,12,13] The sero-prevalence of HBsAg among mothers and the youngest children living with HBsAg positive mothers in upper part of Dolpa were 17 % and 48 % respectively.[14]

This study has shown that the prevalence of the infection among the pregnant women was low (< 0.32 %), mimicking the various previous reports and study.[2,11] However, the infection was clustered in the indigenous ethnicities, nearly threefold higher infection compared to other than indigenous ethnicities.

One-fourth of the total participants consumed drinks, containing alcohol. Almost all the pregnant women from indigenous background had taken various forms of alcohol; the commonest form of drinks was *Jad* and *Chhyang* (a local fermented alcohol). Various studies have suggested that alcohol helps increasing the sexual risk behavior and unsafe sexual relationship that could help increasing the risk of transmission of the virus.[15] The alcohol not only increases the risk of the transmission but also independent risk factor of hepatitis, cirrhosis, and HCC.[16] Thus, indigenous pregnant women were in double burden of risk because of alcohol use and the hepatitis B infection.

The piercing, receiving tattoos, exposure with non-sexual household members, and direct blood contact were the commonest prevailing risk factors, which could transmit the infection. But this study could not establish the association with prevailing risk factor and diseases because of small number of sample size. However, various studies have revealed that the explored prevailing risk factors have strong association with the infection.[17]

The serological findings of the mother showed that three out of 32 participants were found to have anti HBs reactive report in the same person. The study is not able to answer the coexistence but other studies have suggested that the coexistence is associated with increased "a" determinant variability during chronic carriage, the coexistence could be considered potential reservoirs of immune escape variants.[18,19] One-fourth of the infections were highly infectious (HBeAg +) during the study, more than half respondent had antibody against HBeAg which suggested highly infectious nature of the infection in the past. More than two-third babies born with HBeAg + mothers were infected with virus (HBsAg+), and only one-third babies born from HBeAg-ve mother were infected. The mother's HBeAg has associated with increased rate of mother-to-child transmission. Perinatal

HBV transmission can be prevented providing hepatitis B immunoglobulin and hepatitis B vaccine to their infants soon after birth, ideally within 24 hours of birth.[8] However, there is no universal pregnancy screening and provision of immunoglobulin and active vaccination at birth in Nepal, the existing hepatitis B vaccination are provided at 6, 10, and 14 weeks of birth.[20] The National Immunization program needs to be updated along with a combination of maternal and child health care services to address the problem.[1,8]

One-fifth of newborn was infected with the virus (HBsAg+) at birth. The known fact is that a majority of the baby infected with the virus at the perinatal period will be chronic carrier,[8] nearly one-fourth of them will eventually die from HBV-related liver disease, including cirrhosis and hepatocellular carcinoma.[1,8,21] The chronic carriers are a constant source of new infections for the susceptible person.

On top of that the indigenous people are at high risk of the infection such as seven out of every 10 victims of trafficking are indigenous women and girls, majority of school drop-out are indigenous students, and indigenous youth make up the largest migrant workers and prisoners in Nepal.[7] Moreover, the poverty and social exclusion of indigenous people are the main barriers to equitable access to education.[22,23]

Given the epidemic, prevailing risk factors and plausible facts, the indigenous ethnicities are at the risk of infection and its squeal. A public health intervention is required to combat the infection through various activities that have been proved effective already at the global level such as at birth vaccination, counseling, catch up vaccination, care and treatment along with health education and awareness programs aiming to achieve the national goal and international commitment to combat viral hepatitis.

It is a hospital based study could have some diseases biased or bias in health seeking behavior of various subpopulation or individuals. In addition, Nepal had faced a disastrous earthquake, 7.8 Richter scale, during the study period; it might have an effect on the research in various ways such as access to facilities, quality of services at the facility, and transportation that were not counted in the study. This study has shown that the infection was clustered in the indigenous population and possesses the already known risk factors that are responsible for the transmission of the infection such as alcohol consumption, low level of awareness against hepatitis B infection including other risk factors-piercing, tattooing, exposure to hepatitis B infected household members, direct blood contact, blood transfusion and injecting drug not prescribed by a doctor were also presented. This study has shown the prevalence and mother to newborn transmission rate of the infection, however, not able to identify the association of the infection and risk factors due to small subset sample size of newborn population.

CONCLUSIONS

The prevalence of hepatitis B infection among the pregnant women attended the hospital was low. However, the proportion of the infection among the indigenous ethnicity was significantly high compared to other caste/ethnicities, which suggests the clustering of the infection among the indigenous ethnicity.

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