

## Prevalence of hepatitis B virus infection among pregnant women attending prenatal care at Mae Sai Hospital in Thailand: A retrospective cross-sectional study

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### ABSTRACT

**Background:** Hepatitis B virus (HBV) infection is a serious public health problem worldwide and a major cause of liver diseases. Pregnant women with HBV infection are a reservoir for the virus and can transmit the infection to their children. Most infants (90%) infected with HBV develop chronic infection and 25% die prematurely from liver cancer or cirrhosis.

**Objective:** To assess the prevalence of HBV infection among pregnant women attending prenatal care at Mae Sai Hospital, a border region in Northern Thailand.

**Materials and methods:** This retrospective cross-sectional research study collected data from the hospital records database between January 2019 and September 2023. All pregnant women were tested for serum HBsAg marker by the STANDARD Q HBsAg Test. Statistical analyses were conducted using IBM SPSS version 29.0, with logistic regression used to detect the associations between variables at a significance level of  $p < 0.05$ .

**Results:** The study population comprised 2962 pregnant women, with 29.98% Thai and 70.02% non-Thai divided into Burmese (48.12%) and other ethnic groups (51.88%). The overall prevalence rate of HBV infection among pregnant women was 4.9% (95%CI=4.1-5.7). The HBV prevalence rates of Thai pregnant women and non-Thai pregnant women were 2.9% (95%CI=1.8-4.2) and 5.7% (95%CI=4.7-6.9), respectively. Two variables (nationality and year of birth) were associated with hepatitis B infection. Non-Thai pregnant women had a 2-fold (95%CI=1.998-3.161,  $p=0.003$ ) greater chance of HBV infection than Thai pregnant women, while Thai pregnant women born before the implementation of the national vaccination program had a 4.2-fold (95%CI=1.757-10.037,  $p=0.004$ ) greater chance of HBV infection than those born after the program implementation.

**Conclusion:** Results showed a lower prevalence of hepatitis B virus infection in pregnant women compared to previous studies. Nationality and vaccine implementation were identified as associated factors with hepatitis B infection. Raising awareness, promoting preventive measures, and implementing screening before pregnancy planning, or receiving the HBV vaccine to prevent infection during pregnancy are essential to stop the transmission of the hepatitis B virus to newborns.

### Introduction

Hepatitis B virus (HBV) is an emerging global health problem as either acute or chronic infection. The World Health Organization (WHO) 2024 Global Hepatitis Report stated that the number of deaths from viral hepatitis is increasing. Worldwide, 254 million people live with hepatitis B, while only 3% (7 million people) living with chronic hepatitis B infection had received antiviral therapy

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at the end of 2022.<sup>1</sup> Those living with chronic hepatitis B have a high risk of progression in the long term to diseases such as chronic hepatitis, liver cirrhosis, hepatocellular carcinoma, and even death.<sup>2</sup> Chronic hepatitis B (CHB) is defined by the presence of detectable HBsAg in the blood for longer than six months.<sup>3</sup> Age of exposure is a key factor in determining the risk of chronic infection. The probability of developing chronic hepatitis B infection during the perinatal period is high at 70 to 90% compared to 5 to 10% for those acquiring infection during adulthood.<sup>4</sup>

The risk of HBV transmission to newborn infants is 70 to 90% due to the simultaneous positivity of mothers with HBsAg and HBeAg seromarkers. By contrast, there is a 10 to 40% risk of HBV transmission if mothers test positive for only HBsAg.<sup>5</sup> Therefore, pregnant women attending antenatal care should be screened for HBsAg and Anti-HBs. HBV is vaccine-preventable, and immunization offers more than 95% protection against the development of chronic infection.<sup>6</sup> HBV vaccination should be administered at birth for infants exposed to the virus.<sup>7</sup> In Thailand, the Thailand National Strategies (TNS) have implemented a national health benefit package for infants born after 1992 including the viral hepatitis B vaccine. The first stated aim of the TNS was to eliminate viral hepatitis by 2016, while the latest strategy (2022-2030) has the goal of eliminating viral hepatitis B as a major public health threat by 2030.<sup>8</sup> Despite the presence of vaccines, HBV infection remains a major obstacle to public health in Thailand. In 2023, the Department of Disease Control, Ministry of Public Health announced that 2.2 to 3 million Thais were living with chronic HBV infection, with a prevalence of 4 to 5% in those born before 1992. The goals of the national strategy are to reduce viral hepatitis B incidence by 95% and the mortality associated with viral hepatitis B by 65% by 2030.<sup>9</sup>

This cross-sectional study assessed the prevalence of hepatitis B virus infection among pregnant women attending antenatal care (ANC) at Mae Sai Hospital in Chiang Rai. This secondary hospital has a capacity of 90 beds and is in the northernmost part of Thailand near the Myanmar border, serving Thai, Burmese, and other ethnic groups such as Mong and Karen who are living in Thailand without Thai identity documentation. This assessment evaluated the potential development of chronic liver disease and liver cancer.

### Materials and methods

All pregnant women attending antenatal care (ANC) at Mae Sai Hospital between January 2019 and December 2023 were included in this study. They underwent a blood test to screen for HBV infection during the initial prenatal visit, and HBsAg screening was conducted by the STANDARD Q HBsAg Test. The sensitivity and specificity of the device were rated at 100% by the company provided and at 98% (95% CI: 94.29-99.63) and 100% (95% CI: 98.12-100%), respectively by the Department of Medical

Sciences, Thailand. Data were retrospectively collected from the electronic database of Mae Sai Hospital. Inclusion criteria were pregnant women attending ANC at Mae Sai Hospital who had HBsAg serology marker data, while pregnant women without this data were excluded. The research was conducted in accordance with the ethical guidelines outlined in the Declaration of Helsinki, The Belmont Report, the CIOMS guidelines, the International Conference on Harmonization in Good Clinical Practice or ICH-GCP, and 45CFR 46.101(b), and was approved by the University of Phayao Human Ethics Committee No. HREC-UP-HSST1.2/131/67. All the pregnant women were self-identified as indigenous people with de-identified codes.

### Statistical analysis

All data were analyzed using SPSS statistical software (IBM SPSS version 29.0). Continuous and categorical variables were presented as numbers and percentages. Categorical data were analyzed and compared using the chi-square test, with logistic regression used to detect the associations between variables at a significance level of  $p < 0.05$ .

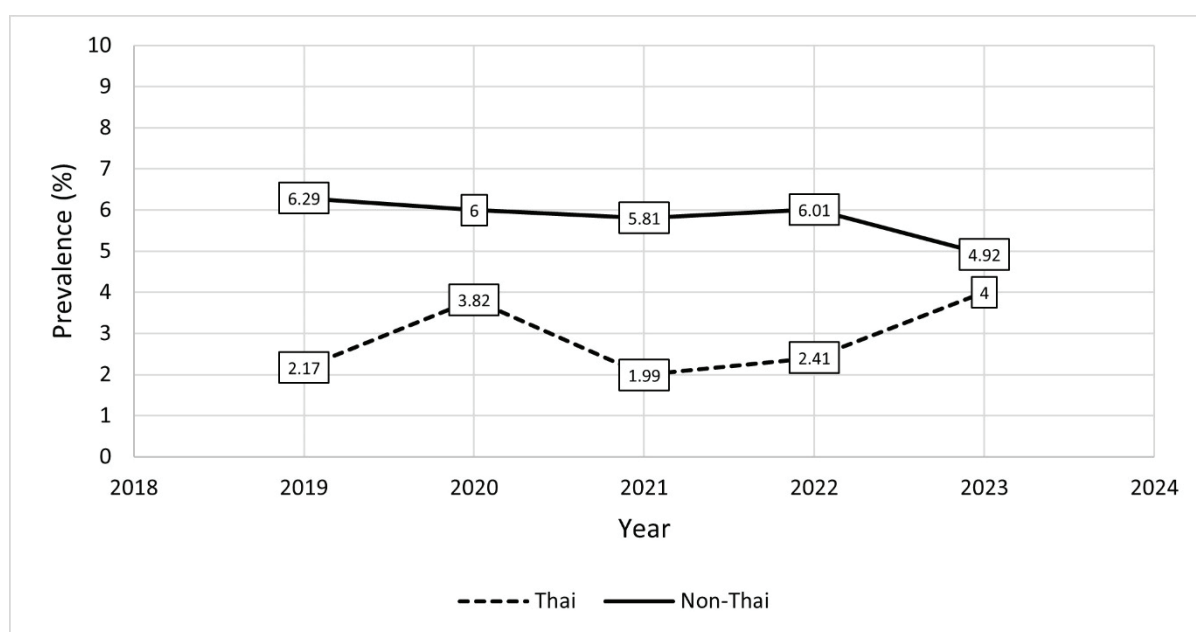
### Results

Between January 2019 and December 2023, 2,692 pregnant women were admitted to the antenatal care unit at Mae Sai Hospital and included in the analysis. Table 1 shows the demographics of the pregnant women. The sample was divided into the HBsAg positive and HBsAg negative groups, and 131 pregnant women were HBsAg positive with a prevalence rate of 4.9% (95%CI=4.1-5.7). The participants were also segregated by nationality and age. Approximately 30% and 70% were Thais and non-Thais, respectively. The non-Thai group consisted of Burmese (48.1%) and other ethnicities (51.9%). Based on the nationality distribution, the prevalence of HBsAg positive in the Thai group and non-Thai group was 2.9 % (95%CI=1.8-4.2) and 5.7% (95%CI=4.7-6.9), respectively. The prevalence rate of HBsAg positive was highest in the 31-40 age group. The prevalence of HBsAg positivity had the same tendency by age group in the Thai and non-Thai populations. Multivariate analysis showed that nationality not age group was associated with hepatitis B infection; non-Thai pregnant women had a 2-fold (95%CI=1.998-3.161,  $p=0.003$ ) greater chance of HBV infection than Thai pregnant women. Based on the annual distribution, the number of HBV-infected subjects in each year was 4/184 (2019), 5/131 (2020), 3/151 (2021), 4/166 (2022), and 7/175 (2023) for the Thai group, and 28/445 (2019), 21/350 (2020), 15/258 (2021), 17/283 (2022), and 27/549 (2023) for the non-Thai group. The prevalence rate of HBsAg positive in the Thai group was between 1.99 and 4.0%, while the prevalence rate of HBsAg positive in the non-Thai group was between 4.92 and 6.29% (Figure 1).

**Table 1.** Prevalence and univariate and multivariate analyses of the factors associated with HBV infection in pregnant women.

|              | HBsAg             |                   | Total<br>N (%) | $\chi^2$<br>( <i>p</i> value ) | Univariate analysis |             |                | Multivariate analysis |             |                |
|--------------|-------------------|-------------------|----------------|--------------------------------|---------------------|-------------|----------------|-----------------------|-------------|----------------|
|              | Positive<br>N (%) | Negative<br>N (%) |                |                                | OR                  | 95% CI      | <i>p</i> value | OR                    | 95% CI      | <i>p</i> value |
| Nation group | 131 (4.9)         | 2,561 (95.1)      | 2,692          | 0.006**                        |                     |             |                |                       |             |                |
| Thai         | 23 (2.9)          | 784 (97.1)        | 807 (2.0)      |                                | 1.00                |             |                |                       |             |                |
| Non-Thai     | 108 (5.7)         | 1,777 (94.3)      | 1,885 (70.0)   |                                | 2.072               | 1.311-3.275 | 0.002**        | 1.998                 | 1.262-3.161 | 0.003**        |
| Age (years)  | 131               | 2561              | 2,692          | 0.160                          |                     |             |                |                       |             |                |
| <20          | 17 (3.8)          | 433 (96.2)        | 450            |                                |                     |             | 0.164          |                       |             |                |
| 21-30        | 62 (4.4)          | 1,334 (95.6)      | 1,396          |                                | 1.184               | 0.685-2.047 | 0.546          |                       |             |                |
| 31-40        | 49 (6.3)          | 729 (93.7)        | 778            |                                | 1.712               | 0.947-3.010 | 0.062          |                       |             |                |
| >40          | 3 (4.4)           | 65 (95.6)         | 68             |                                | 1.176               | 0.335-4.123 | 0.801          |                       |             |                |

**Note:** \*\*significance level at  $p < 0.01$ , \*\*\*significance level at  $p = 0.001$ .

**Figure 1.** Distribution of HBV prevalence in pregnant women between 2019 and 2023. The solid line represents the tendency of the prevalence rate of non-Thai pregnant women, while the dashed line represents Thai pregnant women.

The vaccine program was implemented in children born after 1992 by the Department of Disease Control, Ministry of Public Health of Thailand, and in pregnant women born before 1992 and born after 1992 at 36.7% and 63.3% respectively. The prevalence rate of HBsAg positive significantly decreased in Thai pregnant women from 1.5% to 0.5% ( $p = 0.001$ ), whereas non-Thai pregnant women recorded a slight decrease in the prevalence rate. However, the prevalence rate of HBsAg positive

significantly decreased between women born before and after 1992 ( $p = 0.002$ ). Multivariate analysis showed that the vaccine implementation program was an associated factor in hepatitis B virus infection; Thai pregnant women born before the implementation of the national vaccination program had a 4.2-fold (95%CI=1.757-10.037,  $p = 0.004$ ) greater chance of HBV infection than Thai pregnant women born after the implementation (Table 2).

**Table 2.** Prevalence and univariate and multivariate analyses identifying vaccine implementation as an associated factor in HBV infection of Thai pregnant women.

| Nation group | Prevalence of Hepatitis B viral infection in pregnant women |                           | Total | $\chi^2$<br><i>p</i> value | Univariate analysis |             |                | Multivariate analysis |             |                |
|--------------|---|---------------------------|-------|----------------------------|---------------------|-------------|----------------|-----------------------|-------------|----------------|
|              | N (%)   |                           |       |                            | OR                  | 95% CI      | <i>p</i> value | OR                    | 95% CI      | <i>p</i> value |
|              | Born before 1992 (N=988)                                    | Born after 1992 (N=1,704) |       |                            |                     |             |                |                       |             |                |
| Thai         | 15 (1.5)  | 8 (0.5)                   | 23    | 0.001***                   | 1.745               | 1.227-2.481 | 0.002**        | 1.684                 | 1.183-2.396 | 0.004**        |
| Non-Thai     | 50 (6.8)  | 58 (5.0)                  | 108   | 0.1042                     | 1.384               | 0.937-2.045 | 0.102          |                       |             |                |
| <b>Total</b> | 65 (6.6)  | 66 (3.9)                  | 131   | 0.002**                    |                     |             |                |                       |             |                |

**Note:** \*\*significance level at  $p < 0.01$ , \*\*\*significance level at  $p = 0.001$ .

## Discussion

The hepatitis B virus causes both major and common infectious diseases of the liver. HBsAg positivity indicates active acute or chronic infection and may range from asymptomatic infection or mild disease to severe or rarely, fulminant hepatitis. Acute infection is usually a self-limiting disease with a case fatality rate of 0.5 to 1%, while chronic infection, defined by the presence of detectable HBsAg in the blood for longer than six months, has a high fatality rate. Age of exposure is a key factor in developing the risk of chronic infection. Hepatitis B infection in childhood is responsible for 95% of chronicity. This retrospective cross-sectional study involved 2,692 pregnant women attending antenatal care at Mae Sai Hospital, a facility located in a region of high population mobility and ethnic diversity along the Thai Myanmar border. The overall prevalence of HBV infection in pregnant women in this study was 4.87%, and lower than the rate of hepatitis B infection in pregnant women at Umphang Hospital, also located along the Thai-Myanmar border, with an overall prevalence rate of 6.7%.<sup>10</sup> The rate of hepatitis B infection in pregnant women at the Thai-Myanmar border was 8.3%.<sup>11</sup> Previous studies of HBV infection in pregnant women reported a prevalence rate of 11.40% in a Rohingya camp, 8% in Eastern Ethiopia, and 11.74% in a mountainous region of Southern China, all higher than the rate in our study.<sup>11-13</sup> Based on the nationality distribution, Thai pregnant women showed a lower prevalence than non-Thai pregnant women at 2.9% versus 5.7%. Thai pregnant women had a low prevalence rate compared to a previous study of pregnant women at Chiang Mai University Hospital, located in the northern part of Thailand, and a high prevalence rate compared to Thai pregnant women in the central and northeast areas of Thailand.<sup>14-17</sup> The prevalence rate in these studies tended to increase with age, consistent with our study. This occurred due to the impact of the HBV immunization implementation in Thailand, which was introduced in 1992, and because of increased knowledge in the young population.

However, despite the implementation of the vaccine program in 1992, Thai pregnant women born after 1992 were still infected with the hepatitis B virus, possibly because the HBV-neutralizing antibodies were still below the protective level. The Centre for Disease Control (CDC) considers that people who have received three doses of

hepatitis B vaccine and tested positive for anti-HBs (>10 mIU/mL) are immune to hepatitis, while those who do not respond to vaccination or have a low level are thought to remain susceptible to infection. Participant information concerning vaccination medical history or boosting was not included in our study. Shakeri *et al.* revealed that 10 years after having the hepatitis B vaccine, the protection rate was 96.5%.<sup>18</sup> Anti-HBs levels decrease rapidly in the first year after hepatitis B vaccination in children but this decrease slows down in the following years. If the anti-HBs level remains above 10 mIU/mL, protection can continue for up to 24 years.

Adults who received routine hepatitis B vaccination in the newborn period had 71% protection when they reached adulthood.<sup>19</sup> However, a booster dose should be given to women planning for a pregnancy to negate the chance of hepatitis B infection.

## Limitations

The findings of this one-center, hospital-based, retrospective study may not accurately represent all pregnant women, and further validation is required in other regions among larger population groups. Follow-up assessments of the severity of infection were not conducted through hepatitis B profiling and comprehensive historical data on boosting or receiving HBV vaccinations in pregnant women were lacking, while the follow-up analyses of maternal and neonatal outcomes encountered problems with data access.

## Conclusion

The prevalence of hepatitis B in Thai pregnant women at Mae Sai Hospital was 2.85%, and lower than the prevalence rate in non-Thai pregnant women. The overall prevalence of HBV infection in pregnant women in this study was 4.87%, and lower than the rate of hepatitis B infection in pregnant women compared to previous studies. The overall prevalence rate in this study was less than the goal of the Department of Disease Control, Ministry of Public Health, which aims to eliminate viral hepatitis B as a major public health threat by 2030. The prevalence rate of HBV infection significantly decreased in Thai pregnant women born after the implementation of the national vaccination program. However, steps to prevent maternal HBV infection should be followed

by women planning for pregnancy by undergoing HBV testing, especially those belonging to high-risk non-Thai populations.

### Conflict of interest

The authors declare that this research was conducted in the absence of competing interest.

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