

## RESEARCH ARTICLE

## Determinants of Detectable Anti-hepatitis B in Fertile Age Women from Indonesia

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### Abstract

Hepatitis B (HBV) is still a major health problem worldwide, as evidenced by the large number of people infected with hepatitis. There are around two billion people infected with HBV, and an estimated 350 million are in chronic conditions. Hepatitis B is a ninth-order disease that causes death in mothers and their babies. The HBV infection in pregnant women is critical because of vertical or perinatal transmission. This study's purpose was to analyze data of the HBsAg and anti-HBs fertile age women, pregnant women, and postpartum mothers from National Basic Health Research Data 2007. The method is a retrospective study using secondary data from the Basic Health Research in 2007. The number of samples in the form of data on respondents of fertile age women are women aged 15 to 49 years. Data screened and matched with that examined pregnancy/have had a postpartum examination/never checked neonates/had examined their toddlers. One thousand three hundred two (1,302) respondents were eligible to be sampled in this analysis. The variables analyzed were age and anti-HB titers in women of childbearing age 15 to 49 years who were not protected against hepatitis B, as much as 74.65% of the total 1,302 people. Three hundred thirty (330) respondents had anti-HBs titers. This study concludes respondents who are not married age 15–20 years showed relationship with negative anti-HBs antibodies.

**Keywords:** Anti-hepatitis B titer, fertile age women, hepatitis B virus, postpartum mothers, pregnant women

### Introduction

Hepatitis B is still a significant health problem in the world. It is proven by the large number of people infected with hepatitis.<sup>1</sup> The prevalence of chronic hepatitis B infection varies worldwide, ranging from <1% in low-endemic regions to 30% in highly endemic areas. There are around two billion people infected with HBV, and an estimated 350 million are in chronic conditions.<sup>1</sup> HBV is a ninth-order disease that causes death to mothers and their babies.<sup>2</sup> In Nigeria, despite effective vaccine administration, it is still declared an HBV hyperendemic area with an estimated prevalence of 12%.<sup>2</sup>

Regions declared endemic intermediate if the prevalence of HBsAg is around 1–17% and the risk of infection is approximately 20–60%, covering Southern Europe, Southern America, and Russia. Fertile age women (FAW) are women in a state of reproductive organs functioning properly between the ages of 20–45 years. The peak of fertility in women is in the age range of 20–29 years. At this age, women have a 95% chance of getting pregnant. At the age of 30–39

years, the percentage decreases to 90%, and after entering the age of 40 years, the chance of pregnancy becomes 40%, then it will reduce to 10% if women are over 40 years old.<sup>3,4</sup>

In countries with high HBV endemicity, where the prevalence of HBsAg is  $\geq 8\%$ , the transmission pattern is usually vertical at birth from a chronically infected mother or horizontally during early childhood from being caused by bites, skin lesions, or unhealthy habits. About 45% of the world's population, those living in African and Asian countries, the Amazon Basin, and parts of the Middle East, live in high endemicity areas with a lifetime risk of infection of more than 60%. Only about 12% of the world's population lives in low-endemicity regions, such as the United States, Western Europe, and Australia, where the prevalence of HBsAg is <1% and the lifetime risk of infection is <20%.<sup>2,5</sup>

Transmission in low-endemicity areas is generally horizontal in adulthood, usually through sexual transmission and contaminated needles in medical procedures or injection drug use. The results of the Basic Health Research in 2007 showed a prevalence of hepatitis of 9.4%.

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It can be said that every one person out of 10 Indonesians has ever been infected with hepatitis B.<sup>6</sup>

This paper describes the number of respondents (fertile age women)—including pregnant and postpartum mothers with neonates. Mothers with under-fives have a risk in their body because there is no anti-hepatitis B antibody titer, so they can be affected by hepatitis B.

## Methods

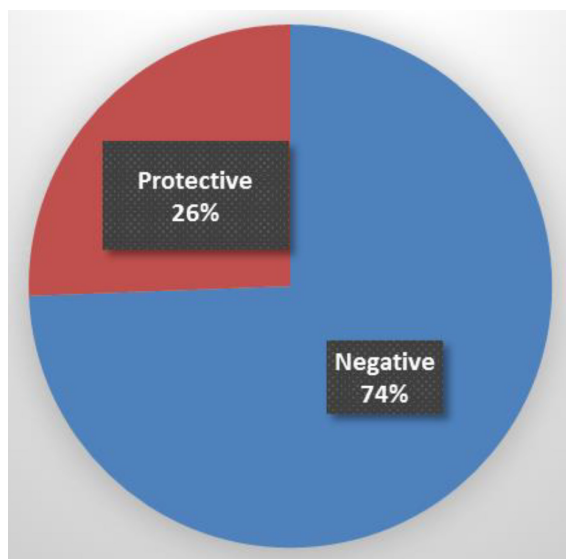
The method used is a retrospective using secondary data from the Basic Health Research 2007 conducted by the National Institute of Health Research and Development of the Ministry of Health Republic of Indonesia. The data used are secondary data from the Basic Health Research 2007. It is in the form of biomedical data that can be linked to the data of public health. Samples are from respondents of fertile age women (FAW) at the Basic Health Research 2007 aged 15 to 49. Respondents in this study are the respondent in the last 12 months since the Basic Health Research 2007 data collection. Respondents have examined their pregnancy and had a postnatal health check. It also includes respondents who examined neonates under five years old. The data is linked to the biomedical data, the anti-hepatitis B antibody titer data. After the screening process, the information is FAW aged 15 to 49. Data can be matched with those who have examined pregnancy/have had a postpartum examination, checked neonates/had examined their toddlers; 1,302 respondents were eligible in this analysis. In comparison, the number of samples of women of childbearing age who have anti-hepatitis B antibody titers was 7,325 respondents.

This study had received ethical approval from the Health Research Ethics Committee of the National Institute of Health Research and Development of the Ministry of Health Republic of Indonesia, number: KS.02.01.2.1.4739.

## Results

The results of anti-hepatitis B antibody titer examination from 7,325 respondents were negative for 5,451 and positive for 1,873 respondents. The percentage of the antibody results can be seen in Figure.

Table 1 shows the relationship FAW between individual characteristics and anti-hepatitis B antibodies by the age group of fertile women



**Figure Results of the Anti-HBs Antibody Examination**

(15–49 years), showing that several variables have a statistically significant relationship. In the work variable, it was found that women of fertile age who did not work had a risk of 1.367 times (OR=1.367) not having antibodies/negative and statistically significant ( $p=0.000$ ). Education women of high reproductive age risk 1.129 times (OR=1.129) not having antibodies/negative and statistically significant ( $p=0.016$ ). The following variables are significant: women of childbearing age who are not married have a risk of 1.458 times (OR=1.458) of not having antibodies/negative and statistically significant ( $p=0.000$ ). The age group (20–49 years old), the socio-economic variable of the poor, and the variable of women who did not check their health were statistically unrelated.

Multivariate analysis of independent variables is marriage, education, occupation, age group, socioeconomic level, and health checked. Multivariate analysis using binary logistic or logistic regression by a stepwise method including all independent variables and then corresponding  $p>0.25$  were excluded in the analysis.

Table 2 shows the results of multivariate analysis, where all variables were included and analyzed simultaneously. It turned out that only one significant variable, the unmarried in marriage variable, had a significant relationship with anti-hepatitis B antibodies with a risk of 1.459 times compared to those who were married and statistically significant ( $p=0.000$ ). Furthermore,

**Table 1 Relationship Characteristic of Individuals with Titer Antibody Anti-hepatitis B in Fertile Age Women (15–49 Years)**

Individual Characteristics	Anti-hepatitis B Antibodies			OR	95% CI	p
	Negative	Protective	Total			
Age						
20–49	4,606	1,667	6,273	0.673	0.572–0.791	0.000
15–19	846	206	1,052			
Occupation						
Not work	1,149	306	1,455	1.367	1.190–1.571	0.000
Work	4,303	1,567	5,870			
Education						
Higher	3,569	1,174	4,743	1.129	1.012–1.259	0.016
Lower	1,883	699	2,581			
Marriage						
No	1,423	365	1,787	1.458	1.281–1.660	0.000
Yes	4,029	1,508	5,537			
Socioeconomic						
Poor	3,245	1,076	4,321	1.090	0.980–1.212	0.060
Rich	2,207	797	3,003			
Women checks health						
No	5,244	1,800	7,044	1.022	0.779–1.342	0.460
Yes	208	73	281			

**Table 2 Multivariate Analysis the Determinants of Individual Characteristics with Anti-hepatitis B Antibody Titers in FAW**

Variables	Value	Sig	Exp (B)	95% CI	Percentage Correct
Marriage	0.378	0.000	1.459	1.282–1.661	
Constant	-1.739	0.000	0.176		
Overall percentage					74.4

the overall percentage was 74.4% of marriage variables could answer the relationship between individual characteristic variables and anti-hepatitis B antibodies, whereas other variables determined the rest.

## Discussion

The analysis of maternal risk factors checked for pregnancy, delivery, puerperium, neonates, and toddlers; the anti-HBs antibody titer examination results showed no significant relationship. At the same time, the age variable had a significant association with  $p=0.010$ . It proves that age prioritizes managing the hepatitis B virus (HBV). Age factors influence the presence of anti-hepatitis B antibody titers (anti-HBs). The

results of the Basic Health Research, 2007, the relationship between the age of respondents with anti-hepatitis B antibody titer data is significantly related to the group of respondents aged 46–49 years.<sup>6</sup> Other research shows that anti-HBs titers decrease with increasing human age, especially after age 15. The research about pregnant women infected with hepatitis B can transmit the virus to their baby during pregnancy or delivery, so screening is necessary to determine the prevalence of pregnant women with hepatitis B in Malang.<sup>7</sup> The screening was carried out in two public health centers of Malang city, i.e., Dinoyo and Kedungkandang, two public health centers of Malang regency, i.e., Sumberpucung and Gondanglegi, and Hermina Hospital. Participants were given counseling, anamnesis, vital signs

checks, and blood sample collection. The serum of participants was tested for HBsAg and Anti-HBs. The method used was ELISA.<sup>7</sup>

In another study, 156 pregnant women participated in the screening. The mean age of participants was 28,5±5,8 years old, and the mean age at marriage was 22 years. Hepatitis B prevalence was 1%, and 8% positive anti-HBs were found in patients with negative HBsAg. The other research is about a centrifuge to produce serum. The serum is issued in HBsAg examination with the immunochromatography method, while HBsAg examination is based on double-antibody sandwich immunoassay for HBsAg determination. Sampling was carried out for one month. The studies of hepatitis B antigen surface (HBsAg) and anti-HBs in pregnant women are screening for vertical transmission of hepatitis B.<sup>8,9</sup>

The research by Sinaga et al.<sup>10</sup> aimed to determine the results of HbsAg and anti-HBs examination in pregnant women in Sentani. The serum sample of pregnant women in this research was 60. The method of HBsAg and anti-HBs examination used is the Immunochromatography method. Beginning with taking venous blood in pregnant women, then doing was carried out using HBsAg rapid test brand SD Bioline with sensitivity >99% specificity >99% and anti-HBs test strip brand Answer with sensitivity >99% specificity >99.5%. This research used a descriptive analysis method to determine the results of HBsAg and anti-HBs examination in pregnant women. HBsAg and anti-HBs examinations were conducted for 13% HBsAg positive infected with hepatitis B, and as many as 87% showed negative results. The anti-HBs examination showed that 15% had hepatitis B antibodies, and 85% were negative.

The results of our analysis have the same results from research on seroprevalence from pregnant women who attend routine antenatal care in South Ethiopia and Uganda. The study in South Ethiopia aimed to estimate seroprevalence and associated factors of HBV infection among pregnant women attending the Antenatal Clinic (ANC) of Arba Minch Hospital. The overall seroprevalence of HBV infection was 4.3% (95% CI=2.2–6.9%). Multivariate analysis showed a history of abortion (AOR=7.775; 95% CI=1.538–39.301) and having multiple sexual partners (AOR=7.189; 95% CI=1.039–49.755) were independent predictors of HBsAg seropositivity.

In conclusion, the prevalence of HBV infection is intermediate. Therefore, screening for HBV infection should be a routine part of ANC.<sup>11,12</sup>

Anti-hepatitis B titer (anti-HBs) is formed from the results of immunization or individuals who have suffered from hepatitis and recovered so that the body has developed immunity against hepatitis B. It is also necessary to analyze the relationship between immunization with anti-hepatitis B antibody titer. In this study, the age of respondents and antibody titer increased. It is likely that older respondents had hepatitis B but were cured. Studying the relationship between ever having hepatitis B with an antibody titer is necessary. The results of the study by Chibwe et al.<sup>13</sup> showed that anti-HBs were detected using enzyme immunoassays. Health workers must emphasize routine HBV screening among pregnant women, plus appropriate management in developing countries.

Acute hepatitis B can become chronic depending on when someone is infected. If an infection occurs as a baby, then the possibility of acute hepatitis B developing into a chronic disease in about 90% of the total infants infected with HBV. The risk goes down when we get older. About 25–50% of children between 1–5 years infected with the hepatitis B virus are also at risk of becoming chronic. The risk decreases to 6–10% when someone over five years old is infected. Most people with chronic hepatitis B are infected at birth or early childhood. If someone has been infected with chronic hepatitis B since childhood, then it is likely that 25% of infected people will die if they do not get treatment. Whereas if someone is infected with hepatitis B during adulthood, chances are 90% of patients will recover, and the virus will disappear in 6 months.<sup>14,15</sup>

Hepatitis B can be prevented by vaccination. Anti-HB antibodies can appear in response to hepatitis B vaccination. One series of vaccinations can produce enough antibodies in 95% of healthy people. Anti-HBs antibody titers will decrease along with the age of immunization. At an older age, immune disorders will decrease anti-HB titer. Hepatitis B immunization giving will form active immunity against infections caused by the hepatitis B virus in infants, toddlers, and adults. Giving hepatitis B immunization when newborns are born for up to 7 days to break the chain of transmission from mother to baby during delivery.<sup>16,17</sup>

The cross-sectional study results were

conducted in Southeastern Turkey between January and April 2013 with a representative sample of community-based agriculture (n=705). The results obtained are the prevalence of HBsAg, anti-HBs, anti-HBc, anti-HBe antibodies, and seropositive, respectively 5.7%, 25.9%, 28.9%, 28.9%, 16.4%, and 36.7%. There was no relationship between HBsAg and household size, age, education level, parity, and place of birth. In contrast, HBsAg prevalence was higher in seasonal migrant workers and people living in urban areas. The prevalence of anti-HB antibodies was significantly higher in women  $\geq 35$  years old, those with high parity, and those who gave birth without the help of a health professional ( $p < 0.05$ ). The risk for HBV infection in the seasonal migration group was 4.3 times higher compared to local workers ( $p = 0.00$ ; OR=4.3; 95% CI=2.2–8.4), with a prevalence rate of 11%.<sup>18</sup>

The importance of the HBV screening test of pregnant women was also carried out by Yi et al.<sup>19</sup> and Kambuno et al.<sup>20</sup> Their study suggested screening pregnant women to find out whether they are infected with hepatitis B. Early immunization of babies born to women infected with hepatitis B is highly recommended, and check HbsAg for those women going to marry.

### Conclusions

In this analysis, there was no relationship between FAW, who examined their pregnancy and postpartum health, and FAW, who examined neonates and infants with HBs antibody titers. However, there was a significant relationship between FAW age groups and antibody titers anti-HBs. That is in the age group 15–20 years, and respondents who are not married have a relationship with negative antibodies anti-Hbs.

### Conflict of Interest

The authors declare that there are no competing interests. All authors read, approved, and have the same contribution to the manuscript.

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### References

1. Hwang EW, Cheung R. Global epidemiology of hepatitis B virus (HBV) infection. *NAJMS*. 2011;4(1):7–13.
2. Ugwuja EI, Ugwu NC. Seroprevalence of hepatitis B surface antigen and liver function tests among adolescents in Abakaliki, South Eastern Nigeria. *IJTM*. 2010;6(1):3690.
3. Rossi C, Shrier I, Marshall L, Cnossen S, Schwartzman K, Klein MB, et al. Seroprevalence of chronic hepatitis B virus infection and prior immunity in immigrants and refugees: a systematic review and meta-analysis. *PLoS One*. 2012;7(9):e44611.
4. Xin X, Wang Y, Cheng J, Zhang Y, Peng Z, Xu J, et al. Seroepidemiological survey of hepatitis B virus infection among 764,460 women of childbearing age in rural China: a cross-sectional study. *J Clin Virol*. 2016;81:47–52.
5. Pusat Data dan Informasi, Kementerian Kesehatan Republik Indonesia. Situasi dan analisis hepatitis [Internet]. Jakarta: Kementerian Kesehatan Republik Indonesia; 2014 [cited 2022 May 14]. Available from: <https://pusdatin.kemkes.go.id/resources/download/pusdatin/infodatin/infodatin-hepatitis.pdf>.
6. Badan Penelitian dan Pengembangan Kesehatan, Departemen Kesehatan Republik Indonesia. Riset kesehatan dasar (Riskesdas) 2007 [Internet]. Jakarta: Departemen Kesehatan Republik Indonesia; 2008 [cited 2022 May 24]. Available from: [http://labdata.litbang.kemkes.go.id/images/download/laporan/RKD/2007/lap\\_rkd07.pdf](http://labdata.litbang.kemkes.go.id/images/download/laporan/RKD/2007/lap_rkd07.pdf).
7. Mustikah S, Hasanah D. Prevalensi infeksi hepatitis B pada ibu hamil di Malang. *JKB*. 2018;30(1):76–80.
8. Allain JP, Opare-Sem O. Screening and diagnosis of HBV in low-income and middle-income countries. *Nat Rev Gastroenterol Hepatol*. 2016;13(11):643–53.
9. Souza MT, Pinho TLRd, Santos MDC, Santos Ad, Monteiro VL, Fonsêca LMB, et

- al. Prevalence of hepatitis B among pregnant women assisted at the public maternity hospitals of São Luís, Maranhão, Brazil. *Braz J Infect Dis*. 2012;16(6):517–20.
10. Sinaga H, Latif I, Pangulu N. Pemeriksaan hepatitis B surface antigen (HbsAg) dan anti-Hbs pada ibu hamil sebagai skrining penularan hepatitis B. *J Ris Kesehat*. 2018;7(2):80–4.
  11. Yohanes T, Zerdo Z, Chufamo N. Seroprevalence and predictors of hepatitis B virus infection among pregnant women attending routine antenatal care in Arba Minch Hospital, South Ethiopia. *Hepat Res Treat*. 2016;2016:9290163.
  12. Bayo P, Ochola E, Oleo C, Mwaka AD. High prevalence of hepatitis B virus infection among pregnant women attending antenatal care: a cross-sectional study in two hospitals in northern Uganda. *BMJ Open*. 2014;4(11):e005889.
  13. Chibwe E, Silago V, Kajoro E, Juma M, Mkumbo E, Minja CA, et al. Antihepatitis B surface antigen and hepatitis C antibodies among pregnant women in an urban area of Mwanza city, Tanzania. *J Pregnancy*. 2019;2019:7917894.
  14. Fan L, Owusu-Edusei K Jr, Schillie SF, Murphy TP. Antiviral treatment among pregnant women with chronic hepatitis B. *Infect Dis Obstet Gynecol*. 2014;2014:546165.
  15. Mukhtar NA, Toy BC, Burman BE, Yu A, Chen AH, Berman P, et al. Assessment of HBV preventive services in a medically underserved Asian and Pacific Islander population using provider and patient data. *J Gen Intern Med*. 2015;30(1):68–74.
  16. Dwivedi M, Misra SP, Misra V, Pandey A, Pant S, Singh R, et al. Seroprevalence of hepatitis B infection during pregnancy and risk of perinatal transmission. *Indian J Gastroenterol*. 2011;30(2):66–71.
  17. Teshale EH, Kamili S, Drobeniuc J, Denniston M, Bakamutamaho B, Downing R. Hepatitis B virus infection in northern Uganda: impact of pentavalent hepatitis B vaccination. *Vaccine*. 2015;33(46):6161–3.
  18. Yentur Doni N, Simsek Z, Keklik Z, Gurses G, Zeyrek FY. Epidemiology of hepatitis B in the reproductive-age female farmworkers of southeastern Turkey. *Hepat Mon*. 2014;14(11):e22120.
  19. Yi W, Pan CQ, Hao J, Hu Y, Liu M, Li L, et al. Risk of vertical transmission of hepatitis B after amniocentesis in HBs antigen-positive mothers. *J Hepatol*. 2014;60(3):523–9.
  20. Kambuno NT, Bessie MF, Tangkelangi M, Djuma AW. Risk factors of intra-familial hepatitis B virus transmission among hepatitis B patients in Kupang, Indonesia. *GMHC*. 2019;7(2):151–6.