



Efficacy and Safety of Tenofovir in Preventing Perinatal Hepatitis B in Jakarta

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Abstract: Vertical transmission of hepatitis B virus (HBV) remains a major public health challenge in Indonesia, particularly among pregnant women with high viral loads. Tenofovir disoproxil fumarate (TDF) has been recommended to prevent perinatal transmission; however, local data regarding its efficacy and safety remain limited. This study aimed to evaluate Analyzing the effectiveness and safety of TDF in HBsAg-reactive pregnant women and its relationship with the infant's HBsAg status is necessary. An observational cohort study was conducted on 103 HBsAg-reactive pregnant women at five referral health facilities in Jakarta. Maternal effectiveness was measured by changes in SGPT and SGOT levels before and after therapy using the Wilcoxon test. Safety was assessed based on adverse events, pregnancy complications, and renal function using the chi-square test. Infant effectiveness was analyzed based on HBsAg status and tested using multivariate logistic regression. TDF significantly reduced SGPT and SGOT levels ($p < 0.001$). No significant association was found between TDF duration and adverse events, complications, or renal impairment ($p > 0.05$). Ninety-one-three percent of infants were HBsAg non-reactive, and 93.2% received complete hepatitis B vaccination. Complete vaccination ($OR = 414.52$; $p < 0.001$) and the absence of pregnancy complications ($OR = 0.048$; $p = 0.021$) were the main protective factors. TDF is safe and effective in preventing vertical transmission of HBV. Successful prophylaxis is highly dependent on infant vaccination and maternal health. These results support the integration of TDF into the national hepatitis B elimination program.

Introduction

Hepatitis is an inflammatory condition of the liver that can arise from a wide range of etiologies, including viral and bacterial infections, autoimmune disorders, drug-induced liver injury, alcohol consumption, hepatic steatosis, and exposure to toxic substances (1). The principal viral agents responsible for hepatitis are hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV), and hepatitis E virus (HEV) (2). Among these, hepatitis B represents a major global public health concern, particularly in developing countries with high endemicity, including Indonesia. According to World Health Organization (WHO) estimates, approximately 296 million people worldwide were living with chronic HBV infection in 2019, and more than 820,000 deaths occur annually due to HBV-related complications, such as liver cirrhosis and hepatocellular carcinoma (3).

In 2015, an estimated 257 million individuals globally were living with chronic HBV infection, while approximately 71 million were affected by chronic HCV infection (4). Co-infection with hepatitis viruses among people living with human immunodeficiency virus (HIV) remains a substantial

public health challenge, with an estimated 2.9 million individuals co-infected with HCV and approximately 2.6 million co-infected with HBV (4, 5). In Indonesia, a nationwide early screening program for hepatitis B among pregnant women was launched in 2020, enrolling 2,682,297 participants; of these, approximately 1.68% (45,108 pregnant women) tested positive for hepatitis B infection (6). In the Southeast Asian region, hepatitis B continues to be the leading cause of chronic liver disease (7). Data from the National Basic Health Research Survey (Riskesdas) indicate that the prevalence of hepatitis B surface antigen (HBsAg) in the general Indonesian population reached 7.1%, classifying Indonesia as a country with moderate-to-high hepatitis B endemicity (8). As the capital city of Indonesia, Jakarta has more comprehensively documented hepatitis B prevalence data than other regions, based on reports from the Jakarta Provincial Health Office in 2022 (9).

Mother-to-child transmission (MTCT) accounts for the majority of chronic hepatitis B virus (HBV) infections among children in endemic regions. Approximately 95% of infants infected through perinatal transmission develop chronic HBV infection, particularly in the absence of timely passive and active immunoprophylaxis (10). In response, the Indonesian

Ministry of Health plans to expand antiviral treatment services for pregnant women to prevent MTCT of HBV across 1,388 primary and referral healthcare facilities nationwide in 2024 (11).

The cornerstone of MTCT prevention includes administration of the hepatitis B vaccine birth dose (HB0) within 24 h of birth, followed by completion of the HB1-HB3 vaccination series, as well as hepatitis B immunoglobulin (HBIG) for infants born to mothers who are positive for hepatitis B surface antigen (HBsAg) (12, 13). However, the effectiveness of immunoprophylaxis is markedly reduced among mothers with high viral loads (HBV DNA $\geq 200,000$ IU/mL), in whom viral breakthrough and immunoprophylaxis failure may occur (14, 15). These findings underscore the need for additional maternal antiviral interventions.

In Indonesia, several challenges continue to hinder the prevention of vertical HBV transmission, including suboptimal hepatitis B screening coverage among pregnant women, limited availability of HBIG in primary healthcare facilities, and insufficient education regarding hepatitis B prevention strategies (14). According to the Indonesian Ministry of Health (2022), coverage of timely HB0 administration within 24 h of birth remains below the World Health Organization (WHO) elimination targets, reflecting persistent systemic gaps in implementation (14).

Tenofovir disoproxil fumarate (TDF), a nucleotide analogue reverse transcriptase inhibitor, is recommended by international clinical guidelines as a first-line antiviral therapy for pregnant women with high HBV viral loads (16, 17). Evidence from observational studies and meta-analyses demonstrates that initiation of TDF during the third trimester significantly reduces maternal HBV DNA levels and lowers the risk of perinatal transmission (18, 19). These findings have been further validated by randomized, double-blind clinical trials conducted in Thailand (20).

In addition to its antiviral efficacy, TDF has demonstrated a favorable safety profile during pregnancy. The European Association for the Study of the Liver (EASL) reports no increased risk of congenital anomalies, fetal growth restriction, or obstetric complications, including preeclampsia, associated with TDF exposure (16). Furthermore, global pharmacovigilance data and cohort studies support its safety during pregnancy and breastfeeding (18, 21). The WHO also endorses TDF as a key component of the global strategy for hepatitis B elimination (3).

Despite robust international evidence, data from Indonesia remain limited, particularly studies involving HBsAg-positive pregnant women across diverse socioeconomic and clinical settings. Such locally generated evidence is essential to assess the feasibility, effectiveness, and contextual applicability of antiviral prophylaxis within Indonesia's healthcare system (14). Therefore, this study aimed to evaluate the efficacy and safety of TDF among HBsAg-reactive pregnant women at referral healthcare centers in Jakarta and to assess its impact on infant HBsAg status. Additionally, this study sought to identify key determinants of successful MTCT prevention including treatment duration, hepatic fibrosis status, pregnancy-related complications, and adherence to infant immunization to support evidence-based national policy development and implementation. The findings of this study are expected to contribute to closing knowledge gaps and to strengthen the integration of antiviral prophylaxis into antenatal care programs, particularly in high-burden urban settings.

Experimental Section Subject

This study was conducted at healthcare facilities in Jakarta that were officially designated by the Indonesian Ministry of Health to provide tenofovir disoproxil fumarate (TDF) prophylaxis for the prevention of mother-to-child transmission of hepatitis B virus. Study participants were recruited between February and April 2025. Ethical approval was obtained from the Research Ethics Committee of the Faculty of Pharmacy, Universitas Pancasila (Approval No. 104/KEPK-FFUP/IV/2025). The study population consisted of pregnant women receiving TDF prophylaxis therapy.

The inclusion criteria were pregnant women of any age who received TDF prophylaxis at designated healthcare facilities in Jakarta; infants born to mothers undergoing TDF prophylaxis, regardless of whether they had completed the hepatitis B immunization schedule at the age of 9–12 months (HB0, hepatitis B immunoglobulin [HBIG], and HB1-HB3); and pregnant women with a documented HBV DNA level greater than 200,000 IU/mL. Exclusion criteria included incomplete medical records and cases in which either the mother or the infant had died.

During the study period, a total of 103 pregnant women received TDF prophylaxis and were included in the analysis. Participants were recruited from five healthcare facilities that had been formally appointed by the Ministry of Health to implement TDF prophylaxis, in accordance with the Decree of the Minister of Health of the Republic of Indonesia No. HK.01.07/MENKES/15/2023 (22).

Research Question

This study was designed to address critical gaps in locally generated evidence regarding the use of tenofovir disoproxil fumarate (TDF) for the prevention of perinatal hepatitis B virus (HBV) transmission in Indonesia. Although substantial international evidence supports the efficacy and safety of TDF, data from the Indonesian healthcare setting remain limited, where heterogeneity in maternal viral load, adherence to infant vaccination, and variations in clinical management may substantially influence clinical outcomes.

Accordingly, this study aimed to address the following research questions: (1) What is the efficacy of TDF in reducing hepatic inflammation and preventing vertical transmission of HBV among HBsAg-reactive pregnant women in Jakarta? This objective includes evaluation of changes in maternal serum transaminase levels (SGPT and SGOT) before and after TDF therapy, as well as assessment of the proportion of infants who test negative for HBsAg at 9–12 months of age, (2) Is TDF prophylaxis safe for both mothers and infants? Safety outcomes include maternal adverse events, renal function parameters, pregnancy outcomes, and neonatal growth indicators, (3) Which maternal and neonatal factors are significantly associated with successful prevention of HBV mother-to-child transmission? This analysis focuses on the influence of maternal HBV viral load, hepatic fibrosis status, pregnancy-related complications, adherence to antiviral prophylaxis, and completeness of infant hepatitis B immunization on prophylactic effectiveness.

By addressing these objectives, this study seeks to generate robust local evidence to inform the integration of TDF-based antiviral prophylaxis into Indonesia's national hepatitis B elimination strategy, thereby strengthening evidence-based maternal and child health policies and clinical decision-making across diverse healthcare settings and programmatic contexts.

Study design

This study employed an observational cross-sectional design. The research was conducted at healthcare facilities in Jakarta, including both primary- and referral-level facilities that implemented the tenofovir disoproxil fumarate (TDF) prophylaxis program. The study population comprised pregnant women receiving TDF prophylaxis therapy.

Study effectiveness outcomes in mothers included changes in serum alanine aminotransferase (SGPT) and aspartate aminotransferase (SGOT) levels, while effectiveness outcomes in infants were assessed based on hepatitis B surface antigen (HBsAg) status. Safety outcomes for both mothers and infants were also evaluated, including maternal adverse drug reactions, pregnancy-related complications, and the occurrence of congenital anomalies in infants.

Procedure

The research procedure began with the identification and review of medical records of pregnant women who received tenofovir disoproxil fumarate (TDF) prophylaxis between January and August 2024. Records of infants born to these mothers between March and July 2024 were subsequently identified. Hepatitis B surface antigen (HBsAg) testing in infants was conducted at the age of 9–12 months, with examinations performed between December 2024 and April 2025.

Data analysis

Data analysis was performed to (1) describe the baseline characteristics of the study population, (2) evaluate the efficacy of tenofovir disoproxil fumarate (TDF) on maternal biochemical parameters and infant hepatitis B surface antigen (HBsAg) outcomes, (3) assess the safety profile of TDF in both mothers and infants, and (4) identify independent determinants associated with successful prevention of vertical hepatitis B virus (HBV) transmission. All statistical tests were two-tailed, and a p -value <0.05 was considered statistically significant.

Descriptive and preliminary analyses

Continuous variables were summarized as mean $\pm$ standard deviation (SD) for normally distributed data or as median with interquartile range (IQR) for non-normally distributed data. Categorical variables were presented as frequencies and percentages. Data normality was assessed using the Shapiro-Wilk test, while homogeneity of variances was evaluated with Levene's test. Potential outliers were cross-checked against original medical records. Sensitivity analyses were conducted with and without outlier inclusion to evaluate the robustness of the results.

Bivariate analysis

Paired comparisons of maternal biochemical markers serum glutamic-pyruvic transaminase (SGPT/ALT) and serum glutamic-oxaloacetic transaminase (SGOT/AST) before and after TDF therapy were performed using the paired t -test for normally distributed data or the Wilcoxon signed-rank test for nonparametric data. Associations between categorical variables, including infant HBsAg status and maternal or neonatal characteristics, were examined using the chi-square test or Fisher's exact test when expected cell counts were <5 . Variables with a p -value <0.25 in bivariate analyses, as well as variables of established clinical relevance, were considered for inclusion in multivariate

models.

Multivariate logistic regression analysis

Multiple logistic regression was applied to identify independent predictors of successful HBV transmission prevention, defined as HBsAg-negative status in infants aged 9–12 months. Model refinement was conducted using a backward likelihood ratio approach. Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were reported to quantify associations. Model calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test, and discriminatory ability was evaluated using the area under the receiver operating characteristic (ROC) curve (AUC). Multicollinearity was assessed using the variance inflation factor (VIF), with VIF values >5 considered indicative of significant multicollinearity.

Handling of missing data

Data completeness was verified prior to analysis. Records with incomplete or inconsistent key variables were excluded during initial data cleaning. For variables with $<5\%$ missing data, complete-case (listwise deletion) analysis was applied. When missing data exceeded 5% and were deemed missing at random (MAR), multiple imputation using chained equations (MICE) with 20 iterations was performed. Results from imputed datasets were compared with complete-case analyses to assess the robustness of findings, and both were reported where appropriate.

Sensitivity and subgroup analyses

Sensitivity analyses were conducted to examine the stability of model estimates under alternative assumptions regarding outliers and missing data. Prespecified subgroup analyses were performed based on maternal viral load ($<1,000,000$ IU/mL vs. $\geq 1,000,000$ IU/mL), duration of TDF therapy (≤ 3 months vs. >3 months), completeness of infant hepatitis B vaccination, and maternal fibrosis status. To control for inflation of type I error due to multiple comparisons, Bonferroni correction or false discovery rate (FDR) adjustment was applied where appropriate.

Software and reproducibility

All statistical analyses were performed using IBM SPSS Statistics version 29.0 (IBM Corp., Armonk, NY, USA) and R software version 4.2 or later (R Foundation for Statistical Computing, Vienna, Austria). Statistical syntax, data dictionaries, and reproducible R scripts were archived and are available from the corresponding author upon reasonable request to ensure analytical transparency and reproducibility.

Ethical and analytical transparency

All analyses were prespecified and aligned with the study's *a priori* hypotheses. Any exploratory or post hoc analyses were explicitly identified as such. Decisions regarding variable selection, data transformation, and imputation assumptions were fully documented in the statistical appendix to ensure methodological transparency.

RESULTS

Characteristics

Characteristics of maternal respondents

The majority of study participants were aged 20–35 years (72.8%), as summarized in **Table 1**. Maternal age is a relevant factor influencing both the risk of vertical HBV

Table 1. Characteristics of Pregnant Women Undergoing Prophylaxis.

Respondent Characteristics	Frequency	Presentation
Age		
< 20 Years	1	1%
20 – 35 Years	75	72.8%
> 35 Years	27	26.2%
Pregnancy Status		
Primigravida (Gravida 1)	35	34%
Multigravida (Gravida >1)	68	66%
Mother's Viral Load		
< 1 Million Copies	20	19.4%
1 million - < 10 million copies	13	12.6%
10 Million - < 50 Million Copies	13	12.6%
50 Million - < 100 Million Copies	8	7.8%
100 Million - < 200 Million Copies	14	13.6%
> 200 Million Copies	35	34%

transmission and the effectiveness of antiviral therapy. Women of reproductive age generally demonstrate better awareness of treatment adherence and infant immunization, which may contribute to improved prevention outcomes, as reported in previous studies (23).

In addition, most participants were multigravida (66%), reflecting the demographic profile of pregnant women in Indonesia, where a substantial proportion of women of productive age have had prior pregnancies (24).

Regarding virological characteristics, **Table 1** shows that 19.4% of participants had an HBV DNA level <1 million IU/mL, whereas 34.0% had a high viral load ($\geq 200,000$ IU/mL). Elevated maternal viral load is a well-established predictor of mother-to-child transmission of HBV, even in the presence of combined passive-active immunoprophylaxis in neonates (24). Consequently, pregnant women with high viral loads are strongly recommended to receive antiviral therapy during the third trimester to reduce transmission risk.

Overall, the baseline characteristics of participants in this study suggest that pregnant women attending referral healthcare facilities in Jakarta remain at considerable risk for HBV vertical transmission, particularly due to the substantial proportion of mothers with high HBV DNA levels ($\geq 200,000$ IU/mL).

Characteristics of child respondents

Based on **Table 2**, the infants included in this study comprised 53.4% females and 46.6% males. This distribution reflects the generally balanced sex ratio observed in the general population. Infant sex is not known to directly influence the risk of vertical hepatitis B virus transmission; however, reporting sex distribution remains essential for comprehensive characterization of the study population.

Based on **Table 2**, the infants included in this study consisted of 53.4% females and 46.6% males, reflecting a generally balanced sex distribution consistent with that of the general population and indicating the absence of sex-related selection bias in the study sample. Infant sex is not known to directly influence the risk of vertical hepatitis B virus (HBV) transmission; however, it is reported as part of

Table 2. Characteristics of Babies Born.

Respondent Characteristics	Frequency	Presentation
Gender		
Man	48	46.6%
Woman	55	53.4%
Vaccination Status		
Complete	96	93.2%
Incomplete	7	6.8%
HBV Infection Examination Status (9-12 months after birth)		
Positive	9	8.7%
Negative	94	91.3%
Baby's Birth Weight		
< 2500 grams	8	7.8%
≥ 2500 grams	95	92%
Baby's Length at Birth		
Normal (> 48 cm)	29	28%
Abnormal (≤ 48 cm)	74	72%
Malformations in babies		
There is	0	0%
There isn't any	103	100%

the comprehensive characterization of the study population. The rate of complete HBV vaccination among infants was notably high, reaching 93.2%, indicating strong implementation of the national hepatitis B immunization program at referral health facilities in Jakarta. Complete HBV vaccination plays a critical role in reducing the risk of infection among infants born to HBsAg-positive mothers (24). According to the World Health Organization (WHO) guidelines, administration of a birth dose within 24 h followed by two to three additional doses can prevent more than 90% of perinatal HBV transmission (24). Nevertheless, 6.8% of infants had not yet received the complete HBV vaccination schedule. This finding warrants particular attention, as delayed or incomplete vaccination is associated with an increased risk of chronic HBV infection, especially among infants born to mothers with high viral loads (24).

HBV screening results revealed that 8.7% of infants remained HBV-positive despite maternal antiviral therapy during pregnancy. This finding is consistent with previous studies demonstrating that although combined maternal antiviral therapy and infant immunoprophylaxis substantially reduce vertical transmission, a small proportion of infections may still occur, particularly in cases of very high maternal viral load or suboptimal immunoprophylaxis (24). Conversely, the majority of infants (91.3%) tested HBsAg-negative, underscoring the high effectiveness of the combined prevention strategy applied in this study.

Overall, the infant characteristics observed in this study indicate substantial success in preventing vertical HBV transmission at referral health facilities in Jakarta. However, further improvements are needed to achieve complete vaccination coverage and to strengthen preventive strategies for mothers at higher risk of transmission, particularly those with high viral load or suboptimal adherence to perinatal care protocols, to further minimize residual transmission risk.

Effectiveness in mothers

Maternal effectiveness was assessed by comparing biochemical parameters before and after prophylactic therapy using the Wilcoxon signed-rank test, as the data consisted of paired, non-normally distributed observations. The parameters evaluated included serum glutamic pyruvic transaminase (SGPT/ALT) and serum glutamic oxaloacetic transaminase (SGOT/AST) levels measured prior to and following Tenofovir Disoproxil Fumarate (TDF) prophylaxis in pregnant women.

The administration of Tenofovir Disoproxil Fumarate (TDF) in pregnant women with chronic hepatitis B infection aims not only to prevent vertical transmission to the infant but also to reduce hepatic inflammatory activity, which is reflected by decreased serum transaminase levels, particularly SGPT (ALT), as summarized in **Table 3**. In this study, comparative analysis of SGPT levels before and after TDF therapy was conducted among 103 pregnant women using the Wilcoxon signed-rank test.

Descriptive analysis demonstrated that the mean maternal SGPT (ALT) level prior to therapy was 38.23 U/L (SD 25.84), with values ranging from 12 to 211 U/L. Following Tenofovir Disoproxil Fumarate (TDF) prophylaxis, the mean SGPT level decreased to 24.20 U/L (SD 12.86), with a minimum of 9 U/L and a maximum of 103 U/L.

Paired comparison using the Wilcoxon signed-rank test revealed that 100 respondents (97.1%) experienced a reduction in SGPT levels (negative ranks), while only 3 respondents (2.9%) showed an increase (positive ranks), with no participants demonstrating unchanged values. The test yielded a Z statistic of -8.171 with a p-value < 0.001, indicating a statistically significant reduction in SGPT levels after TDF administration.

These findings confirm the effectiveness of TDF in reducing hepatic inflammatory activity among HBsAg-positive pregnant women, as reflected by the significant decline in serum SGPT levels. This result is consistent with previous studies which reported that TDF therapy during pregnancy significantly reduced maternal transaminase levels and improved overall liver biochemical profiles (21).

TDF is both safe and effective in controlling disease activity while simultaneously reducing the risk of mother-to-child transmission of HBV (23).

Furthermore, a local study conducted at Cipto Mangunkusumo Hospital (RSCM), Jakarta, reported that TDF therapy not only resulted in significant reductions in SGPT levels but also markedly suppressed maternal HBV DNA to <50 IU/mL at 28 weeks postpartum, thereby preventing deterioration of liver function and reducing the risk of fibrosis progression and cirrhosis (25).

Collectively, these results indicate that TDF administration in pregnant women with chronic HBV infection provides dual clinical benefits: effective prevention of perinatal HBV transmission and significant improvement in maternal liver function, as evidenced by the substantial reduction in SGPT levels. SGOT (AST) analysis is summarized in **Table 4**.

Descriptive analysis revealed that the mean maternal SGOT (AST) level prior to Tenofovir Disoproxil Fumarate (TDF) therapy was 50.57 U/L (SD 35.15), with values ranging from 22 to 270 U/L. Following TDF administration, the mean SGOT level declined to 32.10 U/L (SD 12.37), with a minimum of 17 U/L and a maximum of 111 U/L, indicating improvement in hepatic status after antiviral prophylaxis.

Table 3. Average SGPT Levels Before and After Tenofovir Disoproxil Fumarate (TDF) Therapy in Pregnant Women with HBV infection.

Parameter	N	Mean	Elementary School	Min	Max	Normal Reference Values
SGPT before therapy	103	38.23	25.84	12	211	0 - 32 U/L
SGPT after therapy	103	24.20	12.87	9	103	
p-value 0.000 < 0.05						

Table 4. Average SGOT Levels Before and After Tenofovir Disoproxil Fumarate (TDF) Therapy in Pregnant Women with HBV infection.

Parameter	N	Mean	Elementary School	Min	Max	Normal Reference Values
SGOT before therapy	103	50.57	35,152	22	270	0 - 31 U/L
SGOT after therapy	103	32.10	12,366	17	111	
p -value 0.000 < 0.05						

Inferential analysis using the Wilcoxon signed-rank test demonstrated a statistically significant difference between SGOT levels before and after therapy (Z = -8.794; p < 0.001). A total of 102 out of 103 respondents (99.0%) exhibited a reduction in SGOT levels (negative ranks), while only one respondent (1.0%) showed an increase (positive ranks), with no tied observations.

The significant reduction in SGOT levels further supports the therapeutic effectiveness of TDF in attenuating hepatic inflammation among HBsAg-positive pregnant women. These findings are consistent with prior studies indicating that TDF not only suppresses HBV replication but also improves hepatocellular injury, as reflected by reductions in transaminase enzymes, including SGOT and SGPT (24).

Moreover, Terrault et al. reported that short-term TDF administration during pregnancy is both safe and effective in improving liver biochemical profiles without inducing clinically significant hepatotoxicity (24). Collectively, the present findings reinforce existing evidence that TDF therapy in pregnant women with chronic HBV infection confers substantial clinical benefits, particularly in improving maternal liver function while maintaining a favorable safety profile.

Safety for mothers

Maternal safety data related to prophylactic therapy were subsequently analyzed using the Chi-square test to evaluate the association between independent variables reported adverse effects, SGPT levels, pregnancy-related complications, and serum creatinine levels and the dependent variable, namely the duration of prophylactic TDF therapy in pregnant women.

Based on the statistical analysis presented in **Table 5**, no statistically significant association was observed between the duration of Tenofovir Disoproxil Fumarate (TDF) therapy and the occurrence of adverse effects, changes in SGPT levels, pregnancy-related complications, or alterations in serum

Table 5. Security Test **Table Use** of TDF in Mothers.

Variables	Duration of Prophylaxis		p -value
	≤ 3 Months (%) (N=71)	> 3 Months (%) (N=32)	
Side effects during prophylaxis			
There is	20 (28)	7 (22)	0.630
There isn't any	51 (72)	25 (78)	
SGPT levels after prophylaxis			
Normal (<32 U/L)	61 (86)	26 (81)	0.565
Abnormal (>32 U/L)	10 (14)	6 (19)	
Pregnancy complications during prophylaxis			
There is	11 (15)	4 (12)	0.772
There isn't any	60 (85)	28 (88)	
Creatinine levels after prophylaxis			
Normal (<1)	68 (96)	30 (94)	0.645
Abnormal (>1)	3 (4)	2 (6)	

creatinine levels among pregnant women receiving TDF for the prevention of perinatal hepatitis B virus (HBV) transmission (24).

These findings are consistent with previous studies which reported that TDF use during pregnancy is generally well tolerated and associated with a favorable safety profile, characterized by mild and transient adverse effects, with rare occurrences of renal dysfunction or serious obstetric complications. Moreover, existing evidence indicates that initiation of TDF therapy during the second or third trimester is not associated with an increased risk of major adverse maternal or fetal outcomes (24).

Taken together, the results of this analysis suggest that the duration of TDF prophylaxis, whether administered for less than three months or more than three months, remains clinically safe for pregnant women, supporting its use as an effective strategy for the prevention of vertical HBV transmission.

Effectiveness in infants

The effectiveness of prophylaxis in infants was evaluated using Chi-square analysis to examine the associations between multiple independent variables including maternal SGPT levels, maternal viral load, maternal fibrosis status, maternal adverse effects, maternal serum creatinine levels, pregnancy complications, infant birth weight, infant length at birth, hepatitis B vaccination status, adherence to prophylactic therapy, and mode of delivery and the dependent outcome, namely HBsAg status in infants at follow-up.

The Relationship between Maternal and Neonatal Factors and HBsAg Status in Infants

The bivariate analysis examining the associations between selected maternal and infant factors and HBsAg status in infants identified several variables significantly associated with HBV transmission risk, as presented in **Table 6**.

Mother's Viral Load: A statistically significant association was observed between maternal viral load and infant HBsAg status ($p = 0.011$). Infants born to mothers with viral loads >1 million IU/mL exhibited a higher risk of HBV infection compared with those born to mothers with viral loads <1

million IU/mL. This finding is consistent with previous studies which demonstrated that elevated maternal HBV DNA levels are a major determinant of vertical transmission risk despite immunoprophylaxis (24).

Maternal Fibrosis Results: Maternal fibrosis status was also significantly associated with infant HBsAg positivity ($p = 0.001$). Infants born to mothers with cirrhosis had a substantially higher likelihood of being HBsAg positive. Cirrhosis reflects advanced chronic liver disease, which is often accompanied by sustained viral replication and impaired immune regulation, thereby increasing the risk of mother-to-child transmission. These findings suggest that fibrosis staging may be a useful component of risk stratification in maternal HBV management. This finding aligns with evidence who identified cirrhosis as an independent risk factor for vertical HBV transmission (26).

Table 6. Variable Test Independent to Variables Dependent Effectiveness in Infants.

Variables	HBsAg Status in Infants		p -value
	Positive (%)	Negative (%)	
Maternal SGPT results before prophylaxis			
Normal	6 (7)	81 (93)	0.144
Abnormal	3 (19)	13 (81)	
Mother's viral load			
< 1 million IU/mL	1 (2)	55 (98)	0.011
> 1 Million IU/mL	8 (17)	39 (83)	
Maternal Fibrosis Results			
Cirrhosis	4 (57)	3 (43)	0.001
Non-Cirrhosis	5 (5)	91 (95)	
Side effects for mother			
There is	5 (17)	24 (83)	0.113
There isn't any	4 (5)	70 (95)	
Maternal Creatinine Level			
Normal	7 (78)	2 (22)	0.059
Abnormal	91 (97)	3 (3)	
Maternal Pregnancy Complications			
There is	3 (21)	11 (79)	0.103
There isn't any	6 (7)	83 (93)	
Baby's weight at birth			
< 2500 grams	2 (25)	6 (75)	0.114
≥ 2500 grams	7 (7)	88 (93)	
Baby's body length at birth			
Normal	2 (7)	27 (93)	1.00
Abnormal	7 (9)	67 (91)	
Infant vaccination status			
Complete	3 (3)	93 (97)	0,000
Incomplete	6 (86)	1 (14)	
Maternal Prophylaxis Compliance			
Obedient	1 (2)	50 (98)	0.031
Not obey	8 (15)	44 (85)	
Mother's Delivery Method			
Normal	7 (10)	66 (90)	1.00
SC	2 (7)	28 (93)	

Vaccination Status: A highly significant association was identified between infant hepatitis B vaccination completeness and HBsAg status ($p < 0.001$). Infants who did not receive complete HBV immunization were at markedly higher risk of HBV infection, underscoring the critical role of timely and complete vaccination in preventing perinatal transmission (24).

Maternal Compliance with Prophylaxis: Maternal adherence to TDF prophylaxis was significantly associated with infant HBsAg status ($p = 0.031$). Infants born to mothers with poor adherence to antiviral therapy were more likely to be HBsAg positive. Adequate adherence is essential for effective viral suppression during late pregnancy, thereby minimizing intrauterine and peripartum transmission risk (24).

Variables Without Significant Relationship

Several variables including maternal SGPT levels ($p = 0.144$), maternal adverse effects during therapy ($p = 0.113$), maternal serum creatinine levels ($p = 0.059$), pregnancy-related complications ($p = 0.103$), infant birth weight ($p = 0.114$), infant birth length ($p = 1.000$), and mode of delivery ($p = 1.000$) were not significantly associated with infant HBsAg status.

These findings indicate that certain maternal biochemical parameters and perinatal outcomes do not independently predict vertical HBV transmission. Instead, the risk of transmission appears to be primarily driven by virological and immunoprophylactic factors, particularly maternal viral load, severity of liver disease as reflected by fibrosis status, and the timeliness and completeness of infant immunization, as well as maternal adherence to antiviral therapy.

This pattern underscores the central role of viral suppression and immunization strategies in preventing mother-to-child transmission of HBV, rather than reliance on nonspecific biochemical markers or delivery-related factors.

Safety for babies

Infant safety outcomes were evaluated using Chi-square analysis to examine the association between infant anthropometric parameters specifically birth weight and birth length as independent variables, and the duration of maternal Tenofovir Disoproxil Fumarate (TDF) prophylaxis as the dependent variable, as presented in **Table 7**.

Based on the Chi-square test results, no statistically significant association was observed between the duration of maternal prophylaxis and neonatal body length ($p = 0.161$) or birth weight ($p = 0.430$). As the obtained p-values exceeded the predefined significance threshold ($\alpha = 0.05$), the null hypothesis was retained. Although descriptive analysis indicated a higher proportion of infants with body

length < 48 cm in the group whose mothers received prophylaxis for less than three months (47 of 71 infants), as well as a higher proportion of infants with birth weight $< 2,500$ g in the same group (7 of 71 infants), these differences did not reach statistical significance.

These findings suggest that neonatal anthropometric outcomes are likely influenced by factors beyond the duration of antiviral prophylaxis, including maternal nutritional status during pregnancy, overall maternal health, placental function, and genetic determinants. This interpretation is consistent with previous evidence which emphasizes that fetal growth is multifactorial and shaped by both maternal and intrauterine environmental factors (27).

Multivariate logistic regression

Multivariate analysis was performed using multiple logistic regression. Independent variables with a p-value < 0.25 in the bivariate analysis were selected for inclusion in the backward stepwise multiple logistic regression model. This threshold was applied to ensure that potentially important predictors were not excluded prematurely. The following variables were therefore considered as candidate independent predictors in the multivariate logistic regression analysis, allowing for a systematic assessment of their independent effects while controlling for potential confounding factors.

Based on **Table 8**, a total of five independent variables were included in the multivariate logistic regression analysis, namely maternal SGPT levels, maternal viral load, pregnancy-related complications, infant vaccination status, and maternal adherence to antiviral prophylaxis, reflecting both maternal clinical status and infant-related factors relevant to perinatal HBV transmission risk.

In contrast, six other variables including maternal fibrosis status, maternal adverse effects, maternal serum creatinine levels, infant birth weight, infant birth length, and mode of delivery were not entered into the multivariate model. These variables were excluded not only because their bivariate p-values exceeded 0.25, but also due to sparse data issues, whereby at least two cells in the corresponding contingency tables had expected frequencies of fewer than five observations, which limited the reliability of parameter estimation.

Inclusion of such variables would have violated the assumptions of logistic regression and potentially resulted in model instability, as reflected by inflated or implausible odds ratio estimates [Exp(B)]. Therefore, exclusion of these variables was necessary to ensure the validity, robustness, and interpretability of the final multivariate model, as well as to maintain adequate model parsimony and statistical reliability. Based on **Table 9**, three variables remained statistically significant in the multivariate logistic regression analysis ($p \leq 0.05$), indicating a meaningful association between the independent variables pregnancy complications, infant hepatitis B vaccination status, and maternal adherence to prophylaxis and infant HBsAg outcomes, after adjustment for other covariates included in the model. These findings suggest that both maternal clinical factors and infant preventive interventions independently contribute to the risk of HBV mother-to-child transmission. Collectively, this multivariate model highlights the critical importance of integrated maternal management and timely infant immunization in optimizing perinatal HBV prevention outcomes within routine clinical practice settings and national public health programs in Indonesia nationwide.

Table 7. Variable Test Independent with Variables Dependent Safety for Babies.

Variables	Duration of Prophylaxis		p -value
	≤ 3 Months (%)	> 3 Months (%)	
Baby weight			
< 2500 grams	7 (10)	1 (3)	0.430
≥ 2500 grams	64 (90)	31 (97)	
Baby's body length			
< 48 cm	47 (64)	26 (81)	0.161
≥ 48 cm	24 (36)	6 (19)	

Table 8. Selection Results Variables Independent Variables Entered in Multivariate Regression Test Logistics Multiple.

Variables	p -value	Fixed Value	Information
SGPT value	0.144	p- value < 0.25	Multivariate Entry
Mother's viral load	0.011	p- value < 0.25	Multivariate Entry
Fibrosis Status	0.001	p- value < 0.25	Not Entering Multivariate
Side Effects for Mother	0.113	p- value < 0.25	Not Entering Multivariate
Maternal Creatinine	0.05	p- value < 0.25	Not Entering Multivariate
Pregnancy Complications	0.103	p- value < 0.25	Multivariate Entry
Baby weight	0.114	p- value < 0.25	Not Entering Multivariate
Baby's body length	1.00	p- value > 0.25	Not Entering Multivariate
Vaccination	0,000	p- value < 0.25	Multivariate Entry
Prophylaxis Compliance	0.031	p- value < 0.25	Multivariate Entry
Delivery Methods	1.00	p- value > 0.25	Not Entering Multivariate

Table 9. Analysis Results Multivariate Regression Logistics Double in the Final Stage.

Variables	B	Sig	Exp (B)
Pregnancy Complications (Reference: pregnant women without complications)	-3,034	0.021	0.048 (95% CI 0.04 – 0.637)
Giving Infant Vaccines (Reference: fully vaccinated baby)	6,027	0,000	414,523 (95% CI 17,867 – 9617,161)
Prophylaxis Compliance (Reference: pregnant women comply with prophylaxis)	2,268	0.097	9.663 (95% CI 0.064 – 140.555)
Constant	-2,230	0.086	

Pregnancy Complications

The variable pregnancy complications demonstrated a regression coefficient (B) of -3.034 with a p-value of 0.021, and an odds ratio Exp(B) = 0.048 (95% CI: 0.004-0.637). This finding indicates that the presence of pregnancy-related complications was significantly associated with a reduced likelihood of successful prevention of vertical HBV transmission, reflected by a higher probability of infants testing HBsAg positive.

Pregnancy complications may compromise the effectiveness of prophylaxis through several mechanisms, including altered drug pharmacokinetics, impaired hepatic metabolism, reduced placental perfusion, or decreased adherence to antiviral therapy. These findings highlight the critical importance of early identification and intensive management of pregnancy complications to optimize the effectiveness of antiviral prophylaxis (18).

Infant Hepatitis B Vaccination Status

Infant hepatitis B vaccination status emerged as the strongest protective factor against vertical transmission. The regression analysis yielded a coefficient of B = 6.027 (p < 0.001), with an odds ratio Exp(B) = 414.523 (95% CI: 17.867-9,617.161). This indicates that infants who received complete hepatitis B vaccination were more than 400 times more likely to remain HBsAg negative compared with infants with incomplete vaccination.

Despite the wide confidence interval likely reflecting sparse events this finding is consistent with extensive evidence demonstrating that timely administration of HB0 and hepatitis B immunoglobulin (HB1g) within 24 h of birth,

followed by completion of the vaccination series, can reduce perinatal HBV transmission by more than 90%, even among mothers with high viral loads (28). From a clinical pharmacy perspective, these results reinforce that active immunization remains an indispensable component of HBV mother-to-child transmission prevention, even in the presence of effective antiviral therapy.

Maternal Adherence to Antiviral Prophylaxis

Maternal adherence to TDF prophylaxis showed a positive regression coefficient (B = 2.268) with an odds ratio Exp(B) = 9.663 (95% CI: 0.664-140.555), although the association did not reach statistical significance (p = 0.097). While this variable did not meet the conventional threshold for significance, the direction and magnitude of the association suggest a clinically meaningful trend, indicating that mothers who adhered to prophylactic therapy were more likely to give birth to HBsAg-negative infants.

Adherence to antiviral therapy is influenced by multiple factors, including health literacy, perceived side effects, social and family support, engagement with healthcare providers, and access to medication. These findings underscore the importance of patient-centered counseling and adherence support, particularly within antenatal care and community pharmacy settings (29).

Comparison With Previous Studies

The results of this study are consistent with those who demonstrated that tenofovir prophylaxis initiated in the third trimester significantly reduced vertical HBV transmission among mothers with high viral loads (>200,000 IU/mL), particularly when combined with complete infant

immunization (17). Similarly, Hu et al. reported effective viral suppression without adverse renal outcomes among pregnant women receiving tenofovir, with most fully vaccinated infants remaining uninfected (19). This supports the favorable safety profile of tenofovir in maternal antiviral therapy.

Further emphasized that prophylaxis adherence during pregnancy and complete infant vaccination represent complementary protective mechanisms antivirals reducing intrauterine transmission and vaccination preventing peripartum and postnatal transmission (13). Overall safety of tenofovir during pregnancy, although slight differences in infant growth parameters were noted and warrant further investigation (30). Such observations underscore the importance of continued postnatal monitoring to ensure optimal long term infant outcomes.

Overall Interpretation

In summary, the multivariate analysis identified pregnancy complications, infant vaccination completeness, and maternal adherence to prophylaxis as key determinants influencing the success of preventing vertical transmission of hepatitis B in Jakarta. Infants born to mothers with pregnancy complications, incomplete vaccination, or poor adherence to antiviral therapy represent a high-risk group requiring enhanced clinical monitoring and targeted interventions.

These findings provide important local evidence to support the integration of comprehensive antiviral prophylaxis, robust immunization programs, and adherence-focused antenatal care into Indonesia's national hepatitis B elimination strategy.

CONCLUSION

Overall, the prevention of vertical transmission of hepatitis B requires an integrated and multidisciplinary approach, encompassing effective management of pregnancy-related complications, timely and complete infant vaccination, and optimal adherence to antiviral prophylactic therapy.

Pregnancy complications were shown to have a significant negative impact on the success of vertical transmission prevention, as pregnant women experiencing complications had a lower likelihood of preventing HBV transmission to their infants. These complications may interfere with antiviral effectiveness through altered pharmacokinetics, impaired maternal health status, or reduced adherence to therapy.

In contrast, hepatitis B vaccination administered to newborns was identified as a highly significant protective factor, substantially increasing the likelihood of successful prevention of vertical transmission. The markedly high effectiveness of complete vaccination underscores its central role in HBV elimination strategies, particularly when administered promptly after birth.

Maternal adherence to antiviral prophylaxis with tenofovir disoproxil fumarate demonstrated a positive trend toward improved prevention outcomes, although statistical significance was not achieved in this study. Nevertheless, this finding highlights the clinical importance of adherence as a modifiable factor that can enhance the effectiveness of prophylactic interventions.

Collectively, the findings of this study provide important evidence to inform the development of integrated immunological and pharmacological intervention strategies

for the prevention of vertical hepatitis B transmission. The implementation of a comprehensive strategy focusing on optimized management of pregnancy complications, expanded coverage of hepatitis B vaccination, and strengthened support for maternal adherence to antiviral prophylaxis is essential to achieving national and global hepatitis B elimination targets.

Declarations

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Conflict of Interest

The authors declare no conflicting interest.

Data Availability

Ethics Statement

This observational study was approved by the Universitas pancasila. Written informed consent was obtained from all participants. Approval ethics has obtained from Committee Ethics Faculty of Pharmacy, Pancasila University with number letter 104/KEPK-FFUP/IV/2025

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Additional Information

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