Medic Center

VIÊM GAN VIRUS B & THAI KỲ

- Dữ liệu mới từ TAF.

PGS. TS. BS. Phạm Thị Thu Thủy
Trung Tâm Y Khoa MEDIC, TP. Hồ Chí Minh

1

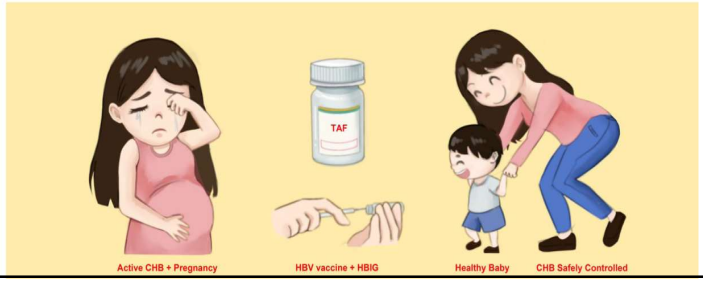
NỘI DUNG

I, Đặt vấn đề.

II, Viêm gan siêu vi B & thai kỳ.

III, Điều trị HBV ở phụ nữ mang thai: Dữ liệu mới từ TAF.

IV, Kết luận.



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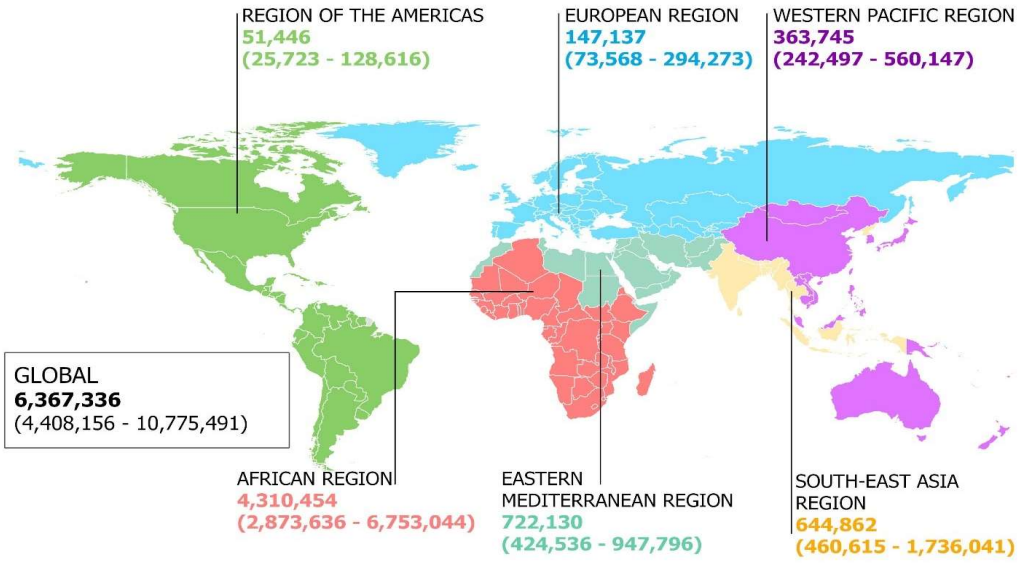
Estimated number of hepatitis B virus infection among children under 5 by WHO region, 2019



Source: World Health Organization. Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021. Available at https://www.who.int/publications/i/item/9789240027077

3

The Lancet Regional Health - Western Pacific 16 (2021) 100267

Contents lists available at ScienceDirect

The Lancet Regional Health - Western Pacific

journal homepage: www.elsevier.com/locate/lanwpc

Research paper

Hepatitis B virus infection among 90 million pregnant women in 2853 Chinese counties, 2015-2020: a national observational study

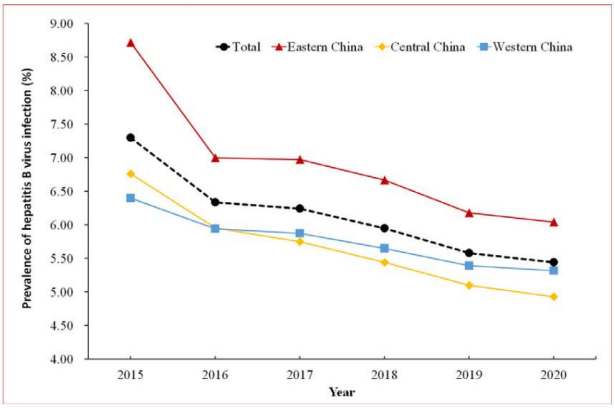


Table 1
Trends of HBV prevalence among pregnant women in mainland China, 2015-2020

Year	Pregnant women tested for HBV (n)	HBsAg positive (n)	HBsAg prevalence (%, 95 CI)	p for trend
2015	13 928 840	1 016 578	7.30 (7.28, 7.31)	<0.001
2016	18 229 199	1 154 938	6.34 (6.32, 6.35)	
2017	17 385 461	1 085 777	6.25 (6.23, 6.26)	
2018	15 038 592	894 889	5.95 (5.94, 5.96)	
2019	14 355 042	801 072	5.58 (5.57, 5.59)	
2020	11 936 522	649 577	5.44 (5.43, 5.45)	
Total	90 873 656	5 602 831	6.17 (6.16, 6.18)	

Figure 1. Trends of HBV prevalence among pregnant women in different regions.

J. Liu, X. Wang, Q. Wang et al.

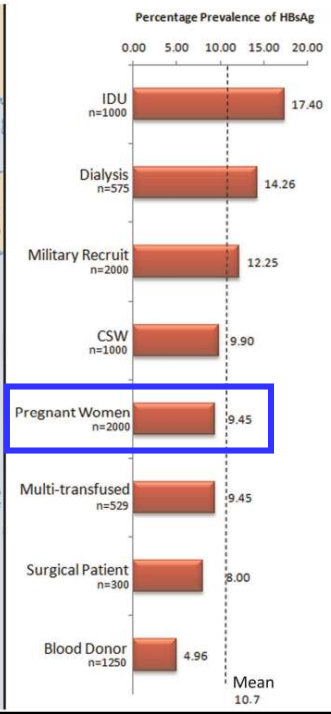
4

Map of Viet Nam Depicting the Prevalence of HBsAg in 5 Regions.

The map depicts the percentage HBsAg positives in Ha Noi, Hai Phong, Da Nang, Khanh Hoa and Can Tho. To the right is a graph depicting the prevalence of HBsAg in each of the study groups in the 5 study sites in Viet Nam.

n = 8654

Linda Dunford et al. A Multicentre Molecular Analysis of Hepatitis B and Blood-Borne Virus Coinfections in Viet Nam . PLoS ONE | www.plosone.org June 2012 | Volume 7 | Issue 6 | e39027



5

Research Article

Hepatitis B Infection and Mother-to-Child Transmission in Haiphong, Vietnam: A Cohort Study with Implications for Interventions

Biomed Res Int. 2020; 2020: 4747965.
Published online 2020 Aug 20. doi: 10.1155/2020/4747965

Pham Minh Khue,[1] **Nguyen Thi Thuy Linh**,[1] **Vu Hai Vinh**,[2] **Luu Vu Dung**,[3] **and Bang Nguyen Van**[4]

[1]*Faculty of Public Health, Haiphong University of Medicine and Pharmacy, Haiphong, Vietnam*
[2]*Department of Tropical and Infectious Diseases, Viet-Tiep Hospital, Haiphong, Vietnam*
[3]*Department of Biochemistry, Haiphong Gyneco-Obstetric Hospital, Haiphong, Vietnam*
[4]*Department of Pediatrics, Hanoi Medical University, Hanoi, Vietnam*

Correspondence should be addressed to Pham Minh Khue; pmkhue@hpmu.edu.vn

Received 27 April 2020; Revised 28 July 2020; Accepted 5 August 2020; Published 20 August 2020

Academic Editor: Roberto Amerigo Papini

Background. There is little data available on HBV infection and mother-to-child transmission (MTCT) in Vietnam. *Objective*. This study is aimed at assessing the prevalence of HBV infection and the current situation of MTCT in Haiphong, Vietnam. *Methods*. A transversal survey of 1721 pregnant women followed by an observational prospective cohort study of 183 HBV-infected women was conducted at Haiphong Gyneco-Obstetric Hospital. Women were followed up up to 12-month postpartum; use of prevention measures and the MTCT rate were evaluated. HBV infection in children was defined by a HBsAg-positive test at 12 months of age. *Results*. At baseline, 183 of 1721 pregnant women (10.6%) tested HBsAg positive. Among them, 23.0% were HBeAg positive, 26.2% had a detectable load of HBV DNA, and 13.1% had a HBV DNA load ≥ 200,000 IU/mL. All women underwent MTCT prevention antiviral therapy. At delivery, 98.9% of newborns receive a HBV vaccine birth dose, and 82% received HBIG. At 12 months of age, 94.7% have received the scheduled HBV vaccines. Eight percent of infants born from followed-up women were HBsAg positive. The mother's HBeAg-positive status was associated with a higher risk of HBV infection in infants. *Conclusion*. The HBV prevalence and MTCT rates are high in Haiphong. A strong national plan to increase the access to preventive measures and to monitor results is needed in order to decrease this prevalence.

6

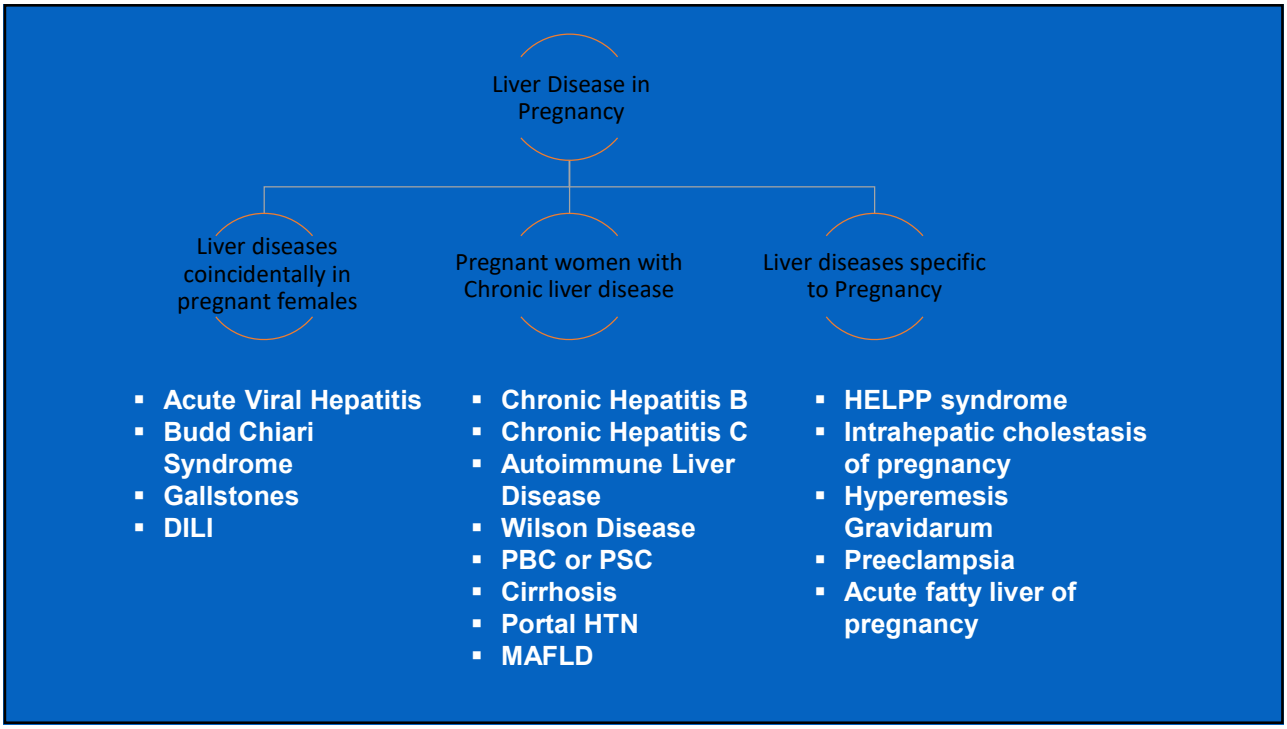
Scientifc Reports | (2021) 11:8676

Hepatitis B virus infection among pregnant mothers and children after the introduction of the universal vaccination program in Central Vietnam

Masami Miyakawa[1], Lay-Myint Yoshida[2,3]✉, Hien-Anh Thi Nguyen[4], Kensuke Takahashi[5], Tho Huu Le[6], Michio Yasunami[5], Koya Ariyoshi[5], Duc-Anh Dang[4] & Hiroyuki Moriuchi[1,3]

A birth cohort study was conducted in Khan Hoa Province, central Vietnam between 2009 and 2012 to determine the seroprevalence of hepatitis B virus (HBV) in pregnant women and their children, and associated risk factors. We enrolled 1987 pregnant women with their babies at the birth phase, and 12.6% (95% confidence interval [CI]: 11.1–14.0) of mothers were hepatitis B surface antigen (HBsAg)+. At 2-year follow-up phase, 1339 (67.4%) children were enrolled of whom 76.6% completed hepatitis B vaccines (HepB) and 1.9% (95% CI: 1.2–2.7) were HBsAg+. When mothers were hepatitis B e antigen (HBeAg)+, 28.3% of children have got infected even with complete HepB. HBV infection in mothers, hepatitis B surface antibody (anti-HBs antibody) below the seroprotective level in children, and mothers with pre-pregnancy low body mass index were associated with HBV infection in children. Meanwhile, HBV infection in children, older maternal age, no or incomplete doses of HepB, and boys were associated with anti-HBs antibody below the seroprotective level in children. Our birth cohort study determined a low rate of congenital HBV infection and associated risk factors in Vietnam, however further studies are needed to advance prevention including anti-viral therapy in pregnant women at high risk.

7



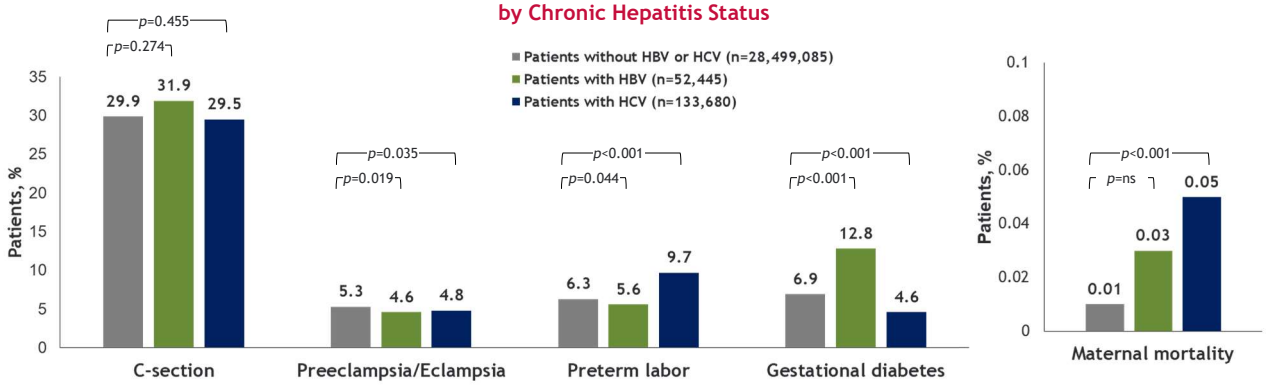
8

II, Viêm gan siêu vi B & thai kỳ.

Pregnancy Complications in Patients with HBV or HCV

Retrospective, nationwide, 7-year study utilizing the National Inpatient Sample database from 2012-2018

Outcomes of Pregnancy-Related Admissions by Chronic Hepatitis Status

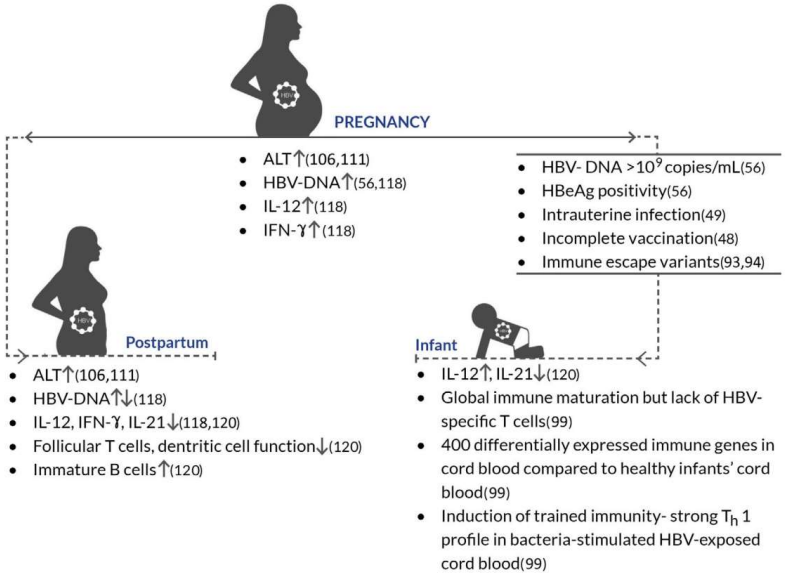


Patients with CHB were associated with a higher rate of gestational diabetes, and patients with HCV were associated with higher rates of preterm labor and all-cause in-hospital maternal mortality during pregnancy, compared to uninfected controls

Chen B, et al. AASLD 2021. 891

9

Schematic representation of immunologic changes in the peripartum period in mothers with CHB and their infants



JOSHI AND COFFIN. Hepatitis B and Pregnancy: Virologic and Immunologic Characteristics. Hepatology Communications, Vol. 4, No. 2, 2020.

10

Guidelines: HBV Infection and Pregnancy.

- All pregnant women should be screened for HBV[1]
- Risk of chronic HBV infection linked to age of exposure; ~90% infants, 5% adults[2]
- HBIG and HBV vaccine should be administered to newborns of HBsAg-positive mothers <12 hr after delivery[1]
- HBV therapy should be discussed with expectant mothers[1]
- HBV flares are uncommon in pregnancy (~9%)[3]

1. Terrault. Hepatology. 2018;67:1560. 2. Weinbaum. MMWR Recomm Rep. 2008;57:1.
3. Chang. Am J Gastroenterol. 2016;111:1410.

11

Liver Function Tests and Pregnancy.

- ALT, AST may be slightly lower or unchanged in second and third trimesters
- Total bilirubin and INR do not change
- AFP increases
- Albumin and hemoglobin decreased from hemodilution
- ALP increases from placental source

Tram. Am J Gastroenterol. 2016; 111:176.

12

Summary of proposed modes of HBV MTCT and underlying mechanisms

PRENATAL (INTRAUTERINE) *3%-8%*	NATAL (AT BIRTH) *~35%*	POSTNATAL (POSTPARTUM) *Variable rates reported depending on age of infection and country of origin*
1. **Placental infection** • Through maternal vascular endothelium to endovascular extravillous trophoblasts(35) • Infection of Hofbaeur cells (placental macrophages)(36) • Transcytosis – entry mechanism for HBV into trophoblasts; HBV-specific receptors may be present in only the early stages of infection(37) • Increased ASGPR (receptor involved in endocytosis of HBV) in placental and maternal circulating dendritic cells(38) • Paracellular routes from maternal blood to fetal capillaries – through placental leakage(39), transmission through HBV within maternal PBMC(40,41) 2. **Germline infection** HBV-infected oocytes and embryo(42,43)	1. **Microtransfusion – mixing of maternal and fetal blood**(44) 2. **Direct contact with infected fluid in maternal genital tract**(45) 3. **Swallowing of infected fluids**(44)	1. **Early horizontal transmission – from close contact with infected mothers**(46,47) 2. **Incomplete or delayed vaccination (immunoprophylaxis failure)**(48,49) 3. **Breastfeeding – HBsAg detected at high concentrations in breast milk; however, no significant difference in infection rates between breastfed and non-breastfed infants**(50,51)

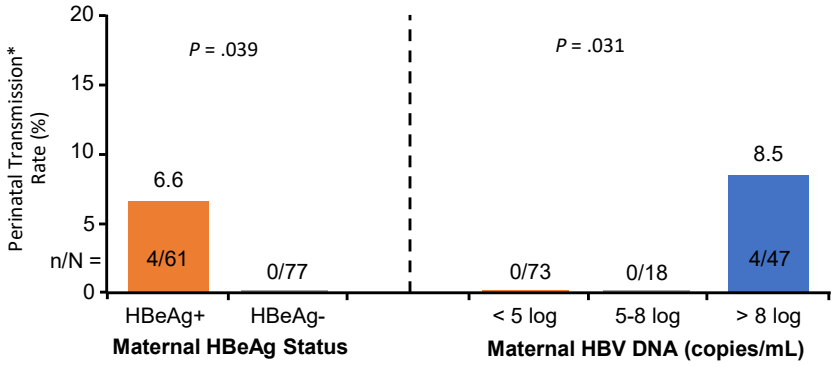
ASGPR, asialoglycoprotein receptor.

JOSHI AND COFFIN. Hepatitis B and Pregnancy: Virologic and Immunologic Characteristics. Hepatology Communications, Vol. 4, No. 2, 2020.

13

Perinatal HBV Transmission Is Related to Maternal eAg status and HBV DNA Level

- All infants received HBIG + first dose HBV vaccine within 12 hrs of birth and additional doses of HBV vaccine at 2, 4, and 6 mos



*Perinatal transmission = HBsAg positive at Mo 9.

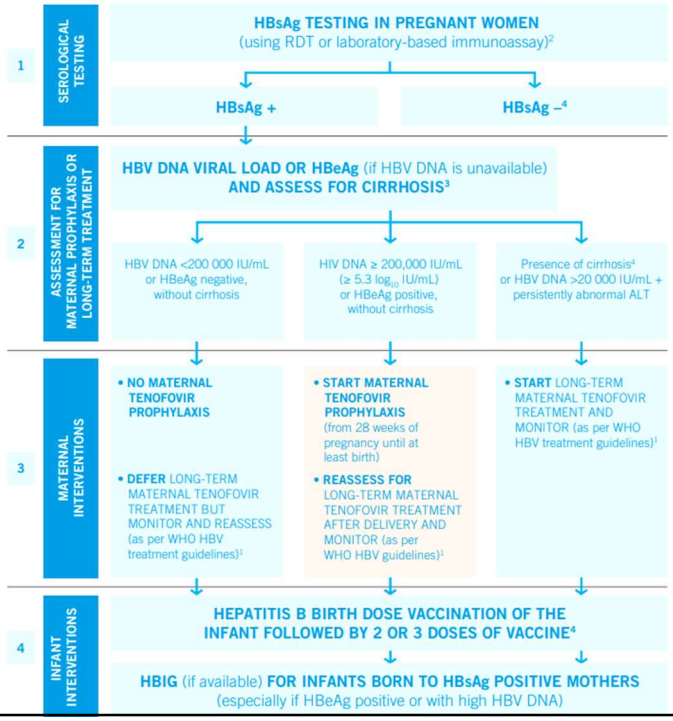
Wiseman E, et al. Med J Aust. 2009;190:489-492.

14

World Health Organization

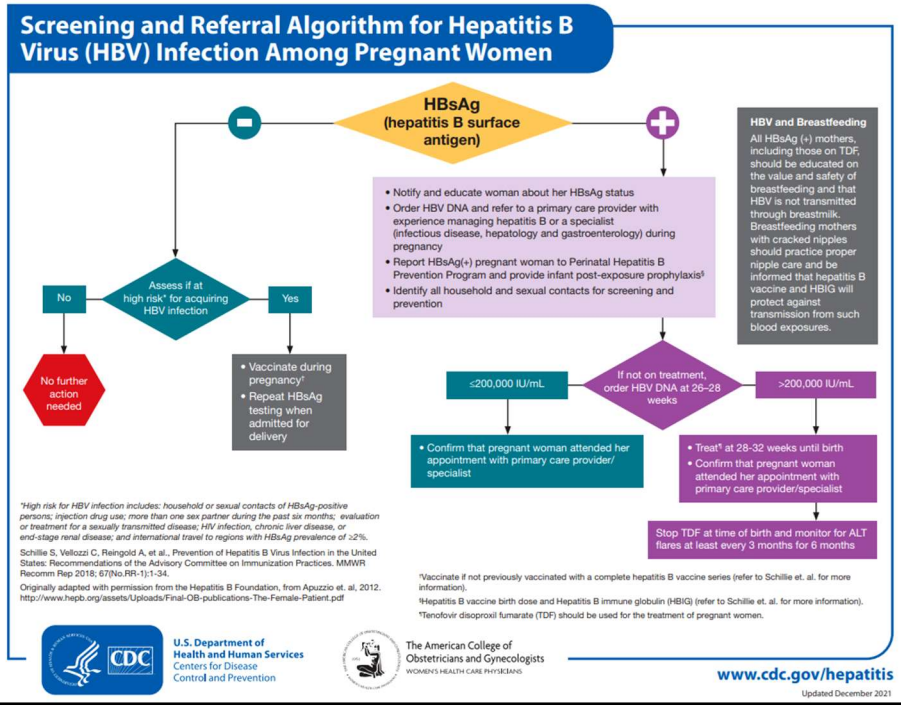
JULY 2020

Algorithm on maternal and infant interventions for prevention of mother-to-child transmission, and assessment of eligibility of mother for treatment for her own health



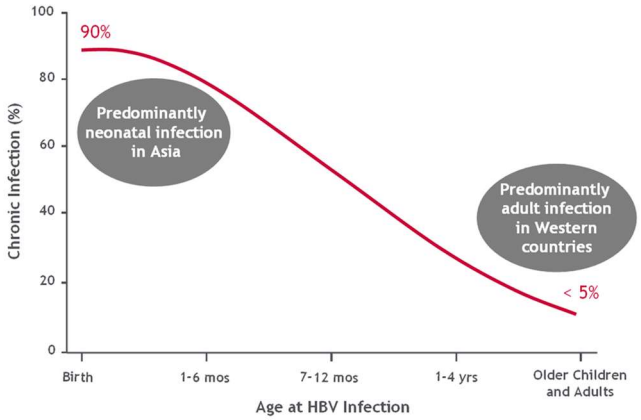
PREVENTION OF MOTHER-TO-CHILD TRANSMISSION OF HEPATITIS B VIRUS: GUIDELINES ON ANTIVIRAL PROPHYLAXIS IN PREGNANCY. WHO JULY 2020.

15



16

Preventing Perinatal HBV Transmission: Why Is It So Important?



Progression to Chronic Infection is Dependent on the Age at Acute HBV Infection

Asian Liver Center. *2007 Physician's Guide to Hepatitis B: A Silent Killer*. http://liver.stanford.edu/files/2007Handbook.pdf. Accessed November 7, 2007.

17

Clinical Practice Guidelines

JOURNAL OF HEPATOLOGY

EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection☆

European Association for the Study of the Liver*

Journal of Hepatology 2017 vol. 67 j 370–398

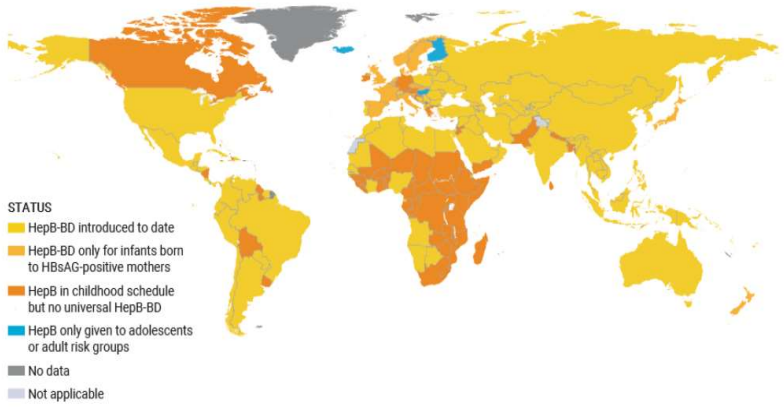
The prevention of HBV perinatal transmission, which is considered to occur mainly at delivery, and causes the majority of chronic HBV infection is based on the combination of HBIG and vaccination given within 12 h of birth. This prophylaxis reduces the rate of perinatal transmission from >90% to <10%.[1] HBIG and vaccine failures occur almost exclusively in HBeAg-positive women with high HBV DNA levels (>200,000 IU/ml) and/or HBsAg level above 4–4.5 $\log_{10}$ IU/ml.[198–201] NA prophylaxis could be also useful in the few HBeAg-negative women with high levels of viremia but normal ALT levels.[198–201] These mothers should be informed that utilising a NA to reduce their viremia levels increase the effectiveness to HBIG and vaccination. LAM, TBV or TDF prophylaxis has been used in this setting during the last trimester of pregnancy. Of them, TDF is the preferred agent due to its characteristics mentioned previously. In a randomised study in pregnant HBsAg-positive women with high HBV DNA levels (>200,000 IU/ml), the rate of mother to child HBV transmission at post-partum week 28 was 0% in those treated with TDF compared to 7% in the placebo control group per protocol analysis having a similar safety profile.[198] If NA therapy is given as prophylaxis, *i.e.*, only for the prevention of perinatal transmission, its duration is not well defined (stopping at delivery or within the first 3 months after delivery). The potential advantage of stopping at delivery is no interference in breast feeding. In addition, TDF ameliorated maternal ALT elevations which can occur during pregnancy or early after delivery in untreated mothers.[202]

18

Global Progress Report on HIV, viral hepatitis and sexually transmitted infections, 2021.

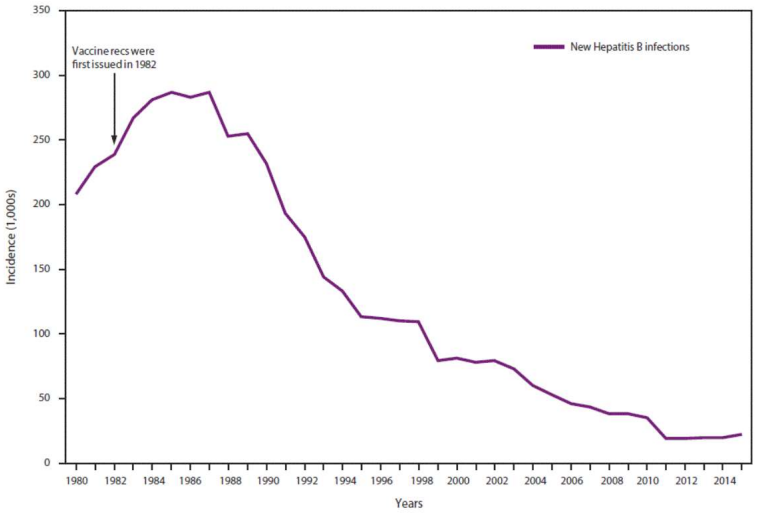
World Health Organization

Hepatitis B birth dose vaccination strategies in the national immunization programme, April 2021



19

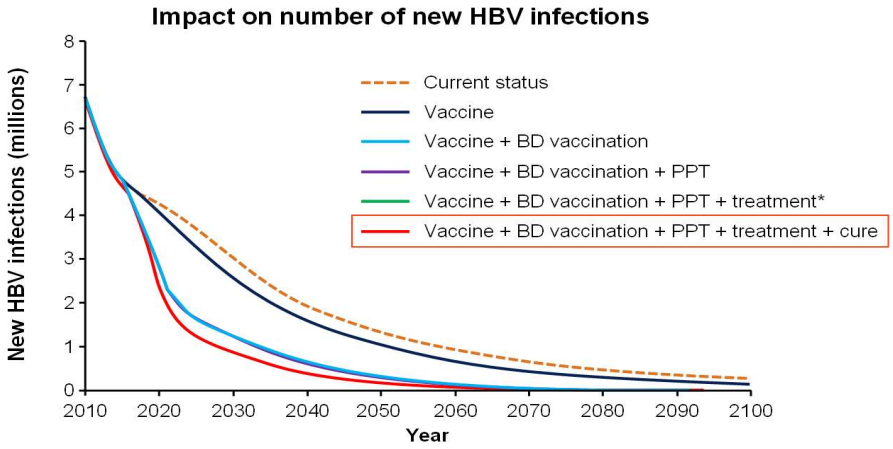
Incidence of hepatitis B virus infection — National Notifiable Diseases Surveillance System, United States, 1980–2015



Sarah Schillie et al. Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. CDC. January 12, 2018 / 67(1);1–31

20

GIẢI PHÁP TỐI ƯU NÀO ĐỂ GIẢM LÂY NHIỄM HBV



*Green line is overlapped by red line.
BD: birth dose; PPT: peripartum antiviral therapy.

Nayagam S, et al. Lancet Infect Dis 2016;16:1399–408

21

III, Điều trị HBV ở phụ nữ mang thai: Dữ liệu mới từ TAF.

Generic Name	Trade Name	Manufacturer	Date Approved for CHB
Interferons			
Interferon alfa-2b, recombinant	Intron® A	Schering Corporation	1992
Peginterferon alfa-2a	Pegasys®	Roche Laboratories	2005
Nucleosides/Nucleotides			
Lamivudine	Epivir-HBV®	GlaxoSmithKline	1998
Adefovir dipivoxil	Hepsera®	Gilead Sciences	2002
Entecavir	Baraclude®	Bristol-Myers Squibb	2005
Telbivudine	Tyzeka®	Idenix and Novartis	2006
Tenofovir DF	Viread®	Gilead Sciences	2008
Tenofovir alafenamide	Vemlidy®	Gilead Sciences	2016

Điều trị HBV như thế nào.

FDA Approved Therapies for CHB

U.S. Food and Drug Administration (FDA)
https://www.fda.gov/forpatients/illness/hepatitisbc/ucm408658.htm Accessed May 18, 2018

22

Goals of HBV Therapy

Goal of CHB Treatment:
To prevent liver-related morbidity and mortality associated with CHB through suppression of HBV replication
(HBV DNA undetectable <10 IU/mL)

↓

Associated with normalization of ALT, loss of HBeAg, and improvement in liver histology

Concomitant goal of antiviral treatment in pregnancy:
Decrease risk of HBV transmission to infant

Terrault. Hepatology. 2016;63:261.

23

BỘ Y TẾ

Số: 3310/QĐ-BYT

CỘNG HÒA XÃ HỘI CHỦ NGHĨA VIỆT NAM
Độc lập - Tự do - Hạnh phúc

Hà Nội, ngày 29 tháng 7 năm 2019

QUYẾT ĐỊNH

VỀ VIỆC BAN HÀNH HƯỚNG DẪN CHẨN ĐOÁN, ĐIỀU TRỊ BỆNH VIÊM GAN VI RÚT B

2. Phòng lây truyền từ mẹ sang con

- Tiêm vắc xin VGVR B liều sau sinh cho tất cả trẻ em theo chương trình tiêm chủng mở rộng.

- Trẻ sinh ra từ mẹ có HBsAg dương tính: tiêm kháng huyết thanh VGVR B và vắc xin VGVR B trong vòng 24 giờ sau sinh. Nên tiêm cùng thời điểm nhưng ở hai vị trí khác nhau. Sau đó tiêm đầy đủ các liều vắc xin VGVR B cho trẻ theo quy định của chương trình tiêm chủng mở rộng.

- Đối với các trường hợp thai phụ có tải lượng HBV DNA > 200.000 IU/mL (> 10^6 copies/mL) hoặc HBsAg định lượng > 10^4 IU/mL, tư vấn điều trị dự phòng lây truyền HBV từ mẹ sang con

+ Dùng TDF từ tuần 24 - 28 của thai kỳ, nếu muộn hơn thì nên bắt đầu ít nhất 4 tuần trước sinh và liên tục đến 4 - 12 tuần sau sinh

+ Theo dõi tình trạng của mẹ gồm triệu chứng lâm sàng, AST, ALT mỗi 4 - 12 tuần, tải lượng HBV DNA trong vòng 24 tuần sau sinh để phát hiện VGVR B bùng phát.

+ Xét nghiệm HBsAg và anti-HBs cho trẻ > 12 tháng tuổi để đánh giá tình trạng nhiễm HBV.

- Không chống chỉ định nuôi con bằng sữa mẹ ở những người mẹ có HBsAg dương tính và mẹ đang sử dụng TDF để điều trị bệnh hoặc điều trị dự phòng

24

SUMMARY OF MAJOR GUIDELINE RECOMMENDATIONS FOR HBV MANAGEMENT IN PREGNANCY

	AASLD 2018[6]	EASL 2017[7]	APASL 2016[8]
HBV-DNA threshold for treatment	>2 x 10^5 IU/mL (10^6 copies/mL) or HBsAg >4log IU/mL	>2 x 10^5 IU/mL (10^6 copies/mL)	10^6-10^7 IU/mL (5 x 10^6 copies/mL)
Treatment initiation gestational age	28-32 weeks	28-32 weeks	28-32 weeks
Preferred drug	TDF (LMV or TBV alternative)	TDF (LMV or TBV alternative)	TDF (LMV or TBV alternative)
Therapy discontinuation	At delivery or up to 12 weeks after delivery; postpartum ALT monitoring suggested every 3 months for 6 months	12 weeks after delivery	At delivery or 4-12 weeks after delivery
Breastfeeding	Not contraindicated. Risk of low-level antiviral exposure to infants should be discussed with mothers	Not contraindicated in untreated and TDF-treated women	Discouraged while mothers are on antiviral therapy
Mode of delivery	Cesarean section is not indicated	No comment	No comment

JOSHI AND COFFIN. Hepatitis B and Pregnancy: Virologic and Immunologic Characteristics. Hepatology Communications, Vol. 4, No. 2, 2020.

25

Tenofovir prophylaxis to prevent mother-to-child transmission of HBV

World Health Organization

JULY 2020

New recommendation

WHO recommends that pregnant women testing positive for HBV infection (HBsAg positive) with an HBV DNA ≥ 5.3 $\log_{10}$ IU/mL (≥ 200,000 IU/mL)[1] receive tenofovir prophylaxis from the 28th week of pregnancy until at least birth, to prevent mother-to-child transmission of HBV. This is in addition to three-dose hepatitis B vaccination in all infants, including timely birth dose *(conditional recommendation, moderate quality of evidence).*

Use of HBeAg testing, where HBV DNA testing is not available, to determine treatment eligibility for tenofovir prophylaxis to prevent mother-to-child transmission of HBV

New recommendation

WHO recommends that in settings in which antenatal HBV DNA testing is not available, HBeAg testing can be used as an alternative to HBV DNA testing to determine eligibility for tenofovir prophylaxis to prevent mother-to-child transmission of HBV[2] *(conditional recommendation, moderate quality of evidence).*

PREVENTION OF MOTHER-TO-CHILD TRANSMISSION OF HEPATITIS B VIRUS: GUIDELINES ON ANTIVIRAL PROPHYLAXIS IN PREGNANCY. WHO JULY 2020.

26

AASLD Guidance: HBV Treatment Options

TRƯỜNG HỢP GẶP PHẢI:

1, Phụ nữ đang điều trị TAF có thai ngoài ý muốn.

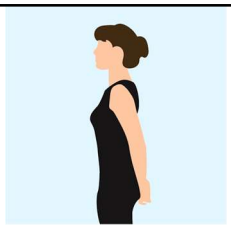
2, Phụ nữ mang thai có loãng xương.

3, Phụ nữ mang thai có bệnh thận mạn.

Terrault. Hepatology. 2018;67:1560.

27

1, Phụ nữ đang điều trị TAF, có thai ngoài ý muốn.



28

2, Phụ nữ mang thai có loãng xương.

Pregnancy Associated Osteoporosis Group UK

Pregnancy Associated Osteoporosis

The Pregnancy Associated Osteoporosis group *are an Expert Patient group.*

Pregnancy Associated Osteoporosis is also known as PLO (Pregnancy and Lactation Osteoporosis)

What is PAO?

This disease is a severe but rare form of osteoporosis affecting women who are pregnant or postpartum. It is associated with frail bones that break with little or no trauma, particularly in the spine, causing debilitating back or hip pain and related complications, possibly long-term.

How common is PAO

The true incidence of PAO is unclear as misdiagnosis is common. It is currently estimated to occur in 4-8 in one million pregnancies.

How is PAO diagnosed?

Diagnosis is usually made through the discovery of multiple low or no impact vertebral compression fractures (VCF) and/or sacral/pelvic/hip or other fractures, confirmed by MRI and/or X-ray. A DEXA (bone density scan) may show that bone mineral density is in the osteoporotic range.

When do PAO fractures occur?

Fractures may present at any point in pregnancy or postpartum, but are most common in the last trimester during childbirth or in the first 12 weeks postpartum.

What causes PAO?

Causes of the disease are not fully understood yet. Large decreases in bone mineral density (BMD) may increase susceptibility to osteoporotic fractures. All women lose BMD during pregnancy and breastfeeding, but this is usually regained naturally after weaning and does not cause issues.
Women with PAO may:

- Experience a greater drop in bone mineral density relative to the average and/or
- Enter pregnancy with a low baseline BMD, making them more susceptible.

29

Pregnancy Associated Osteoporosis Group UK

What are the known risks for development of PAO?

PAO can occur with no apparent risk factors (idiopathic) .

Some risk factors have been identified in some women who develop PAO:

- Inadequate nutritional intake before or during pregnancy impacting bone health:
- Hyperemesis
- Coeliac Disease, Crohn's or other malabsorption issue.
- Dietary restrictions (i.e. vegan diet without adequate calcium intake, and nutrients vital to health and wellbeing)
- History of eating disorder or low BMI (<20)
- Vitamin D deficiency
- Medical history of bone problems
- PAO diagnosed in a previous pregnancy
- Osteopenia or osteoporosis diagnosed prior to pregnancy
- History of fractures prior to pregnancy, including childhood
- Family history of osteoporosis or fragility fractures
- Genetic variants leading to bone formation issues
- Amenorrhea, exercise-induced or otherwise
- Renal stones/hypercalciuria
- Medical treatments that may negatively impact BMD:
- Progestogen-only contraception (including Depo-Provera)
- Anticoagulants before or during pregnancy (including low molecular weight heparin)
- Thyroid hormone
- Corticosteroids
- History of cancer treatment

30

Case Report
Obstet Gynecol Sci 2017;60(1):133-137
https://doi.org/10.5468/ogs.2017.60.1.133
pISSN 2287-8572 · eISSN 2287-8580

Obstetrics & Gynecology Science

Pregnancy-related osteoporosis and spinal fractures

Ka Yeong Yun[1], Si Eun Han[1], Seung Chul Kim[1], Jong Kil Joo[2], Kyu Sup Lee[1]

[1]Medical Research Institute, Pusan National University Hospital, Busan, [2]Department of Obstetrics and Gynecology, Pusan National University School of Medicine, Busan, Korea

Pregnancy-related osteoporosis is a very rare condition characterized by the occurrence of fracture during pregnancy or the puerperium. Despite its relative rarity, it can be a dangerous condition that causes severe back pain, height loss and disability. Normal physiologic changes during pregnancy, genetic or racial difference, obstetrical history and obstetrical disease, such as preterm labor or pregnancy-induced hypertension, are presumed risk factors of pregnancy-related osteooporosis. However, exact etiology and pathogenesis are uncertain. The management and natural history are still poorly defined. Traditional medications for osteoporosis are calcium/vitamin D and bisphosphonate. Concerns with bisphosphonate include accumulation in bone and fetal exposure in subsequent pregnancies. The newly developed medication, teriparatide, has shown good results. We report six cases of pregnancy-related osteoporosis and spinal fracture with literature review.

Keywords: Fractures, compression; Osteoporosis; Pregnancy

31

Qian et al. BMC Musculoskelet Disord (2021) 22:926
https://doi.org/10.1186/s12891-021-04776-7

BMC Musculoskeletal Disorders

RESEARCH Open Access

Pregnancy- and lactation-associated osteoporosis with vertebral fractures: a systematic review

Ying Qian[1], Lei Wang[2], Lili Yu[3] and Weimin Huang[2*]

Abstract

Background: To review, analyze and characterize the pregnancy and lactation-related osteoporosis (PLO) with vertebral fractures based on the extraction data in the previous studies.

Methods: A comprehensive literature search of electronic databases including the PubMed, Embase and Web of Science was conducted from January 1st,1990 to December 1st, 2020. The enrolled data were pooled to analyze the baseline characteristics, clinical features, risk factors and treatment options.

Results: A total of 65 articles with 338 cases were enrolled for data extraction. The enrolled cases aged from 19 to 47 years, with a mean value of 35.7 years old. The average body mass index (BMI) was 22.2 kg/m^2 ranged from 16.0 to 39.0 kg/m^2. Of the 173 cases, 149 cases with vertebral fractures occurred in the first pregnancy, 19 cases in the second pregnancy, four cases in the third pregnancy and one case in the fourth pregnancy. Up to 91.5% of the back pain occurred within the last 3 months of pregnancy and the first 3 months after delivery. The most involved vertebral levels were L2, L1 and T12 accounting for 32.6% of all the fractures. The average fracture numbers were 4.4 levels per patient. The lumbar Z-scores were mostly recorded with a mean value of − 3.2 ranged from − 7.8 to 0.

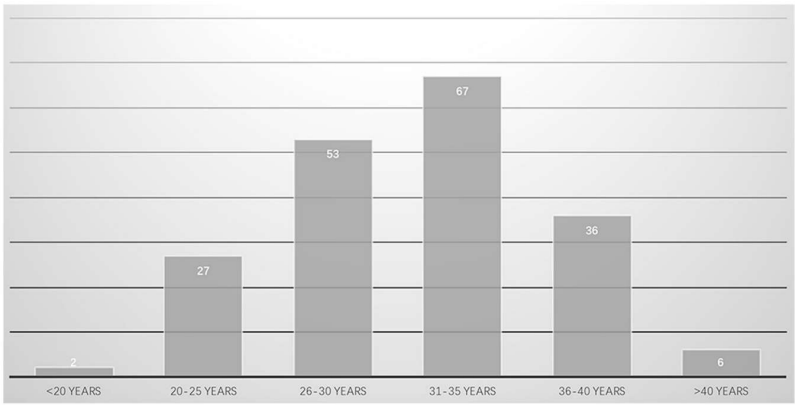
Conclusions: PLO with vertebral fractures is a rare clinical entity, which is more likely to occur in older and thinner pregnant women. Back pain is the clinical complaint and mostly occurs in the late pregnancy and early lactation periods. Most vertebral fractures appear in the first pregnancy but it can occur in any time of pregnancy. Thoracolumbar region is the mostly involved region. As compared with postmenopausal osteoporotic fractures, PLO usually has multiple levels fractures. Bisphosphonates are the most widely used treatment so far, however, many factors need to be taken into account to decide which drug to choose in PLO and further studies are necessary for clear recommendation in the future.

Keywords: Pregnancy, Lactation, Osteoporosis, Vertebral fractures, Systematic review

32

The age distributions of the included population

All the included PLO patients aged 19 to 47years. A total of 191 cases documented the detailed age information with a mean age of 35.7years. Of the 191 cases, 6 cases over 40years old accounting for 3.1%, 109 cases over 30years old accounting for 57.1%, 29 cases under 26 years old accounting for 15.2%.

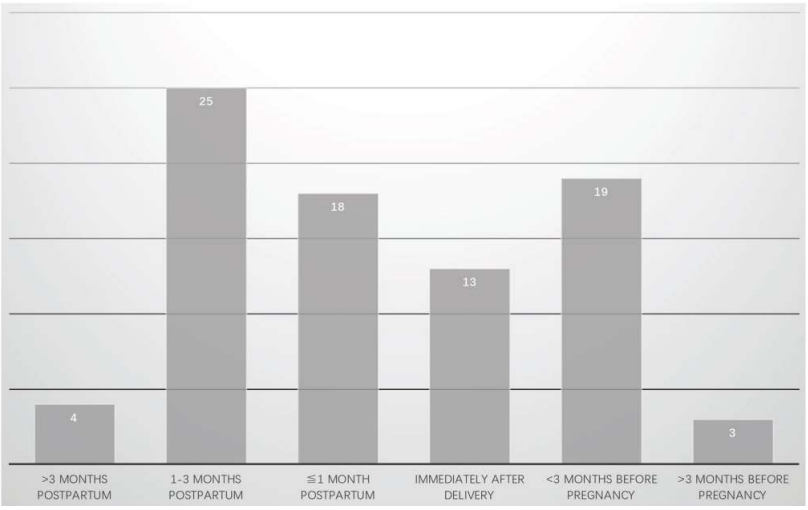


Ying Qian et al. Pregnancy- and lactation-associated osteoporosis with vertebral fractures: a systematic review. BMC Musculoskelet Disord (2021) 22:926

33

Symptom onset time of the included patients

Te earliest time of symptom onset was determined at the 5th month pregnancy, while the latest was at 9 months postpartum. Of the 82 cases with defnite symptom onset time, 75 cases (91.5%) with back pain occurred during the last 3 months of pregnancy and the frst 3 months after delivery



Ying Qian et al. Pregnancy- and lactation-associated osteoporosis with vertebral fractures: a systematic review. BMC Musculoskelet Disord (2021) 22:926

34

Crude prevalence of osteoporosis, by age group, among Vietnamese adult women living in Hanoi City in 2003 who participated in a survey of osteoporosis

Age group (years)	No.	Normal (%)	Osteoporosis (%)
20–29	369	99.2	0.8
30–39	383	97.9	2.1
40–49	407	96.3	3.7
50–59	405	91.6	8.4
60–69	403	69.5	30.5
70–79	217	43.8	56.2
≥80	48	20.8	79.2
Total	2,232	84.6	15.4

Vu Thi Thu Hien et al. Determining the Prevalence of Osteoporosis and Related Factors using Quantitative Ultrasound in Vietnamese Adult Women. Am J Epidemiol 2005;161:824–830

35

3, Phụ nữ mang thai có bệnh thận mạn.

Managing pregnancy in chronic kidney disease: improving outcomes for mother and baby

This article was published in the following Dove Press journal:
International Journal of Women's Health
14 July 2016
Number of times this article has been viewed

Alyssa Fitzpatrick[1]
Fadak Mohammadi[2]
Shilpanjali Jesudason[1–3]

[1]Women's and Babies Division, Women's and Children's Hospital, [2]Central and Northern Adelaide Renal and Transplantation Service, Royal Adelaide Hospital, [3]Department of Medicine, University of Adelaide, Adelaide, South Australia, Australia

Abstract: Parenthood is a central focus for women with chronic kidney disease, but raises important fears and uncertainties about risks to their own and their baby's health. Pregnancy in women with background kidney disease, women receiving dialysis, or those with a functioning kidney transplant poses a challenging clinical scenario, associated with high maternal–fetal morbidity and potential impact on maternal renal health. Improvements in care over recent decades have led to a paradigm shift with cautious optimism and growing interest regarding pregnancies in women with chronic kidney disease. In this review, we discuss obstetric and renal outcomes, and practical aspects of management of pregnancy in this complex cohort.

Keywords: renal, obstetric, fetal, transplant, drugs

Pregnancy and the kidney

The prevalence of chronic kidney disease (CKD) is rising, and may affect 3% of women in their childbearing years.[1] Preexisting CKD of any stage impacts upon maternal and perinatal outcomes. The challenging nature of these pregnancies underscores the need for careful prepregnancy planning in known CKD patients, early identification of new-onset maternal CKD, management of pregnancy with shared decision making, and a patient-centered approach, in an integrated specialized obstetric and nephrology service. This review provides an overview of key issues in clinical management for women with CKD and their infants and discusses strategies for preconception counseling for those planning pregnancy.

International Journal of Women's Health 2016:8 273–285

36

› Nephrol Dial Transplant. 2009 Dec;24(12):3744-50. doi: 10.1093/ndt/gfp320. Epub 2009 Jul 3.

Kidney function and future risk for adverse pregnancy outcomes: a population-based study from HUNT II, Norway

John Munkhaugen [1], Stian Lydersen, Pål Richard Romundstad, Tor-Erik Widerøe, Bjørn Egil Vikse, Stein Hallan

Affiliations + expand

PMID: 19578097 DOI: 10.1093/ndt/gfp320

Abstract

Background: Current knowledge on prepregnancy reduced kidney function and the risk of adverse pregnancy outcomes mainly relies on small studies in selected populations. We aim to investigate whether reduced kidney function is associated with the risk of adverse pregnancy-related outcomes in the general population.

Methods: A population-based study linking all women attending the Second Health Study in Nord-Trøndelag, Norway (1995-97) and subsequent pregnancies registered in the Medical Birth Registry. Multivariable random-effect logistic regression analysis was used to explore the association between renal function and study outcome.

Results

Over an 11-year period, 3405 women gave birth to 5655 singletons (mean time 4.7 ± 2.5 years after the HUNT 2 Study). In all, we identified 885 (17.7%) cases with our main study outcomes (preeclampsia, $n = 204$; small for gestational age, $n = 537$; preterm birth, $n = 285$). The characteristics of the women who attended the HUNT 2 Study and subsequently became pregnant are presented in Table 1. The mean eGFR was 107.6 ± 19.4 ml/min/1.73 m^2 and microalbuminuria calculated by multiple imputation was present in 3.2% of the women. The overall prevalence of CKD was 3.3%, and CKD stages 1, 2 and 3 occurred in 2.4%, 0.8% and 0.1%, respectively. No women with CKD 4 or 5 gave birth during the follow-up period.

37

Wiles et al. BMC Nephrology (2019) 20:401
https://doi.org/10.1186/s12882-019-1560-2

BMC Nephrology

THE RENAL ASSOCIATION founded 1950

GUIDELINES Open Access

Clinical practice guideline on pregnancy and renal disease

Kate Wiles[1*], Lucy Chappell[2], Katherine Clark[3], Louise Elman[4], Matt Hall[5], Liz Lightstone[6], Germin Mohamed[4], Durba Mukherjee[4], Catherine Nelson-Piercy[7], Philip Webster[8], Rebecca Whybrow[9] and Kate Bramham[10]

Introduction

Background

Chronic kidney disease (CKD) is estimated to affect 3% of pregnant women in high-income countries, (Piccoli et al., 2018, #13860) which equates to between 15,000–20,000 pregnancies per year in England. The prevalence of CKD in pregnancy is predicted to rise in the future due to increasing maternal age and obesity.

Although CKD is not a barrier to reproduction in most women, the risk of adverse pregnancy outcomes is increased in women with CKD including pre-eclampsia, fetal growth restriction, preterm delivery and accelerated loss of maternal renal function. CKD impacts on communication, decision-making, and the surveillance and management of women before, during, and after pregnancy.

Existing guidance on the management of CKD in pregnancy includes the UK Consensus Group on Pregnancy in Renal Disease (ISBN 978–1,107,124,073) and expert review. Neither Kidney Disease Outcomes Quality Initiative (KDOQI) or National Institute of Health and Care Excellence (NICE) have produced specific guidance on the management of renal disease in pregnancy. Published guidance containing information relevant to the care of women with CKD in pregnancy includes:

- KDOQI Clinical Practice Guideline for Haemodialysis, 2015.
- KDIGO Clinical Practice Guideline for the Evaluation and Management of CKD, 2012
- KDIGO Clinical Practice Guideline for Glomerulonephritis, 2012
- KDIGO Guideline for the Care of Kidney Transplant Recipients, 2009.
- KDIGO Clinical Practice Guidelines for Nutrition in Chronic Renal Failure, 2008.
- NICE: Intrapartum Care for Women with Existing Medical Conditions or Obstetric Complications and their Babies [NG121], 2019.
- NICE: Urinary Tract Infection (Lower) Antimicrobial Prescribing [NG109], 2018
- NICE: Urinary Tract Infection (Recurrent) Antimicrobial Prescribing [NG112], 2018.
- NICE: Antenatal Care for Uncomplicated Pregnancies [CG62], 2008, updated 2017.
- NICE: Vitamin D supplement use in specific population groups [PH56], 2017
- NICE: Diabetes in Pregnancy: Management from Pre-conception to the Post-partum Period [NG3], 2015.
- NICE: Antenatal and postnatal mental health: clinical management and service guidance [CG192], 2014, updated 2018

38

Published in final edited form as:
Am J Kidney Dis. 2019 January ; 73(1): 119–130. doi:10.1053/j.ajkd.2018.06.006.

Renal Disorders in Pregnancy: Core Curriculum 2019

Maria L. Gonzalez Suarez, MD, PhD[1], **Andrea Kattah, MD**[2], **Joseph P. Grande, MD, PhD**[3], and **Vesna Garovic, MD, PhD**[2,*]

[1]Division of Nephrology, Department of Medicine, University of Mississippi Medical Center, Jackson, MS;

[2]Division of Nephrology and Hypertension, Department of Medicine, Mayo Clinic, Rochester, MN;

[3]Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN

Abstract

As the incidence of chronic kidney disease (CKD) increases and women pursue pregnancy at more advanced ages, the management of renal disease in pregnancy has become increasingly relevant to the practicing nephrologist. Women with renal disorders face several challenges in pregnancy due to increased physiologic demands on the kidney and risk for disease progression, the potential teratogenicity of medications, and the increased risk of complications such as preeclampsia and preterm delivery. Challenges posed by an underlying disease process in pregnancy, such as autoimmune disease or diabetes mellitus (DM), necessitate an interdisciplinary team to ensure good maternal and fetal outcomes. Rates of acute kidney injury (AKI) in pregnancy are generally declining worldwide, but remain a significant public health concern in developing countries. Pregnancy may also be the first time that a woman is diagnosed as having renal disease or hypertension. An understanding of what constitutes normal physiologic changes in pregnancy is critical in a diagnostic evaluation. In this review, we will review the physiologic changes in pregnancy, the causes and management of AKI in pregnancy, hypertensive disorders of pregnancy, and how to care for women with CKD of various etiologies, including the use of anti-hypertensives and immunosuppressants.

39

Điều trị HBV ở phụ nữ mang thai: Dữ liệu mới từ TAF.

TAF hiệu quả & an toàn cho phụ nữ mang thai trong nhiều nghiên cứu.

Multicenter, prospective study of 60 pregnant women who were receiving TAF or switched to TAF were followed until at least post-partum Month 7

Maternal Characteristics	n=60
Mean age, years ± SD	30±5
Mean gestational age at TAF initiation, weeks ± SD	1.0 ±13.7
Mean ALT, U/L ± SD	113±93
Mean HBV DNA, $\log_{10}$ IU/mL ± SD	4.6±3.5
Mean TAF treatment duration, weeks ± SD	82±20
Maternal Outcomes	**n=60**
Virologic breakthrough, n (%)	2 (3)

Infant Outcomes	n=59*
MTCT at month 7, n (%)	0
Breast fed, n (%)	43 (73)
Congenital defects or malformations, n (%)	0

*One mother who initiated TAF at 12 weeks of pregnancy underwent induced abortion at 23 weeks of gestation due to the diagnosis of cleft lip and palate for the fetus.

Physical and neurological development of infants was normal at birth, 7 months, and 12 months

TAF administered throughout pregnancy in women with active CHB was generally safe for both mothers and infants, and reduced the MTCT rate to 0%

Infants received standard immunoprophylaxis and were followed until at least postpartum Month 7.
Zeng Q-L, et al. EASL 2021. #990

40

Antiviral kinetics of tenofovir alafenamide and tenofovir disoproxil fumarate over 24 weeks in women of childbearing potential with chronic HBV

Background/purpose: Use of tenofovir disoproxil fumarate (TDF) improves patient outcomes in preventing mother-to-child transmission (pMTCT) of the hepatitis B virus (HBV) in mothers with chronic HBV and high viral loads. Given the lack of data for tenofovir alafenamide (TAF) in pMTCT, rates of early viral suppression with TAF and TDF were evaluated in women of childbearing potential (WOCBP) participating in 2 randomized, double-blind, Phase 3 studies in chronic HBV.

Methods: In a patient subset meeting WOCBP criteria and with baseline HBV DNA >200,000 IU/mL, rates of viral suppression with TAF or TDF in achieving the target of HBV DNA <200,000 IU/mL at weeks 12 and 24 were assessed. Multivariate logistic regression was used to identify factors predictive of failure to suppress HBV DNA to the target level.

Results: In 275 of 1298 (21%) patients meeting WOCBP criteria with high viral load, 93% and 96% had HBV DNA <200,000 IU/mL at weeks 12 and 24, respectively. Results for TAF (n = 194) vs TDF (n = 81) treatment were similar at weeks 12 and 24 (94% vs. 90% and 97% vs. 93%), respectively. High baseline HBV DNA level, genotype D infection, and prior interferon (week 24 only) were predictive of failure to achieve the target level. Both treatments were well tolerated with TAF showing less impact on renal and bone parameters.

Conclusions: In WOCBP with high VL, no differences were found between TAF and TDF in reducing HBV DNA to levels associated with lower transmission risk. These data support ongoing studies of TAF for pMTCT.

Calvin Q Pan et al. PLoS One . 2021 May 13;16(5)

41

Efficacy and safety of tenofovir alafenamide fumarate for preventing mother-to-child transmission of hepatitis B virus: a national cohort study

Background: Data on tenofovir alafenamide fumarate (TAF) for preventing mother-to-child transmission of hepatitis B virus (HBV) are lacking.

Aims: To investigate the efficacy and safety of TAF therapy for preventing hepatitis B mother-to-child transmission.

Methods: Mothers with chronic HBV infection, positive for hepatitis B e-antigen and with HBV DNA >200 000 IU/mL received TAF for preventing mother-to-child transmission were enrolled retrospectively from multiple centres with data collection on mother-infant dyads up to postpartum week 24-28. Primary measurements were the mother-to-child transmission rate and infants' malformation rate. Secondary assessments included maternal HBV DNA reduction at delivery, and maternal or infant adverse events during follow up.

Results: Among 71 mothers enrolled, the mean (±SD) age was 30.3 (±2.2) years. TAF was initiated during the second or third trimester and continued to delivery with a mean (±SD) duration of 12.8 (±4.0) weeks. At delivery, 85.9% (61/71) of the mothers achieved HBV DNA <200 000 IU/L. Seventy-three infants (two sets of twins) were born from mothers treated with TAF and none had congenital defects or malformations. All infants received HBV immunoglobulin and vaccine at birth with additional HBV vaccinations at one and six months. At age 24-28 weeks, all infants had negative hepatitis B surface antigen and undetectable levels of HBV DNA (<100 IU/mL). Body weight, height, and head circumferences were comparable to national standards for physical development. No severe adverse effects were reported in either mothers or infants.

Conclusions: TAF for highly viraemic mothers effectively prevented mother-to-child transmission of hepatitis B. There were no safety concerns for either mothers or infants with 24-28 weeks of follow up.

Yang Ding et al. Aliment Pharmacol Ther. 2020 Oct;52(8):1377-1386.

42

Tenofovir Alafenamide to Prevent Perinatal Hepatitis B Transmission: A Multicenter, Prospective, Observational Study

Background: Few safety and effectiveness results have been published regarding the administration of tenofovir alafenamide fumarate (TAF) during pregnancy for the prevention of mother-to-child transmission (MTCT) of hepatitis B virus (HBV).

Methods: In this multicenter prospective observational study, pregnant women with HBV DNA levels higher than 200 000 IU/mL who received TAF or tenofovir disoproxil fumarate (TDF) from gestational weeks 24-35 to delivery were 1:1 enrolled and followed until postpartum month 6. Infants received immunoprophylaxis. The primary endpoint was the safety of mothers and infants. The secondary endpoint was the hepatitis B surface antigen (HBsAg)-positive rate at 7 months for infants.

Results: In total, 116 and 116 mothers were enrolled, and 117 and 116 infants were born, in the TAF and TDF groups, respectively. TAF was well tolerated during a mean treatment duration of 11.0 weeks. The most common maternal adverse event was nausea (19.0%). One (0.9%), 3 (2.6%), and 9 (7.8%) mothers had abnormal alanine aminotransferase levels at delivery and at postpartum months 3 and 6, respectively. The TDF group had safety profiles that were comparable to those of the TAF group. No infants had birth defects in either group. The infants' physical and neurological development at birth and at 7 months in the TAF group were comparable with those in the TDF group. The HBsAg positive rate was 0% at 7 months in all 233 infants.

Conclusions: Antiviral prophylaxis with TAF was determined to be generally safe for both mothers and infants and reduced the MTCT rate to 0%.

Qing-Lei Zeng et al. *Clinical Infectious Diseases*, Volume 73, Issue 9, 1 November 2021, Pages e3324–e3332

43

Tenofovir Alafenamide for Pregnant Chinese Women With Active Chronic Hepatitis B: A Multicenter Prospective Study

BACKGROUND & AIMS: **Data on long-term tenofovir alafenamide (TAF) therapy for pregnant women with active chronic hepatitis B (CHB) (immune clearance and reactivation phases, currently and previously diagnosed) and their infants are lacking.**

METHODS: **Pregnant women with active CHB treated with TAF and tenofovir disoproxil fumarate (TDF) were enrolled in this multicenter prospective study, and infants received immunoprophylaxis. The primary outcomes were rates of adverse (safety) events in pregnant women and defects in infants and fetuses. The secondary outcomes were virologic responses in pregnant women, infants' safety, hepatitis B surface antigen (HBsAg) status, and growth conditions.**

RESULTS: **One hundred three and 104 pregnant women were enrolled and 102 and 104 infants were born in the TAF and TDF groups, respectively. In the TAF group, the mean age, gestational age, alanine aminotransferase level, and viral loads at treatment initiation were 29.3 years, 1.3 weeks, 122.2 U/L, and 5.1 $\log_{10}$ IU/mL, respectively. TAF was well-tolerated, and the most common adverse event was nausea (29.1%) during a mean of 2 years of treatment. Notably, 1 (1.0%) TAF-treated pregnant woman underwent induced abortion due to noncausal fetal cleft lip and palate. No infants in either group had birth defects. In the TAF group, the hepatitis B e antigen seroconversion rate was 20.7% at postpartum month 6, infants had normal growth parameters, and no infants were positive for HBsAg at 7 months. The TDF group had comparable safety and effectiveness profiles.**

CONCLUSIONS: **TAF administered throughout or beginning in early pregnancy is generally safe and effective for pregnant women with active CHB and their infants.**

Qing-Lei Zeng et al. Clinical Gastroenterology and Hepatology 2021 Dec 11;S1542-3565(21)01306-9

44

TAF for Prevention of HBV Vertical Transmission

- Multicenter, real-world, TDF-controlled study (N = 207)
- **Eligibility**
  - Maternal age >20 yr
  - All pregnancy stages
  - Newly diagnosed with active CHB (treatment naive)
  - Previously diagnosed with active CHB (receiving non-TAF regimen; continue TDF or switch to TAF or TDF from another regimen)
- **Primary endpoints**
  - **Maternal safety:** perinatal adverse events and complications, ALT flare and kidney function at delivery, and postpartum Mo 3 and 6
  - **Infant safety:** structural defects at birth, Apgar scores at 1 min, and abnormal conditions from birth to 7 mo
  - **Infant** anthropometric indexes at birth and 7 mo
- **Secondary endpoints**
  - **Maternal:** rate of undetectable HBV DNA, ALT normalization, and HBeAg and HBsAg loss
  - **Infant:** HBV serologic markers at 7 mo

Zeng. AASLD 2021. Abstr OA19.

45

TAF for Prevention of HBV Vertical Transmission: Maternal Safety

Safety Result, n (%)	TAF (n = 103)*	TDF (n = 104)*
Perinatal adverse events in ≥10% of women		
•Nausea	30 (29.1)	33 (31.7)
•Anorexia	23 (22.3)	21 (20.2)
•Fatigue	19 (18.4)	20 (19.2)
•Vomiting	11 (10.7)	11 (10.6)
Complications in ≥2% of women		
•Premature rupture of membranes	13 (12.6)	14 (13.5)
•Preterm labor	3 (2.9)	4 (3.8)
•Gestational hypertension	3 (2.9)	4 (3.8)
•Pneumonia	1 (1.0)	4 (3.8)

*All *P* values >.05 for TAF vs TDF group.

Zeng. AASLD 2021. Abstr OA19.

46

TAF for Prevention of HBV Vertical Transmission: Infant Efficacy

- Perinatal transmission rate was 0% at 7 mo
  - Positive anti-HBs: 99.0% and 100% of infants in TAF and TDF groups, respectively

Maternal Efficacy Result at Postpartum Mo 18, % (n/N)	TAF (n = 103)*	TDF (n = 104)*
HBV DNA target not detected		
•Treatment-naive group	100 (19/19)	100 (22/22)
•Switchover or continuation group	100 (11/11)	100 (10/10)
ALT normalization		
•Treatment-naive group	94.7 (18/19)	95.5 (21/22)
•Switchover or continuation group	100 (11/11)	100 (10/10)
HBeAg seroconversion		
•Treatment-naive group	22.0 (13/59)	21.1 (12/57)
•Switchover or continuation group	30.4 (7/23)	29.0 (9/31)

*All *P* values >.05 for TAF vs TDF group.

Physical and neurological development of infants was normal at birth, 7 months, 12 months, and 18 months

TAF and TDF were generally safe and effective for infants

Zeng. AASLD 2021. Abstr OA19.

47

What's New in the Guidelines | NIH - Clinical Info HIV.gov

Recommendations for Use of Antiretroviral Drugs During Pregnancy

- The Panel continues to recommend dolutegravir (DTG) as a *Preferred* ARV drug for pregnant people, irrespective of trimester, and for people who are trying to conceive. The most recent data from the Tsepamo study in Botswana indicate that, although the prevalence of infant neural tube defects (NTDs) with periconception use of DTG was higher than the prevalence of NTDs in infants born to women who were receiving efavirenz and women without HIV, the prevalence was not significantly increased compared with women with HIV receiving non-DTG ARV regimens at conception. Based on these and other data, the Panel has removed bulleted recommendations with DTG-specific cautions.
- Based on additional data about the use and safety of tenofovir alafenamide (TAF), the Panel now recommends TAF as a *Preferred* nucleoside reverse transcriptase inhibitor for ARV regimens in people who are pregnant or are trying to conceive.
- Available data about weight gain with TAF and with DTG during pregnancy have been reviewed and incorporated in this section.
- Oral cabotegravir (CAB) and the new long-acting injectable regimen of CAB and rilpivirine (RPV) have been classified as *Not Recommended* for use in pregnancy and as *Insufficient Data* for persons who are trying to conceive or who become pregnant while on this regimen.
- Revisions have been made to the sections listed below to incorporate the Panel's updated recommendations about ARV drugs during pregnancy and for people who are trying to conceive.

What's New in the Guidelines

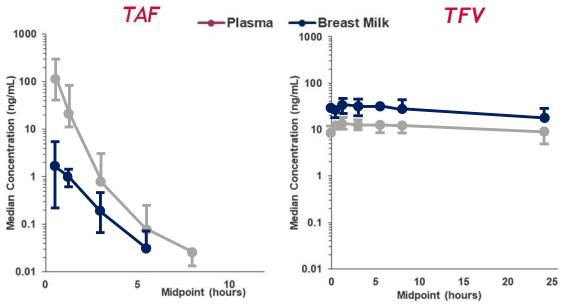
Updated: Mar. 17, 2022
Reviewed: Mar. 17, 2022

48

Pharmacokinetics of TAF in Breast Milk

Phase IV, open-label, single-arm, multicenter study evaluating PK of TAF and TFV in 10 breastfeeding women with CHB

Concentrations Over Time



Pharmacokinetics

	Half Life (hours)	C_{max} (ng/mL)	T_{max} (hours)	AUC_{all} (ng*h/mL)
Plasma TFV	40.5 (18.5-65.1)	16.7 (11.3-19.9)	1.25 (0.7-2.6)	207.4 (146.4-305.6)
Plasma TAF	0.9 (0.7-1.1)	166.5 (84.5-354.8)	0.5 (0.5-1.1)	149.9 (70.9-214.3)
Breastmilk TFV	27.7 (20.0-35.4)	53.1 (29.6-57.8)	5.5 (3-8)	584.7 (453.7-1015.8)
Breastmilk TAF	0.8 (0.8-3.3)	2.3 (0.9-11.6)	0.5 (0.5-1.3)	2.9 (2.4-3.4)

The relative infant dose of TAF is 0.07% of maternal dose of drug, well below accepted standard of safe exposure (<10%)

Concentrations of TAF and TFV were low in breastmilk with negligible exposure to infants

Lower limit of quantification: TFV 1.00 ng/mL for blood/breastmilk and 10.0 ng/mL for urine; TAF 0.05 ng/mL for blood/breast milk.

Kayes T, et al. AASLD 2021. 772

49

Medic Center

IV, Kết luận.

- Viêm gan B là bệnh hay gặp ở nước ta: Tỉ lệ nữ mang thai nhiễm HBV cũng cao.

  Tất cả phụ nữ mang thai phải được xét nghiệm HBV để có hướng xử trí thích hợp.

- Phụ nữ có thai đang điều trị HBV thì cứ tiếp tục điều trị với thuốc TDF: Tiếp tục thuốc TDF hoặc chuyển đổi qua TDF nếu dùng thuốc khác.

  TDF là thuốc được đề nghị dùng cho phụ nữ có thai theo đa số các guideline.

- Có chiến lược tư vấn kiến thức lây lan cho tất cả các phụ nữ nhiễm HBV, đặc biệt điều trị dự phòng lây từ mẹ sang con đúng chỉ định.
- Được phép cho con bú trong khi điều trị thuốc kháng siêu vi B.
- Với các dữ liệu an toàn và hiệu quả mới, TAF có thể sẽ được xem xét cho phép để điều trị HBV ở phụ nữ có thai.

50

51