

論文内容要旨

Intermediate hepatitis B virus infection
prevalence among 1622 pregnant women in rural
Burkina Faso and implications for mother-to-child
transmission

(妊婦 1622 人を対象としたブルキナファソ農村部における B 型肝炎ウイルス感染疫学状況と HBV 母子感染への影響に関する考察)

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【Background】

In countries highly endemic to hepatitis B virus (HBV) infection, mother-to-child transmission (MTCT) is the main transmission mode. The risk of MTCT increases in pregnant women with high viral load (HBV DNA >200,000 IU/mL) or positive for Hepatitis B e antigen (HBeAg). Therefore, in 2020, the World Health Organization (WHO) recommended screening pregnant women for Hepatitis B surface Antigen (HBsAg) and administering antivirals to HBsAg-positive pregnant women with viral load >200,000 IU/mL or those positive for HBeAg if the viral load is unavailable.

Burkina Faso, in West Africa, is endemic to HBV infection and the prevalence is higher in rural areas (BMC Public Health, 2018). Our previous study in Nanoro, rural Burkina Faso in 2018 revealed an HBsAg prevalence of 6.3% in mothers of children under 5 years old, indicating a potential risk for MTCT (BMC Infectious Diseases, 2020). However, there is no routine HBV screening for pregnant women in Burkina Faso, so pregnant women at high risk of MTCT is unknown, and HBV prevention measures are insufficient. Previously, we demonstrated that dried blood spot (DBS) technology is highly performant in detecting HBV seromarkers and is an effective tool for HBV research in resource-limited countries (GastroHep, 2021). Therefore, the purpose of this study is to confirm the prevalence of HBsAg in pregnant women in rural Burkina Faso and to determine the proportion of those with high viral load or HBeAg-positive using DBS samples, to implement effective prevention measures.

【Methods】

This study is part of a large-scale longitudinal research aiming to prevent HBV MTCT in Burkina Faso. Within this research, we conducted a cross-sectional study in three peripheral health centers in Yako, rural Burkina Faso, among pregnant women visiting these hospitals for antenatal care between February and November 2021. The minimum required sample size was calculated to be 1,431. Pregnant women were recruited using a consecutive sampling method after obtention of their informed consent. A questionnaire was administered to collect their characteristics and potential HBV risk factors.

All pregnant women were tested for HBsAg using a rapid diagnostic test approved by WHO for official use (Determine HBsAg 2, Abbott Laboratories, IL, USA, analytical sensitivity of 0.1 IU/mL). DBS samples were collected from HBsAg-positive pregnant women using the Hemospot™ device (Spot on Sciences, CA, USA) and stored at -20 degrees until shipment to Hiroshima University for laboratory analyses. HBV seromarkers were detected by chemiluminescent enzyme immunoassay (CLEIA, Fujirebio, Japan) using our previously published method, which compared DBS samples to paired serum samples and showed a sensitivity for HBsAg, HBeAg, and HBeAb of 89.3%, 100%, and 100%, respectively, and 100% specificity for all three seromarkers (GastroHep, 2021). Molecular analyses (real-time PCR, nested PCR, partial genome sequencing) were performed to measure HBV viral load and

identify genotypes. Multivariable analysis was performed to assess factors associated with HBsAg positivity, with a significant level set at 0.05.

【Results】

A total of 1,622 pregnant women were recruited, with a mean age of 25.1 ± 6.0 years (range 15-46 years). Of them, 106 were positive for HBsAg by rapid test, giving a prevalence of 6.5%. similar to our previous study in Nanoro. By multivariable logistic regression analysis, factors associated with HBsAg positivity were age 25-34 years (aOR=2.24, p=0.005), having never heard of HBV (aOR=1.63, p=0.022), and female genital mutilation (aOR=2.25, p=0.013).

Of the 106 positives for HBsAg by rapid test among 1622 pregnant women, one participant was missing DBS sample, and three were negative for HBsAg by CLEIA, so 102 HBsAg-positive cases by CLEIA were tested for HBeAg and HBeAb. The prevalence of HBeAg was 22.6% (23/102) and decreased with age (p=0.040), while HBeAb was positive at 66.7% (68/102) and increased with age (p=0.005). Of the 102 HBsAg-positive samples by CLEIA, 8 were excluded for an insufficient amount in DBS, and we could quantify viral load in 94 HBsAg-positive samples. The median viral load was 193,580.0 IU/mL in HBeAg-positive cases and was significantly higher than the median viral load of 12,011 IU/mL in HBeAg-negative cases (p<0.001).

Of the 94 HBsAg-positive pregnant women in which viral load was quantified, 18 (19.1%) had a viral load greater than 200,000 IU/mL. Genotype could be identified in 63 samples, and genotype E was predominant at 58.7% (37/63), followed by genotype A (36.5%, 23/63), B (3.2%, 2/63), and C (1.6%, 1/63). Viral load >200,000 IU/mL was lower in genotype A (2/23, 8.7%) than in genotype E (13/37, 35.1%), while the HBeAg positivity rate was higher in genotype A (36.1%, 9/23) than in genotype E (24.3%, 9/37).

Overall, among 94 samples, HBeAg sensitivity to predict viral load >200,000 IU/ml, the cut-off for antiviral prophylaxis recommended by the WHO was 55.6% (10/18), and the specificity was 86.8% (66/76). Among 63 samples with identified genotypes, 16 (25.4%) had viral load >200,000 IU/ml, of which 13 (81.2%) were genotype E, 2 (12.5%) were genotype A and 1 (6.3%) was genotype B. The sensitivity of HBeAg in predicting high viral load was lower in genotype E (53.8%, 7/13) than in genotype A (100%, 2/2), while the specificity was higher in genotype E (91.7%, 22/24) than in genotype A (66.7%, 14/21).

【Conclusion】

This large-scale study among 1,622 pregnant women confirmed HBsAg prevalence of 6.5% in rural Burkina Faso, as previously reported, and also revealed for the first time that among HBsAg-positive pregnant, 19.1% (viral load >200,000 IU/mL) to 22.6% (HBeAg-positive) are at risk of MTCT. This situation is alarming for HBV elimination by 2030. To address this issue, antenatal care programs in Burkina Faso should urgently implement routine HBsAg screening for all pregnant women, particularly in rural areas. In addition,

vaccination of babies at birth and administering antivirals to pregnant women should also be initiated as recommended by the WHO and Burkina Faso guidelines for the prevention of MTCT of HBV.

According to the WHO guidelines, HBeAg can be used in countries where viral load testing is unavailable, with 88.3% sensitivity to detect viral load over 200,000 IU/mL. However, this study in Burkina Faso revealed 55.6% sensitivity for HBeAg to detect high viral, meaning that almost half of the pregnant women with a viral load over 200,000 IU/mL were HBeAg-negative and would not receive treatment. The lower sensitivity in this study seems to be due to genotype E. Therefore, this study alerts caution in using HBeAg as an alternative to viral load testing in genotype E-predominant countries.

Given the high incidence of HBV in Africa, it is essential to use efficient tools adapted to this region to control MTCT. One of these tools is DBS, which can be used in resource-limited countries, as demonstrated in this study. Although HBeAg testing is more available in developing countries, this study showed that it is not sensitive enough to decide on antiviral prophylaxis in pregnant women in Africa. Therefore, there is an urgent need to develop affordable and easy-to-use point-of-care viral load tests.

In conclusion, this study provided valuable data for establishing evidence-based prevention measures for HBV MTCT in Burkina Faso and other African countries, which can contribute to the global effort to eliminate HBV.