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Major Article

Hepatitis B prophylaxis in newborns: A cross-sectional study of 7-year attendance in a public hospital of Brazil

Alex S. Jorge MSc [a,*], Barbara S. Horvath [a], Claudia Ariati [a], Jessica C. Silva [a], Lucas B. Lima [a], Josana D. Horvath [b], Jorge Juarez Vieira Teixeira PhD [c], Dennis Armando Bertolini PhD [c]

[a] Medical and Pharmaceutical Science Centre, West Parana State University, Cascavel, Paraná, Brazil
[b] Specialized Centre in Infectious and Parasitary Diseases, Cascavel, Paraná, Brazil
[c] Department of Clinical Analysis and Biomedicine, State University of Maringa, Maringa, Paraná, Brazil

Key Words:
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Background: Children with vertically transmitted hepatitis B virus develop chronic infection up to 90% of the time. This study aimed to verify the prevalence of hepatitis B surface antigen (HBsAg) in pregnant patients treated in a Brazilian public hospital and analyze the prophylactic measures in newborns.

Methods: A cross-sectional study was conducted by collcting data in the electronic charts of patients who attended the obstetric and maternity departments, from January 1, 2010, to December 31, 2016, and evaluating the results of pregnant women's HBsAg, prophylaxis in newborns, and clinical follow-up. The data were tabulated and analyzed using Microsoft Excel software.

Results: Among the 7,763 participating patients, 109 were reactive to HBsAg, and 3 were indeterminate. However, only 28 had correct information on HBV prophylaxis with the parturient and newborn in the chart, and only 16 completed the follow-up.

Conclusions: Most of the HBsAg-positive pregnant women (75%) did not have prophylactic information in the charts, and almost 50% of the pregnant women and newborns who had appropriate prophylaxis did not return for medical follow-up. Failure of prophylaxis can promote vertical/perinatal transmission of hepatitis B virus in newborns of mothers who are HBsAg positive.

BACKGROUND

Approximately 257 million people are infected with hepatitis B virus (HBV) worldwide, and 15.0%-40.0% of infected individuals will develop cirrhosis, hepatic failure, or hepatocellular carcinoma.[1,2] In Brazil, viral hepatitis is classified as a serious public health problem, and in 2017, almost 600 thousand cases were reported; of which 31.7% were HBV.[3]

Identifying the etiologic agent through serological tests makes the search for adequate prevention and control measures possible. Therefore, regular exams should be performed, which play an important role in the prevention, diagnosis, screening, and follow-up of patients with the disease.[4]

HBV is primarily transmitted through percutaneous or mucosal exposure to blood or body fluids contaminated with HBV. The forms of contagion may be sexual intercourse, percutaneous inoculation (through sharp objects), and vertical transmission, either transplacentally, during delivery, or during breastfeeding.[2,5,6] Vertical transmission accounts for 35%-40% of new hepatitis B cases worldwide. Chronic infection occurs in 90% of infants infected in the neonatal period, especially those whose mothers tested positive for hepatitis B surface antigen (HBsAg-HBV) and HBV "e" protein (HBeAg) during delivery and whose detection indicates high levels of viral replication.[7]

Neonatal HBV infection may be asymptomatic, which increases the risk of developing complications and increase morbidity and mortality.[5,8] The risk of developing hepatocellular carcinoma in children infected with HBV is estimated to be 200 times greater than that of the general population, and prenatal diagnosis is extremely important for its prevention.[5] Studies have shown that immunoprophylaxis immediately after birth, with administration of the vaccine and hepatitis B immunoglobulin (HBIG), prevents neonatal HBV infection in >95% of cases.[9,10]

Immunization of the mother against hepatitis B during pregnancy is safe, and primary childhood vaccination with a recombinant vaccine provides long-term protection against the disease.[11]

* Address correspondence to Alex S. Jorge, MSc, West Paraná State University, Rua Universitária 1169, Cascavel, Paraná, 85819-110, Brazil.
E-mail address: alex.huop@gmail.com (A.S. Jorge).
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Table 1
Epidemiologic data of the 109 pregnant women who were reactive for HBsAg in WPUH between January 1, 2010, and December 31, 2016

Sector	Obstetric center	Maternity					
	83.5%	16.5%					
Marital status	Single	Married	Widowed	Stable union	NR		
	15.6%	30.1%	0.9%	39.3%	14.1%		
Religion	Catholic	Evangelical	Atheist	NR			
	72.5%	9.2%	2.8%	15.5%			
Ethnicity	White	Brown	Black	NR			
	74.3%	11.9%	2.8%	11.0%			
Education	<8 y	8 y	<12 y	12 y	Graduated	NR	
	5.5%	20.2%	14.7%	13.7%	3.7%	42.2%	
Location	Urban area	Countryside	NR				
	58.7%	3.7%	37.6%				
Town	Cascavel	Other cities					
	81.7%	18.3%					
Age	15-20 y	21-25 y	26-30 y	31-35 y	36-40 y	Up to 40 y	NR
	14.7%	22.9%	13.8%	21.1%	7.3%	9.2%	11.0%

HBsAg, hepatitis B surface antigen; *NR*, not reported in the medical record.

According to the Centers for Disease Control and Prevention, the American College of Obstetricians and Gynecologists, and the Brazilian Ministry of Health, immunoprophylaxis should be performed with the vaccine along with HBIG that are administered in the first 12 h of life of newborns with HBV-infected mothers.[12]

Owing to the need to improve prenatal care and immunization of newborns of HBV-infected mothers, the Brazilian Ministry of Health established the Humanization Program for Pre-Natal and Birth through Ordinance 569, published in the Federal Official Gazette on June 8, 2000, section 1, page 4. This program aims to reduce the rates of maternal and perinatal morbidity and mortality, increasing pregnant women's access to prenatal care by investing in obstetric and neonatal care.[13]

The follow-up of the pregnant woman in the prenatal period allows serological tests to be performed, which enables prevention and early treatment of vertically transmissible diseases.[4]

The lack of awareness and availability of preventive measures against HBV infection is a serious public health problem, mainly because it is a silent disease.[4] Appropriate practices should be adopted for the prevention and detection of infection in pregnant women, contributing to reduced effects on the spread of this infection. Thus, health professionals who attend pregnant women during prenatal care and delivery should have adequate knowledge and periodic training to perform the necessary measures to prevent the infection.[12] This study aimed to verify the prevalence of HBsAg-HBV in female patients treated in the maternity and obstetric center of a public hospital in the Western Region of Paraná State, Brazil, and to evaluate the administration of appropriate prophylaxis in newborns (administration of the vaccine and HBIG) to prevent vertical transmission.

METHODS

A retrospective cross-sectional study was conducted through the collection of data in electronic medical records (Tasy; Philips Healthcare, Amsterdam, Netherlands) at the Western Paraná University Hospital (WPUH) in pregnant women visited from January 1, 2010, to December 31, 2016. To avoid vertical transmission of HBV, investigators verified the age, city of origin, and existence of no other preexisting diseases; the results of HBsAg serological tests; and evaluated the administration of prophylaxis in newborns with mothers who tested positive or had indeterminate status of their serological test. The referral data of puerperae and newborns were verified at the Specialized Center for Infectious and Parasitary Diseases (SCIPD) in the city of Cascavel, Paraná State, Brazil, which is the reference center for the follow-up and treatment of patients who attended the 10th Regional Health of Paraná State. Data were tabulated using Excel software (Microsoft Excel; Microsoft Corp, Redmond, WA).

This study was approved by the Committee of Ethics in Research with Human Beings under No. 2191947.

RESULTS

WPUH is the largest public hospital in the Western Region of Cascavel City, Paraná State, Brazil, with 245-bed capacity. With a monthly average admission of >6,000 patients, it is the preferred treatment center in cases in which highly complex obstetric care is needed. All of the patients in the study originated from cities that belong to the 10th Regional Health Center of the Western Paraná, with the majority residing in urban areas. The mean age of pregnant women was 28.1 years, with a standard deviation of 8.64 years. The possible duplication of care of the same pregnant woman was considered as an individual event between subsequent pregnancies or properly excluded when the patient was hospitalized more than once during the same puerperal period. The epidemiologic profile of patients in this study is shown in Table 1 and Figure 1.

During the study period, 12,548 HBsAg tests were requested at the WPUH, which were performed in the hospital's own laboratory using i1000sr Immunology Analyzer methodology (Abbott Architect, Abbott Park, IL), presenting 217 (1.73%) who tested positive, 7 (0.06%)

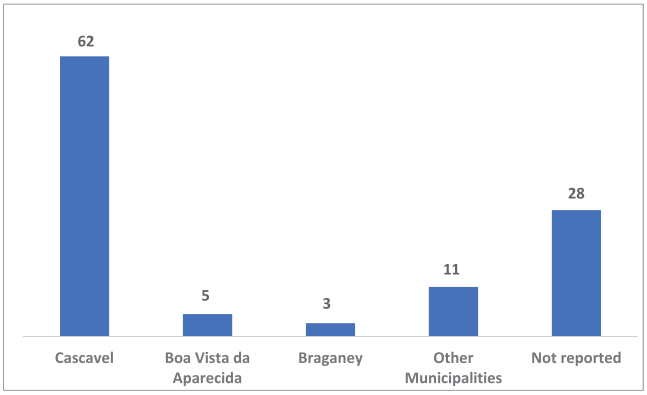

Fig 1. Number of pregnant women per city with HBsAg-reactive result. Other municipalities correspond to 1 patient per city: Catanduvas, Corbélia, Espigão Alto do Iguaçu, Guaraniaçu, Ibema, Jaciaba, Nova Aurora, Foz do Iguaçu, Santa Lucia, Três Barras do Paraná, and Vera Cruz do Oeste.

Table 2
Results of HBsAg serologies for patients in WPUH between January 1, 2010, and December 31, 2016

	Year							
HBsAg (serology)	2010 (n)	2011 (n)	2012 (n)	2013 (n)	2014 (n)	2015 (n)	2016 (n)	Total (n)
Reactive	25	21	33	23	39	31	45	217
Undetermined	2	0	0	1	2	0	2	7
Nonreactive	772	871	983	1,130	2,157	2,537	3,872	12,324
Total	799	892	1,016	1,154	2,198	2,568	3,921	12,548

HBsAg, hepatitis B surface antigen; *WPUH*, Western Paraná University Hospital.

who were undetermined, and 12,324 (98.2%) who were nonreactive. Among the total number of exams requested, 7,763 were requested exclusively for women who visited the obstetric and maternity center. A total of 109 tested positive, and 3 were undetermined. Repeat serology was not requested for indeterminate results (Table 2).

Among the 112 records with reagent or indeterminate results, only 28 (25%) newborns were reported to receive prophylaxis and administered with the HBV vaccine and HBIG immediately after birth, and information on the procedures performed was reported in other medical records (75%).

Among the 109 HBV carriers, 1 (0.92%) also had hepatitis C virus and syphilis infection, 1 had syphilis (0.92%), and 1 (0.92%) was a carrier of HIV. When compared with the data of patients registered by the SCIPD, the data of 109 charts with a reactive result of this study presented only 16 compatibilities (14.7%) (ie, only 16 reactive pregnant women returned for follow-up according to the region's reference service).

DISCUSSION

Vertical transmission is considered when the child is infected by the mother until the first year of life,[14] persisting as a chronic disease in most individuals.[15] The serological examination for HBsAg screening is part of the protocol examinations requested for pregnant women at WPUH who do not have a recent HBsAg serology, making it important to carry out the examination immediately, allowing prophylaxis with the newborn immediately after birth, and reducing the possibility of vertical transmission.[16] According to official data released by the Brazilian Health Ministry, 91,824 pregnant women attended the 10th Regional Health agency of Paraná State from 2010-2015.[17] In the same period, the WPUH registered 22,197 births in the sectors related to this study, and no consolidated data were available in 2016,[18] giving an approximate annual average of 3,700 deliveries. Our data indicated an annual average of 1,109 requested HBsAg tests (ie, approximately 30% of pregnant women arrived without prior knowledge of the serological condition for hepatitis B).

Serological conditions of the pregnant women in our study was expected to be elucidated even during pregnancy, because all health care services in Paraná State must follow the protocols defined by the Brazilian Public Health System and Paraná State Health Secretary. The public health system offers, free of charge, 8 visits in the prenatal/postpartum period: 7 visits in the prepartum period (4 in the first and second trimester [2 each trimester] and 3 in the third trimester), and 1 visit in the postpartum period. Serological testing for HBsAg was performed during the prenatal phase, preferably in the first trimester. These visits and serological tests are performed at primary health care units.[19,20] The percentage of pregnant women who received prenatal care in this region was <70%, consistent with results in other Brazilian regions.[21] Knowledge about serological conditions during pregnancy allows for interventions to immunize the mother or to minimize the risk of vertical transmission.[22,23]

Although the presence of HBeAg in HBsAg-positive pregnant women is a predominant factor for vertical HBV transmission,[24] testing protocols at public health systems, including the WPUH, do not include detection of HBeAg in HBsAg-positive pregnant women. HBeAg serology was available on medical request at any time, however, detection of this marker was requested in only 4 pregnant women; of these, only 2 had their exams performed (nonreactive HBeAg); and only these 2 women and their newborns had their prophylaxis noted in medical records. The request for the HBeAg analysis represents an important additional factor that would reinforce the need for immunoprophylaxis, because the presence of reactivity to HBeAg with HBsAg may represent a risk of up to 90% of vertical infection probability.[14,25]

The results of reactivity for HBV found in patients treated in WPUH (1.73%) were similar to the study by Gonçalves et al,[26] who found that 1.80% of pregnant women attended at Hospital Base de São José do Rio Preto tested positive. The prevalence of HBV in pregnant women in Brazil varies according to the region studied, resulting in HBsAg generally below 1%,[27–29] but a higher prevalence was expected in our data, considering a higher endemic of HBV in this region in Brazil.[30]

Only 28 (25%) of the newborns with reactive or indeterminate mothers for HBsAg received the appropriate prophylactic measures, with the vaccine and HBIG, because only those files had this information. Considering that most of the medical records do not contain all the necessary information regarding the changes that occurred in pregnant women and newborns, whether prophylactic measures have not been performed or recorded in their medical records cannot be confirmed. HBV (recombinant HBsAg) has been a part of the national obligatory protocol in the neonatal vaccine schedule since 1998. The first dose is administered within 12-24 hours postpartum at hospital units to all newborns regardless of mothers' hepatitis B status, and the second and third doses are administered 30 and 180 days post-birth, respectively, at health care units.[31,32]

According to the same national protocol, newborns of HBsAg-positive mothers must receive HBV plus HBIG within 12 hours of birth in different muscle groups in the hospital unit.[32,33] Considering that this is a well-defined protocol and is recommended by the Brazilian Ministry of Health, this prophylactic measure may have been instituted in the WPUH without it being appropriately recorded. This may have led to the electronic medical records reflecting a low medical adherence. This lack of information is worrisome, because if complete data were found, a large number of newborns were possibly exposed without prophylaxis, increasing the chances of neonatal HBV infection.[14,25,34]

Among the 81 records that did not have information on the initiation of prophylaxis in women and newborns, 2 were discharged before the serological result was ready, 5 had communication notes for epidemiologic surveillance, and 3 were referred to SCIPD. In cases for possible discharge and where the serological examination for HBsAg has not yet been performed, a rapid test for HBsAg may be performed, which has good results in terms of sensitivity and specificity, besides the easy

execution and speed of the result.[35,36] This facilitates direct medical decision for prophylaxis, minimizing possible harm to the newborn when released without the mother's serological knowledge.

Patients from the public or private sector, with serological tests reactive for HBsAg in the municipalities belonging to the 10th Health Regional of the State of Paraná, including pregnant women, should be referred for follow-up, treatment, and control to SCIPD in the city of Cascavel. Among the 28 pregnant women attended and with the correct immunoprophylaxis, only 16 were followed up in the specialized center, and 3 of them were chronic carriers of the disease. This low adherence may be caused by more than 1 explanation and may be a failure of hospital counseling as well as patients' own decisions because pregnant women have the freedom to choose if they wanted to undergo follow-up at the specialized center. Another hypothesis is that the patient chose to undergo follow-up outside the public network; however, the probability of this choice is low considering the population served by the WPUH, which mostly involve people with low financial resources and without private health insurance coverage. No measures were available to determine pregnant women's knowledge about their serological status, disease significance, and the importance of specialized follow-up, which could have improved their adherence to the referral service.

All patients (mothers and children) from the 10th Regional Health Service who were admitted to the SCIPD had adequate serological follow-up to verify the vertical or perinatal transmission. Vertical and perinatal transmission were not recorded during the study period, even considering the 3 pregnant women in our study who were chronic carriers of HBV. Brazilian effectiveness studies have reported good results for vaccines and immunoglobulin;[37,38] however, our study findings cannot be inferred in a similar manner because only a few children underwent serological follow-up post-immunization.

Although this study was conducted in the largest public hospital and for a considerable period of time, we cannot confirm that it reflects the regional reality, because they were not correlated with the data from other hospital units. Another possible bias of this study is that data of pregnant women who eventually visited with a recent reaction of serological test for HBsAg and for whom prophylaxis was prescribed without the request of a new examination were not collected.

CONCLUSIONS

Among all the records of pregnant women who were reactive to the serological test for HBsAg, 75% had no solicitation notes for vaccine prophylaxis and with HBIG. This loss of information implies that the prophylaxis did not actually happen, which increases the possibility of vertical transmission of hepatitis B. Although the electronic medical record system allows storage of many epidemiologic data and prescriptions, we perceive that the adherence of those responsible for these notes was low. All information pertinent to the patient's medical data should be recorded, as it is part of his or her health history and, if consulted, may mark future actions to promote patient well-being.

Few pregnant women with reactive results (16/109) are registered in the specialized center for infectious diseases, either due to lack of correct referral, ignorance of the pathology, or own choice. To improve adherence levels, referral of the mother and newborn to the reference service should be established as an obligatory protocol.

Few children underwent serological follow-up postimmunization, impairing the evaluation of prophylactic efficacy.

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