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RESEARCH REPORT

Applicability and efficacy of a model for prevention of perinatal transmission of hepatitis B virus infection: Single center study in Egypt

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Abstract

AIM: To identify possible maternal risk factors for hepatitis B virus (HBV) acquisition and assess the efficacy of immunoprophylaxis given to infants born to hepatitis B virus surface antigen (HBsAg) positive mothers.

METHODS: Screening of 2000 pregnant females was carried out using rapid test and confirmed by enzyme immunoassay. A questionnaire consisting of 20 questions about the possible risk factors for acquisition of HBV infection was filled for every pregnant HBsAg positive female in addition to at least 2 pregnant HBsAg negative females for each positive case. Infants of HBsAg positive women were offered passive and active immunoprophylaxis within the 1st 48 h after birth, in addition to 2nd and 3rd doses of HBV vaccine after 1 and 6 mo respectively. Infants were tested for HBsAg and hepatitis B surface antibodies (HBsAb) at six months of age.

RESULTS: HBsAg was confirmed positive in 1.2% of tested pregnant women. Risk factors significantly associated with HBV positivity were; history of injections (OR = 5.65), history of seeking medical advice in a clinic (OR = 7.02), history of hospitalization (OR = 6.82), history of surgery (OR = 4) and family history of hepatitis (OR = 3.89) ($P < 0.05$). Dropout rate was 28% for HBsAg women whose rapid test was not confirmed and could not be reached to provide immunoprophylaxis for thier newborns. Immunoprophylaxis failure was detected in only one newborn (3.7%) who tested positive for HBsAg at 6 mo of age; and vaccine failure (seronegative to HBsAb after 4 doses of the vaccine) was detected in another one (3.7%). The success rate of the immunoprophylaxis regimen was 92.6%.

CONCLUSION: This pilot study shows that a successful national program for prevention of perinatal transmission of HBV needs to be preceded by an awareness campaign to avoid a high dropout rate.

Key words: Egypt; Hepatitis B virus; Hepatitis B virus surface antigen positive mothers; Immunoprophylaxis; Perinatal transmission

Core tip: Perinatal transmission of hepatitis B virus (HBV) is still a threat in Egypt despite a successful immunization program for infants. In this work we tried to assess the risk factors for maternal acquisition of HBV and study a model for prevention of perinatal transmission of HBV. To achieve our aim we screened 2000 pregnant women for hepatitis B virus surface antigen. Risk factors for HBV acquisition were mostly related to medical care. We encountered a high drop-out rate of women who could not be reached to offer their newborns immunoprophylaxis. For those who received immunoprophylaxis after birth, a success rate of 92.6% was achieved. An awareness campaign has to precede implementation of a national program for prevention of perinatal transmission of HBV.

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INTRODUCTION

An estimated 350 million persons worldwide are chronically infected with hepatitis B virus (HBV)[1]. Perinatal transmission is the most common mode of transmission worldwide[2]. To prevent perinatal transmission, women should be screened for hepatitis B virus surface antigen (HBsAg) during the first prenatal visit and, if seronegative but at high risk, screened again in late pregnancy[3].

Transmission presumably occurs during birth, however, viral transmission may occur in utero *via* transplacental leakage[4].

Specific factors that directly correlate with the development of the HBsAg-positive state in the infant (in the absence of effective prophylaxis) are (1) the maternal HBsAg titer; (2) maternal hepatitis B e antigen (HBeAg) positivity (up to 90% of infants born to HBeAg-positive mothers develop chronic hepatitis B; infants of HBeAg-negative carrier mothers have a 20% risk)[5-7]; (3) HBV DNA in maternal serum[8]; (4) HBsAg-positive cord blood; (5) HBsAg-positive siblings[5,9,10]; or (6) when vaccine is offered later than 48 h after birth[11].

Administration of hepatitis B immunoglobulin (HBIG) and concurrent hepatitis B vaccine have been shown to be 95% efficacious in the prevention of perinatal transmission of HBV, the efficacy is lower for maternal carriers with very high serum HBV DNA levels (> 10^8 IU/mL)[12-14].

The aim of this work was to identify the prevalence and possible maternal risk factors for HBV acquisition, introduce a model for prevention of perinatal transmission of HBV and assess the efficacy of active and passive immunoprophylaxis administered within the first 12-48 h after birth to infants born to HBsAg positive mothers.

MATERIALS AND METHODS

Ethics

The study protocol was approved by the Review Board and Ethical Committee of Kasr Alainy School of Medicine, Cairo University. All pregnant females were screened for HBsAg after obtaining a verbal consent.

Study subjects

This cohort prospective study was conducted on a convenient sample of two thousand pregnant women coming for routine antenatal care at the Outpatient Clinic of the Obstetrics Department and Center for Social and Preventive Medicine, Kasr Al-Ainy School of Medicine, Cairo University, Cairo, Egypt. The study as well included 12 pregnant women known to have HBV infection who came to the Pediatric Hepatology Outpatient Clinic for consultation about immunoprophylaxis for their coming babies. All infants born to HBsAg positive mothers were included in this study. This group was included to increase the number of newborns receiving immunoprophylaxis.

Each positive HBsAg mother-infant pair was assigned a unique study ID number (1-35).

The study consisted of 2 phases: Phase 1 (Figure 1): Screening for HBsAg: Two thousand pregnant women were screened for HBsAg by rapid test (one step HBsAg test). Screening was carried out from May 2010 to July 2011. If HBsAg was detected by the rapid test, enzyme immunoassay was done for confirmation. Hepatitis B surface antibodies (HBsAb), hepatitis B core antigen IgM (HBcIgM), hepatitis B virus core antibody (HBcAb) total, HBeAg, HBeAb and quantitative DNA by PCR were also done on the same serum sample. All tests were done at the Clinical Pathology Department, Kasr Al-Ainy School of Medicine, Cairo University. Results of all confirmatory tests were reported to all pregnant females by phone. Phase 2: Follow up of HBsAg positive women and their newborns: Women with positive HBsAg were contacted and the prevention of perinatal transmission of HBV infection to their babies was explained to them. A contact cell phone number was given to each HBV positive pregnant female for immediate contact at the onset of labor pains in order to administer immunoprophylaxis for their newborns.

A questionnaire consisting of 20 questions about the possible risk factors for acquisition of HBV infection was filled for every pregnant HBsAg positive female in addition to at least 2 pregnant HBsAg negative females for each positive case.

Family members of HBsAg positive mothers were also screened for HBsAg by rapid test whenever possible. Cases found positive for HBsAg whether pregnant females or their family members, were instructed to seek medical

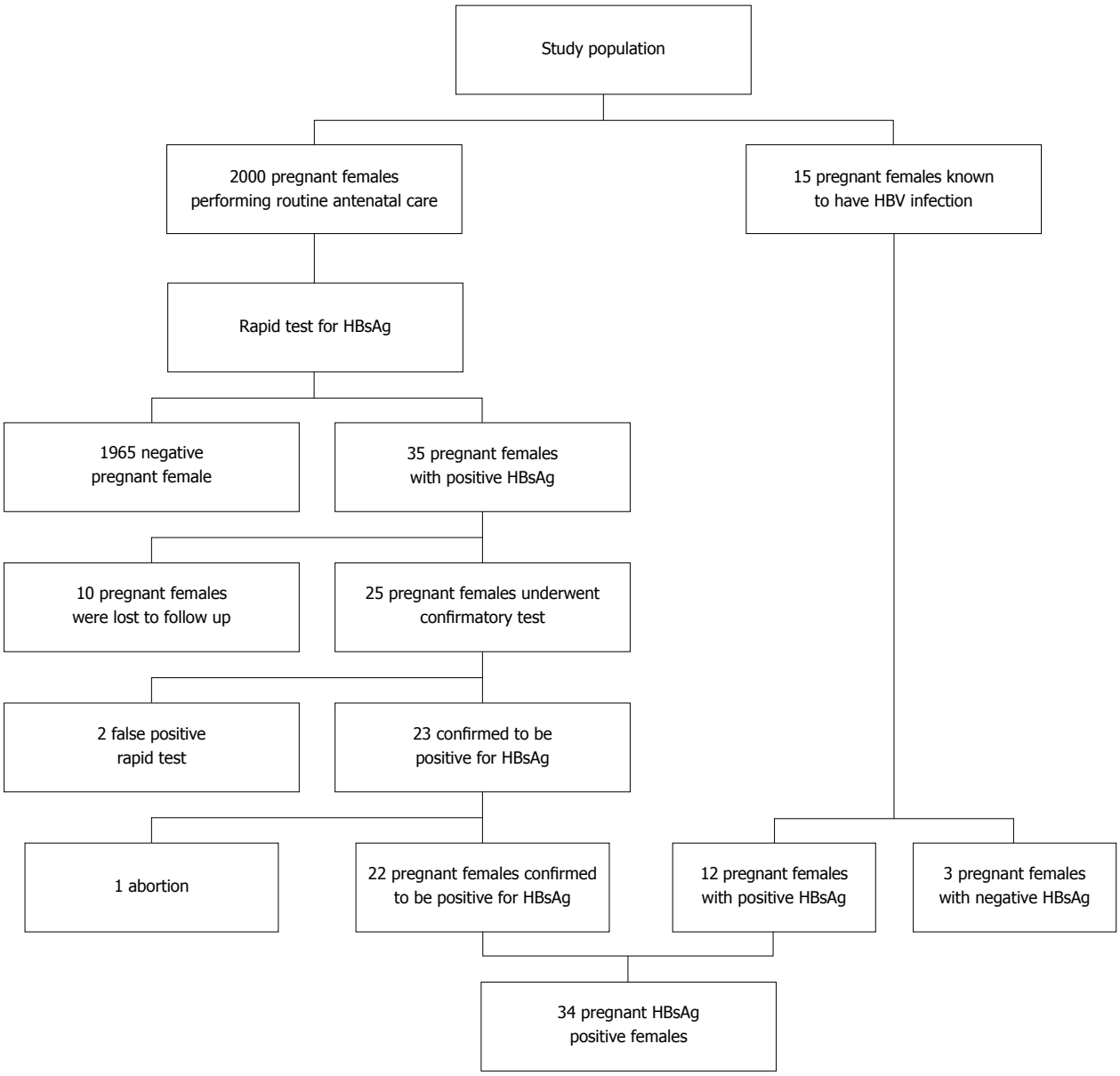

Figure 1 Flowchart of selecting hepatitis B virus surface antigen positive females. HBsAg: Hepatitis B virus surface antigen; HBV: Hepatitis B virus.

advice with hepatologists. Pediatric cases were referred to the Pediatric Hepatology Unit at Cairo University Pediatric Hospital for medical care where the test for HBsAg was repeated using enzyme immunoassay. Seronegative family members were instructed to receive the vaccine against HBV.

Immunoprophylaxis was carried out from May 2010 till March 2012. Newborns encountered within the first 48 h after delivery received both 0.5 mL of HBIG (HepaBIG) and 0.5 mL of recombinant HBV vaccine (Euvax: 20 μg purified HBsAg/mL) intramuscularly at two different sites. They received two more doses of HBV vaccine at the age of 1 and 6 mo.

All newborns given immunoprophylaxis were tested for HBV viral load by quantitative real time PCR at birth before vaccination.

At six months of age, the infants were tested for HBsAg and HBsAb. Infants seronegative for HBsAb at 6 mo of age were re-tested at 7 mo, one month after the 3rd dose of HBV vaccine. Those who were seronegative again at 7 mo were given a fourth dose of the vaccine and re-tested one month later (at 8 mo of age).

Statistical analysis

All collected questionnaires were revised for completeness. Data was entered then transferred to SPSS for analysis. Simple descriptive statistics (arithmetic mean and standard deviation) were used for summary of quantitative data, and frequencies were used for qualitative data. Bivariate relationships were displayed in cross tabulations *i.e.*, the association of HBV infection with potential risk factors. Comparisons of proportions were performed using the χ^2 and Fisher's exact tests where appropriate. Odds ratios (OR) and 95%CI were generated as estimates

Table 1 Risk factors for acquisition of hepatitis B virus in the studied population *n* (%)

	HBsAg negative (*n* = 82)	HBsAg positive (*n* = 35)	*P* value	OR	95%CI
Occupation					
Housewife	77 (93.9)	35 (100)	0.320	-	-
Working	5 (6.1)	0 (0)			
HBV vaccination	4 (4.9)	0 (0)	0.315	-	-
History of injections	34 (41.5)	28 (80)	< 0.001	5.65	2.2-14.42
History of medical clinic attendance	43 (52.4)	31 (88.6)	< 0.001	7.02	2.27-21.71
History of hospital admission	34 (41.5)	29 (82.9)	< 0.001	6.82	2.55-18.23
History of sutures	54 (65.9)	29 (82.9)	0.064	2.50	0.93-6.74
History of surgeries	41 (50)	28 (80)	0.003	4	1.57-10.18
History of drained abscesses	5 (6.1)	4 (11.4)	0.440	1.98	0.50-7.89
History of urinary catheter	32 (39)	20 (57.1)	0.071	2.08	0.93-4.65
History of blood transfusion	7 (8.5)	3 (8.6)	1	1	0.24-4.13
History of endoscopy	4 (4.9)	3 (8.6)	0.420	1.82	0.38-8.63
History of dental treatment	42 (51.2)	23 (65.7)	0.140	1.82	0.80-4.15
History of schistosomiasis	0 (0)	0 (0)			
History of nail care	6 (7.3)	5 (14.3)	0.301	2.11	0.59-7.44
Ear piercing	81 (98.8)	35 (100)	1	-	-
Circumcision	81 (98.8)	32 (91.4)	0.075	0.13	0.01-1.27
History of cauterization	1 (1.2)	0 (0)	1	0.69	0.62-0.78
History suggestive of previous hepatitis	1 (1.2)	0 (0)	1	-	-
Family history suggestive of hepatitis	16 (19.5)	17 (48.6)	0.001	3.89	1.65-9.20

HBsAg: Hepatitis B virus surface antigen.

of associations. All statistical analyses were performed using SPSS version 15.

RESULTS

Seroprevalence of HBsAg

In phase 1 of the study, screening for HBsAg was done for a total of 2000 pregnant women by rapid test. The test was positive in 35 (1.75%) pregnant women, but only 25/35 women came back to do the confirmatory test by enzyme immunoassay. Four refused to come back, and six women could not be reached by phone. The confirmatory test revealed 2 false positive results. Thus a total of 23 HBsAg positive women were detected by the confirmatory test giving an overall HBsAg prevalence of 1.2%.

Another group of 15 pregnant women who gave history of HBV infection sought our help for immunoprophylaxis. One of these pregnant women was Korean; 12/15 women were positive for HBsAg. At the end of phase 1 of the study a total of 35 HBsAg positive women were enrolled.

Risk factors for HBsAg positivity among the studied pregnant women

Interview questionnaire was conducted for all 35 HBV positive study participants and 82 HBV negative women to assess the risk factors for HBV positivity.

The mean age for HBsAg positive women was 27.1 ± 4.8 years and median was 27 years, while for the HBsAg negative women the mean age was 25.9 ± 4.8 and median 25.5 years. No significant difference was observed as regards the age of positive and negative women (*P* value = 0.18).

Most of the study population came from Giza and Cairo governorates (51.3% and 41.9% respectively). Table 1 shows the comparison of patient characteristics of the HBV positive and negative women enrolled in the study. Risk factors significantly associated with HBV positivity were; history of injections (OR = 5.65), history of seeking medical advice in a clinic (OR = 7.02), history of hospitalization (OR = 6.82), history of surgery (OR = 4) and family history of hepatitis (OR = 3.89) ($P < 0.05$).

Screening for HBsAg by rapid test for the family members of the HBsAg positive mothers was offered; 21/35 families agreed to be screened. Not all family members within the same family came for screening. Only 48 members were screened; 17 (35.5%) husbands, 29 (60.5%) children, 1 (2%) mother and 1 (2%) brother. Ten (20.8%) had positive HBsAg while the other 38 (79.2%) were negative. The positive cases were 4 (40%) husbands, 5 (50%) children and 1 (10%) mother. The 10 positive cases were confirmed using enzyme immunoassay.

Laboratory tests done for the HBsAg positive mothers

Table 2 shows the laboratory profile for recruited HBsAg positive pregnant women.

All HBsAg positive pregnant women were negative for HBsAb and HBcIgM, while they were all positive for HBcAb total. Two women (5.7%) were negative for HBeAg, HBeAb and HBV DNA markers. Only 3/35 women (8.6%) were positive for HBeAg and 29/35 (82.9%) were positive for HBe Ab. HBV DNA was positive in 18/35 (51.4%) (Figure 2). A total of 14 cases had positive results for HBeAb and HBV DNA combined, while only 3 cases were positive for HBeAg and HBV

Table 2 Hepatitis B virus markers profile of hepatitis B virus surface antigen positive pregnant women recruited in the study

Study ID	HBsAg	HBeAg	HBeAb	PCR	HBsAb	HBcIgM	HBcTotal
2	+ve	-ve	+ve	+ve (509)	-ve	-ve	+ve
4	+ve	-ve	+ve	+ve (213)	-ve	-ve	+ve
7	+ve	-ve	+ve	+ve (90)	-ve	-ve	+ve
8	+ve	-ve	+ve	+ve (2530)	-ve	-ve	+ve
9	+ve	-ve	+ve	+ve (147)	-ve	-ve	+ve
13	+ve	+ve	-ve	+ve (54700)	-ve	-ve	+ve
14	+ve	-ve	+ve	+ve (387)	-ve	-ve	+ve
15	+ve	-ve	+ve	+ve (1790)	-ve	-ve	+ve
16	+ve	-ve	+ve	+ve (12500)	-ve	-ve	+ve
17	+ve	+ve	-ve	+ve (314000)	-ve	-ve	+ve
18	+ve	-ve	+ve	+ve (989000000)	-ve	-ve	+ve
21	+ve	-ve	+ve	+ve (832)	-ve	-ve	+ve
23	+ve	-ve	+ve	+ve (4010)	-ve	-ve	+ve
26	+ve	+ve	-ve	+ve (39000000)	-ve	-ve	+ve
28	+ve	-ve	+ve	+ve (79)	-ve	-ve	+ve
30	+ve	-ve	+ve	+ve (272)	-ve	-ve	+ve
31	+ve	-ve	-ve	+ve (64)	-ve	-ve	+ve
35	+ve	-ve	+ve	+ve (72)	-ve	-ve	+ve

Cases number 1, 3, 5, 6, 10-12, 19, 20, 22, 24, 25, 27, 29, 32-34 were positive for hepatitis B virus surface antigen (HBsAg) and HBcTotal, and negative for hepatitis B surface antibodies (HBsAb), hepatitis B core antigen IgM (HBcIgM), hepatitis B e antigen (HBeAg), hepatitis B e antibody (HBeAb) and hepatitis B virus (HBV) PCR.

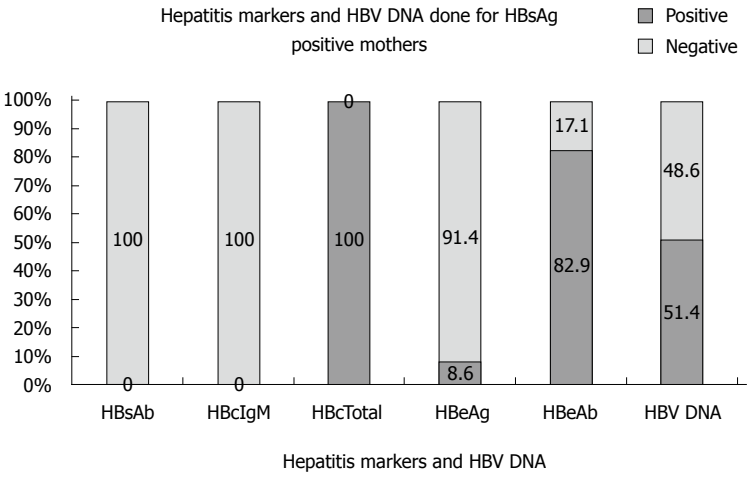

Figure 2 Hepatitis markers and hepatitis B virus DNA done for hepatitis B virus surface antigen positive mothers. HBsAb: Hepatitis B surface antibodies; HBcIgM: Hepatitis B core antigen IgM; HBcAb: Hepatitis B virus core antibody; HBsAg: Hepatitis B virus surface antigen; HBV: Hepatitis B virus; HBeAg: Hepatitis B e antigen; HBeAb: Hepatitis B e antibody.

DNA combined (Table 2).

Outcome of pregnancy

Only one of the HBsAg positive women had an abortion; while the remaining 34 women had delivered their babies. Thirteen women (38.2%) had normal vaginal delivery while 21 (61.8%) had a cesarean section. Newborns were 20 (58.8%) full term females and 14 (41.2%) full term males. The only infant who got infected was a male, delivered by cesarean section. Twenty-five (83.4%) infants were exclusively breast fed till the age of 6 mo.

HBV immunoprophylaxis

A total of 30/34 (88.2%) infants received the HBIG and the first dose of HBV vaccine within the first 48h after birth and the second dose of HBV vaccine at the age of 1 mo. At the age of 6 mo only 27/30 (90%) infants came back for the third dose of HBV vaccine, while 3/30 (10%) infants were lost to follow up and did not get the third dose (cases number 18, 30 and 34).

Among the 30 infants who received the HBIG, a total of 22 (64.7%) infants received the HBIG within the first 12 h following delivery, 4 (11.76%) received it within 12-24 h (one of them is case number 4 with HBsAg positive and HBsAb negative at 6 mo of age) and 5 (14.7%) received it within 24-48 h (Table 3).

One infant (1/34, 2.9%) came for the first time at the age of 9 d, thus received the first dose of HBV vaccine at 9 d and did not receive the HBIG (case number 1), the second and third doses of HBV vaccine were then admin-

Table 3 Hepatitis B immunoglobulin and hepatitis B vaccine administered to the infants born to hepatitis B virus surface antigen positive women *n* (%)

		Age of administration	*n* = 34
HBIG	Not Given		3 (8.8)
	Given	1st 12 h	22 (64.7)
		12-24 h	4 (11.8)
		24-48 h	5 (14.7)
HBV vaccine	1st dose	1st dose within 48 h of delivery	31 (91.2)
		1st dose at the age of 9 d	1 (2.9)
		1st dose at the age of 2 mo	2 (5.9)
	2nd dose	2nd dose at age 1 mo	32 (94.1)
		2nd dose at age 4 mo	2 (5.9)
	3rd dose	3rd dose at 6 mo	31 (91.2)
	4th dose	4th dose at 7 mo	3 (8.8)

HBIG: Hepatitis B immunoglobulin; HBV: Hepatitis B virus.

istered at the ages of 1 mo and 6 mo respectively.

Two infants (2/34, 5.9%) did not receive the HBIG and followed the Ministry of Health routine vaccination schedule at 2, 4 and 6 mo of age (cases number 13 and 15). One infant (1/34, 2.9%) was completely lost to follow up (case number 24).

Laboratory tests done for the infants

Table 4 shows the laboratory and immunoprophylaxis profile of the studied infants.

Testing for HBV DNA was done for only 30 infants immediately after delivery, only 1 (3.3%) was positive (case number 18). This infant's mother was Korean and had very high maternal viremia (989000000 copies/mL), this infant was lost to follow up at the age of 6 mo.

HBsAg and HBsAb status were tested for only 30 infants at the age of 6 mo. Only 1 infant (1/30, 3.3%) had positive HBsAg and negative HBsAb (case number 4). This infant had a negative HBV DNA at delivery; his mother was negative for HBeAg. He was a male and was delivered by cesarean section. The mother's quantitative HBV DNA was only 213 copies/mL (Table 1). On screening, her elder 3-year-old daughter was positive for HBsAg by rapid test.

Among the 29 HBsAg negative children, a total of 26 (89.7%) infants had positive HBsAb and three (10.3%) had negative HBsAb (cases number 1, 9 and 28). HBsAb status was tested again for these three infants one month after the 3rd vaccine dose; all 3 infants were still negative for HBsAb. Thus a 4th dose of HBV vaccine was administered and the HBsAb status was re-tested 1 mo after the 4th vaccine dose, two infants became HBsAb positive (cases number 1 and 28) and only one of the three infants remained negative (case number 9).

Thus among the 27 infants receiving both HBIG and HBV vaccine within the 1st 48 h after birth and who completed the three doses of HBV vaccine (at 1 and 6 mo), a total of 23 infants (85.2%) were seropositive for HBsAb and negative for HBsAg at the age of 6 mo, two infants (7.4%) (cases number 1 and 28) developed the HBsAb at the age of 7 mo (one month after the fourth dose of HBV vaccine), one infant (3.7%) (case number 9) remained HBsAb negative at the age of 8 mo (one month after a fourth dose of HBV vaccine), and one infant (3.7%) (case number 4) was positive for HBsAg and negative for HBsAb at 6 mo of age. Thus immunoprophylaxis failure (HBIG and HBV vaccine failure) was detected in only 3.7% (1/27), and vaccine failure (seronegative to HBsAb after 4 doses of the vaccine) was detected in another 3.7% (1/27). Hence, the success rate of the followed immunoprophylaxis regimen was observed in 92.6% (25/27) of infants.

DISCUSSION

HBV infection is a major health problem. Perinatal transmission of HBV is one of the most important routes of transmission and yet can be preventable. Identifying HBV infected mothers is very important to identify infants who will benefit from immunoprophylaxis; therefore antenatal screening is highly recommended. Screening and further immunization of newborns of HBV infected mothers can protect them from later serious sequelae of cirrhosis and hepatocellular carcinoma.

The prevalence of HBV in pregnant females in the present study was 1.75% and confirmed in 1.2%. This prevalence is slightly lower than expected. The prevalence of HBsAg in Egypt is of intermediate endemicity (2%-8%). Nearly 2-3 million Egyptians are chronic carriers of HBV[15-17].

Risk factors for acquisition of HBV among our pregnant females point to lack of standard precautions among health care facilities. Most of the possible risks were related to medical care, injections and surgeries. This highlights the importance of emphasizing application of infection control policies and practices in all health care facilities[18] to ensure prevention of transmission of blood borne infections.

One fifth of screened family members were HBsAg positive; half of them were offsprings. Horizontal transmission within families has been previously reported[19-23]. Prevention of horizontal transmission of HBV is of utmost importance for controlling HBV infection in a community.

After screening 2000 pregnant females for HBsAg, 28.6% of positive cases dropped out. Besides the 6 mothers who could not be reached to be informed about the results, four refused to come for confirmation. This is higher than drop outs (12.6%) reported in the thyroid screening program which has been successfully established in Egypt since the year 2000. Dropout rate was defined as the number of positive screened babies who did not come for confirmation/total number of positive screened babies[24].

Difficulties that might face this program include difficulty reaching the patients, high incidence of drop outs and sometimes denial to admit the possibility of being HBV infected. This high percentage gives an insight about the importance of awareness campaigns that have

Table 4 Profile of infants born to hepatitis B virus surface antigen positive women recruited in the study

Case number	HBV DNA at birth	HBIG within 48 h of delivery	First dose of HBV vaccine within 48 h of delivery	Second dose of HBV vaccine at age of 1 mo	Third dose of HBV vaccine at age of 6 mo	Fourth dose of HBV vaccine at age of 7 mo	HBsAg at age of 6 mo	HBsAb at age of 6 mo	HBsAb 1 mo after 3rd dose of vaccine	HBsAb 1 mo after 4th dose of vaccine
1	-	No	No[1]	Yes	Yes	Yes	-ve	-ve	-ve	+ve
4	-ve	Yes[2]	Yes	Yes	Yes	No	+ve	-ve	-ve	-
9	-ve	Yes[3]	Yes	Yes	Yes	Yes	-ve	-ve	-ve	-ve
13	-	No	No[4]	No[4]	Yes	No	-ve	+ve	-	-
15	-	No	No[4]	No[4]	Yes	No	-ve	+ve	-	-
18	+ve	Yes[3]	Yes	Yes	No	No	-	-	-	-
24	-	No	No	No	No	No	-	-	-	-
28	-ve	Yes[3]	Yes	Yes	Yes	Yes	-ve	-ve	-ve	+ve

[1]The infant received the first dose of HBV vaccine at the age of 9 d; [2]Hepatitis B immunoglobulin (HBIG) at 12-24 h after birth; [3]HBIG within the first 12 h after birth; [4]Infants received the first and second doses of the hepatitis B virus (HBV) vaccine at the age of 2 and 4 mo respectively. Cases number 2, 3, 5-8, 10-12, 14, 16-17, 19-23, 26, 27, 29, 31-33, 35 were negative for HBV DNA at birth, received HBIG and first dose of HBV vaccine within 48 h after birth, received second and third doses of HBV vaccine at 1 and 6 mo of age respectively, were HBsAg negative and HBsAb positive at 6 mo of age; Cases number 30 and 34 were negative for HBV DNA at birth, received HBIG and first dose of HBV vaccine within 48 h after birth, received second dose of HBV vaccine at 1 mo, and were lost to follow up at 6 mo; Case number 25 had an abortion. HBsAb: Hepatitis B surface antibodies; HBsAg: Hepatitis B virus surface antigen.

to precede implementation of a national program for prevention of vertical transmission of HBV. Lack of follow up in a tertiary care center like Cairo University Hospitals poses a question of how would be the response to follow up in a primary care center in a rural area. A successful program should include; easy screening tests, available confirmatory tests, prevention methods and therapy for positive cases. Rapid tests for HBsAg detection have low cost. Positive results can be further confirmed using immunoassay. One rapid test costs one tenth of one immunoassay test. In our study all pregnant females were informed that this service was for free. One researcher only was in charge of the whole procedures. Cell phones were the only way of communication with the pregnant females. Service recipients could respond more if they were informed that the screening, confirmatory tests and immunoprophylaxis are for free, if more than one health care provider were in charge, if more than one cell phone was known or a written complete address was taken. Home visits for cases that drop out could lower the percentage of lack of follow up. We believe that if the study was performed on a larger national scale, the number of dropped out cases would be much less.

In Egypt, primary health care units provide medical care for attending pregnant females. Some investigations are done routinely for these females *e.g.*, hemoglobin percent, blood group including Rh and serum glucose. We suggest doing screening for HBsAg during the same visits. There is a special attention in rural areas to tetanus toxoid coverage. We suggest doing screening for HBsAg during the same visits in rural areas. Screened women could have their HBsAg status documented on their health cards.

Another limitation for the program is the price of HBIG. HBIG is expensive, with no available 0.5 mL single dose preparation. The only available suitable preparation in Egypt is 1 mL single use vial preparation. The cost of this vial is 265 LE. The vial cannot be reused or saved for future use as it contains no preservative; therefore partially used vials should be discarded immediately. For a national program, availability of 0.5 mL preparation will reduce the cost.

Both HBIG and HBV were intended to be administered to all newborns of HBsAg positive pregnant females within 12 h after delivery; 22 newborns (71%) were given within the first 12 h after delivery, 4 (12.9%) within 12-24 h and 5 (16.1%) within 24-48 h. Delay in immunoprophylaxis was because the mothers did not contact the researchers after delivery although they were given a contact phone. According to Samuels and Cohen[25]; the hepatitis B vaccination can be delayed by more than 24 h after the baby's birth but it should definitely be administered before the baby is 7 d old.

Out of the 27 infants with known outcome, one showed immunoprophylaxis failure (HBIG and HBV vaccine failure) and was found to be HBsAg positive. Hence, the success rate of our immunoprophylaxis is 96.3%. HBV vaccination and HBIG administration within 24 h after birth, followed by two additional vaccine doses (at 1 and 6 mo) in order to complete the 3-dose vaccine series, has been demonstrated to be 85%-95% effective in preventing acute and chronic HBV infection in high-risk infants (infant whose mother is positive for both HBsAg and HBeAg)[26]. Failure of vaccine plus HBIG to interrupt mother-to-child transmission of HBV is influenced by maternal serum HBeAg-positive status[27,28] and maternal HBV DNA of $\geqslant 10^7$ copies/mL[27]. The only infant in our study who showed immunoprophylaxis failure was born to an HBeAg negative mother, whose DNA viral load was only 213 copies/mL. This baby had a negative quantitative HBV DNA at birth. Infection is thus suspected to be acquired either during delivery or after birth. On screening, this infant's elder sister was HBsAg positive. If a previous child was HBV positive, concerns about the risk of perinatal transmission may be higher[29].

Despite immunoprophylaxis, between 3.7% to 9.9% of infants still acquire HBV infection[30-37]. Failure of passive and active immunoprophylaxis in this setting may be the result of in utero transmission of HBV infection, perinatal transmission related to a high inoculum, and/or the presence of surface gene escape mutants[38].

In conclusion, this is the first pilot study on HBV immunoprophylaxis for infants born to HBsAg-positive mothers in Egypt. Although the present study revealed an HBsAg prevalence among Egyptian pregnant women less than 2%; still a national program for screening for HBV infection in pregnant women is a mandate in Egypt. Most risk factors for maternal HBV acquisition were related to medical care, which calls for a re-enforcement of infection control practices in medical facilities. The dropout rate in this study is high. A national program has to be preceded by an awareness campaign. HBIG 0.5 mL preparations have to be made available to match the limited financial resources. In both rural and urban areas, screening of pregnant females for HBsAg could be done during the same visits for tetanus toxoid coverage and the HBsAg status documented on their health cards. HBIG and HBV vaccine can be administered to newborns during the first post natal visit that the Ministry of Health recommends for thyroid screening and zero polio vaccine dose, the 2nd HBV vaccine dose during the last visit post natal visit which is at 40 d, and the 3rd HBV vaccine dose with the rest of their routine immunization.

COMMENTS

Background

Despite the introduction of hepatitis B vaccine in the expanded program of vaccination in Egypt since 1993, perinatal transmission of hepatitis B virus (HBV) remains a threat. Egypt lies within the intermediate zone of endemicity (2%-8%). Hepatitis B virus surface antigen positive pregnant women can transmit the infection to their babies. It is of importance to define the risk factors residing behind acquisition of infection. It is, as well, high time to introduce a model for the prevention of perinatal transmission of HBV.

Research frontiers

Definition of possible risk factors for HBV acquisition among adult females may assist in implementation of measures for prevention of HBV infection. In the present study, many risk factors lie within the medical practice, which points to the importance of implementation and enforcement of infection control policies and procedures in Egyptian medical facilities. Although immunoprophylaxis for prevention of perinatal transmission of HBV has been practiced for many years, some countries, including Egypt, still lack a national program. Implementation of a national program includes many facets besides financial resources including public awareness and utilization of previous successful models.

Innovations and breakthroughs

This is the first pilot study published from Egypt about a model for prevention of perinatal transmission of HBV. The drop-out rate in the pilot study, calls for an awareness campaign to precede implementation of a national program.

Applications

This study demonstrates how a preventive program can be applied to prevent perinatal transmission of HBV, putting in consideration the study limitations.

Terminology

"Perinatal transmission" has replaced an older synonym "vertical transmission" that describes the transmission of an infection from a pregnant mother to her newborn during the perinatal period: intrauterine, intranatal or early postnatal.

Peer review

This study has screened 2000 pregnant females in Egypt using rapid test and confirmed by enzyme immunoassay to identify the prevalence and possible maternal risk factors for HBV acquisition. This program focused on maternal risk factors associated with HBV positivity and the efficacy of active and passive immunoprophylaxis. In spite of the high dropout rate, this cohort prospective study including 2000 cases does provide some useful information and make practical recommendation for further research.

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