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Hepatitis B Viral Markers In Pregnant Women and Newborn Infants in Korea

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A study of the 5,284 pregnant women who delivered at St. Columban's Hospital in Mokpo City between April 1, 1985 to June 30, 1987 was conducted to determine the presence of hepatitis B viral (HBV) markers in the mothers and infants and to evaluate their effects. Medical histories, physical examinations, liver function studies and the ELISA test for HBV markers were reviewed.

The following results were obtained:

1) Of the 5,284 pregnant women, 448 (8.48%) were positive for HBsAg. Three hundred and thirty four women tested positive for HBsAg; 130 (38.92%) were HBeAg positive, 105 (31.44%) were HBeAg and anti-HBe negative, and 99 (29.64%) were anti-HBe positive.

2) Women positive for HBsAg exhibited a slight increase in toxemia ($p<0.1$), and no significant difference in postpartum hemorrhage ($0.05< p<0.1$) and the severity of hyperemesis.

3) SGPT was significantly higher in HBeAg positive women than in HBeAg negative women ($p<0.01$), and it was significantly more elevated in both eclamptic and preeclamptic women than in normal pregnant women ($p<0.005$).

4) The frequency of congenital malformation, spontaneous abortion, infantile death and physiologic jaundice was increased in the newborns of chronic HBV carriers, while women with active hepatitis B experienced more premature births.

5) Mother to infant transmission of HBsAg and HBeAg was high in the HBeAg positive group (18.0%, 42.7%) respectively, but very low in the HBeAg negative group (7.8%, 0.0%). Mother to infant transmission of antibodies was in the order of anti-HBc (95.5%), anti-HBe (91.2%) and anti-HBs (75.0%).

The effects of the HBV carrier state in pregnant women included increases in toxemia, postpartum hemorrhage, congenital malformations and premature births, however none of them were statistically significant.

There was a significant difference in the elevation of SGPT between toxemic and normal pregnant women, and between HBeAg positive and HBeAg negative carrier women.

The mother to infant transmission rate of HBeAg was more frequent than that of HBsAg.

Key Words: *HBV markers, Pregnant Women, Newborn Infants*

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INTRODUCTION

There are an estimated 200 million hepatitis B carriers in the world[1~4], and most of them are in the Pacific Ocean area of Asia. Although variations are observed between countries and ethnic groups, on the average 8 to 10% of the adults from South East Asia are chronic hepatitis B carriers[5].

While 8 to 10% of the population of Korea are chronic hepatitis B carriers, about 70% of the population have been exposed to HBV[6]. The prevalence of HBsAg begins to increase during the primary school years and peaks in the early twenties[7,8]. Both perinatal and horizontal transmission during childhood are sources of infection in this country.

The risks associated with the transmission of HBV from mother to infant vary according to the profile of the mother. Among mothers who are positive for HBeAg, the risk of transmitting HBV to their infants is 80 to 90% and 80 to 90% of those infants will become chronic carriers[9~13]. The frequency of HBeAg in chronic hepatitis B is about 40 % in this country[14] in contrast to the less than 4% in North America and Northern Europe[15]. Vertical transmission accounts for 20 to 40% of the world' s carriers (50 million)[2,16~18]. We suggest more than 40% of the total number of chronic hepatitis B carriers in this country are a direct result of perinatal transmission.

There is no specific drug for the treatment of acute viral hepatitis B and the available treatment has little effect in altering the course of the disease. Ten to fifteen percent of those infected become chronic hepatitis B carriers and are the source of endemic infection[3]. Therefore, the most effective way to decrease the population of chronic hepatitis B carriers is to prevent perinatal transmission from mother to infant.

There are a few reports about long term observation of perinatal transmission of HBV and non-A, non-B viruses. Our study of perinatal transmission included medical histories, physical examinations and EIA testing for HBV markers in all pregnant women who delivered at St. Columban's Hospital in Mokpo City. The results of the study reveal the prevalence of HBV markers in pregnant women and newborns and the effects of HBV on newborns and pregnant women.

MATERIALS AND METHODS

Five thousand, two hundred and eighty four pregnant women who delivered at St. Columban's Hospital in Mokpo, Jollanamdo, Korea from April 1, 1985 to June 30, 1987 were tested for HBsAg, and HBsAg positive carrier women were tested for HBeAg and anti-HBe. Medical histories included incidence of spontaneous abortion, premature birth, stillbirth, infantile death, congenital malformation and severe physiologic jaundice. The severity of hyperemesis and toxemia and the amount of postpartum hemorrhage were noted.

Peripheral venous blood was drawn from mothers before delivery, and from newborns within several hours after birth (before injection of HBIG). HBsAg, anti-HBs, anti-HBc, HBeAg and anti-HBe were assayed by the ELISA technique (Abbott Diagnostics, North Chicago, Ill). All sera were stored in at $-20℃$, and tests were repeated as necessary.

RESULTS

1. Effect of HBV on Pregnancy

Of the 5,284 pregnant women, 448 (8.48%) were positive for HBsAg.

There were 127 cases of toxemia among the 5, 284 pregnant women (Table 1), with a frequency of 3.35% in the HBsAg positive women, and 2.32% in the HBsAg negative women. These 127 patients

Table 1. Frequency in Toxemia of Pregnancy According to HBsAg Positivity

HBsAg	Toxemia			Normal pregnancy	Total
	Eclampsia	Preeclampsia	Total (%)		
HBsAg (+)	1	14	15 (3.35)	433	448
HBsAg (−)	10	102	112 (2.32)	4724	4836
Total	11	116	127 (2.40)	5157	5284

$P > 0.1$

were evaluated reference to: teenagers, over 35 years of age, twins, multipara, hypertension, diabetes mellitus and renal disease. Of the 111 toxemia cases among the HBsAg negative women, 49 cases (44.1%) had one of the above associated conditions, and 6 of 16 cases (37.5%) of toxemia in the HBsAg positive women had one of the above associated conditions (Table 2).

SGPT elevation was noted in 6.9% (8/116) of the preeclamptic women and in 27.3% (3/11) of the eclamptic women. One hundred and seventy five cases of postpartum hemorrhage were noted (Table 4). The frequency of positive HBsAg was 8.3% (426/5,109) in the women who had normal amount of bleeding (less than 500cc) and 12.6% (22/175) in the women who experienced severe hemorrhage (more than 500cc). Although HBsAg positive women hemorrhaged more, it was not statistically significant. Table 5 lists possible causes of hemorrhage.

The women were evaluated with respect to the severity of hyperemesis (Table 6). The frequency of positive HBsAg was 8.5% in 3,286 cases of mild or no hyperemesis, 9.4% in 666 cases of moderate hyperemesis and 8.4% in 1,332 cases of severe hyperemesis. There was no significant difference in HBsAg positivity and the severity of hyperemesis.

2. Effect of HBV on the Fetus

The incidences of spontaneous abortion, premature birth, stillbirth, infantile deaths, congenital malformations, and severe physiologic jaundice were noted. In this pregnancy, HBsAg positive women accounted for 8.29% of the 217 cases of premature birth, 6.85% of the 73 cases of stillbirth, 9.09% of the 55 cases of congenital malformations

Table 2. HBsAg and Associated Conditions in Toxemia of Pregnancy

Associated conditions	HBsAg	
	No. negative (%)	No. positive (%)
<20 years	2	0
>35 years	8	0
Twins	6	1
Multipara	22	4
Hypertension	5	0
Diabetes	0	0
Renal disease	6	1
Known	49 (44.1)	6 (37.5)
Unknown	62	10
Total	111	16

Table 3. Elevation of Serum SGPT at Delivery

Subject	No. of abnormal (%)	No. of normal (%)	Total
Eclampsia	3 (27.3)	8 (72.7)	11
Preeclampsia	8 (6.9)	108 (93.1)	116
Normal pregnancy*	64 (1.2)**	5093(98.8)	5157
Total	75 (1.4)	5209 (98.6)	5284

$P < 0.005$ Eclampsia to normal
$P < 0.005$ Preeclampsia to normal
$0.05 < P < 0.1$ Eclampsia to preeclampsia
* Normal pregnancy ; No toxemia of pregnancy
** 64 cases : Elevation of SGPT (> 50IU) due to hepatitis A (2), B (17), unidentified (44), drugs (1).

Table 4. Postpartum Hemorrhage and HBsAg

Amount of postpartum hemorrhage	No. of cases	No. of HBsAg (%)
<500 cc	5109	426 (8.3)
>500 cc	175	22 (12.6)
Total	5284	448 (8.5)

$0.05 < P < 0.1$

Table 5. HBsAg and Causes of Postpartum Hemorrhage

Cause	No. of women	
	HBsAg (−)	HBsAg (+)
Large episiotomy	4	1
Laceration of perineum	2	0
Atony		
Overdistended uterus	11	2
Prolonged labor	8	2
Vigorous oxytocin	10	1
Other	35	4
Uterine infection	9	0
Rapid labor	4	1
Placenta retention	60	9
Placenta abruptio	4	0
Placenta previa	4	0
Total	151 (3.1)	20 (4.5)

and 10.59% of the 236 cases of severe physiologic jaundice, while in previous pregnancy by the medical history, 10.45% of the 134 cases of prematurity, 11.11% of the 90 cases of stillbirth, 13.64% of the 22 cases of congenital malformations, 11.69% of the 77 cases of infantile deaths and 10.11% of the 811 cases of spontaneous abortions. All of the incidences of fetal wastage except stillbirth seemed to be increased, but not statistically significantly, in the chronic HBV carriers (Table 7).

The frequency of prematurity was 4.11% (197/4,792) in HBsAg negative and normal SGPT women, 3.71% (16/431) in HBsAg positive healthy carrier women, 11.76% (2/17) in active hepatitis B women, and 10.00% (1/10) in HBsAg negative and SGPT above 100IU women. All of the above findings were not significant statistically (Table 8).

3. Effect of HBV in Pregnancy on the Newborn Infant

Among the 334 HBsAg positive women, 130 (38.92%) were HBeAg positive, 105 (31.44%) were HBeAg and anti-HBe negative, and 99 (29.64%) were anti-HBe positive (Table 9).

The level of serum SGPT in HBeAg positive healthy carrier women was significantly higher than in HBeAg negative healthy carrier women ($p<0.01$) (Table 10).

Table 6. Positive Rates of HBsAg According to Severity of Hyperemesis

Severity of hyperemesis	No. of cases	No. of HBsAg (%)
None to mild	3286	279 (8.5)
Moderate	666	57 (8.6)
Severe	1332	112 (8.4)
Total	5284	448 (8.5)

We studied the prevalence of HBV markers in 218 newborns whose mothers were chronic HBV carriers according to maternal HBeAg/anti-HBe status at the delivery (Table 11). HBsAg was positive in 16 neonates (18.0%) of 89 HBeAg positive mothers, 6 neonates (9.5%) of 63 HBeAg and anti-HBe negative mothers, and 4 neonates (6.1%) of 66 anti-HBe positive mothers. HBeAg was positive in 38 neonates (42.7%) of 89 HBeAg positive mothers and negative in all neonates (0.0%) of the 129 HBeAg negative mothers.

The mother-to-infant transmission of HBV markers at delivery was studied (Table 12). The HBsAg positivity was 11.2% in 221 cases. The HBeAg positivity was 37.8% in 90 cases. The anti-HBe positivity was 91.2% in 68 cases. The anti-HBs positivity was 75.0% in 20 cases. The anti-HBc positivity was 95.5% in 222 cases.

Table 7. Positive Rates of HBsAg with Possible Adverse Effects on the Fetus

	Present pregnancy No. positive /No. cases (%)	Previous pregnancy No. positive /No. cases (%)
Prematurity	18/217 (8.29%)	14/ 134 (10.45%)
Stillbirth	5/ 73 (6.85%)	10/ 90 (11.11%)
Cong. malformation	5/ 55 (9.09%)	3/ 22 (13.64%)
Physiologic jaundice	25/236 (10.59%)	
Infantile death		9/ 77 (11.69%)
Spontaneous abortion		82/ 811 (10.11%)
Total	53/581 (9.12%)	118/1134 (10.41%)

Table 8. The Frequency of Premature Birth

Pregnant women	No. of women	No. of premature birth	%
HBsAg (−) SGPT →	4792	197	4.11%
HBsAg (+) SGPT →	431	16	3.71%
HBsAg (+) SGPT ↑	17	2	11.76%
HBsAg (−) SGPT (40 − 100)	34	1	2.94%
HBsAg (−) SGPT > 100	10	1	10.00%
	5284	217	

HBV markers were found in several neonates whose mothers were negative. The anti-HBe positivity was 4.0% in 173 cases. The anti-HBs positivity was 4.1% in 221 cases. The anti-HBc positivity was 36.8% in 19 cases.

DISCUSSION

It is a well known fact that alterations in certain liver function tests can occur during a normal pregnancy:[19~24] including retention of BSP, a modest increase in alkaline phosphatase, cholesterol and α_1 and α_2 globulins, reduced serum albumin, urea and uric acid concentrations. These changes, with or without clinical evidence of liver disease, are divided into three types: 1) abnormalities peculiar to the stage of pregnancy; 2) abnormalities superimposed upon pregnancy; and 3) abnormalities not peculiar to pregnancy[25,26]. Among these, jaundice due to viral hepatitis which is included in number three is the most common cause of jaundice in pregnant women.

Over 30 kinds of viruses can cause hepatitis in man, and at least six, A, B, D and 3 types of non-A, non-B have implications for pregnant women and

Table 9. Maternal HBeAg/Anti-HBe Status at Delivery

Maternal HBeAg/Anti-HBe at delivery	No. of HBsAg (+)	(%)
HBeAg (+)	130	(38.92)
HBeAg (−), Anti-HBe (−)	105	(31.44)
Anti-HBe (+)	99	(29.64)
Total	334	(100.00)

Table 10. The Level of Serum SGPT at Delivery

Subjects	Number	Mean (U/L)
Control *	4,638	13.63
HBsAg (+) HBeAg (−)	229	15.08 ± 6.76
HBsAg (+) HBeAg (+)	130	18.24 ± 7.79

* Control : SGPT < 40, HBsAg (−), Toxemia (−)
P < 0.01 by students' t-test

Table 11. Mother-to-Infant Transmission of HBV Markers According to Maternal HBeAg/Anti-HBe Status at Delivery

Mother / Neonate			HBsAg (+) HBeAg (+) AntiHBe (−)	HBsAg (+) HBeAg (−) AntiHBe (−)	HBsAg (+) HBeAg (−) AntiHBe (+)	Total
sAg	eAg	eAb				
+	+	−	15 (16.9)	0	0	(7.6)
−	+	−	23 (25.8)	0	0	(9.3)
+	−	−	1 (1.1)	5	0	(2.9)
+	−	+	0	1	4	(2.3)
−	−	−	48	52	9	
−	−	+	2	5	53	
Total			89	63	66	218

Table 12. Mother-to-Infant Transmission of HBV Markers at Delivery in 241 Mothers and their Infants

HBV markers	Mother No. positive	Infant No. positive (%)	Mother No. negative	Infant No. positive (%)
HBsAg	221	27 (11.2)	20	0 (0.0)
HBeAg	90	34 (37.8)	151	0 (0.0)
Anti-HBe	68	62 (91.2)	173	7 (4.0)
Anti-HBs	20	15 (75.0)	221	9 (4.1)
Anti-HBc	222	212 (95.5)	19	7 (36.8)

newborn infants[28]. A hepatitis A virus infection during pregnancy is of no major risk to the fetus[29]. There is a brief viremic period[28], but no chronic carrier state and no transmission to the newborn[29]. There has been no study of hepatitis A infection and pregnant women in Korea. This may be due to the nearly 100% positivity of anti-HAV in the thirty year age group in Korea[7,8]. Of the 5,284 pregnant women surveyed, only two exhibited a positive IgM anti-HAV and elevated SGPT.

The Delta agent requires the presence of HBV for replication and infection[30]. Hepatitis D has been reported to be transmitted from mother to infants[31]. The transmission and prevention of hepatitis D infection may be similar to those of hepatitis B. Although Korea is an endemic area for hepatitis B, there seems to be very few cases of hepatitis D infection. One investigator reported that there was not one Delta agent positive patient among chronic liver disease patients due to HBV[32]. Another researcher reported that 1.6% of the patients with chronic liver disease due to HBV were positive for anti-Delta[33]. Recently a researcher reported that anti-Delta was detected in only 1 case out of 40[34]. Thus there is no risk of perinatal transmission of hepatitis D in Korean pregnant women.

Non-A, non-B hepatitis resemble hepatitis A and B in epidemiological chracteristics[28]. The importance of vertical transmission remains uncertain, although there is evidence that women who develop non-A, non-B hepatitis during the third trimester of pregnancy are more likely to transmit the infection to their babies than those who become ill earlier in their pregnancy[29]. There are several reports that 15 to 35% of acute viral hepatitis in adult Koreans in non-A, non-B hepatitis, but there is no report evaluating the perinatal transmission of non-A, non-B hepatitis in Korea. Presently the authors are studing this and will issue a report in the near future.

Hepatitis B, the most common and virulent form in Korea, has been studied thoroughly since serologic tests became available. Many investigations on the maternal effects of viral hepatitis have been conducted. Most early reports from the less well developed areas of the world such as India[35~41], the Middle East[42~44] and Africa[45,46] suggested that both the frequency and severity of viral hepatitis were far greater in pregnant women. However, some of the data might have been included a third agent, non-A, non-B hepatitis, which appears to be responsible for the extraordinarily high fatality rate in pregnant women. Sherlock[22] proposed that malnutrition and hormonal changes in late pregnancy were possible factors. Haenmerli[47] reported that inadequate prenatal care, together with anemia or other diseases were responsible.

Many reports from the developed countries of Europe[48,49] and America[50,51] showed that viral hepatitis has no greater adverse effect on pregnant women than on non-pregnant women.

The percentage of positive HBsAg as determined by EIA in our study was 8.48% and was higher than the RPHA method of Jun et al[7] 5.9%, Eum et al[52] 5.2%, Lee et al[53] 3.6%, Goo et al[54] 7.1%, Lee et al[55] 5.0%, Shin et al[56] 6.1%, but was similar to that of Baek et al[57] 7.4% by the EIA method and Jang et al[58] 9.1% in 350 nonpregnant young women by the RIA method.

The prevalence of HBsAg may differ according to race and locality. Carla Rosendahl[15] reported that the positivity of HBsAg in Germany was 1.2% in 8,918 pregnant women, but that half of the carriers were of Asian origin. The positivity of HBsAg was 11% in 1,272 pregnant women in Ovamboland, South West Africa[59].

Although there is no report on the frequency of toxemia in pregnant HBV carriers, we observed 127 cases of toxemia of pregnancy in 5,284 pregnant women, and the statistics indicate that the frequency of toxemia of pregnancy was higher in HBsAg positive women ($p > 0.1$).

To verify the relationship between toxemia and HBV carriers, we studied 127 parients with toxemia of pregnancy with reference to; teenagers, women over 35 years of age, twins, multipara, hypertension, diabetes mellitus, and renal disease (Table 2)[60]. Of the 111 cases of toxemia of pregnancy in HBsAg negative women, 49 cases (44.1%) had one of the above associated conditions. Of the 16 cases of toxemia of pregnancy in HBsAg positive women, 6 cases (37.5%) had one of the above associated conditions. Thus we suggest that toxemia of pregnancy is more frequent in HBV carriers.

Yoo et al[61] reported that the level of serum SGPT in severe preeclamptic women was elevated significantly more than that of mild preeclamptic women, but there was no significant difference between eclamptic and mild preeclamptic women. But in our data the level of serum SGPT in eclamptic women (mean 18.11 ± 13.03 U/L) was significantly higher than in preeclamptic women (mean 37.30 ± 17.56 U/L) ($p < 0.01$).

We studied 175 cases of postpartum hemor-

rhage in 5,284 pregnant women. The HBsAg positivity was 8.3% in cases with bleeding of less than 500 ml, and 12.6% in cases with postpartum hemorrhage more than 500 ml ($0.05<p<0.1$). We studied 175 cases of postpartum hemorrhage in relation to immediate causes; large episiotomy, laceration of perineum, atony (overdistended uterus, prolonged labor, vigorous oxytocine infusion, others), uterine infection, precipitate labor, retained placenta, abruptio placenta, and placenta previa[62]. Of the 4,836 cases of HBsAg negative women, 151 cases (3.1%) had apparent causes. Of the 448 cases of HBsAg positive women, 20 cases (4.5%) had apparent causes. Causes of postpartum hemorrhage were more frequent in HBsAg positive carriers, suggesting that postpartum hemorrhage is slightly more frequent in HBV carriers but not significantly, and that it can be an indirect effect.

There are numerous reports of the effect of viral hepatitis on the fetus during pregnancy. In early studies, many reports showed an increased frequency of prematurity, stillbirth, intrauterine death, congenital malformations and abortion during pregnancy as consequence of hepatitis[35~40.42,44,63~65]. In later studies from Western countries, an unusual increase in fetal wastage has not been noted[48,50,51,66~68]. But the risk of prematurity seemed to be increased, especially if the mother was infected in the last trimester[51,69~71].

In Korea, Lee et al[53] reported that prematurity was 7.6%, abortion 1.8%, stillbirth 1.8% in 225 pregnant women. Shin et al[56] reported that stillbirth was 2.45%, congenital malformations 0.49% in 817 pregnant women. But they could not compare because there was no case of fetal wastage in HBV carrier women.

In our study, of 5,284 pregnant women, there were 217 prematurity cases, 73 stillbirth cases, 55 congenital malformations cases, 236 severe physiological jaundice cases in this pregnancy. In previous pregnancy history taking, there were 134 prematurity cases, 90 stillbirth cases, 22 congenital malformations cases, 77 infantile death cases and 811 spontaneous abortion cases. When we compare the data by the positive and negative groups of HBsAg, all of the incidences of fetal wastage seemed to be increased in the chronic HBV carriers, but not statistically significantly. The HBsAg positivity in cases with stillbirth was similar to that of normal delivery. This can be possible because some of the women who had intrauterine death might have gone to another hospital before fullterm and we studied nearly fullterm pregnant women who visited our hospital for delivery.

The prevalence rate of HBeAg in chronic HBV carriers is less than 4% in North America and Northern Europe and is 40 to 50% in the Far East and South East Asia. In this country Baek et al[57] reported that HBeAg positive was 45%. HBeAg and anti-HBe negative 5%, anti-HBe positive 50% in 40 HBsAg positive pregnant women. Eum et al[94] reported that HBeAg positive was 45.4%, HBeAg and anti-HBe negative 18.2%, and anti-HBe positive 35.4% in 11 HBsAg positive pregnant women. In our study, among 334 HBsAg positive pregnant women, 130 cases (38.92%) were HBeAg positive, 105 cases (31.44%) HBeAg and anti-HBe negative, and 99 cases (29.64%) anti-HBe positive.

The presence of HBeAg is considered a serum marker for active viral replication as well as for potential infection and is used as a prognostic marker for perinatal transmission of the HBV[10,72~75]. HBeAg is usually detected in serum together with HBV-DNA polymerase and HBV DNA and therefore reflects the presence of the complete virion (Dane particles)[17,71,76,77].

If the mother is positive for both HBsAg and HBeAg, about 80 to 90% of infants will become infected and approximately 90% of these infected infants will become chronic HBV carriers[11]. If the HBsAg positive carrier mother is HBeAg negative, the transmission occurs in 25% of the cases. If anti-HBe is positive, the transmission occurs in 12 % of the cases. Notably if the mother is HBeAg negative, transition to chronic HBV carrier is rare[13,28].

Carla Rosendahl[15] reported that in a Western European population the risk of perinatally acquired HBV infection in the infants of anti-HBe positive carrier mothers is small, and that passive immunization of this group is not necessarily indicated.

But Sherlock reported that HBV DNA was found in 40% to 50% of anti HBe positive patients in some region and race which means a high rate of infection also. Shou-Dong Lee et al[78] reported that 10% of HBeAg negative carrier mothers had detectable HBV DNA in their sera which may be a more sensitive and direct indicator for the infection and the risk of perinatal transmission of HBV. Myron J. Tong[79] reported that HBV infection occured in 37.5% of infants born to HBeAg-negative mothers. He suggested that if the mother is HBsAg positive, regardless of the HBeAg/anti-HBe status, we should provide immunoprophylaxis for the

newborn infant. However fatal cases of neonatal hepatitis B virus infection have been reported in infants born to such women[80~82].

HBeAg/anti-HBe status of the mother is important not only in perinatal transmission but also in postnatal infection. Beasley et al[83] observed that the incidence of HBV infections during the second and third year of life in 105 children whose mothers were HBsAg carriers. If the mother was HBsAg positive, the incidence of infection was 57.1%, HBeAg negative and anti-HBe negative 20.4%, anti-HBe positive 11.3%.

Some researchers suggested the possibility of transplacental transmission of HBV[18]. But many investigators observed that many HBsAg-positive neonates have been perfused at delivery with their mother's blood and this HBsAg may disappear within a few weeks of birth[84].

The authors are continuing to observe the rate of chronic carriers in neonates born to carrier mothers. The HBV profile in neonates at birth was reviewed and was related to the mother's HBeAg/anti-HBe status. In our study, among 218 carrier mothers, HBsAg was positive in 16 neonates (18.0 %) out of 89 HBeAg positive mothers, 6 neonates (9.5%) out of 63 HBeAg negative, anti-HBe negative mothers, and 4 neonates (6.1) out of 66 anti-HBe positive mothers.

Goudeau et al[85] reported that HBsAg was positive in 4 neonates (30.8%) from 13 HBeAg positive mothers and 5 neonates (16.7%) from 30 HBeAg negative, anti-HBe negative mothers. There was no anti-HBe positive mother.

In Korea Baek et al[57] reported on 40 neonates born to carrier mothers and Eum et al[71] reported on 8 neonates born to carrier mothers. The incidence of HBsAg positivity was similar but the two studies used the cord blood of neonates which proved to be inaccurate[86~91].

There are several reports of maternal-infant transmission of hepatitis B virus infection at birth. Theoretically the virus can pass through the placenta by maternal-fetal transfusion at delivery. Papaevangelou et al reported that anti-HBc crosses the placenta freely, but Dane particles can cross only when the placenta barrier is ruptured. Shiraki et al[84] reported that most of newborn infants who were infected in the perinatal period exhibited HBs-antigenemia about 3 to 5 months after birth. Arakawa et al reported that IgG-bound HBeAg can freely pass through the placenta[92,93]. Noriyuki et al[94] observed that within 1 month after birth, HBeAg titers decreased rapidly and again increased at the age of 2 months in accordance with HBsAg positive conversion.

The maternal-infant transmission of HBV markers was quite variable by the investigators, Baek et al[57] reported that the HBsAg positivity was 60% in 40 cases and the anti-HBs positivity was 80. 9% in 250 cases. Lee et al[55] reported that the HBsAg positivity was 17.6% in 74 cases and the HBeAg positivity was 80.0% in 15 cases. Goudeau et al[85] reported that the HBsAg positivity was 13.0 % in 46 cases, the HBeAg positivity was 7.7% in 30 cases and the anti-HBe positivity was 0.0% in 30 cases.

In our study the HBsAg positivity was 11.5% in 227 cases, the HBeAg positivity was 37.7% in 78 cases, the anti-HBe positivity was 81.8% in 55 cases, the anti-HBs positivity was 85.7% in 28 cases, and the anti-HBc positivity was 95.9% in 194 cases. The transmission rate of HBeAg was 3.5 times higher than that of HBsAg in the peripheral blood of newborn infants at birth. The order of the transmission rate of antibodies is anti-HBc, anti-HBe, and anti-HBs. Generally antibodies seemed to cross the placenta freely especially anti-HBc, but antigens seemed to be more restricted. But HBeAg might cross the placenta more easily than HBsAg and 23 cases (25.8%) of newborn infants whose mothers (89 cases) were positive both for HBsAg and HBeAg showed HBeAg positive only. These results were simlar to the study of Arakawa et al[92] and that of Yeh YS et al[93]. We noted the appearance of HBV markers in a few neonates whose mothers were negative. The anti-HBc positivity especially was very high (36.8%).

The present study shows the prevalence of markers in pregnant women and maternal-infant transmission of HBV markers and the effect of HBV on the fetus, newborn infants and women. We are going to collect more cases and observe the real effect of HBV especially on prematurity, toxemia of pregnancy, and postpartum hemorrhage. We hope also to classify liver disease and to find the importance of vertical transmission of non-A, non-B hepatitis in pregnant women.

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