Impacts of Vaccination on Hepatitis B Viral Infections in Korea over a 25-Year Period

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Key Words

Epidemiology · Hepatitis B vaccine · Hepatitis B virus · Korea

Abstract

Background: Hepatitis B virus (HBV) vaccination has effectively reduced the acute and chronic infection rates in recent years. Since 1983, HBV vaccination has been recommended for all neonates in Korea. **Methods:** This article reviews the impacts of HBV vaccination throughout the past 25 years in Korea. Before the introduction of the HBV vaccination program, approximately 8% of the general Korean population tested positive for hepatitis B virus surface antigen (HBsAg). **Results:** The percentage of vaccinated infants has surpassed 98.9% since 1990. The HBsAg carrier rate in the general population decreased to 3.7% in 2007. In particular, the prevalence of HBsAg decreased to 0.44% in teenagers and to 0.2% in children younger than 10 years. In addition, administration of the HBV vaccine may have reduced the risk of hepatocellular carcinoma among adults. Despite the administration of hepatitis B immunoglobulin and the HBV vaccine to children with HBsAg-positive mothers, the failure rate of HBV immunoprophylaxis was 4.2% in 2008. In Korea, there have been no reported cases of HBV surface gene variants

such as G145R. **Conclusions:** The prevalence of HBV carriers in Korea was markedly reduced after the introduction of the universal HBV vaccination program. Korea is now classified as an area of intermediate endemicity for HBV.

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Introduction

Hepatitis B virus (HBV) infection is a serious public health problem worldwide and a major cause of chronic hepatitis, cirrhosis, and hepatocellular carcinoma (HCC) [1]. At least 2 billion people, or one third of the world's population, have been infected with HBV and an estimated 1 million people die each year from acute and chronic sequelae secondary to HBV infection [2]. In addition, more than 400 million people, or 6% of the world's population, are chronic carriers of HBV. Approximately 4.5 million new cases of HBV infection occur worldwide each year, and one fourth of these cases progress to liver disease [3]. There is a marked difference in the geographic distribution of carriers, ranging from 10–20% in South-East Asia and Sub-Saharan Africa to less than 1% in Northern Europe and America [1, 4]. Approximately 75% of chronic carriers live in Asia and the Western Pacific [1,

4]. In low endemic areas, most HBV infections are acquired via horizontal transmission among adolescents and young adults. Conversely, in areas of high endemicity, the most common route of transmission is perinatal and the infection is often acquired during the preschool years [2, 4]. The risk of becoming an HBV carrier is 90% in cases of perinatal infections, between 25 and 30% for infected infants and children under 5 years of age, and less than 10% for infected adults [2, 4]. More than 25% of infants and older children who acquire HBV infection will eventually develop HBV-related HCC or cirrhosis. Adults who have had chronic HBV infection since childhood develop HCC at a rate of 5% per decade, which is 100 to 300 times the rate among uninfected persons [1, 4]. In Korea, HCC is both the third most common and the third most deadly cancer. The age-standardized mortality rate for HCC is 33.9 per 100,000 men and 10.9 per 100,000 women. The annual death rates from HCC were 21.4 per 100,000 persons in 1996 and 22.4 per 100,000 persons in 2006 [5, 6]. The number of deaths from liver cancer increased from approximately 5,789 in 1983 to 9,966 in 1994, then remained steady at 9,500 per 100,000 persons in 2006 [7, 8]. With regards to the etiological agents of HCC, approximately 65–75% of patients test positive for hepatitis B virus surface antigen (HBsAg), and 10–20% of patients test positive for antibodies to HCV (anti-HCV) [9, 10]. Because less than 10% of HCC cases are non-B or non-C, surveillance of hepatitis carriers is the most important tool for the prevention of HCC in Korea. Although current antiviral treatments using interferons or nucleoside/nucleotide analogs are effective against chronic HBV, chronic carriage of the virus is more difficult to eliminate. Considering that most HBV infections in Korea occur vertically, universal infant vaccination is the key to the elimination and subsequent eradication of HBV. Therefore, the combined efforts of vaccination and effective treatment regimens may eventually lead to the eradication of HBV.

The first HBV vaccine, derived from human carrier plasma, was approved for use in the United States in 1981. In 1991, the WHO recommended that all countries implement a policy of universal HBV vaccination by 1997 [11]. Most countries have incorporated universal HBV vaccination into their national infant immunization programs. The estimated global coverage rate of infant HBV vaccination increased from less than 1% in 1990 to 30% in 2000, and from nearly 50% in 2004 to 69% in 2008 [12]. As of 2008, 177 of the 193 WHO member states (92%) had initiated HBV vaccination programs [13]. This program reduced not only the rate of persistent infection and the

total prevalence of HBV in the younger generation but also the occurrence of childhood HCC and fulminant hepatitis [14]. In Korea, hepatitis B has significantly declined in the past decades as a result of the HBV vaccination program and the introduction of other public health measures such as use of universal precautions in medical settings and blood screening tests. Thus, this article reviews the impacts of HBV vaccination in Korea over the past 25 years.

Strategy for the Prevention of HBV Infection in Korea

Korea was classified as an area of high endemicity before the implementation of the universal HBV vaccination program. The first domestic plasma-derived HBV vaccine became available in Korea in 1982, and HBV vaccination has been recommended for all neonates since 1983. The first national HBV vaccination program began in 1985 for newborn infants whose mothers were HBsAg carriers. A national HBV vaccination program for school-aged children was launched in Korea in 1988, and HBV vaccination was incorporated into the national vaccination guidelines in 1991. In 1995, Korea began universally vaccinating newborn infants to prevent the perinatal transmission of HBV. A national program to prevent the vertical transmission of HBV was launched in 2002 [15]. In Korea, most cases of HBV infection occur when the virus is transmitted from carrier mothers to infants during the perinatal period, and from other horizontal sources to infants and children. Over the past 25 years, Korea has adopted a series of strategies to eliminate HBV infection and prevent transmission of the virus [16]. These strategies involve the universal vaccination of infants and adolescents, and the screening of all pregnant women for HBsAg to prevent perinatal HBV transmission. Since 1983, HBV vaccination at 0, 1 and 2 months or at 0, 1 and 6 months after birth has been compulsory for all neonates born in Korea. To prevent perinatal transmission, infants born to HBsAg-positive mothers and mothers of unknown HBsAg status receive the HBV vaccine and hepatitis B immunoglobulin (HBIG) within 24 h of birth. The HBV vaccine is also recommended for high-risk groups (e.g. homosexual men, health-care workers, drug users, people with multiple sexual partners, people who live with chronically infected persons, chronic hemodialysis patients, HIV-infected patients and other immunocompromised persons).

Fig. 1. Changes in the prevalence of HBV carriers over the past 25 years, after the introduction of HBV vaccine in Korea. Since 1983, HBV vaccination has been recommended for all neonates in Korea. Data were adapted from [22, 27].

In Korea, approximately 79.7% of neonates born after 1983 and 98.9% of neonates born after 1990 received the HBV vaccine [17]. However, a study [18] of 2,072 elementary school students in 1993 revealed that only 69.8% of the children had received all 3 doses of the HBV vaccination schedule. In general, a protective antibody response occurs after the first dose in 30–50% of healthy adults aged 40 years or younger. This protective response occurs in 75% of healthy adults after the second dose, and in more than 90% of healthy adults after the third dose [14]. Data obtained from a Korean survey of national immunity in 2007 revealed that after the completion of the 3-dose HBV vaccination regimen, approximately 95% of individuals exhibited protective concentrations of the anti-HBs antibody [19].

Impacts of HBV Vaccination in Korea over a 25-Year Period

Changes in the Prevalence of Chronic HBV Carriers

According to several studies published in the 1980s and early 1990s, the prevalence of chronic HBV carriage ranged from 8–10% before the introduction of the HBV vaccine (fig. 1) [20–22]. In 1990, Oh and Joung [23] reported that the prevalence of HBsAg positivity was 5.27% among 173,342 school students (aged 7–18 years) born before the vaccination program was introduced. Kim et al. [24] conducted a study of 498,206 male army draftees

between 1993 and 1999 to evaluate HBV infection. The majority of the draftees were born before the launch of the universal vaccination program and were 20 years old. Thus, the draftees received the HBV vaccine as school-aged children rather than as infants. Among these draftees, positivity of HBsAg gradually decreased from 5.8% in 1993 to 4.3% in 1999. Jang et al. [25] also reported that the overall prevalence of HBsAg among more than 600,000 subjects older than 6 years was 8.3% in 1995, 4.8% in 1996, 3.4% in 1997 and 1998, and 2.6% in 1999. Subgroup analysis revealed that the rates of HBsAg carriage among subjects aged 6–19 years were 8.2% in 1995, 3.9% in 1996, 2.1% in 1997, 2.6% in 1998 and 1.3% in 1999. Hence, the rate of HBsAg carriage declined from 8.2% in 1995 to 1.3% in 1999. Most of the subjects were born after the introduction of the universal vaccination program. However, the rates of HBsAg carriage among subjects older than 20 years during the same years were 8.9, 6.4, 5.9, 5.4 and 5.4%, respectively, and the rates decreased from 8.9% in 1995 to 5.4% in 1999. For all years, the rates of HBsAg carriage were significantly lower among subjects aged 6–19 years than among subjects older than 20 years. Jang et al. [26] also reported that between 1997 and 1999, the prevalence of HBsAg among 120,220 school students (age range 7–18 years; born between 1981 and 1992) was 2.5%. The rate of HBsAg carriage among elementary school students (born between 1987 and 1992) was 1.4%, which was significantly lower than the rates of HBsAg carriage among junior high school students (3.2%; born between 1982 and 1986) and senior high school students (3.4%; born between 1981 and 1983). During the same years, the overall rate of HBsAg carriage decreased significantly from 2.8 to 1.9%. Although many epidemiological studies have assessed HBV infection in Korea, most of the studies were based on unrepresentative or small populations from selected communities. The Korean Ministry for Health, Welfare and Family Affairs performed the National Health and Nutrition Survey of 4 cohorts, aged 10 years or older, in 1998, 2001, 2005 and 2007 to investigate the epidemiological characteristics of HBV infection in Korea [27]. As the survey was based on a representative sample of the entire nation and used a stratified multistage probability sampling design, these data provide a comprehensive picture of the distribution of HBV in Korea. Data obtained from the first National Health and Nutrition Survey in 1998 revealed that the rates of HBsAg seropositivity in children aged 10 years and older were 5.1% in males and 4.1% in females [28]. Among children and adolescents younger than 20 years, the seropositivity rates were 2.1% in males and 2.7% in

females. The peak ages for seropositivity were 20–29 years in males and 30–39 years in females, after which time the rates remained the same until the subjects reached 50–59 years. The rates then decreased in both males and females. According to these nationwide surveys, the prevalence of HBsAg positivity in persons older than 10 years decreased from 4.6% in 1998 to 3.7% in 2007. The rate of HBsAg carriage among subjects between 10 and 18 years old declined from 2.2% in 1998 to 0.2% in 2005 [27]. A 2007 survey of national immunity conducted by the Korea Centers for Disease Control showed the prevalence of HBsAg was 0.2% in children aged 4–6 years [19]. Similarly, the Korean Ministry of Education, Science and Technology conducted student health examinations in 2006 to investigate the epidemiological characteristics of HBV infection in Korea. The prevalence of HBV infection among junior high school students was 0.44% [29]. Data obtained from the fourth National Health and Nutrition Survey of Korea in 2007 revealed that the prevalence of HBsAg was 3.7% among males and females aged 10 years and older [27]. The prevalence of HBsAg was higher in men (4.3%) than in women (3.2%), and the total number of HBV carriers was estimated to be more than 1,800,000 persons in 2007 [27]. A sustained decline of HBV infection is expected in the future, whereupon the prevalence of HBV infection in Korea will eventually be as low as that in Western countries.

Changes in HBV Surface Antibody Positivity

The rates of HBV surface antibody (anti-HBs) in 332,780 students aged 6–17 years increased sharply, from 21.7% in 1988 to 54.1% in 1993 [30]. In 1993, Lee et al. [18] examined the prevalence of anti-HBs among 2,072 elementary school students, and found that the anti-HBs seropositive rate was 88.9% among children aged 6–7 years and 75.8% among children aged 12–13 years. Jang et al. [26] also reported in the late 1990s that the prevalence of anti-HBs among 120,220 students aged 7–18 years was 47.4%. In 1998, the first National Health and Nutrition Survey found that the anti-HBs seropositive rate was 57.0% in males and 58.9% in females [28]. An et al. [31] reported that, between 2003 and 2005, the rates of anti-HBs by age were 78.6% for infants aged 6–12 months, 62.7% for children aged 1–3 years, 51.9% for children aged 4–6 years, 49.5% for children aged 7–12 years, 63.4% for adolescents aged 13–15 years and 72.2% for adolescents aged 16–18 years. A 2007 survey of national immunity conducted by the Korea Centers for Disease Control revealed that the anti-HBs prevalence was 56.0% in children aged 4–6 years [19].

Fig. 2. Changes in anti-HBc positivity over the past 25 years, after the introduction of HBV vaccine in Korea. Since 1983, HBV vaccination has been recommended for all neonates in Korea. Data were adapted from [32, 33].

Changes in HBV Core Antibody Positivity

During the 1980s, 11% of newborn babies in Korea became infected with HBV during the perinatal period. Thereafter, the prevalence of HBV core antibody (anti-HBc) increased with increasing age. The anti-HBc positivity rate was nearly 30% among children younger than 10 years. Among adults in their forties, the infection rate reached approximately 70% (fig. 2) [32]. After the introduction of the vaccine program, Lee et al. [18] reported that the anti-HBc seropositive rate in 1993 was 7.1% among children aged 6–7 years and 15.6% among children aged 12–13 years. During the late 2000s, the prevalence of anti-HBc decreased with decreasing age and was 10.6% in adults younger than 30 years. These data may reflect the effects of universal HBV vaccination in Korea. The proportion of anti-HBc was highest in adults aged 50–59 years (52.4%) and decreased with decreasing age [33].

Changes in the Epidemiologic Profile of Acute Hepatitis B

The epidemiologic profile of acute HBV infection in Korea continues to change in response to the universal HBV vaccination program. Concerning the etiology of acute viral infection during the early 1990s, the prevalence rates of acute viral hepatitis A, B, D and non-A/non-B were 3.4, 60.3, 0.9 and 35.3%, respectively, with HBV infection being the most common cause [34]. According to data reported between 2006 and 2008 [35], the majority (70%) of

Fig. 3. Age distribution of acute hepatitis B in the 1980s and 2000s. The peak age was 20–29 years in the 1980s, and 30–39 years in 2000s. Data were adapted from [37].

cases of acute viral infection were caused by the hepatitis A virus, while HBV accounted for only 5%. Therefore, the incidence of acute hepatitis B dramatically declined after the introduction of the HBV vaccination program. According to the 2008 Guidebook of the Hepatitis B Vertical Transmission Prevention Program of the Korean Ministry for Health, Welfare and Family Affairs [36], the incidence of acute hepatitis B in adult males older than 30 years was 17 per 100,000. After the implementation of the HBV vaccination program, the peak age of acute hepatitis B has also changed (fig. 3). Cases of acute hepatitis B peak in adults aged 20–29 years. The majority of acute hepatitis B cases in the early 1980s occurred in people aged 10–29 years (60.0%). The decline in the incidence of acute hepatitis B after the introduction of the HBV vaccination program was more striking in adults aged 10–29 years, who were born after the introduction of HBV vaccination. On the other hand, the incidence of acute hepatitis B in the early 2000s was highest among adults aged 30–39 years, who were born before the introduction of the HBV vaccination program [37]. Other cohort studies from Korea also demonstrated that HBV infection occurs commonly in adulthood [38, 39]. Thus, HBV transmission may still occur in unvaccinated and uninfected adults, and HBV vaccination is able to prevent the spread of infection within the family and as a result of direct contacts during adulthood. Therefore, an adult without a complete set of previous vaccinations should be given ‘catch-up’ HBV vaccinations to prevent acute HBV infection.

Changes in the Incidence of HCC

A Taiwanese study demonstrated a decline in the incidence of HCC in children after the implementation of the universal hepatitis B vaccination [40]. Importantly, a large-scale cohort study [41] performed in Korea reported that HBV vaccination protected against the development of HCC in adult men. With regards to the incidence among unvaccinated and uninfected people (table 1), the relative risks of HCC among the chronically infected and among the unvaccinated and infected were 18.1 (95% CI 14.2–22.9) and 0.34 (95% CI 0.19–0.60), respectively. The relative risk of HCC among the vaccinated group was 0.58 (95% CI 0.31–1.09). That is, the incidence of HCC was lower in the vaccinated group than in the unvaccinated group. This study suggests that HBV vaccination significantly decreases the incidence of HCC, even in adulthood. However, the follow-up period was only 4 years, and HCC requires several decades to evolve from the HBV carrier state. Thus, long-term follow-up studies will be needed to verify these findings. Along with a decrease in HBsAg carrier status, HCC development is expected to decrease in the near future.

Immunoprophylaxis Failure

Epidemiological studies in the 1980s found that 6.57% of pregnant women in Korea were HBsAg positive [22]. The prevalence of HBsAg in pregnant women was 4.1% in 1990, 3.4% in 1995 and 3.3% in 2002 [42]. A survey conducted by the Korea Centers for Disease Control and Prevention [43] also reported that the prevalence of HBsAg in pregnant women was 3.4% in 1995 and 3.2% in 2006. HBV e antigen (HBeAg) positivity was found in 53.1% of HBsAg-positive mothers and in 50.7% of their HBV-infected newborns [32]. During the 1980s, 11% of newborn babies in Korea were infected with HBV via maternal transmission during the perinatal period [32]. In particular, the vast majority (i.e. 65–93%) of unvaccinated infants born to HBeAg-positive mothers became infected [44, 45]. Chung et al. [46] also reported that 45% of HBsAg-positive mothers were HBeAg positive. Between 40 and 80% of all mothers of HBsAg-positive children are HBsAg positive. The HBsAg carrier rate for siblings ranges from 33 to 67% [47, 48]. In addition, the vertical transmission rate was 48.3% in children born to HBsAg-positive mothers. In contrast, the paternal transmission rate was low, and 21.4% of the children had HBsAg-positive fathers [47]. Another study also examined the rates of perinatal transmission between siblings with HBsAg-

Table 1. Association between HBV vaccination and risk of HCC among male adults

Serological profiles and vaccination status	Incidence rate of HCC	Relative risk of HCC (95% CI)
HBsAg- and anti-HBs-		
non-vaccinee (the unvaccinated and uninfected group)	13.7	1.0
vaccinee (the vaccinated group)	8.0	0.58 (0.31–1.09)
HBsAg- and anti-HBs+ (the unvaccinated and infected group)	4.4	0.34 (0.19–0.60)
HBsAg+ and anti-HBs- (the chronically infected group)	215.9	18.1 (14.2–22.9)

Data retrieved from Lee et al. [41].

Table 2. Overall prevalence of HBV infection in siblings by age and parental HBsAg status

	>20 years old	10–19 years old	<10 years old
HBV prevalence in siblings by HBsAg-positive			
parent	24.2% (136/561)	12.8% (44/345)	2.1% (4/192)
mother	54.7% (110/201)	33.3% (28/85)	7.6% (2/26)

Adolescents older than 20 years were born before any systematic HBV vaccination began, children younger than 10 years old were born after Korea's universal vaccination program for newborn infants had been implemented, and those between 10 and 19 years old were born in an intermediate phase where certain groups received vaccination. Data taken from Kong et al. [49].

Table 3. Vaccine failure rates in infants according to HBeAg status and HBV DNA levels of HBsAg-positive mothers

Maternal HBeAg status	Maternal HBV DNA titer (copies/ml)	Vaccine failure rate
Positive	$\geq 5 \times 10^7$ $< 5 \times 10^7$	47.9% (156/326) 36.7% (11/30)
Negative	$\geq 5 \times 10^7$ $< 5 \times 10^7$	30.8% (4/13) 7.0% (34/485)

$\geq 5 \times 10^7$ copies/ml is considered a high level of HBV DNA, $< 5 \times 10^7$ is considered a low level. Data retrieved from the Report of the Korea Centers for Disease Control and Prevention, 2004 [54].

positive parents (table 2). The overall prevalence of HBV infection in siblings by age and parental HBsAg status was similar to those of the past reports above.

Before the introduction of the HBV vaccine, nearly 90% of infants born to HBeAg-positive mothers were infected at birth [44, 45]. By administering HBIG and the HBV vaccine to all neonates born from HBsAg-positive mothers, 88–95% of all cases of perinatal transmission of HBV could be eliminated [44, 45]. However, despite the adequate administration of HBIG and the HBV vaccine at birth, about 5–10% of cases of perinatal transmission of HBV could not be completely prevented [50, 51]. Although the cause of prophylaxis failure is still unclear, high levels of maternal viremia and intrauterine infections probably play a role [50–53]. According to a 2004 report by the Korea Centers for Disease Control and Prevention [54], vertical transmission in infants was uniquely associated with the mother's HBeAg seropositivity and HBV DNA levels. HBsAg-positive rates in 854 infants according to the HBeAg status and HBV DNA levels of

their HBsAg-positive mothers are shown in table 3. Among the 356 neonates born to HBeAg-positive mothers, 167 (46.9%) were HBsAg positive. Conversely, of the 498 infants born to HBeAg-negative mothers, 39 (7.8%) were HBsAg positive. Of note is that the data in the table show that irrespective of maternal HBeAg status, more than 30% of infants born to women with high HBV DNA levels were HBsAg-positive. This study revealed the importance of perinatal transmission of HBV from HBeAg-positive mothers to their children. In addition, the levels of HBV DNA in carrier mothers are associated with vertical HBV transmission. Song et al. [55] evaluated the failure of HBV immunoprophylaxis in 144 children who received HBIG and the HBV vaccine, and who were born to HBsAg-positive mothers with detectable HBV DNA. Among the 144 participants, 17 (11.8%) experienced immunoprophylaxis failure. The rates of HBV immunoprophylaxis failure were 12% among children born to mothers who were HBsAg positive, 0% to HBeAg-negative mothers, 21% to HBeAg-positive mothers, 0% to mothers

with undetectable HBV DNA and 27% to mothers with detectable HBV DNA. Another study by Kang et al. [56] also reported that the failure rate of HBV immunoprophylaxis was 7.4% and all such cases had been born to HBeAg-positive mothers. According to the 2008 Guidebook for the Hepatitis B Vertical Transmission Prevention Program of the Korean Ministry for Health, Welfare and Family Affairs [36], the rate of anti-HBs among 33,634 subjects who completed the 3-dose HBV vaccination schedule was 85.1%. Despite adequate HBV vaccination, 1,414 children (4.2%) experienced immunoprophylaxis failure, defined as HBsAg seropositivity. These reports confirmed again that maternal transmission is the primary reason for vaccine failure and the primary problem that must be addressed. Therefore, maternal HBeAg and HBV DNA levels should be assessed prior to childbirth to identify children at high risk of immunoprophylaxis failure. The effectiveness of strategies to reduce maternal HBV activity during the perinatal period should also be further elucidated.

Another mechanism of vaccine failure involves HBV surface gene mutants. The immune pressure of hepatitis B immunization and HBIG promotes the selection of HBV surface gene mutants. In particular, S-gene HBV mutants (i.e., the prototype G145R mutation, in which a single amino-acid substitution of glycine to arginine occurs at amino acid 145 of the 'a' determinant of the surface antigen) have been identified in Italy and elsewhere [57–59]. Such mutants can potentially escape neutralizing anti-HBs antibodies and infect vaccinated people. In Taiwan, the prevalence of surface gene mutants was approximately 20% in HBsAg carrier children [59]. However, the prevalence of HBV surface gene mutants in Korea remains unclear. In Korea, 9 of 31 children (29%) with perinatal prophylaxis failure had a nucleotide substitution at the 'a' determinant of the surface antigen. However, amino acid substitutions were identified in only 2 cases (6.5%). In one case, a child was infected by the wild-type virus and a virus that expressed variants of the I126S mutation. In the other case, a child was infected by the wild-type virus and a virus containing the S114A + I126S mutation. Surface gene variants such as G145R were not found in the patients [60]. In another study [61], 2 patients were infected by mutant strains of the virus, with 1 strain containing W74S and F85Y substitutions and the other containing T63I, W74S and T131N substitutions. Neither patient had surface gene variants such as G145R. Therefore, compared with previous studies in other nations, gene surface variants do not appear to play an important role in perinatal immunoprophylaxis failure in Korea.

Inadequate administration of HBV vaccine may be a cause of perinatal immunoprophylaxis failure. A report by Kim et al. [62] revealed that in 91.9% of 341 hospitals, HBV vaccination and immunoglobulin injections were performed within 12 h after birth in more than 90% of neonates. Furthermore, 84.4% of the hospitals refrained from administering HBIG to mothers of unknown HBsAg status until a complete report was obtained. Such a delay in providing the initial dose of the vaccine increases the risk of HBV infection in the child. Increasing the HBIG coverage rates among infants born to HBsAg-positive mothers is an important way to prevent mother-to-infant transmission. Data obtained from a 2008 study of the Hepatitis B Vertical Transmission Prevention Program revealed that the second or third dose of the HBV vaccine was administered at appropriate times in only 80% of infants [43]. Therefore, the rate of vaccination coverage must be increased to minimize the risk of HBV transmission and ensure timely administration of the HBV vaccine. These data suggest that considerable variation exists in the administration of perinatal prophylaxis and that failure to provide appropriate immunoprophylaxis remains an important cause of perinatal HBV infection, especially among infants born to unscreened women.

Conclusion

Hepatitis B vaccination has effectively reduced the infection and chronicity rates of HBV and related complications. Prior to the introduction of the HBV vaccine, the HBsAg carrier rate among the general Korean population was approximately 8%. Since 1983, HBV vaccination has been recommended for all neonates in Korea. The overall prevalence of HBV vaccination has exceeded 99% since 1990. The HBsAg carrier rate in the general population decreased to 3.7% in 2007, with a HBsAg carrier rate of 0.44% among teenagers and of 0.2% among children younger than 10 years. In addition to the changes in HBV markers that occurred after the introduction of the HBV vaccination program, the HBV vaccine appears to reduce the risk of HCC. However, acute HBV infection may still occur in unvaccinated and uninfected adults. In those cases, catch-up vaccination will be needed. Despite adequate administration of HBIG and the HBV vaccine in children with HBsAg-positive mothers, the vaccine failure rate was 4.2%. No cases of surface gene variants such as G145R have been reported in Korea. Despite considerable effort to reduce HBV infection via the universal vaccination of all newborn and school-age children, a large

proportion of the population was previously infected with HBV and still harbors the virus.

In conclusion, the prevalence of HBV carriage in Korea was much lower after the introduction of a universal HBV vaccination program. Korea is now classified as an area of intermediate endemicity for HBV; however, unvaccinated and uninfected adults may require supplemental vaccination to protect against HBV infection. Despite universal HBV vaccination, many people are infected with HBV and will become infected in the future. The prevention of complications in infected individuals, such as cirrhosis and hepatocellular carcinoma, requires appropriate therapeutic agents.

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Disclosure Statement

The authors declare that there is no conflict of interest regarding this study.

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