Chapter

# Epidemiology of Hepatitis B Virus

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## Abstract

Hepatitis B virus (HBV) is a double-stranded DNA hepadnavirus. It is an important cause of acute 5and chronic hepatitis and hepatocellular carcinoma. Worldwide about 2 billion people show serological evidence of exposure and about 400 million have active infection. High prevalence areas include sub-Saharan Africa, China, and southeast Asia. HBV was known at onset as the etiology of what is called "serum hepatitis", this is the most common form of viral hepatitis transmitted parenterally. It is also a cause of both acute and chronic hepatitis of great significance. Hepatitis B virus has an incubation period that varies between 1 and 6 months. The clinical features of acute infection resemble those of the other viral hepatitides. Death from fulminant hepatitis occurs in about 1%. Following acute infection, there is either complete recovery (with long-term immunity) or persistent infection. The latter occurs in 5–10% infected adults, 30% infected children and 90% infants infected at birth; it is more common in the immunocompromised.

**Keywords:** hepatitis B, viral hepatitis, epidemiology, incidence, prevalence, distribution

## 1. Introduction

Hepatitis B Virus (HBV) is a double-stranded DNA hepadnavirus. It is an important cause of acute and chronic hepatitis and hepatocellular carcinoma. Worldwide about 2 billion people show serological evidence of exposure and about 400 million have active infection. High prevalence areas include sub-Saharan Africa, China, and Southeast Asia [1, 2].

HBV has remained a public health issue of global concern in the presence of multiple efforts to eradicate this viral disease through individualized and mass screening, education, and immunization programs [3]. The current estimates have shown that about 400 million individuals throughout the world have chronic HBV infection [1, 3]. Those infected with HBV have 15–40% risk of developing complications such as cirrhosis, hepatic failure, or hepatocellular carcinoma (HCC); and 15–25% of them have the risk of death from related HBV liver disease. About 60–80% of people are diagnosed with HCC and 500,000–1.2 million people die every year due to chronic HBV infection. It is established that HBV infection is the 10th leading cause of death globally.

HBV was known at onset as the etiology of what is called "serum hepatitis", this is the most common form of viral hepatitis transmitted parenterally. It is also a cause of both acute and chronic hepatitis of great significance [4]. Hepatitis B virus has an incubation period that varies between 1 and 6 months. The clinical features of acute infection resemble those of the other viral hepatitides. Death from fulminant hepatitis occurs in about 1%. Following acute infection, there is either

complete recovery (with long-term immunity) or persistent infection. The latter occurs in 5–10% infected adults, 30% infected children and 90% infants infected at birth; it is more common in the immunocompromised.

The prevalence of HBV infection varies widely [1–7], with rates ranging from 0.1–20% in different parts of the world. There is high prevalence of hepatitis B surface antigen (HBsAg) positivity rates above 8% in areas of high viral infection endemic prevalence such as the Far East, Sub-Sahara in Africa, the Amazon basin, and some parts of the Middle East. In these settings, there is presence of serologic evidence of prior hepatitis B virus infection anti-hepatitis B core antigen in most cases: positive anti-HBc or anti-HBs. Regions such as India, Japan, Middle East, Eastern & Southern Europe, parts of central Asia and south America are areas with intermediate chronic HBV infection prevalence (2–7% positive HBsAg). The regions with low chronic HBV infection prevalence (below 2percent positive HBsAg) include the USA, Australia, Southern South America, and Northern Europe. Throughout the world 45% of the global population live in high prevalence areas generally. People immigrating from high to low endemic regions have shown patterns that have a greater impact on the epidemiology of HBV; e.g., Migration of individuals from countries in South East Asia resulted in increased prevalence of chronic hepatitis B in the USA.

## 2. Modes of transmission of hepatitis B virus

We have two major modes of transmission of hepatitis B virus in the world [1–3]: perinatal and horizontal transmissions. The perinatal transmission occurs during child delivery from infected mothers to their babies, this mode of spread accounts for the majority of transmissions in the world. The second mode is horizontal transmission, that can occur through open wounds (cuts and scratches), blood transfusion, poor infection prevention practices to curve blood-borne infections in health facilities, sexual transmission and risky health behaviors such as piercing of the body, unsafe drugs injection, body tattoos and scarification using unsterilized instruments & other equipment. Developing chronic hepatitis B virus infection depends on the mode of spread of the virus, as the risk decreases with age at infection for susceptible individuals. About 90% of infections acquired during perinatal period will become chronical. Up to 20–60% of under 5 infections (1 to below 5 years of age) and 5–10% of adults and older children will develop chronic HBV infection.

Hepatitis B virus can be found in body fluids such as blood, saliva, vaginal fluids and menses, semen; and in less amount in breast milk, perspiration, urine, tears of infected people. HBV is easily spread through contact with body secretions, the virus resists to breakdown and can live long outside the human body. Heterosexual & other sexual activities and unsafe use of drugs by people who inject drugs account for most transmissions of the virus in regions with low prevalence.

Vertical or perinatal transmission of HBV is commonly observed in countries in the Far East Asian and Oceania regions. Mothers with high viral load have higher chances of transmitting the virus to their new born. Infection during child birth occurs in 5–20% of babies born to HBsAg positive, HBeAg-negative women. While most perinatal infections occur in babies born to chronically infected mothers, those with acute HBV infection in the 3rd trimester are also very likely to transmit the virus. Only less than 2% of perinatal transmissions occur in-utero.

The horizontal transmission during early childhood is significant in some regions in particular Sub-Saharan Africa, Alaska, and the Mediterranean, where perinatal transmission is less common as compared to Asia. There is lower prevalence of positive HBeAg correlates in mothers with less efficient spread during child

birth. Nonetheless, by the time the child is 10 years old, about 90% of children in rural Sub-Saharan regions of Africa will show evidence of past exposure to the virus. In the same population, HBeAg wean off in early in contrast to Asians, and most of them are HBeAg-negative by the reproductive age.

There is a possibility that these observations in epidemiologic variations are secondary to genotypic differences in hepatitis B virus. The accurate mode of spread in early childhood is not known, it is however thought that it occurs through blood and body secretions (not apparent) from family members or peers/playmates that inoculate the virus into cuts (scratches or abrasions) to the skin or other mucosal lesions.

The laboratory tests specific for HBV have revealed the fact that transmission through blood and blood products, and parenteral transmissions seem to be especially blood related. It is however important to note that infectivity does not solely appear by blood-to-blood contact. It has been observed that certain experimentations render the viral transmission by mouth is ineffective. The infection may be endemic in semi-closed and closed settings and mentally handicapped facilities. It is more common in urban settings among adults and those living in deprived socio-economic states. Marked differences can be observed for the infection prevalence and the carrier states in various geographical areas and between people with different ethnic and socio-economic statuses.

Enough evidence exists to show the transmission of HBV by intimate and sexual contacts. People who are sexually promiscuous, especially those active homosexual males who change partners regularly, have very high chances of acquiring hepatitis B virus infection. The surface antigen for HBV has been detected in blood and various body secretions like semen, menses and vaginal fluids, saliva, breast milk (including colostrum) and serous fluids. These body fluids have been implicated in the transmission of the virus. Therefore, hepatitis through contact is of major importance. The virus may be accidentally transmitted from inoculation of small amount of blood or fluids contaminated with blood during medical or surgical interventions, vaccination with inadequately sterilized equipment such as needles and syringes, drug-injections, tattooing, piercing of ear and nose, acupuncture, razors, shared toothbrushes, towels and other linens contaminated with blood. Other factors related to transmission in specific climates in the tropics and warn-countries are important to note; including ritual circumcision, blood-letting, repeated bites by bloodsucking arthropod vectors, traditional tattooing and scarification. However, findings on the role which biting insects play in the transmission of HBV are conflicting. HBsAg has been detected in multiple species of mosquito and bedbugs either trapped in the wild or fed experimentally on infected blood in laboratories. No convincing outcome for replication of hepatitis B virus in insect has been shown. Also, there is no evidence in epidemiology for mechanical transmission of HBV by insects.

HBsAg has been reported present in feces, urine and bile, often as a result of blood contamination. HBV is not known to be transmitted through fecal-oral mode and urine. Urine is not infectious unless it is blood contaminated. There is no evidence to show airborne transmission of the infection. Clustering of HBV can be seen in family settings but this is not associated with genetic factors and does not imply venereal or maternal transmission. The mechanisms of HBV intrafamilial transmission is yet to be established.

## 3. Donation of tissues and blood

As a standard of care, blood donors are now universally screened for hepatitis B with HBsAg test [1]. This had markedly reduced the risk of infection transmission

through transfusion. Countries around the world with negligible prevalence have also added anti-HBc tests to detect chronic carriers with low viral load who may not be detected with HBsAg test. These two tests decrease HBV infection rates to about 2.5–15.3 per million units of blood in settings with low prevalence rates. Developed countries like Canada, USA, Australia, Japan, etc. perform other more sensitive tests/nucleic acid tests additionally. However, the benefits in terms of incremental yield and other clinical advantages of nucleic acid tests over rapid tests (serologic) in these regions with low HBV prevalence, and the need for additional serologic tests, has not been established. Since about 90% of adults individuals have serologic evidence of ongoing or past HBV infection, anti-HBc is not to be used as a screening test in settings with high burden of hepatitis B. Therefore, in these settings, HBsAg is the only screening test being used. Nevertheless, in these settings, occult hepatitis B is seen in 3–30% of people with positive HBc and negative HBsAg. We now know that HBsAg-negative, positive hepatitis B DNA blood carries about 10% risk of transmission. In Taiwan, the risk of transmission of Hepatitis B infection through transfusion was approximated recently to be 100 per million units, with donor screening strategy using HBsAg test alone. This means that it is 7–40 times higher than in settings with low prevalence. The nucleic acid tests had a yield estimated to be at least 20 times higher in settings with high prevalence as compared to those with low prevalence, where it is currently in use. This has rendered it more cost saving per infection averted in these settings. Anti-HBc screening test is strategy is more cost-effective compared to nucleic acid tests in areas with lo prevalence despite the potential role of nucleic acid testing in these areas. The sensitivity and specificity of nucleic acid tests vary in most high prevalence settings. There is need to develop newer HBsAg assays with improved sensitivity to address this issue.

The other potential spread of occult or subclinical hepatitis B virus is from tissues and organs donation. Undetected viral load at time of tissue donation may be more frequent among tissue donors than blood donors according to estimates. To prevent infection following tissue or organ transplant, the easiest way is to exclude HBc-positive donors. This approach may not be practical in settings with high prevalence where most people have prior exposure to the virus. Consequently, the nucleic acid test is good additional measure to screening strategies for tissue donors to reduce the chances of transmission. The challenge, however, remains to reduce the turnaround time for results of nucleic acid test performed in clinical transplant facilities.

## 4. Mother to child transmission

HBV can be transmitted to infants born from carrier mothers during child labour and delivery. This is the single most important factor that determines the prevalence of HBV infection in some settings, especially the Southern parts of Eastern Asia and China. The chances of acquiring HBV infection in infant may approximate 90% and seem to be associated with ethnic groups. Pediatric infections are particularly important because a big number of these infants will be carriers. Hepatitis B infectivity is directly associated with the presence of high titres of HBsAg and/or HBeAg in the mother's blood stream. About95% of new born babies are infected around delivery time when HBeAg is present in their mother's circulation. The prevalence of HBeAg among mothers who carry the virus as well as mother to child' infectivity varies significantly in various settings and ethnic groups.

In South-East Asia, about 30–50% of HBsAg carrier mothers also carry HBeAg in their circulation. Perinatal transmissions are estimated to account for about 50% of the carriers in this population. These infections are frequent in babies born

from mother of West Asian and Afro-Caribbean decent. In the contrary, Caucasian women present fewer perinatal transmissions and carrier states. Mother to child transmission of infection and the carrier state patterns are different in regions such as Africa, where HBeAg is less common in carriers and the infection to their babies is frequently seen during the first 5 years of life resulting in horizontal transmission. The transmission of hepatitis B infection to infants born from non-carrier women by contact with other playmates who are infected from their carrier mothers is another mode of spread of the virus.

The considerable risk of hepatitis B infection during perinatal period from mothers with acute HBV infection is possible, especially during the 3rd trimester or within 2 months post-delivery. Transmission in-utero is not common, since HBV does not cross the intact placenta and the limited number of intrauterine infections are probably due to maternal blood leakage into the fetal blood stream associated with a tear in the placenta.

The exact mechanism of infection during perinatal period is not known but it is probable that this happens during delivery or shortly after birth due to maternal blood leakage into the fetal blood stream or the ingestion/inadvertent inoculation of maternal blood into the baby's circulation. The majority of infants infected during labour and delivery become chronic carriers.

HBeAg is a serologic marker for hepatitis B DNA viral load. Infections during perinatal period occur almost always in mothers who are positive for hepatitis B but can also occur in women who have very high viral load, hepatitis B virus DNA greater than 200,000 IU/ml in their blood. If the child is not immunized, his/her risk of acquiring hepatitis B virus during delivery is almost 100% when the mother has a positive HBeAg. The famous Taiwan study by Palmer Beasley as reported by Zuckerman [1] in the 1970s when there was no vaccine available showed that 85% of positive HBeAg mothers had their babies developing chronic infection vs only 32% of the negative ones. There is an approximated 90% risk of infants who acquired infection during perinatal period becoming chronically infected.

To reduce mother to child transmission of hepatitis B virus, incorporating the birth immunization dose into the HBV immunization schedule is the most effective strategy. This dose, if followed by two more doses, can significantly reduce the prevalence of chronic infection in babies born from positive HBeAg mothers by about 90%, and by about 100% from negative HBeAg mothers. The birth dose is particularly important in in settings were an important proportion of mothers with positive HBsAg and positive HBeAg at the same time. Such settings include the Pacific Islands, South East-Asia, and China. In these regions, if the birth dose is missed, HBV vaccine' effectiveness could reduce to about 50–75%. In other areas of the world such as Sub-Sahara in Africa, and Russia where less than 25% of pregnant mothers with a positive HBsAg have also positive HBeAg, the consequences of missing the birth dose are still significant but not as severe. The expended immunization program should include a dose of hepatitis B immunoglobulin at birth to babies born to mothers with positive HBsAg. This has the potential to reduce further the chances of transmission to below 5%. A randomized controlled trial by Beasley et al. demonstrated that the birth dose of hepatitis B immunoglobulin administered to babies born to mothers with both positive HBsAg and HBeAg lead to only 6% of these babies seroconverting to positive HBsAg as compared to 88% of babies in the placebo arm.

## 5. Horizontal spread

The horizontal spread of hepatitis B virus is very likely to lead to chronic state if it occurs in young children [1, 3, 6]. This was demonstrated in several studies

conducted before the HBV vaccine was made available. Research conducted in Senegal revealed that half the children who had horizontal transmission of HBV before they were 2 years old developed chronic infection. In another research on 1280 people who had hepatitis B virus negative sero-markers in rural Alaskan conducted in the 1970s revealed that 29% of children below 5 years old, out of 189 individuals who acquired the infection over a four-year period, had chronic hepatitis B against 16% of children between 5 and 10 years old, and only 8% for adults above 30 years old. The birth dose of hepatitis B vaccine together with the subsequent doses can reduce the acquisition of infection in the early months of life as well as prevent perinatal transmission in settings where the risk of chronicity through horizontal transmission of the infection is great.

Horizontal transmission, if it occurs in young children and some adults, this is because of high likelihood of infectious hepatitis B virus found on surfaces. The research conducted in Alaska many years ago, before the availability of viral DNA testing, the hepatitis B surface antigen was found in the environment on samples from table tops from school lunch room, toys, feeding bottles, and walls in houses where positive HBsAg individuals lived. Hepatitis B viral replication was possible at room temperature after at least 7 days. There is possibility that the virus can be spread through broken skin and mucosa from people with chronic infection on to surfaces, infecting thereby other people with open lesions. The horizontal transmission can also happen through non-sterile objects and procedures such as injections from healthcare providers or drug-injection, tattooing, scarification, sexual route, dialysis, emergency procedures, etc.

Young adults in the USA have increased horizontal transmission of HBV through unsafe drug-injection use in some places. There was 114% increase in the acute hepatitis B infection between 2006 and 2013 in West Virginia, Kentucky, and Tennessee. This increase was seen mostly in white populations between 30 and 39 years old who had a drug-injection history. In health care facilities, the outbreaks of hepatitis B can also increase the horizontal spread of the virus. The prevention of horizontal spread entails the combination of several measure such as education, good infection prevention and control practices, and immunization of household contacts to hepatitis B infected individuals and other people at high risk of HBV infection.

### 5.1 Vaccination

Hepatitis B vaccine is now available for over decades now. It is highly effective infection prevention measure among people at high risk of developing the disease [8]. The USA implemented universal immunization in 1991 and saw the incidence of acute infection decrease by 89% in adolescents and young children. With this exercise, the disparities in prevalence of chronic hepatitis B infection between races have reduced. Hepatitis B virus is endemic in Alaska, but following immunization, the incidence of new infections has markedly decreased. With this achievement, the incidence of hepatic cirrhosis and hepatocellular carcinoma is expected to reduce as well in the next few decades. Taiwan is one of the nations that adopted universal vaccination earlier. Its prevalence of positive surface antigen than was between 15–20% has reduced to 7% among adolescents and young children.

## 6. Chronic carriers

The concept “carrier state” is defined as persistence of HBsAg in blood circulation for more than 6 months, based on longitudinal researches. This state maybe

associated hepatic changes comprising minor damage in the nuclei of liver cells to persistent liver inflammation, chronic active hepatitis, liver cirrhosis, and hepatocellular carcinoma. The integration of the HBV DNA may occur at several places or at unique site of the host genome in carriers of HBV with or without histological evidence of hepatic disease. The majority of carriers have HBsAg in their circulation with or without other markers of the viral infection (HBeAg, HBV DNA, DNA polymerase). The continued expression of HBsAg is suggestive of integrated viral DNA resultant. Some HBV carriers may have HBV DNA in their liver but with no surface antigen expression, this is called "latent viral infection".

There are a number of risk factors that have been established in accordance to the "carrier state". The carrier state is most common in male gender, it is more likely to follow infections acquired in childhood than those acquired in adulthood, it occurs most often in individuals with natural or acquired immune deficiencies. The carrier state develops in only about 5–10% of infections acquired in adult life.

Carriers' prevalence among adults who appear healthy, especially the blood donors vary by region. The global population can be grouped in to three regions by prevalence of hepatitis B virus infection:

a. Hyperendemic regions: here, the infection includes almost always several countries of South-East Asia, China, the Western Pacific, and the sub-Saharan region of Africa. In these settings, infection in early life is very common. The proportions of carriers in these regions range from above 5–20%.

b. Intermediate endemic regions: here, the prevalence of hepatitis B infection range from 20–50% generally (by serologic markers like HBsAg, anti-HBs and anti-HBc), and that of carriers from 1–5% overall. It is seen in countries in the Northern region of Africa, the middle East, South America, and parts of Southern and Eastern Europe.

c. Low prevalence regions: here, less than 10% of the general population have evidence of hepatitis B virus infection by serologic markers, and a carrier rate of less than 0.1%. Nevertheless, the prevalence of HBV infection and carriers vary considerably in these settings within ethnic groups. These regions include northern Europe, the USA, Canada, most Western Europe, New Zealand, and Australia.

With the advent of HIV/AIDS, the hepatitis B virus coinfection with HIV has become a major concern of late because of synergic negative effects of both viruses. HIV coinfection increase the chances of hepatic disease progression related to hepatitis B virus while hepatitis B coinfection augment antiretroviral therapy related liver toxicity.

## 7. Distribution of hepatitis B by age

It has been recognized two different patterns of hepatitis B infection by age distribution [1, 8, 9]. Individuals with high burden of HBV, infection is often acquired early during childhood. The highest infection and carrier rates are usually seen among children and young adults while the lowest is prevalent among older individuals. The HBeAg has been found more frequently in young carriers than in their adult counterparts. In contrast, HBe antibody is more common in older individuals. These results are in keeping with the possibility of young carriers being most infective.

In settings where this viral infection is not commonly observed, the highest prevalence of HBsAg occurs in populations between the age of 20 and 40 years old. The highest rates of hepatitis B infections are seen in populations at increased risk of contact with blood or blood products, e.g., health care workers, certain groups of patients, IV drug users, and male promiscuous homosexuals.

There is need to understand that the prevalence of hepatitis B infection, the age distribution of this infection, the carrier state. This change is drastic in some regions with the implementation of routine program of expanded hepatitis B vaccination.

## 8. Hepatitis B genotypes

There are six HBV genotypes grouped A-F based on phylogenetic analysis of complete viral genome classification [10, 11]. The most disseminated genotypes throughout the world are A and D. In contrast, B and C genotypes are restricted to East Asia, and E genotype to sub-Saharan Africa. The genotype F on the other hand is more diverse from other genotype classes and is seen in aboriginal Americans. All the genotype classes have a common immunodominant area on the surface antigen that is called "a determinant". This determinant span amino acids 124–147 and is hydrophilic. It is taught to be a form of two major and one minor loops with cysteine disulphide bonds. The "a" determinant target primarily the neutralizing antibodies induced by vaccination. The available hepatitis B vaccines have common major immunization response to "a" epitope with subsequent protection against all subtypes of HBV.

## 9. Burden of HBV in developing countries

HBV has an intermediate to high endemicity levels in developing countries [12–16]. Recently, the incidence of acute infection has decreased in several countries. The prevalence of chronic carriers of HBsAg has also decreased, this is as a result of the introduction of universal immunization coverage for hepatitis B virus in the 1990s. A few other countries are still not able to implement these interventions, especially in their rural and highly endemic regions. There is lack of sufficient information on the epidemiology of hepatitis B virus in many Eastern Europe and Latin-America countries.

### 9.1 Epidemiology

#### *9.1.1 Africa*

The entire Africa is known to be highly endemic continent for hepatitis B virus. The infection occurs with more than 8% hyperendemicity for chronic carriers of surface antigen in the general population in countries of Sub-Sahara like Nigeria, Cameroon, Burkina Faso, Gabon, and Namibia. Some other countries such as Zambia, Kenya, Senegal, Ivory Coast, Liberia, and Sierra Leone experience intermediate endemicity (2–8%). The following countries are considered to have low HBV endemicity (below 2%) in Africa: Morocco, Algeria, and Egypt.

Children in Africa are at high risk of acquiring hepatitis B infection. The hepatitis B markers seroconversion rates vary from 10.2–60.5% annually in Somalian children between 1 and 10 years old. The highest rates are seen in children with a low socio-economic situation. In South Africa, the highest rate of hepatitis B

infection in Children (5–6 years old) was 15.7%. The infection is often acquired by these children through parenteral horizontal transmission route from siblings and parents. Unsafe sharing of toiletries and sharpening, cutting, scraping or scratching instruments in the daily activities accounts for such a high horizontal transmission. In addition, cultural practices like scarification and tattooing and sexual promiscuity greatly increase the chance of hepatitis B infection. Hepatitis B transmission by transfusion of blood and blood products still occurs and is taught to have an epidemiological impact in some regions in Sub-Saharan countries.

### *9.1.2 Asia*

The Arabian region or South-Western Asia accounts for 10% of territories in Asia. The Arabian Peninsula (Saudi Arabia, Bahrain, the Unites Arab Emirates, Oman, and Yemen included) together with Kuwait have a positive e antigen prevalence from 1.5 to above 8%. The HBsAg-positive prevalence in the Gaza Strip is 3.5% in the general population and 3.8% in blood donors.

Arab countries have implemented the WHO-recommended Expanded Program on Immunization, and hepatitis B virus immunization programs started in these countries have now covered a large proportion of their population. This has successfully reduced the hepatitis B virus endemicity.

Saudi Arabia is the first Arab country to adopt an HBV immunization program. It has seen a steady decline in positive surface antigen prevalence observed in children aged between 1 and 12 years, from 7% in 1989 to 0.31% in 1997 and zero% in 2008.

Cambodia is one of the western Pacific countries with the hepatitis B Virus prevalence at 4.6% in the adult population and 6% in blood donors. In this country, high anti-HBc rates have been reported (58.6% and 72.4%) in different studies, suggesting a principal role played in the past by horizontal transmission in childhood and adulthood.

China also started the universal HBV immunization program of newborn babies in 1992. In this country, the prevalence of surface antigen carriers decreased from 9.8% in 1992 to 7.18% in 2006. The immunization coverage rate at the end of 2005 was 20% lower in rural areas than in the urban areas, a difference that has steadily decreased in recent years. China has gone from a high to an intermediate endemicity level in a short period of time despite the suboptimal immunization coverage. The prevalence of anti-HBs was higher in fully immunized children (63.2–74.3%) than in non-immunized subjects (21.1–34.8%) because of the universal hepatitis B immunization campaign.

### *9.1.3 Eastern Europe*

There are very few epidemiological studies conducted on hepatitis B virus infection in Eastern Europe which do not provide conclusive evidence on the spread of hepatitis B at the level of generalization of routine immunization in this large geographic region.

In a recent study from Bulgaria, positive surface antigen prevalence in persons below 20 years old, targeted by hepatitis B immunization, was significantly lower than that found in non-vaccinated persons aged over 20 (1% against 4.8%). The hepatitis B surface antigen-positive seroprevalence in the general population was 3.8% in studies performed in Bulgaria, 5.6% in Romania and from 4.4–13% in different studies in Serbia, with wide variations within single countries that reflect the different socio-economic conditions between rural and urban areas. In these studies, males showed higher rates of hepatitis B surface antigen positivity than females.

### *9.1.4 Latin America*

The epidemiological information on hepatitis B virus is insufficient and in pieces in Latin America. About 7–12 million Latin Americans are carriers of hepatitis B chronic infection according to estimates. The rate of positive surface antigen individuals varies between countries, the highest being recorded in the 20–40 age groups possibly because of horizontal transmission. Recently, progress from intermediate to low endemicity levels have been registered in some tropical countries in Latin America such as Venezuela, Colombia, and Panama. Hepatitis B infection still provides a heavy socioeconomic burden in many developing nations despite universal immunization programs introduced in the 1990s. These programs need to be extended without fail to cover the rural areas in countries where hepatitis B vaccination is demonstrating its efficacy in reducing the transmission of the virus. Countries that are still unable to adopt a universal immunization program for newborn babies need to receive support from international health organizations to implement this.

## 10. Burden of HBV in the United States

There are approximately 700,000 to greater than 2 million people with chronic HBV infection in the USA. It is difficult to obtain accurate approximations of individuals burdened with chronic HBV infection in the world and in the USA in particular due the asymptomatic nature of the disease in most people infected with the virus [9]. This results in more people not diagnosed, passive surveillance, and underreporting. With the introduction of universal immunization in the USA, there is increased immunity among children and adolescents. Despite this progress, the number of adults infected with chronic hepatitis B has been increasing because of immigration of infected individuals from highly endemic settings. It is estimated that about 70% of hepatitis B infections in the USA are from foreign-born individuals. About 40,000–45,000 subjects from hepatitis B virus endemic settings (with chronic hepatitis B infection prevalence above 2%) immigrate to the USA legally. The total number of immigrants from Eastern Asia and Sub-Saharan Africa living in the USA is estimated above 3.9 million.

The National Health and Examination Survey (NHANES, 2011 & 2012) revealed that about 850,000 Americans are living with Chronic hepatitis B. Non-Hispanic individuals represent approximately 5% of the United States population. The oversampling of this group revealed that about half of all chronic hepatitis B infections (400,000) in the USA are seen among non-Hispanic Asians. The rates of acute hepatitis B infection have remained about 1 per 100,000 population since 2009 in the USA. These have been reported mainly from non-urban as compared to urban areas. The highest rate of acute hepatitis B infection in the USA is reported among African American adult populations. Of late, between 2006 and 2013, there was an increase in incidence of acute hepatitis B infection in Tennessee, West Virginia, and Kentucky, among white populations between the age of 30 and 39 years old who reported common risk factor such as drug-injection use.

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