

REVIEW ARTICLE

GLOBAL INITIATIVES IN HEALTHCARE: HEPATITIS B IMMUNIZATION

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Summary

Global healthcare is a political variable that involves both political as well as nongovernmental agencies and refers to health of the whole planet regardless of the geographical and political boundaries. Global healthcare initiatives are programs that address specific global health issues or diseases. The most important objective of a global health initiative is to achieve a major improvements in global populations' health outcomes regardless the geographic location. Global health programs bring and use various resources to improve, prevent and resolve worldwide health issues.

Key words: World Health Organization; Global Alliance for Vaccines and Immunization; hepatitis B; immunization; global health

INTRODUCTION

Between 1998 and 2000 the World Health Organization (WHO) (24) launched several global health initiatives including Global Alliance for Vaccines and Immunization. The purpose of these specific programs was to increase the use of recently licensed vaccines and to improve childhood immunization status worldwide. In attempt to prevent leading causes of death as well as sources of chronic diseases in children the WHO (24) included in this specific initiative the hepatitis B immunization.

Hepatitis B

Hepatitis B is a liver infection caused by the hepatitis B virus (HBV). This virus is transmitted from an infected person to someone who is not infected by bodily fluids during sexual contact, sharing needles or from a mother to a baby during birth (5). While in some patients, HBV infection may result in a short-term disease, in others this virus may cause chronic illness that can lead to serious health issues as liver cirrhosis and liver cancer. The most efficient way to prevent HBV infection is early immunization.

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The purpose of this paper is to show the importance of immunization in prevention of communicable diseases. More specifically, this paper will discuss prevention of HBV infection. This paper will demonstrate that newborn immunization is the most effective way to prevent spread of HBV infection and that is the best way to protect children as well as future generations from chronic HBV infection worldwide.

Global Health and Global Health Initiatives

Life expectancy and mortality differs greatly across the world. This imperative health disparity is a result of the higher risk of communicable diseases in low-income countries and inequalities in healthcare development, research and pattern of health transition (12). Global health initiatives play critical role in prevention of communicable diseases by creation and facilitation of global immunization frameworks. One of such initiatives, launched in Switzerland in January 2000, is the Global Alliance for Vaccines and Immunization (GAVI). According to the WHO (23) GAVI is a international coalition consisting of national governments and international organizations as: United Nations Children's Fund; WHO; World Bank; Bill and Melinda Gates Children's Vaccine Program; Rockefeller Foundation; International Federation of Pharmaceutical Manufacturers Associations; and multiple additional research and public health institutions. While GAVI is a new alliance it will continue to build upon the work of its predecessor, the Children's Vaccine Initiative.

When addressing life expectancy and mortality it is always important to consider vulnerable populations, in particular children. According to the U.S. Government (18) 8.1 million children die annually from diseases that are treatable or vaccine preventable conditions. Lack of child immunization significantly increases child mortality rates and ultimately result in considerably shorter life expectancy at birth, especially for infants in developing countries (9). Hepatitis infection affects life expectancy and mortality of people worldwide including children. Due to its worldwide prevalence, HBV viral infection represents major global health problem.

Hepatitis infection

Hepatitis infection is an inflammation of liver that can be caused by multiple viruses. These viruses include hepatitis A, B, C, D, and E. HBV is spread through percutaneous and per mucosal exposure to infected blood or other bodily fluids (21). According to *Sellier et al.* (14) one-third of the world's population has serological evidence of current or past HBV infection. Concerning is mainly the prevalence of chronic HBV infection. Currently there are approximately 240 billion people across the world with chronic HBV infection, with highest occurrence in Africa and Asia. It is estimated, that 650 000 people die annually as a result of chronic HBV infection, most commonly due to liver cirrhosis and liver cancer (21). The most common transmission of HBV that accounts for majority of HBV infections around the world is from mother to infant during delivery (14). Approximately 90% of HBV infections acquired during infancy result in chronic illness (5). Approximately 25% of chronically infected infants eventually die due to liver failure resulting from cirrhosis or hepatocellular carcinoma (26). *Su et al.* (16) emphasize that a universal immunization prevents HBV infection when given in early childhood. More specifically, neonatal immunization is the best way to protect infants and children from chronic HBV infection. According to the CDC (4) 70%-95% of perinatal HBV infections are prevented with completion of HBV vaccine series if started within the first day of life. Within the United States the current practice is to immunize all infants with first dose of hepatitis B vaccine within 12 hours after delivery. If the mother is positive for the hepatitis B surface antigen (HBsAg) the infant also receives hepatitis B immune globulin (HBIG) within the initial 12 hours of birth (4).

Illustrative Situation

An ethical dilemma arises when mother's hepatitis surface antigen (HBsAg) status is unknown either due to lack of prenatal care or coincidentally missing prenatal records. Even if the HBsAg test is repeated, the short postpartum hospitalization may not allow for the laboratory results to be available prior to patient's discharge. The dilemma is whether an infant born to mother with unknown HBsAg should be immunized with HBIG in addition to the standard hepatitis B vaccine, especially if the mother's life style predisposes her to high risk of HBV infection and it's uncertain that her infant will have timely follow-up with a pediatrician. Global health policies are pertinent in this situation as it is very important to prevent neonatal HBV infection worldwide by development and application of a universal vaccination plan. The WHO (22) recommends active immunization with HBIG prophylaxis

in conjunction with hepatitis B vaccination for newborn infants whose mothers are HBsAg positive. According to the CDC (3) hepatitis B vaccine should be administered within 12 hours of delivery to all infants born to mothers with unknown HBsAg status. In the case that mother's status is unknown at discharge from hospital, the CDC (3) recommends that infant's private pediatric provider is alerted and if the mother is determined as HBsAg positive the private pediatrician administers HBIG within 7 days after delivery.

Unfortunately, the currently available policies and recommendations don't address a situation when a high-risk mother with history of poor medical compliance and unknown HBsAg status is discharged from a postpartum unit. Some providers choose to immunize infant with HBIG prior to discharge from the hospital, especially when they have any indication that the mother may not follow up with a private pediatrician in timely manner. Others providers prefer to counsel mother on importance of an early follow up care but choose to immunize the infant only with hepatitis B vaccine.

Inconsistent practice is inappropriate at any healthcare facility and must be resolved while utilizing shared governance. Team of nurses, physicians, healthcare leaders and patient representatives should collaborate to develop clear policies and procedures that would guide healthcare providers in their routine practice. In addition, healthcare leaders and providers, in effort to prevent perinatal HBV infection, should focus on development and appropriate utilization of electronic medical records (EMR). Nation-wide EMR could be used not only to track patients' education and completed immunizations, but it could also reinsure timely access to prenatal screening results and would eliminate the need to re-test patients while delaying the treatment. Healthcare leaders and providers have the opportunity to improve patients' health by full utilization of EMR and by synchronizing these valuable resources with hospital electronic documentation.

Patient education should include the importance of prenatal screening, means of hepatitis transmission and importance of routine hepatitis B immunization. For mothers who are HBsAg negative but are at risk for HBV infection (e.g., injection-drug use, more than one sex partner in the previous 6 months or an HBsAg-positive sex partner, evaluation or treatment for a sexually-transmitted disease) the prenatal care should include hepatitis B vaccine series and their HBsAg status should be re-checked at delivery (3). If the mother is HBsAg positive the prenatal education needs to include the importance of infant's hepatitis B and HBIG immunization as well as treatment of chronic HBV. Origin of the infection should be investigated and additional assistance as for example substance abuse treatment should be offered (3).

Global Health

Simple and specific definition of global health is important as many different terms were used in the past. Diversity in terminology may create confusion in the current meaning of global health. Especially the term of international health continues to be used as a synonym for global health. However, the international health is specifically associated with the development of aid and humanitarian assistance by the Ministries of Health within the World Health Organization (1). Global health incorporates numerous disciplines while integrating multiple parties rather than be directed by one organization or one discipline. *Beaglehole and Bonita* (1) defined global health as "collaborative trans-national research and action for promoting health for all".

During the last decades the importance of global health increased dramatically. Global health is influenced by the world's globalization, more specifically by the increased movement of persons or goods and the ultimate increased global dissemination of infectious as well as non-infectious diseases (6). Due to the complexity of global health, countries need to cooperate to effectively protect the global population. According to the U.S. Department of Health and Human Services (DHHS) one of the most essential principles of public health is that a single country can't protect health of its population alone and without the help from the rest of the world. Global health initiatives are ideal task-force tools to address global health concerns.

Global Health Initiatives

Global health initiatives pursue significant improvement in health of people across the world and are generally developed by high-income countries. The U. S. Government (18) created global health initiatives to promote and

assist with sustainable effective, efficient and country-led public health programs that would deliver essential health care within their individual regions. These global health initiatives focus on improving health of women, newborns and children by addressing issues with infectious disease; reinsuring delivery of clean water and nutrition; and considerably enhancing health of vulnerable populations. Besides the improvement in health, these efforts will stimulate growth of multiple sectors and result in enhanced economic development by increased job opportunities, improved education, developed agriculture, enhanced gender equality and positively influenced political stability (18).

Other example of global health initiative is the GAVI, that is grounded on innovative public-private partnership, and which plays critical role in prevention of communicable diseases by creation and facilitation of global immunization. GAVI's main focus is to improve vaccination coverage by financing and facilitating global immunization frameworks in 73 low-income countries (2). One of the main goals is to decrease childhood mortality to 68 per 1000 life births. By 2013, GAVI already avoided six million future deaths from immunization preventable diseases by vaccinating 440 million children in low-income countries (2). As HBV is one of the most common sources of chronic diseases in children, the hepatitis B vaccine is included in the GAVI's global immunization framework.

Hepatitis B Virus

HBV is a member of *Hepadnaviridae* family and is a major pathogen causing acute and chronic inflammation of liver that often results in liver cirrhosis and hepatocellular carcinoma (25). The occurrence of HBV infection is common. *Sellier et al.* (14) in their retrospective study of 11417 women projected that approximately 30% of the world's population has some evidence of current or past HPV infection. In the U. S. the prevalence of HBV involves 4.9 % of the total population (11). Majority of adults with acute form of HBV recover completely, unless they suffer from fulminant form of HBV. According to the CDC, (4) fulminant hepatitis occurs only in about 1% to 2% of acutely infected persons but approximately 200 to 300 Americans die annually as fatality rate of fulminant HBV is 63% to 93%. WHO estimates that approximately 360 million people currently suffer from chronic infection that may result in serious illness and death. Viral hepatitis accounts for at least one million deaths every year (22).

When the virus is transmitted from an infected person to a new host, the incubation period may vary significantly. On average the incubation period is 75 days, but may range from 30 to 180 days (22). More specifically, the HBsAg may be detected by blood test within 30-60 days after the initial infection and later can be noticed during widely variable period of time. It is important to know that up to 40% of HBsAg positive patients may carry the hepatitis B e-antigen (HBeAg), which is linked to significantly higher infectivity (22).

As stated earlier, neonatal and childhood HBV illness results in chronic HBV infection. In their review, *Wu and Chang* (25) identified that most of these children initially present with immune-tolerant status, followed by immune clearance phase with various degrees of liver injury during puberty with subsequent seroconversion of hepatitis B e antigen (HBeAg) and finally the consequent inactive phase of the chronic disease. HBeAg seroconversion during the first 3 years of life accompanied by liver damage significantly increased risk of childhood hepatocellular carcinoma. It is important to monitor the HBV markers in patients with chronic infection as early intervention can improve their long-term outcomes (25).

Modes of HBV transmission differ between geographical areas and depend highly on HBV endemicity. The WHO (22) defines HBV endemicity by prevalence of HBsAg in general population of specific geographical area. More specifically, in highly endemic area the HBsAg prevalence is higher than 8%, while the 2-7% prevalence represents intermediate endemicity and prevalence rate lower than 2% is typical for low endemicity areas (8). In countries with high endemicity the main concern is HBV transmission from mother to child and transmission between young children. This infection pattern is a result of HBV presence in blood and vaginal secretions as well as other bodily fluids including saliva and tears (8). In their article review *Joshi, James, Quaglia, Westbrook, and Henegham* (10) identified that mother to child transmission is responsible for most of the HBV infection worldwide. In areas with low endemicity the main route of infection is sexual transmission and the use of contaminated needles, especially in population of drug users, while the mother to child infection accounts only for about one third of chronic infections (22).

Vaccination

Timely prenatal screening and appropriate vaccination can particularly prevent mother to child and child-to-child HBV infections and speed up the process of HBV elimination. Based on the CDC (4) recommendation all newborn infants in the U.S. should receive their first dose of hepatitis B vaccine within 12 hours of delivery. This first dose of hepatitis B vaccine is the single most successful measure in prevention of HBV infection and its possible consequences of chronic infection. Consequently, early immunization and completion of the subsequent hepatitis B vaccines series prevents 70%–95% of perinatal HBV infections and protects the newborns from household HBV infection (4). In retrospective study of 2226 patients *Su et al.* (16) determined that universal hepatitis B vaccination program is efficient prevention of acute hepatitis B infection as represented by declined incidence of this infection in population of adolescents and young adults. In fact *Su et al.* (16) suggested that due to epidemiology of acute hepatitis B infections, available surveillance data and high coverage of the hepatitis B series in childhood there may not be a need for booster hepatitis B vaccination in the population of adolescents and young adults who were immunized as infants.

The immunization recommendations are different for all infants born to HBsAg-positive mother. These at risk infants should be immunized with HBIG and hepatitis B vaccines within 12 hours after delivery (11). However it is estimated that only 50% of expected births to HBsAg-positive pregnant women are identified. Therefore, infants born to unidentified HBsAg-positive mothers will not receive the needed immunoprophylaxis (11). It is important to note that this current immunization practice and CDC recommendation may not always be effective in prevention of hepatitis B infection from HBsAg-positive mother to her newborn infant. In a retrospective study of 621 infants of HBsAg-positive mothers *Zou et al.* (26) found that in spite of the recommended immunization protocols a significant portion of infants didn't respond immunologically to the vaccination and some presented with immunoprophylaxis failure. In hope to prevent immunoprophylaxis failure the study aimed to determine the effects of three doses of hepatitis B vaccine in combination with two-doses of HBIG. The study concluded that this protocol achieved 95.7% protective levels of antibody to HBsAg at 7 months of age and is an effective way to prevent mother to infant transmission of hepatitis B (26). Even though further studies on evaluation of long-term immunological status of these patients are needed, additional doses of HBIG vaccination maybe a reasonable solution in future prevention of HBV infection.

Unfortunately, increasing numbers of newborns don't receive the currently recommended vaccines as their parents decline to immunize them. In recent national survey Pew Research Center (13) found that nearly 10% of Americans believe that vaccines are not safe for healthy children. According to this survey 15% of younger adults, 18-29 years old, believe that vaccines are unsafe. However, only 4% of Americans over the age 65 share the same opinion (13). These public opinions influence immunization rates within the United States and may negatively affect community immunity. In their report *Fine, Eames, and Heymann* (7) indicate that the idea of community immunity is based on indirect protection to unvaccinated individuals within fully immunized populations. Yet these unimmunized individuals are still fully susceptible to an infection if exposed. The goal of comprehensive community immunity is to protect individuals who are unable to be immunized due to true contraindications to the vaccine (7). If 15% of the population is not immunized due to personal beliefs the community immunity threshold will be breached and outbreaks of preventable diseases will occur. This situation creates ethical issues especially for the populace of people who can't be immunized due to complex medical issues.

Addressing and screening high-risk groups in an inadequately immunized community may become an important reality within the U.S. High-risk groups not only significantly increase the incidence of the disease but also are often responsible for outbreaks (7). Vaccinating at least 80% of the high-risk population could prevent these outbreaks. Even though preferential vaccination of highly transmitting groups results in lower percentage of overall immunization coverage when compared to usual vaccination models it has the potential to protect the entire population and strengthen the community immunity (7). Based on information provided by Lam et al. (11) the risks factors for hepatitis B infection include: co-infection with hepatitis C or HIV; history or current treatment of sexually transmitted disease; inmate presence in correctional facility; multiple sex partners in last 6 months; patient or patient's parents born in regions with high HBV endemicity especially if the patient was not vaccinated as an infant; recent use of intravenous drugs; sex partner or household contact with a person is HBsAg positive; and patient who is undergoing hemodialysis. Patients with these high risk factors should be routinely screened and preferentially immunized to prevent any form of HBV infection transmission.

Implications for Healthcare Leaders and Providers

Global health continues to transform as it is influenced by the phenomenon of globalization. Population growth, increased life expectancy and changes in age specific mortalities are additional factors affecting this ongoing transformation process. When creating global health policies and initiatives and establishing research priorities, it is important for the healthcare providers and leaders not only to be involved in the process, but also to recognize that the same healthcare system models can't be used for both the developing and developed countries. Addressing health disparities of individual countries is an ethical obligation for the healthcare leaders, providers and nurses (15). It is historically given that healthcare is closely interconnected with global health and while the global health impacts the healthcare, healthcare leaders and providers have the potential in return to improve the global health.

There are many aspects of the global health that affects how healthcare leaders and providers practice in different part of the world and how they address different global health issues. Vaccination as prevention of communicable diseases continues to be one of the critical global health priorities. In the specific case of HBV infection the global health needs to influence the healthcare leaders and providers by: guiding the development of ethnically acceptable policies and procedures; development of prenatal education; reinsuring adequate prenatal care; prenatal HBsAg screening; follow up care for HBsAg positive mothers and their infants; and development of electronic documentation when feasible. However the most important part is to involve local people in these transformations, as they know best what may work in their local setting and what is important for their specific population.

Description of Major Global Health Policy Principles

The U.S. Government (20) outlined seven core principles to guide its involvement in global health. These principles are based on the Paris Declaration on Aid Effectiveness and are embedded in the U.S. Government's global health programming to reinsure that the global health policies outcomes are measurable and sustainable. The U.S. Government (20) defined and described the following global health principles:

- The woman, girls and gender equality principle focuses on addressing the gender inequalities and disparities responsible for compromising the health of all females.
- The sustainable country-owned principle allows the donor country to create health systems that are in the course of the time will be owned and operated by the local government and its native people.
- The health system strengthening principle comprises of proven, cost-effective interventions and technologies that are used to treat and prevent diseases. The idea is to sustain continuing investment in the health sector and to create value that would be interesting for additional investors including the local government and private sector.
- Promoting global health partnership is a principle that brings together a variety of donors, organizations and partners to address all health needs and to achieve health outcomes more effectively and efficiently.
- The integration principle combines a variety of health activities with other sectors that can yield improvement in overall health; an example is the issue of immunization and sanitation.
- The research and innovation principle is based on achievement of measurable outcomes and encourages scientific innovation by U.S Government funded research.
- Improvement in metrics, monitoring and evaluation is an important principle that allows monitoring and evaluation of the programs' implementation, processes and future needs.

Best Course of Action for a Healthcare Leaders and Providers

The most important course of action for a healthcare providers and leaders involved in prevention of hepatitis B infection is undoubtedly education. Declining numbers of immunized individuals within the U.S, and the recent outbreaks of measles shows that immunization is truly a global health issue, regardless the economical status of the individual country. The recent national survey showed that parents who choose not to immunize their children had a poor understanding of the immunization importance. Some of them were skeptical about effectiveness of vaccines and distrusted the pharmaceutical companies while others simply did not understand why healthy children should be immunized (13). Parents need to learn that vaccination provides their children with immunity without getting sick first.

Conclusion

U. S. Government (18) recognizes that health is the most important part of human progress as it determines whether parents can provide for their families, children can be educated, women can survive pregnancy and delivery, and infants can grow to become healthy adults. In parts of the world where health services are easily accessible families and communities thrive. However, when health services are not accessible the communities unravel (18). Immunization and prevention of acute as well as chronic diseases within our global population is one of the most important determinants of global health.

Disclosure statement

The authors proclaim that they have no competing interests.

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