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VACCINATION AGAINST HEPATITIS B IN ECUADOR: RISK GROUPS, COMORBIDITIES AND TOXIC HABITS IN NON-RESPONDING INDIVIDUALS.

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ABSTRACT

Introduction; Hepatitis B virus is a viral agent that chronically infects humans, with an estimated 400 million people at permanent risk of developing cirrhosis and/or hepatocellular carcinoma. Immunization against hepatitis B (HB) is effective and safe, it is one of the most effective interventions for immunoprevention. However, there is a population group that does not respond to vaccination. **Objective**: to analyze the lack of response to anti-HB vaccine in the Ecuadorian population and its association with risk groups, comorbidities and toxic habits. **Methods**: A documentary design was applied through the analysis of different selected sources of scientific databases under inclusion and exclusion criteria, published in the last 10 years. The prevalence of HB shows endemicity in different regions. Health care providers are one of the groups with the highest risk of becoming infected, as well as newborns of seropositive mothers. The identified factors associated with the lack of response to vaccination are obesity, celiac disease, advanced age, immunocompetence, male sex, co-infections, smoking, drug addiction and alcoholism. **Conclusion**: Hepatitis B remains a major health problem throughout the world. Compliance of the complete administration of hepatitis B vaccine schedule is encouraged as established by health authorities in favor of children and people at risk, especially health personnel. Monitoring of antibodies and dose reinforcement is also advised.
Keywords: hepatitis B, vaccines, occupational risks, immunization

INTRODUCTION

Hepatitis B (HB) is a liver infection of viral etiology and of acute or chronic evolution which has a worldwide distribution that can give rise to a number of very significant acute symptoms as well as chronic diseases. It involves important transmission mechanisms, directly linked to the socioeconomic, health and cultural conditions of different regions (1).

This pathology can be prevented through vaccines, which are safe, easy to obtain and effective, and by prophylactic treatment with antivirals during pregnancy. In addition to vaccinating children under one year of age, including the dose at birth, WHO recommends using prophylactic treatment with antivirals to prevent HBV transmission from mother to child. Pregnant women with high levels of HBV DNA (viral load) or with the presence of HBV e-antigen (HBeAg) (or both) have a high risk of transmitting the virus to the child, even if they are infants who have received the dose at birth and the complete vaccine against HB (2).
The Ministry of Public Health through the Surveillance System of Ecuador (SIVE), from week 48 of year 2020, reported a total of 135 confirmed cases of HB in the section of immunopreventable diseases. And in 2019, it was reported a total of 339 cases confirmed in the Ecuadorian population. In 2016, Ecuador was part of the hepatitis prevention plan proposed by WHO in order to comply with vaccination as prevention, detect the disease early and provide the necessary therapy to those who need it.(3).

The World Health Organization (WHO) launched the global strategy against viral hepatitis in 2016 in order to reduce the impact of this problem. It aimed at reducing cases of HBV and HCV by 30% and reduce mortality by 20% by 2020. Ecuador has joined the plan, showing a significant decrease in cases in the last four years. However, for specialists, the numbers may be higher given that many cases go undiagnosed(5).

The development of seroprotection induced by the vaccine was performed by determining the anti-HBV surface antigen antibody. However, it has been shown that of 100% of people vaccinated against HBV, 4 to 10% have a low or no immune response to the anti-HBV vaccine.(1). It is estimated that the reasons that do not allow generating such a response vary between non-genetic factors and genetic factors. Non-genetic factors include age, obesity, drug addiction, smoking, alcoholism, infections, immune suppression and the vaccination route, and genetic factors such as those suffering from celiac disease and the presence of Human Leukocyte Antigen in its HLA DR3, HLA DR7, HLA DQ2 and HLA B8 haplotypes. These are associated with a poor or null response to the hepatitis B vaccine (<10mIU/ ml), in 30-40% of the vaccinated population(8).
Semra (6), reported that in 2014 HBV infection continued to be a public health problem worldwide. It is an endemic disease in some parts of the world and its greatest strength is to cause serious liver diseases. Differences in host immune response may be one of the reasons for the diverse clinical presentations of virus infection. Polymorphisms of the genes encoding proinflammatory and anti-inflammatory cytokines, which are responsible for the regulation of the immune response, can affect the clinical presentation of the infection. In particular, polymorphisms of genes encoding cytokines such as interleukin (IL)-1, IL-6, IL-8, IL-10, IL-18, IL-28, interferon-γ, tumor necrosis factor-α, tumor growth factor-β1 and regulatory molecules,(13).
HBV infection is part of the tenth cause of mortality in the world due to its form of presentation. It causes almost 600 thousand deaths annually. Serious complications such as liver failure and hepatocarcinoma occur more frequently in patients with chronic infection. Although there are immunization programs, HB infection is present in Latin America. According to WHO, this disease remains as silent epidemic because patients carrying the virus do not realize they have it for years and decades until it manifests itself.(22).

HBV Subtypes, genotypes, and mutations

HBsAg comprises a neutralizing epitope identified as a determinant. Other HBsAg determinants have been described: d/y and w/r. It thus defines four HBV subtypes: adw, adr, ayw and ayr. Certain amino acid substitutions in this epitope, particularly in the region of amino acids 137 to 147, can render the determinant unrecognizable by routine screening tests or by vaccine-induced antibodies. Although, in theory, the selection pressure exerted by vaccination or antiviral treatments can boost the replication of these mutants, their possible clinical importance has not yet been elucidated and they have not been shown to constitute a danger to public health.(23).

HBV viral proteins

The four genes that modify the viral proteins are translated into seven proteins, four of which are the antigens that would produce the immune response in the infected individual.(25):

- HB surface antigen (HBsAg): structural protein, which is an association of three proteins: large, medium and small, as mentioned above, with a lipid bilayer envelope. The small protein is the one found in greater quantity, carrying the necessary signal for the assembly of large and medium proteins.(25).
- Ag. Do "core" - HbcAg: the MAI core encoded for the two proteins: the one of the viral capsids-Ag of the core (25).
- Ag. "e" – HbeAg: anti-HBe is found in patients with reduced or incomplete viral synthesis. Persistence of HBeAg in the blood in acute viral hepatitis is associated with an increased risk of chronic hepatitis or cirrhosis.(25).
- The polymerase gene encodes a protein: the viral reverse transcriptase. This polypeptide has at least four enzymatic activities required for the synthesis of genomic DNA(25).
- Protein X: is associated with a regulatory function: transactivator of several promoters, and has shown transforming capacity in cell cultures. It has been related to the genesis of hepatocarcinoma(25).

Transmission

In areas with high endemicity, HB is usually transmitted from mother to child during childbirth, which is called perinatal or horizontally transmission. It happens in the household environment through exposure to infected blood, especially from infected children to healthy children during first five years of life(26).

Transmission can also occur through needle sticks, tattoos, body piercing, and exposure to infected blood or body fluids such as saliva, semen, and vaginal and menstrual fluids. Sexual transmission can also occur, especially in unvaccinated men who have sex with other men. Infection in adulthood becomes chronic in less than 5% of cases, while in infants and young children this proportion is 95%. The virus can also be transmitted through the reuse of needles and syringes in health centers or through injecting drugs(26).

Prevention against HBV infection: immunization and other strategies

Chronic HBV infection is a common cause of liver disease worldwide, with a disproportionately high burden in South-Eastern Asia. Vaccines and nucleoside or nucleotide drugs are available, which reduce both new infection rates and the development of liver disease in HBV-positive people who adhere to long-term suppressive therapy. Although there is still considerable value in optimizing access to virus suppression regimens, the scientific and medical communities have embarked on a concerted journey to identify new antiviral drugs and immune interventions aimed at curing infection (31).

Hepatitis virus immunization can be classified into passive and active immunization. Passive vaccination is carried out with immunoglobulin against hepatitis B (IGHB) that provides temporary immunity and active vaccination is the administration of the vaccine that produces long-term immunity. In endemic areas, the main route of infection arises from maternal transmission (32).

The result of perinatal transmission, results in a very high chronic infection rate of 90%. Therefore, the best time for initial HBV vaccination should be within 24 hours of birth, followed by subsequent doses of HBV vaccine during infancy (32). On the other hand, other strategies that are easy to apply for the prevention of HBV infection are to control the presence of the virus in blood products before being applied to new individuals, the correct sterilization of steel materials that are frequently used in health centers. And finally, it is important to be careful when performing body piercings and thus help to prevent the horizontal transmission of the virus.

The Center for Disease Control and Prevention (CDC) in Atlanta, USA, suggests that hepatitis B vaccine must be administered to all patients who consult for a sexually transmitted disease, on the grounds that these pathologies share the same route of transmission(16). In Latin America, especially, the following indications are suggested for immunization against hepatitis B virus:

- All children and anyone under the age of 18.
- People with occupational risk (workers in health areas).
- Patients with end-stage chronic kidney disease, including those on predialysis, hemodialysis and peritoneal dialysis, and patients with chronic liver disease.
- Sexual contacts of HBV carriers and HIV infection.
- People who have had more than one sexual partner in six months, a history of a sexually transmitted disease, men who have sex with men.
- People who get injectable illicit drugs.

Lack of response to hepatitis B virus (HBV) vaccination has been associated with interleukins implicated in Th1 functioning, including interleukin-8 (IL-18) and interferon-γ (IFN-γ). IL-18 and IFN-γ have also been linked to the development of different types of immune-mediated inflammatory conditions, including type 1 diabetes, celiac disease, rheumatoid arthritis, obesity, and systemic lupus erythematosus (33).

Methods

The methodological design used for this research is documentary and descriptive.

Search strategy.

In the present work, a search for journal articles based on keywords or MESH terms (in English and Spanish) was developed. It included: epidemiology, Hepatitis B, risk groups, vaccines, and demography. These were available in scientific databases such as SciELO, PubMed, Elsevier, Latindex and Redalyc. Other information was also collected from official websites such as the World Health Organization, the Ministry of Public Health of Ecuador, the Pan American Health Organization and the Centers for Disease Control and Prevention of the United States.

Inclusion criteria. selection of full-text articles published in the period from December 2006 to December 2021 in Spanish, English and Portuguese languages. It addressed the epidemiology of Hepatitis B, the causes of non-response to vaccination and groups identified as non-responders.

Exclusion criteria. All those studies carried out in vitro or other biological systems other than humans were excluded.

Ethical criteria. In this research, copyright was respected, making an adequate citation and referencing of the information according to Vancouver standards, as well as safeguarding intellectual property.

Results

Epidemiology of hepatitis B globally and in Ecuador.

Hepatitis B is one of the most transmitted infectious diseases in the world. It is estimated that 5% of the population is infected worldwide. This means that approximately 300 million people, who are infected, are the so-called chronic carriers (36, 37). HB cases are highly variable depending on the region studied. The World Health Organization of Western Pacific and African regions have the highest prevalence rates of this disease, with an adult infection rate of 6.2 % and 6.1%, respectively (38).

It is clearly detailed that the Western Pacific Region is one of the regions that reports the most cases of HB according to the sources consulted. This is due to the lack of information about the disease, especially in undeveloped countries or in areas with low coverage or access to vaccination programs services. At a global level in the European Union, the burden of chronic hepatitis disease due to HBV was estimated at 4.7 million and the prevalence of HBsAg in the general population at 0.9% (0.7-1.2) in 2015. The prevalence is higher in Eastern and Southern countries (39)(Table 1).

Table 1. Distribution of Hepatitis B cases worldwide

Region/country	Million cases/ prevalence (%)	Reference
Western Pacific Region	115 (6.2-8)	(37,47,44)
Africa Region	60 (6.1-15)	(39,47,60)
Eastern Mediterranean Region	21 (3.3-5)	(40,47)
South East Asia Region	39 (2.0)	(41-47)
Europe Region	4.7 (0.9-2)	(42,47)
North America	7 (0.7-2)	
Latin America	<2	(44, 60.59)
Total	257 (19.90)	

In Ecuador, a total of 78 cases of hepatitis B has been registered. According to data from the Ministry of Public Health during 2020 until epidemiological week 20 (first quarter of the year), the most affected provinces are Esmeraldas with 28.2% representing 22 cases, followed by the province of Pichincha with 24.4% representing a total of 19 cases(40)(table 2).

Table 2. Distribution of cases of Hepatitis B in Ecuador. Year 2020.

Province	cases	Percentage
Esmeraldas	22	28.2
Pichincha	19	24.4
Manabi	6	7.7
Guayas	5	6.4
Morona-Santiago	4	5.1
Pastaza	4	5.1
Santo Domingo de los Tsachilas	3	3.8
Zamora Chinchipe	3	3.8
Azuay	two	2.6
Bolivar	two	2.6
Imbabura	two	2.6
Orellana	two	2.6
Canar	1	1.3
Chimborazo	1	1.3
Gold	1	1.3
Napo	1	1.3
Total	78	100

Source: Ministry of Public Health, 2020 (40).

Main risk groups in response to vaccination against Hepatitis B.

In relation to the identification of the main risk groups in response to vaccination against HB, according to WHO, the main method of prevention against Hepatitis B is vaccination. It is recommended that it must be included in vaccination programs worldwide. It should be given to all infants and people with risk behaviors. In areas where mother-to-child transmission of HBV is common, the first dose should be given as soon as possible after birth (within the first 24 hours). Complete vaccination induces antibodies that reach protective concentrations in more than 95% of infants, children, and young adults. Protection lasts at least 20 years. All children and adolescents under 18 years of age who have not been previously vaccinated should be vaccinated. This has allowed a 68% decrease in the prevalence of HBV infection among children in America regardless of country of origin and within 10 years after the beginning of universal HB vaccination. Recent studies seem to indicate that the administration of the recombinant HBV vaccine intradermally is very effective and could represent a more useful strategy than the intramuscular way (41).

In a study conducted in India with 454 individuals, who completed all three doses of the vaccine and had post-vaccination estimates of their antibody titers, a total of 98.9% had titers greater than >10mLU/Ml and a 1. 1% titers <10mLU/Ml(42). In the city of Ghana, 89.2% had titers greater than >10mLU/Ml and 10.8% titers less than 10mLU/Ml (43). In Colombia, when reviewing the titers of anti-HBs antibodies, 98% obtained results greater than 10 IU/ml. It is considered as reactive to the doses of the vaccines and thus they reached protective titers.(44). In Ecuador, it was identified in health personnel at a Hospital of Medical Specialties, taking into account the number of vaccinations, that 33% did not generate serum levels lower than 10 IU/ml and 67% managed to generate adequate seroprotection with values higher than 10 IU /ml (45).

Regarding the inmates in a study carried out in Switzerland, 5.9% had a chronic infection (HBsAg +), 32.4% had resolved HBV (anti-HBc +, but HBsAg -), and 14.0 % had a serological profile compatible with immunization (anti-HBc-, anti-HBs +). Just under half of the inmates had no detectable HBV markers, meaning they were neither carriers of HBsAg nor immune and therefore they were susceptible to HBV infection (46). In Korea, the prevalence of HBV markers was studied in 218 newborns whose mothers were chronic carriers of HBV according to maternal HBeAg/anti-HBe status at delivery. HBsAg was positive in 16 newborns (18.0%) of 89 HBeAg-positive mothers, 6 newborns (9.5%) of 63 negative HBeAg and anti-HBe mothers, and 4 newborns (6.1%) of 66 mothers positive for anti-HBe. HBsAg was positive in 38 infants (42.7%) of 89 HBsAg-positive mothers and negative in all infants (0.0%) of 129 HBsAg-negative mothers (47) (table 3).

Table 2. Risk groups defined by the generation of antibody titers (Anti HBs).

Reference	Country	Risk group
HEALTH CARE PROVIDERS		

		Alternatives	Frequency	Percentage
Thomas et al. (42)	India	Nonreactive <10mIU/mL	5	1
		Reactive >10mIU/mL	449	99
		Total	454	100
Obiri-Yeboah et al.(43)	Ghana	Nonreactive <10mIU/mL	7	eleven
		Reactive >10mIU/mL	58	89
		Total	65	100
Tamayo Diaz (48)	Colombia	Nonreactive <10mIU/mL	two	two
		Reactive >10mIU/mL	101	98
		Total	103	100
Puma Strap et al.(49)	Ecuador	Nonreactive <10mIU/mL	278	67
		Reactive >10mIU/mL	136	33
		Total	414	100
INMATES				
Getaz et al.(fifty)	Switzerland	HBsAg +		6
		anti-HBc +		32
		anti-HBs +		14
		anti-HBc -, HBsAg -		48
		Total		100%
PREGNANT AND NEWBORN WOMEN				
Ryoo-young (51)	Korea	HBsAg +	38	42
Brown et al. (52)	USA	HBsAg +	2263	100

Comorbidities and toxic habits associated with the lack of response to the hepatitis B vaccine.

In an observational study with an analytical component, adult patients with Chronic Kidney Disease in a three days a week hemodialysis treatment at the National Hospital of Itauguá during 2015 were included. AntiHBsAg was determined in all of them, 89 subjects were included, of which 47% had an inadequate response to the HBV vaccine. There was a slight male predominance, age, smoking habit, comorbidities and nutritional status by BMI. These were non-significant risk factors for inadequate response to the HBV vaccine. However, those with years of hemodialysis and uremia were significantly related to this poor response (53).

In another study, the immunological response to the HB vaccine was determined in doctors, nurses and medical students in Paraguay. The results were that the mean BMI was 24.7±3.8 kg/m2, and adequate serum levels of anti-HBs in 64% of the health personnel were detected. Obesity was a factor associated with poor response to the vaccine (p= 0.02). Sex, age, time since last dose, and smoking were factors that were not significantly associated with lack of response to the vaccine. (54).

In immunocompetent patients there are factors that influence an inadequate response to the hepatitis B vaccine, such as advanced age, male sex, low BMI, cigarette and alcohol consumption(16). In immunocompromised patients, being a young patient is a positive predictor of vaccination against HB(55). When the vaccine is administered, it interacts with the antigen-presenting cells present in the blood (HepBsAg-specific B cells) This epitope is lysed and processed in the major histocompatibility complex (MHC) II, which later presents it to the surface of the TH-2 cells. These TH-2 cells become activated and stimulate the differentiation of B lymphocytes into plasma cells. These cells release antibodies against hepatitis B (HepBsAb) in large quantities, as well as induce the development of memory B and T cells. These memory cells play an important role in long-term protection(56). This would be explained because after vaccination in immunocompetent patients, protection against HBV is maintained by the immune memory of the subject after the decrease in antibodies, or even after the loss of antibodies. This does not happen in immunosuppressed individuals. To assess the outcome of immunization, anti-HBs titer ≥ 100 mIU/mL is often preferred as a correlate of longer protection against infection, especially in subjects at risk. In our study, the cut-off point was 10 mIU/mL, because anti-HBs values can be lower in immunosuppressed patients.(57).

Many studies from retrospective studies to randomized controlled trials have found a correlation between undetectable levels of HIV viral load, a high CD4 T cell count and greater vaccination success. Viral load appears to be more important than TCD4, despite the fact that there is a positive correlation between the CD4 count and the time of vaccination(58).

Discussion

Hepatitis B virus (HBV) infection is a global public health problem. Global estimates suggest that more than 2 billion people have been infected with HBV and that 248 million of these people are chronically infected (defined as HBsAg positivity). About 15% to 25% of people with chronic HBV infection die of cirrhosis or liver cancer.

The Global Burden of Disease Study(44), estimated that there were 686,000 deaths caused by HB in 2013 and an age-standardized death rate of 5.9 per 100,000 globally, of which 300,000 deaths were attributed to liver cancer and 317,400 deaths to secondary liver cirrhosis and hepatitis B. This rate represents a substantial global burden, with wide global geographic variation. The prevalence of hepatitis B (HBsAg) is highest in the sub-Saharan African and Western Pacific regions, considered high-intermediate to high endemicity countries (5% to ≥ 8% prevalence), and prevalence estimates exceed 15% in several countries. The lower intermediate regions (2%–4.99%) include eastern Mediterranean and European regions. The regions of America and Western Europe are considered to be of low endemicity, with a prevalence of HBsAg generally less than 2%. However, there has been an overall decrease in HBsAg prevalence over time in most countries, but with notable increases in African and Eastern European countries (42,43, 47-52).

In the United States, estimated figures of chronic HB infection range from 700,000 to more than 2 million people. The number of chronically infected people worldwide and in the United States is challenging because the disease is asymptomatic in most infected people, leading to underdiagnosis, and passive surveillance often results in underreporting.(59). Despite the decrease in cases of chronic hepatitis B among children and adolescents, due to the increase in immunity following the recommendations of universal vaccination, the number of adults with chronic infection has increased as a result of the immigration of infected people from countries highly endemic. It is estimated that up to 70% of HBV infections in the United States occur among people born abroad (60).

The integration of HB vaccination into national immunization programs has led to substantial reductions in hepatitis B virus (HBV) transmission in previously endemic countries. The key strategy for the control of the HBV epidemic is the dose at birth and childhood vaccination(61). A study of health workers in China to evaluate HB vaccination status found that the complete vaccination rate among health workers and the desire to be vaccinated are low. Education campaigns and national HB vaccination policies targeting health workers are needed, particularly for older health workers who may be at higher risk (62), as supported by this documentary research.

On the other hand, Khan et al.(63), detail in their research that district-level variation in HB vaccination is spatially heterogeneous and clustered in India, with a strong neighborhood effect. HB vaccine uptake among Indian children depends primarily on their socioeconomic and demographic characteristics.

Generally, a large part of the world population is not fully trained with information regarding antiviral vaccines and the importance of suffering from this infection. For this reason, many of them do not go to places where it is available. This is explained in detail in a cross-sectional analytical study carried out with doctors, nurses, laboratory workers, health assistants, pharmacists and radiographers who work in the state of Yobe. It was shown that 151 (82.97%), 81 (44. 51%), 85 (46.70%) and 33 (18.13%), respectively, of health workers surveyed, had extensive knowledge about everything related to HBV and good knowledge of the HB vaccine. It correlated with those who had completed the three doses of vaccination (64).

According to the sources consulted, it is explained that Ecuador is not an endemic country for HB, compared to other South American countries. However, the Ministry of Public Health (MSP) establishes that although the national rate is below 8%, there are people who have hepatitis, but they were never diagnosed because they did not go to the doctor in a timely manner (42). According to WHO, it is determined that approximately 37% of HBV infections among health workers in the world are due to the result of occupational exposure. Likewise, in a study carried out on nursing students, it was determined that there may be a prevalence of infection that could reach 11.1%, or up to three times more than in the general population, given that the professionals are exposed to biological risks. Moreover the risk is higher during the training process, due to the lack of experience, which increases the risk of accidents in their practices and hospital stays (18).

According to the latest report from the European Center for Disease Control, the most likely mode of transmission of acute hepatitis B cases in 2017 was heterosexual transmission (27%), followed by nosocomial transmission (16%), homosexual transmission between men (13%).), non-occupational exposure (10%) and shared use of drug injection equipment (10%) (43). The explanation for the low response could be due to the decrease in memory B cells, altered B cells and B cell phenotypes in viremic patients vaccinated against HIV. It may also be due to the lack of response that was found in patients who had increased regulatory T cells(22).

It has been described that patients older than 50 years and TCD4 less than 200 are the most important factors that make them non-responders to the HB vaccine. In the study by Pollak et al. (65), TCD4 cell count, at the time of vaccination, was found to be the only negative predictor of response to HBV vaccination in HIV-infected Vietnamese adult patients. They mention the importance of vaccinating newly infected patients with advanced immunosuppression. On the other hand, in vaccinated patients who are on ART after 1 year, no differences were observed in CD4 gains in responders and non-responders to the HB vaccine.

Further research should be carried out on the response to HB vaccination in immunocompetent and immunodeficient populations through cohort studies. It should be defined which of the groups, identified as being at risk with current known factors, are responsible for the lack of response or inadequate response after vaccination with three doses of HBV vaccine.

Conclusions.

Hepatitis B, a life-threatening liver infection, is a major health problem throughout the world. The highest prevalence of hepatitis B is found in the Western Pacific and African regions, where it is endemic. In North America the prevalence is low. In Latin America, including Ecuador, hepatitis B is not endemic due to prevention by vaccination. However, it is estimated that there could be an underreporting of cases due to the need to improve information systems, data collection and surveillance, especially the monitoring of resistance mutations related to antiviral drugs.

Health care providers are at greater risk of contracting hepatitis B, as they have an important source of transmission such as permanent exposure to infected biological fluids. Newborns make up another part of the risk groups because of their mothers, who are seropositive for the surface antigen of the hepatitis B virus, and the risk of transmitting it to their babies is 80 to 90% This makes them chronic carriers. Obesity, celiac disease, advanced age, immunocompetence, male sex, co-infections, smoking, drug addiction and alcoholism have been significantly associated with lack of response. In addition, they could lead to an increased risk of leaky mutations of Hepatitis B virus vaccine.

Recommendations

Fulfilling the complete administration schedule of hepatitis B vaccine is encouraged, as established by health authorities for children and for people at risk, especially health care providers. Monitoring of antibodies and dose reinforcement is also advised. In universities, vaccination of students in health scenarios must be requested in order to protect the health of young people, and also because they are less aware of preventive care, as in the case of Hepatitis B, a sexually transmitted infection.

Routine vaccination of all children living in the Amazon basin is recommended, as well as in other areas since they report more frequent cases. It is paramount to implement routine vaccination for security coverage of the country.

It is necessary to increase the spread of relevant scientific advances that may lead to a cure for the disease and widely inform the scientific community, general population and health authorities about it. In addition, promoting research in populations should be done, since the lack of response to the vaccine is a feature.

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