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Article

Immune Response to GeneVac-B® (rDNA I.P. Hepatitis B Vaccine) in Vaccinated Persons with a Standard Schedule in Bobo-Dioulasso, Burkina Faso

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Abstract: GeneVac-B® was recently licensed in Burkina Faso and is widely used for population vaccination. This study aimed to evaluate the immune response in people fully vaccinated against hepatitis B with the GeneVac-B® vaccine in Burkina Faso under actual conditions of use. This cross-sectional study included individuals fully vaccinated with GeneVac-B®. For each consenting participant, sociodemographic and clinical data were collected using a structured questionnaire. Approximately 4 mL of whole blood was collected for immunological (anti-HBs, HBsAg, anti-HCV and anti-HIV) and biochemical (blood glucose, total cholesterol, and triglycerides) testing. The anti-HBs titer was used to determine the immune response. A total of 392 participants were included in the study. The mean age was 35.5±15 years. Approximately 56.1% had been previously exposed to HBV. Three hundred eighty (380) participants had an anti-HBs titer ≥ 12 mIU/mL, a seroprotection rate of 96.9%, and 12 had a titer < 12 mIU/mL, a nonresponse rate of 3.1%. Among the nonresponders, 11 (11/12; 91.7%) had high total cholesterol levels (> 240 mg/dL), and 8 (8/12; 66.7%) were older than 40 years of age. The results showed an excellent immune response to GeneVac-B® in our study population. However, age > 40 and high total cholesterol appear to be factors associated with nonresponse.

Keywords: Hepatitis B; GeneVac-B®; immune response; nonresponse factors; Burkina Faso

1. Introduction

Hepatitis B virus (HBV) infection remains a significant public health problem worldwide despite the availability of prevention methods and effective antivirals [1]. According to the "Global Progress Report on Human Immunodeficiency Virus (HIV), viral hepatitis and sexually transmitted infections" produced by the World Health Organization (WHO) in 2021, the number of chronic HBV carriers worldwide is estimated at 296 million (95% CI: 228 - 423 million). With 82 million (95% CI: 62 -115 million) chronic carriers, Africa is particularly affected by this scourge. In 2019, 1,500,000 (95%

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CI: 1,100,000 - 2,600,000) new infections were recorded worldwide, including 990,000 (95% CI: 660,000 - 1,600,000) in the African region. In addition, hepatitis B caused 820,000 (95% CI: 450,000 - 950,000) deaths worldwide in 2019, including 80,000 (95% CI: 47,000 - 110,000) in Africa [2]. Burkina Faso, a country located in West Africa, is endemic for HBV infection. The Prevalence in the general population is estimated to b9% [3,4].

HBV infection can be prevented by vaccination. Safe and effective vaccines have been available since the early 1980s [5]. To control this infection, since 1990, the WHO has recommended vaccination of children, exhorting countries to introduce the hepatitis B vaccine as part of their Expanded Programme on Immunization (EPI). Moreover, vaccination is thought to be the most effective means of prevention, as it has prevented 210 million new infections since the global vaccination program was implemented [6,7]. However, several factors can influence the achievement of seroprotection following the administration of the hepatitis B vaccine. Among these factors are age (mainly over 40), male sex, alcohol consumption, obesity, chronic diseases, infections such as HIV, and genetic factors [8–13] . Biological factors such as high cholesterol levels, high triglycerides [14], and the microbiota [15] also influence the degree of seroprotection achieved. So, several studies evaluating the immune response to hepatitis vaccines have been conducted worldwide [16–20].

Following WHO recommendations, Burkina Faso introduced the hepatitis B vaccine into its EPI in 2006. This vaccine (DTwP-HepB-Hib, Biological E. Limited, India) is administered with other vaccines according to the following schedule: 2, 3, and 4 months (M2, M3, M4) of life after birth. In 2022, the first dose was administered at birth with a monovalent vaccine (Euvax B® Pediatric, LG Chem, South Korea). In addition to this prevention strategy, which mainly targets newborns, there are monovalent vaccines in Burkina Faso (Engerix B® and Euvax B®) used primarily for immunizing the adult population. However, their cost is an obstacle to their accessibility. Full immunization with one of these vaccines would cost an average of €37. Recently, the GeneVac-B® vaccine was licensed in our country. GeneVac-B® is a product of the SERUM INSTITUTE OF INDIA PVT LDT and is administered according to the conventional three-dose vaccination schedule: 0, 1 and 6 months (M0, M1, M6). It is a branded generic vaccine that is accessible and affordable (€3/dose). These characteristics make it a good tool for preventing HBV infection in countries with limited resources. High response rates have been reported in previous studies evaluating the efficacy of GeneVac in healthy infants, adolescents, and adults [21–26] However, all these evaluation studies were conducted in India, highlighting the need to conduct such studies in local countries before using them on a large scale. Given the various factors that can influence the vaccine response, to our knowledge, there is no data on the efficacy of GeneVac-B® under our actual conditions of use. To fill this data gap, this study was carried out to assess the immune response in people fully vaccinated with the GeneVac-B® vaccine at the Bobo-Dioulasso "Assaut-Hépatites" Centre, Burkina Faso.

2. Materials and Methods

2.1. Study Design – Study Population – Setting

This cross-sectional study was conducted between September 2021 and July 2023. All people who had been vaccinated according to the standard vaccination schedule (3 doses: M0, M1, M6; M: month) in Burkina Faso with the GeneVac-B® vaccine at the "Assaut-Hépatites" Center. Thus, all participants who agreed to return for post-vaccination biological analyses 1 to 3 months after administering the last dose of vaccine and from whom we obtained informed consent were included in this study. For participants under 18 years old, consent from the parents or guardians was obtained after obtaining the child's assent. Participants' inclusion and data collection (sociodemographic and biological) were carried out at the Bobo-Dioulasso "Assaut-Hépatites" Center. This is a viral hepatitis Advice-Screening, Vaccination, and Management center that was established in 2018. It is located in the city of Bobo-Dioulasso and receives patients from different regions of Burkina Faso. The biological analyses were conducted at the Clinical Microbiology and Immunology Laboratory of the Institut de Recherche en Sciences de la Santé (IRSS) and the Clinical Biology Laboratory of the "Assaut-

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Hépatites" Center. These laboratories have the technical facilities required to perform serological and molecular analyses.

2.2. Sample Size – Sampling

The sample size was determined using Cochran's formula: $N = Z^2 p (1-p)/m^2$, where N = minimum required sample size, Z = 1.96, the standard normal variation (p-value: 0.05 and 95% confidence interval), p = seroprevalence of anti-HBs (we assumed that 50% of the Burkinabe population was anti-HBs-positive) and m = precision at 5% at 95% confidence interval. According to this formula, the sample of participants to include was 384 participants.

Participants meeting the inclusion criteria were enrolled progressively until the required sample size was reached. Once the participant's eligibility had been established, a detailed explanation of the purpose and procedure of the study was given, followed by a request for consent to participate in the study. Each participant was given a unique identification number to avoid duplication during the study period.

2.3. Data and Sample Collection

Sociodemographic and clinical data were collected using a structured questionnaire during individual participant interviews. The data were collected by nurses trained in research ethics and filling in the data collection forms. The main data collected were age, sex, weight, height, alcohol consumption, and smoking habits.

Approximately 4 mL of whole blood was collected from each participant by venipuncture at the elbow crease. The sample was taken in a dry tube under rigorous aseptic conditions and labeled. The samples were centrifuged at 4000 rpm for five [5] minutes, and the serum was aliquoted into two well-labeled cryotubes (patient identification number, date of collection). One cryotube of serum was used to measure antibody titers, and other serological tests and biochemical parameters were used for this study. The second cryotube was stored at -80°C for future studies.

2.4. Hepatitis B Vaccine (rDNA) I.P.

GeneVac-B® is manufactured by Serum Institute of India PVT LTD.212/2, Hadaspar, Pune 411028, INDIA. It is an infectious recombinant DNA Hepatitis B Vaccine. It contains purified surface antigens of the virus obtained by culturing genetically engineered Hansenula polymorpha yeast cells with the surface antigen gene of the hepatitis B virus. The hepatitis B surface antigen (HBsAg) expressed is purified through several chemical steps and formulated as a suspension of the antigen adsorbed on aluminum and thiomersal is added as preservative. GeneVac-B® is indicated for active immunization against Hepatitis B infection in subjects considered at risk of exposure to HBV-positive material. The route of administration is intramuscular injection. A series of 3 shots can prevent the disease: 6, 10, and 14 weeks for infants / 0, 1, and 6 months for children, adolescents, and adults / 0, 1, and 2 months (for rapid protection)

2.5. Laboratory Analyses

- Quantification of anti-HBs antibodies titer

Anti-HBs antibodies were detected using the VIDAS® Anti-HBs Total II kit (Biomérieux, Marcy-l'Etoile, France) on the Mini VIDAS automated system. The test principle combines the sandwich enzyme-linked immunosorbent assay with fluorescence end-point detection (ELFA). Before using each reagent kit, calibrations were performed with VIDAS® AHBS S1 calibrators according to the protocol provided by the manufacturer. VIDAS® AHBS C1 and VIDAS® AHBS C2 controls were used for quality control. To perform the assay, samples were first programmed on the instrument using the number assigned to each sample, and then 200 µL of serum from each sample was pipetted into the sample well of a cartridge. The analysis was then started, during which the automated system took two fluorescence measurements at 450 nm in the reading cuvette. The first reading considers the bottom of the cuvette before the substrate is brought into contact with the cone (SPR). The second

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reading is taken after the substrate has been incubated with the enzyme in the cone (SPR). The relative fluorescence value (RFV) was calculated and corresponds to the difference between the two measurements. The instrument calculated the results automatically using a calibration curve and expressed it in mIU/mL. The result is obtained after 60 minutes. The measurement range extends from 3 to 500 mIU/mL. VIDAS Anti-HBs Total II is calibrated against the international standard (WHO Second International Standard 07/164 for Anti-hepatitis B surface antigen (Anti-HBs) immunoglobulin). Results are interpreted in accordance with Table 1.

Table 1. Interpretation of anti-HBs antibodies results according to the manufacturer.

Titer (mUI/mL)	Interpretation
Titer < 8	Negative
8 ≤ Titer < 12	Equivocal
Titer ≥ 12	Positive

- Detection of anti-HBc antibodies

Anti-HBc total antibodies were also detected using the VIDAS® Anti-HBc Total II (HBCT) kit (Biomérieux, Marcy-l'Etoile, France) on the Mini VIDAS automated system. It is a fluorescent enzyme linked immunosorbent assay (ELFA) based on the principle of inhibition. The assay reagents are ready-to-use and pre-dosed in sealed reagent strips. The reaction medium is introduced into the Solid Phase Receptacle (SPR) and withdrawn several times. After dilution, the sample is incubated in the SPR. Anti-HBc antibodies (IgM and IgG) present in the sample bind to the recombinant HBc antigen coating the interior of the SPR. Unbound sample components are removed during the wash steps. The solid phase is then incubated with the conjugate. This conjugate binds to HBc antigenic sites on the solid phase that are not bound by serum antibodies. Unbound conjugate is washed away. In the final detection step, the substrate (4-methylumbelliferyl phosphate) enters and exits the SPR. The conjugated enzyme catalyzes the hydrolysis of this substrate to a fluorescent product (4-methylumbelliferone) whose fluorescence is measured at 450 nm. Fluorescence intensity is inversely proportional to the amount of anti-HBc antibody present in the sample. Results are automatically analyzed by the instrument and expressed as an index calculated against a standard.

Table 2. Interpretation of anti-HBc total antibodies results according to the manufacturer.

Index	Interpretation
i < 1	Presence of anti-HBc antibodies
1 ≤ i < 1.4	Equivocal result
i ≥ 1.4	Absence of anti-HBc antibodies

- Detection of HIV-1/2 antibodies

HIV infection was investigated using the Determine™ HIV-1/2 (Abbott Rapid Diagnostics (Pty) Ltd., South Africa). This is a qualitative in vitro visual reading immunoassay for detecting anti-HIV-1 and anti-HIV-2 antibodies in human serum, plasma, or whole blood. The Determine™ HIV-1/2 test detects a wide variety of HIV subtypes. Its procedure is simple, fast, and easy to use, delivering results in 15 minutes. In Africa, according to the manufacturer, the Determine™ HIV-1/2 has a sensitivity of 99.91% and a Specificity of 99.75%.

- Detection of anti-HCV antibodies

The STANDARD Q HCV Ab (SD Biosensor, Republic of Korea) Test was used to test for anti-HCV antibodies. This is a rapid immunochromatographic test for qualitatively detecting HCV-specific antibodies in human serum, plasma, or whole blood. Results are obtained after five [5] minutes. According to the manufacturer, it has a sensitivity of 100% and a specificity of 97.67%.

- Biochemical tests

The samples were analyzed using CYANSmart (Cypress Diagnostics, Belgium) to look for certain biochemical factors that could influence the vaccine response. CYANSmart is a semi-automated device for the quantitative determination of various biochemical substances. In this study, it was used to measure creatinine, total cholesterol, triglycerides, and blood glucose. The samples were prepared manually outside the instrument. After an incubation period (in or out of the instrument), the samples were measured in a flow cell, and the analyzer calculated the results. These calculations can be made because there is a relationship between the amount of light reflected or transmitted and the concentration of substances in the sample.

All the biological analyses were realized according to the procedures provided by the manufacturer and following good laboratory practice by well-trained and experienced technicians. The biologist responsible for coordinating the biological analyses supervised the handling and ensured the analyses were carried out correctly.

2.6. Ethics Statement

The ethics committee of the Institut de Recherche en Sciences de la Santé (IRSS), known as the Comité d'Ethique Institutionnel pour la Recherche en Santé (CEIRS), approved this study (A024-2023/CEIRES), and written informed consent was obtained from all participants. A enrolled number was attributed to each participant for anonymizing data used.

2.7. Statistical Analysis

Variables were entered using the computer software Excel and analyzed with STATA 14.0 (Texas/USA). The categorical variables were expressed as percentages (with a confidence interval of 95% [95% CI] for the response and non-response frequencies), and the chi-squared or Fisher exact test was used for comparison. The quantitative variable (age) was expressed as mean ± standard deviation.

3. Results

3.1. Characteristics of the Study Population

A total of 392 participants were enrolled in this study. Of these, 204 (52%) were female, for a sex ratio of 0.94. The mean age of the participants was 35.5 ±15.3 years, with the majority (259; 66.1%) aged between 18 and 49 years. One hundred and seven (27.3%) participants were overweight with a body mass index (BMI) between 25 and 29.9, and 84 (21.4%) were obese (BMI > 30). Twelve (3.1%) were smokers, and 112 (28.6%) regularly consumed alcohol. Regarding biological characteristics, 113 (28.8%) had abnormal blood glucose levels (> 6.1 mmol/L), 18 (4.6%) had abnormal creatinine levels (> 123.7 µmol/L), 111 (28.3%) high total cholesterol levels (> 240 mg/dL) and 65 (16.6%) high triglycerides levels (150 -199 mg/dL). In addition, 11 (2.8%) participants were positive for HIV, and one (0.3%) had previously been in contact with the hepatitis C virus. Table 3 summarizes the sociodemographic and clinical characteristics of study participants.

Table 3. Sociodemographic and clinical characteristics of study participants.

Characteristics	Enrolled effectif (n)	Frequence (%)
Gender		
Female	204	52.0
Male	188	48.0
Age groups (year)		
<18	58	14.8
18-49	259	66.1
50 and +	75	19.1
Body Mass Index (BMI)		
<18.6	37	9.5
18.5-24.9	164	41.8
25 -29.9	107	27.3

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≥ 30	84	21.4
Alcohol consumption		
Yes	112	28.6
No	280	71.4
Smoking		
Yes	12	3.1
No	380	96.9
Blood glucose		
Normal: 3.3 – 6.1mmol/L	279	71.2
Abnormal: > 6.1mmol/L	113	28.8
Creatininemia		
Normal: 53 -123.7 µmol/L	374	95.4
Abnormal : > 123.7 µmol/L	18	4.6
Cholesterol Total		
Normal : < 200 mg/dL	173	44.1
Suspect high: 200 -239 mg/dL	108	27.55
High : > 240 mg/dL	111	28.3
Tryglycerides		
Normal : <150 mg/dL	285	72.7
High : 150 -199 mg/dL	65	16.6
Hypertriglyceridemic : 200 -499 mg/dL	42	10.7
HIV		
Positive	11	2.8
Negative	381	97.2
Anti-HCV		
Positive	1	0.3
Negative	391	99.7

3.2. Immune Response to GeneVac-B®vaccine

Participants' anti-HBs titer ranged from 0.0 to > 500 mIU/mL. The majority of participants (280/392; 71.40%) had an anti-HBs titer> 500 mIU/mL and 8 (8/392; 2.04%) had not seroconverted. Of the 392 participants, 380 had an anti-HBs titre ≥ 12 mIU/mL, corresponding to a seroprotection of 96.9% (95% CI: 94.7 - 98.4), and 12 a titer < 12 mIU/mL, representing a non-response rate of 3.1% (95% CI: 1.6 - 5.3). Among the 137 subjects aged 40 and over, non-response affected 8 (5.84%), compared with 4 (1.57%) of the 255 subjects aged under 40, p = 0.029. The distribution of anti-HBs titer by study participants by sociodemographic and clinical characteristics is represented in Table 4.

3.3. Previous Exposure to HBV

Anti-HBc Total II (HBCT) assays were performed on 155 randomly selected specimens. Of these, 56.12% (87/155) were positive, indicating prior exposure to HBV prior to vaccination. One specimen had an equivocal result. Of the 87 anti-HBc-positive specimens, 63.21% (55/87) had an anti-HBs titer > 500 mIU/mL, compared to 89.55% (60/67) of anti-HBc-negative specimens. In addition, seroprotective anti-HBs titers were detected in 96.55% (84/87) of anti-HBc-positive specimens versus 100% (67/67) of anti-HBc-negative specimens.

Table 4. Seroprotection of study participants by sociodemographic and clinical characteristics (n = 392).

Characteristics	Anti-HBs		*p*
	< 12 mUI/ml	≥ 12 mUI/mL	
	n (%)	n (%)	
Gender			0.244
Female	4 (1.96)	200 (98.04)	
Male	8 (4.26)	180 (95.74)	
Age groups (year)			0.27
<18	0 (0.00)	50 (100.00)	
18-49	8 (3.09)	252 (96.91)	
50 and +	4 (5.33)	71 (94.67)	
Body Mass Index (BMI)			0.24
<18.6	0 (0.00)	37 (100.00)	
18.5-24.9	8 (4.88)	156 (95.12)	
25 -29.9	1 (0.93)	106 (99.07)	
≥ 30	3 (3.57)	81 (96.43)	
Alcohol consumption			0.75
Yes	4 (3.57)	108 (96.43)	
No	8 (2.86)	272 (97.14)	
Smoking			0.28
Yes	1 (8.33)	11 (91.67)	
No	11 (2.89)	369 (97.11)	
Blood glucose (mmol/L)			0.52
Normal: 3.3 – 6.1	10 (3.58)	269 (96.42)	
Abnormal: > 6.1	2 (1.77)	111 (98.23)	
Creatininemia (µmol/L)			0.10
Normal: 53 -123.7	10 (2.67)	364 (97.33)	
Abnormal: > 123.7	2 (11.11)	16 (88.89)	
Cholesterol Total (mg/dL)			0.005
Normal: < 200	1 (0.58)	172 (99.42)	
Suspect high : 200 -239	3 (2.78)	105 (97.22)	
High : > 240	8 (7.21)	103 (92.79)	
Tryglycerides (mg/dL)			0.96
Normal : <150	9 (3.16)	276 (96.84)	
High : 150 -199	2 (3.08)	63 (96.92)	
Hypertriglyceridemic > 200	1 (2.38)	41 (97.62)	
HIV			1.00
Positive	0 (0.00)	11 (100.00)	
Negative	12 (3.15)	369 (96.85)	
Anti-HCV			1.00
Positive	0 (0.00)	1 (100.00)	
Negative	12 (3.07)	379 (96.93)	

3.4. Characteristics of Nonresponsders

A total of 12 (3.1%) participants did not respond positively to the GeneVac-B® vaccine. Descriptively, of the non-responders, 8 (8/12; 66.66%) were male, 8 (8/12; 66.66%) were over 40 years of age, 3 (3/12; 25.0%) were obese, 4 (4/12; 33.33%) were regular alcohol drinkers, and 11 (11/12; 91.66%) had high cholesterol rate.

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4. Discussion

This cross-sectional study was designed to assess the immune response in people fully vaccinated against hepatitis B with the GeneVac-B® vaccine in Burkina Faso under actual conditions of use. Our results show that 96.9% of participants developed an excellent humoral response, and 3.1% failed to achieve a protective level of anti-HBs. This result aligns with the protection level expected for second-generation vaccines. Indeed, it is estimated that for these vaccines, around 5 to 10% of the vaccinated population do not induce protective immunity [27]. Similar response rates have been reported in previous studies evaluating the efficacy of GeneVac in healthy infants, adolescents, and adults in India [21–26]. This result also highlights that, given the low cost of the GeneVac-B® vaccine on the market in Burkina Faso (around €3 per dose), it could represent a good tool for preventing HBV infection and controlling the disease.

The non-response rate of 3.1% obtained in our study aligns with the evaluation data reported for this vaccine. It could be due to some characteristics linked to the participants. According to the literature, various factors such as age over 40, male gender, BMI > 25, smoking, chronic alcoholism, and chronic diseases such as diabetes, hypertension, renal failure, and HIV infection can have a negative impact on the vaccine response [12,13,28,29]. The same applies to some high biochemical parameters such as cholesterol, triglycerides, and lipoprotein levels [14], genetic factors [30], and microbiota [15]. Given the small number of participants (12/392) who did not respond favorably to the vaccine in our study, logistic regression analyses could not be performed to establish an association between these parameters and immune non-response. However, when describing the characteristics of non-responders, we found that 8 (66.66%) were male, 8 (66.66%) were over 40 years of age, 3 (25.0%) were obese, 4 (33.33%) drank alcohol regularly, and 11 (91.66%) had high cholesterol. Although these data are not statistically significant, post-vaccination serological surveillance of people with these characteristics could be effective in controlling infection, pending a large-scale study to assess the impact of these factors. In addition, administering a booster dose or restarting the vaccination schedule could result in seroprotection, as has been reported in some studies [31].

Of a randomly selected sample, 56.12% had been exposed to HBV prior to vaccination. By measuring total anti-HBc after vaccine administration, we were unable to determine the presence of natural immunity after exposure to HBV. Furthermore, statistical analysis showed that there was no significant difference in the titer of very high anti-HBc (> 500 mIU/mL) between the two groups (63.21% in anti-HBc positive samples versus 89.55% in anti-HBc negative samples). The same was true for seroprotection, which was 96.55% in anti-HBc-positive samples versus 100% in anti-HBc-negative samples. A study to assess the extent to which natural immunity is established after prior exposure to HBV in areas of high virus circulation would contribute to a better application of the hepatitis B vaccination policy.

Our study had certain limitations. Firstly, due to the small number of non-responders, we did not perform a logistic regression analysis to identify the associated factors with non-response to the vaccine. A large-scale study would, therefore, be necessary to determine the factors that might affect response to the hepatitis B vaccine in our context. Secondly, cellular immunity responses were not assessed, especially as it is well-known that cellular immunity plays a crucial role in HBV vaccination. Finally, our study only included urban residents, whose characteristics may differ from those of rural residents and influence vaccination response [30].

5. Conclusions

The results showed an excellent humoral response to GeneVac-B® in our study population. Given its cost and availability on the market, this vaccine could be a good tool for preventing hepatitis B infection in Burkina Faso. However, 12 (3.1%) participants did not respond favorably to the vaccine despite this positive result. It would, therefore, be necessary to carry out regular post-vaccination evaluation studies to assess immunity against HVB infection. A large-scale sero-study should also be conducted to identify the non-response factors better.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Comité d'Ethique Institutionnel pour la Recherche en Santé (CEIRS) (A024-2023/CEIRS du 18 Octobre 2023).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper.

Data Availability Statement: Data generated during this study are available from the corresponding author upon reasonable request.

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Conflicts of Interest: The authors declare no conflict of interest.

References

1. Spearman CW, Andersson MI, Bright B, Davwar PM, Desalegn H, Guingane AN, et al. A new approach to prevent, diagnose, and treat hepatitis B in Africa. BMC Global Public Health. 2023 Nov 2;1(1):24.
2. World Health Organization. Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021 [Internet]. 2021 [cited 2024 Feb 6]. Available from: https://www.who.int/publications-detail-redirect/9789240027077
3. Lingani M, Akita T, Ouoba S, Sanou AM, Sugiyama A, Tarnagda Z, et al. High prevalence of hepatitis B infections in Burkina Faso (1996–2017): a systematic review with meta-analysis of epidemiological studies. BMC Public Health. 2018 Dec;18(1):551.
4. Meda N, Tuaillon E, Kania D, Tiendrebeogo A, Pisoni A, Zida S, et al. Hepatitis B and C virus seroprevalence, Burkina Faso: a cross-sectional study. Bull World Health Organ. 2018 Nov 1;96(11):750–9.
5. Aspinall EJ, Hawkins G, Fraser A, Hutchinson SJ, Goldberg D. Hepatitis B prevention, diagnosis, treatment and care: a review. Occupational Medicine. 2011 Dec 1;61(8):531–40.
6. Rémy V, Largeron N, Quilici S, Carroll S. The economic value of vaccination: why prevention is wealth. Journal of Market Access & Health Policy. 2015 Jan;3(1):29284.
7. Nayagam S, Thursz M, Sicuri E, Conteh L, Wiktor S, Low-Beer D, et al. Requirements for global elimination of hepatitis B: a modelling study. The Lancet Infectious Diseases. 2016 Dec;16(12):1399–408.
8. Filippelli M. Hepatitis B vaccine by intradermal route in non responder patients: An update. WJG. 2014;20(30):10383.
9. Thomas R, Fletcher G, Kirupakaran H, Chacko M, Thenmozhi S, Eapen C, et al. Prevalence of non-responsiveness to an indigenous recombinant hepatitis B vaccine: A study among South Indian health care workers in a tertiary hospital. Indian Journal of Medical Microbiology. 2015 Feb;33:S32–6.
10. Tagliabue C, Principi N, Giavoli C, Esposito S. Obesity: impact of infections and response to vaccines. Eur J Clin Microbiol Infect Dis. 2016 Mar 1;35(3):325–31.
11. Van Den Ende C, Marano C, Van Ahee A, Bunge EM, De Moerlooze L. The immunogenicity and safety of GSK's recombinant hepatitis B vaccine in adults: a systematic review of 30 years of experience. Expert Review of Vaccines. 2017 Aug 3;16(8):811–32.
12. Yang S, Tian G, Cui Y, Ding C, Deng M, Yu C, et al. Factors influencing immunologic response to hepatitis B vaccine in adults. Sci Rep. 2016 Jun 21;6(1):27251.
13. Zimmermann P, Curtis N. Factors That Influence the Immune Response to Vaccination. Clinical Microbiology Reviews. 2019 Mar 13;32(2):10.1128/cmr.00084-18.
14. Guo D, Dai J, Ju R, Zhou Q, Wang N, Wu C, et al. The relationship between triglyceride, cholesterol and lipoprotein levels, and immune responses to hepatitis B vaccine. Front Med. 2023 Mar 30;10:1131373.
15. Lynn DJ, Benson SC, Lynn MA, Pulendran B. Modulation of immune responses to vaccination by the microbiota: implications and potential mechanisms. Nat Rev Immunol. 2022 Jan;22(1):33–46.
16. Vivian Efua SD, Armah D, Delali Adwoa W. Hepatitis B virus vaccination post serological testing and antibody levels of vaccinated health care workers in Accra, Ghana. Vaccine: X. 2023 Aug;14:100294.
17. Anutebeh EN, Tatah L, Feteh VF, Aroke D, Assob JCN, Choukem SP. Immune response to hepatitis B vaccine following complete immunization of children attending two regional hospitals in the Southwest region of Cameroon: a cross sectional study. BMC Infect Dis. 2021 Dec;21(1):1205.

 doi:10.20944/preprints202405.0333.v1

18. Ocan M, Acheng F, Otike C, Beinomugisha J, Katete D, Obua C. Antibody levels and protection after Hepatitis B vaccine in adult vaccinated healthcare workers in northern Uganda. Borrow R, editor. PLoS ONE. 2022 Jan 21;17(1):e0262126.
19. Norizuki M, Kitamura T, Komada K, Sugiyama M, Mizokami M, Xeuatvongsa A, et al. Serologic testing of randomly selected children after hepatitis B vaccination: a cross-sectional population-based study in Lao People's Democratic Republic. BMC Infect Dis. 2019 Dec;19(1):507.
20. Miao N, Zheng H, Sun X, Zhang G, Wang F. Protective effect of vaccinating infants with a 5 μg recombinant yeast-derived hepatitis B vaccine and the need for a booster dose in China. Sci Rep. 2020 Oct 23;10(1):18155.
21. Vijayakumar V, Hari R, Parthiban R, Mehta J, Thyagarajan S. Evaluation of immunogenicity and safety of Genevac B: a new recombinant hepatitis B vaccine in comparison with Engerix B and Shanvac B in healthy adults. Indian Journal of Medical Microbiology. 2004 Jan;22(1):34–8.
22. Shivananda, Somani V, Srikanth BS, Mohan M, Kulkarni PS. Comparison of Two Hepatitis B Vaccines (GeneVac-B and Engerix-B) in Healthy Infants in India. Clin Vaccine Immunol. 2006 Jun;13(6):661–4.
23. Kulkarni-Munje A, Malshe N, Palkar S, Amlekar A, Lalwani S, Mishra AC, et al. Immune Response of Indian Preterm Infants to Pentavalent Vaccine Varies With Component Antigens and Gestational Age. Front Immunol. 2021 Apr 23;12:592731.
24. Sapru A, Kulkarni PS, Bhave S, Bavdekar A, Naik SS, Pandit AN. Immunogenicity and Reactogenicity of Two Recombinant Hepatitis B Vaccines in Small Infants: A Randomized, Double-Blind Comparative Study. Journal of Tropical Pediatrics. 2007 Oct 1;53(5):303–7.
25. Velu V, Nandakumar S, Shanmugam S, Jadhav SS, Kulkarni PS, Thyagarajan SP. Comparison of three different recombinant hepatitis B vaccines: GeneVac-B, Engerix B and Shanvac B in high risk infants born to HBsAg positive mothers in India. WJG. 2007;13(22):3084.
26. Velu V, Nandakumar S, Shanmugam S, Jadhav SS, Kulkarni PS, Thyagarajan SP. Comparison of three different recombinant hepatitis B vaccines: GeneVac-B, Engerix B and Shanvac B in high risk infants born to HBsAg positive mothers in India. WJG. 2007;13(22):3084.
27. Di Lello FA, Martínez AP, Flichman DM. Insights into induction of the immune response by the hepatitis B vaccine. WJG. 2022 Aug 21;28(31):4249–62.
28. Zeeshan M, Jabeen K, Ali ANA, Ali AW, Farooqui SZ, Mehraj V, et al. Evaluation of immune response to Hepatitis B vaccine in health care workers at a tertiary care hospital in Pakistan: an observational prospective study. BMC Infect Dis. 2007 Dec;7(1):120.
29. Liu F, Guo Z, Dong C. Influences of obesity on the immunogenicity of Hepatitis B vaccine. Human Vaccines & Immunotherapeutics. 2017 May 4;13(5):1014–7.
30. Zimmermann P, Curtis N. Factors That Influence the Immune Response to Vaccination. Clin Microbiol Rev. 2019 Mar 20;32(2):e00084-18.
31. Xu L, Zhang L, Kang S, Li X, Lu L, Liu X, et al. Immune Responses to HBV Vaccine in People Living with HIV (PLWHs) Who Achieved Successful Treatment: A Prospective Cohort Study. Vaccines. 2023 Feb 9;11(2):400.