



RESEARCH ARTICLE

Evaluating the Effect of Hepatitis B Vaccination on Serological Markers in Ile-Ife, Osun State, Nigeria: A Cross-Sectional Study

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Abstract

Hepatitis B (HB) is a public health issue in Nigeria which the introduction of the HB vaccination through the National Programme of Immunization (NPI) in 2004 has not been able to eliminate due to various challenges.

This cross-sectional study measured hepatitis B virus (HBV) serological markers for infection and immunity among individuals of ages between 0 - 32 years which are divided to two cohorts/era namely *Pre-vaccine* and *Vaccine* era in Ile-Ife, Nigeria based on the introduction time of hepatitis B vaccine to the National Programme on Immunization in Nigeria. Venous blood samples were screened for the presence of hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), hepatitis B envelope antigen (HBeAg), hepatitis B envelope antibody (HBeAb), and hepatitis B core antibody (HBcAb) using a rapid diagnostic kit.

Among the 150 participants screened, 6 (4.0%) had HBsAg in them, with those born after the introduction of HB vaccine in 2004 having a higher prevalence of 2.6% (n = 4/150), while those born before had 1.3% (n = 2/150). Although the HB vaccination records were not sighted for any one of the participants, HBsAb detection was observed to be 1.2%, while HBeAb and HBcAb markers' prevalence were 34.0% and 16.0%, respectively.

Only 1 (0.6%) of those born during the vaccine era had HBsAb, while 64 (83.12 %) of the same era had no detectable HBsAg indicating yet a high percentage of the population being susceptible to the HBV infection. This suggests the need to deliberately consider in-depth studies on the process and outcome of the hepatitis B vaccination in Ile-Ife. It is evident that HBV is widespread, possibly due to both vertical and horizontal transmission in the study area. Concerted efforts to ensure herd immunity that will culminate in the eradication of viral hepatitis in 2030 as proposed by the WHO is necessary.

Keywords

Vaccination, Markers, Antibodies, Antigens, Hepatitis B virus, Ile-Ife

Abbreviations

HBV, HBsAg, HBsAb, HBeAg, HBeAb, and HBcAb

Introduction

Hepatitis B remains a global health challenge, primarily affecting the liver and often progressing silently without overt symptoms. While many infected individuals remain asymptomatic, clinical manifestations when present, include fatigue, malaise, appetite loss,

nausea, dark urine, abdominal discomfort, and jaundice [1]. Hepatitis B constitutes a major global health burden, with an estimated 254 million chronic infections and 1.1 million deaths in 2022, primarily due to cirrhosis and hepatocellular carcinoma, despite the availability of safe and effective vaccines. Regional disparities in prevalence are significant, with the highest burdens



Citation: Unogwa GC, Adesina OA, Oyebola BF, et al. (2025) Evaluating the Effect of Hepatitis B Vaccination on Serological Markers in Ile-Ife, Osun State, Nigeria: A Cross-Sectional Study. J Infect Dis Epidemiol 11:334. doi.org/10.23937/2474-3658/1510334

Received : October 14, 2025 : **Accepted:** November 18, 2025 : **Published:** November 21, 2025

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in the WHO Western Pacific Region (97 million) and African Region (65 million), compared to the South-East Asia (61 million), Eastern Mediterranean (15 million), European (11 million), and Americas (5 million) Regions, while annual incidence remains high at approximately 1.2 million new infections [2].

The transmission of this hepatotropic virus occurs through exposure to infected blood or biological fluids, with common routes including perinatal transmission (mother to child), unsafe medical practices, unprotected sexual contact, and needle sharing. The infection can manifest as acute or chronic disease, with chronic cases carrying long-term risks of severe liver damage, including fibrosis and cancer [3].

Nigeria maintains the highest hepatitis B burden in sub-Saharan Africa and ranks among the top three globally, with an estimated 17.8 million people (8.1% of the population) living with chronic infection in 2022, contributing significantly to approximately 70,000 annual deaths primarily from cirrhosis and liver cancer, despite only 1% of that eligible receiving antiviral treatment [4].

National surveillance data highlight an 8.6% prevalence among adults aged 15-49 years, marked by significant gender disparities: Males exhibit nearly double the prevalence (11.1%) compared to females (6.1%) [5]. To combat this epidemic, Nigeria introduced the HBV monovalent vaccine into its National Immunization Program (NIP) in 2004, administered to infants at 6, 10, and 14 weeks of age. By 2012, the program expanded to include a pentavalent vaccine (HB-DPT), combining HBV with diphtheria, pertussis, tetanus, and *Haemophilus influenzae* type B (Hib) [6].

These strategic updates aimed to streamline immunization schedules while broadening protection against multiple diseases. One of the ways to assess the effectiveness of vaccination efforts is through serological markers that emerge at distinct stages of HBV infection or immunity. Collectively, HBV markers enable clinicians to determine active infection, viral clearance, immunity status, or asymptomatic carriage, offering a nuanced understanding of both individual and population-level HB trends. This study has the objective to determine the prevalence of the five HBV serological markers among individuals born before and after the implementation of the hepatitis B vaccine in Ile-Ife, Nigeria.

Methods

Venous blood samples were collected from 150 participants (aged 0-32 years) who were residents or recipients of healthcare services across four healthcare facilities namely Oba Aderemi Primary Health Centre, Enuowa Primary Health Center, State Hospital Oke-Ogbo, and the Health Centre, Obafemi Awolowo University, all in Ile-Ife, Osun State, Nigeria: The study, approved by

the Health Research Ethics Committee of the Institute of Public Health, Obafemi Awolowo University, Ile-Ife (Approval Number: IPH/OAU/12/2307, enrolled both symptomatic and asymptomatic individuals attending these facilities. Those declining consent, people with chronic liver diseases, and immuno-compromised individuals were exempted from the study. The cohort was stratified into two groups based on HBV vaccination timelines: a *pre-vaccine group* (born before 2004) and a *vaccine-era group* (born in or after 2004). The sera obtained from the collected venous blood samples were screened for HBV markers (HBsAg, HBsAb, HBeAg, HBeAb, HBcAb) using a Colloidal Gold rapid diagnostic kit, (China). The data collected from the questionnaires and laboratory analysis were analyzed using the Statistical Package for Social Sciences (SPSS) version 23 to determine and compare the prevalence of both eras.

Results

The 150 participants involved in this study cut across different categories of people. The median as well as the modal age of the participants was 20 years while the mean age was 17.3 years. Table 1 provides more details about the study participants, with the categorization into two eras, the pre-vaccine and vaccine eras.

The prevalence obtained for each of the HBV serological markers according to differentiation to eras showed that in all, 6 (4.0%) tested positive for HBsAg, 2 (1.2%) for HBsAb, 1 (0.6%) for HBeAg, 51 (34.0%) for HBeAb, and 24 (16.0%) for HBcAb. Further details according to the two eras are shown in Table 2.

It is worth noting that 3 (4.11%) of those who claimed to have been vaccinated in the *vaccine era* had no detectable HBsAb in them, while 1(1.37%) in the *pre-vaccine era* who claimed not to have been vaccinated had detectable HBsAb. Also, HBeAb was found in 2(2.60%) of those who declared to have been vaccinated. Details of the HBV markers' distribution according to the eras are shown in Table 3. Table 3: Distribution of HBV serological markers according to vaccination status and era.

Discussion

It is obvious that the universal and catch-up vaccination programmes of the WHO have good intentions, yet the challenge of achieving the set goals globally is not abating especially in the developing world. As expected, hepatitis B vaccine should provide immunity but some of the outcomes of the vaccination recorded in this study appear to be contrary to the expected results even though this needs to be further substantiated before it can be said to be a problem. Not much has been done to evaluate sero-conversion in the vaccine recipients in Nigeria and the responses of some of the participants in some studies can be misleading. However, this study with those born after

Table 1: Demographic characteristics of study participants.

Demographic factors		Era		Total (%)
		Pre-vaccine era (%)	Vaccine era (%)	
Sex	Male	25 (16.7)	31(20.7)	56(37.3)
	Female	48(32.0)	46(30.7)	94(62.7)
Total		73(48.7)	77(51.4)	150(100.0)
Age Group (Years)	0 - 5	0(0.0)	22(14.6)	22(14.6)
	6 - 10	0(0.0)	15(10.0)	15(10.0)
	11 - 15	0(0.0)	8(5.3)	8(5.3)
	16 - 20	0(0.0)	32(21.3)	32(21.3)
	21 - 25	60(40.0)	0(0.0)	60(40.0)
	26 - 30	12(8.0)	0(0.0)	12(8.0)
	31& above	1(0.7)	0(0.0)	1(0.7)
Total		73(48.7)	77(51.4)	150(100.0)
HB Vaccination	Yes	3(2.0)	9(6.0)	12(8.0)
	No	70(46.6)	68(45.3)	138(92.0)
Total		73(48.7)	77(51.4)	150(100.0)
HB vaccine doses received	1 Dose	0(0.0)	2(1.3)	2(1.3)
	2 Doses	3(2.0)	4(2.6)	7(4.7)
	3 Doses	0(0.0)	2(1.3)	2(1.3)
	Not Sure	0(0.0)	1(0.7)	1(0.7)
	None	70(46.6)	68(45.3)	138(92.0)
Total		73(48.7)	77(51.4)	150(100.0)

Table 2: Distribution of HBV serological markers among the study participants,

		Era		Total (%)
		Pre-vaccine era (%)	Vaccine era (%)	
HBsAg	Positive	2(1.3)	4(2.6)	6(4.0)
	Negative	71(47.3)	73(48.7)	144(96.0)
HBsAb	Positive	1(0.6)	1(0.6)	2(1.2)
	Negative	72(48.0)	76(50.6)	148(98.7)
HBeAg	Positive	0(0.0)	1(0.6)	1(0.6)
	Negative	73(48.7)	76(50.6)	149(99.3)
HBeAb	Positive	28(18.7)	23(15.3)	51(34.0)
	Negative	45(30.0)	54(36.0)	99(67.0)
HBcAb	Positive	15(10.0)	9(6.0)	24(16.0)
	Negative	58(38.7)	68(45.3)	126(84.0)
Total		73(48.7)	77(51.3)	150(100.0)

Table 3: Distribution of HBV serological markers according to vaccination status and era.

			HB vaccine received		Total
			Yes (%)	No (%)	
HBsAg	Pre-vaccine	Positive	0 (0.00)	2 (2.74)	2
		Negative	3 (4.11)	68(93.15)	71
	Vaccine	Positive	0(0.00)	4(5.20)	4
		Negative	9(11.69)	64(83.12)	73
HBsAb	Pre-vaccine	Positive	0(0.00)	1(1.37)	1
		Negative	3 (4.11)	69(94.52)	72
	Vaccine	Positive	0(0.00)	1(1.30)	1
		Negative	9(11.69)	67(87.01)	76
HBeAg	Pre-vaccine	Positive	0(0.00)	0(0.00)	0
		Negative	3 (4.11)	70(95.89)	73
	Vaccine	Positive	0(0.00)	1(1.30)	1
		Negative	9(11.69)	67(87.01)	76
HBeAb	Pre-vaccine	Positive	0(0.00)	28(38.36)	28
		Negative	3 (4.11)	42(57.53)	45
	Vaccine	Positive	2(2.60)	21(27.27)	23
		Negative	7(9.09)	47(61.04)	54
HBcAb	Pre-vaccine	Positive	0(0.00)	15(20.55)	15
		Negative	3 (4.11)	55(75.34)	58
	Vaccine	Positive	0(0.00)	9(11.69)	9
		Negative	9(11.69)	59(76.62)	68

the introduction of HB vaccine in 2004 having a higher HBsAg prevalence of 2.6% ($n = 4/150$), while those born before had 1.3% ($n = 2/150$) is calling for more thorough investigation. The reason why some of these participants claimed to have been vaccinated and yet without detectable HBsAb in them is also begging for answers. It could, however, be that they were not actually vaccinated or something else happened. The 8.6% prevalence of HBsAg among adults aged 15-49 years in Nigeria reported by Oluwatosin and others [5] and that of 4% reported in this study may not be far from the same reasons such as perinatal exposure, unsafe medical care, and traditional cultural practices about scarification and tattooing that use non-sterilized tools as reported by Basimane, et al., [7], which still make Nigeria a country with one of the highest HBV burden rates in the world. These challenges are still there and their impacts in eradicating hepatitis B transmission cannot be overlooked.

It is not unlikely that another obstacle to the vaccine protection against hepatitis B lies in the unfinished vaccine courses, as recorded in the 6.0% of participants in the vaccine-time cohort. The incomplete vaccination schedules result in inadequate protection against HBV infection because the protection rate revealed only 1.2% HBsAb positivity. Perieres and colleagues, [8] in a systematic review harvested various factors including caregivers' time constraints, lack of knowledge regarding vaccination, unavailability of vaccines or personnel in healthcare facilities, missed opportunities for vaccination, and poor access to vaccination services among others as reasons for non-vaccination and under-vaccination among children and adolescents in Sub-Saharan Africa. The distance barriers that prevent rural residents from accessing health facilities can contribute to their inability to finish what they have started and it could also be due to improper orientation or education about the consequences of not completing the vaccine dosage. Although Nigeria is said to have recorded a higher full immunization coverage than Mozambique [9] and Ethiopia [10], yet the available data recorded 62.6%, 82%, and 76.4% in 2007, 2011, and 2021 coverage respectively [11].

Attending several immunization sessions for caregivers in remote locations produces both transportation expenses and unattended opportunities that result in patients dropping out of care [12]. Low adherence gets worse because children and their caregivers hold incorrect cultural beliefs about vaccines and they distrust government health information [13]. Weak systems in Nigeria face additional challenges from the use of Tritanrix-HB because it requires strict cold storage maintenance to preserve its potency and, hence, its effectiveness. The improper storage of vaccines continues to spread widely throughout the healthcare sector. Irregular power supplies coupled with poor refrigeration facilities and lacking education

among healthcare staff disrupts the cold chain throughout Nigeria [14]. Hepatitis B vaccine potency suffers from improperly stored conditions since the recombinant protein becomes denatured making it less effective in getting the body ready to fight against hepatitis B. Nigeria can implement Rwandan-style solar-powered refrigeration and temperature monitoring technology which has helped Rwanda to solve its cold chain challenge in a way [15]. Since the HBV genotype E, predominant in West Africa, exhibits unique antigenic determinants in its surface protein [16], this may be connected to some genetic factors that can serve to explain the infection status of individuals carrying HBsAg and the effect of it after the administration of the hepatitis B vaccine. Furthermore, a study has reported that HBsAb seroconversion rates were 15% lower in children with HBV genotype E than children with HBV genotype A during a Gambian trial [17]. This difference suggests weaker immune responses from vaccines produced from genotypes A or D toward genotype E of the hepatitis B virus. More structural and genetic studies are necessary to unravel the reduced vaccine seroconversion rate in HBV genotype E infected children as reported above. There is an urgent need for vaccine development against local HBV variants if this is later further confirmed as a challenge to the eradication of viral hepatitis. Research on genotype-targeted vaccine development like those launched in Southeast Asia for genotype C has the potential to improve vaccine effectiveness [18] if such is adopted in Nigeria.

The high seroprevalence of past infection markers, 34.0% for HBeAb and 16.0% for HBcAb confirms wide spread of HBV exposure, consistent with Nigeria's hyperendemic status. The extremely low detection rate of HBeAg (0.6%) indicates most people infected with HBV have either cleared the virus or remain in a non-replicating state because their immune system controls the infection rather than vaccine protection. The pattern emerges from natural protection acquired through early-life exposure to HBV because vertical transmission affects between 30-50% of chronic HBV cases in sub-Saharan Africa [1]. The gap in reported risk activities and actual transmission routes might stem from participant tendency to hide sensitive behavior or different primary routes of virus transmission. The mismatch between identified risks versus transmission pathways may also be attributed to study participants concealing stigmatized actions because of social preference effects. The high rates of past HBV infection markers (HBeAb: 34.0%; HBcAb: 16.0%) provide evidence that perinatal transmission through mother-to-child routes and horizontal transmission by any of shared razors, toothbrushes and traditional scarification methods are likely factors that drive the HBV spread most significantly in this population. The high prevalence of hepatitis B in Nigeria matches its classification as hyperendemic because 30–50% of chronic cases emerge through vertical transfer yet silent

endemicity persists through horizontal transmission [1,19]. Further investigating HBV transmission in this population should consider strategies to decrease the unwillingness of the participants to declare the whole truth and to ensure the correctness of the information obtained from them. Public health initiatives need to promote wider antenatal HB screening methods along with household safety education while fostering local leader involvement to defeat vaccine avoidance beliefs. The reason for the 45.3% from the vaccine-era that are yet to be vaccinated needs to be addressed.

Conclusion

Nigeria's hyperendemic hepatitis B burden can be said to persist due to gaps in immunization compliance, cold chain failures, and potential antigenic mismatches between vaccines and circulating genotype despite vaccination efforts. The low protection due to the presence of the HBsAb reflect systemic shortcomings especially in the vaccine-era cohort compared to the pre-vaccine group. This underscores unresolved challenges, including incomplete vaccine dosage and logistic barriers. Silent transmission is also evident through high detection of HBeAb and HBcAb which imply past infection, while perinatal and horizontal transmission routes sustain endemicity. Without urgent reforms, the risks of perpetuating preventable morbidity and mortality through hepatitis B is high. There are yet a lot to be done in a population like this where vaccine dosages are not completed and appropriate conditions for vaccine storage and administration are not accompanied with the updated studies on the immunological changes produced by a vaccine in situations where there are genotypic diversities as in HBV if the elimination of viral hepatitis will be achieved as proposed by the WHO.

Acknowledgments

The authors wish to acknowledge the cooperation of all the participants in this study and the assistance of the medical personnel in all the medical facilities where blood samples were collected from for their support and cooperation.

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