

A 4-Year Cross-Sectional Study of Hepatitis B Virus Infection among Pregnant Women: Need for Policy Decision

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Abstract

Background: The elimination of hepatitis B virus (HBV) in Nigeria, especially among pregnant women requires commitment from the government and health policy makers. This is predicated on comprehensive surveillance and epidemiological data. The objective of the current study is to provide the epidemiological data and unique perspectives that will inform accurate advocacy and influence policy decisions.

Materials and Methods: A 4-year cross-sectional study was conducted among 2,428 consecutively recruited consenting pregnant women attending antenatal care at the University College Hospital, Ibadan, Oyo State, Nigeria. Venous blood was screened for HBsAg using Enzyme Linked Immunosorbent Assay (ELISA). HBsAg sero-negative samples were further tested for other HBV serological markers (anti-HBc, HBeAg and anti-HBe) by ELISA. Socio-demographic and clinical details were obtained using a semi-structured questionnaire.

Results: Overall HBsAg prevalence was 5.1% (2,305/2,482). Twenty three (1%) of the HBsAg sero-negative women tested positive to both anti-HBc and anti-HBe while 5.3% and 0.8% tested positive to only anti-HBc and anti-HBe, respectively. Additionally, 6.4% (38/594) of the HBV fully vaccinated pregnant women tested positive to HBsAg.

Conclusion: Hepatitis B is endemic among Nigerian pregnant women. Serological patterns indicated possible occult hepatitis B infection. More political commitment from government and policy makers is urgently required.

Keywords: Hepatitis B; Pregnant Women; Policy; Nigeria

Introduction

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV). It is a major global health problem affecting over 360 million people/individuals worldwide with attendant mortality of 880,000 from liver related complications. Occult hepatitis B infection has been estimated to be about 58 million [1,2], with chronic hepatitis B infection putting people at high risk of death from cirrhosis and liver cancer. Transmission of hepatitis B virus is majorly by blood or body fluid contacts, unsafe sexual exposure and by vertical transmission [3,4].

Despite the increasing incidence of hepatitis B, there is no national policy, or guidelines specifically for hepatitis B elimination [2]. Prior to year 2017 about 194 nations had approved the Global Health Sector Strategy (GHSS). Unfortunately, only a few have come up with national road maps and made requisite commitments toward realization for the elimination of the infection [2,5]. Pregnant women remain a vital target in the elimination effort and strategy against the spread of the virus Infection as vertical transmission has a greater risk of progression to chronic hepatitis B infection, liver cirrhosis and hepatocellular carcinoma [6].

Increased hepatitis B vaccination rates had reduced hepatitis B prevalence from 4.7% in the year 2000 to 1.3% five years after. The global coverage of birth dose vaccination is still poor at 39% [2,7]. Nayagam, *et al.* identified five important factors critical for hepatitis B elimination, these are rapid expansion of the infant vaccination coverage; increased birth dose vaccination; vaccination effectiveness; peripartum medication; testing and management scale up [7].

HBV infection occurs mainly during infancy and early childhood, with mother to child transmission (MTCT) accounting for approximately half of the transmission routes of chronic HBV infections. The risk of maternal-infant transmission is related to the HBV replicative status of the mother which correlates with the presence of HBeAg marker as 90% of HBeAg-positive mothers transmit HBV infection to their offspring compared to only 10%-20% of HBeAg-negative mothers. Routine screening of pregnant women and provision of hepatitis B immune globulin and hepatitis B vaccine to their infants within 12 hours of birth is therefore vital to perinatal HBV transmission.

Objective of the Study

The objective of this study is to proffer the epidemiological data and unique perspectives of hepatitis B infection among pregnant women. This will inform accurate advocacy and influence policy decisions.

Materials and Methods

Study area, design and population

The study was conducted at the University College Hospital in Ibadan, Nigeria. The hospital is a tertiary care centre that provides acute, chronic, referral and emergency services to the Southwest region of Nigeria and the country at large.

The cross-sectional study was conducted on 2,428 consecutively recruited, consenting pregnant women who visited the hospital from December 2016 to December 2020. Blood samples were collected after obtaining the socio-demographic and clinical details through administration of a semi-structured questionnaire.

Inclusion and exclusion criteria

Consenting pregnant women attending antenatal booking clinic were enrolled. Exclusion criteria were: declination of consent for sample collection, known hepatitis B status or women who were acutely ill at the time of sample collection.

Sample collection and laboratory processing

Five milliliters of blood was aseptically collected and centrifuged at 3500RPM for 5 minutes prior to storage at -80°C up until the time of analysis. HBsAg detection was done by Enzyme linked immunosorbent assay (ELISA) (3rd generation; BIORAD, France). HBsAg negative samples were further screened for other serological HBV markers (anti-HBc, HBeAg and anti-HBe) using DIA-PRO ELISA kits (Diagnostic Bioprobes Milano, Italy). Enzyme linked immunosorbent assay uses both monoclonal and polyclonal antibodies in its solid-phase simultaneous sandwich assay. Using an ELISA plate reader, the readings were taken at an optical density of 450 nm. Tests were run, validated and interpretation of results was done with strict adherence to the instructions of the manufacturer.

Ethical approval

The joint Ethical Committee of the University of Ibadan and University College Hospital, Ibadan approved the study before commencement (UI/EC/18/0264). Each participant gave written informed consent before enrollment into the study.

Data analysis

Analysis of obtained data was done using Epi info version 7.2. Significant association was determined at $p < 0.05$.

Results

A total of 2,428 pregnant women were recruited into this study, majority (2412, 99.3%) of whom were married and above the age of 30 years (1296, 53.4%). A large proportion of the participants were literate (2292, 94.4%) with ten or more years of formal education and were mainly non-health workers (2335, 96.2%). One fourth (622, 25.6%) of the pregnant women were primiparous while three quarter (1806, 74.4%) were multiparous.

Overall, HBsAg prevalence among the pregnant women was 5.1% (122 /2,482). HBsAg seropositivity was higher among those above 30 years of age (5.3 vs 4.8%) and among the married group (5.1 vs 0%) compared to those below 30 years of age and single, respectively. The non-health worker group had a higher HBsAg prevalence (119, 5.1%) than their colleagues in the health profession (4, 4.3%). The infection was more prevalent among the less educated participants (9, 6.6%) compared with their educated counterparts (114, 5.0%). Primigravida women had lower HBsAg seropositivity rate (28, 4.5%) compared to those with multigravida women (95, 5.3%). No significant relationship was however established between HBsAg seropositivity and the socio-demographic characteristics of participants (Table 1).

Table 1: Socio-demographic distribution and HBsAg seropositivity among participants.

Variables	Groups	Total tested (%)	HBsAg negative (%)	HBsAg positive (%)	X ² (p-value)
Overall prevalence		2428 (100)	2305 (94.9)	123 (5.1)	
Age	≤ 30	1132 (46.6)	1078 (95.2)	54 (4.8)	0.3853 (0.53)
	>30	1296 (53.4)	1227 (94.7)	69 (5.3)	
Marital status	Single	16 (0.7)	16 (100)	0 (0)	0.8595 (0.35)
	Married	2412 (99.3)	2289 (94.9)	123 (5.1)	
Occupation	Health workers	93 (3.8)	89 (95.7)	4 (4.3)	0.1176 (0.73)
	Non health workers	2335 (96.2)	2216 (94.9)	119 (5.1)	
Education	≤ Secondary	136 (5.6)	127 (93.4)	9 (6.6)	0.7213 (0.40)
	Post secondary	2292 (94.4)	2178 (95.0)	114 (5.0)	
Parity	Primiparous	622 (25.6)	594 (95.5)	28 (4.5)	0.5537 (0.46)
	Multiparous	1806 (74.4)	1711 (94.7)	95 (5.3)	

Twenty three (0.98%) of the 2,360 HBsAg negative women tested positive to both anti-HBc and anti-HBe while those positive to anti-HBc only and anti-HBe only were 122 (5.17%) and 18 (0.76%), respectively. All participants were seronegative to HBeAg.

Table 2: Presence of other HBV serological markers among HBsAg-negative pregnant women.

Other HBV markers	Prevalence (%)	Interpretation
Anti-HBc	122 (5.3)	Resolved or occult hepatitis B infection
anti-HBe	18 (0.8)	Convalescent state
Anti-HBc and anti-HBe	23 (1.0)	Convalescent state

Table 3 showed that 83.4% (2024) of the antenatal attendees had not been previously vaccinated and HBsAg seropositivity rate among the non-vaccinated group was 4.8%. However, 26 (6.4%) of the vaccinated pregnant women were also seropositive for HBsAg. There was a significant association between previous HBV seropositive results and current HBsAg seropositivity. Pregnant women who had scarification either as a child or an adult had a higher HBsAg seroprevalence rate (5.7% and 5.9% respectively) compared to those who had no scarification; although no significant relationship was established. Hepatitis B seropositivity was higher among those with history of contact with HBV patient (11, 6.5%) compared with those who had no contact (5.0%). HBsAg seropositivity rate was also higher among those with previous history of other sexually transmitted infections (112, 5.7%), surgical and dental procedure (5.7 vs 4.8%), circumcision as an adult (5.2% vs 5.0%) and history of HIV infection (6.5% vs 5.0%). However, no significant association was established between all these clinical features/risk factors and HBsAg seropositivity rate.

Table 3: Distribution of HBsAg seropositivity according to participants' reported risk factors.

Variables	Groups	Total tested (%)	HBsAg negative (%)	HBsAg positive (%)	X ² (p-value)
Previous HBV vaccine	Yes	404 (16.6)	378 (93.6)	26 (6.4)	1.8907 (0.17)
	No	2024 (83.4)	1927 (95.2)	97 (4.8)	
Previous HBV screening	Yes	594 (24.5)	556 (93.6)	38 (6.4)	2.8985 (0.09)
	No	1834 (75.5)	1749 (95.4)	85 (4.6)	
Previous Positive HBV results	Yes	12 (0.5)	9 (75.0)	3(25.0)	9.9643 (0.00)
	No	2416 (95.5)	2296 (95.0)	120 (5.0)	
Scarification as a child	Yes	758 (31.2)	715 (94.3)	43 (5.7)	0.8441 (0.36)
	No	1670 (68.8)	1590 (95.2)	80 (4.8)	
Scarification as an adult	Yes	557 (22.9)	524 (94.1)	33 (5.9)	1.1082 (0.29)
	No	1871 (87.1)	1781 (95.2)	90 (4.8)	
History of contact with HBV patient	yes	170 (7.0)	159 (93.5)	11 (6.5)	0.7500 (0.39)
	No	2258 (93.0)	2146 (95.0)	112 (5.0)	
History of other STI	Yes	141 (5.8)	133 (94.3)	8 (5.7)	0.1150 (0.73)
	No	2287 (94.2)	2172 (95.0)	115 (5.0)	
History of surgical and dental procedure	Yes	680 (28.0)	641 (94.3)	39 (5.7)	0.88 (0.35)
	No	1748 (72.0)	1664 (95.2)	84 (4.8)	
Circumcision as an adult	Yes	534 (22.0)	506 (94.8)	28 (5.2)	0.0449 (0.83)
	No	1894 (88.0)	1799 (95.0)	95 (5.0)	
HIV status	Yes	92 (3.8)	86 (93.5)	6 (6.5)	0.4214 (0.52)
	No	2336 (96.2)	2219 (95.0)	117 (5.0)	
History of unsafe injection	Yes	10 (0.4)	10 (100)	0 (0)	0.5358 (0.46)
	No	2418 (99.6)	2295 (94.9)	123 (5.1)	

Discussion

The effective control of Hepatitis B among pregnant women is central to the elimination of hepatitis B infection among the general population. The overall HBsAg prevalence among pregnant women in this study was 5.1% which connotes intermediate endemicity. This observation is at variance with earlier reports of 6.8 - 10.5% from the same region of the country [8-11]. This could be as a result of increased community awareness, accessibility to prophylactic health care services such as vaccination and variation in the diagnostic methods used as well as in sample sizes. In previous similar studies, the sample sizes were less than 500 as compared with the over two thousand participants enrolled in the current study. The northern region of Nigeria had earlier reported higher prevalence rates in the range of 7 - 12.3% [12-16]. In contrast to our finding in the South-west zone of Nigeria, reports from the South-South zone were less than 5% [17,18]. The observed inter-regional differences could be a result of the different socio-demographic characteristics and social lifestyles across each region.

Different African countries have reported varied prevalence of HBsAg seropositivity among pregnant women. While Mali, Gambia and Burkina Faso reported a high range of 9.2 - 17.3% [19-21], other countries such as Rwanda, Uganda and Sudan reported a comparatively lower prevalence rate of 2.4 - 4.9% [22,23]. More developed nations like the United States and Western Europe reported much lower HBsAg prevalence of less than 2% [24]. This could be due to more advanced testing coverage, improved HBV vaccination services and political commitment from the government.

A hundred and twenty two of the HBsAg sero-negative women (5.3%) tested positive to anti-HBc. This could either imply a resolved state of the infection or an indication of occult hepatitis B infection. This finding is however higher than 0.9% found among apparently healthy hospital attendees [25]. Eighteen (0.8%) of the HBsAg negative population tested positive to anti-HBe. The presence of this marker signifies a convalescent state. In such individuals, HBV infectivity is low but still possible. Twenty three (1.0%) tested positive to both anti-HBc and anti-HBe in spite being negative to HBsAg. The detection of these two markers shows that the pregnant women are within the convalescent stage.

The married and older (above 30 years) pregnant women had a higher infection rate. This was consistent with previous studies [10,26] and might be due to the fact that they are more likely to be sexually exposed. This finding is however at variance with some other studies which found higher prevalence among pregnant women below 30 years [27,28]. Furthermore, non health workers had a higher HBsAg prevalence rate compared to their colleagues in the health sector. Better knowledge on HBV prevention practices among this group might be a possible explanation. It may also be due to better education as well as improved socioeconomic status. The infection was more prevalent among the less educated participants (6.6%) compared to their educated counterparts (5.0%). This may give credence to the belief that the more the awareness and education, the lesser the spread of the virus. This report is in keeping with other similar studies in Nigeria [27-30].

Primigravida women had lower infection rate (4.5%) compared to multigravida women (5.3%). Reports have shown a proportionate rise in HBV infection with multiple childbirths [10,31]. This finding informs the need to review some vital processes within the health care system which might be contributory to the possible infection during pregnancy and delivery.

Majority (83.4%) of the antenatal attendees had never been vaccinated against HBV making them susceptible to HBV infection. However, 26 (6.4%) of the previously vaccinated pregnant women were HBsAg seropositive. The current study could not distinguish between possible pre-pregnancy HBV infection or possibility of immune escape mutants, where previously negative individuals tested positive afterwards. A possible mutation could have occurred in the virus conferring on it the ability to "escape" the resisting immune defense of the host. A typical pattern had long been demonstrated first in Italy [32] and recently in Ibadan, Nigeria [33]. A significant association was observed between previous HBV results and HBsAg seropositivity. Twenty five percent (3/12) of the pregnant women with previous

HBV results of greater than 6 months earlier were still HBsAg seropositive. A positive test result after six months of initial detection of the virus defines a chronic state of HBV infection. This implies that this set of pregnant women is chronically infected with hepatitis B. A similar multi-centre study within the Southwest region had earlier observed a reduction in HBsAg prevalence among pregnant women with previous HBV results [10].

Pregnant women who had scarification either as a child or an adult had a higher prevalent rate of the infection compared to those who had no scarification. Although no significant relationship was established, this finding underlies scarification as a potential means of contracting HBV. Furthermore, participants with no history of unsafe injection had a higher rate of infection thus suggesting that they contracted the virus through other route. Hepatitis B infection was higher among those with history of contact with HBV patient (6.5%) compared with those who had no contact (5.0%). HBsAg seropositivity rate was higher among those with history of other STIs. Hepatitis B is a sexually transmitted virus with transmission pathway similar to other STIs. Higher HBsAg seroprevalence was also observed among those with history of surgical and dental procedure thus suggesting possible surgical exposure to HBV. Circumcised pregnant women also had higher prevalence rate of the infection, thus justifying the contributory role of female genital mutilation to development of hepatitis B infection in females. Strict adherence to infection prevention control measures in carrying out any invasive or non-invasive procedures will go a long way in reducing HBV transmission. Co-infection with HIV was 6.5%. This observation is similar to other reports from within [27] and outside the country [34,35].

Conclusion

Hepatitis B is endemic among pregnant Nigerian women. Serological patterns indicated possible occult hepatitis B infection and immune escape mutants. More political commitment from government and policy makers is urgently required to actualize a generation free of hepatitis B virus infection.

Study Limitation

We could not perform molecular analysis such as HBV DNA and sequencing due to lack of funds as this could have fully confirmed the occult hepatitis B infection status of those positive for only anti-HBc and the escape mutants established among HBsAg-positive vaccinated pregnant women.

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