# Viral Hepatitis B and C infections in adolescents born pre- and post-Hepatitis B vaccine introduction in Calabar, Nigeria

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## Abstract

Hepatitis B and C Virus (HBV, HCV) infections are major contributors to the burden of chronic liver diseases globally. In 2004, the Nigerian Government introduced the HBV vaccine into the National Program on Immunization (NPI) to curb the HBV infection. This study aimed to determine the prevalence and associated factors of HBV and HCV infections among adolescents in secondary schools in Calabar, Cross River State, South-South Nigeria, in the pre- and post-vaccination era. This was a school-based, cross-sectional study. Six hundred and sixty secondary school adolescents aged 10-20 years were recruited using a multistage sampling technique. Hepatitis B Surface Antigen (HBsAg) and HCV antibody screening were done respectively on the study participants using the rapid chromatographic immunoassay method. The relationship between sociodemographic variables and Hepatitis B infection was described. A p-value of less than 0.05 was considered significant. The mean age of the participants was 14.85±2.11 years. Six participants were positive for HBsAg, giving an overall prevalence of 0.9%. The positive adolescents were from public schools, and the age group mostly positive was 16 years and above (2.1%). None of the screened adolescents was positive for HCV antibody. Though the prevalence of HBV infection was low, most of those who tested positive were delivered before the introduction of the HBV vaccine into the NPI schedule. Modalities to vaccinate young people delivered before the introduction of the Hepatitis B vaccine into the NPI schedule should be developed.

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## Introduction

Hepatitis B and C Virus (HBV, HCV) infections are major global public health problems, with an estimated 296 million and 58 million people living with chronic liver infections worldwide as of 2019, respectively.[1,2] The highest prevalence of HBV infection is in East Asia and sub-Saharan Africa.[1] The clinical spectrum of HBV and HCV infection is broad, ranging from asymptomatic infection to cirrhosis and hepatocellular carcinoma.[1,2] Annually, the World Health Organization (WHO) marks World Hepatitis Day to increase awareness about these viruses, with the aim of eliminating viral hepatitis by 2030.[3] In Nigeria, systematic review studies in children showed a prevalence of HBV viral infection ranging between 4.1% and 44.7%, varying from one locale to another, with the pooled result being 11.5%.[4] HBV can be prevented by vaccination, and the Nigerian government introduced the HBV vaccine into the National Program on Immunization (NPI) schedule in 2004.[5] This made it mandatory for all newborns to be vaccinated. However, this was not extended to children outside the newborn period.[5] The prevalence of HBV and HCV depends on the geographic region and risk factors they are exposed to.[4,6] This study, therefore, aimed to determine the prevalence and associated factors of HBV and HCV infections among adolescents in secondary schools in Calabar delivered before the HBV vaccination era in 2004 and the post-vaccination era. The baseline data from this research will be useful in planning preventive measures.

## Materials and Methods

### Study location

This study was conducted in Calabar, the capital of Cross River State in South-South Nigeria. Calabar has two Local Government Areas (LGA); Calabar Municipality and Calabar South. The population of Calabar Municipality is 183,681, while Calabar South is 191,515.[7] There are 32 public and 15 private secondary schools in Calabar. The Efiks and Quas form the major ethnic groups in these LGAs. The occupations of the residents include civil service, trading, public service, farming, artisanship, and manual labor.

### Study design

This was a cross-sectional study carried out from July to September 2019. The minimum sample size was calculated using the Cochran formula.[8] Adoga *et al.*[9] found the prevalence of HBV to be 6.5% among adolescents, which was used to calculate the sample size. The minimum sample size thus determined was 584. Allowing for a 10% non-participation rate, the approximate minimum sample size was adjusted to 660.

### Study population

Study participants were adolescents aged 10 to 20 in selected private and public secondary schools in Calabar who were born before 2004, during the pre-vaccinated and post-vaccinated period before the introduction of HBV into the NPI schedule.

### Sampling technique

A multistage sampling method was used; this involved five stages. The first, third, and fourth stages applied stratified random sampling, while the second and fifth stages used simple random sampling. The first stage was by stratified random sampling based on the location of schools in Calabar Municipality and Calabar South LGA. In the second stage, a total of 20 schools were selected by simple random sampling through balloting; of these 20 schools, 14 were in Calabar municipality and six in Calabar South, giving a ratio of approximately 2:1. Hence, for every two schools selected in Calabar Municipality, one was selected in Calabar South. Therefore, four Calabar Municipality schools and two Calabar South schools were selected for the study. Each of the six selected schools was stratified in the third stage based on classes. For each school with six classes (JS 1, 2, 3, SS 1, 2, and 3), one-sixth of the sample size for the school was equally allocated to each class; for those with classes less than these, the sample size was calculated equally among them. In the fourth stage, each class was stratified based on streams in the class. The number of children recruited from the class was equally allocated among the streams. The fifth stage involved the final recruitment of the study participants from a particular stream.

### Ethics approval

Ethical clearance for the conduct of this study was obtained from the Cross River State Health Research Ethics Committee and the Cross River State Ministry of Education. Written informed consents were obtained from the parents or guardians of study participants. In addition, assents were also obtained from the study participants before the commencement of the study.

### Data collection

Data collection instruments were pre-tested on the students in the public schools in Calabar but were not included in the final study. A semi-structured self-administered questionnaire was used for data collection. Participants were stratified into social classes based on the Ogunsanya social class classification.[10]

### Laboratory investigations

Two milliliters (2 mL) of venous blood was obtained from each participant under an aseptic procedure into a properly labeled serial number-tagged clean plain bottle and allowed to clot. Serum was separated and used for the analyses. Hepatitis B Surface Antigen (HBsAg) and HCV Antibodies (HCV-Ab) were detected using different commercially available rapid chromatographic immunoassays for the qualitative detection of HBsAg and HCV-Ab both manufactured by ABON™ (Abon Biopharm Co., Hangzhou, China). The qualitative assays were performed using one-step test strips for the detection of HBsAg and HCV-Ab in serum samples. Tests were performed within one hour of specimen collection and separation. Only clear, non-haemolyzed serum samples were used. The test strips and quality control sera were allowed to equilibrate to room temperature (15-30°C) prior to testing. The test strip was immersed vertically in the serum for at least

**Table 1.** Socio-demographic characteristics (N=660).

| Variable | Frequency (n) | Percentage (%) |
|---|---|---|
| Age | | |
| 10 | 185 | 28.0 |
| 11-15 | 253 | 38.3 |
| 16-20 | 222 | 33.7 |
| Sex | | |
| Male | 172 | 26.1 |
| Female | 488 | 73.9 |
| Ethnicity | | |
| Efik | 248 | 37.6 |
| Ejagham | 90 | 13.6 |
| Ibibio | 113 | 17.3 |
| Annang | 47 | 7.1 |
| Igbo | 41 | 6.2 |
| Yoruba | 15 | 2.3 |
| Other | 106 | 16.1 |
| Number of persons in the household | | |
| 1-4 | 93 | 14.1 |
| >4 | 567 | 85.9 |
| Father's occupation | | |
| Civil servant | 343 | 52.0 |
| Farmer | 43 | 6.5 |
| Trader | 103 | 15.6 |
| Artisan | 171 | 26.0 |
| Mother's occupation | | |
| Civil servant | 251 | 38.0 |
| Farmer | 90 | 13.7 |
| Trader | 213 | 32.3 |
| Artisan | 106 | 16.0 |
| Father's education | | |
| Tertiary | 428 | 64.8 |
| Secondary | 176 | 26.7 |
| Primary | 23 | 3.5 |
| Incomplete primary | 33 | 5.1 |
| Mother's education | | |
| Tertiary | 370 | 56.1 |
| Secondary | 212 | 32.1 |
| Primary | 41 | 6.2 |
| Incomplete primary | 21 | 5.6 |
| Social class | | |
| High | 290 | 43.9 |
| Middle | 211 | 32.0 |
| Low | 159 | 24.1 |

10-15 seconds with arrows pointing toward the serum sample (as indicated on the test strip). The test strip was then on a non-absorbent flat surface, and the timer started. The immunochromatographic took place within a few minutes, and the result was exactly 15 minutes later. The HBsAg assay has manufacturer-reported specificity, sensitivity, and accuracy of >99.0%, 97.0%, and 98.5%, respectively, while the HCV-Ab antibody assay has a reported specificity, sensitivity, and accuracy of >99.0%, 98.6%, and 99.3% as well respectively.

### Data analysis

Data was analyzed using Statistical Package for Social Sciences (SPSS) for Windows, Software Version 22.1. (SPSS Inc., Chicago, USA). Categorical variables were compared using the Chi-square test. Binary logistic regression was performed to evaluate socio-demographic variables independently associated with HBV infection. A p-value of less than 0.05 was considered statistically significant.

## Results

### Socio-demographic characteristics of study participants

Tables 1-3 show the socio-demographic characteristics and medical history of study participants. A total of 660 adolescents participated in the study, of which 488 (73.9%) were females. The mean age of the study population was 14.85±2.11 years. The majority of the participants were of the Efik tribe, 248 (37.6%). The most common occupation of fathers was civil service, with 343 (52.0%) and 428 (64.8%) of the fathers having tertiary education. Most mothers were civil servants 251 (38.0%), and 370 (56.1%) of the mothers had a tertiary level of education.

### Sero-prevalence of Hepatitis B and Hepatitis C among study participants

Six participants were positive for HBsAg with an overall sero-prevalence of 0.9%. None of the study participants was positive for HCV antibody (0%).

### Relationship between socio-demographic factors and Hepatitis B infection

A Chi-square test of independence was conducted to explore the relationship between socio-demographic factors (age group, sex, schools attended, and social class of students) and HBV infection among secondary school students in Calabar. The results showed that sex was significantly associated with HBV infection (p=0.048; $X^2$=4.83), with the prevalence of HBV infection relatively higher among male study participants compared to female students (2.8% *vs* 0.5%). Age group, schools attended by students, and students' social class were not significantly associated with HBV infection.

## Discussion

The overall prevalence of HBV infection among the adolescents in this study was 0.9%. The prevalence of 0.9% is lower than that of 1.2% observed in the same geographic region involving adolescents in school born in the pre-vaccination era of 2004.[11] HBV positivity increased with increasing age, though there was no significant association. Adolescents 16 years or older delivered during the pre-vaccination era had a positivity rate of 2.1% compared to those 15 years of age or lower with 0.8%. The increased prevalence in children 16 years and older may be because there

**Table 2.** Medical history of study participants.

| Variable | Frequency (n) | Percentage (%) |
|---|---|---|
| Previous blood transfusions | 35 | 5.3 |
| Past history of surgery | 26 | 3.9 |
| HBV vaccination status | 44 | 6.7 |
| Known sickle cell patient | 24 | 3.6 |
| Sharing of sharp objects (blades, clippers, manicure/pedicure) | 218 | 33.0 |
| Alcohol intake | 163 | 24.7 |
| Herbal medications | 102 | 15.4 |
| Injection from quacks | 82 | 12.4 |
| Native scarification marks | 59 | 8.9 |
| Native tonsillectomy/surgical procedure | 52 | 7.9 |
| Female genital mutilation | 29 | 4.4 |
| Intravenous drug abuse | 23 | 3.5 |
| Family history of chronic liver disease | 17 | 2.6 |

HBV, Hepatitis B Virus.

**Table 3.** Relationship between sociodemographic factors and Hepatitis B infection among study participants.

| Variable | Hepatitis B infection status | | $X^2$ | p |
|---|---|---|---|---|
| | Positive (%) | Negative (%) | | |
| Age group | | | | |
| ≤10 | 0 (0.0) | 185 (100.0) | 1.79 | 0.409 |
| 11-15 | 2 (0.8) | 251 (99.2) | | |
| 16-20 | 4 (2.1) | 118 (97.9) | | |
| Sex | | | | |
| Male | 4 (2.8) | 168 (97.2) | 4.83 | 0.048** |
| Female | 2 (0.5) | 486 (99.5) | | |
| Schools | | | | |
| Public | 6 (3.6) | 408 (96.4) | 3.32 | 0.505 |
| Private | 0 (0.0) | 252 (100.0) | | |
| Social class | | | | |
| High | 1 (0.4) | 289 (99.6) | 2.43 | 0.297 |
| Middle | 3 (1.9) | 208 (98.5) | | |
| Low | 2 (1.8) | 157 (98.7) | | |

**Fisher's Exact Test

was no access to the HBV vaccine. At this age, most adolescents are very active and explore their world while indulging in certain risky behaviors like sexual activities and drug abuse.[12] The low prevalence seen among the study population aged 15 years or less may be due to the increased awareness and uptake of the HBV vaccination introduced into the NPI schedule in Nigeria in 2004.[5] Odusanya *et al*.[13] showed a low prevalence of 1.3% among vaccinated children in a rural community in Western Nigeria when compared to non-vaccinated children with a prevalence of 4.6%. Ezeilo *et al*.[14] in Enugu, South-East Nigeria, also showed a low prevalence of 1.1% among 159 vaccinated children.

Positivity for HBsAg was significantly associated with the sex of the adolescents. Male adolescents were more likely to be positive than female adolescents. This finding corroborates studies from other researchers, where there was a significant association between sex and HBsAg positivity.[11,15,16] Male adolescents tend to be more adventurous, which may be responsible for the higher prevalence amongst males compared to female adolescents.

Positive adolescents were all from the government public schools and none from the privately owned schools. Though this was not significantly associated with the positivity to HBsAg, Aderibigbe *et al*.[17] also reported that students attending public schools had a higher risk of exposure than those attending private schools. A study in Abidjan[18] found a significant association between school type and risk for HBV infection suggesting that students from high socioeconomic background have a reduced risk exposure level for HBV infection when compared to their counterparts from lower socio-economic background who often attend public schools. Therefore, there is a need for more educational awareness in these schools on the mode of spread of HBV and ways of preventing the infection.

In this study, the major risk exposures for HBV infection were found to be the sharing of sharp objects, needle prick injuries, injection from quack doctors/nurses, history of blood transfusion, and unprotected sex. This aligns with factors reported by other authors from other parts of the country. Aderibigbe *et al*.[17] and Ndako *et al*.[19] reported risk factors for HBV infection among their respondents as contact with blood and other body fluids, sharing sharp objects, body piercing activities, and sexual exposure, while Ugwuja *et al*.[20] reported factors such as unsafe injection, tribal marks/circumcision/scarification, and blood/blood products transfusions.

Socio-economic class, exposure to risk factors such as traditional practice of scarification incisions, tattoos, use of intravenous drug abuse, and unsafe sexual exposure were not significantly associated with HBV infection in this study population. This corroborates with Al- Faleh *et al*.[21] in Saudi Arabia, who demonstrated that socio-economic status was not significantly associated with HBV positivity in children in their population. Uleanya and Obidike[12] in Enugu also found no significant relationship between socio-economic status and HBV positivity in their study. This may be because of equal exposure to the risk factors of HBV among children of different social classes. However, in this study, it was observed that adolescents from the higher social class had no positive for HBV compared to those from the middle and lower social classes. This is similar to findings in another study in Enugu.[12] This may be because people in the higher socioeconomic class are less likely to indulge in activities that may promote infection with HBV, such as sharing sharp objects, injections from quack doctors/nurses, native tonsillectomy, and scarification marks. Chukwuka *et al*.[22] in Ebonyi State, Nigeria, showed no significant association between the cultural practice of scarification marks and ear piercing and HBV infection. This is in contrast to the study by Eke *et al*.,[23] who showed that scarification marks and tattooing were significantly associated with positivity to HBV infection in Enugu, Nigeria. Regarding HCV infection, none of the adolescents was reactive to HCV antibody (0.0%). This shows a similar prevalence among children aged 10 to 16 years from Southern Brazil, where there was no report of positivity to HCV antibody.[24,25] A previous study carried out earlier to this present study in Calabar, Nigeria, among 744 secondary school adolescents showed a prevalence of 0.3%.[26] These data appear to corroborate the low or absence of HCV infection among adolescents within these age groups in this geographic region.

The limitation of this study is that being a cross-sectional study limits the ability to draw conclusions about the outcome of the infections. However, being a school-based study, this could reflect the true nature of the infections in the community amongst this age groups.

## Conclusions

The seroprevalence of HBV infection was 0.9%, and HCV was 0% among the study participants. Though the prevalence of HBV infection was low, most of the positive adolescents were delivered before the introduction of the HBV vaccine into the NPI schedule in Nigeria. Modalities to vaccinate young people born before the introduction of the HBV vaccine into the NPI schedule should be developed.

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