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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 a bid to curb the HBV infection, the Nigerian Government introduced the HBV vaccine into the National Program on Immunization (NPI) in 2004.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 multi-staged sampling technique. Hepatitis B Surface Antigen (HBsAg) and HCV antibody screening were done respectively on the study participants using rapid chromatographic immunoassay method. The relationship between sociodemographic variables and Hepatitis B infection were 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 positive were delivered before the introduction of the HBV vaccine into the NPI schedule. Modalities to vaccinate young people delivered before the introduction of Hepatitis B vaccine into the NPI schedule should be developed.

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 the 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% to 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 NPI schedule in 2004.[5] This made it mandatory for all new-borns to be vaccinated. However, this was not extended to children outside the new-born 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 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] in their study found the prevalence of HBV to be 6.5% among adolescence, which was used to calculate the sample size. The minimum sample size thus determined was 584. Allowing for a 10% non-participation rate, approximate minimum sample size was adjusted to 660.

Study population

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

Sampling technique

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 location of

schools into 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 schools in Calabar Municipality and two schools in Calabar South were selected for the study. In the third stage, each of the six selected schools was stratified 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 to be 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. Clearance was also obtained from Cross River State Ministry of Education. Written informed consents were obtained from 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 in the students in the public schools in Calabar, but not included in the final study. A semi-structured self-administered questionnaire was used for

data collection. Participants were stratified into social class based on the Ogunsanya classification of social class.[10]

Laboratory investigations

Two millitres (2 mL) of venous blood was obtained from each participant under aseptic procedure into a properly labelled 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, P.R. China). The qualitative assays were performed using one-step test strips for 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 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 to take place within a few minutes and the result was exactly 15 minutes after. 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 analysed using Statistical Package for Social Sciences (SPSS) for Windows, Software Version 22.1. (SPSS Inc., Chicago, IL, USA). Categorical variables were compared using the Chi-square test. Binary logistic regression was performed to evaluate socio-demographic variables that were independently associated with HBV infection. A p-value of less than 0.05 was considered statistically significant.

Results

Socio-demographic characteristics of study participants

Table 1 shows the socio-demographic characteristics 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. Majority of the participants were of the Efik tribe 248 (37.6%). The commonest occupation of fathers was civil service 343 (52.0%) and 428 (64.8%) of the fathers had tertiary education. Most mothers were civil servants 251 (38.0%) and 370 (56.1%) of the mothers had tertiary level of education.

Sero-prevalence of HBV and HCV among study participants

Six participants were positive for HBsAg with an overall sero-prevalence of 0.9%. None of the study participants was positive to 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 social class of students 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 the prevalence 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 of age 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 was no access to the HBV vaccine and at this age most adolescents are very active and explore their world while indulging in certain risky behaviour 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 the female. This finding corroborates studies from other researchers where there was significant association between sex and HBsAg positivity.[11, 15,16] Male adolescents tend to be more adventurous, and this may be responsible for the higher prevalence amongst males compared to female adolescents.

Adolescents who were positive 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 the 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 sharing of sharp objects, needle prick injuries, injection from quark doctors/nurses, history of blood transfusion and unprotected sex. This is in consonance 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 of 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] working, 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 none positive for HBV compared to the middle and lower social class. 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 of sharp object, injection from quark doctors/ nurses, native tonsillectomy and scarification marks. Chukwuka *et al*.,[22] working in Ebonyi State, Nigeria, showed no significant association between the cultural practice of scarification marks and ear piercing to HBV infection. This is in contrast to the study by Eke *et al*.[23] who showed that presence of 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 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 group in this geographic region.

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

Conclusions

The sero-prevalence of HBV infection was 0.9% and HCV was zero percent 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 HBV vaccine into the NPI schedule be developed.

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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

Table 2. Medical history of study participants.

Past medical history	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 sharps (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

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

Variable	Hepatitis B infection status		X^2	p-value
	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