Research

Prevalence and Socio-Demographics of Hepatitis B Surface Antiginaemia among Secondary school Children in an urban community Southeast Nigeria: A Cross sectional study

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Abstract

Background: Hepatitis B virus (HBV) is responsible for a prevalent infectious disease in the world which is of public health importance due to its risk of chronicity with attendant high morbidity and mortality. Although it is a vaccine preventable disease, Nigeria is still highly endemic for HBV. The aim of the study was to determine the seroprevalence of Hepatitis B surface antigenemia and sociodemographic characteristics among secondary school students in Onitsha.

Methods: This is a cross sectional descriptive study of Hepatitis B surface antigenemia in secondary schools' students in Onitsha, South-East Nigeria. Participants were recruited using a multi-staged sampling technique and their HBsAg status was determined using Monalisa™ HBsAg Ultra ELISA kit.

Results: Out of the 751 students assessed, 57 were sero-positive to HBsAg giving a prevalence of 7.6%. The prevalence was more in males than females and students in the higher socioeconomic class were least affected. The highest prevalence was observed among students within the age group of 14-16years. Only 4.3% of the students had received HBV vaccine.

Conclusion: The endemicity of Hepatitis B in the study population calls for urgent action. This is because the infected students can be reservoirs for horizontal transmission. Furthermore, asymptomatic HBV infection can progress to chronic complications like liver cirrhosis and hepatocellular carcinoma. Therefore, the introduction of vaccination of adolescents against HBV in the school health program will be an effective way of controlling the high prevalence of HBV infection in this population.

Keywords: Prevalence, Endemicity, Hepatitis B Virus (HBV), sociodemographic

Introduction

Hepatitis B virus (HBV) infection is one of the common infectious diseases in the world and a major public health problem worldwide. It can be transmitted sexually, also by blood and blood products transfusion. The presence of Hepatitis B surface antigen (HBsAg) in blood serves as the most useful marker of HBV infection[1]. Despite the availability of methods by which this virus can be detected and surveillance activities that have been put in place to reduce its transmission, the virus continues to constitute a threat to health.

The global disease burden of Hepatitis B virus is substantial due to its high morbidity and mortality. Its epidemiology is geographically disparate such that the number of people estimated to be chronically infected with HBsAg in various WHO regions is as follows:116 million in Western Pacific Region, 81 million in the African Region, 60 million in the Eastern Mediterranean Region, 18 million in the South-East Asia Region, 14 million in the European Region and 5 million in the Region of the Americas[2]. This data indicates that a reasonable number of the world's populations living with the hepatitis B virus are in sub-Saharan Africa. Countries are classified as having low endemic rates (< 2% of the population has the antibody to HBsAg), intermediate endemic rates (2-8% positive for HBsAg), or high endemic rates (>8% positive for HBsAg)[3].

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The major challenge of hepatitis B viral infection is its chronicity, as defined by persistence of hepatitis B surface antigen for more than 6 months[4]. WHO estimates that there are about 1.5 million new Hepatitis B virus infections each year and that in 2019 there were about 296 million people worldwide who were chronic carriers of HBV, 10.5% of all people estimated to be living with hepatitis B (about 30.4 million people) were aware of their infection, while 22% (about 6.6 million) of the people diagnosed with HBV were on treatment with an estimated 820,000 deaths mostly from cirrhosis and hepatocellular carcinoma[2]. Early hepatitis B diagnosis can benefit those with chronic HBV-associated liver disease as treatment with Interferon-α-2b (IFN-α2b) and antiviral drugs - nucleos(t)ide analogues like Lamivudine, Tenofovir and Entecavir can slow the progression of the liver disease to cirrhosis and thus avoid or delay the need for liver transplantation[2]. These drugs are however expensive and not readily available.

In May 2016, WHO adopted a global hepatitis strategy[5] with the goal of eliminating viral hepatitis as a public health threat by 2030. However, the burden of viral hepatitis B in Africa is still high with a prevalence of 6.2% and new infection rates are said to be highest among children[6]. Nigeria falls within the hyper endemic region of Sub-Saharan Africa. Studies in Nigerian children have reported prevalence rates of HBsAg ranging from 1.2% to 44.7% with risk factors for transmission varying from one region to another[5,6,7]. A national survey of the sero-prevalence of HBV in the general population in 2016 was reported as 12.2%[11]. On the other hand, systematic reviews and meta-analysis of data collated across the country, demonstrated a downward trend with an overall pooled HBV prevalence of 13.8% and 9.5% in 2013 and 2019 respectively[6,12].

Hepatitis B is a vaccine preventable disease, thus in 1992 the World Health Organization (WHO) recommended the inclusion of hepatitis B vaccination in all national immunization programs independent of hepatitis B carrier rate[13]. Nigeria approved the inclusion of hepatitis B vaccine in its National Program on Immunization (NPI) in 1995, however, its widespread implementation was delayed until 2004 when the monovalent HBV vaccine was added to the routine infant immunization and subsequently changed to the polyvalent vaccine which is given at 6, 10, and 14 weeks of age[14]. After its introduction about 2 decades ago, the Hepatitis B vaccine coverage increased steadily from 18% in 2005 to 41% in 2008 to 66% in 2010 to a peak of 70% in 2014 followed by an unfortunate decline to 33% in 2017 and then a rise to 57% in 2020[15].

Methodology

Study Location: This study was carried out in secondary schools in Onitsha, one of the important cities in the southeastern part of Nigeria. It is a major commercial centre in Nigeria and sub-Saharan Africa. It consists of Onitsha North and Onitsha South local government areas and is located at the intersection of 6°10' North and 6°47' East with a population of about 1.5 million people. The town lies on the east bank of the River Niger, just south of its confluence with the Anambra River. The inhabitants are predominantly Igbo by tribe and mainly traders. English and Igbo are commonly spoken languages[16]. Most of the schools that participated in the study had school Health center that provides basic health care services to school children by certified health workers. They have the capacity to refer students that will need specialist care.

Study Population: According to the data obtained from the Post Primary Schools Commission Onitsha, and the zonal education offices of Onitsha North and South local government areas, there are 66 approved secondary schools in the area with an estimated population of about 22,000 students - 13,604 students are in public schools and 8,500 in private schools.

Study Design: This was a descriptive cross-sectional study conducted over the period of June 2014 – March 2015.
Inclusion criteria: Secondary school children in Onitsha that gave their assent and whose parents gave their consent for the study.
Exclusion criteria: Students with recent (less than 1 month) Hepatitis B vaccination with evidence of immunization card documentation to avoid false positive HBsAg results.

Ethical Approval/Considerations: Ethical approval for the study was obtained from the Ethics and Research committee of Nnamdi Azikiwe University Teaching Hospital, Nnewi. Thereafter, permission was secured from the Post Primary Schools Service Commission, Onitsha as well as from the Principals and Class teachers at the selected schools/classes. An informed consent was obtained from parents/guardians of students under the age of 18years and assent from all subjects. Participation was entirely voluntary, and subjects were

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assured they could withdraw if they wished to. Each subject and/or parent was informed of the result of the serology at the end of the study and referred to the appropriate health facility where indicated.

Sample Size Determination: The sample size was calculated using the Cochran's formula:[17]
$n = z^2pq/E^2$
n= minimum desired sample size p= proportion of target population estimated to have the characteristic from previous studies. The prevalence of 7.6% (0.076) reported by Chukwuka et al[7] was used
q= 1.0 - p = 1 – 0.076 = 0.924
E= margin of standard error (degree of accuracy desired) set as 2% [0.02]
z= standard deviation usually set at 1.962 which corresponds to the 95th confidence interval
N = 1.96 x 1.96 x 0.076 x 0.924/0.02 x 0.02
= 0.269772518 / 0.0004 = 674.4
To make allowance for dropouts due to inadequate blood sample or inappropriately filled questionnaires, a total number of 780 students were recruited and proportionately distributed. At the end of the study, the number of subjects that remained was 751

Sampling Technique: A multi-staged sampling technique was used to recruit subjects for the study who were all students at Secondary schools in Onitsha.
Stage 1: This involved sorting the schools into groups. Firstly, they were divided into two major groups- Public and Private which seen to be distributed in with a ratio of 1:2 in the study area. There were more private secondary schools than the public secondary schools. Though the private schools were more than the public schools, the public schools had more student population than the private schools in the ratio of 1:1.6.
The schools were further sorted into sub-groups based on the types/composition of the schools as follows: male only, female only and co-educational (mixed) schools. By way of simple proportion of their population, this translated into a ratio of 1:1:2 respectively.
Stage 2: Based on the ratio of the population of the schools (1:1:2), a total number of 8 schools [i.e., 2x total ratio (4)] were selected for the study in a ratio of 1:1:2 representing male only, female only and co-educational respectively from both private and public schools. This was achieved through balloting. Furthermore, using the ratio of 1:1.6 for population of students in the private: public schools, a total number of 120 students were selected from each public school and 75 from each private school to obtain a grand total of 780 subjects.
Stage 3: In each selected school, with the consent of the principal, the total number of classes was obtained, and the classes used were determined by simple random sampling (balloting).
Stage 4: In the selected classes, systematic sampling was applied using the class registers as a sampling frame. A student was chosen at random to be the starting point. Thereafter, other choices were made at regular intervals until the total number desired from the school was reached. The interval for each school was calculated as follows:
K= N ÷ n
Where K is sampling interval, N is sample population, n is sample size
The sampling interval varied from school to school depending on their population. For example, the population of the 'female only' public school used was 1054. The sample interval (k) was calculated as follows:
K=1054 ÷ 120 = 8.78
Thus, apart from the first student who was randomly selected, every 9th student was recruited.
The selected students were given forms to obtain the consent of their parents. The first section of the questionnaire was given to the students to get input from their parents where necessary.

Data Collection: Data was obtained from selected students and their parents with the aid of self-administered questionnaires to obtain their sociodemographic variables. The mode of communication was in simple English language to obtain correct information. Confidentiality of the information provided was assured. The questionnaires were coded with numbers corresponding to the blood sample of the same individual. The socioeconomic class was determined from the parents' occupation and educational status using the Oyedeji classification[18].

Specimen Collection, Storage and Analysis: Three milliliters (3mls) of venous blood were collected from the subjects that met the inclusion criteria using Ethylene Di-amine Tetra-acetic Acid (EDTA) bottles under aseptic conditions in the school clinic. The blood samples were taken to the haematology laboratory for separation of plasma by centrifugation at 6,000 revolutions per minute (rpm) for 5 minutes and then stored at -20^{0}C in micro vials. After the sample collection, the assay for HBV was carried out in five batches using Monalisa™ HBsAg Ultra ELISA kit from

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BIO-RAD (Redmond, USA) with Lot number 3K0071. The kit had a sensitivity of 100% and specificity of 99.96%. Appropriate measures were taken to ensure the maintenance of the cold chain (+2-8^{0}C) until the time of use when the reagents were allowed to reach room temperature. The contents of the Monalisa™ HBsAg Ultra ELISA kit and their respective labels are: Micro plate (R1), Concentrated Washing Solution 20X (R2), Negative control (R3), Positive control (R4), Conjugate Diluents (R6), Conjugate (R7), Substrate Buffer (R8), Chromogen Pink Colored (R9) and Stopping Solution (R10).

The results of the tests were returned to the students using the codes assigned to each subject at the time of sample collection. Those who tested positive for HBsAg were referred to the Nnamdi Azikiwe University Teaching Hospital, Nnewi for further management. Those who tested negative were counseled to avoid risky behaviors that could predispose them to the infection.

Data Analysis: Statistical analysis of the derived data was computed using the statistical package for social sciences (SPSS) version 20. Simple descriptive statistics such as means, standard deviations and proportions were used to describe the data. Chi square test was used to explore the association between HBsAg status and the assessed categorical variables. The level of statistical significance was set at $p < 0.05$.

Results

A total number of 751 secondary school students were finally enrolled into the study. Out of these, 57 tested positive to HBsAg with a prevalence rate of 7.6%. Three hundred and five of the respondents were males and 446 females with a male: female ratio of 1:1.5. The age range was 11years to 24years while the commonest age group was the group 14-16 years (65.1%). The mean age was 15.73 (SD 1.54). The least common age group was the group ≥20 years (1.5%) which is not surprising considering that at that age most students are no longer in secondary school. Table 1 showed the socio-demography of the respondents.

Table 2 depicts the prevalence of HBsAg according to age, sex, social class and family size. HBsAg was detected in 57 (7.6%) subjects comprising 30 males (52.6%) and 27 females (47.4%). This difference was however not statistically significant ($\chi^2 = 3.694$, P = 0.055). Among the age groups, the group 14-16 years had the highest proportion of HBsAg positive respondents- 33 (57.9%) and there was a statistically significant association between age and HBsAg positivity ($\chi^2 = 23.505$, P = 0.000). One hundred and forty-eight (21.0%) respondents belonged to the upper socioeconomic class while 327 (43.5%) and 240 (32.0%) belonged to middle class and lower class respectively. Twenty-six (3.4%) of respondents did not provide sufficient data to determine their social class. More HBV infections were found in the middle class. The commonest number of persons per household was 3-5 persons per household 497 (66.2%) with an average of 5.20 ± 1.63 persons per household and 2.77 ± 1.11 persons per room. However, there was no significant association between the respondents' social class (χ^2= 3.679, P = 0.596), family size ($\chi^2 = 2.559$, P = 0.278), religion ($\chi^2 = 1.179$, P = 0.555) and their HBsAg status.

Table 1: Sociodemographic Characteristics of Respondents

Variables	Frequency	Percent
Age (yrs)		
11-13	50	6.7
14-16	489	65.1
17-19	201	26.8
≥20	11	1.5
Sex		
Male	305	40.6
Female	446	59.4
Religion		
Christianity	733	97.6
Islam	7	0.9
Traditional religion	7	0.9
Tribe		
Igbo	707	94.1
Hausa	7	0.9
Yoruba	17	2.3
Ijaw/Urhobo/Efik	13	1.7
Igala/Igbira	5	0.6
Esan	2	

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Table 2: Association between HBsAg Status and Sociodemographic Variables

Variable	HBsAg Status Positive (%)	Negative (%)	Total	χ^2	P-value
Gender					
Male	30(52.6)	275(39.6)	305(40.6)	3.694	0.055
Female	27(47.4)	419(60.4)	446(59.4)		
Age (years)					
11-13	5(8.8)	45(6.5)	50(6.7)	23.505	<0.001*
14-16	33(57.9)	456(65.7)	489(65.1)		
17-19	14(24.6)	187(26.9)	201(26.8)		
≥20	5(8.8)	6(0.9)	11(1.5)		
Religion					
Christianity	57(100)	676(98.0)	733(98.1)	1.179	0.555
Islam	0(0.0)	7(1.0)	7(0.9)		
Traditional religion	0(0.0)	7(1.0)	7(0.9)		
Family size					
<3	2(3.5)	24(3.5)	26(3.5)	2.559	0.278
3.5	43(75.4)	454(65.4)	497(66.2)		
>5	12(21.1)	216(31.1)	228(30.4)		
Social class					
Upper class	9(15.8)	149(21.6)	158(21.1)	3.679	0.596
Middle class	24(42.1)	303(43.9)	327(43.8)		
Lower class	22(38.6)	218(31.6)	240(32.1)		
Insufficient data	2(3.5)	20(2.9)	22(2.9)		

Table 3: Association between Positivity and HBV Vaccination

Variable	HBsAg Status +ve(%)	-ve(%)	Total	χ^2	P-value
HBV Vaccination					
Yes	4(7.0)	28(4.0)	32(4.3)	1.945	0.378
No	44(77.2)	581(83.8)	625(83.3)		
I don't know	9(15.8)	84(12.1)	93(12.4)		
Time of vaccination					
>One month<one year	1(25.0)	9(32.1)	10(31.3)	0.08	0.773
Greater than one year	3(75.0)	19(67.9)	22(68.7)		

4.3% of the subjects received Hepatitis B vaccination and 93% of those who were seropositive to HBsAg had not received the protective vaccination.

Discussion

The prevalence rate of 7.6% in the study population confirms the endemicity of HBV infection in Nigeria and places the study area in the category of intermediate endemicity. This high rate may be explained by the fact that most of the students were born before the introduction of the HBV vaccine in the National Immunization schedule or did not have access to this vaccination thereafter. The implication of asymptomatic HBV infection in the study age group is that they may become chronic carriers of the virus and serve as reservoirs for subsequent transmission to others. The prevalence rate obtained in this study incidentally corresponds to that reported by Chukwuka *et al*[10] among primary school pupils in Nnewi, South Eastern Nigeria possibly due to its proximity to the index study area. This is however unexpected as his study population was primary school pupils compared to secondary school students in this study. One would expect the seroprevalence rate to increase among the adolescent

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age range because of horizontal transmission as observed by Adetunji et al[19].

In contrast, the seroprevalence rate obtained in this study is lower than the pooled national prevalence of 12.1% - 13.6% in the general population and 11.5% among children reported by different meta-analytic studies in Nigeria[6,11,12]. Intra country differences also exist with high prevalence values among students in the Northern Nigeria (9% in Jos[20], 11.4% in Maiduguri[21], 12.5% in Zaria[22], 18.4% in Kaduna[23], and 44.7% in Borno[7]). On the other hand, relatively low or intermediate prevalence values were noted in Southern Nigeria (1.2% in Calabar[7], 2.9% in Ibadan[19], 3.1% in Enugu[24], 4.1%[8] and 6.5% in Ebonyi[25]) with a few exceptions like 13.9% among children admitted to the children's emergency room (CHER) in Benin Teaching Hospital[26]. This wide variation could be due to differences in subject selection, sensitivity of methods applied as well as diverse socioeconomic and demographic risk factors that favor horizontal transmission of HBV. Furthermore, low immunization coverage in some parts of Northern Nigeria accounts for the high prevalence in that region. In comparison to other Sub-Saharan African countries, the prevalence rate obtained in this study is lower than the pooled prevalence rate of 14.3% among adolescents[27] and high school students[28] in Ghana 11.2% in Cameroon[29], 17% in Sierra Leone[30] and 18.5% in Benin republic[31] but greater than that of 4.4% in Ethiopia[32]. Remarkably, in a study in Mexico[33], out of over 1500 adolescents and young adults screened for markers of HBV, no HBsAg was detected indicating no acute or chronic infection. In like manner, notwithstanding the contribution of immigrants from high HBV endemic regions, very low prevalence rates are reported in developed countries like South Africa (0.4%)[34], United States (0.36%)[35] and EU/EAA member states (0.9%)[36]. These are attributed to the gains of the successful implementation of universal infant hepatitis B vaccination as well as school-based programs for adolescents.

This study demonstrated an increasing prevalence of HBV with age peaking at the age group 14-16 years and declining afterwards as was the case in some other studies.[7, 20,25,37] In addition, the association between age of respondents and their HBsAg status was statistically significant. This corroborates reports that infection in later childhood plays a more important role in HBV transmission in Nigeria and some other African countries[25,30]. This is unlike China and some other Asian Countries where vertical transmission predominates[38]. This phenomenon may be explained by the fact that the risk of HBV infection evolving into chronicity is inversely related to the age of infection so HBV infection acquired horizontally is more likely to resolve spontaneously than that acquired vertically which in most cases leads to chronicity[39,40]. Exceptions may occur however if there are factors in the infected individual that reactivate HBV or delay the clearance of the virus as in people with HBV-HIV co-infection with the resultant risk of chronicity and advanced liver disease[30].

More males than females were seropositive to HBsAg, though the difference was not statistically significant. This suggests that males and females were equally exposed to HBV as corroborated by many studies[8,19,21-25,28,37] however a few authors have had contradictory findings[7,20]. The higher male prevalence is likely because adolescent males are prone to engage in risky practices that promote the horizontal transmission of HBV such as sexual activity and illicit drug use. Conversely, *Anigilaje and Olutola*[41] reported more female subjects than male being dually infected with HIV and HBV and the reason was not explicit.

Only 4.3% of the study population was vaccinated against HBV and there was information about the number of doses received. This reveals that despite our improvement in reducing the incidence of this vaccine preventable disease among children through infant immunisation[14,15], majority of our adolescent and adult population are still exposed to the risk of contracting HBV and its complications. This reflects in the high overall population prevalence of chronic Hepatitis B (CHB) infection in Nigeria[6,11,12]. This can be addressed by adopting catch up vaccination for the older population particularly for high-risk groups. Voluntary testing can also be encouraged, and appropriate treatment commenced where indicated.

Implications of the finding: This study revealed that the study area has intermediate endemicity to HBS Antigenaemia, with low HBV vaccine coverage. Therefore, there is need to create awareness among health workers and policy makers to increase the frequency of catch-up vaccination for adolescents. This can increase HBS Vaccine coverage and subsequently reduce the prevalence of HBSAg infection with its attendant chronic complications.

Limitation: The limitation stems from the fact that being a cross-sectional study, the outcome of the sero-positive participants could not be ascertained, hence the need to conduct a similar study with a prospective study design, where the participants can be followed up to

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determine the outcome/prognosis of HBSAntiginaemia in the study area.

Conclusion

Out of seven hundred and fifty-one secondary school students in Onitsha, South East Nigeria who were screened for Hepatitis B surface antigen, 57 of them (7.6%) were seropositive. The prevalence of 7.6% places the study area in the category of intermediate endemicity. It is worrisome that majority of the subjects were not vaccinated against HBV, which is vaccine preventable, thus exposing them to the possibility of contracting the highly contagious virus and developing its long-term complications. This thus highlights the importance of increased surveillance, scaling up of immunization and school health programmes to achieve the WHO target of a 90% reduction in new cases of HBV infection as well as an associated 65% decline in Hepatitis B-related mortality by the year 2030.

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