

Seroprevalence and Correlates of Hepatitis C Virus Infection in Secondary School Children in Enugu, Nigeria

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Abstract

Background: Although children comprise a small fraction of the burden of hepatitis C virus (HCV) infections, which is a major global health challenge, a significant number of them develop chronic HCV infection and are at risk of its complications. **Aim:** The aim of the current study was to determine the prevalence and associated factors of HCV infection in school children in Enugu urban. **Subjects and Methods:** This was a cross-sectional seroepidemiological study involving children aged 10–18 years selected using multistage systematic sampling in Enugu metropolis, Southeast Nigeria. The anti-HCV was tested using a 3rd generation enzyme-linked immunosorbent assay. Data were analyzed using SPSS Version 16.0 with the level of significance set at $P < 0.05$. **Results:** Four hundred and twenty children were selected and screened comprising 210 (50.0%) males and females. The seroprevalence of anti-HCV was 4 (1.0%). Three (75%) out of the four positive cases for the anti-HCV were females while one was a male giving a male to female ratio of 0.3–1. Traditional scarifications/tattoos were the putative risk factors observed to be significantly associated with anti-HCV seropositivity. **Conclusion:** This study has demonstrated an anti-HCV seroprevalence of 1.0% among children aged 10–18 years in Enugu with traditional scarification as the predominant associated risk factor. Proper health education including school health education and promotion of behavioral change among the public on the practice of safe scarifications/tattoos should be encouraged in our setting.

Keywords: Anti-hepatitis C virus, Children, Prevalence, Risk factors

Introduction

Hepatitis C virus (HCV) is a hepatotropic virus and the cause of the majority of the cases of the formerly called “transfusion – related non-A, non-B hepatitis” with profound effect in the liver.^[1,2] HCV infection is one of the leading public health challenges globally accounting for about 115 million infections; 11 million of whom are children younger than 15 years of age. Similarly, about 80 million cases of the total global infections are viremic out of which 5 million are

children <15 years.^[3] Sub-Saharan Africa with a prevalence of 5.3% and an estimated 32 million infected people with HCV have the largest global burden.

Generally, worldwide geographic prevalence and genotypic variations exist with reasons that are poorly understood.

Earlier studies about two and half decades ago, prior to the wide application of routine screening of blood and plasma-derived

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products for anti-HCV showed prevalence ranging from 0.4% to 14.5% in some series.^[2-6]

HCV is transmitted primarily through percutaneous exposure.^[7] In children, generally, perinatal (vertical) acquisition of HCV is the most prevalence route of transmission, with about 5% of infants born to mothers with HCV viremia having HCV through vertical transmission.^[1] In addition, maternal co-viral infections in pregnancy including HIV, as well as high HCV, and RNA positive viral titers have been shown to increase the risk of transmission.^[1]

In the developing countries, the most common route of transmission is unscreened-/poorly screened blood or plasma – derived products.^[8] Other putative routes of HCV transmission include overuse and unsafe injection practices, intravenous drug use, tattooing, body piercing, and sharing of household nail clippers, razor blades, and toothbrushes.^[9,10]

HCV is the most likely hepatotropic virus leading to chronic hepatitis. Generally, about 6–9% of HCV-infected children have been observed to achieve sustained spontaneous viral clearance during a 6–year follow-up irrespective of the route of HCV infection acquisition.^[1,10] Studies have alluded to the fact that though majority of cases of HCV infections acquired in childhood appear benign, about 25% of them could develop liver cirrhosis and liver failure in childhood and occasionally hepatocellular carcinoma after 20–30 years following acute infections.^[11,12]

HCV infection remains a major public health challenge particularly in developing countries where poverty and ignorance shape people's perception of disease and its determinants in addition to the fact that there are no available effective vaccines owing to the high mutability of the viral genome. Moreover, immunoglobulins currently produced lack viral antibodies as anti-HCV viral screening is conducted on all donor blood and plasma derived products.^[1]

Pediatric HCV infection has generally not received its desired attention,^[13] particularly in developing countries, where the healthcare costs including economic impact for the HCV-infected children as well as their family contacts have been estimated at millions of the United States of American Dollars.^[14]

Few studies have been reported on the seroepidemiology of HCV infections in Nigerian children,^[15] where children under 15 years of age account for about 43–45% of the 177 million Nigerian population.^[16]

Hence, the aim of the current study is to determine the prevalence and risk factors of HCV infection in secondary school children in Enugu, Nigeria.

Subjects and Methods

Study design

This was a cross-sectional seroprevalence study conducted among secondary school children in Enugu metropolis (consisting of 3 local governments area namely: Enugu metropolis (consisting of 3 local government areas namely: Enugu East, Enugu North, and Enugu South local government areas) conducted between June 16, 2014 and July 31st, 2014.

Study sample size determination

The sample size for the study was calculated using the formula below.^[17]

$$N = Z^2pq/d^2$$

where N = The desired sample size when the population is more than 10,000.

Z = The standard variation usually set at 1.96 (which corresponds to 95% confidence interval).

P = The population in the target population estimated to have a particular characteristic (Prevalence of HCV infection in children reported in Ibadan, South West Nigeria, by Okonko *et al.* was 0.9% which is equal to 0.09.^[15]

$$q = 1.0 - p, \text{ i.e., } 1.0 - 0.09 = 0.91$$

d = degree of accuracy desired; set at 0.05.

Therefore, the minimum sample size, $n = (1.96)^2 (0.09)(0.91) / (0.05)^2$

Hence, applying the formula stated above, the minimum sample size was 126 subjects. An attrition rate of 20% was anticipated, so the adjusted minimum sample size will be 151 school children.

Schooling system in study locale

Enugu is the capital city of Enugu State South Eastern Nigeria. Enugu State has an estimated population of about 3 million people,^[18] while Igbo is the major ethnic group.

In Nigeria, children under 15 years of age account for about 43–45% of the 177 million Nigerian population.^[16]

Evidence from the Nigerian Demographic and Health Survey reveals that among children of secondary school age, 35.1% were attending secondary schools. Thus, the secondary school net attendance rate in Nigeria could be shielding the fact that many children are in school at a level that is not appropriate for their age.^[19] The secondary school age in Nigeria is from 12 to 17 years; however, in the southern parts of Nigeria, children much younger than 12 years could well be found already in secondary schools.

Study sampling/population

A multi-staged sampling method was used to select the study population who were secondary school children as follows: A list of all the public secondary schools in the five densely populated areas of Enugu urban was drawn from where schools were selected by simple random sampling. There were about twenty schools spread over the five densely populated areas of the Enugu metropolis (Abakpa Nike, Trans Ekulu/ GRA, Emene, Achara Layout/Uwani, and New Haven/ Independence Layout). One school was selected by simple random sampling method from each of these areas representing three coeducational, one all boys and one all girls schools. Each school has JS classes I to SS class 3, (i.e., Classes I to VI). Each class has an average of about 150 students. Among the selected schools, the students were stratified according to their classes and in each class, they were further stratified based on their sex. The subjects were subsequently selected by the application of systematic sampling method where the first child was selected by simple random sampling, and every other fifth child was also selected. Fifteen children were selected from each class and about ninety children from each school, giving a total of 450 children selected. Furthermore, about thirty selected children refused to continue with the study because of lack of parental consent in 23 of them while seven said they cannot withstand blood-letting even after series of counseling, giving a refusal rate of 6.7%. In all, 420 school children were recruited.

Permission for the study

Ethical approval for the study was sought from the Health Ethics and Research Committee of the University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu. Permission to conduct the study was obtained from the Ministry of Education Enugu State, Nigeria, while consent was obtained from the respective school principals and parents/caregivers and assents from the students as well.

Questionnaire

Information obtained from the semi-structured questionnaire designed for the study included: Biodata of each child and parents (age, sex, parental highest educational attainment, and occupation) and child's medical history including past history of blood transfusion, native uvulectomy, sharing of toothbrush/razor blades/hair clippers or other sharps, traditional scarifications/tattoos, circumcision, surgery, alcohol use, past history of jaundice/liver disease, intravenous drug use, and multiple sexual partners.

Each child's social classification was derived using the method proposed by Oyedeji.^[20] Here, the social class of each child was determined based on the occupational status and highest educational attainment of the parents. The scores were summed and the mean (approximated to the nearest whole number) obtained. The mean score was used to assign the child to one of the socioeconomic Classes (I to V). The social classes of the subjects were further stratified into upper (social classes

I and II), middle (social class III), and lower (social classes IV and V).

Procedure for field work

Two research assistants who were house officers were trained for two consecutive days by the investigators, who are pediatricians. In the course of the training, the investigators and research assistants practiced on how to administer and fill the questionnaires and method of collection of the blood samples.

The questionnaire was pretested and validated 2 weeks prior to the commencement of the study and the content found not to be ambiguous.

Prior to the commencement of the study the investigators and research assistants visited the selected schools to familiarize themselves with the school authorities and students of the selected schools. During the familiarization visits, the students and teachers were given a brief talk on viral hepatitis with special reference to hepatitis C, its mode of transmission, prevention, and control. Moreover, the objective of the study was explained to the students. The selected students were given a consent form to take home to their parents for approval and signing and brought back the next day. On the following days, the respective school halls were used for the retrieval of the consent forms.

One semi-structured questionnaire per student was administered and completed by the investigators and each student.

Exclusion criteria

Subjects who had symptoms and signs suggestive of liver disease were excluded.

Procedure

Venous blood (5 ml) was obtained from each participant and tested for antibody to HCV (anti-HCV) using a third generation assay (ELISA) manufactured by ABON Biopharm (Hangzhou) Co., Ltd., P.R. China (Number: 11559996501). This test kit has a sensitivity of 99.0% and specificity of 98.6%.^[21]

Data analysis

Data were analyzed using the statistical package for social sciences (SPSS) software Version 16.0 (Chicago, IL, USA) and presented as percentages, frequencies, whereas bivariate analysis was used to determine the predictive risk factors for HCV infection.

Results

A total of 420 children aged 10–18 years comprising 210 males and females were studied, giving a male to female ratio of 1:1. The social class distribution of the study subjects is as shown in Table 1.

The overall mean age was 14.26 (2.017), whereas the median age was 14.0.

The mean age for males was 13.97 (2.135), whereas among the females, it was 14.40 (1.946).

Four out of the 420 subjects tested positive to the anti-HCV giving an overall seroprevalence of 1% [Table 1].

75% (3/4) of the anti- HCV cases were females, whereas one was a male giving a male to female ratio of 0.3:1. See Table 2. Two were aged 10, whereas the others were between 12 and 13 years.

The putative risk factors were more frequent in the anti-HCV seropositive subjects compared to the anti-HCV negative cases [Table 3].

When the putative risk factors were subjected to bivariate analysis, only traditional scarification/tattoo was statistically significant ($P < 0.01$) which are shown in Table 4.

Discussion

The seroprevalence of hepatitis C in the current study was 1.0% which is comparable to findings in a similar study in Nigeria with a reported prevalence of 0.9%.^[15] It is, however, low when compared with other reports in some parts of sub-Saharan Africa.^[22,23] It is pertinent to state that several recent studies on the seroprevalence of hepatitis C reported in Nigeria were with other co-morbidities including sickle cell anemia,^[24-26] HIV,^[27] and hepatitis B virus co-infections.^[28]

However, the 1.0% seroprevalence of HCV reported in the current study could possibly be an underestimation of the actual prevalence as evidence from the Nigeria demographic and health survey reveals that among children of secondary school age, 35.1% were attending secondary schools,^[19] implying that a greater percentage of the children are out of school and as such are not accounted for.

Although children represent a small fraction of the global burden of HCV infections, a substantial proportion of them have been reported to have chronic HCV infection and are at increased risk for the development of its complications including chronic liver cirrhosis, liver failure, and hepatocellular carcinoma at later age.^[3] This necessitates the need to screen at risk children for hepatitis C viral infection.

Among the putative risk factors studied, only native scarifications/tattoos were significantly prevalent among subjects who tested positive to HCV antibodies compared to those who were seronegative. This implies that there is a significant contribution to the disease burden by this unwholesome practice. Similar observations have been made by Ejiofor *et al.*^[26] in Enugu. The chance of

Table 1: Sociodemographic characteristics of the study population

Variables	Frequency (n=420)	Percentage (100.0)
Age (years)		
10-12	140	33.3
13-15	140	33.3
16-18	140	33.3
Sex		
Male	210	50.0
Female	210	50.0
Social class		
1	39	9.3
2	97	23.1
3	109	26.0
4	93	22.1
5	82	19.5

Table 2: Prevalence of hepatitis C according to sex

Sex	Hepatitis C antibody		
	Negative (n=416)	Positive (n=4)	Total (n=420)
Male	209 (99.5)	1 (0.5)	210
Female	207 (98.6)	3 (1.4)	210
Total	416 (99.0)	4 (1.0)	420

Table 3: Distribution of risk factors of hepatitis C infection among the anti-hepatitis C virus positive cases

Risk factors	Hepatitis C			
	Negative		Positive	
	No	Yes	No	Yes
Previous blood transfusion	92.3	7.7	100.0	0.0
Native uvulectomy	87.0	13.0	100.0	0.0
Sharing of toothbrush	82.2	17.8	75.0	25.0
Sharing razor blades, or clippers	37.0	63.0	0.0	100.0
Traditional scarification/tattooing	87.5	12.5	50.0	50.0
Injections from quacks	41.3	41.3	50.0	50.0
Circumcision	53.8	46.2	75.0	25.0
Previous surgery	95.9	4.1	100.0	0.0
Intravenous drug use	100.0	0.0	100.0	0.0
Use of alcohol	97.6	2.4	100.0	0.0
Multiple sex partners	98.1	1.9	75.0	25.0
Past history of jaundice/liver disease	97.1	2.9	100.0	0.0

transmitting HCV-related infections through scarification in the subjects for conditions such as febrile convulsions, visible cardiac pulsations, enlarged abdominal organs particularly splenomegaly, or even for esthetic reasons may likely be substantial following the fact that such practices might have occurred several years ago and most importantly some of them may have co-morbidities likely to result in anemia requiring blood transfusion with its attendant risks if not screened for hepatitis C.

However, such children with known sickle cell disease, HIV infection were excluded from the study. HCV principal route

Table 4: Bivariate analysis of the risk factors for hepatitis C virus infection among subjects

Risk factors	Correlation coefficient (<i>r</i>)	<i>P</i>
Social class	-0.012	0.81
Previous blood transfusion	0.016	0.75
Traditional uvulectomy	0.028	0.58
Sharing toothbrush	-0.006	0.91
Sharing razor blades/clippers	-0.076	0.12
Traditional scarifications/tattoos	-0.149	<0.01
Injection from quacks	0.034	0.50
Circumcision	0.041	0.40
Surgery	0.042	0.40
Use of alcohol	0.029	0.56
Past history of jaundice	0.013	0.79
Family history of liver disease	0.018	0.72

of transmission is exposure to contaminated blood.^[29] In the current study, none of the positive cases for anti-HCV reported past history of blood transfusion.

Further, perinatal/vertical transmission is one form of HCV transmission, even though it is a known less common mode of infection. In the current study, we could not directly ascertain the proportion of subjects with positive anti-HCV from maternal HCV positively.

The females had higher seroprevalence compared to males. This is in contrast to a similar Nigerian study by Okonko *et al.*^[15] where more males were found to have higher positivity.

The reason for the higher female predilection may be uncertain. However, females are traditionally more likely to have had ear piercing in infancy as well as native aesthetic scarifications hence increasing the chances of HCV transmission in them if the instruments applied were unsterile.

Socioeconomic status has been observed to be associated with the transmission of some similar viral infections like hepatitis B virus infection as reported by Ugwuja and Ugwu^[30] Others have reported varying findings showing that social class does not influence hepatitis B viral infection in children.^[31] Though social class, as well as educational attainment of the children and parents, was not statistically associated with the prevalence of hepatitis C seropositivity, in the current study, it is possible that because the majority of the children studied were from upper- and middle-socioeconomic backgrounds with higher educational attainment they may have limited exposure to the possible risk factors for hepatitis C viral infection following their improved environmental and behavioral conditions and hence the low hepatitis C seroprevalence as observed in them.

The four positive subjects were aged between 10 and 13 years. Though we could not sight similar local studies on adolescent population, similar studies in Ugandan^[22] had revealed higher positivity in younger age.

Even though other risk factors reported in this study were not significantly related to anti-HCV positivity such as injections from quacks, sharing of clippers, razor blades, native uvulectomy, and circumcision. It is important to note that such unhealthy practices could result in transmission of blood-related infections including hepatitis B or C and even HIV.^[29,32-34]

Till date, pediatric HCV infections have not received the desired attention it deserves probably due to the fact that the proportion of infected children is small and that majority of perinatal and early childhood infections are either cleared or the few infected ones may not all develop the chronic stigmata of the disease in childhood. However, the burden of HCV infection should be appreciated in children

Conclusion

This study has highlighted the burden of HCV infection in adolescent child population in Enugu with traditional scarification/tattooing being the most prevalent associated risk factor.

Adequate health education including school health education and promotion of behavioral change among the general public to practice safe scarifications/tattooing should be encouraged to limit the spread of the infection.

Limitation of the study

Inability to determine the maternal HCV serostatus of the study subjects which could be a risk factor for its transmission.

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Conflicts of interest

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