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PREVALENCE AND RISK FACTORS FOR HEPATITIS C AND HUMAN IMMUNODEFICIENCY VIRUS CO-INFECTION AMONG CHILDREN IN ENUGU, NIGERIA

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Abstract

Background: Hepatitis C virus (HCV) and Human Immunodeficiency virus (HIV), are major public health challenges in the developing world especially sub-Saharan Africa. The aim of this study was to determine the prevalence and risk factors of Hepatitis C virus infection among children infected with HIV.
Methods: This was a cross-sectional study conducted at the Paediatric HIV Clinic, UNTH, Enugu between July and December 2009. Antibodies to HCV were analyzed by newer generation rapid chromatographic immunoassay method using the Chromatest one step HCV test kit. The data was analysed using the Statistical Package for Social Sciences (SPSS) version 15 statistical software. The chi squared test was used to test for significant association of categorical variables. A *p*-value of <0.05 was accepted as significant.
Results: One hundred and eighteen children HIV-infected children, aged between eighteen months to fifteen years were included in the data analysis. Eight of the HIV infected subjects were positive for HCV, giving an HIV-HCV co-infection prevalence of 6.8%. Co-infection was more prevalent among males and in those in age group 11-15 years. Blood transfusion, irrespective of frequency ($p<0.015$), and injections for immunization ($p<0.049$) were the significant risk factors noted
Conclusion: There is need for strengthening of existing preventive strategies against HCV and HIV infections such as screening of donor blood and safe injection practices in our locality.

Key words: Hepatitis C, Human immunodeficiency virus, Co-infection

Introduction

Infection with HCV has become a major global concern because of its worldwide distribution and its propensity to progress to chronicity in up to 70-80% of cases with subsequent increase in mortality and morbidity (Alter, 2007). About 30% of chronically infected persons progress to liver cirrhosis and ultimately to liver failure and hepatocellular carcinoma (Hoofnagle, 1997; Esteban et al, 1999). According to WHO, an estimated 150 million people (3% of the world's population) are chronically infected, with 3-4 million newly infected persons each year (WHO, 2000). Africa has a major share of this burden, accounting for 31.9 million infections and the highest prevalence of 5.3% (Madhara et al 2002), compared to South East Asia and Middle East with 2.15% and 4.6% respectively while America and Europe have prevalences less than 2% (WHO, 2000).

Human immunodeficiency virus (HIV) which is the aetiologic agent of acquired immune deficiency syndrome (AIDS) has also assumed a pandemic proportion worldwide. World Health Organization (WHO) and United Nations Joint Programme on AIDS (UNAIDS) data show that 33.2 million people are estimated to be living with the disease worldwide with an average of 1500 new infections per day (WHO/UNAIDS, 2009). Sub-Saharan Africa accounts for 68% (about two- thirds) of the total global burden. Of the 2.3 million children estimated to be infected worldwide, 90% live in sub-Saharan Africa of which Nigeria accounts for 10% (WHO/UNAIDS, 2009).

HCV shares similar modes and risk factors for transmission with HIV. These include transfusion of unscreened blood, heterosexual activity, use or sharing of unsterile needles, illicit intravenous drug use (IDU) and, traditional practices like scarification, tattooing, circumcision among others. Hepatitis C can also be transmitted via mother to child transmission (MTCT), a major mode of transmission of HIV in children (about 90%). This transmission is increased from a rate of 5% to up to 20% in the presence of maternal HIV/HCV co-infection (NIH, 2002). Generally, transmission efficiency is determined by the amount of virus in a body fluid and the type and extent of contact (Mboto et al, 2006). Thus when HIV/HCV co-infection occurs due to similar routes of infection and behavioral risk factors which they share, a new management challenge is presented.

HIV has also been shown to increase the infectivity of HCV. It worsens the clinical picture in patients already at risk of hepatotoxicity following the use of some Highly Active Retroviral Therapy (HAART) like Nevirapine (Valet-Richards et al, 2006). Both infections have rapid replication rates and are refractory to complete eradication by currently available therapy. There is, however, little experience and knowledge of the use of the available treatment options for HCV like Pegylated Interferon and Ribavirin for HCV in children in our region.

Sub Saharan Africa as noted earlier, is endemic for both infections and replete with factors which propagate their transmission, therefore is at risk of emergence of a "third epidemic" (Mboto et al, 2006). While there are data on the burden of this co-infection in adults, the converse is true for children. This study was thus undertaken to highlight the burden of the co-infection among children in this environment and determine the risk factors associated with it. Such information will add to the wealth of knowledge of the disease and will assist policy makers in initiating guidelines for the management and prevention of both infections, ultimately forming a basis for further research in this evolving area of HIV research.

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Methods

Area of Study

The study site was the University of Nigeria Teaching Hospital (UNTH), Ituku-Ozalla, a tertiary medical facility. The hospital, is a referral centre, serving mainly the Eastern States of Nigeria. The Paediatric HIV Clinic provides care to about 250 HIV–infected children.

Study design

The study was cross sectional in nature. The advantage of using cross sectional design was that reasonable sample size could be achieved in a relatively short time.

Inclusion and exclusion criteria:

Subjects included were those aged between 18 months-15 years whose HIV status have been confirmed by Western Blot technique. Subjects with indeterminate HIV status where excluded.

Data collection

The Paediatric HIV Clinic was visited on the clinic days during which 120 subjects who consented and met the inclusion criteria were enrolled consecutively over a six month period, (July 1st to December 31st, 2009). Subjects were recruited for the study after informed consent from their Caregivers and assent from the older children. Structured questionnaire was used to obtain patient's biodata, occupation and educational status of parents or guardian; and possible risk factors for HCV transmission. About 3 mls of blood was drawn from the subjects for HCV assay by the researchers or trained assistants. The blood was quickly transferred to a plain sterile bottle and centrifuged within 3 hours of collection. The sample analysis was done with support from the Haematology Department of UNTH, Ituku-Ozalla.

Sample Analysis: The serum specimens were assayed immediately for HCV antibodies with the Newer Generation, one step Hepatitis C Virus test Kit a newer generation rapid chromatographic enzyme immunoassay for the qualitative detection of antibody to hepatitis C virus in serum or plasma (Chromatest - Linear Chemicals, Spain ref:4230220). The text kit is stable at room temperature (2-30^{0}C) and has a relative sensitivity of 100% and specificity of 99.6%. It also has an internal control mechanism, whereby the appearance of a line in the control region validates the test and vice versa.

Data Analysis

The data was analyzed after entering into a computer data base using the Statistical Package for Social Sciences (SPSS) version 15 statistical software (Chicago Il, USA). Chi square was used to test for significant associations of categorical variables. The odds ratio (OR) of risk factors were calculated. A *p*- value of <0.05 was accepted as significant.

Ethical considerations

Approval to conduct the study was obtained from the Hospital Research Ethics Committee of UNTH. Subjects who were positive for HCV and their caregivers were counseled on the nature of the infection and possible routes of transmission to others. It was emphasized however, that this is a screening test that may require further testing. They were, subsequently, referred to the clinicians at the HIV clinic for further assessment and follow up.

Results

Two of the tests that did not show a line in the control region were invalidated, thus 118 HIV infected subjects age between 18 months and 15 years were analysed. The distribution of the study population according to age and sex is as shown in Table 1. The subjects comprised of 68 males and 50 females with a male to female ratio of 1.36:1. Their ages ranged from 1.5 to15 years (mean 6.88 $\pm$3.83 years). Majority of the study population (47.5%) were in the age range 1.5-5 years. The least represented was the age group 11-15 years, accounting for 22.2% of the total population. There was no statistical significance between males and females (p>0.449).

Among those HCV positive, the ages ranged from 3 to14 years, with a mean age of 10.1$\pm$ 4.2 years (Table 2) Six were males and two were females, giving a male: female ratio of 3:1. Four (50%) of the HCV infected subjects are in the age group 11-15 years and the least in age group 1.5-5 years. The reverse is observed among the HCV negative subjects. There was no significant association between age and HCV positivity among both groups (p>0.135).

All HCV infected and non-infected subjects had received intramuscular injections as shown in Table 3. History of blood transfusion was recorded in 33.1% which was significant, (p<0.015) and 59.3% of them were circumcised. None had a positive history of sexual exposure or use of intravenous drugs. Some of the subjects had more than a single risk factor.

The odds ratio of the risk factors that had significant association with HCV positivity in these HIV positive children are shown in Table 4. Those with history of blood transfusion were 7 times as likely to be HCV positive than those who had not been transfused (Odds ratio – 7). Receiving injection for immunization was 0.23 times as likely to lead to HCV positivity (Odds Ratio – 0.23). The other risk factors did not show any significant association with HCV positivity.

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Table 1: Age and sex distribution of all subjects

Age group (years)	N Males %	N Females %	N Total %	*p*
1.5 -5	29 42.6	27 54.0	56 47.5	0.45
6-10	22 32.4	14 28.0	36 30.5	
11-15	17 25.0	9 18.0	26 22.0	
Total	68 100	50 100	118 100	

Table 2: Distribution of subjects according to HCV positivity

Age group(yrs)	Males		Females		Total	
	HCV-ve(%)	HCV+ve(%)	HCV-ve(%)	HCV+ve(%)	HCV-ve(%)	HCV+ve(%)
1.5- 5	29 (46.8)	0	26 (54.2)	1(50)	55 (50)	1 (12.5)
6 - 10	19 (30.6)	3 (50)	14 (29.1)	0	33 (30)	3 (37.5)
11-15	14 (22.6)	3 (50)	8 (16.7)	1(50)	22 (20)	4 (50)
	62 (100)	6 (100)	48 (100)	2(100)	110 (100)	8 (100)

+ve: *p*- 0.135

Table 3: Distribution of risk factors examined among all respondents

Risk factor	**HCV infected n (%)**	**HCV non- infected n (%)**	***p***
History of receiving injections	8 (6.8)	110 (93.2)	1.000
History of circumcision	6 (8.6)	64 (91.4)	0.294
History of blood transfusion	6 (15.4)	33 (84.6)	0.015*
History of scarification or tattoo	3 (13.0)	20 (87.0)	0.186

Table 4: Showing the odds ratio (OR) of different factors examined with a positive HCV test in the children.

Factors examined	*P*-values	OR
History of Blood transfusion	0.015*	7
High rate of blood transfusions (>3)	0.350	
History of receiving injection	1.000	
- from a chemist shop	0.352	
- from a native doctor	0.068	
- from nurse at home	0.308	
- for immunization	0.049*	0.23
- for drug administration	0.060	
Use of a needle of unknown status	0.434	
Low socioeconomic status	0.543	
History of scarification and tatooing	0.186	
History of circumcision	0.294	

OR = odds ratio

Discussion

In this study, the prevalence of HCV/HIV co-infection is 6.8%. This figure is lower than 13.8% recorded in Tanzanian children (Telatela et al., 2007) but similar to the range of 4-10% obtained among Nigerian adults at Lagos (Lesi et al., 2007), Jos (Agwale et al., 2004) and Ibadan (Otegbayo et al, 2008) using different methods of HCV assay. The prevalence of HCV in the general population determines the prevalence in the different groups studied therein. A prevalence of 8% was documented for the general population in Nigeria in 1996 (Oni et al., 1996). Marginal improvement in health care practices (blood screening for HIV, HCV and other infections, use of disposable syringes) since then, may have led to the slight drop in prevalence noted since then.

The highest frequency of HCV positivity was documented among children in the age bracket 11-15 years. This is in consonance with a similar study on HIV infected Tanzanian children (Telatela et al., 2007) which showed high frequency of positivity of HCV in children in the 10-15 years group compared to younger age ranges, representing an increase in HCV positivity with increasing age. This can be attributed to greater cumulative exposure to risk factors for HCV infection as a person gets older. The lower prevalence noted in the 1.5 – 5 year age group found in this study is similar to the findings as documented by Agbede et al. who recorded a zero prevalence among pre-school age children (Agbede et al., 2006). These may suggest a relatively low level of vertical transmission as also suggested by some other authors (Sulkowski, 2008; Menendez et al., 1999) irrespective of the HIV status of the cohorts.

More males than females were positive for HCV in this study. The preferential care of the male child in our environment may have exposed them to more risks of acquiring HCV as they are given both orthodox and non-orthodox treatment when sick, both of which are associated with varying degrees of HCV transmission. Also circumcision, a known risk factor for HCV transmission is carried out more on them than on females.

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This finding, though not significant, correlates with the findings in a large study in USA with 21,509 participants with a M:F ratio of 2:1 attributed to the more active lifestyle of males with attendant risks of exposure to HCV than females (Armstrong et al., 2006). Otegbayo et al. (2008) however documented a greater female preponderance of HCV positivity in their studies among adults but they had more female subjects among their cohorts which could have explained their finding.

The significant risk factors for HCV positivity found among the studied cohort were blood transfusion and injection for immunization. Odds ratio for history of blood transfusion was 7, indicating that subjects with history of blood transfusion are 7 times more likely to be HCV positive than those without. In a similar study at Jos (Inyama et al., 2005), blood transfusion was found as a significant risk factor. A WHO study (Hauri A et al., 2004), attributed up to 40% new HCV infections in the developing world to healthcare contaminated injections which can include injections for immunizations especially if disposable needle and syringes are not used. This may thus explain our finding of a higher chance of co-infection with injections for immunization. The study among Tanzanian HIV infected children did not document any significant risk factor and suggested possibly MTCT as the reason for the high prevalence documented. Other risk factors like scarification, circumcision and heterosexual activities have been documented as risk factors for HCV infection in different cohorts. These studies do not negate each other, but support the fact that the prevalence and risk factors for each region or age group depends on the predominant socio-cultural activity and life style found among them. It is suggested that children being an age group with different peculiarities and lifestyle from adults will have different risk factors as shown by this study. Sexual exposure and intravenous drug use were neither documented as significant risk factors from this study nor in any of the reviewed works among Paediatric cohorts, thus showing their low relevance in contributing to HCV in children especially in our sub-region.

In conclusion, the increasing access to HAART means improved quality of life and increased life expectancy for HIV-infected children. Co-infection with HCV however cuts short these aspirations as patients now live long enough to suffer from consequences of HCV on the liver. Since treatment of HCV is still in evolution even in developed countries, prevention would be a most worthwhile alternative. More emphasis should be placed on screening of blood for transfusion for HCV, in addition to other blood transmissible diseases and safe injection practices. Increasing awareness of the disease and its modes of transmission prevalent in our region should be carried out among health care workers, especially those who have direct contact with patients since nosocomial transmission can take place. The general populace will also benefit from similar health education. These will aid in making an appreciable impact in reducing the burden of this disease generally, and among HIV infected persons in particular. More studies which will require a larger cohort of patients, followed up over a period of time, are needed to evaluate further the effect of both infections and the role of various risk factors in causing these diseases in the Paediatric age group.

Competing interests: The authors declare no conflicts of interest related to this study.

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