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RESEARCH ARTICLE

High Anti-HCV Seroprevalence and Low Performance of ICT Strip in Diagnosing Hepatitis C Virus Infection in Children in Enugu Metropolis

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Abstract:

Background:

The lack of a vaccine for Hepatitis C virus (HCV) places children at a high risk of contracting the infection. It becomes necessary to accurately diagnose this infection for proper treatment as well as identifying potential risk factors for effective management.

Aim:

This study was conceived to assess the test performance of the commonly used Immunochromatographic test (ICT) strip and identify the associated clinical manifestations and risk factors of HCV in children in Enugu Metropolis.

Method:

A cross-sectional study involving randomly selected 270 children below six years of age was conducted in Enugu Nigeria. The subjects were screened for anti-HCV by ICT and Enzyme-Linked Immunosorbent Assay (ELISA) and the demographic, signs and symptoms and risk factors were collected.

Results:

A total of 50 out of 270 children were positive for anti-HCV with a seropositivity of 18.5%. ICT strip had a very low sensitivity of 38.00% with an accuracy of 88.52% in detecting anti-HCV. The presence of dark urine was associated (p = 0.01) with HCV infection.

Conclusion:

A seroprevalence of 18.5% of Anti-HCV was found in children below six years old in Enugu metropolis and the performance of ICT in diagnosing HCV infection was poor compared to ELISA.

Keywords: Hepatitis C virus, Immunochromatographic test strip, ELISA, seroprevalence, Children, risk factors.

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1. INTRODUCTION

Hepatitis C virus (HCV) is a globally prevalent virus and a leading cause of morbidity and mortality which calls for public health concern [1]. Recently, the seroprevalence of the disease burden is estimated to be over 185 million infections worldwide as against 170 million infections in early 2000 [2] with an increase of 2.8% in the last 15 years [3]. Prolong HCV infection can lead to liver cirrhosis, liver failure, hepatocellular cancer, and possibly death [4]. Presently, HCV is the leading cause of death in HIV patients who are on highly active antiretroviral drugs [5].

HCV is transmitted through infected blood or blood-derived body fluids. Thus, the likely primary means of HCV transmission especially in developing countries include blood transfusion from unscreened donors, exposure of blood through the use of contaminated or inadequately sterilized medical instruments and needles for surgical and dental procedures, performing activities that cause skin breaks such as tattooing, ear and body piercing, the use of unsterilized objects for rituals and traditional medicine such as circumcision, scarification, face marks, acupuncture etc [2, 6].

HCV is highly genetically diverse with 7 main genotypes, of which each genotype has about 67 sub-types [7, 8]. With this high genetic diversity, the development of a vaccine as well as some pan-genotypic drugs has been a major challenge [9]. As such, there is no existing vaccine for HCV, although clinical trials for potential vaccines are ongoing [10]. The lack of a vaccine places children at a high risk of contracting HCV since at this stage in life, their immune system is not fully developed. More so, children are at high risk of prolong HCV infection to develop to chronic liver disease and other liver complications [11]. With this vulnerability of children to HCV infection and no available vaccine, effective management of the disease will depend on routine screening of infected individuals for proper treatment. Also, identifying the possible means of transmission of the virus will help prevent contraction of the infection.

The most commonly used screening tool for HCV infection in Nigeria today is the Immunochromatographic test (ICT) strips because it is very rapid with results obtained in less than 10 minutes, relatively cheap and affordable, and doesn't require expertise in performing the test. Though developed by different diagnostic and pharmaceutical companies across the world, the mode of action of these ICTs is similar and is based on the common principle of antibody present in plasma or serum to migrate upward by capillary action and react with recombinant antigen present on the chromatographic membrane of the strip thereby generating a colour line in the test region. Usually, the manufacturers claim that these test strips have relatively high sensitivity, specificity and accuracy but querying performances have been reported [12] as the very low level of the anti-HCV antibodies may not be detected by the strips. More so, in case of poor diagnosis, a presumptive diagnosis can aid clinicians to screen individuals for vital signs of clinical manifestations. Thus, it is necessary to routinely assess the performance of the commonly used ICT test for HCV screening and also, identify the associated signs and symptoms as well as potential risk factors for effective management of the disease.

2. MATERIALS AND METHODS

2.1. Study Area

This study was a hospital based cross-sectional study carried out at Enugu State University Teaching Hospital (ESUTH) and Favor Child Pediatrics Hospital in Enugu. Enugu is the capital of Enugu State located in South Eastern Nigeria with latitude and longitude coordinates of 6.459964 and 7.548949.

2.2. Study Population

The study population consisted of children with minor illnesses and fever who attended the hospitals. Subjects who met the criteria for inclusion which includes children less than 71 months old (less than six years) and whose parents and guardians provided a written informed consent were randomly selected and recruited for the study. Within the period of February to August 2017, a total of 270 children were recruited based on the calculated sample size using the formula: $N = Z^2pq/d^2$, where z = Normal standard deviation at 1.96 which corresponds to 95% confidence interval; p = Prevalence of Hepatitis C virus infection; q = 1-p; and d = degree of accuracy/ precision expected = 0.05.

2.3. Data Collection

After the recruitment, a structured interviewer-administered questionnaire on the predisposing factors to HCV infection was used to obtain participants data. The data collected include demographic, socioeconomic, background knowledge about HCV, its screening, associated signs and symptoms as well as risk factors and preventive measures.

2.4. Sample Collection and Serological Screening for Anti-HCV

After the participants were interviewed, three millilitres of blood was collected through venous puncture and transferred into sterile plain bottles. The blood was then centrifuged at 1500 rpm for 5 minutes to obtain the serum. The serum was aliquot and transported to the National Arbovirus and Vectors Research Center (NAVRC) Enugu for Enzyme-Linked Immunosorbent Assay (ELISA) analysis and later to the Microbiology laboratory of Godfrey Okoye University Enugu for ICT assay. Anti-HCV antibody was screened using anti-HCV ELISA test kits by Fortress Diagnostics Limited, United Kingdom and HCV one step Hepatitis C test ICT strip by Biogate Laboratories Ltd, Canada according to the manufacturer's protocol.

2.5. Data Analysis

The seropositivity (%) of anti-HCV was calculated as (presence of anti-HCV / total population) x100. The specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of ICT test for HCV infection was calculated from true positive (TP), true negative (TN), false negative (FN) and false positive (FP). Sensitivity was calculated as TP/(TP + FN) x100, specificity as TN/(TN + FP) x100, NPV as TN/(TN + FN) x100, PPV as TP/(TP + FP) x100 and accuracy as ((TP+ TN)/sample size) x100.

2.6. Statistical Analysis

Data was analyzed using Statistical Package for Social Science (SPSS) version 16. Results were expressed in frequencies and proportion, and presented in tables. Pearson chi-square ($\chi 2$) test was used to determine the association between ICT and ELISA tests in diagnosis HCV infections. Also, $\chi 2$ was used to determine the association of various parameters including socio-demographic characteristics as well as signs and symptoms with HCV infections. The odd ratio (OR) was generated using a binomial logistic regression model to determine the independent contribution of risk factors to HCV infection. All statistical analysis employed a two-sided test and 95% confidence interval (CI) for *p*-value determination. A *p*-value ≤ 0.05 was considered statistically significant.

3. RESULTS

Among the 270 subjects, 50 were tested positive for anti-HCV by ELISA giving a seropositivity of 18.5%. The ELISA assay was more effective and reliable than the ICT strips in diagnosing anti-HCV as it detected 50 positive subjects as against 19 for ICT strips. As such ICT test had a low potential in detecting anti-HCV positive subjects with a sensitivity of 38.00% (19/50), but was very effective in screening subjects without HCV as all anti-HCV negative subjects were confirmed negative by ELISA, resulting to a specificity of 100%. More so, the PPV, NPV and accuracy of ICT test were 100%, 87.65% and 88.52%, respectively. The performances of the two tests are summarized in Table **1**. As shown in Table **2**, the seroprevalence of anti-HCV was insignificantly greater ($\chi 2$: 0.014; $p = 0.514$) in females (11.1%) than males (7.4%), and thus was not associated with gender. Also, though the prevalence of HCV infection was greatest (5.6%) in the age group of 48-59 months (4 years^{+}), HCV was not associated ($\chi 2$: 2.099; $p = 0.914$) with age group. The presence of HCV infection in children was not associated with the patients/guardians level of education ($\chi 2$: 5. 246; $p = 0.073$) and marital status ($\chi 2$: 2.234; 0.525). Evaluating clinical signs and symptoms of subjects showed dark urine to associate significantly ($p< 0.05$) with HCV infection while no subject with jaundice was HCV positive. Moreover, fever, joint pain, itchy skin, loss of appetite, fatigue and abdominal pains did not show any significant association ($p> 0.05$) with the infection (Table **3**). Potential risk factors of the parents or guardians of patients such as the presence of tattoo mark, alcohol intake, sharing of items, dental procedure and blood transfusion were observed to be associated significantly ($p<0.05$) with HCV infection with OR of 6.000, 1.898, 3.195, 2.184 and 2.984, respectively. Among these factors, the presence of a tattoo mark showed the greatest risk.

Table 1. Comparison between ICT and ELISA techniques in diagnosing HCV.

Test		HCV- ELISA			$\chi 2$	*p*-value
		Positive (%)	Negative (%)	Total (%)		
HCV-ICT	Positive	19 (7.0)	0 (0.0)	19 (7.0)	89.93	0.000
	Negative	31 (11.5)	220 (81.5)	251 (93.0)		
	Total	50 (18..5)	220 (81.5)	270 (100)		

Legend: Legend: HCV: hepatitis C virus, HCV-ICT: immunochromatographic test strip for HCV, HCV-ELISA: enzyme linked immunosorbent assay for HCV, $\chi 2$: Chi-square, OR: odd ratio, CI: confidence interval. %: percentage.

Table 2. Association of anti-HCV seroprevalence with some study characteristic of participants.

Variables			HCV-ELISA		
Child	**Positive (%)**	**Negative (%)**	**Total (%)**	**χ2**	***p*-value**
Sex **Male** **Female**	20 (7.4) 30 (11.1)	86 (31.9) 134 (49.6)	106 (39.3) 164 (60.7)	0.014	0.514
Age **0-6 months** **7-11 months** **12-23 months (1 yr)** **24-35 months (2 yrs)** **36-47 months (3 yrs)** **48-59 months (4 yrs)** **60-71 months (5yrs)**	1 (0.4) 2 (0.7) 1 (0.4) 10 (3.7) 8 (3.0) 15 (5.6) 13 (4.8)	4 (1.5) 16 (5.9) 3 (1.1) 52 (19.3) 39 (14.4) 65 (24.1) 41 (15.2)	5 (1.9) 18 (6.7) 4 (1.5) 62 (23) 47 (17.4) 80 (29.6) 54 (20.0)	2.099	0.914
Guardian/Parent					
Level of Education **Non-formal College/University** **Postgraduate**	12 (4.4) 32 (11.9) 6 (2.2)	67 (24.8) 103 (38.1) 50 (18.5)	79 (29.3) 135 (50.0) 56 (20.7)	5.246	0.073
Marital Status **Married** **Separated** **Single** **Divorce**	38 (14.1) 0 (0.0) 12 (4.4) 0 (0.0)	177 (65.6) 3 (1.1) 38 (14.1) 2 (0.7)	215 (79.6) 3 (1.1) 50 (18.5) 2 (0.7)	2.234	0.525

Table 3. Association of anti-HCV seroprevalence with signs and symptoms of participants.

		HCV-ELISA			
Variables	**Positive (%)**	**Negative (%)**	**Total (%)**	**χ2**	***p*-value**
Fever **Present** **Absent**	42(15.6) 8 (3.0)	177(65.6) 43(15.9)	212 (81.1) 51(18.9)	0.334	0.362
Jaundice **Present** **Absent**	0 (0.0) 50 (18.5)	19 (7.0) 201 (74. 4)	19 (7.0) 251 (93.0)	4.645	0.018
Joint pain **Present** **Absent**	8 (3.0) 42 (15.6)	21 (7.8) 199 (73.7)	29 (10.7) 241 (89.3)	0.770	0.141
Itchy Skin **Present** **Absent**	2 (0.7) 48 (17.8)	11 (4.1) 209 (77.4)	13 (4.8) 257 (95.2)	1.807	0.177
Loss of appetite **Present** **Absent**	22 (8.1) 28 (10.4)	114 (42.2) 106 (39.3)	136 (50.4) 134 (49.6)	0.996	0.200
Weakness/fatigue **Present** **Absent**	19 (7.0) 31 (11.5)	102 (37.8) 117(43.3)	121 (44.8) 148 (54.8)	1.441	0.486
Abdominal Pains **Present** **Absent**	14 (5.2) 36 (13.3)	53 (19.6) 167 (61.9)	67 (24.8) 203 (75.2)	0.334	0.340
Dark Urine **Present** **Absent**	9 (3.4) 41 (15.2)	10 (3.7) 210 (77.8)	19 (7.0) 251 (93.0)	13.212	0.01

Table 4. Binomial logistic regression analyses for potential risk factors of HCV infection based on ELISA assay.

Variables (N =270)		HCV-ELISA		OR	95% CI for OR		*p*-value
	Present (%)	**Absent (%)**	**Total (100%)**		**Lower**	**Upper**	
Multiple sex partners							
Yes	7 (2.6%)	15 (5.6%)	22 (8.1%)	2.225	0.856	5.784	0.094
No	43 (15.9%)	205 (75.9%)	248 (91.9%)				
Tattoo marks							

(Table 4) contd.....

Variables (N =270)		HCV-ELISA		OR	95% CI for OR		*p*-value
	Present (%)	Absent (%)	Total (100%)		Lower	Upper	
Yes	12 (4.4%)	11 (4.1%)	23 (8.5%)	6.000	2.468	14.584	0.0001
No	38 (14.1%)	209 (77.4%)	247 (91.5%)				
Alcohol intake							
Yes	40 (14.8%)	142 (52.6%)	182 (67.4%)	2.197	1.042	4.633	0.035
No	10 (3.7%)	78 (28.9%)	88 (32.6%)				.
Piercing							
Yes	30 (11.1%)	139 (51.5%)	169 (62.6%)	0.874	0.466	1.639	0.675
No	20 (7.4%)	81 (30.0%)	101 (37.4%)				
Surgery							
Yes	12 (4.4%)	29 (10.7%)	41(15.2%)	2.080	0.975	4.436	0.054
No	38 (14.1%)	191 (70.7%)	229 (84.8%)				
Liver disease							
Yes	2 (0.7%)	28 (10.4%)	30 (11.1%)	0.286	0.066	1.241	0.076
No	48 (17.8%)	192 (71.1%)	240 (88.9%)				
Share Items							
Yes	26 (9.6%)	51 (18.9%)	77 (28.5%)	3.590	1.898	6.788	0.0001
No	24 (8.9%)	169 (62.6%)	193 (71.5%)				
Dental procedure							
Yes	16 (5.9%)	39 (14.4%)	55 (20.4%)	2.184	1.098	4.344	0.024
No	34 (12.6%)	181 (67.0%)	215 (79.6%)				
Blood transfusion							
Yes	11 (4.1%)	19 (7.0%)	30 (11.1%)	2.984	1.317	6.761	0.007
No	39 (14.4%)	201 (74.4%)	240 (88.9%)				

4. DISCUSSION

HCV infection is a life-threatening viral infection and a leading cause of liver disease, thus, a major public health problem in the world [13, 14]. With no existing vaccine against HCV [15], young children remain the most vulnerable infectious group of the society. As such, effective diagnosis especially in young children is important for prompt treatment. ICT strips are commonly used for routine screening of HCV infected subject, thus, it was necessary to assess their performance. In this study, ICT strip showed a poor performance characterised by a low sensitivity of 38.0% in detecting HCV when compared to ELISA assay as the standard. Though this strip had a high specificity (100%) and accuracy (84. 52%), the low sensitivity suggests that some infected subjects may not be diagnosed by the strip. The fact that ICT strips are routinely used for screening HCV infection poses a major challenge as false negative subjects may harbour the infection for a long time which may develop to chronic liver disease or hepatocellular carcinoma [16]. ELISA has been considered very reliable in diagnosing HCV infection but its routine use may not be feasible due to its high cost and longer time of analysis compared to ICT strips. Thus, periodical assessment of the performance of ICT strips by health practitioners is necessary to identify the most reliable ICT strip for routine use. More so, ELISA should be used as a confirmatory test when indiscriminate result of ICT strips is found.

Based on ELISA assay, anti-HCV was found to have a seropositivity of 18.5% and was higher compared to other previous studies conducted in children in Nigeria [17 - 19]. This seroprevalence was far higher than the reported rate of 2.1%-2.8% in Sub-Saharan Africa and the highest rate of 2.8% in West African sub-region [20]. Also, this prevalence is high compared to other findings across Africa such as 4.3% in Northern Ethiopia [21] and 1.8% in Ghana [22] but comparable to 16.0% in Rwanda [23]. The high seroprevalence of this infection in children suggest that the transmission rate has increased and thus calls for public health concern. More so, the low seroprevalence of anti-HCV was observed in children below 23 months old while high seroprevalence was found in children between 48-71 months of age but there was no significant relationship between age and seroprevalence of anti-HCV ($\chi^2 = 2.185$, $p > 0.05$). This suggest that older children may be at a higher risk of contracting the infection probably because they are more active than the younger ones so they can play, move around and thus gets exposed to the infection easily.

Though more than half of individuals with early HCV infection are usually asymptomatic, chronic infection for over 30 days may tend to manifest symptoms [24]. Dark urine ($p = 0.01$) was found to be associated with HCV while fever,

jaundice, itchy skin, joint pain, depression or weight loss, loss of appetite, fatigue and abdominal pain were not associated with the infection. Dark urine is a clinical manifestation commonly observed in individuals with chronic liver disease, thus it may be likely that some of the HCV infected individuals may develop liver disease.

With high seroprevalence of anti-HCV, is it believed that the rate of transmission may have increased thus it was necessary to identify the possible associated risk factors for transmission. Several risk factors such as multiple sex partners, practice of homosexuality, too much alcohol intake, intravenous drug use, presence of tattoo or tribal marks, sharing of personal items such as toothbrush, body piercing, history of any liver disease, blood transfusion, dental procedure and history of surgery etc. have been documented from previous studies to be associated with HCV infection [25 - 27] and thus could be a potential source of transmission from parents/guardians to children. Thus, our assessment of such risk factors in this study showed the presence of tattoo mark, shared items, alcohol intake, dental procedure and blood transfusion as potential risk factors of HCV infection. This finding concords with previous studies which have equally shown these factors as potential means of transmission of HCV infection [21, 23, 28].

CONCLUSION

This study showed a high anti-HCV seroprevalence of 18.5% in children below 6 years of age and this infection was associated with dark urine. Also, the presence of tattoo mark, sharing of items, alcohol intake, dental procedure and blood transfusion were found to be potential risk factors of transmission from parents/ guardians to children. ICT strip showed a poor performance in diagnosing HCV infection compared to ELISA assay with a sensitivity of 38%. The poor performance of ICT strip calls for general public health concern as false negative subjects are at risk of liver disease and eventually death due to prolong unidentified infection. Thus, a more effective diagnosis such as ELISA should be done for confirmation of inconclusive diagnosis by ICT strips especially when a subject is manifesting clinical signs and symptoms. Effective control measures should be undertaken by the society, health practitioners, stakeholder, public health advocates, etc. for the prevention of the risk factors and better management of HCV infection.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study design was reviewed and approved by the ethical committee of ESUTH Enugu, Nigeria with approval no: ESUTHP/C-MAC/RA/034/165.

HUMAN AND ANIMAL RIGHTS

No Animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Written informed consent was obtained from all parents or guardians willing to include their children in the study.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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