

Post-transfusion hepatitis C seroprevalence in Tanzanian children

JESSE KITUNDU, ABEL MSENGI, MECKY MATEE*, MAULID FATAKI, THEODORA KAZIMOTO, ROSE MPEMBENI†, EMMANUEL MNUBHI & FESTUS KALOKOLA

*Departments of Paediatrics and Child Health, †Epidemiology and Biostatistics and *Microbiology and Immunology, Muhimbili University College of Health Sciences, Dar es Salaam, Tanzania*

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Summary In Tanzania, children with malaria-associated anaemia are frequently given blood transfusions, and donor blood is not screened for hepatitis C virus (HCV) infection. To determine the seroprevalence of HCV infection in Tanzanian children previously transfused with blood, 184 children (92 transfused, 92 not transfused) aged between 15 and 59 months matched for age and sex were screened for HCV antibodies by the particle agglutination test using Serodia® anti-HCV (Fujirebio Inc., Japan). The overall prevalence of HCV infection was 7.1% (13/184). HCV seropositivity was 5.4% (5/92) among children with a history of blood transfusion and 8.6% (8/92) among the non-transfused. There was no significant difference in the prevalence of HCV infection between transfused and non-transfused children. None of the factors investigated, such as gender, the nutrition and HIV serostatus of the children and the marital and education status of their mothers, was associated with HCV seropositivity. Further studies are recommended to identify the factors associated with HCV infection in Tanzanian children.

Introduction

Hepatitis C virus (HCV) infection is a major public health problem. It is estimated that it has affected over 200 million people worldwide, about 3% of the world's population, and is responsible for chronic liver disease.^{1,2} The infection is transmitted predominantly by blood and exposure to body fluids. The risk of acquiring HCV infection from blood transfusion varies between 20 and 40% in countries where donor blood is not routinely screened for HCV,³ depending on the prevalence of infection, the number of transfusions and what

screening programmes there are in a particular area.⁴

Other routes of transmission are from mother to child (vertical) and through injecting with contaminated syringes and needles (horizontal).¹ Vertical transmission has been reported in 5% of pregnancies but can be as high as 25% if a mother is also HIV-positive.^{5,6} In developed countries where HCV infection rates are relatively low, ranging between 1 and 2%, the risk is estimated to be one in 103,000.^{1,7}

In most developing countries, blood transfusions are given frequently and donor blood is not screened routinely for HCV infection, favouring an increased risk of infection. In these countries, the prevalence of HCV infection is reported to be high (5–24%), although

Reprint requests to: Dr Jesse A. Kitundu, Dept of Paediatrics and Child Health, Muhimbili University College of Health Sciences, PO Box 65001, Dar es Salaam, Tanzania. E-mail: jkitundu@muchs.ac.tz

low prevalence rates of around 1% have been reported in some East African countries.⁸⁻¹⁰

A recent study in Dar es Salaam found an HCV seroprevalence of 8% among blood donors at Muhimbili National Hospital (MNH),⁴ where there are approximately 6,000 transfusions a year, which suggests that approximately 480 units are tainted with HCV.⁹ Usually, more than 70% of these transfusions are given to children aged less than 5 years.^{4,11,12} Figures show that 2,050 (82.5%) of 2,482 children admitted to the medical paediatric wards of MNH between June 1998 and June 1999 received blood (unpublished report).

The policy in Tanzania is that all blood donations should be screened anonymously for all transfusion-associated pathogens. However, in the 181 health care facilities with blood transfusion services, donor blood is screened only for HIV and syphilis.¹³ In view of the large number of blood transfusions in children < 5 years in Tanzania and the potential to transmit HCV, the risk of HCV infection attributable to blood transfusion needs to be determined.

We report a study to determine the prevalence of HCV infection in Tanzanian children with a history of blood transfusion.

Patients and methods

Study design

This was a cross-sectional, case-controlled clinical study conducted by the Departments of Paediatrics and Microbiology and Immunology of MNH, Dar es Salaam from August 1999 to January 2000. MNH is a tertiary referral hospital and the majority of children (about 80%) are referred from other city hospitals, health centres, dispensaries and up-country health facilities; the remainder are self-referred.¹⁴

The study population was all children admitted to the medical paediatric wards and those attending paediatric medical outpatient clinics during the study period. Blood-transfused children were enrolled if they were aged

between 15 and 59 months and had received a blood transfusion 4 or more weeks prior to the study. Verbal consent was obtained from the mother or guardian. When a case was enrolled, an age- and sex-matched control was identified and enrolled within 2 weeks. The controls were children with no history of blood transfusion. Children were excluded from the study if any information was missing, about blood transfusion, for example, or the exact date of birth, or if their mothers/guardians refused consent to inclusion in the study. Exclusion from the study did not in any way affect the further management of the children.

Mother interviews

Upon enrolment into the study, mothers/guardians were interviewed according to a structured questionnaire developed for the purpose. Briefly, the information sought included name, address, age and sex of the child, maternal education, marital status, history of fever, jaundice, joint swelling, abdominal pain, cough, convulsions, diarrhoea and date of blood transfusion. Experienced paediatricians conducted the interviews, and all questionnaires were checked for correct entry by the principal investigator (JAK).

Subject assessment

A thorough physical examination was done on all children according to the principles of paediatric practice.¹⁵ Anthropometric measurements including weight and length were taken in order to determine the children's nutritional status.

As soon as they were admitted, children were weighed, lightly clothed, using a Salter weighing scale with an accuracy of 10 g. Children with diarrhoeal dehydration were weighed after correction of the dehydration within 4-6 hours. The height of children over 24 months was measured to the nearest cm using a stadiometer. In children younger than 24 months, recumbent length was measured to the nearest mm using a standard length board with a fixed headpiece, a measuring

tape and a movable foot-board. Age was calculated in months as the difference between date of data collection and date of birth recorded on the mother/child health card. Children's nutritional status was expressed as *Z*-scores, weight-for-length, weight-for-age and height-for-age. Children whose weight-for-length was < -2 *Z*-scores were considered wasted and designated stunted if length/height-for-age was < -2 *Z*-scores. The rest were considered to be of normal nutritional status.¹⁶

Laboratory investigations

About 2 ml of venous blood was taken from the anterior cubital vein using disposable syringes/needles, put into sterile tubes, left to clot and then centrifuged at 1,500 rpm for 10 min to separate the sera, which were then stored in 1.5-ml Nunc tubes (Nunc™, Denmark) at -20°C until assay. Before assay, the sera were removed from the deep freezer and allowed to reach room temperature.

Anti-HCV serology

Anti-HCV antibody (anti-HCV) in the sera was detected by Serodia® anti-HCV (Fujirebio Inc., Japan), a particle agglutination test. The test is based on the principle that gelatin particles sensitized with recombinant antigens are agglutinated in the presence of antibodies to HCV in plasma/serum specimens. The testing procedure and interpretation of results were done according to the manufacturer's instructions.

HIV serology

Anti-HIV antibodies were detected by Enzygnost HIV 1 + 2 ELISA (Behring, Marburg, Germany) and the reactive samples were confirmed by Wellcozyme ELISA (Wellcozyme Recombinant, Murex Diagnostics, Kent, UK). Samples reactive to both tests were considered positive for anti-HIV antibodies. None of the tested sera had discordant reactivity.

Statistical analysis

Data were entered, cleaned, validated and analysed using Epi Info and SPSS software.^{17,18} The χ^2 and Fisher's exact tests were used to estimate the significance of differences between cases and controls and also to test for associations. A *p*-value of ≤ 0.05 was taken to indicate significance. Seroprevalences of anti-HCV and anti-HIV were expressed as percentages. An association was considered significant if the corresponding confidence interval did not include 1.0.

The study was approved by the Ethics Committee of Muhimbili University College of Health Sciences.

Results

A total of 205 children were enrolled in the study, most of them (69%) aged between 15 and 34 months. However, 21 (8.4%) were excluded from the study for various reasons, including unknown exact date of birth and lack of consent. Thus, 184 children, 92 with a history of blood transfusion (cases) and 92 non-transfused (controls) formed the study group.

Table I shows that there were no significant differences between cases and controls with regard to gender or mean age, nor between their mothers with regard to marital and educational status.

Table II summarizes the nutritional and clinical characteristics of the two groups. Most of the children (145/184, 79%), transfused and non-transfused, were of normal nutritional status (weight for length > -2 *Z*-scores). Of the 21% who were malnourished, 15 were cases and 24 controls. The difference was not statistically significant. In the analysis of symptoms and clinical signs on admission, only jaundice was significantly more frequent among cases (12%, 11/92) compared with controls (4.3%, 4/92, OR 2.99, 95% CI 0.82–11.7, $p = 0.005$), while fever, abdominal pain, cough and convulsions were significantly more common among controls ($p \leq 0.05$). Fever, abdominal pain, cough

TABLE I. Demographic characteristics of the two study groups (92 blood-transfused children, 92 not transfused)

	Blood transfused n (%)	Not transfused n (%)
Male	45 (48.9)	48 (52.1)
Female	47 (52.0)	44 (48.0)
<i>Age (mths)</i>		
15-24	35 (38.0)	34 (37.0)
25-34	29 (31.0)	36 (39.0)
35-44	18 (20.0)	15 (16.0)
45-59	10 (11.0)	7 (8.0)
Mean age	32.2	30.3
<i>Marital status</i>		
Married	70 (76.1)	76 (82.6)
Co-habiting	15 (16.3)	10 (10.8)
Single/divorced	7 (7.6)	6 (7.6)
<i>Maternal education</i>		
None	2 (2.2)	1 (1.1)
1-6 yr	15 (16.3)	12 (13.0)
7 yr	69 (75.0)	64 (69.5)
> 7 yr	6 (6.5)	15 (16.3)

and convulsions were more common in the controls but the difference was not significant.

Table II also shows that 13 children had IgG anti-HCV antibodies, five of them (5.4%) cases and eight (8.6%) controls. There were no increased odds for anti-HCV antibodies among children with a history of blood transfusion. Twenty-five children had IgG anti-HIV antibodies, eight (8.7%) cases and 17 (18.4%) controls. HIV seropositivity was not associated with an increased risk of HCV infection.

Table III shows that neither maternal education nor marital status was associated with HCV seropositivity.

Table IV summarizes the clinical features during admission of the HCV-seropositive and seronegative children. None of the clinical parameters, including wasting and stunting, was associated with HCV seropositivity.

Discussion

This is the first study of hepatitis C virus infection in Tanzanian children. Most of the

children were aged between 15 and 34 months, which reflects the admission pattern at Muhimbili National Hospital.

The overall prevalence of HCV in both transfused and non-transfused children was 7.1%, similar to that in blood donors (8%) reported from the same setting in 1999 by Matee *et al.*⁴ Nonetheless, blood transfusion did not influence the seroprevalence of HCV infection. This is rather unexpected in view of the high rate of HCV infection in blood donors and the large number of transfusions given to children. That the prevalence of HCV infection among the transfused children was not greater suggests other important sources of HCV transmission. Recent studies in the USA have reported that most HCV transmission is by intravenous drug abuse and sexual contact.³ In Tanzania, parenteral exposure to blood via contaminated and inadequately sterilized instruments and needles used in medical and dental practice and in traditional medicine as well as vertical transmission could be important sources of transmission. These factors, however, were not investigated in this study. The few factors that were investigated, such as gender, nutritional status of the child and marital status of the mother, were not associated with HCV seropositivity. Some epidemiological studies have shown that the mode of transmission in 20-40% of patients with HCV is unknown.^{7,19} It is important to note that even in this population, where HIV seroprevalence is high, HCV was not associated with HIV seropositivity. In fact, all HCV infection was in HIV-seronegative children, implying that the occurrence of the two viruses was not associated, despite sharing a common epidemiology. This is contrary to the findings of several other studies.²⁰⁻²²

It is imperative that population-based, epidemiological studies be done to investigate the associated factors and their relative contribution to HCV infection. Such studies will enable the prioritization of preventive measures, taking into account that available resources are scanty.

With regard to the clinical features analysed, cough, fever, abdominal pain and convulsions

TABLE II. Clinical characteristics of the two study groups (92 blood-transfused children, 92 not transfused)

	Blood transfused <i>n</i> (%)	Not transfused <i>n</i> (%)	OR	95% CI	<i>p</i> -value
<i>Nutritional status</i>					
Weight/length < -2 Z-score (wasted)	15 (16.3)	24 (26.1)	1.81	0.83-4.0	
<i>Clinical symptoms</i>					
Fever	38 (41.3)	57 (62.0)	0.43	0.83-4.0	0.005
Jaundice	11 (12.0)	4 (4.3)	2.99	0.82-11.7	0.05
Joint swelling	2 (2.2)	7 (7.6)	0.27	0.04-1.49	
Abdominal pain	6 (6.5)	16 (17.4)	0.33	0.11-0.97	0.02
Diarrhoea	1 (1.1)	2 (2.2)	0.49	0.02-7.11	
Cough	5 (5.4)	21 (22.8)	0.19	0.06-0.58	0.0007
Convulsions	1 (1.1)	6 (6.5)	0.16	0.01-10.6	0.05
<i>Serology</i>					
HCV + ve	5 (5.4)	8 (8.6)	0.6	0.16-2.14	
HCV - ve	87 (94.6)	84 (91.4)			
HIV + ve	8 (8.7)	17 (18.4)	0.5	0.2-1.33	
HIV - ve	84 (91.3)	75 (81.6)			

Fever, jaundice, abdominal pain, convulsions and cough were statistically significant ($p \leq 0.05$).

were found to be commoner in the non-transfused group and the difference was statistically significant ($p = 0.005$). This finding probably reflects the common presenting symptoms of the non-transfused controls during the study. None of the clinical features or symptoms was associated with HCV serostatus, in keeping with findings in other studies.^{1,23,24}

In conclusion, the studied child population

had a high prevalence of HCV infection (7.1%) which was not attributable to blood transfusion. Although HIV seroprevalence was high at 13.6%, which conforms with an earlier figure of 19.6% in hospitalized children in the same place,²⁵ it was not associated with the occurrence of HCV.

TABLE III. Prevalence of HCV antibody by marital status and maternal education*

	HCV-positive <i>n</i> = 13 (%)	HCV-negative <i>n</i> = 171 (%)
<i>Marital status</i>		
Single/divorced	10 (76.9)	138 (80.7)
Married	2 (15.1)	21 (12.3)
Co-habiting	1 (8.0)	12 (7.0)
<i>Maternal education</i>		
No formal	0 (0)	3 (1.8)
< 7 yr	5 (38.5)	22 (12.9)
7 yr	7 (53.8)	126 (73.6)
> 7 yr	1 (7.7)	20 (11.7)

* No significant difference in any of the parameters studied ($p > 0.05$).

TABLE IV. Clinical features/symptoms on admission in children with and without HCV antibody*

	HCV-positive <i>n</i> = 13 (%)	HCV-negative <i>n</i> = 171 (%)
Fever	7 (53.8)	88 (51.5)
Yellow colouration	0 (0)	15 (8.8)
Swelling of joints	0 (0)	8 (4.7)
Abdominal pain	1 (7.7)	21 (12.3)
Diarrhoea	1 (7.7)	2 (1.2)
Cough	1 (7.7)	25 (14.6)
Convulsions	1 (7.7)	6 (3.5)
Weight-for-length < -2 Z-score (wasting)	3 (23.1)	34 (58.1)
Length-for-age < -2 Z-score	5 (38.0)	60 (33.0)

* No significant difference in any of the parameters studied ($p > 0.05$).

Further studies are recommended to discover the factors that might explain the occurrence of HCV in the study population.

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