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CC –BY **Hepatitis c virus antibodies in
mother-infant blood pair in Zaria**

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Abstract: Objectives: To determine the prevalence of Hepatitis C virus (HCV) antibodies in mother-infant pair, and risk factors for vertical transmission of HCV in ABUTH Zaria.

Method: One hundred mother-infant pair had serological determination for HCV antibodies from birth to 28days and a repeat at 6weeks after delivery. HIV antibody test and serum alanine transaminase level estimation were done for the mothers at the time of enrolment. Data including mothers' demography, pregnancy and delivery history, relevant past medical history as well as physical examination of all babies were obtained and entered into a pro-forma designed by the researcher. Data was analyzed using SPSS version 15.0.

Results: Prevalence of HCV antibodies was 5% and 6.8% in

mothers and babies respectively at enrolment, while vertical transmission occurred in 60%. Five (5%) mothers had raised serum alanine transaminase. There was no new infection during the follow up period. There was no statistical significance between multiple sexual partners, history of prior blood transfusion, and or jaundice and maternal HCV infection.

Conclusion: This study has been able to establish Mother to Child Transmission (MTCT) of HCV in our community (Zaria), This is of public health significance. The findings of this study further corroborate the need for more public enlightenment on routes of transmission and prevention of HCV infection .It is thus recommended to institute screening of antenatal care attendees and women of reproductive age.

Introduction

Hepatitis C virus, a blood borne infectious single stranded RNA virus of the Flaviviridae family¹ is the commonest cause of almost all percutaneously acquired non A non B Hepatitis and one of the leading causes of chronic liver disease³. Its genetic and antigenic variability allows it to escape immune surveillance causing persistent infection and making development of an effective preventable vaccine difficult till date.

Hepatitis C virus infection has a global prevalence of 3% with about 170million people infected.⁴ It has a variable prevalence with the highest reported in Egypt.

Acute infections are usually asymptomatic or subclinical in about 70% cases but result in chronic infections in up to 85% of cases. Liver cirrhosis develops in 20-30% of chronic infections over the next 20-30years and hepatocellular carcinoma over the next ensuing 10 years in 5-10% cases.^{4,5}

Hepatitis C virus infection affects all age groups, and acute infection in children proceed to chronic infections at the same rate as in adults with vertically transmitted infections becoming chronic in majority of paediatric cases.⁶ There is no effective treatment to prevent transmission from infected pregnant women to their unborn

babies and drugs used to treat viral hepatitis are contraindicated in pregnancy, and till date there is no effective preventive vaccine against hepatitis C virus due to its extensive genetic and antigenic variability which allows the virus to escape immune surveillance and thus causing persistent infection.⁴

The rising global prevalence of Hepatitis C virus with bulk of the disease burden in Africa and its attendant sequelae of chronic liver disease with no preventive vaccine till date makes it a problem of public health significance. Prior to 1990, the predominant mode of transmission documented in children was through contaminated blood products in the United States, but vertical transmission is now the commonest.⁷ There is a dearth of local studies to document similar findings in our environment.

This study was carried out to determine the prevalence of HCV antibodies in paired maternal infant serum and determine risk factors for vertical transmission in a tertiary hospital setting.

Materials and methods

This was a descriptive longitudinal study conducted at the Paediatric, Obstetrics and Gynecology wards and PMTCT clinic of Ahmadu Bello University Teaching Hospital between May 2009 and February 2010. The hospital is located in Zaria, Kaduna state. It maintains 3 comprehensive health centres at Yakawada, Banzazzau and Sabon-Gari and is a referral centre for neighbouring states.

The labour ward records about 50 to 100 deliveries monthly with peak during the months of August to October.

Consecutive babies delivered at or presenting within the first 28 days of life at ABUTH and their mothers were enrolled into the study after obtaining consent from their mothers. Babies who had blood transfusion, scarification, uvelectomy or native circumcision prior to presentation were excluded. Mothers and babies who had positive tests were referred to the adult and paediatric gastroenterology clinics of ABUTH for further evaluation, follow up and subsequent management.

Ethical approval was obtained from the Medical and ethical committee of ABUTH.

Data collection was by administering questionnaires to mothers and laboratory investigations.

The questionnaire included maternal demography, address and GSM phone numbers, present and past pregnancy and delivery history (parity, place and mode of delivery, cord severing instrument feeding option), as well as relevant past medical history (jaundice, blood or blood component transfusion, intravenous drug use, alcohol and dialysis).

All the babies were fully examined, their ages, sex, weight, length and signs like jaundice were sought for and recorded and entered into a proforma.

Five millilitres of maternal venous blood was obtained, allowed to clot and centrifuged. The serum was used for HCV antibody (IgG) using Biomill diagnostic rapid test kit, HIV antibody test using Determine test and serum ALT. 1ml of babies blood was also obtained, centrifuged and serum used for HCV IgM antibody using a 2 step 3rd generation indirect ELISA. The HCV antibody test for both mothers and babies were repeated six weeks after the first test in those who turned up for the second visit.

Data analysis was done using SPSS version 15.0. Results were presented in figures, tables and graphs as appropriate. Students' t-test was used to compare means of normally distributed continuous variables, while differences between proportions were evaluated by the Chi square test. A p-value of less than 0.05 was considered statistically significant in comparative analysis.

Results

A total of one hundred mother-infant pair (including 2 sets of twins) were enrolled giving a total of 100

mothers and 102 babies. Sixty-two (62%) mothers and 63(61.7%) babies completed the study. Five (5%) mothers and 7(6.8%) babies had positive HCV antibody test giving a prevalence of 5% and 6.8% in mothers and babies respectively at enrolment. Only 1 mother out of the five with positive HCV antibody test at enrolment turned up for the second test after 6 weeks and still tested positive.

Out of the 102 babies enrolled, 6(5.9%) died before completion of the study. Two were a set of preterm very low birth weight twins who were on admission in SCBU for problems of prematurity and succumbed. The remaining four died at home as reported by their mothers when they were contacted to be reminded of their second appointment. One was said to have had diarrhoea and the remaining 3 had febrile illnesses with convulsions in one of them.

Seven mothers relocated to far places before due date for second test, nine mothers declined the second test for themselves and their babies while remaining 17 mother-infant pair were lost to follow up despite using means of contacting them including use of GSM numbers and contact addresses given at the time of enrolment.

The mothers ages ranged between 18 and 40 years with 66(66%) in age bracket 26-40 years, with one third of them aged 18-25 years signaling peak reproductive age. Ninety-eight mothers received antenatal care, 89% of the pregnancies were carried to term and the rest were preterm deliveries. Seventy one mothers were breastfeeding their babies and the remaining 29 were on replacement feeds.

One hundred and two babies were enrolled (two sets of twins inclusive) of which 56(55%) were males and 46 were females giving a M: F ratio of 1:0.8. Thirty two male and 31 female babies completed the study accounting for 61.7% of the initial population. Their ages ranged from 4 hours to twenty eight days at enrolment. Twelve babies were preterm and low birth weight, two of which were very low birth weight and six were macrosomic. The birth weights ranged between 1.4kg and 4.5kg with a mean of 3kg±0.56.

One mother became widowed 2 weeks prior to delivery and one also got divorced also during the course of the pregnancy. Eighty two mothers were in monogamous marriages and 18 were in polygamous settings. Four out of five mothers with positive antibody test were in monogamous while the fifth was in a polygamous setting. There was no statistical significant association between being married and maternal HCV infection. ($\chi^2=0.107$ df=2, p=0.948)

Eighty six mothers were in their first marriages, 13 in second marriages and 1 was in her 3rd marriage. Four out of 5 mothers with a positive HCV antibody test were in their first marriages while the fifth was in her second marriage. The only mother with a positive HCV antibody test both at enrolment and follow up was in her first marriage and in a monogamous setting. The remaining 4 mothers did not turn up for the second test. There was no significant statistical association between

order of marriage and maternal HCV infection.

Marital status, type and order of marriage might reflect multiplicity of sexual partners which is a route of acquisition of HCV infection in mothers.

Twelve mothers had a positive history of jaundice, one was still jaundiced at the time of enrolment but she was negative for the HCV antibody test both at enrolment and at the second test. Two out of the remaining eleven had positive HCV antibody test at enrolment but did not turn up for the second test. The remaining nine were negative for HCV antibody test at enrolment, six of them took the second test and remained negative. The remaining three were lost to follow up. The mother with positive antibody test at enrolment and follow up had no prior history of jaundice. There was no statistically significant association between history of jaundice and maternal HCV infection. ($X^2=3.97$ $df=1$, $p=0.050$). Table 1

Table 1: relationship between history of jaundice and maternal HCV positivity

	HCV Positive	HCV Negative	Total
Jaundice			
Yes	2	10	12
No	3	85	88
Total	5	95	100

Five out of the 100 mothers enrolled gave a history of receiving blood transfusion in the preceding 6 weeks to 10 years prior to enrolment. All five of them and the two of them that turned up for the second test were negative for HCV antibodies. All five mothers with positive test had no prior history of blood transfusion. History of blood transfusion was not associated with increased risk of maternal HCV infection ($X^2=0.336$, $df=1$, $p=0.562$). Insert table 2

No new infection was documented during the follow up period.

Table 2: General characteristics of mothers

Characteristic	Frequency	(%)
<i>Marital status</i>		
Married	98	(98)
Divorced	1	(1)
Widowed	1	(1)
<i>Parity</i>		
Primipara	30	(30)
Multipara	63	(63)
Grandmultipara	7	(7)
<i>Age</i>		
18-25 Years	34	(34)
26-40 Years	66	(66)
<i>History of blood transfusion</i>		
Yes	5	(5)
No	95	(95)
<i>Alcohol consumption</i>		
Yes	2	(2)
No	98	(98)
<i>Indiscriminate use of sharp objects</i>		
Yes	4	(4)
No	96	(96)

In this study, 5 out of 100 mothers enrolled had positive HCV antibody test. The babies of three mothers out of the five with positive antibody test at enrolment had positive IgM antibody test (3 mother infant pair out of 5 mothers with positive HCV antibody and positive Ig M antibody respectively at enrolment) suggesting a vertical transmission rate of 60%. Only one of the 5 mothers turned up for the second test and still tested positive but her babies (set of twins who were also positive at enrolment died before due date for the second test, one other baby remained positive, while the 4th tested negative at second test and remaining three were lost to follow up (table 3)

Table 3: Maternal versus baby HCV status at enrolment and follow up

S/No	Enrolment		Follow up	
	Mother	Baby	Mother	Baby
1	Positive	Negative	LFU	LFU
2	Positive	Positive	Positive	Died
		Positive		Died
3	Positive	Negative	LFU	LFU
4	Positive	Positive	LFU	LFU
5	Negative	Positive	LFU	LFU
6	Negative	Positive	Negative	Negative
7	Positive	Positive	LFU	LFU
8	Negative	Positive	Negative	Positive

LFU (Lost to follow up).

Five out of the seven babies with positive IgM antibody test were being breastfed and the remaining two were on formula feeds. Three babies with positive test (set of twins inclusive) were being breastfed were born to mothers with a positive test .however there was no statistical significance between breastfeeding and HCV infection in the babies

Five mothers had raised serum ALT levels but none of them was HCV antibody positive, whereas all five mothers with positive HCV antibody had normal serum ALT levels.

Discussion

The prevalence of HCV infection in this study was 5% and 6.8% in mothers and their babies within 28 days of delivery respectively. The prevalence in mothers is similar to findings of 5% in Benin city⁸ and 6% in Maiduguri⁹ among pregnant women. It is comparable to 5% and 4.3% in Tanzania¹⁰ and Democratic Republic of Congo⁸ respectively. A lower prevalence of 0.4% in Calabar⁸, 1.6% in Abuja¹¹. And 1.8% in Cameroun¹², an immediate neighbouring country was reported.

In contrast a higher prevalence of 9.2%¹³ was found in South-Western part of Nigeria where up to 90.8% of the mothers had traditional facial scarification marks suggesting percutaneous transmission. Egypt had the highest documented prevalence in pregnancy of 19%¹⁴.

The higher rates found in this study and other studies above the global prevalence of 3% may be a reflection of high burden of the infection in Sub-Saharan Africa

with Nigeria being the most populous in the region. Other possible explanations for the differences may be due to peculiarities of transmission routes which can be affected by sociocultural practices, low risk of sexual route of transmission and varying rates of intravenous drug use in different regions. Intravenous drug use was found to be notably high in Egypt and other developed countries.

The Five mothers with positive test were aged between 22-36years. This is in conformity with documented high prevalence noted in women in reproductive age bracket as reported in Abuja¹¹, Maiduguri⁹ and Benin⁸ in age groups 15-20years, 20-29years, and 30-34years respectively. A study among healthy female Pakistani university students found a prevalence of 5.2%¹⁵ which also reflects women in childbearing age group. A high prevalence of 13.2 %¹⁶ was reported in an apparently healthy population in Keffi Nasarawa State. These findings further corroborate the asymptomatic or subclinical nature of acute HCV infection.

The prevalence of 6.8% among newborns in this study was higher than 1.1 % obtained in newborns in South-western Nigeria, but comparable to 9% among Egyptian newborns. A rate of 1.6%¹⁷ was reported in Pakistani children aged between 1-5years, and 0.4%¹⁸ in American under 12s. The lower prevalence rates among the Pakistani and American children compared to findings in this study in newborns may be due to spontaneous resolution of some acute infections over time as documented in studies where children were followed up for long periods with resultant loss of HCV antibodies and negative viral antigen detection tests where earlier tests had been positive.

The variation in prevalence rates between mothers and their babies may also be due to the difference in the diagnostic tests used. IgM antibody assay used for the babies tends to rise earlier in acute infections and thus earlier detected than IgG antibody detection which was used in mothers. It may also be possible that the mothers might have recovered from their own acute infection while the infection in babies persisted as in most perinatally acquired infection progressing to chronic infections.

Vertical transmission rate in this study was 60%. Some previous studies found a rate of 5%^{6,19}. A study from South-western Nigeria found 12%¹³ while no case of vertical transmission was reported in a Camerounian study where 76% of the mothers had detectable HCV RNA and 6.7% of the mothers had HIV co-infection¹². Favourable outcome of pregnancy and low rate of HCV transmission may be explained by the endogenous production of interferon (alpha, beta, gamma) as described in the placental environment. The finding in this study may be due to the small number of HCV positive mother infant pair (3 out of 5). This number can be said to be too small for meaningful deduction.

Another Egyptian study documented a vertical transmission rate of 47.4%¹⁴, and 74% of the mothers had detect-

able HCV RNA denoting another risk factor for vertical transmission as has been shown by previous studies. In this study, 2 out of the 7 babies with positive IgM were born to mothers who had negative HCV antibody test, but one of the mothers had elevated serum ALT which reflects active viral replication and viremia which is another risk factor for vertical transmission. The discordance between mother and baby could be due to false positive result in the baby. Additionally the algorithm for diagnosis for HCV infection states that positive antibody tests should be confirmed by supplemental confirmatory tests like RIBA or qualitative HCV RNA detection to rule out false positives, the rate of which varies depending on the prevalence of the infection in any given population. Supplemental tests were not done in this study.

Other risk factors for acquisition of HCV infection are percutaneous exposure to blood and blood products prior to 1990(ref20). None of the 5mothers with prior history of blood transfusion were positive for HCV antibody test, however they were all transfused between 1999 and 2009 when screening kits for HCV had become available and risk of transmission said to have been reduced to about 1 in 100,000. Blood transfusion was also not a significant risk factor for maternal HCV in this study and studies by Mbotto et al¹⁰ and Bassey et al¹¹, it was however found to be a key risk factor for maternal HCV infection in a study in Egypt¹⁴ within the same time frame. Other risk factors for the Egyptian study included raised serum ALT and parenteral treatment for schistosomiasis¹⁴. The history of blood transfusion and parenteral treatment for schistosomiasis in the Egyptian study point to risk associated with percutaneous transmission of HCV prior to identification of HCV and availability of test kits for its diagnosis. Probably repeated studies done later might have shown reduction in rates and even risk factors for its acquisition. Prior blood transfusion and raised serum ALT were not significant risks for maternal HCV infection in this study and others probably because of increased safety of blood transfusion due to screening of donors for risk factors associated with transmission of infectious diseases and availability of highly sensitive and specific test kits for diagnosis of transmissible infectious diseases.

No mother affirmed to intravenous drug use among the studied cohort, and of the four mothers that responded positively to indiscriminate use of injections at patent medicine states for different ailments, none was positive for HCV antibody test both at enrolment and follow up, as opposed to the high prevalence obtained for a similar risk in Egypt due to the now discontinued mass emetine tartar injections for treatment of schistosomiasis with recycled and improperly sterilized syringes in the 70s . The study in Calabar estimated similar risk by obtaining history of female circumcision and sharing blades¹³. It was however not found to be a significant risk for acquisition of HCV infection.

Tribal scarification marks in mothers was not associated

with risk of HCV infection in this study and Calabar study¹⁰.

Heterosexual transmission resulting from multiple sexual partners did not appear to be a significant risk factor for HCV infection as was assessed in this study using marital status, order of marriage and marriage set up. This is in keeping with low risk of sexual transmission documented in two previous studies.

Twelve mothers had a positive history of jaundice of which 2(16%) had positive HCV antibody test. Two out of 7 babies with positive test were born to mothers who had prior history of jaundice, one of the mothers had HCV/HIV co-infection. Maternal history of jaundice was not a statistically significant risk factor for both maternal HCV infection and its vertical transmission in this study.

Conclusion

This study has been able to establish maternal to child transmission of HCV in our community Zaria. This is of public health significance. There is the need for more public enlightenment programmes about HCV acquisition routes, prevention, and integration of screening for HBV

and HCV into routine antenatal care services.

Larger multicenter studies should be conducted to compare and identify risk factors for maternal HCV infection and its vertical transmission.

Authors Contributions

Abdullahi FL: Planning, literature search, data collection, analysis writing of the manuscript

Yakubu AM: Revised the manuscript and supervised the conduct of the study.

Mukhtar HM: Review of drafts of the manuscript and supervision.

Conflict of interest: None

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