Vertical transmission of hepatitis C virus in low to middle socio-economic pregnant population of Karachi

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Abstract

Purpose To determine the rate of vertical transmission (transmission from mother to child) of hepatitis C virus in low to middle socio-economic pregnant women.

Methods This study was conducted at Sarwar Zuberi Liver Centre (SZLC) in collaboration with the department of Gynaecology and Obstetrics, Civil Hospital Karachi (CHK) and Abbasi Shaheed Hospital (ASH) for a period of 4 years from September 2005 to December 2009. Total 18,000 women seeking antenatal care were screened for hepatitis C antibodies (Anti-HCV) using 4th generation ELISA technique. Positive 1,043 women were further offered HCV ribonucleic acid (RNA) by polymerase chain reaction (PCR). Six hundred and forty women agreed to have PCR done, and 510 PCR positive women were finally included in the study, followed till delivery and treated if required. Newborns of 510 PCR positive mothers were advised HCV-RNA by PCR from 3 to 12 months of age and Anti-HCV at 18 up to 24 months and followed up to 3 years.

Results 1,043/18,000 (5.79%) mothers were Anti-HCV positive, of which PCR results of 640 mothers are available where 510/640 (79.7%) were PCR positive, 357/510 (70%) delivered by spontaneous vaginal delivery (SVD), 33 (6.4%) by forceps delivery, 70 (13.7%) had elective, and 50 (9.8%) had emergency caesarian section. Premature rupture of membranes (PROM) was present in 81 mothers. Data of 510 babies from 3 months to 3 years of age was available of which only 215 had their laboratory tests done (HCV-RNA-PCR in 86 and Anti-HCV in 129). Mean birth weight (kg), height (cm) and OFC (cm) were 2.74 ± 0.43 , 52.4 ± 7.5 , and 35 ± 4 . Apgar score median at 1 and 5 min was 7 (range 2–10), 8 (range 4–10), respectively. Low birth weight was present in 49 (9.6%), 37 (7.2%) had history of Neonatal Intensive Care Unit (NICU) admission. PCR of none of the 86 babies done at 3–12 months was positive. Five babies out of 129 were Anti-HCV positive at 18 months of age. Of this, 3/5 was HCV-RNA-PCR positive. Rate of vertical transmission of HCV was 1.39.

Conclusion In spite of the high hepatitis C positivity in pregnant population, the rate of vertical transmission to the neonate is low.

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Introduction

Hepatitis C virus (HCV) infection is an important cause of chronic liver disease (CLD) accounting for an estimated 40% of cases in developed countries [1] and is a major public health problem in the developing world. World Health Organization (WHO) estimates worldwide HCV carriers to be 130 million [2]. According to a report

recently published by the National Health Survey of Pakistan, conducted by the Pakistan Medical and Research Council (PMRC), the prevalence rate of HCV in our population is approximately 4.9% [3]. This rate is increasing steadily due to the unavailability of a vaccine and our inability to curtail the risk factors involved in the spread of infection. The risk factors for transmission of infection have been identified previously [4]. As HCV is one of the blood-borne infections, like hepatitis B virus (HBV) and human immunodeficiency virus (HIV), so a possibility of vertical transmission cannot be ruled out [5]. Several studies have shown the transmission from mother to baby in the womb or during the process of birth and this risk of perinatal infection for HCV was documented to range from 3 to 15% in different populations [2]. This transmission was believed to occur in utero, as a consequence of a high viral load in mother [2, 6, 7].

Other international data suggest that perinatal transmission of HCV occurs at the time of birth in about 5% of infants born to HCV antibody (Anti-HCV) positive women almost exclusively from mothers who are HCV-RNA positive [8, 9]. A study from Canadian Paediatric society documented the rate of transmission of chronic HCV infection from pregnant women to their infants to be approximately 5% but also states that 25% of infected infants will clear the virus spontaneously [10]. This spontaneous clearance of infection is also supported by other studies [11] where HCV genotype is not known to influence the transmission risk [7].

Overall seroprevalence of HCV in the paediatric population from 12 to 18 years is 0.4%. The prevalence of HCV antibody positivity in our antenatal population is estimated at around 4–6% [12].

Vertical transmission of HCV in babies can be detected either by HCV-RNA-PCR at 3 months of age onwards or by Anti-HCV (ELISA) from 18 months onwards [13, 14]. Universal screening of newborns and mothers is not recommended by majority of the clinicians but some centers recommend screening of all mothers and newborns for the transmission of viral hepatitis routinely [15]. Considering our scenario where prevalence rate for this infection in general population is 4.9% [3], we decided to conduct this study on HCV-RNA positive mothers and their newborns, the objective being to determine the rate of vertical transmission in our cohort of patients from low-middle socioeconomic population of two tertiary care centers, Civil Hospital Karachi (CHK) and Abbasi Shaheed Hospital (ASH).

Patients and methods

Multicentre observational study was undertaken involving Sarwar Zuberi Liver Centre (SZLC) and Department of

Obstetrics and Gynaecology CHK, Dow University of Health Sciences (DUHS) and ASH, Karachi Medical and Dental College (KM&DC). The study was started in September 2005. A total of 18,000 pregnant women from low to middle socioeconomic group (which was defined on the basis of monthly income from less than Rs. 5,000 (\$ 60) up to Rs.15,000 (\$ 180), Kacha (huts) or Pakka (cemented) house, ownership of house) seeking antenatal care at the out-patient department of CHK and ASH were screened for viral hepatitis B and C. Initial screening was performed using the 4.0 generation ELISA assay (DiaSorin S.p.A. 13040 SALUGGIA (VERCELL)–ITALY CE Marked). Patients who were positive for Anti-HCV were further tested for HCV-RNA-PCR (HCV Qualitative) by QIAamp Viral RNA Extraction and Qiagen HCV RG RT-PCRvkit from Qiagen GmbH, Qiagen Strasse 1, D-40724 Hilden (CE, IVD Marked) using Rotor-Gene 6000 Instrument of Corbett Life Sciences, and included in the study. Out of 1,043 Anti-HCV positive women, 640 agreed to have their HCV-RNA-PCR done. HCV viral load of the mothers was also done when available. PCR positive 510 mothers were finally included in the study. Those women with co-morbidities, such as HBV infection (by screening for HBsAg on 4th generation ELISA), thalassemia minor (ruled on Hb electrophoresis), diabetes mellitus (DM) ruled by fasting and random blood sugar levels, hypertension (ruled by history or continuous monitoring) or previous history of interferon therapy for treatment of HCV were excluded. Spouse of patient who was HCV-RNA-PCR positive was also screened for Anti-HCV and HBsAg.

Babies ($n = 510$) of HCV PCR positive mothers were enrolled but only 215 babies were screened as parents did not allow the remaining babies to be screened. They preferred to have the screening done after 3 years of age. Of those parents who agreed 86/215 had HCV-RNA-PCR done at the age of 3–12 months and 129/215 had HCV antibody. Mothers and their babies were followed and given treatment if indicated according to the American Association for the Study of Liver Diseases (AASLD) guidelines [16–18].

Labour details were documented including duration and premature rupture of membranes (PROM), mode of delivery, birth weight, gender and Apgar score. Mothers were encouraged to breastfeed for a minimum period of 6 months as breastfeeding is not a source to transmit the infection [19]. Newborns were followed at recommended intervals of 6, 12, 18 and 24 months. All 510 PCR positive mothers and only 215 babies could be followed to the end of the study.

Data were analyzed using SPSS version 10.0. Means and standard deviation were obtained for age, gender, height, weight, and OFC.

Results

The age range of pregnant women was from 18 to 45 years (mean 27.6 ± 5.25 SD).

A total of 18,000 antenatal patients were screened for HCV antibody. Anti-HCV positive women were 1,043 (5.79%). HCV-RNA results of 640 delivered patients collected of which 510 (79.7%) were positive (Table 1). HCV-RNA qualitative done in our cohort of patients had a lower detection limit of 80 copies/ml by real time and the viral load in mothers done ranged from 584 to 1,70,00,000 copies/ml.

Out of the data of 510 PCR positive delivered patients, a majority of 357 (70%) had delivered by spontaneous vaginal delivery (SVD), 33 (6.4%) by forceps delivery, 70 (13.7%) had elective, and 50 (9.8%) had emergency caesarian section. Out of 510 babies, females were 285 (55.8%), rest were male babies. The mean birth weight (kg) was 2.74 ± 0.43 SD, height (cm) 52.4 ± 7.5 SD, OFC, 35 ± 4 SD. Apgar score median at 1 and 5 min was 7 (range 2–10), 8 (range 4–10), respectively.

Table 2 shows the newborn details. Newborns/babies with low birth weight were 49, of which 37 had history of Neonatal Intensive Care Unit (NICU) admission due to reasons other than viral hepatitis. The anthropometric and clinical data of 510 babies are presented. However, laboratory tests of only 215 babies could be done due to the reluctance of parents to have their children tested. HCV-RNA-PCR at age of 3–12 months was done in 86 whereas 129, at 18–24 months had there Anti-HCV done. Anti-HCV done in 129/215 babies of which only 5/129 (3.87%) babies were HCV antibody positive at the age of 18 months. Of these, five Anti-HCV positive babies, three were HCV-RNA-PCR positive by real time with a low viral load ranging between 80 and 150 copies/ml. HCV-RNA-PCR was done in 86/215 babies, at 3–12 months of age and none were positive. Overall 3 out of 215 babies were HCV-RNA-PCR positive (1.39%).

Table 1 Maternal data of 18,000 pregnant women from low to middle socio-economic tertiary care hospital screened for HCV and vertical transmission to baby

	<i>N</i>	(%)
Anti-HCV positive	1,043/18,000 ^a	5.79
HCV-RNA-PCR + ve	510/640 ^b	79.7
Vertical transmission rate ^c	3/215 ^d	1.39

^a 18,000 women were screened in 4 years

^b Women agreed to have PCR done

^c Rate number of persons experiencing a particular event during a given period/the number of persons who are at risk of experiencing the particular event during the same period $\times$ 100

^d Number of babies tested

Discussion

HCV positivity has been reported in approximately 1–4% pregnant women [20] and vertical transmission has been estimated to approximate 5% of population [21]. WHO estimates rate of vertical transmission to be 3–15% in different populations and exclusively in HCV-RNA-PCR positive mothers [2]. The transfer of HCV from mother to child is almost invariably restricted to children whose mother is viremic, and the rate of transmission seems to be influenced by maternal viral load [6, 7]. More recent reports have continued to confirm clearly that maternal viral load is a key determinant for vertical transmission, regardless of maternal HIV status [8, 9]. We conducted this study in two different settings to determine the rate of vertical transmission in our middle to low socioeconomic pregnant population. In our study, maternal age ranges from 18 to 40 years whereas, children from 3 months to 3 years were included.

Determining the rate of vertical transmission of HCV is complicated due to the inconsistent criteria for defining infection in young children. A previously published local data from Islamabad, Pakistan showed the prevalence of HCV in pregnant women to be 6%. In the study, 13/18 women (72%) were PCR positive but rate of vertical transmission was not analyzed [22]. These figures are similar with our study except that we tried to analyze the rate of vertical transmission also by applying the formula for rate which includes the number of persons experiencing a particular event during a given period/the number of persons who are at risk of experiencing the particular event during the same period.

As suggested by various other studies, children born to Anti-HCV positive mothers should be screened at 18–24 months of age and when the mother is HCV-RNA-PCR

Table 2 Outcome of babies born to HCV-RNA-PCR positive mothers from low to middle socioeconomic population at two tertiary care hospitals of Karachi

Characteristics (<i>n</i> = 510*)		
Mean birth weight (kg)	2.74 ± 0.43	
Mean birth height (cm)	52.4 ± 7.5	
Mean OFC (cm)	35 ± 4	
Babies screening results (n = 215 [†] /510)		
Anti-HCV (age 12 months or >)		
(<i>n</i> = 129/215)	Positive	Negative
	5	124
	(3/5 were HCV-RNA-PCR +ve)	
HCV-RNA-PCR (up to age of 3 months)		
(<i>n</i> = 86/215)	0	86

n number, *kg* kilogram, *PCR* polymerase chain reaction

* Total number of babies of HCV-RNA- PCR +ve mothers

[†] No. of babies who allowed laboratory screening

positive, a single HCV-RNA test of the baby at a minimum of 3 months of age is recommended because it is a very sensitive and specific test [14]. Our study so far shows HCV-RNA-PCR positivity in only 3 out of 215 (1.39%) infants of HCV-RNA-PCR positive mothers. The rate of vertical transmission in our study comes out to be 1.39 per year.

All mothers in our study were encouraged to breastfeed their babies for at least a period of 6 months after which weaning was started and mothers were put on treatment for HCV if the repeat HCV-RNA-PCR was positive and genotype was determined. Multiple observational studies have proved that breastfeeding is safe and not an additional risk for infection transmission [8, 17].

In our study, majority of the women had uneventful normal vaginal delivery; follow up of the infants showed only five anti-HCV positive and three HCV-RNA-PCR positive cases. These children include babies from 3 months to 3 years of age. Further studies are needed to document and support this data to set the national guidelines for prevention, screening, and treatment of HCV amongst pregnant women and their newborns. However, HCV positive women should bear children, contrary to popular beliefs, but if there is a possibility, they should plan their pregnancy after HCV therapy.

Conclusion

Rate of vertical transmission of HCV infection in low/middle socioeconomic population presenting at a tertiary care hospital of Karachi, Pakistan was 1.39, suggesting that vertical transmission of HCV is not a major route of HCV infection in our population despite high PCR positivity rate in pregnant population.

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