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Original Article

Mother to Child Transmission of Hepatitis C Virus in Asymptomatic HIV Seronegative Pregnant Females of Malwa Region of Punjab (North India)

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ABSTRACT

***Background*:** Study reports on the transmission of HCV infection from mother to child are limited in India and almost lacking from Punjab (Malwa region), where the infection is reported to be on the rise.
***Aim*:** To determine the rate of perinatal transmission in asymptomatic HIV seronegative pregnant females of Malwa region of Punjab.
***Methods*:** In this prospective follow up study, a total of 829 of the 841 consecutive healthy pregnant females who were negative for antiHIV antibodies and HBsAg were tested for antiHCV antibodies by third generation ELISA. HCV seropositive females were further tested for HCV-RNA by RT-PCR. Babies born to viraemic mothers were tested for the presence of anti HCV antibodies and HCV-RNA at birth, at 6 months and at 12 months of age.
***Results*:** Out of 829 pregnant females, 35 (4.22%) were positive for antiHCV antibodies and of these 35, 17 (48.58%) had detectable HCV-RNA. Of the 17 babies born to HCV viraemic mothers, 5 (29.4%) were positive for antiHCV antibodies and 3 (17.64%) for HCV-RNA at birth. Only one of these three, could be followed till 12 months of age and remained positive for both antiHCV antibodies and HCV-RNA. This gave the rate of perinatal transmission as 5.88% (1 of 17) among HCV-RNA positive pregnant females. Among the study of risk factors, history of unsafe therapeutic injections was observed as a statistically significant ($p<0.0001$).
***Conclusion*:** 5.88% rate of perinatal transmission of the present study shows that this is not an uncommon route of transmission of HCV in Malwa region of Punjab. However, more studies are urgently needed to know the exact extent and other aspects of this route of transmission to prevent further spread.

KEYWORDS: Hepatitis C virus, asymptomatic pregnant females, perinatal transmission, mother to child transmission, unsafe therapeutic injections.

Introduction

HCV infection is a serious global health problem with an estimate of more than 170 million carriers worldwide who are at risk of developing liver cirrhosis and / or hepatocellular carcinoma[1,2]. The principle route of transmission of HCV is exposure to contaminated blood / blood products. Perinatal transmission is one of the less common modes of acquiring HCV infection[2-4]. With the availability of effective screening methods for the detection of HCV, transfusion associated HCV infection in children have almost completely disappeared. Consequently, mother to child transmission has become the most important mode of spread of HCV infection in children[3-5]. The reported rate of thistransmission ranges between 0-37% among the children born to asymptomatic antiHCV positive mothers[3,5-7]. In France, it was estimated to be less than 6% and in Egypt it was as high as 36%[6]. Not many studies on this subject have been conducted in India. A study from South India reported the transmission to 11.1% and from North India to 25% children born to HCV seropositive mothers[3,5]. We studied the rate of perinatal transmission in an area of North India (Malwa region of Punjab) where HCV infection is reported to be on the rise and adequate information on the subject is lacking[8,9].

Material and Methods

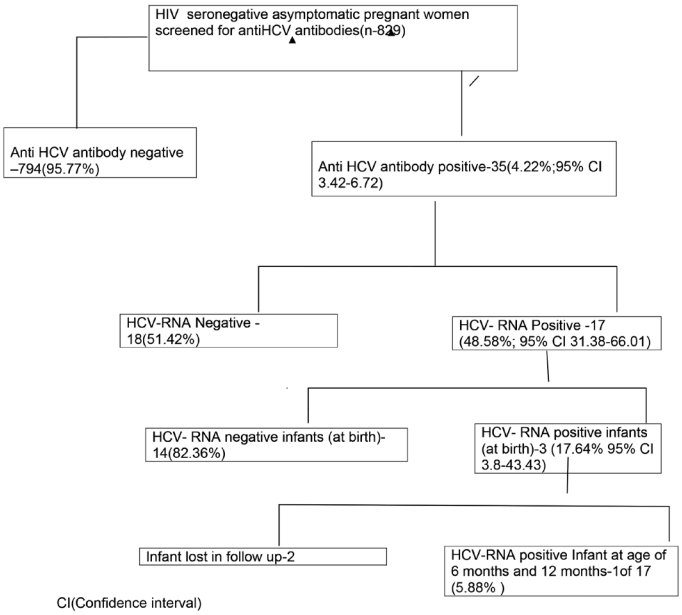
A total of 841 healthy pregnant females who attended the Department of Obstetrics and Gynecology of our tertiary care hospital during the period February 2014-January 2015 were tested for antibodies against HIV1 and 2(Microlisa-HIV ELISA- J Mitra and co.) and HBsAg (SD HBsAg ELISA 3.0-SD Biostandard diagnostics) after taking their written consent. Out of 841, 829 who were found to be negative for antiHIV antibodies and HBsAg were enrolled in the study.Anti HCV antibodies in these females were detected by third generation ELISA (HCV ELISA- J Mitra and co.). The initially reactive samples were retested in duplicate and were considered ELISA positive if at least two of the three were reactive. TheHCV status, sociodemographic characters and clinical history of these females were recorded. The HCV seropositive pregnant females were further tested for HCV-RNA by RT-PCR(HCV-Real-TM-Sacace biotechnologies) and followedtill the birth of their babies. The babies were tested for anti HCV antibodies andHCV-RNA (by RT-PCR) at birth (within 3 days of birth) and at 6 months and 12 months of age. The study was approved by the Institutional Ethical Committee.

Statistical Analysis:Data was compiled and analyzed with appropriate statistical test using SPSS version 22.0 (2013,Armonk,NY)

Results

Design and follow up of the study are shown in **figure 1**. Out of the 829 antiHIV antibody and HBsAg negative asymptomatic pregnant females, 35 were found to be positive for antiHCV antibodies which gave the prevalence of antiHCV as 4.22% (95% CI3.42-6.72). Among these 35 females, HCV-RNA was detected in 17 (48.58%; 95% CI 31.38-66.01). **Table 1** shows the age and risk factor profile of HCV seropositive (group 1) and seronegative (group 2) females. The majority of these pregnant females were in the age group of 20-25 years and the age range of the two groups was comparable (p=0.98 **table 1**).The analysis of risk factors revealed that the use of unsafe therapeutic injections was the only identifiable risk factor which

Figure 1:



played statistically significant role in the transmission of HCV (both for antiHCV positivity (p <0.0001-**table 1**) and HCV viraemia i.e. HCV-RNA positivity (p=0.0059-**table 2**). The viral load in the HCV-RNA positive mothers ranged between 4650 to >50,000 IU/ml. Of the 17 babies born toviraemic mothers, 5 (29.4%) were found to be positive for antiHCV antibodies and 3 (17.6%) for HCV-RNA at birth. Only one of these three, could be followed

Table 1: Age and Risk factor profile of HCV seropositive and seronegative pregnant females.

Age and Risk Factors	HCV seropositive (n=35)	HCV seronegative (n=794)	p value	Odds ratio
Mean age	25.49+3.89 years	25.75+ 4.31 years	0.98	
Blood transfusion	0	25 (3.14)	0.61	-
Dilatation and curettage	1 (2.86)	18 (2.26)	0.81	1.26
Abortions	2 (5.71)	70 (8.81)	0.52	0.628
Still births	0	2 (0.25)	1	-
Previous Deliveries	13 (37.14)	377 (47.48)	0.23	0.653
Surgeries	10 (28.6)	312 (39.29)	0.20	0.617
Dental Treatment	4 (11.43)	70 (8.81)	0.59	1.359
Jaundice	5 (14.29)	62 (9.09)	0.36	1.667
Unsafe therapeutic injections	20 (57.14)	42 (5.29)	<0.0001	23.873
Tattooing	2 (5.71)	70(8.81)	0.52	0.628
HCV status of husband / other members of family	2 (5.71)	0	0.27	-

Figures in parentheses represent percentage.
*p <0.05 significant.

Table 2: Risk factors analysis of HCV RNA positive (n=17) and HCV RNA negative (n=18) pregnant females.

Risk Factors	HCV Seropositive (n=35)		p value
	HCV RNA positive (n=17)	HCV RNA negative (n=18)	
Blood transfusion	0	0	1
Dilatation and curettage	1 (5.88)	0	0.48
Abortions	2 (11.76)	0	0.22
Still birth	0	0	1
Previous delivery	7 (41.18)	6 (33.33)	0.73
Previous surgery	6 (35.29)	4 (22.22)	0.47
Dental treatment	2 (11.76)	2 (11.11)	1
Jaundice	4 (23.53)	1 (5.56)	0.11
Unsafe therapeutic injections	14 (82.35)	6 (33.33)	0.005
Tattooing	1 (5.56)	1 (5.56)	0.96
HCV status of husband / other members of family	0	0	0

Figures in parentheses represent percentage.
*p<0.05 significant.

till 12 months of age and remained positive for both antiHCV antibodies and HCV-RNA.The remaining two were lost in the follow up.

Discussion

There is great variability in the antiHCV antibody positivity in the studies conducted on the antenatal women[2,3,5,6]. Although the prevalence of 4.2% observed in the present studyfalls in the range of 0.12-5.8% reported in other epidemiological studies but is higher than that observed in developed countries and some Indian studies[3,5,7,10,11]. This could be attributed to geographical variation, relatively smaller sample size and adequacy and efficacy of the laboratory tests employed. Earlier studies from India have shown no evidence of exposure to any particularrisk factor in substantial proportion of antiHCV positivity in antenatal females[5]. However in our study population,history of unsafe therapeutic injections was observed as astatistically significant ($p<0.0001$) risk factor (**Table 1**). This suggests that parenteral exposure continues to be a major transmission route for HCV infection. According to a status report of HCV infection in India (2014), 38% of infections in India may be attributed to unsafe medical injections and the rate is increasing steadily due to the unavailability of vaccine and our inability to curtail the risk factors[12].

As the transfer of HCV from mother to child is almost invariably restricted to children born to HCV-RNA positive mothers,it is important to know the presence of HCV-RNA in HCV seropositive mothers. In the present study 48.57% (17/35) of the anti-HCV antibody positive females had shown the presence of HCV-RNA. This is slightly lower than that reported in other studies (64-75%) on asymptomatic pregnant females[5,13], but comparable to that of Parthiban *et al* (44.4%) from South India[3]. Risk factors analysis of HCV-RNA positive and negative mothers showed that HCV-RNA positivity was significantly associated with the history of unsafe therapeutic injections. Rest of the risk factors (**Table 2**) did not influence HCV-RNA positivity which is similar to the findings of Kumar *et al*.[11].

Diagnosis of vertical transmission is made by identifying HCV-RNA in the mother and the child. A consensus from the National Institutes of Health recommends that the children are classified as HCV infective if their serum sample is found to be positive for HCV-RNA on at least two follow up visits or antiHCV antibodies at the age of 12 months[14]. In the present study, three of the 17 (17.65%) children born to viraemicmothers were HCV-RNA positive at birth. But unfortunately only one of these three could be tested at 6 and after 12 months of age and continued to show persistent viraemia (presence of HCV RNA and antiHCV antibodies). The child was born by normal vaginal delivery which was not prolonged. As the other two children were lost during follow up, their HCV-RNA and antiHCV antibody status remained unknown. This gave the rate of vertical transmission (with certainty) as 5.8% (1 of 17) among HCV-RNA positive mothers which is less than that reported in the two other Indian studies (25% and 28.6%)[3,5] had all the three children been available for the tests on the follow up visits, the rate of HCV transmission would have been different. However, arecent study from Karachi (Pakistan) which reported antiHCV positivity of 5.79% in pregnant females estimated very low rate of vertical transmission (1.39%)[13]. Such wide variations in the vertical transmission of HCV could be related to differences in the sample size, maternal social status, duration of follow up and the other methodological differences between the studies and the risk factors involved in the transmission of HCV infection. The principle risk factors known to be associated with perinatal transmission are maternal viral load and HIV co infection[4,14]. Our study included only HIV seronegative females and all the three mothers who showed perinatal transmission had high HCV viral load (above 50,000 IU/ml). More recent reports have confirmed clearly that maternal viral load is the key determinant for vertical transmission, regardless of maternal HIV status[5,13].The other risk factors influencing vertical transmission of HCV are mentioned as HCV genotype, mode of delivery and breast feeding. However data collected to this date regarding all these factors is controversia[l5].

There are certain limitations of the present study. Because of financial constraints, we could not

characterise the pattern of genotypes of HCV of the infected mother baby pairs which would have helped to confirm the source of infection in the new born babies. Parthiban et al. revealed the persistent presence of mixed genotypes 1a and 4 throughout the follow up period in the babies born to HCV-RNA positive mothers[3]. Also, because we could not follow all theantiHCV and HCV-RNA positive children till 12 months of age, we are unable to comment on the transient nature of viraemia and antiHCV seroconversion in these children. Both these are well known entities in children born to antiHCV and RNA positive mothers[3,5]. However, the present study confirms that perinatal transmission of HCV is not uncommon in the Malwa region of Punjab. But further studies are needed to know the extent of infection and other aspects of mother to child transmission of HCV in this region where HCV seropositivity is reported to be high in the general population as well as in antenatal females[8,9]. This would help to formulate the national guidelines for screening, treatment and prevention of HCV infection among pregnant females and the children born to them.

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