

Transmission of Anti-HCV from Mother to Infant and its Natural Course

Ijaz-ul-Haque Taseer¹, Shahid Irshad Rao², Athar Razzaq³, Sohail Safdar¹, Ahsanullah Mirbahar¹
PMRC Research Centre¹, Department of Gynecology & Obstetrics², Department of Pediatric Medicine³, Nishtar
Medical College and Hospital, Multan.

Abstract

Background: Anti HCV is transferred from positive mother to her newborn. To prevent this transfer of anti HCV, many health care providers stop the mother from breast feeding and recommend the checking of the newborn for anti HCV. If found positive, they take it as a chronic infection and recommend treatment of the child as soon as possible. Prohibition from breast feeding not only pushes these neonates towards nutritional deficiencies but also make them prone to infections. The testing also stigmatizes the mother and her newborn for life. The literature proves that this antibody transfer is passive and clears in majority of cases without any residual disease. Mother to infant transfer of anti-HCV and its natural course in Pakistani population is not known.

Objectives: To determine the frequency of anti-HCV positivity and its natural course in infants born to anti-HCV reactive mothers.

Subjects and Methods: Anti-HCV reactive mothers were registered from gynecology department and labor room of Nishtar Hospital Multan from 07-10-2010 to 07-04-2011, using non probability purposive sampling. The ALT of mothers was also checked. The babies born to these mothers were checked for anti- HCV by ELISA and ALT at 0 day (at the time of birth) and then at 6, 12, 18 and 24 months using venous blood samples. Data was entered and analyzed using SPSS-11.

Results: Out of 35 anti-HCV reactive mothers; only one had ALT above the upper limit of normal (> 40 IU/L). A total of 35 babies were born to these mothers, out of whom 34(97.1%) were reactive to anti-HCV at the time of birth and only one was non reactive. At 6 months 2 babies had expired and 3 were lost to follow up, leaving 30 babies. Out of these 30 babies 11 became non-reactive and 19 were still reactive for anti-HCV at 6months. At 12 months, all 19 anti-HCV reactive cases became non reactive, indicating passive transfer of antibodies from the mother to these neonates which they lost by 12 months. ALT of all babies except 3 was raised at 6 months (> 40 IU/L) which became normal during the subsequent visits.

Conclusion: Almost all children born to anti-HCV positive mothers were reactive at the time of delivery but they all became non-reactive by the age of 12 months indicating passive transfer of anti HCV from the mother to the neonate.

Key words: Anti-HCV, vertical transmission, pregnant ladies.

Introduction

Almost 2-3% of the world's population is HCV reactive¹. The virus has a high tendency to progress to chronic hepatitis C infection². The overall prevalence of hepatitis C virus in Pakistan is 5% with pockets of high infection in different provinces and subsets of population³. Though most transmission of HCV occurs through a breach in the mucosal membrane or skin but vertical transmission has also been reported in some studies, either in utero, during labor or after birth⁴⁻¹¹. The rate of mother to infant transmission ranges from 0-17 % in mothers who are not co-infected with HIV and from 0-44% in mothers co-infected with HIV^{9,12-19}. Babies born to HCV/HIV co-infected mothers are at four fold increased risk for vertical transmission of HCV¹⁵.

The transmission of HCV mostly occurs when there is high viral load in the mother ($> 10^6$ viral RNA copies per ml)^{14,15}. As viral levels fluctuate therefore it is appropriate that these should be measured during the 3rd trimester¹⁵. Passive trans-placental transfer of anti-HCV IgG antibodies occur from mother to infant¹⁵ which usually disappear within 12-18 months after birth^{9,12,15,20,21}. Babies born to mothers with high viral load, lose anti-HCV antibodies later than those born to HCV RNA negative mothers, therefore it is recommended to delay the HCV testing till 18-24 months of age^{20,21}. Reactive anti-HCV with negative HCV RNA in a child indicates past exposure while positive HCV RNA and raised ALT on 2 occasions 6 months apart points towards infection^{4,12,15,21,22}.

As there is limited knowledge regarding the natural course of anti-HCV in babies, therefore, the health care providers recommend screening of all babies born to these mothers, and if the infant is found positive the mother is stigmatized and is blamed to be the source of HCV transmission.

The present study was conducted to see whether anti-HCV reactive mothers transmit HCV to their new borns or not and if yes, how long the anti-HCV reactivity lasts.

Subjects and Methods

Using a non-probability purposive sampling technique, all anti-HCV reactive pregnant women coming to the gynecology department and labor room of Nishtar Hospital Multan from 07-10-2010 to 07-04-2011 were registered and included in the study. The participating women were explained about the study and informed written consent was taken. Ethical clearance was obtained

Corresponding Author:

Ijaz-ul-Haque Taseer
PMRC Research Centre
Nishtar Medical College and Hospital
Multan.
Email: dritaseer@hotmail.com

from Institutional Ethical Review Committee, Nishtar Hospital Multan. All demographic information, anti HCV (ELISA) and ALT levels were recorded on a questionnaire. Babies born to these mothers were also registered and checked for anti- HCV by ELISA and ALT at 0 day (at the time of birth), 6, 12, 18 and 24 months. If two consecutive blood samples of the baby were non-reactive for anti-HCV, the baby was not followed further. Data were entered and analyzed using computer program SPSS-11. Frequencies and percentages were calculated for study variables like past history of hepatitis C, family history of hepatitis C and anti-HCV status of the baby at different intervals.

Results

Data of 35 anti-HCV reactive mothers were entered. Only one mother had a raised ALT (> 40 IU). Previous history of jaundice was present in 06 (17.1%) mothers while family history of HCV was present in 10 (28.5%) mothers. Only 1 husband was anti-HCV positive. Detailed information of mothers and their families is given in Table and Figure.

Table: Information of participating mothers and their families.

Characteristics	Yes n(%)	No n(%)	Total
Family History of HCV	10(28.6)	25 (71.4)	35
HCV Status of Husband	1(2.9)	34 (97.1)	35
History of Jaundice in mother	6(17.1)	29 (82.9)	35
Any other child with HCV	1(2.9)	34 (97.1)	35

Out of 35 babies born to these mothers, 20 (57.1%) were males and 15(42.9%) females. All 35 newborns were tested for anti HCV (ELISA) at birth using venous blood samples and 34(97.1%) were found positive. At 6 months out of 35 cases, 2 expired and 3 were lost to follow up, leaving 30 cases that were again tested for anti-HCV. At 6 months 11(36.7%) infants became anti-HCV non-reactive while 19(63.3%) were still anti-HCV positive. One case that was non-reactive at the time of birth was again non-reactive at 6months therefore this case was labeled as negative and dropped from further testing. Thirty cases were again checked at 12 months including the previous 19 who were reactive at 6 months. Out of 30 cases, 19 became negative and 11 were still HCV reactive. At 18 months all cases became anti-HCV negative therefore the study was stopped and no checking was done at 24 months.

The study showed that maternally transferred passive antibodies were seen in all except one case at birth but all these infants became anti-HCV negative by 12 months. All 35 mothers were tested for ALT levels only one (2.85%) had ALT levels more than 40 IU/L. ALT was tested in all 35 babies at the age of 6 months

and only 3(8.57%) had raised ALT more than 40 IU/L. All the remaining babies including those who had raised ALT levels at 6 months of age showed normal ALT levels during the subsequent visits.

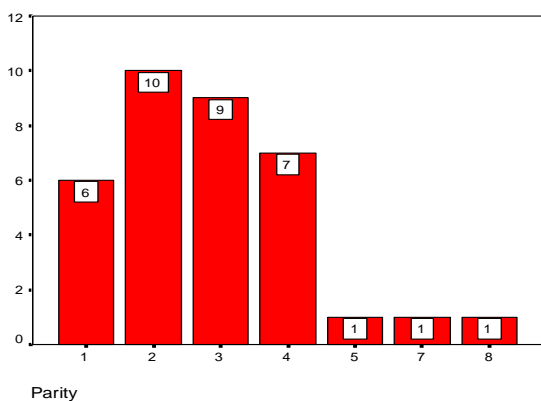


Figure: Parity of the anti-HCV positive mothers.

Discussion

In the present study passive transfer of maternal HCV antibodies was seen in the neonates, which disappeared in all cases by the age of 12 months. Maternal antibodies freely cross placenta and transfer passively from mother to infant. Many studies have been done on the natural course of HCV antibodies in infants born to anti-HCV reactive mothers and almost all have reported that these antibodies are found in all newborns but they usually disappear at 12-18 months of age²⁰. Babies who vertically acquire HCV also clear maternal antibodies during first 18 months of life and develop their own antibodies either after resolution of maternal antibodies or overlapping with it⁹.

Vertical transmission of hepatitis C virus infection has been reported in children especially those whose mother has high viral load ($> 10^6$ viral RNA copies per ml) in 3rd trimester^{4,14,15,23}. The risk is very low in non-viremic mothers⁷.

In present study, 36.6% infants became anti-HCV negative at 6 months and all became negative at 12 months. Ferrero et al reported 37% clearance of anti-HCV at 6 months, 88% clearance at 12 month with few clearing it at 18 months²⁰. England et al reported 57% babies clearing anti-HCV before the age of 6 months and 95% cleared them at 12 months²¹. These results are close to our findings. It has also been reported that clearance of HVC is significantly longer if the mother is has high viral load and is co-infected with HIV but these antibodies are lost earlier if the mother is on HIV treatment^{20,21,24}. The European Paediatric Hepatitis C Virus Network reported vertical transmission rate of 8.3% in HIV co-infected mothers versus 5.5% in non HIV infected mothers (difference insignificant)^{7,9}. Because a significant portion of children spontaneously clear HCV during 1st year of

life therefore early testing may give false positive results and generate anxiety among parents, therefore American Association for Study of Liver Diseases (2009) has recommended that if suspecting vertical transmission, anti-HCV testing may be done at the age of 18 months^{9,25}.

In the present study all the newborns cleared anti HCV at the age of 12 months, therefore as recommended earlier by other workers all testing of anti-HCV and ALT for the detection of vertical transmission should be delayed and if required they may be done between 18 to 24 months. Limitations of study were its small sample size as we wanted to find out whether this is an issue for our population and if yes to what extent. HCV RNA testing was not done due to financial constraints.

Acknowledgement

We are thankful to Pakistan Medical Research Council, Islamabad for funding this project under Research grant No. 4-11-1/10/HPA/RDC/NMC, Multan. We are grateful to all staff of PMRC Research Centre, Nishtar Medical College, Multan who helped us in this research work, especially Mr. M. Ilyas Qaiser for his efforts in data collection. We are thankful to Gyne Unit III especially Dr. Kiran, Dr. Shumaila, Dr. Reena and Dr. Huda for their support in data collection. We also acknowledge Dr. Yaseen, PGR, Paediatric Unit 1 for his assistance. Authors also acknowledge the parents who gave their consent for participation and who co-operated us during follow up of the study.

References

1. Dusheiko G. Hepatitis C. In: Dooley JS, Lock ASF, Burroughs AK, Heathcote EJ. Eds. *Sherlock's diseases of the Liver and biliary system*. 12th ed. 2011. P. 406-26.
2. Mack CL, Gonzalez-Peralta RP, Gupta N, Leung D, Narkewicz MR, Roberts EA, et al. NASPGHAN practice guidelines: diagnosis and management of hepatitis C infection in infants, children and adolescents. *J Pediatr Gastroenterol Nutr* 2012; 54: 838-55.
3. PMRC Report. National survey on prevalence of hepatitis B & C in general population of Pakistan [online] 2007. Available from URL: <http://www.pmr.org.pk/hepatitisbc.htm>.
4. Resti M, Bortolotti F, Vajro P, Maggiore G. Guidelines for the screening and follow up of infants born to anti-HCV positive mothers. *Dig Liver Dis* 2003; 35: 453-7.
5. Indolfi G, Resti M. Perinatal transmission of hepatitis C virus infection. *J Med Virol* 2009; 81: 836-43.
6. Cottrell EB, Chou R, Wasson N, Rahman B, guise J. Reducing risk for mother to infant transmission of hepatitis C virus: a systematic review for the U. S Preventive Services Task Force. *Ann Intern Med* 2013; 158: 109-13.
7. European Paediatric Hepatitis C Virus Network. Three broad modalities in the natural history of vertically acquired hepatitis C virus infection. *Clin Infect Dis* 2005; 41: 45-51.

8. Zuccotti GV, Cucchi C, Torcoletti M, Gemmellaro L, Sala D, Salvini F, et al. Proposal of step wise follow up for hepatitis C seropositive mothers and their infants. *Pediatr Med Chir* 2003; 25: 6-11.
9. University of Washington. [Home page of the University of Washington]. [Online] 2012 May 22 last update. [Cited 2013 April 22]. Available from: URL: <http://depts.washington.edu/hepstudy/hepC/prevention/hcvpnt/discussion.html>.
10. Zuccotti GV, Salvini F, Farina F, Aqostoni C, Riva E, Giovannini M. Longitudinal long term follow up study of children with vertically acquired hepatitis C virus infection. *J Int Med Res* 2006; 34: 215-22.
11. McIntyre PG, Tosh K, McGuire W. Caesarean section versus vaginal delivery for preventing mother to infant hepatitis C virus transmission. *Cochrane Database System Rev* 2006; 18: CD005546.
12. Jara P, Hierro L. Treatment of hepatitis C in children. *Expert Rev Gastroenterol Hepatol* 2010; 4: 51-61.
13. Tajiri H, Miyoshi Y, Funada S, Etani Y, Abe J, Onodera T, et al. Prospective study of mother to infant transmission of hepatitis C virus. *Pediatr Infect Dis J* 2001; 20: 10-4.
14. Powell M, Bailey J, Maggio LA. How should you manage children born to hepatitis C positive women? *J Fam Pract* 2010; 59: 289-90.
15. Robert EA, Yeung L. Maternal-infant transmission of hepatitis C virus infection. *Hepatology* 2002; 36: 106-13.
16. Ogunro PS, Adekanle DA, Fadero FF, Ogungbamigbe TO, Oninla SO. Prevalence of anti-hepatitis C virus antibodies in pregnant women and their offspring in a tertiary care hospital in south western Nigeria. *J Infect Dev Countr* 2007; 1: 333-6.
17. Kazou S. Mother to infant transmission of hepatitis C virus. *Kantansui* 2006; 52 (1): 21-25.
18. Herrine SK, Jefferson T. Mother to child transmission of HCV. The HCV Advocate Medical writers' Circle. April 2006. p1-2 (www.hcvadvocate.org).
19. Syriplulou V, Nikolopoulou G, Daikos GL, Theodoridou M, Pavlopoulou L, Nicolaidou P, et al. Mother to child transmission of hepatitis C virus: Rate of infection and risk factors. *Scand J Infect Dis* 2005; 37: 350-3.
20. Ferrero S, Lungaro P, Bruzzone BM, Gotta C, Bentivoglio G, Ragni N. Prospective study of mother to infant transmission of hepatitis C virus: a 10 year survey (1990-2000). *Acta Obstet Gynecol Scand* 2003; 82: 229-34.
21. England K, Pembrey L, Tovo PA, Newell ML. European Pediatric HCV Network. Excluding hepatitis C virus (HCV) infection by serology in young infants of HCV infected mothers. *Acta Pediatr* 2005; 94: 444-50.
22. Healy CM, Cafferkey MT, Conroy A, Doolely S, Hall WW, Becket M, et al. Outcome of infants born to hepatitis C infected women. *Ir J Med Sci* 2001; 170: 103-76.
23. Parthiban R, Shanmugam S, Velu V, Nandakumar S, Dhevahi E, Thangaraj K, et al. Transmission of hepatitis C virus infection from asymptomatic mother to child in southern India. *Int J Infect Dis* 2009; 13: 394-400.
24. Conte D, Fraquelli M, Prati D, Colucci A, Minola E. Prevalence and clinical course of chronic hepatitis C virus (HCV) infection and rate of HCV vertical transmission in a cohort of 15250 pregnant women. *Hepatology* 2000; 31: 751-55.
25. Ghany M, Strader DB, Thomas DL, Seef LB. Diagnosis, management and treatment of hepatitis C: an update. *Hepatology* 2009; 49: 1335-74.