

Prevalence & risk factors for hepatitis C virus among pregnant women

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Background & objectives: Information on hepatitis C virus (HCV) infection in pregnant women in India is scanty. This study was carried out to investigate the prevalence of HCV within an obstetric population in north India and to identify the various risk factors for the viral infection.

Methods: A total of 8130 pregnant women from antenatal clinic were subjected to anti-HCV testing by third generation ELISA. Anti-HCV positive seropositive women were further tested for HCV-RNA, hepatitis B and HIV. The women were evaluated for the presence of following known risk factors for HCV infection.

Results: Eighty four (1.03%) pregnant females had HCV antibodies. Of these, 46 (54.8%) were positive for HCV-RNA, 4(4.8%) tested positive for HBsAg, while none tested positive for HIV. The mean age and parity of the anti-HCV antibody positive women was 24.36 ± 3.6 yr and 0.9 ± 0.8 , while that of the anti-HCV antibody negative women was 24.13 ± 3.6 yr and 0.8 ± 0.8 respectively. Of the 84 anti-HCV positive women, 52 (61.9 %) did not have any identifiable risk factors. The risk factors variables did not have significant association with HCV positive status.

Interpretation & conclusion: Prevalence of hepatitis C in pregnant women was 1.03 per cent. None of the known risk factors was found to be significantly associated with the HCV infection. Hence case identification and consequent management pose a particular problem and routine screening is not a viable option in our resource- poor setting.

Key words Anti-HCV antibody - hepatitis C virus infection - pregnancy - prevalence - risk factors

Hepatitis C virus (HCV) is one of the major aetiological agents of parenterally acquired hepatitis. HCV infection is asymptomatic in a large proportion of cases (65-75%) and revealed only accidentally by abnormal liver function tests and /or anti-HCV positivity. The long-term morbidity and mortality is far greater than its counterpart hepatitis B in terms of

chronic active hepatitis (70%), cirrhosis (20-30%), hepatocellular carcinoma and liver failure¹. Anti-HCV screening of blood products introduced during the early 1990s has minimized this mode of HCV acquisition, leaving vertical transmission from infected mothers as the predominant mode of infection in children. Approximately 7-8 per cent of hepatitis C virus-positive

women transmit hepatitis C virus to their offsprings with a higher rate of transmission seen in women co-infected with HIV².

The worldwide literature on HCV prevalence has increased considerably over the past decade, yet few surveys have been conducted on national level. Several studies of pregnant women in Europe reported relatively low anti-HCV prevalence when second or third generation ELISAs were used. In an antenatal survey from England, the prevalence of anti-HCV in antenatal clinic attenders in Greater London area and Northern and Yorkshire region was found to be 0.43 per cent (of 25938 women) and 0.21 per cent (of 16675 women) respectively³. The HCV prevalence of 0.38 and 0.20 per cent were seen in inner and outer districts of London respectively⁴. Another UK study of an antenatal population in the West Midlands found an overall HCV prevalence of 0.14 per cent⁵. In a national survey among 30,259 childbearing women throughout Scotland, the HCV seroprevalence was found to be 0.29-0.40 per cent⁶.

Little is known about hepatitis C virus infection in pregnant women in India. The seroprevalence of anti-HCV antibody in the healthy general population of India was found to be 1.5 per cent each in 234 voluntary blood donors and 65 pregnant women⁷. HCV infection was not detected in 250 randomly selected antenatal women in Shimla (Himachal Pradesh)⁸. In our preliminary study, 14 of 1900 (0.73%) pregnant females were tested anti-HCV seropositive⁹. There are no large scale studies on the estimates of the prevalence of HCV infection and risk behaviour of HCV infection in low risk Indian population. We therefore undertook this study to assess the prevalence of HCV infection within an obstetric population attending a tertiary care hospital in New Delhi, India and to determine whether various risk factors for HCV infection could be identified.

Material & Methods

The study recruited a cohort of consecutive 8130 healthy pregnant women at the antenatal clinic of Department of Obstetrics and Gynecology of Maulana Azad Medical College and Lok Nayak Hospital, New Delhi, India (May 2004 to August 2006). Assuming the average prevalence of HCV infection to be 0.2 per cent (based on data available from western countries) and with a precision of 0.04 (20% of true estimate) and at a probability level of 10 per cent, it was estimated that nearly 8000 pregnant women need to be screened. Seventeen women were excluded who declined to

participate (15) or who had liver diseases (2). The characteristics of these 17 women were comparable to that of those included in the study and were not taken for analysis in this paper. The Institute Ethics Committee approved the study. All women attending the antenatal clinic, who gave their consent to participate, were evaluated by a questionnaire. It dealt with detailed demographic characteristics and factors that could put a woman at risk for acquiring hepatitis C. The women with previous liver disease were excluded. Anti-HCV antibodies were detected by commercially available third generation ELISA diagnostic kits (SP-NANBASE C-96 3.0, manufactured by General Biological Corp, Taiwan). The initially reactive samples were re-tested in duplicate and considered ELISA positive if at least two of three results were reactive. All anti-HCV antibody positive samples were tested for HCV-RNA by a reverse transcriptase polymerase chain reaction (RT-PCR). RNA was extracted by using the acid guanidinium-phenol-chloroform method as described by Chomczynski and Sacchi¹⁰. All HCV antibody positive women were further tested for HBsAg, HBcIgG, HBeAg (kits manufactured by General Biological Corp, Taiwan) and human immunodeficiency virus (HIV) by Microlisa-HIV Elisa Kit manufactured by J. Mitra & Co. Pvt. Ltd., New Delhi, India. Each of the HCV positive patients was invited to participate in an interview with the first author (AK) at a subsequent antenatal visit for counselling. Serological results were told to them and they were counseled for the need of further postpartum follow up with the hepatologist.

Data were analyzed using SPSS for Windows version 9.0. (SPSS Inc., Illinios, USA). Univariate analysis for categorical variables was performed using X² and Fisher's exact test. Continuous variables were compared using Student's t-test. The anti-HCV seropositive women constituted the study group whereas anti-HCV seronegative women constituted the controls. $P < 0.05$ was considered significant.

Results

Eighty four (1.03%) of the 8130 pregnant women tested positive for anti-HCV antibodies. Of these, 46 (54.8%) were positive for HCV-RNA by RT-PCR. Among the 84 anti-HCV positive pregnant women, 4 (4.8%) tested positive for HBsAg, while none of these tested positive for HIV.

The mean age of the study group (n= 84, anti-HCV antibody positive) was 24.36 ± 3.6 yr, while that of the control group (n=8046 anti-HCV antibody negative)

was 24.13±3.6 yr. The age distribution of the two groups was comparable with the majority of the patients in either group were in the age group of 21-25 yr (Table I). The mean parity of the study was 0.9±0.8 and that of the control group was 0.8±0.8. The subjects in the control group had a greater range varying from zero to six while that in the study group had a smaller range (0 to 3). Both study and control groups had similar educational qualifications (Table I). There was no significant difference between HCV-RNA positive and negative women in their demographic characteristics,

Among the known risk factors for HCV infection, previous blood transfusions, dilatation and curettage (D&C), previous abortions, acupuncture and tattooing, previous surgery, multiple sexual partners and intravenous drug abuse were studied as independent variables. Of 8130 pregnant women, 257 (3.2%)

received blood transfusion before the index pregnancy, 1114 (13.7%) reportedly underwent D&C, 1270 (15.8%) had history of abortion, 839 (10.3%) had tattoo application and/or acupuncture and 1017 (12.5%) had history of any surgery before the index pregnancy (Table II). None of the women declared that they had multiple sexual partners or ever injected drugs. Of the 84 anti-HCV positive women, 52 (61.9%) did not have any identifiable risk factors. In spite of lack of statistical association among the anti-HCV positive subjects as well as HCV-RNA positive women, a particular trend of risk factors was visible in the studied variables. As none of the known or studied risk factors for HCV positivity came out to be significant on univariate analysis, multivariate analysis was not feasible.

Discussion

This study represents a large-scale, single hospital based report to define the seroprevalence of hepatitis C virus-specific antibodies in an urban population of pregnant women and to evaluate the risk factors in this group. The seroprevalence of hepatitis C antibodies of 1.03 per cent in an antenatal population was similar to the findings of other epidemiologic studies (1-5%)^{1,11-14}.

The highest greatest prevalence of infection occurs among individuals of reproductive age^{15,16}. Age is a known risk factor for hepatitis C infection; seropositivity has been reported to increase until the age 40 and then declines over time¹⁷. This can be explained by the greater probability of exposure of these women to risk factors. In our study of predominantly young pregnant women, the prevalence was found to increase up to the age of 25 but decrease after that. But the lack of association may be due to less number of subjects in the older age group. Leikin *et al*¹⁸ have reported a higher mean parity of HCV positive patients

Table I. Age, parity and literacy status of the pregnant population

Characteristics	Anti-HCV antibody	
	Seropositive (N=84)	Seronegative (N=8046)
Age (yr)		
17-20	14 (16.7)	1377 (17.1)
21-25	43 (51.2)	4414 (54.9)
26-30	23 (27.4)	1869 (23.2)
31-35	4 (4.7)	339 (4.2)
> 35	00 (0.0)	47 (0.6)
Parity		
Nullipara	32 (0.9)	3423 (1.1)
Multipara	52 (99.1)	4623 (98.9)
Literacy status		
Illiterate	22 (26.2)	1897 (23.6)
Upto Metric	40 (47.6)	4438 (55.2)
Upto 12th	9 (10.7)	895 (11.1)
Graduate	11 (13.1)	669 (8.3)
Postgraduate	2 (2.4)	147 (1.8)

Values in parentheses are percentages

Table II. Risk factors analysis in pregnant population

Risk factors	1	2	3	4	5	6	7	8
	HCV positive (N=84)	RNA positive (N=46)	RNA negative (N=38)	P value (2&3)	O.R (95% CI) (2&3)	HCV negative (N = 8046)	P value (1&6)	O.R (95%CI)(1&6)
Blood transfusion	4(4.8%)	3(6.5 %)	1(2.3%)	0.6	2.5(0.2-25.8)	253(3.1%)	0.3	1.5(0.6-4.2)
Dilatation & curettage	12 (14.3%)	8(17.4 %)	4(10.5 %)	0.5	1.7(0.4-6.4)	1102(13.7%)	0.9	1.0(0.6-1.9)
Abortions	12 (14.3%)	8(17.4 %)	4(10.5 %)	0.5	1.8(0.4-5.9)	1270(15.8%)	0.8	0.9(0.5-1.6)
Acupuncture &/or tattooing	04 (4.8%)	2(4.3 %)	2(5.3 %)	1.0	0.8(0.1-6.0)	835(10.4%)	0.1	0.4(0.1-1.2)
Surgery	10 (11.9%)	0	10(26.3%)	-	-	1007(12.5%)	1.0	0.9(0.5-1.8)

O.R, odds ratio
95% C.I = 95% confidence Interval

in their study. Although the mean parity of both the groups was similar, the prevalence of anti-HCV among the multiparous females was more than nulliparous females in our study.

It was found that 54.8 per cent of the anti-HCV antibody positive pregnant women had detectable HCV-RNA in their blood, a figure that is slightly lower than that found in most of the studies (64-75%) on asymptomatic pregnant women^{3,19-22}. The prevalence of HCV-RNA is important for mother to child transmission.

Earlier studies have found an association between the prevalence of HCV infection and the known risk factors of this infection *i.e.*, blood transfusion, intravenous drug abuse, multiple sexual partners, and homosexuality¹²⁻¹⁴. In a study from northern Italy, the principal risk factors were history of intravenous drug abuse (32%) and exposure to blood products (24%). In the same study, 4 and 2.1 per cent of the patients were found to be anti-HIV and HBsAg positive respectively²².

In a study from Pakistan²³ when previous vaginal deliveries with episiotomy, previous surgeries, blood transfusions, and D&C for abortion or dysfunctional uterine bleeding were taken as independent variables, only past history of surgical procedures was found to be the most important factor for transmission of hepatitis C virus infection. It has been reported that in resource-poor countries, the risk of iatrogenic HCV infection is high²⁴. Sexual transmission of hepatitis C virus also probably occurs, although the importance of spread by this route remains unclear. The presence of cosmetic alterations in the form of body piercing or tattooing should be taken into consideration whenever assessing the risk of an individual having HCV antibodies.

The present study showed that a substantial proportion (up to 62%) of women with HCV had no evidence of exposure to any known risk factors in their history. This compares well with the observation that 40 to 73 per cent of the women had no obvious risk factors for HCV infection at the time of booking^{19,22,25,26}. It has been found that selective antenatal screening policy based on risk factors, failed to identify over half of infected patients¹⁹. Moreover, screening of asymptomatic pregnant women for hepatitis C virus infection is not cost-effective²⁷. Routine screening is not recommended currently during pregnancy for asymptomatic women without risk factors for HCV infection^{2,25}.

With a prevalence of the HCV infection equivalent to elsewhere in the world but with no significantly associated risk factor, identification of HCV infection here poses a greater public health problem. In this situation, the modules based on selective screening for high risk factor analysis will fail to identify over half of the infected patients. Therefore, targeted screening is not appropriate and universal screening would present cost constraints especially in resource-poor countries. Further research is necessary to understand the causes and implications of this observation and to give future directions.

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