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Hepatitis C Virus Infection during Pregnancy in Upper Egypt

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Abstract

Background: It is estimated that 150–200 million people, or 3% of the world's population, are living with chronic hepatitis C**.**

Objective: to identify the prevalence of HCV among pregnant women and infants of infected women and detect risk factors and the rate of vertical transmission.

Methods: 3000 births of pregnant women aged between 18 to 43 years were randomized and prospectively screened using HCV antibody and HCV polymerase chain reaction (PCR) analysis to identify the risk of pregnancy on HCV and HCV on pregnancy and the prevalence of HCV among pregnant women and infants of infected women to identify the rate of vertical transmission.

Results: A total of 3000 pregnant women attending perinatal care were screened. Forty four (1. 46%) showed HCV-positive antibodies, vertical transmission (13.6%) and six (0.2%) of

newborns tested positive within the first 24 hours post-delivery. Three-fourth (33/44) of the HCV positive pregnant women had a history of surgical intervention. However, 50% (22/44) had history of Cesarean section and blood transfusion (11/44).

Conclusion: The prevalence of HCV in pregnant women in Egypt is lower than previously reported. Risk factors for transmission suggest that there is a correlation between the age and parity of the studied women and the incidence of hepatitis C infection. Hepatitis C virus infection was found more among those women with past history of previous surgery or blood transfusion. Further studies are needed to explore this issue. Incidence of vertical transmission of HCV in Egypt is not more different than in other countries and it plays no role in the high endemicity in Egyp

Key words: Hepatitis C virus, vertical transmission, pregnant women.

Introduction

It is estimated that 150–200 million people, or 3% of the world's population, are living with chronic hepatitis C. About 3–4 million people are infected per year, and more than 350,000 people die yearly from hepatitis C-related diseases. During 2010 it is estimated that 16,000 people died from acute infections while 196,000 deaths occurred from liver cancer secondary to the infection **(Lozano R. et al., 2012)**.

Rates have increased substantially in the 20th century due to a combination of intravenous drug abuse and reused but poorly sterilized medical equipment.

Rates are high (>3.5% population infected) in Central and East Asia, North Africa and the Middle East, they are intermediate (1.5%-3.5%) in South and Southeast Asia, sub-Saharan Africa, Andean, Central and Southern Latin America, Caribbean, Oceania, Australasia and Central, Eastern and Western Europe; and they are low (<1.5%) in Asia Pacific, Tropical Latin America and North America **(Mohd et al.,2013)**.

Worldwide, the seroprevalance of HCV in pregnant women is thought to be anywhere from 0.15% to 2.4% in the United States and European countries and much higher in countries like Egypt where it is estimated to be as high as 8.6% **(Abdul Qawi et al., 2010)**.

The prevalence of HCV infection in children ranges from 0.05% to 0.36% in studies carried out in the United States and Europe and is much higher in developing countries where it can range from 1.8% to 5%. Insufficient screening of transfused blood and blood products and parenteral exposure continue to be the major causes of HCV transmission in developing countries. In the United States and other developed countries, vertical transmission is the major route of HCV infection. In the United States, an estimated 240 000 children have antibodies to HCV, with seroprevalences of 0.1–0.2% **(Armstrong et al., 2006).**

Patients and Methods:

This prospective study was conducted at AL Azhar University hospital, Assuit to identify the risk of pregnancy on HCV and HCV on pregnancy and the prevalence of HCV among pregnant women and infants of infected women to identify the rate of vertical transmission. The study population included all pregnant women who were admitted at the obstetric department.

The study was done on 3000 patients from March 2014 to June 2015 and the following for each patient was done, Careful history for sociodemographic characteristics (age, education and residence), Obstetric characteristics (gestational age and parity), the possible risk factors (e.g. history of surgery or blood transfusion, tattooing, and circumcision), general examination for: Body weight and height, Vital signs, Lower limbs examination, Abdominal examination and obstetric examination.

Basic investigations: Maternal venous blood samples will be obtained for tests of HCV. Ultrasonography will be done for viability of fetus and congenital anomalies.

Serological testing of infants

Infected patients who tested positive were called back to get a peripheral blood sample from their infants. HCV antibody testing was done first on the infants and then positive HCV antibody samples were tested for HCV-RNA. Infants were considered uninfected if they had never been positive for HCV RNA or if they cleared anti-HCV antibodies after 6 months of age. Infants were

considered to have perinatal mother-to-infant transmission if they were HCV-RNA positive at any time following birth or showed anti-HCV antibodies after 6 months of age. They were considered to have transient perinatal HCV infection if they were positive for HCV RNA at the 6-month visit, but negative for both anti-HCV and HCV-RNA after the 6-month visit. The children continuing to have HCV-RNA after the 6-month visit were considered to have persistent perinatal HCV infections. Anti-HCV antibodies detected in the blood of children whose mothers tested positive for anti-HCV antibodies 2-6 months after delivery were considered to be maternally acquired.

Results

Among 3000 pregnant women screened for HCV Forty four (1.46% prevalence) showed positive antibodies in both ELISA and real time PCR HCV-RNA. All HCV-positive women had a history of surgical intervention and/or blood transfusion. Of total 44 HCV-positive pregnant women, 22 (50%) had underwent cesarean section surgical intervention and 11 (25%) had blood transfusion. A strong statistical significant association ($p<0.001$) was noticed with age, parity, medical diseases, surgical history and blood transfusion for HCV vertical transmission. Among neonates born to HCV-RNA positive women, 6 babies (13.6%) were positive for HCV antibodies and HCV-RNA, of which 4 babies were delivered through cesarean section and other 2 by normal vaginal delivery (NVD).

Table 1: Rapid test, HCV antibody and PCR results of all studied patients (n=3000)

	No.	**%**
Rapid test		
Positive	50	1.67
Negative	2950	98.33
HCV ab		
Positive	47	1.57
Negative	2953	98.43
PCR		
Positive	44	1.46
Negative	2956	98.54

Table 2: HCV PCR of the fetus of all studied patients (n=2800)

Result	No.	%
Positive	6	0.19
Negative	2994	99.81

Table 3: PCR of positive HCV antibody patients (n=44)

	No.	%
High viremi	**5**	**11.4**
Moderate viremia	**15**	**34.1**
Low viremia	**24**	**54.5**

Table 4: HCV PCR of the fetus of positive HCV antibody patients (n=44)

	No.	%
Positive	6	13.6
Negative	38	86.4

Table 5: Maternal Risk Factors for HCV Infection

	HCV antibody				P. value
	Positive (n=44)		Negative (n=2956)		
	No.	%	No.	%	
Age of discovery, Mean±SD	29.8±4.6		26.3±4.5		<0.001**
≤19 years	0	0.0	71	2.37	<0.001**
20-29 years	21	47.7	2179	72.63	<0.001**
30-39	22	50.0	704	23.47	<0.001**
40-49	1	2.3	2	0.07	0.564
Parity					
Nulliparous	1	2.3	384	12.80	0.059
Primipara	3	6.8	593	19.77	0.046*
Multipara	33	75.0	1848	61.60	0.123
Grand para	7	15.9	131	4.37	0.001**
BMI					

	HCV antibody				P. value
	Positive (n=44)		Negative (n=2956)		
	No.	%	No.	%	
Normal	32	72.7	2048	68.27	<0.001**
Overweight	10	22.7	748	24.93	<0.001**
Obese	1	2.3	135	4.50	<0.001**
Morbid obesity	1	2.3	25	0.83	<0.001**
Residence					
Urban	20	45.5	1443	48.10	0.772
Rural	24	54.5	1513	50.43	0.771
Medical disease					
Free	41	93.2	2793	93.10	0.966
Diabetes mellitus	0	0.0	49	1.63	-
Hypertension	1	2.3	72	2.40	0.671
Cardiac	0	0.0	29	0.97	-
Thyroid	1	2.3	11	0.37	0.427
Gall Bladder Stone	1	2.3	1	0.03	0.007**
Anemia	0	0.0	1	0.03	-
Surgical history					
No	10	22.7	2489	82.97	<0.001**
yes	34	77.3	467	15.86	<0.001**
Blood transfusion					
Yes	11	25.0	0	0.00	<0.001**
No	33	75.0	2956	98.53	<0.001**
US in first trimester					
Free	40	90.9	2956	98.53	<0.001**
Fatty liver	3	6.8	0	0.00	-
Mild splenomegaly	1	2.3	0	0.00	-
US in second trimester					
Free	34	77.3	2956	98.53	<0.001**
Fatty liver	6	13.6	0	0.00	-
Mild splenomegaly	4	9.1	0	0.00	-

	HCV antibody				P. value
	Positive (n=44)		Negative (n=2956)		
	No.	%	No.	%	
US in third trimester					
Free	33	75.0	2956	98.53	<0.001**
Fatty liver	6	13.6	0	0.00	-
Mild splenomegaly	5	11.4	0	0.00	-
Delivery					
Cesarean section	22	50.0	0	0.0	-
Vaginal delivery	22	50.0	0	0.0	-

** Statistically significant difference (p<0.01)

Table 6: Relation between mother HCV antibody and child HCV

	HCV antibody				P. value
	Positive (n=44)		Negative (n=2956)		
	No.	%	No.	%	
child HCV					
Positive	6	13.6	0	0.0	<0.001**
Negative	38	86.4	2956	100.0	<0.001**

** Statistically significant difference (p<0.01)

Table 7: characters of +ve and -ve vertically transmitted patients

		HCV PCR of the fetus				P. value
		Positive (n=6)		Negative (n=38)		
		No.	%	No.	%	
Age	20-29 years	2	33.3	19	50.0	0.749
	30-39	3	50.0	19	50.0	0.660
	40-49	1	16.7	0	0.0	0.284
Parity	Nulliparous	0	0.0	1	2.6	0.284
	Primipara	0	0.0	3	7.9	0.874

		HCV PCR of the fetus				P. value
		Positive (n=6)		Negative (n=38)		
		No.	%	No.	%	
	Multipara	5	83.3	28	73.7	0.987
	Grandmultipara	1	16.7	6	15.8	0.585
Abortion	0	5	83.3	21	55.3	0.394
	1	1	16.7	6	15.8	0.585
	2	0	0.0	7	18.4	0.585
	3	0	0.0	3	7.9	0.874
	4	0	0.0	1	2.6	0.284
BMI	Normal	4	66.7	28	73.7	0.893
	Overweight	2	33.3	8	21.1	0.886
	Obese	0	0.0	1	2.6	0.284
	Morbid obesity	0	0.0	1	2.6	0.284
Medical disease	Free	6	100.0	35	92.1	0.874
	Hypertension	0	0.0	1	2.6	0.284
	Thyroid	0	0.0	1	2.6	0.284
	Gall stone	0	0.0	1	2.6	0.284
Surgical history	yes	5	73.3	31	81.6	0.7
	No	1	16.7	9	23.7	0.886
Number of surgeries	1	0	0.0	1	2.6	0.284
	2	0	0.0	8	21.1	0.501
	3	4	66.7	6	15.8	0.025*
	4	0	0.0	3	7.9	0.874
Blood transfusion	Yes	4	66.7	7	18.4	0.042*
	No	2	33.3	31	81.6	0.042*
Rapid test	Positive	6	100.0	37	97.4	0.284
	Negative	0	0.0	1	2.6	0.284
HCV antibody	Positive	6	100.0	38	100.0	-
US in first trimester	Free	6	100.0	34	89.5	0.944
	Fatty liver	0	0.0	3	7.9	0.874
	Mild splenomegaly	0	0.0	1	2.6	0.284

		HCV PCR of the fetus				P. value
		Positive (n=6)		Negative (n=38)		
		No.	%	No.	%	
US in second trimester	Free	5	83.3	29	76.3	0.886
	Fatty liver	0	0.0	6	15.8	0.684
	Mild splenomegaly	1	16.7	3	7.9	0.944
US in third trimester	Free	4	66.7	29	76.3	0.988
	Fatty liver	0	0.0	6	15.8	0.683
	Mild splenomegaly	2	33.3	3	7.9	0.257
Delivery	Cesarean section	4	66.7	18	47.4	0.660
	Vaginal	2	33.3	20	52.6	0.660
Fetus HCV ab	Positive	6	100.0	38	100.0	1.000

Discussion

Globally, it was estimated that, Hepatitis C virus genotype 4 is the cause of approximately 20% of the 180 million cases of chronic hepatitis C in the world. HCV-4 infection is common in the Middle East and Africa; currently more than 180 million people had HCV antibodies; (prevalence of 2.8 percent). HCV prevalence is highest in Egypt at >10% of the general population and China has the most people with HCV (29.8 million) **(Heintges T et al., 1997).**

Fulminant hepatitis C is rare. Nevertheless, the long-term liability of acute hepatitis C is significant due to the high rate of chronic infection (HCV-RNA positive in 55 to 85 percent of cases) and chronic hepatitis (elevated serum ALT concentration in 60 to 80 percent of patients with chronic infection).

Approximately 20 to 30 percent of those chronically infected will develop cirrhosis, and a proportion of those patients will develop hepatocellular carcinoma **(Ramachandran P et al., 2012).**

All women should receive antenatal screening for both HBsAg and HCVAb. In the Past, some studies revealed interesting results, that in Egyptian rural villages the prevalence of anti-HCV reaches a mean of 15.5%, with a 30% rate in women aged > 35 years **(Annarosa Floreani, 2013).**

The overall rate of mother-to-child transmission of HCV from HCV-infected, HIV-negative mothers has been estimated at 3%-5%.Co-infection with HIV increases the rate of mother-to-child transmission up to 19.4%.The detection of HCV RNA in the serum of infants in the first 24 hours of life suggests that early intrauterine infection may be possible. Numerous risk factors for vertical transmission have been studied. In general, high viral load defined as at least 2.5×10^6 viral RNA copies/mL, HIV co-infection, and invasive procedures are the most important factors **(Stoszek SK et al., 2006).**

A Japanese study suggested that maternal liver dysfunction, large blood loss at delivery, and vaginal delivery were potential novel risk factors for mother-to-child transmission of HCV **(Hayashida A et al., 2007).** However, pregnancy is not common on top of liver cirrhosis of chronic HCV infection, we experienced many women with esophageal varices and portal hypertension during pregnancy, evaluation of esophageal wall thickness by non-invasive U/S could be very helpful, we preferred cesarean section with prophylactic somatostatin analogues in those with portal hypertension at the time of delivery

According to our survey study of Egyptian pregnant women population in many Egyptian governments mainly in Upper Egypt, 2800 pregnant women screened, 44 women (1.5%) were positive for both HCV antibodies (Ab) and HCV-RNA. Because of known cross-antigencity known between HCV and other diseases, women positive to Ab but negative to HCV-RNA were excluded.

However of those 44 pregnant women Positive to HCV both by Ab and PCR, 33 (75%) had a history of Blood transfusion, however other 10 women (25%) had a surgical history. (Figure 1; determined by decision tree algorithm), which shed light on the source risk factors for HCV vertical transmission, mainly all pregnant women transfused blood, has a PCR positive for HCV.

However 470 pregnant women (16.7%) had history of surgical intervention, only 33 patients has HCV (7.2%).

Whatever CS accounts for 58.8 % of all surgical intervention (20/34), surgical operations are important source for vertical transmission of HCV. Accordingly CS should be discouraged.

We have not found any significant correlation between BMI and HCV infection of overall liver diseases progression or regression.

In another study in a rural district in Egypt of 360 pregnant women we found 6.1% (22/360) of pregnant women were HCV seropositive; of them only 45% (9/20) had viraemia. Risk factors were their age, the age of their husband and the presence of chronic liver disease in the husband **(Khamis HH et al., 2014).**

Also in another study in north India we found that Forty patients tested positive for anti-HCV antibodies among 1,412 patients subjected to anti-HCV testing during study period. Prevalence of HCV during pregnancy was 2.8 % in this study. Among the risk factors studied, previous surgery and blood transfusion were the statistically significant risk factors. There was history of previous major surgery in 16 cases versus 4 controls and was statistically significant (p value 0.002) at $p < 0.05$. History of blood transfusion was present in 4 versus 2 among cases and controls, respectively, and statistically significant (p value 0.004) at $p < 0.05$. Sexual transmission was not the risk factor **(Goyal LD et al., 2014)**.

Study of 1500 pregnant women that were randomly selected when coming in antenatal care outpatient clinicin Etay El-Baroud general hospital El-Behira governorate of Delta Egypt in the period from the 1stof November 2012 till the end of March 2014out of 1500 pregnant women, 156 (10.4%) were positive for HCV antibody. Only 123 (8.2%) were positive for HCV-RNA.HCV infection was associated with older age **(Edessy M et al., 2015).**

Out of 123 infants tested at first month, 85 (69.1 %) were positive for HCV antibody, but only14 (11.4%) were positive for HCV-RNA at birth. After 6 months, only 5 (4 %) remained positive for HCV RNA.

The prevalence of HCV in pregnant women in Egypt is lower than previously reported. Risk factors for transmission suggest that there is a correlation between the age and parity of the studied women and the incidence of hepatitis C infection. Hepatitis C virus infection was found more among those women with past history of previous surgery or blood transfusion. Further studies are needed to explore this issue. Incidence of vertical transmission of HCV in Egypt is not more different than in other countries and it plays no role in the high endemicity in Egypt **(Edessy M et al., 2015).**

Also in another study all pregnant women attending Cairo University Faculty of Medicine Obstetrics and Gynecology antenatal clinic were approached for HCV screening. Of 2514 women screened, a total of 54 women were viremic (2.1%) and delivered 56 infants. Of those, 51 infants

of 49 women were tested at 12 months of age. Only 7 infants were viremic, with an HCV VT rate of 14.3% (7 of 49). Median HCV RNA in the infants was 2100 IU/mL. None of the maternal risk factors analyzed were associated with transmission **(El-Ghazaly H et al., 2015).**

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