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ORIGINAL ARTICLE

Vertical Transmission of Hepatitis C in Pregnant Women and possible risk factor for perinatal outcome at Zagazig University Hospital.

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ABSTRACT

Background: Hepatitis C virus (HCV) considered a serious health problem over the world, which cause chronic liver diseases, cirrhosis, liver failure and hepatocellular carcinoma. In Egypt the prevalence of HCV was 14.7% for positive HCV antibody (Ab) between 15 to 59 years age group during the year 2008, but in the year 2015, there was a significant reduction of in HCV antibody positive and HCV RNA positive individuals (32% and 29% respectively) according to the Egyptian Health Issues Survey (EHIS) and HCV seroprevalence was 10% and 7% viremia between 15 to 59 years age group**.**

Objectives: The aim of this study was to compare the prevalence of HCV RNA positive pregnant women with the general population and discover the possible risk factor for perinatal outcome.

Patients & Methods: This cross-sectional study was performed on 187 pregnant women admitted for labour at Zagazig university hospital between May 2018 to December 2018. **Results:** the results showed that all women in study were comparable as regards mean age with significant association (p=0.001) with increase maternal age, geogravical distribution,socio-economic level, household contact of HCV patient, previous abortion with significant association (p=0.03). The risk factor for HCV infection in study participant varied between visiting dentist, previous blood transfusion without statisyically significant difference.

Conclusions: several risk factors for mother-to-child transmission were determined but none are modifiable and there was no interventions available to prevent vertical transmission.

Keywords: virus carrier, Risk factor, adverse perinatal.

INTRODUCTION

Many studies showed that prevalence of HCV infection in pregnant women ranging between 0.5%-2% in high-income countries and reached 5%-15% in developed countries [1]. Mostly, infected women do not develop manifestations of HCV-mediated clinical during the pregnancy, although many studies reported high increase of gestational cholestasis [2].

The diagnosis of vertical HCV transmission in infants by passive acquired maternal antibodies is complicated as these usually disappeared in age of 12 months. Furthermore, the first PCR assays are more accurate during the first 3 months [3].

Many risk factors were reported for HCV vertical transmission, such as coinfections with HIV, use of intravenous drug, high maternal HCV viral load, delivery mode, preterm labor, membranes rupture and amniocentesis. HCV genotypes and Breast feeding have small effect on vertical transmission [4].

It is necessary to evaluate the vertical transmission especially in high HCV prevalence countries like Egypt [5]. Also, in countries where HCV contained in high-risk populations such as people who inject drugs, where many of them in reproductive age and affected with human immunodeficiency virus (HIV) [6].

PATIENTS AND METHODS

This cross-sectional study was conducted on 187 pregnant women admitted for labour at Zagazig university hospital during May 2018 to December 2018.

Written informed consent was taken from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was carried according to the Ethical Code of World Medical Association (Declaration of Helsinki) for studies including humans.

Inclusion criteria: All pregnant women admitted to Obstetrics and Gynecology Department, Zagazig university Hospitals for delivery during the time of the study and all neonates delivered at Obstetrics and Gynecology Department, Zagazig university Hospitals by women included in study after 3 months.

Exclusion criteria: Evidence of Hepatitis B virus or immunodeficiency virus (HIV) infection. Lacking of prenatal care. Multiple gestations. Liver diseases such as autoimmune liver diseases, alcoholic and nonalcoholic liver diseases

All pregnant women who met the inclusion criteria were submitted to:

Full history taking including : Demographic data (Age, Gestational age, residence, Household contact of HCV patient), **Socio-economic level assessment [**using modified socioeconomic state assessment scale for Egyptian health research **[7]** and **Obstetric history** (Gravidity, Parity and Previous abortion).

Risk factors for HCV infection (Visiting dentist for tooth treatment, repeated injection, previous vaccination, taking IV fluid, surgical procedure, blood transfusion, suture wound, endoscopic procedure, use of patients tools and give injection to patients), **Obstetric risk factors and labor complications (**Caesarean delivery, Gestational diabetes, premature rupture of membranes (PROM), Labor induction, Hypertensive disorders, Polyhydramnion, Oligohydramnion, Placental abruption, Fertility treatment, Non-reassuring Fetal Heart Rate (FHR) patterns and Intrauterine growth restriction (IUGR), **Pregnancy outcomes and neonatal complications:** Meconium-stained amniotic fluid, Low birth weight, Congenital anomalies, HCV RNA positive, preterm delivery, Apgar score and Total perinatal mortality,

Laboratory testing Serum was tested for anti-HCV by ORTHO HCV version 3.0 ELISA [Ortho-Clinical Diagnostics], and the reactive results were tested by RIBA (version 3.0; Chiron). RIBA-positive or indeterminate results were tested for HCV RNA by modified reverse-transcriptase polymerase chain reaction (RT-PCR) (AMPLICOR HCV Test [version 2.0; Roche Molecular Systems]), maternal serum with HCV RNA was tested for viral levels using a branched DNA assay (Quantiplex HCV RNA Assay; Chiron)

anti-HCV negative Serum in HCV-infected infants according to EIA 2.0 was retested by EIA 3.0. The uninfected infants tested by EIA 2.0, the first anti-HCV–negative sample after maternal anti-HCV loss was retested again by EIA 3.0. Serum from infected infants and peripheral venous serum collected at birth from uninfected infants with a negative HCV RNA by AMPLICOR was retested again by nested RT-PCR [8]

Determination of HCV genotype was done by direct sequence of the NS5b region in serum of mothers who transmitted HCV and a random selection of about half of HCV RNA–positive mothers whom not transmit HCV [8]. Done within 24 h of collected sample by standard methods

The antibody to HIV (anti-HIV) Test was done according to EIA (HIVAB HIV-1 EIA; Abbott Laboratories) on serum from all participants and infants born to HIV-infected mothers at age more than 15 months. Results of EIA-reactive serum were confirmed using Western blot (Cambridge Biotech HIV-1 Western Blot Kit; Calypte Biomedical).

HCV RNA was extracted from the breast milk by the MasterPure complete DNA and RNA purification kit (Epicentre Technologies). then, 100 µL of breast milk samples and 50 µL of RNase-free water were mixed with 300 µL of 2× T and C lysis buffer containing 100 µg of proteinase K. After lysis, proteins were removed by protein precipitation reagent, the supernatant containing total nucleic acid was precipitated by isopropanol, and pellet washed with 75% ethanol.

Case definitions: Mothers were defined as HCV positive if their serum was positive for anti-HCV using RIBA or for HCV RNA, but in case of serum testing as RIBA indeterminate and negative HCV RNA were excluded from the analysis

Infants were defined as HCV infected if their serum was positive for HCV RNA on at least 2 follow-up visits or when anti-HCV positive was found at age > 24 months. Infants who were confirmed HCV RNA negative and who seroconverted from positive anti-HCV to negative anti-HCV during follow-up period were considered uninfected.

General abdominal and vaginal examination to determine the way of delivary and risk factor, record information about women progrees or events happened during labour..

Statistical Analysis: The collected data was entered to and analyzed by computer using Statistical Package of Social Services, version 25 (SPSS). Results were presented by tables and graphs. Quantitative data was presented as mean and standard deviation. Qualitative data was presented as frequencies and proportions. Pearson Chi square test (χ^2) and fisher's exact were used to analyze qualitative independent data. P value of ≤0.05 was considered significant .

Sample size: Assuming that the total number of pregnant women attending to Zagazig University hospitals for delivery in 6 months is 3200 women, the prevalence of HCV is 15% and confidence level is 95%, so total sample size is 187 pregnant women, calculated by Epi Info 7 version 7.2.0.1.

RESULTS

Table (1), showed that the mean age of study participants was 26.4 years, mean gestational age was 31.0 years and there was a significant difference for HCV infection regarding Gestational age, Geographic distribution (rural 65.2 % versus 34.8%), parity (primipara 31% versus multipara 69%) and previous abortion (40.3 % had previous abortion versus 59.7% without). **Table (2) and fig. (1)** showed that the most common risk factors for HCV infection in study participants were: Use of patient tools (44.4%), Endoscopic procedure (62.3 %) and repeated injection (23.4%) with no statistical significant difference. **Table (3) and Fig. (2)** showed that 15.0% of study participants had positive HCV antibodies and 5.3% had positive HCV RNA. **Table (4)** showed that 10% of HCV RNA positive neonates had meconium-stained amniotic fluid, 30% had low birth weight and 10% had congenital anomalies. HCV RNA was positive in 20% of study neonates**. Table (5),** showed that there was no statistical significant association between vertical transmission and caesarean delivery, preterm delivery and there was a significant association between vertical transmission and viral load and in infected mother.

Table (1): Demographic characteristics of study participants:

Variables	Study participants (n=187)	
Age (years):		
Mean ± SD Range	26.4 ± 6.2 16.0 – 43.0	
Gestational age (weeks):		
Mean ± SD Range	31.0 ± 4.1 28.0 – 40.0	P < 0.5
Geographic distribution:		
Rural Urban	122 (65.2%) 65 (34.8%)	P < 0.5
Socio-economic level:		
Low Middle	125 (66.8%) 62 (33.1%)	
Household contact of HCV patient:		
Positive Negative	56 (29.9%) 131 (70.1%)	
Parity:		
Primipara Multipara	58 (31.0%) 129 (69.0%)	P < 0.5
Previous abortion:		
Yes No	52 (40.3%) 77 (59.7%)	P < 0.5

Table (2): Risk factors for HCV infection in study participants:

	Study participants	HCV positive		HCV negative	
	No	**No.**	**%**	**No.**	**%**
Previous visit to dentist	116	10	8.6%	106	91.3%
Previous blood transfusion	60	3	5%	54	90%
Repeated injection	64	15	23.4%	49	76.5%
Previous surgeries	84	18	21%	66	78.5%
Endoscopic procedure	19	5	26.3%	14	73.6%

Use of patient tools	9	4	44.4%	5	55.5%

Table (3): Viral markers of hepatitis C infection in study participants:

Variables	Study participants (n=187)	
	No.	**%**
HCV antibodies:		
♦ Positive	28	15.0
♦ Negative	159	85.0
HCV RNA:		
♦ Positive	10	5.3
♦ Negative	177	94.7

Table (4): Pregnancy outcomes and neonatal complications of study participants:

Variables	HCV RNA				χ^2	P
	Positive (n=10)		**Negative (n=177)**			
	No.	**%**	**No.**	**%**		
Meconium-stained amniotic fluid	1	10.0	31	17.5	fisher	**0.99**
Low birth weight	3	30.0	22	12.4	fisher	**0.1**
Congenital anomalies	1	10.0	17	9.6	fisher	0.99
HCV RNA	2	20	0	0.0	fisher	**0.002(HS)**
Preterm delivery	4	40.0	10	5.7	fisher	**0.003(S)**
Low Apgar score at 1 min	2	20.0	10	5.7	fisher	**0.1(NS)**
Low Apgar score at 5 min	4	40.0	10	5.7	fisher	0.003**(S)**

Table (5): Association between vertical transmission and possible risk factors in HCV positive cases:

HCV RNA positive mother N=10	HCV RNA				χ^2	P
	HCV positive baby=2		**HCV negative baby=8**			
	No.	**%**	**No.**	**%**		
Caesarean delivery (n=7)	1	14.2%	6	85.7%	fisher	0.99
PROM(N=5) Less than 6 hours	2	5%	3	25%	fisher	0.4(NS)
High viral load (N=2)	2	100%	0	00.0%	fisher	0.02(S)
Preterm delivery(N=4)	2	50%	2	50%	fisher	0.99

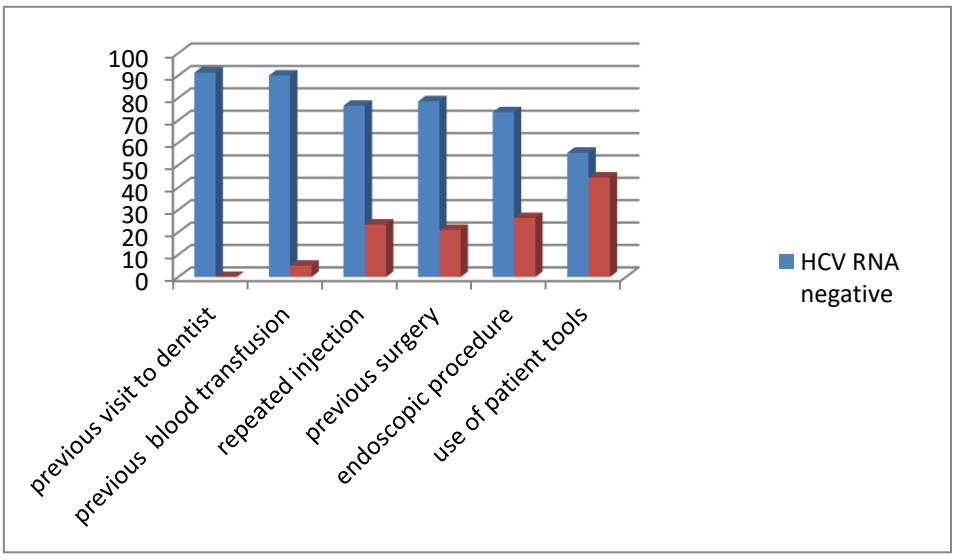

Figure (1): risk factor for HCV infection in study participant.

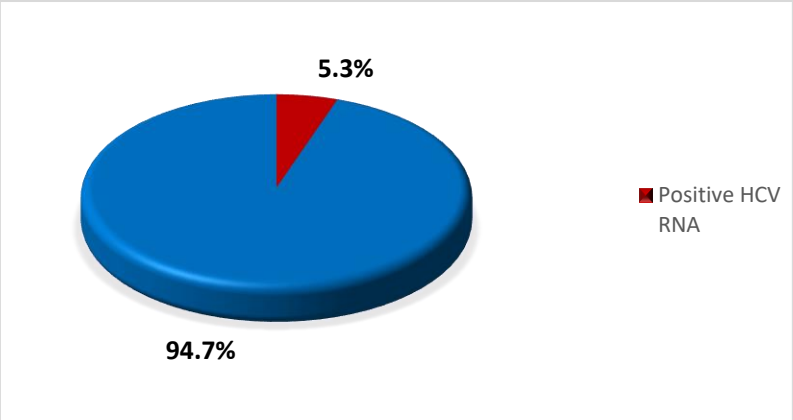

Fig. (2): Viral markers of hepatitis C infection in study participants.

DISCUSSION

It is difficult to diagnose the asymptomatic acute HCV infection in pregnant women unless there was a distinct exposure which allowing accurate timing of seroconversion. The effect of pregnancy on the outcome of acute HCV infection still unknown, but it is supposed that the immunomodulation of pregnancy could support viral persistence rather than clearance **[9]**.

Regarding parity in this study, we noted that a significant difference for HCV infection found between primipara 31% and multipara 69% as seen in (table I). This result agrees with the study of E**lrazek et al. [10]**, who reported that the HCV infection in primipara is 18.53% and in multipara is 58.53%.

In the current study, the risk factors for HCV transmission among study participants was (23.4%), (26.3) of those who had repeated injection, undergo endoscopic procedure respectively, this results agree with the study of **Amr et al. [11]** who found risk Factors associated with HCV infection were the following: having had a repeated injection and undergo endoscopic procedure were (20.1%), (33.1%) respectively.

The current study showed that (21%) of those who had undergone surgical surgery were positive, 44.4% of study subjects having had used tools were also positive, this result consistent with the study of **Awadalla et al. [12]**, who recorded a ratio of (30.1%) for whom undergone surgical procedure and (48.4%) for patients whom used common tools.

The current study showed that there was no statistically significant related to previous visit to dentist (8.6%),and previous blood transfusion (5%).that agree with **Paez et al. [13]** who reported no relation between HCV infection and tooth treatment (3.8%).

The current study showed that the prevalence of HCV in pregnant women is 5%. This result was consistent with the study of **Le Campion et al. [1],** who reported that the prevalence of HCV infection is between 1% and 8% in pregnant in developing countries.

The current study showed a high rate of vertical transmission, from HCV-seropositive, HIV-negative, pregnant women to their newborns (20 per cent) but less than the study of Also **Kassem et al.[14]** who reported that vertical transmission of HCV–RNA was 36 per cent (5/14) for mothers carrying the HCV–RNA which more than our result, also the study of **Zucotti et al. [15]** who reported that among the infants born to the 21 women in whom HCV RNA was detected, the risk of transmission was similar, irrespective of maternal HCV and HIV coinfection (30.7%) or maternal HCV infection alone (25%). This high rate of vertical transmission means that a considerably large number of Egyptian infants acquire HCV infection very early in life through vertical transmission.

The current study showed that the increase of caesarean delivery rate was 20% in HCV RNA positive mothers this result agree with the study of **Prasad et al. [16],** whose noted that the rate of caesarean delivery in HCV infected mother increased by rate of 23%.

In our study, the HCV infection of pregnant women showed significant elevation of preterm labor 40% (p=0.003), and low Apgar scores at 5 min 40% (p=0.03). This result was consistent with **Reddick et al. [17],** who found that infected women with HCV increase the risk of preterm labor and low Apgar scores.

The current study showed that there was no significant association between the risk of vertical transmission and cesarean delivery 14.1% (p=0.99). These results were consistent with the studies of **Ghamar et al. [18],** and **Garcia-Tejedor et al. [19],** who reported that there was no

association between C.S delivery and risk for vertical transmission 10% (p=0.1).

In the current study, the maternal serum HCV RNA viral load is the most common risk factor for vertical transmission (p=0.02). This result was consistent with the study of **Baroncelli et al. [20]** who reported that the first factor for vertical transmission is viral load whereas this risk increase by 70% in HCV RNA positive women..

In this study the rupture of membrane less than 6 hours is not risk factor for vertical transmission 5% (p=0.04). This result was consistent with **Pott et al. [21]** who reported that premature rupture of membrane less than 6 hours, is not considered risk factor for HCV vertical transmission 5% but prolonged rupture of membrane more than 6 hours 60% is risk factor for vertical transmission by exposing the fetus to maternal HCV in the birth canal.

Limitations: This was carried on small number of patients. A larger sample size for a longer time may be able to confirm the results of the current study.

Conclusion: several risk factors for mother-to-child transmission were determined but none are modifiable and there was no interventions available to prevent vertical transmission

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