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Effect Of Hepatitis C Virus On Duration Of Pregnancy And The Incidence Of Congenital Anomalies Of The Fetus

Obstetrics and Gynecology

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ABSTRACT

Background: In spite of reports of raised rates of hypertensive problems, pre-mature births, and cholestasis, the influence of mother HCV infections on gestation complications and obstetrical outcomes hasn't been extensively defined.

Aim of the work: to examine the influence of Hepatitis C virus (HCV) infections during pregnancy on the duration of gestation as well as its possible effect on the incidence of congenital anomalies of the fetus.

Patients and methods: This work was a prospective observational case-control research had been done at Al-Hussein and Sayed Galal hospitals, Al-Azhar University during the period from December 2020 to June 2021. The study included [12]0 HCV infected and 120 HCV uninfected gravid females.

Results: Congenital anomalies in Group (A) show that 7(5.8%) had congenital anomalies while in Group (B) 3(2.5%) had congenital anomalies. Nonsignificant changes have been found among studied groups. Significant changes have been found among studied groups as regard neonatal ICU admission where P=0.005.

Conclusion: Gestations in females who are positive for anti-HCV have elevated rates of poor neonatal and obstetrical results, while correlations among neonatal and obstetrical results and HCV don't essentially mirror a causal association, HCV positivity can be a substitute indicator for raised risk of poor gestation outcome and the HCV-positive gravid populations can need more clinical vigilance in this concern.

Keywords: *Congenital anomalies, pregnant, HCV infection, neonatal ICU.*

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INTRODUCTION

About 185 million persons, or 2.8% of the universal populations, are presently or formerly disorderd with HCV. [1] The valued 4.1 million individuals (1.6%) in the United States with HCV [2] are dwarfed by the 12 million (14.7%) in Egypt. [3]

The prevalence rate of HCV-infections in gravid females in the US was ranging between 1 & 2.4 % [4] and in Egypt between 15.7 & 19%. Regarding to centers for disorders control and prevention and the American college of obstetrics and gynecology strategies, worldwide screening of gravid females isn't endorsed in the US. [5] In spite of having the highest global prevalence of worldwide screening of gravid females, it isn't showed in Egypt, and only risk-based screening is achieved

Vertical HCV transmission during gestation looks to be linked to the expectant mother's viremia rather than the birth route. When a woman's titer is less than 106/mL or she is negative, the virus doesn't seem to be transferred. [6]

The CDC indorses confirmations of a positive EIA with additional recombinant immunoblot assay (RIBA) or RT-PCR for HCV RNA. [7]

The relation between HCV during pregnancy and each of prematurity and congenital anomalies has not been established yet. [6]

PATIENTS AND METHODS

This work was undertaken at Al-Hussein and Sayed Galal hospitals at Al-Azhar University between December 2020 and June 2021 as a prospective observational case-control study. A total of 120 gravid females with HCV infection and 120 gravid females without HCV infection took part in the study.

A control group of 120 gravid females who are known to be infected with HCV will be recruited alongside a group of 120 gravid females who are not infected with HCV.

Cases that were included in the study were chosen based on the following criteria: Patients' age: 18-35 years, Singleton fetus and live fetus, pregnancy in the second or third trimester known to be infected with HCV, patients' age: 18-35 years:

Exclusion criteria of the cases: Patients' age: 18-35 years, Singleton fetus and live fetus, pregnancy in the second or third trimester known to be infected with HCV, patients' age: 18-35 years

History of premature delivery, history of congenital malformed fetus in near family member, females previously infected and treated against HCV, human immuno-deficiency virus, urinary tract infections, renal disorders, DM, pregnancy DM and chronic high blood pressure, any cardiovascular disorder, multiple gestations and history of congenital malformed fetus in the previous pregnancy.

Methods

Patients were subjected to:

Complete history taking: Personal history including name, age, marital state, address menstrual history: involving Menarche age, menstrual disturbances, dysmenorrhea, linked signs, obstetric history including parity and mode of delivery, present history: of chronic disorders and medication, past history of HTN, DM, family history of similar condition or diabetes, history of allergy to any medication and surgical history of operation, laparoscopic interference, treatment of hirsutism by Laser.

Examination: General examination: Evaluation of vital signs and measurement weight, height (BMI). Abdominal and local clinical examination: to assess fundal level and gestational age, scar of preceding surgeries, masses, tenderness or inflexibility and any abdominal or pelvic clinically detectable pathology. Bimanual pelvic examinations of both adenexa, and uterus for recognition of any irregularity of female genitalia

Investigations:

Laboratory: CBC, coagulation profile, detection of albumin in urine sample by boiling or urine analysis, liver and kidney function tests. Virology: A blood sample will be withdrawn from all of the cases at the time of enrolment and to be sent for antibodies screening by ELISA or Rapid test and positive samples will be then examined for quantitative HCV-RNA by PCR. Abdominal U/S: Abdominal ultrasound will be performed using abdominal U/S. All measurements will be performed by a single sonographer with the same machine. Fetal biometry, Amniotic Fluid Index (AFI) measurement, and anomaly scan to check for any congenital anomalies will be done. Once congenital anomalies are suspected, the patient is referred for anomaly scan by 4D US by fetal medicine specialist.

Outcome measures: Primary outcome: Pregnancy age at time of delivery and presence of congenital anomalies of the fetus. Secondary outcome: mode of delivery, apgar score at 1 & 5 min, neonatal delivery mass and ICU admittance.

Ethical approval has been attained from the IRB of faculty of medicine Al Azhar University. Informed verbal agreement was gotten from all involved cases. Secrecy and privacy have been respected in all levels of the work.

The data has been analyzed via IBM SPSS-20.0. software (Armonk, NY: IBM Corp) Qualitative data have been presented as numbers and percent. The Kolmogorov-Smirnov testing has been utilized to verify the normality of distribution Quantitative data have been presented as range (min and max), mean and standard deviation (SD). Significance level was set at the 5% level.

RESULTS

Patients were classified into 2 groups: Group (A): including 120 gravid females infected with HCV. Group (B): including 120 gravid females uninfected with HCV. A nonsignificant differences were found among groups regarding gravidity and abortion where P=0.097. Table (1)

Age	Group (A) (n=120)	Group (B) (n=120)	U	P Value
Min.-Max.	21-37	19-35	7103.00	0.857
Mean± S.D	26.80±5.157	26.63±4.779		
Gravidity				
Min.-Max.	0-5	0-5	6296.50	0.088
Mean± S.D	2.37±1.768	2.74±1.683		
Parity				
Min.-Max.	0-5	0-5	6481.00	0.174
Mean± S.D	2.14±1.579	2.41±1.470		
Abortion				
Min.-Max.	0-3	0-4	6633.50	0.097
Mean± S.D	0.23±0.667	0.33±0.737		

U: Mann-Whitney testing
p: P value for comparison among the groups
*: Statistically significant at P-value <0.05
Table 1: Comparing among both groups as regard to patient's age (years) and patient's obstetric history

History of exposures to risk-factors in Group (A) show that about three quarter of the patients did not have a history of exposures to risk-factors (77.5%) while in Group (B) the majority of the patients didn't had a history of exposure to risk-factors (82.5%). A nonsignificant changes among both groups where P-value=0.317. Table (2)

History of exposure to risk-factors	Group (A) (n=120)		Group (B) (n=120)		P Value
	No.	%	No.	%	
No	93	77.5	99	82.5	0.186
Surgery	10	8.3	5	4.2	
Endoscopy	7	5.8	9	7.5	
Dental treatment	6	5.0	7	5.8	
Blood transfusion	4	3.3	0	0	
Total	120	100	120	100	

p: P value for comparison among the groups
*: significant at P-value <0.05

Table 2: Comparing among the study groups as regard to patient's history of exposure to risk-factors

A statistically significant variances were found among groups regarding each of Hb, platelet, AST, ALT, and INR where P<0.001. Table (3)

	Group (A) (n=120)	Group (B) (n=120)	U	P Value
Hb				
Min.-Max.	10.1-13.4	11.1-14.1	3967.50	<0.001*
Mean± S.D	11.79±0.899	12.57±0.868		
Platelet				
Min.-Max.	195-234	187-264	5820.00	0.010*
Mean± S.D	213.78±11.121	222.09±22.074		
AST				
Min.-Max.	35-81	15-47	130.00	<0.001*
Mean± S.D	57.92±13.083	27.79±7.541		
ALT				
Min.-Max.	38-96	25-52	309.50	<0.001*
Mean± S.D	69.63±15.202	37.98±8.476		
Creatinine				
Min.-Max.	0.6-1.4	0.6-1.0	7005.00	0.711
Mean± S.D	0.82±0.163	0.81±0.140		
Urea				
Min.-Max.	10.0-34.5	10.0-20.0	6299.00	0.094
Mean± S.D	15.01±3.956	15.29±2.800		
INR				
Min.-Max.	0.9-2.7	0.6-1.3	1503.00	<0.001*
Mean± S.D	1.74±0.549	0.97±0.222		

U: Mann-Whitney testing
t: T-Student testing
p: P value for comparison among the groups
*: significant at P-value <0.05

Table 3: Comparing among two groups as regard to patient's laboratory investigations

Significant variances were found among both groups regarding gestational age at time of delivery where P<0.001. Congenital anomalies in Group (A) show that 7(5.8%) had congenital anomalies while in Group (B) 3(2.5%) had congenital anomalies. Nonsignificant variances were found among both groups where P=0.333. Table (4)

Gestational Age at time of delivery	Group (A) (n=120)	Group (B) (n=120)	U	P Value
Min.-Max.	30-40	36-40	3348.00	<0.001*
Mean± S.D	34.74±3.392	37.93±1.538		
Congenital anomalies				
No	113	94.2	117 (97.5)	0.333
Yes	7	5.8	3 (2.5)	
Total	120	100	120 (100)	

U: Mann-Whitney testing
p: P value for comparison among the groups
*: significant at P-value <0.05

Table 4: Comparing among both groups as regard to patient's gestational age at time of delivery (weeks) and patient's congenital anomalies

Neonatal birth weight in Group (A) was ranged between 1734-3194 g with mean±S.D. 2497.42±445.112 g while in Group (B) was ranged between 1822-3815 g with mean±S.D. 2883.18±584.073 g. Significant changes have been found among groups where P<0.001. Neonatal ICU admission in Group (A) show that 22(18.3%) of baby's were admitted to ICU while in Group (B) 7(5.8%) of baby's were admitted to ICU. A significant variances were found among both groups where P=0.005. Table (5)

Neonatal birth weight	Group (A) (n=120)		Group (B) (n=120)		P Value
Min.-Max.	1734-3194		1822-3815		<0.001*
Mean± S.D	2497.42±445.112		2883.18±584.073		
Neonatal ICU admission					
No	98	81.7	113	94.2	0.005*
Yes	22	18.3	7	5.8	
Total	120	100	120	100	

p: P value for comparison among the groups
*: significant at P-value <0.05

Table 5: Comparison between two groups as regard to Neonatal birth weight and patient's neonatal ICU admission

DISCUSSION

In considering the correlations among mothers HCV infections and gestation outcome, the existence of simultaneous risk-factors of poor results, like poor perinatal care and simultaneous medication or alcohol usage, essential to be counted. [8]

So, in this work aim to examine the influence of HCV infections throughout gestation on the duration of gestation as well as its possible effect on the incidence of congenital anomalies of the fetus.

On the other hand, in the present study, as regard abortion in Group (A) was ranging from 0 to 3 with mean± S.D. 0.23±0.667 while in Group (B) was ranged between 0-4 with mean ±S.D. 0.33±0.737. A nonsignificant change was found among groups regarding each of gravidity, parity and abortion.

In a study done by Abdulqawi et al., [9] as regard Parity, it was found that parity>2 among 290 (25) in HCV positive women, and was 41 (49) in HCV negative women, A nonsignificant change was found among groups as regard parity with no differences as regard gravidity nor abortion.

In addition to above findings, we found that as regard history of exposures to risk-factors in Group (A) show that about three quarter of the patients did not have a history of exposures to risk0factors (77.5%) while in Group (B) the mainstream of the cases didn't have a history of exposure to risk-factors (82.5%). A nonsignificant change was found among groups.

While blood transfusions are currently considered a lesser significant risk-factor, it must be measured carefully, particularly in a republic with such an elevated prevalence of the disorder. Our findings are in accordance with those of Sangha et al., [3] who revealed that a history of surgeries, blood transfusions, or injections to manage schistosomiasis elevated the risk of active infections with HCV, non-dependent of the other features.

Abdulqawi et al., [9] reported that as regard history of exposure to risk-factors in HCV positive women showed that 15% had history of blood transfusion, 24 (29) had Major operation, 9 (0.8) had Major accidents, A nonsignificant change was found among groups as regard risk-factors except for blood transfusion.

In the study on our hands, it was revealed that significant changes have been found among groups as regard each of Hb, platelets, ALT, AST, and INR, while there were non-significant differences as regard creatinine and urea.

Our results are supported by the study of McNicholas et al.,[10] which reported that Contributors with HCV infections had higher ALT, AST, and GGT levels at all-time points, and it was revealed that trimester altered the influence of HCV, with HCV-positive cases having higher transaminases in the 1st (and 3rd trimesters, and a leaning to significance for the 2nd trimester.

Several researches propose that the fetuses of mothers with chronic HCV are at elevated risk for opposing newborn results. One research of Pergam et al.,[11] performed that baby of HCV mothers were more expected to be small for pregnancy age, need supported ventilations, be admitted to the ICU, or have lower births weights. Additional research of Connell et al.,[12] performed analogous implications, signifying that baby born to infected moms are at risk for lower delivery weights, pre-term delivery, and congenital irregularities, while confusing factors, like polysubstance abuse, weren't controlled for. A fresher research of Huang et al., [13] established reduced intra-uterine embryonic growing of infants born to HCV mothers.

In a more recent study of Connell et al., [12] utilized delivery certificate record of 1670369 gestations; it was revealed that cases with HCV were more expected to have infants delivered pre-term, with lower delivery weights and congenital irregularities. But that research has many limitations, especially, its retrospective design and the absence of associations with numerous variables, like the usage of tobacco, alcohol or drugs. Certainly, there is no clarification for pre-maturity and lower delivery weights in HCV-negative moms, while raised cytotoxicity of placental natural killer-T cells can be hypothesized possible. [14]

This can explained the findings of our study which stated that Congenital anomalies in Group (A) show that 7(5.8%) had congenital anomalies while in Group (B) 3(2.5%) had congenital anomalies. Nonsignificant changes have been found among groups where P=0.333.

Pergam et al. 11 found that babies born to HCV-positive moms were more expected to be lower delivery weights (OR, 2.17; 95

5CI, 1.24, 3.80), small for gestational age (OR, 1.46; 95 percent CI, 1.00, 2.13), require assisted ventilation (OR, 2.37; 95 percent CI, 1.46, 3.85), and need NICU admittance (OR, 2.37; 95 percent CI, 1.46, 3.85). (OR, 2.91; 95 percent CI, 1.86, 4.55). HCV-positive moms who increased too much weights have elevated hazard of gestation diabetes (OR, 2.51; 95 percent CI, 1.04, 6.03). NICU hospitalization and the need for assisted ventilations still linked to HCV in the non-drug-using population.

This was in agreement with our findings, which demonstrated that neonatal birth weight in Group (A) was ranged between 1734-3194 g with mean±s.d. 2497.42±445.112 g while in Group (B) was ranged between 1822-3815 g with mean±s.d. 2883.18±584.073 g. significant changes were found among groups p<0.001.

In a separate study by Jabeen et al., [15] had a number of 100 cases, and 85 of which were successful. Four pre-mature deliveries happened, one of which was a twin gestation, while 11 spontaneous mis-carriages happened. Following HCV infections, one mis-carriage happened in the gestation. In the PCR-positive cases, there were two infant fatalities because of severe congenital defects. Only one (2.3 percent) of the children born to HCV-RNA positive moms tested positive for the virus.

The scarcity of data in neonates, combined with the rarity of many bad results, has made quantifying the risk of maternal HCV problematic. APGAR scores for children born to HCV exposed and unexposed women seem to be similar 17 in previous literature, which is consistent with our findings, where the APGAR score in Group (A) at 1 minute was ranged between 2-5 with mean S.D. 3.560.562 and increased after 5 minutes to have a mean value of 7.690.683, while in Group (B) at 1 minute was ranged between 2-7 with mean S.D. 3.680.801 a Between groups, nonsignificant change was found.

Also, Neonatal ICU admission in Group (A) showed that 22 (18.3%) of babies were admitted to ICU, whereas 7 (5.8%) of babies were admitted to ICU in Group (B). P=0.005 indicated statistically significant differences across groups. Similar to our findings, Pergam et al., [11] reported that maternal HCV remained strongly associated with NICU admission (OR, 2.80; 95% CI, 1.83, 4.29) and with need for assisted ventilation (OR, 1.82; 95% CI, 1.03, 3.22). Neonates born to HCV-positive drug-using mothers did not have an increased risk of being LBW (OR, 1.19; 95% CI, 0.74, 1.91), prematurity (OR, 1.03; 95% CI, 0.66, 1.61), SGA (OR, 0.97; 95% CI, 0.57, 1.64), or having a low apgar score (OR, 1.12; 95% CI 0.60, 2.08). There was a non-significant trend toward an association between HCV and neonatal jaundice.

A prospective study of Karampatou et al., [8] was conducted on 145 gravid females from British Columbia who were HCV-positive detected a 3.4% rate of intrauterine fetal mortality, 17.9% rate of pre-term delivery, 11.3% rate of small for gestation age, and 12.5% rate of low-delivery-weight infants, which were significantly high in comparison to rates in the general British Columbia population (0.5%, 7%, and 5%, respectively).

CONCLUSION

While associations among obstetrical and neonatal outcomes and HCV mightn't always mirror a causal association, HCV positivity can be a substitute indicator for raised risk of poor gestation outcome, and the HCV-positive gravid women might need more clinical observance in this topic.

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