

## Original Research Article

# Hepatitis C in pregnancy: an observational study highlighting its association with maternal parameters

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## ABSTRACT

**Background:** Pregnancy is a very crucial time in a woman's life. In this period of time, not only multiple physiological alterations effect the usual health status but also makes women more vulnerable to contract infection and face negative sequelae. Hepatitis C, a blood borne viral infection serve the similar fate when encountered by pregnant ladies. This study is based on exploring the prevalence of the Hepatitis C virus seropositivity among pregnant population. Moreover, we also evaluated the major risk factors leading to the infection in these mothers. Besides this, infected mothers were studied for their pregnancy outcomes.

**Methods:** In this study 114 pregnant females were observed for this cross-sectional study. It was conducted in Gynecology Unit- 1, Liaquat University Hospital Hyderabad, for the period of January 2017 to July 2017. Chi square test was applied for statistical analysis on SPSS version 16. The criteria for enrollment in the study was set to be a pregnant lady belonging to age group 20-35 years; having singleton pregnancy; was a booked case at the hospital with compliant to antenatal follow ups; admitted to the labor room for delivery. All the non-pregnant ladies, whom had co morbid conditions such as hypertension or diabetes or had infected with hepatitis B or D were excluded from the study. Furthermore, pregnant ladies with multiple gestion or those who were either diagnosed of hepatitis C prior to conceive or had a previous history of hepatitis C were also excluded.

**Results:** Present study revealed that out of 114, 10(8.8%) pregnant ladies were found seropositive for Hepatitis C virus. Prior history for transfusion of blood was the Foremost risk factor discovered, with 60.5% women reported this. History of surgery was the 2nd commonest factor and 43.9% had this in their medical records. On the other hand, only 8.8% women gave the history for previous evacuation. While observing pregnancy outcomes, we found 48.2% neonates had low birth weight, 41.2% were born preterm and 21.1% had low APGAR score.

**Conclusions:** In a nutshell hepatitis c is prevalent in the pregnant population of this region and showing its effects in the form of compromised pregnancies. History of blood transfusion and previous surgery were found to be chief risk factors in the study.

**Keywords:** Hepatitis C, Maternal variables, Pregnant woman

## INTRODUCTION

Across the globe hepatitis caused by hepatitis C virus has been declared as the major contributor of diseased liver.<sup>1</sup>

Epidemiological studies have reported that around 71 million people among world's population are suffering from the chronic infection caused by the virus.<sup>2</sup> Further, only 50% of them are aware of the fact.<sup>3</sup> The demographic analysis showed that the majority of the effected population belongs to developing countries, ranging from 3 to 20 % or even higher.<sup>4</sup> Since hepatitis C is a blood borne viral illness it is likely to be spread from one person to another, and the frequently encountered modes of transmission include infected blood transfusion, unhealthy injection needle usage and inefficient sterilization of medical equipment other less frequent modes of infection transmission include sexual contact and from mother to baby.<sup>5-8</sup>

Hepatitis C virus can present with variety of manifestations, extending from mild symptoms to chronic liver function abnormalities.<sup>6</sup> During acute disease patient either show symptoms of nausea, jaundice and abdominal discomfort; or may remain asymptomatic.<sup>9</sup> Furthermore, the disease either progress to chronic course or resolve completely.<sup>9,10</sup> The patients suffering from chronic hepatitis C are at risk of developing complications, most important of these are liver cirrhosis and hepatocellular carcinoma.<sup>10</sup> Hepatitis C is associated with great morbidity burden on the society which is still on the verge to rise further, a study stated 43% rise in disability-adjusted life years from 1990 to 2013 caused by hepatitis C virus.<sup>11</sup> Nonetheless the infection is associated with significant mortality, according to WHO this infection engulfed 402,000 precious lives around the world in the year 2015.<sup>2</sup>

Pregnancy brings variety of alterations for the mother's body in order to accommodate and develop the fetus inside the womb.<sup>12</sup> Liver being the center of metabolism for the body, has no different fate when it comes to physiological variations during pregnancy.<sup>12</sup> The physiological mechanism pertains to the deviation in circulatory system of body, which leads to decreased cardiac output supplied to liver, this in turn results in inefficient metabolism.<sup>13</sup> Moreover, pregnancy hormones cause impaired function of smooth muscles in biliary tree which sometimes manifest as cholestasis.<sup>13</sup> Aside of physiological impact of pregnancy, alteration in liver function may occur due to underlying pathology.<sup>13</sup> Pathologies effecting liver specifically during pregnancy include preeclampsia, eclampsia, acute fatty liver of pregnancy and HELLP syndrome. While diseases that can be acquired during pregnancy include gallstones, viral hepatitis.<sup>13</sup>

During pregnancy the diagnosis of hepatitis C infection must be done via ELISA-3 for antibodies, followed by viral load for determining status of infection.<sup>14</sup> Infected pregnant ladies, manifest symptoms in approximately 75% of cases.<sup>9</sup> Though pregnancy does not influence progression of active infection but most of the pregnant women are found to have chronic hepatitis C during pregnancy.<sup>7,15</sup> The usual treatment for this infection is the

combined administration of ribavirin and pegylated interferon alpha. Nevertheless, this combination cannot be used in a pregnant lady because of teratogenic and IUGR (intrauterine growth retardation) effects of these drugs. Moreover, lactating mothers should also avoid this drug combination as the drug can be secreted in breast milk.<sup>16</sup> In the light of above-mentioned facts, specific drug regimens are designed to be used in this significant time of life, by American association for the study of liver disease and infectious disease society of America. Moreover, CDC also supports these guidelines.<sup>17,18</sup>

Recent research work has shown that the age group that encounters most of the hepatitis C cases, has deviated from previously old to nowadays young people, and a significant number of which are women in their fertile age.<sup>19,20</sup> A global survey describes this number to be 35.8%, additionally, among these 0.24% to 4.3% are pregnant ladies.<sup>21</sup> As a matter of fact, hepatitis C have no impact on fertility health of females and because the females hold the desire to conceive despite the infection, the prevalence in pregnant population might reach higher numbers.<sup>22,23</sup> More specifically stating, Pakistan has a high fertility rate which puts women here, in even more danger to encounter hepatitis C while being pregnant.<sup>6</sup> This enhances the risk for vertical transmission of the infection to the next generation.<sup>1,20</sup> Benova L et al, determine this risk round the world as of approximately 5.8%.<sup>24</sup> Among children with hepatitis C infection, 0.2% - 0.4% in European countries and United States while 12 -14% in Africa have acquired the infection via their mother's womb.<sup>14,25</sup> It has been established that higher the viral load, more the chance of transmitting infection to fetus.<sup>24</sup> Other factors associated with greater chance include premature rupture of membranes, HIV co-infection and breast feeding.<sup>8</sup> Furthermore, mode of delivery is declared to have not associated with increased transmission risk.<sup>9</sup> Nevertheless, this infection can be transferred to fetus throughout the pregnancy time.<sup>15</sup> Besides transmission, hepatitis C makes mother and her fetus to bear worse consequences during pregnancy and a difficult upcoming life for the baby with diseased liver.<sup>4,9,26</sup> The commonly encountered pregnancy complications faced by the mothers with hepatitis C infection are intrahepatic cholestasis, gestational diabetes, premature ovarian failure and hypertension.<sup>20,27</sup> Fetal and neonatal compromises associated with hepatitis C are preterm delivery and low birth weight.<sup>9,27</sup> With the aforementioned facts in considerations, American association for the study of liver diseases and the infectious disease society of America formulated guidelines according to which every pregnant lady must undergo the screening for hepatitis C.<sup>18</sup> Similarly screening of new born babies of mothers suffering from hepatitis C is recommended by CDC and American college of pediatrics.<sup>9</sup>

Infection caused by hepatitis C virus, with its chronic and life threatening disease course has profound impact on one's ability to contribute to the society in a positive

manner. And its emerging prevalence has alarmed the healthcare professionals to address the possible means for reduction of further spread at the same time, while dealing with development of more efficient treatment regimens. The abovementioned literature has described the significance of having hepatitis C infection during pregnancy for the mother and the child on its way to this world. In order to deal with this iceberg issue regarding hepatitis C virus infection, this study was conducted. It is aimed to address the prevalence of contracting hepatitis C during pregnancy, major risk factors for the incident and the impact of infection on the pregnancy outcomes.

**METHODS**

This cross-sectional study was performed at Liaquat University Hospital Hyderabad, Gynecology Unit-1, from January 2017 to July 2017 after taking ethical approval. Collection of the data for the study was done according to non-probability purposive sampling. The sample size was calculated by using population proportion (P) for pregnant females suffering from hepatitis C as 8%, absolute precision (d) as 5% and confidence interval as 95%; and it was determined to be 114.<sup>9</sup> Hospital ethical review committee approved the study.

The study was conducted using data from women aged between 20-35 years; having singleton pregnancy at the time of study; who were booked cases with regular follow ups and were admitted for delivery in the hospital. All the females who were either not pregnant or having multiple pregnancies were excluded from the study. Other factors that lead to exclusion of candidates from enrolment in the study were: having co morbid like hypertension or diabetes mellitus; suffering from hepatitis B and /or hepatitis D; possessing past history of hepatitis C infection or diagnosed case of hepatitis C before conception.

The data was obtained from candidates who satisfied the inclusion criteria, after receiving the informed consent. The candidates were asked questions about the past medical history which was significant for acquiring hepatitis C infection. All the candidates were tested for anti HCV antibodies using ELISA method, those who were found positive of antibodies went for testing HCV RNA viral load using PCR. The pregnancy outcomes were also recorded in the context of low APGAR score (<7 at 1 minute), preterm delivery(between 24+0 weeks-36+6 weeks of gestational age) and low birth weight(<2.5 kg).All the information was documented by researchers on formerly designed performa.

**Statistical analysis**

Analysis of the collected data was done on version 16 of SPSS software. Qualitative data was expressed as frequency and percentages. Chi Square test was used to assess the association, p value of <0.05 was take as significant.

**RESULTS**

Total 1 shows 14 Pregnant women, admitted to the labor room of Liaquat university hospital Hyderabad, were studied during this research work. The mean age of study participants was recorded as 27.3±4.6 years. On the other hand, the average results for the current pregnancy were documented as follows:

The mean age of gestation at the time of delivery was 35.1±4.8 weeks. The birth weight of newborn was found to be 2.5±1.0 kg as mean value. The average APGAR score of newly born at 1 minute was 7.93±1.61. To detect hepatitis C in pregnant ladies, ELISA test was done to check antibodies against the virus. In this study 10(8.8%) ladies were found to have positive results for the test, whereas 104(91.2%) were having negative results.

**Table 1: Descriptive data.**

Variables	Mean±SD/ Frequency (%)
Maternal age (years)	27.3±4.6
Distribution of gestational age (weeks)	35.1±4.8
Distribution of birth weight (kg)	2.5±1.0
Distribution of APGAR score	7.93±1.61
Maternal age distribution (years)	<30 years 73(64.0%)
	>30 years 41(36.0%)
Distribution of parity	Primiparity 66(57.9%)
	Multiparity 40(35.1%)
	Grandmultiparity 8(7.0%)
Distribution of gestational age (weeks)	<37 weeks 50(43.9%)
	>37 weeks 64(56.1%)
Distribution of birth weight (kg)	LBW 54(47.4%)
	NBW 60(52.6%)
Frequency of HCV in pregnant women	Positive 10(8.8%)
	Negative 104(91.2%)
Factors leading to HCV	History of surgeries (43.9%)
	History of blood transfusion (60.5%)
	History of vaginal delivery (39.5%)
	History of evacuation (8.8%)
	History of dental surgery (34.2%)
Outcome of pregnant women	APGAR score at one minute (21.1%)
	Preterm delivery (41.2%)
	LBW (48.2%)

When asked about risk factors for contracting HCV, which were encountered by the study candidates, most common factor discovered was history of surgery with 43.9% of women reported this. Similarly, the least common factor was history of evacuation, which was experienced by 8.8% of the study candidates.

**Table 2: Association of HCV with maternal age, parity and gestational age.**

Variables	HCV		p-value	
	Positive	Negative		
Maternal age (years)	<30 years	3(4.1%)	70(95.9%)	0.025
	≥30 years	7(17.1%)	34(82.9%)	
Parity	Primiparity	4(6.1%)	62(93.9%)	0.01
	Multiparity	3(7.5%)	37(92.5%)	
	Grand multiparity	3(37.5%)	5(62.5%)	
Gestational age (weeks)	<37 weeks	2(4%)	48(96%)	0.12
	≥37 weeks	8(12.5%)	56(87.5%)	

During this study considerable number of pregnant ladies observed poor pregnancy outcomes. Of them 41 delivered before term; 48.2% had their babies weighing lower than normal and 21.1% of infants of these mothers suffered lower APGAR score at 1-minute assessment.

Moreover, analysis of relation between positively tested pregnant women for HCV and parity was calculated to have statistical significance (0.01). Among women who were anti HCV positive, 4(6.1%) were primipara; 3(7.5%) were multipara and 3(37.5%) were grand multipara. On the other hand, among women who were negatively tested, 62(93.9%) were primipara; 37(92.5%) were multipara and 5(62.5%) were grand multipara. Another statistically significant (0.025) relation was discovered between HCV infection and maternal age. Accordingly, mothers of age <30 years with positive anti HCV test were 3(4.1%) and with negative test were 70(95.9%). In the same manner mothers with age >30 years who found to be positive for the infection were 7(17.1%) and those with negative results were 34(82.9%).

## DISCUSSION

Where hepatitis C has become a serious threat to health sector globally.<sup>5</sup> Women in their fertile period of life have an increased risk for getting infected with Hepatitis C virus.<sup>28</sup> Kn L et al, worked on the similar context and revealed that about 40% of females suffering from hepatitis C belongs to the fertile age group.<sup>29</sup> The significance to this age group underlies the reason that it has additional dangers when encountered by pregnant females. These women not only are on verge to add more population of hepatitis C virus infected people to the world but also are at risk to face bitter outcomes of the current pregnancy.<sup>9</sup> Researchers suggest an approximate figure of 29,000 for the Hepatitis C suffering mothers delivering babies per annum.<sup>30</sup> Estimation for the prevalence of this infection in pregnant population is the first step to deal with this growing healthcare problem. This study intends to estimate the prevalence of this infection among the pregnant population in this region. During this study, out of 114 enrolled pregnant women, 10(8.8%) participants were discovered to possess Hepatitis C virus infection. Another study on 384 pregnant females was done from 2013-2014 coming to a

hospital in Ethiopia. During this cross-sectional study, the prevalence of HCV was estimated as 0.26 %.<sup>4</sup> A similar study was conducted on primigravidae in Abbottabad. According to this study, the mean age of study participants was 24±5.7 years. Whereas the frequency of HCV antibodies presents in the serum, among these women was calculated to be 13(7.5%).<sup>6</sup> A different study which was executed on 150 ladies, pregnant at the time of study showed that 7(4.66%) ladies were seropositive for Hepatitis C virus.<sup>31</sup> Another similar work demonstrated seropositivity in 3.6% pregnant women.<sup>32</sup> Likewise, researches in Yemen found that 8.5% pregnant females were tested positive for hepatitis C virus on blood examination.<sup>33</sup> Patrick SW et al, studied pregnant ladies suffering from HCV infection from 2009-2014 in Tennessee and USA. it was observed that the number increased by 89% in this period.<sup>34</sup> Multiple studies have described that the variation in the results for prevalence of Hepatitis C virus in pregnant population of different parts of world is associated with the dissimilarity in unhealthy medical practices of blood transfusion and unsterilized equipment usage; socioeconomic status and different diagnostic tools used for the purpose.<sup>4,6</sup>

Although there are several factors that contribute in Hepatitis C virus transmission, however, multiple previous studies have suggested the most common risk factor for contracting HCV particularly in pregnant patients, is through infected blood transfusion.<sup>35</sup> This observed findings were no different and (60.5%) of the pregnant ladies gave the history of prior blood transfusions. A research work executed on 174 pregnant ladies with jaundice resulted in finding that 1.7 % of seropositive study participants for HCV, had previously undergone transfusion of blood.<sup>6</sup> Despite the fact that blood transfusion holds the major share, other factors also serve a significant role in transmitting infection. Therefore, additional noticeable factors found during this study were: past history of surgery which was reported by (43.9%); history of vaginal delivery present in (39.5 %) and history of dental surgery reported by (34.2%) study candidates. Jadoon SM et al, during their analysis for the risks associated with HCV spread among pregnant females, discovered that out of 7.5% candidates whom caught the infection, 9% have had history of surgery before.<sup>6</sup> Furthermore, a study in Baghdad revealed that



even administration of anti-D immunoglobulin therapy is associated with enhanced risk for getting infected with HCV.<sup>26</sup> This study also declares that different obstetrical procedures enhance the chances for spread of hepatitis C virus to the pregnant lady.<sup>26</sup> Besides this Yeung LT et al, proposed that some habits can serve as the additional risk for getting infected with Hepatitis C virus by pennants women such as drug abuse via intravenous or intranasal route and tattooing at home; adding to this HIV infection increase the multiple times.<sup>36</sup>

The most significant impact of hepatitis C in pregnant patients especially the chronic disease, is its negative effects on the developing fetus and the infants.<sup>15</sup> Although several factors play role in worsening impression on fetus such as inefficient perinatal care or I/V drug usage. Nevertheless, alone being an infant to Hepatitis C virus infected mother put them in the greater danger zone.<sup>1,37</sup> In this study, as much as (48.2%) of neonates born to these mothers, had lower than normal birth weight. On the similar note (41.2%) neonates failed to reach the term and were born before term. In addition to this (21.1%) of newborn were documented to have low APGAR score at 1 minute. Likewise, exploring the pregnancy outcomes with maternal Hepatitis C virus infection among 145 infected mothers, Money D et al, observed that 17.9% experienced preterm delivery. Furthermore 12.5% newborns had lower than normal body weight and 11.3% were smaller in size with respect to their gestational age. Additionally, 3.4% fetuses faced death before birth. However, the study found no association of viral load to these poor outcomes.<sup>37</sup> Huang QT et al, executed a meta-analysis to explore the effects of hepatitis C in mother, on the devolving fetus. The observation in this study declare the negative association of the maternal Hepatitis C virus infection on the in-utero growth of the fetus and ultimately results in the lower body weight of the baby at the time of birth.<sup>37</sup> Similar observations were drawn by research work of various studies, according to which, Hepatitis C virus infected mothers have augmented risk for delivering preterm or developing gestational diabetes, hypertension during pregnancy, moreover, the newly born are at increase to have weak physic in term of size and weight.<sup>6,20,15,39</sup> Another study proposed the hazard of developing congenital anomaly among fetus of mothers with hepatitis C virus infection.<sup>40</sup> Nonetheless, maternal Hepatitis C infection is associated with higher chances of requirement for the respiratory support and stay in neonatal intensive care unit.<sup>35</sup> However, the detailed literature review suggests that, where there are many studies supporting the higher negative effects of hepatitis C during pregnancy on its outcomes, many in the data base support no such idea.<sup>20</sup>

A statistical analysis during this study revealed a significant ( $p=0.025$ ) association of maternal age to the seropositivity for Hepatitis C virus in the pregnant population. According to the study results, authors found that increasing maternal age makes women further

vulnerable for contracting the infection, as 3(4.1%) women found positive for hepatitis C infection in the age group of <30 years while 7(17.1%) were tested positive among the group of pregnant ladies with age >30 years. These findings are in parallel with the study results of a work done by Afsheen Z et al, and the statistical significance calculated during their study was ( $p=0.025$ ), further, the most commonly encountered age group of pregnant ladies for Hepatitis C infection was observed to be 26-35 years.<sup>31</sup>

## CONCLUSION

This study shows that there are significant number of ladies coming to hospital for their deliveries have unnoticed HCV in their serum. Yet many females avoid going to hospital for this condition. Therefore, it is suggested that detailed screening programs should be launched in the general population in order to clarify the actual number of HCV infected mothers in this population. Furthermore, past history of blood transfusion and prior surgery was reported by majority of the infected ladies. Steps to minimize the communication of infection via these routes should be addressed. Although many infected women in this study faced poor pregnancy outcomes but efficient antenatal care may help minimize worse cases.

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