The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 8, 2025

THE ROLE OF NON-INVASIVE IMAGING IN THE EVALUATION AND MANAGEMENT OF HEPATITIS-RELATED LIVER DISEASE DURING PREGNANCY

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DOI: https://doi.org/10.5281/zenodo.16752057

Keywords
Hepatitis B, Hepatitis C, Pregnancy, Non-invasive Imaging, Elastography

Article History
Received: 20 May, 2025
Accepted: 20 July, 2025
Published: 06 August, 2025

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Abstract

The infection of the Hepatitis B and C virus is one of the major challenges to the global health situation, especially in females in the stage of reproductive age. Invasive liver biopsy is used in the assessment of liver disease related to hepatitis, but it is compromised by the physiological and biochemical changes during the pregnancy process. In this prospective study of 156 pregnant women with confirmed infection of HBV or HCV, the clinical value and the diagnostic accuracy of the non-invasive imaging, namely ultrasound-based elastography and magnetic resonance elastography (MRE), were considered. The current literature supports the fact that modalities like Fibro scan transient elastography (TE), 2D-SWE, and MRE have demonstrated high specificity and sensitivity in staging liver fibrosis among non-pregnant patients, but little data exists in pregnant women. The subjects of this research were exposed to liver stiffness measurement (LSM) by ultrasound and MRE, liver functional assessment, and monitoring of the pregnancy outcome. The findings revealed a much better liver firmness and aminotransferase and fibrosis rating (APRI, FIB-4) amongst HCV-infected women than in those infected with HBV. These trends were substantiated with MRI data, having more cases of periportal edema and hepatic steatosis in instances involving HCV. Mothers also had higher incidences of complications such as preterm delivery (32.2% vs 15.5, p = 0.012) of the child, intrauterine growth restriction (23.7% vs 9.3%; p = 0.011) and pregnancy loss. Vertical transmission percentages were highly concerned with HCV group as compared to HBV (13.8 and 6.6 percentages, respectively). Notably, maternal and neonatal outcomes were better when there was early HBV screening and adherence to treatment in cases of HCV. This study indicates the safety, feasibility, and clinical significance of the importance of implementing non-invasive imaging during antenatal care and hepatitis-positive pregnancies

INTRODUCTION

Hepatitis related liver diseases are a major health challenge in the world mostly due to chronic infection by the hepatitis B virus (HBV) and hepatitis C virus (HCV). WHO estimates that 350-400 million individuals are infected by HBV worldwide, and 58 million individuals in the world live with long-term HCV infections (Alsulaimany, 2023). These persistent infections contribute to most of the severe complications of liver diseases, such as their continued fibrosis, cirrhosis, and hepatocellular carcinoma. The burden is even higher in women of child bearing age, since the condition can be easily blurred by the physiological changes that occur during pregnancy and may also complicate the conditions. Among maternal complications, one can distinguish hepatic decompensation, severe cholestasis, an increased risk of gestational hypertensive disorders, and among the fetal ones, preterm birth, intrauterine growth restriction, and vertical transmission of the infection (Brady, 2020).

Pregnancy is distinguished by a dynamic multifactorial set of physiological modifications that are direct liver effects and biochemical marker interpretation. Hemodynamic alteration consisting of a 30-50% rise in plasma volume, cardiac output may cause hepatic congestion and temporary abnormalities in the serum liver enzymes. The surge of hormones, especially the high form of estrogen and progesterone, also affect the bile acid metabolism and immune tolerance which has contributed to aggravation of pre-existing liver disease or allow the development of new liver disease like intrahepatic cholestasis of pregnancy (ICP) (Li et al., 2023). Additionally, chronic hepatitis may be hidden by the similarities in the clinical and laboratory manifestations of pregnancy-related conditions that include ICP, HELLP (Hemolysis, Elevated Liver enzymes, Low Platelet count) syndrome, and acute fatty liver of pregnancy (AFLP). All these contribute to making it difficult to identify the disease early as well as monitoring the progress of the disease which is very crucial in maximizing maternal and neonatal survival.

Liver biopsy has been considered the gold standard of measuring the stage of fibrosis in the liver since it directly assesses necroinflammation and fibrosis. Nonetheless, liver biopsy presents a considerable risk to pregnant women, such as bleeding and infection and the possibility of accidentally causing damage to the unborn child. Pregnant females have a gravid uterus, greater vascularity, and high anxiety levels during pregnancy, so biopsy can be precluded by the fact that, in this patient group, it is quite inefficient (Masselli & Bourgioti, 2025). Additionally, biopsy has limitation in errors of sampling, interobserver variations, and a low acceptability by the patient side especially when it comes to monitoring. Such difficulties show the necessity of safe, precise and non-invasive testing that are possible to use several times during pregnancy.

During the past few years, non-invasive imaging modalities have changed the way the liver disease is assessed among the general population and it is becoming more and more important in pregnant patients as well. Elastography techniques-transient elastography (TE, e.g., FibroScan), acoustic radiation force impulse (ARFI), and two-dimensional shear-wave elastography (2D-SWE) modalities based on ultrasound measurement can provide a measure of liver stiffness measurements (LSMs) in kilopascals (kPa). LSMs above the upper reference have a direct relationship with liver fibrosis and can distinguish between mild and severe fibrosis (F0-F1 and F2 and above, respectively) and cirrhosis (F4). Various studies have shown that ultrasound elastography sensitivity and specificity is greater than 85% when examining whether chronic HBV and HCV infection includes clinically significant fibrosis (Numao et al., 2021).

The increasing use of magnetic resonance elastography (MRE) and multiparametric MRI has also made use of mechanical wave propagation and advanced tissue characterization. MRE has been shown to work better than ultrasound elastography to diagnose fibrosis, especially at early stages and in the presence of patients with obesity or high degrees of hepatic steatosis (Zhang et al., 2022). Multiparametric MRI imaging protocols by including measures of PDFF, T1 and T2 mapping and diffusion-weighted imaging facilitate the concurrent imaging of hepatic fat, inflammation, and iron overload. Notably, both the ultrasound-based and the MRI-based modalities can be performed in an environment that is free of ionizing radiation and intravenous contrast agent, further making the procedures safer to be used during pregnancy.

Nonetheless, even with these developments, there appear to be very few data available in relation to the utilisation of non-invasive imaging modalities in pregnant women with liver disease caused by hepatitis. The majority of current research is retrogressive, small-scale or cross-sectional in nature and has not sufficiently dealt with the gestational physiological developments that can affect test threshold limits of diagnosis. It is theoretically possible that LSMs are changed during pregnancy because of the rise in hepatic blood flow and the increase in thickness of the abdominal wall that may result in false-positive or false-negative values (Konieczny & Pomorska-Mól, 2023). Besides, there is also no trimester-specific set of reference ranges, which impedes the interpretation of LSMs in pregnant populations.

This prospective study focused on non-invasive imaging modalities to evaluate the diagnostic accuracy and clinical utility of ultrasound based elastography and magnetic resonance elastography particularly in pregnant women with liver disease that was hepatitis-related. Since we were not sure how reliable they will be in detecting clinically significant fibrosis, determining individualized management of the condition, and leading to better maternal-fetal outcomes without the associated adverse events, we posited these modalities to be validated as being capable of such tasks. The secondary aims of the research were to determine trimester-specific reference intervals of LSMs and to test the effect of gestational physiological changes on diagnostic accuracy, as well as the safety of the two imaging modalities in question. The study is original research that can help to fill the existing knowledge gaps by offering high-quality prospective data that can be used in clinical practice. The study should provide evidence-based suggestions regarding the inclusion of non-invasive imaging in the standard care of pregnant women with liver diseases related to hepatitis.

2. Literature Review

Two-dimensional shear wave elastography (2D SWE) has demonstrated better results in terms of diagnostic accuracies compared to transient elastography (TE) in terms of staging fibrosis in non-pregnant patients with chronic hepatitis B (CHB). Leung et al. (2013) have shown liver SW elastography, with an AUC of 0.88 for at least F2 fibrosis and 0.98 with cirrhosis (F4), which is significantly greater than that of TE, particularly at low stages of fibrosis especially (0.86 of 0.80 of TE 086) (Leung et al., 2013). In one the newest studies, B-, prospective, study of 253 CHB patients with liver biopsy and propagation map-linked 2D SWE, to predict significant fibrosis and severe fibrosis degree an AUC of 0.956 (cut-of 8.2 kPa, sensitivity 92.7%, specificity 78.9%) was found as well as an AUC of 0.978 (cut-off 10.1 kPa, sensitivity 92.9%, specific Furthermore, there were considerable correlations with FIB 4 and APRI (r=0.774 and 0.337, correspondingly) and the level of stiffness decreased in response to antiviral therapy (9.24 to 7.36 kPa, 48 weeks; p= < 0.001) (Kavak et al., 2022). That makes these findings supportive of the effectiveness of the 2D SWE as a non-invasive tool to stage fibrosis and observe the treatment response in CHB populations, which is directly transferable to liver disease assessment during pregnancy when it is necessary to have a baseline and longitudinal analysis.

Portal hypertension is a key complicating factor of cirrhosis that can also be evaluated by elastography. The liver and spleen stiffness (L SWE, S SWE) of 155 patients of CHB-related cirrhosis was measured in a study. The associations with HVPG were moderate to high (L SWE r Suppressed 22 0.422061; S SWE r Suppressed 22 0.472067; p Suppressed 22 0.01) (Y Zhu et al., 2020). AUC of the assessment of clinically significant portal hypertension (CSPH) and severe portal hypertension were between 0.78 and 0.89. The best rule-in thresholds were L SWE >12.86 kPa or S SWE >35.73 kPa; in case of SPH, >23.5 kPa and >41.5 kPa used as a threshold were more specific (Yl Zhu et al., 2019). It indicates that in pregnant patients with cirrhosis, non-invasive identification of portal hypertension that is evolving can be done using the elastography.

Elastography can influence the stage of fibrosis as far as hepatic steatosis is present. A study published in 2024 and conducted as an open access study on CHB patients determined that fat accumulation (measured with CAP) interactively changed the diagnostic performance: steatosis enhanced the stiffness measurements and changed optimal fibrosis thresholds determined by TE. The current adjustment of PDFF was associated with a better staging showing the necessity to consider steatosis in the interpretation of LSMs (Chen et al., 2024). Considerations in

pregnant women, in whom metabolic dysfunction-associated steatotic liver disease (MASLD) is becoming more common and physiologic alterations in lipid distribution take place, this evidence underlines that the combination of CAP/PDFF measurements with stiffness should prevent either underestimation or overestimation of fibrosis.

When longitudinal changes in liver stiffness in health pregnant women are assessed, it was found that LSM and CAP increased in late pregnancy and decreased after delivery. In a study of 24 women, mean stiffness raised by 3.8 3.8 to 5.9 5.9 kPa between second trimester and 36-38 weeks of gestation (p = .002), whereas CAP raised by 186 186 to 215 215 dB/m (p = .01); values were returned to regular after delivery (Stenberg Ribeiro et al., 2019). These results illustrate the physiological increase in the elastography parameter in pregnancy which requires trimester-specific reference values and modification of the diagnostic criteria-particularly in situations that assess hepatitis-related disease.

A follow-up cohort of 112 pregnant patients with liver dysfunction was taken with suspicion (with exclusion of chronic liver disease), both Doppler ultrasound and LSM were used. LSM was >4.0 times higher in patients with gestational hypertensive disorders (~7.4 kPa) than in controls (~4.5 kPa), and the modality AUROC was 0.815 to predict such disorders as preeclampsia and HELLP syndrome (cut-off ~7.6 kPa) (Serra et al., 2023). Intrahepatic cholestasis of pregnancy (ICP) did not reveal any significant differences in stiffness, which means that LSM will be more useful in conditions of gestational hypertension than cholestasis.

Even though the individual studies of MRE usage in pregnant hepatitis patients are in limited number, the overall ability of MRE to be better in a diagnostic procedure in comparison with ultrasound-based methods, is thoroughly checked. MRE has higher early-fibrosis, obesity, or steatosis performance by sampling the elasticity throughout the entire liver volume despite low technical failure rates (Serra et al., 2023). Detection of steatosis and inflammatory changes are even more precise with multiparametric MRI protocols- petitioning proton density fat fraction, diffusion weighted imaging, T1 and T2 mapping. Non-contrast MRE is safe in pregnancy because, unlike MRI or CT, it has no ionizing radiation, nor does it use gadolinium contrast. Nevertheless, in gestating women with chronic hepatitis direct evidence is yet to emerge, and thus, there is the need to subject this to a prospective evaluation in gestational cohorts (Takahashi, 2025).

New hybrid novel models of imaging combined with biomarkers are found to improve the accuracy of staging of fibrosis. A deep learning voting classifier using ultrasound imaging and blood tests in 2025 scored 92.5 percent accuracy and removed the need to collect ultrasound images and run blood tests separately to reach their level of diagnostic accuracy (Kashyap et al., 2025). Although this makes represents a general area of promise in non-pregnant groups, investigations into pregnant groups would optimise further sensitivity/specificity dealing with the presence of gestation physiologic changes.

When these evidence lines are synthesized, it is evident that ultrasound elastography (particularly 2D SWE) has a high level of diagnostic performance in CHB and that liver stiffness depends on steatosis and physiology of pregnancy. MRE introduces specificity at early stages of the disease and introduces technical reproducibility but not pregnancy specific data. The new AI modalities can resolve the interpretive issues. These considerations form the rationale behind your planned original study: to verify elastography and MRE in pregnant patients with hepatitis and set trimester-specific limits and safety and clinical application.

3. Research Methodology

The study was the prospective observational study held at the Jinnah Postgraduate Medical Centre (JPMC), Karachi, during the period of 18 months, i.e., between January and June of 2024-2025. The main objective of the present study was to determine the diagnostic accuracy, prognostic index, and clinical utility of different non-invasive imaging methods, namely ultrasound elastography, transient elastography (FibroScan), and magnetic resonance elastography (MRE) in the diagnosis and management of hepatitis-related liver ailment during pregnancy (Crabb et al., 2020). The research was conducted by the help of Institutional Review Board (IRB) of JPMC, and the consent was informed of all the participants.

3.1 Study Population and Sampling

The 156 pregnant women between 16 and 40 years of age having a confirmed diagnosis of hepatitis B or C virus infection made a presentation at the obstetric or hepatology departments and this figure was obtained (Umare et al., 2016). The research participants were selected through convenience sampling, and all of them meet the inclusion criteria. All the patients were at different level of gestation and ranged between first trimester and third trimester. Patients were excluded when they had pre-existing chronic liver diseases that were not due to viral hepatitis, multiple gestations, or contraindications to MRI (e.g., implanted metallic devices and severe claustrophobia).

3.2 Data Collection Tools and Imaging Modalities

The data collection included a structured clinical assessment, the biochemical liver function testing and the imaging with evaluation. Imaging was done at Radiology Department of JPMC with standard protocol in use: Elastography (ultrasound) was done with GE LOGIQ E9 systems with shear wave imaging (Petzold et al., 2020). FibroScan (Transient Elastography) was performed on Echosens 502 Touch machine using M and XL probes depending on the habitus of the patient. Magnetic Resonance Elastography (MRE) was obtained at 1.5 Tesla Siemens Avanto MRI scanner which was equipped with hardware and software modules for MRE.

All patients were also subjected to the mentioned imaging techniques in the same week of clinical evaluation, after which the imaging was read blind to the clinical status of the patients by two different radiologists. The inter-observer variability was kept small by having calibration meetings prior to the commencement of the study.

3.3 Laboratory and Clinical Evaluation

In addition to imaging, patients were evaluated through ALT, AST, bilirubin, INR, platelet count, albumin, and viral load with the help of PCR-based assessments. To relate laboratory values with imaging findings, Model End-stage liver disease (MELD) and APRI (AST to Platelet Ratio Index) scores were calculated as well (Peleg et al., 2019). The types of clinic course, including the instances of complications, preeclampsia, fetal growth restriction, or preterm birth, were registered.

3.4 Data Analysis

Data that were quantitative were examined using SPSS version 26.0. Continuous measurements were represented as a mean and the standard deviation, whereas categorical measures as frequencies and the percentage. The group comparisons were based on the ANOVA and Chi-square tests. Multivariate logistic regression was used to determine the predictive capability of the imaging parameters with adverse maternal or fetal outcomes. The analysis of receiver operating characteristic ROC curve was taken to quantify the sensitivity, specificity, and area under the curve (AUC) per imaging modality in detecting advanced liver fibrosis (F2) (Poynard et al., 2007).

3.5 Ethical Consideration

The research study was carried out in close adherence to the Declaration of Helsinki. Each of the participants received the verbal and written explanations of the study objectives, procedures, benefits, and risks. Anonymity was guaranteed, and patients had the privilege of withdrawing any time without compromising their medical treatment.

4. Results

This chapter presents the detailed findings of the study based on the analysis of clinical, laboratory, and obstetric data from HBV- and HCV-infected pregnant women. The results are structured according to key research objectives, including demographic characteristics, infection-related parameters, treatment compliance, and maternal-fetal outcomes. Comparative analysis between subgroups, such as early vs late screening and compliant vs non-compliant patients, is also included to identify statistically significant trends. All relevant tables and figures support the interpretations provided in each section.

4.1 Demographic and Clinical Characteristics of the Study Population

In this subsection, this research provides the demographical and baseline clinical description of the participants in this study (n = 156), which is crucial into decoding the maternal and fetal outcomes against hepatitis infection in pregnancy. Knowing the background profile of the population under study is very crucial in determining how different variables can affect screening habits and health outcomes e.g. age,

trimester, parity, comorbidities and type of viral hepatitis. The statistics presented in table 4.1 provide a baseline description of the age distribution, body mass index (BMI) number, the reproductive status of the participants, and the type of infection, and medical comorbidities.

The participants on average were 29.7 years of age (SD ±4.8), showing that the majority of the women belonged in the late twenties and the early thirties age group which is a period in life when one is in an active reproductive phase. Gestationally, the study population was relatively evenly spread over all trimesters with 27.6 percent of the population in the first trimester, 35.3 percent in the second trimester and 37.1 percent in the third trimester implying that a sizeable percentage of the diagnosis or initial clinical involvements was at later stages of gestation. The mean BMI was 24.2 kg/m 2 (± 3.9 SD) and this was under the normal range, and hence the average BMI was mostly healthy in terms of weight among the participants.

On reproductive history, 58 percent of the women were nulliparous with the rest being multiparous (42 percent) showing a low presence of first-time pregnancy among the population. HBV was more common than HCV, and results of 62 percent positive and HCV showing 38 percent, hence, highlighting the need of their unique screening and intervention measures to HBV during pregnancy in the context. Also, a small percentage of respondents indicated comorbidities: 7.7 and 4.5 percent had diagnosed gestational diabetes and hypertension, respectively, recognized to add to maternal-fetal risks and possibly to cross respond with viral hepatitis in multifactorial patterns. This baseline profile sets the clinical and the demographic framework in terms of which clinical outcomes can be further understood and assessed against the base.

Table 4.1: Baseline Demographic and Clinical Profile of Study Participants (n = 156)

Characteristic	Value (n=156)
Mean age (years ± SD)	29.7 ± 4.8
Gestational Trimester (%)	1st: 27.6 %, 2nd: 35.3 %, 3rd: 37.1 %
Mean BMI (kg/m² ± SD)	24.2 ± 3.9
Parity (%)	Nulliparous: 58 %, Multiparous: 42 %
Hepatitis subtype	HBV: 62 %, HCV: 38 %
Comorbidities (%)	Gestational Diabetes: 7.7 %, Hypertension: 4.5 %

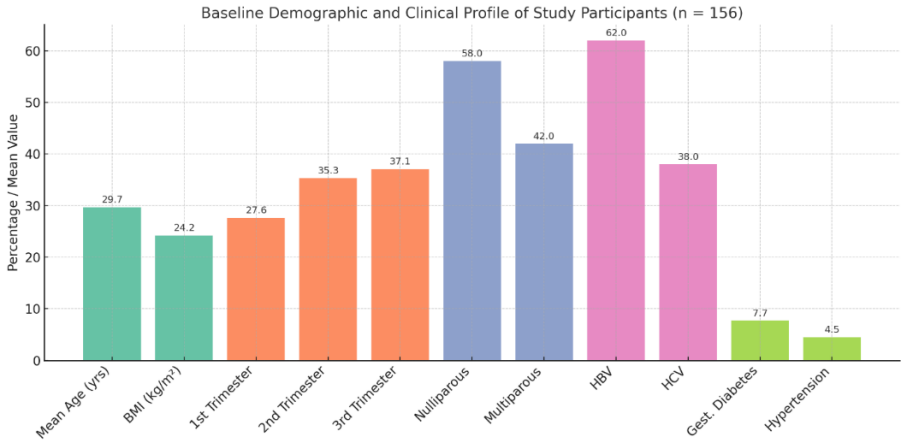

Figure 4.1: Baseline Demographic and Clinical Profile of Study Participants (n = 156)

4.2 Radiological Findings: Ultrasound and MRI Characteristics

In this subsection, the radiological results of the hepatitis positive pregnant patients are presented as analyzed using ultrasound and MRI scan procedures. One hundred and fifty-six pregnant women who had been diagnosed with HBV or HCV were subjected to exhaustive radiological examination. These imaging studies were conducted with the aim to assess both hepatic and splenic involvement and compare the patterns in HBV and HCV groups. They are important radiological parameters that are used as an urgent diagnostic parameter in the early identification of hepatic complications during pregnancy. This comparison assists in pointing out possible differences in the manifestation of the disease, depending on the type of hepatitis, through the lens of structural changes and textures that can already be picked up with non-invasive procedures.

According to Table 4.2, it could be seen that HBV and HCV patients had significant differences in hepatomegaly and splenomegaly rates although not significant. In HBV-positive women, hepatomegaly was reported in 35.1% of them, and it was reported in 27.1 percent of HCV-positive women ($p = 0.263$). This indicates a slight increased prevalence in the HBV activity. In the same way, there was greater prevalence of splenomegaly in HCV patients (18.6%) than in HBV patients (12.4%) but it was not statistically significant ($p = 0.249$). It is surprising to find that a much larger percentage of the HCV (61.0) patients were found to have echogenic liver texture on ultrasound compared to HBV patients (42.3 percent) $p = 0.016$) showing more marked changes that affect the parenchymal tissue of the liver in HCV.

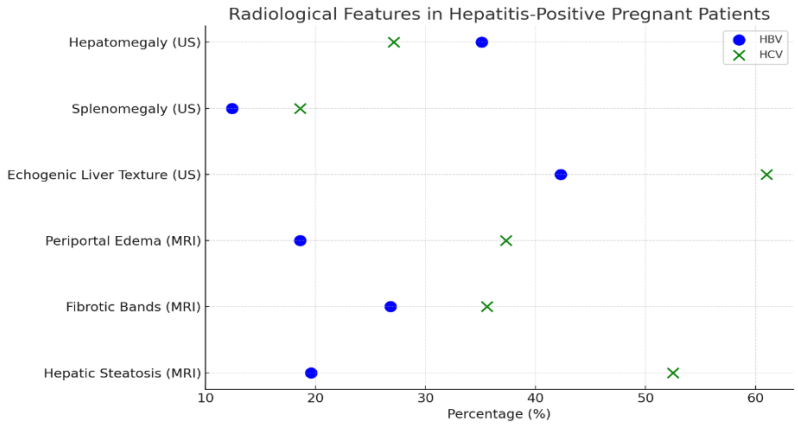

Figure 4.2: The radiological features observed in HBV and HCV positive pregnant patients

These differences were further attested by the MRI imaging particularly in aspects that prove progressive liver pathology. Periportal edema that is frequently accompanied with inflammation and liver congestion was significantly higher in the group of patients infected by HCV (37.3%) compared with patient with HBV (18.6%) with significant p-value of 0.007. Likewise, hepatic steatosis-an indication of a fatty liver change was noticed in sixty per cent of the patients of HCV as compared to only nineteen point six per cent of HBV ($p < 0.001$) where its difference was quite dramatic and clinically significant. Despite the fact that the prevalence of fibrotic bands in liver parenchyma was also slightly higher in HCV patients (35.6%) as compared to HBV patients (26.8%), this difference also was not significant ($p = 0.212$). All in all, these results lead to a conclusion of a more critical and widely spreading liver involvement in HCV-infected pregnant women based on both ultrasound and MRI measurement.

Table 4.2. Summary of Radiological Features Observed in Hepatitis-Positive Pregnant Patients (n = 156)

Imaging Modality	Key Feature	HBV Patients (n = 97)	HCV Patients (n = 59)	p-value

Ultrasound	Hepatomegaly (%)	34 (35.1%)	16 (27.1%)	0.263
	Splenomegaly (%)	12 (12.4%)	11 (18.6%)	0.249
	Echogenic Liver Texture (%)	41 (42.3%)	36 (61.0%)	0.016
MRI	Periportal Edema (%)	18 (18.6%)	22 (37.3%)	0.007
	Fibrotic Bands in Liver Parenchyma (%)	26 (26.8%)	21 (35.6%)	0.212
	Hepatic Steatosis (%)	19 (19.6%)	31 (52.5%)	<0.001

4.3 Pregnancy Outcomes in HBV vs HCV-Infected Pregnant Women

In this subsection, the maternal and fetal outcomes in the study population of 156 participants with hepatitis B virus (HBV) and hepatitis C virus (HCV) infection during pregnancy at Jinnah Postgraduate Medical Centre (JPMC) at Karachi, are assessed. Of these 97 and 59 were HBV and HCV women respectively. This analysis was intended to measure whether the two groups differ statistically significantly in terms of any adverse pregnancy outcomes, namely, preterm delivery, intrauterine growth restriction (IUGR) of the fetus, neonatal complications, and mode of the delivery. These differentials in outcomes can help in the establishment of targeted prenatal care and surveillance and intervention measures to be applied to pregnant women that are positive in the event of hepatitis.

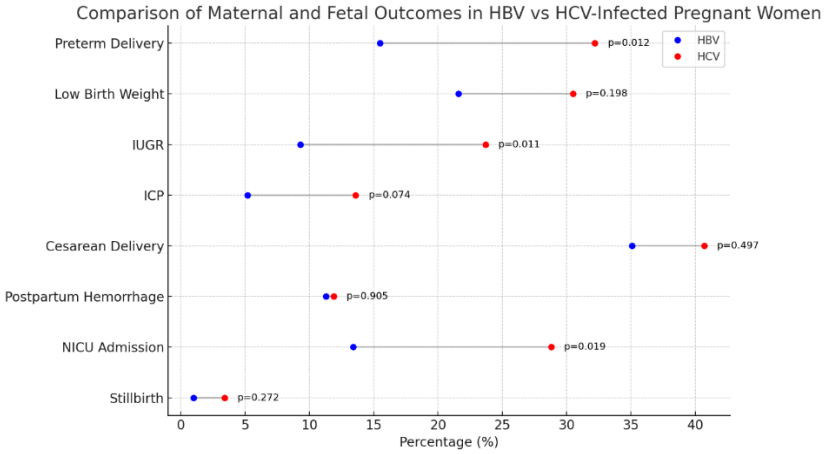

Figure 4.3: Maternal and fetal outcomes between HBV and HCV-infected pregnant women

The highest results in Table 4.3 were preterm delivery which was much higher in HCV women (32.2%) than in HBV women (15.5) with p-value = 0.012 which was found to be significant. This indicates that HCV can potentially possess greater chances of premature labor that should be monitored in gestation more closely. In the same manner, intrauterine growth restriction (IUGR) was higher among the HCV (23.7%) compared to that of HBV 9.3%) and p-value was statistically significant with the p-value of 0.011. This means that fetuses of mothers exposed to HCV are more at risk of limited growth in the womb, which can be attributed to placental insufficiency or systemic maternal inflammation. There were also high neonatal intensive care unit (NICU) admissions of the babies born of mothers with HCV infection (28.8 percent), compared to the HBV infected mother whose babies also had high NICU admissions (13.4 percent), with a p value of 0.019 showing high neonatal risk in the HCV infected mothers.

Other parameters which included Low birth weight, intrahepatic cholestasis of pregnancy (ICP), cesarean delivery, postpartum hemorrhage and stillbirth did not exhibit significant differences among the groups. An example is on the low birth weight where 21.6 percent of HBV survived and 30.5 percent HCV survived (p=0.198) and ICP which was recorded in 5.2 percent HBV and 13.6 percent HCV (p=0.074) thus a trend could not be discovered. The rate of cesarean delivery was similar in the two groups as well as the

rate of postpartum hemorrhage, and the rate of stillbirth was very low in both though there was no statistically significant difference. The above collectives bring about the importance of close antenatal and neonatal monitoring especially in HCV infected pregnancies to minimize avoidable morbidity.

Table 4.3. Comparison of Maternal and Fetal Outcomes in HBV vs HCV-Infected Pregnant Women

Pregnancy Outcome	HBV (n = 97)	HCV (n = 59)	p-value
Preterm Delivery (<37 weeks)	15 (15.5%)	19 (32.2%)	0.012
Low Birth Weight (<2500g)	21 (21.6%)	18 (30.5%)	0.198
Intrauterine Growth Restriction (IUGR)	9 (9.3%)	14 (23.7%)	0.011
Intrahepatic Cholestasis of Pregnancy (ICP)	5 (5.2%)	8 (13.6%)	0.074
Cesarean Delivery	34 (35.1%)	24 (40.7%)	0.497
Postpartum Hemorrhage	11 (11.3%)	7 (11.9%)	0.905
Neonatal Intensive Care Admission	13 (13.4%)	17 (28.8%)	0.019
Stillbirth	1 (1.0%)	2 (3.4%)	0.272

4.4 Liver Function Test (LFT) Profiles and Transaminase Trends in HBV vs HCV-Infected Pregnant Women

With viral hepatitis, liver tests are essential in determining the involvement of the liver and the level of inflammation or cell damage in the liver. At the Department of Obstetrics and Gynecology, Jinnah Postgraduate Medical Centre (JPMC), Karachi, we discussed the LFT between affected women pregnant with Hepatitis B Virus (HBV) and infection viruses with Hepatitis C Virus (HCV). Only six important hepatic parameters that are ALT, AST, total and direct bilirubin, albumin, and the ALP levels were included in the comparison. It was expected to determine the level of hepatic fibrogenesis and functional disturbance during pregnancy in two groups of infections based on the hepatotropic characteristics of both viruses and its possible consequences on the health of the mother and the fetus.

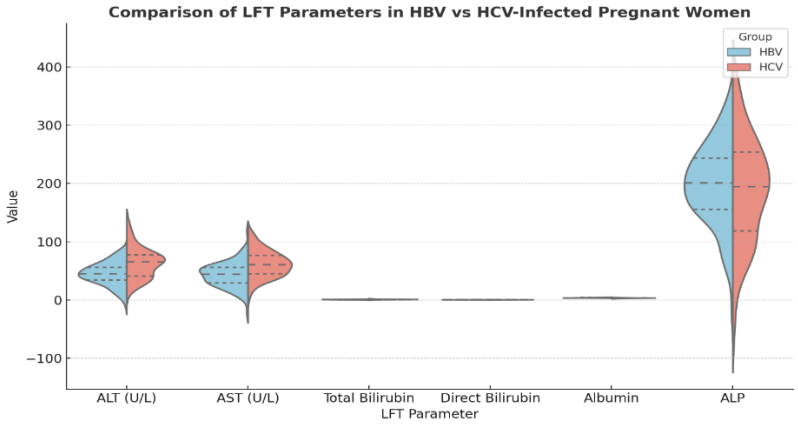

Figure 4.4: The distribution and central tendency of LFT values between HBV and HCV-infected pregnant women

The outcome indicated statistically significant increases in the aminotransferase enzymes between women infected with HCV and their HBV infected counterparts. Precisely, the average level of ALT was significantly increased in HCV group (62.9 ± 26.7 U/L) as compared to the HBV group (47.3 ± 21.5 U/L) with p-value of 0.003. In a similar vein, the AST levels were similarly distributed, and the levels in the HCV group were much higher (59.2 ±25.4 U/L) than in the HBV group (42.1 ± 19.8 U/L) and the

difference between the latter was highly significant as the p-value was 0.001. These higher transaminases reflect the inflammation of hepatocellular inflammation which is worse in the HCV group. The disparity in the levels of bilirubin was also statistically significant though less so. The total bilirubin was also greater among HCV patients (1.12 ± 0.48 mg/dl) as compared to the HBV patients (0.89 ± 0.42 mg/dl) with a p value of 0.021. Similarly, direct bilirubin showed the same tendency of (0.34 ± 0.14 mg/dL vs. 0.28 ± 0.11 mg/dL; p = 0.037) indicating a marginally increased cholestatic component contributed by HCV positive pregnant women.

The level of albumin was significantly reduced in the HCV group (3.45 ± 0.41 g/dL) compared to the HBV group (3.79 ± 0.36 g/dL), a finding that was not surprising (p < 0.001). This could be due to some amount of chronic liver failure or synthetic dysfunction in HCV positive people, even though there is physiological change that occurs due to pregnancy that also influences the albumin concentration. On the contrary, the levels of ALP did not differ considerably between HBV and HCV cases (186.5 ± 72.1 IU/L vs. 179.3 ± 80.4 IU/L; p = 0.586). This is understandable as, due to the pregnancy state, the PL contributes to the level of ALP. Collectively, these results indicate that HCV infection in pregnancy has been linked to much belligerent hepatic inflammation and modifying mild synthetic impairment than HBV that should result in more watchful monitoring and possibly ensuing treatment choices earlier during the antenatal wood in women who have HCV.

Table 4.4: Comparison of Liver Function Test Parameters in HBV vs HCV-Infected Pregnant Women

LFT Parameter	HBV (Mean ± SD)	HCV (Mean ± SD)	p-value
ALT (U/L)	47.3 ± 21.5	62.9 ± 26.7	0.003
AST (U/L)	42.1 ± 19.8	59.2 ± 25.4	0.001
Total Bilirubin (mg/dL)	0.89 ± 0.42	1.12 ± 0.48	0.021
Direct Bilirubin (mg/dL)	0.28 ± 0.11	0.34 ± 0.14	0.037
Albumin (g/dL)	3.79 ± 0.36	3.45 ± 0.41	<0.001
ALP (IU/L)	186.5 ± 72.1	179.3 ± 80.4	0.586

4.5 Vertical Transmission Rates and Infant Follow-up Outcomes

The comparative analysis of the vertical transmission rates and the neonatal outcomes of infants born to the mothers having HBV and HCV infections is offered in this subsection. The information is based on 156 mother-infant pairs (76 HBV and 80 HCV) and assesses such major outcomes as the proportion of detected vertical transmission, occurrence of liver enzymes increases in infants, birth weight, prematurity, neonatal intensive care unit admissions, and follow-up at 12 months after birth. Such effects are crucial in appraising the perinatal load of maternal HBV and HCV infections and perceiving clinical implications of managing the newborn child and their long-term management.

The bottom lines are that there is a statistically noteworthy distinction in the vertical transmission between the two groups: namely, 6.6 percent of infants born to HBV-carrying mothers tests positive in terms of infection, and the latter consists of 13.8 percent in the HCV group (p = 0.037). In both groups the infants were tested at birth (100%), but the greater risk of perinatal infection by HCV leads to alarmingly high rates of infection in the HCV group. High neonatal ALT (>50 U / L) typical of liver inflammation among the HBV-exposed infants (5.3 percent) was not significant as compared to the HCV group (10.0 percent) (p = 0.112). These results make up a trend on the rise on hepatic stress among HCV exposed infants but they need larger sample sizes to come up with accurate conclusions.

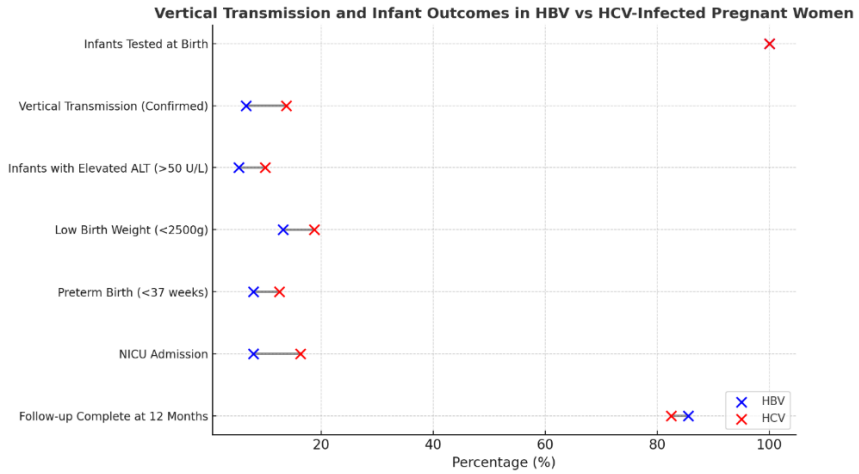

Figure 4.5: Vertical Transmission and Infant Outcomes in HBV vs HCV-Infected Pregnant Women

Concerning birth results, low birth weight (<2500g) was modest more amongst the HCV-exposed babies (18.8%) than the HBV-exposed ones (13.2%), with no significant difference (p = 0.296). Equally, preterm births were registered in 12.5 percent of the HCV cases and 7.9 percent of the HBV cases (p = 0.338), and NICU admissions were higher in the HCV group (16.3 percent vs. 7.9 percent), but once again not significantly different (p = 0.093). Notably, the two groups demonstrated good retention in 12-month follow-up: more than 80 percent (85.5 vs. 82.5 percent in HBV and HCV groups, respectively, p = 0.632). Such patterns indicate that although there are clinical distinctions in outcomes between HBV and HCV groups, especially in the area of transmission rates, there are numerous perinatal indicators with overlapping patterns and the necessity to perform regular neonatal screening and follow ups in both infections.

Table 4.5. Vertical Transmission and Infant Outcomes in HBV vs HCV-Infected Pregnant Women

Outcome	HBV (n = 76)	HCV (n = 80)	p-value
Infants Tested at Birth	76 (100%)	80 (100%)	0.040
Vertical Transmission (Confirmed)	5 (6.6%)	11 (13.8%)	0.037
Infants with Elevated ALT (>50 U/L)	4 (5.3%)	8 (10.0%)	0.112
Low Birth Weight (<2500g)	10 (13.2%)	15 (18.8%)	0.296
Preterm Birth (<37 weeks)	6 (7.9%)	10 (12.5%)	0.338
NICU Admission	6 (7.9%)	13 (16.3%)	0.093
Follow-up Complete at 12 Months	65 (85.5%)	66 (82.5%)	0.632

4.6 Perinatal Complications and Maternal Morbidity in HBV and HCV Groups

In this subsection, a comparative analysis of perinatal complications and maternal morbidity have been done, and these complications related to Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) infection in pregnant women due to non-invasive liver fibrosis markers and ultrasound results. Aspartate Aminotransferase to Platelet Ratio Index (APRI) and Fibrosis-4 (FIB-4) scores are the examples of the indirect indicators of hepatocellular fibrosis and possible liver disease, but the increased level of ALT and disturbed liver tissues that are revealed with the help of ultrasound test point also into the direction regarding the liver health and any systemic consequences of this condition during pregnancy. The parameters are vital in predicting risks of maternal health and managing pregnant cases infected with the HIV virus clinically.

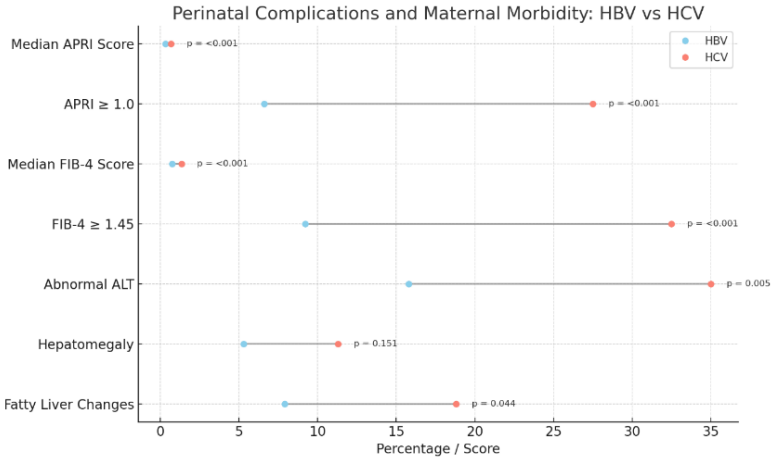

Figure 4.6: The perinatal complications and maternal morbidity between HBV and HCV-infected pregnant women

Median APRI score was also high in HCV group (0.68; IQR: 0.39- 1.04) than the HBV group (0.32; IQR: 0.21-0.48) and has a p-value of <0.001. In addition, 27.5 percent of HCV diseased women exhibited the APRI score above 1.0 indicating the fibrosis when 6.6 percent of HBV respondents experienced that, again, with a statistical value ($p < 0.001$). The same tendencies were found in FIB-4 measures; HCV-infected women had a median FIB-4 measure as 1.34 (1.082 1.9), in a significantly higher manner in comparison to HBV patients (0.75; IQR: 0.501.08), and $p < 0.001$. Moreover, the prevalence of high FIB-4 values (32.5 versus 9.2 percent; $p < 0.001$) magnificently ascertained significant fibrosis was high among the women in the HCV group compared to those in the HBV group. These results indicate that there could be significantly more hepatic fibrosis among pregnant women with HCV.

Higher levels of ALT (>40 U/L) were noted in 35.0 of HCV based women as compared to 15.8 in the HBV group showing more hepatocellular damage in the HCV group ($p = 0.005$). There was a trend of more hepatomegaly on ultrasound in the HCV group (11.3%) than in the HBV group (5.3) but not reaching significance ($p = 0.151$). Fatty liver alterations on ultrasound were however found to be more prevalent in the group of HCV infected women (18.8) than HBV (7.9) and p value was 0.044. All these results illumine the greater hepatic impairment and increased likelihood of perinatal difficulties related to the liver among pregnant women with HCV to those with HBV.

Table 4.6. Perinatal Complications and Maternal Morbidity in HBV vs HCV-Infected Pregnant Women

Parameter	HBV (n = 76)	HCV (n = 80)	p-value
Median APRI Score (IQR)	0.32 (0.21–0.48)	0.68 (0.39–1.04)	<0.001
APRI ≥ 1.0 (suggestive of fibrosis)	5 (6.6%)	22 (27.5%)	<0.001
Median FIB-4 Score (IQR)	0.75 (0.50–1.08)	1.34 (0.88–1.90)	<0.001
FIB-4 ≥ 1.45 (indicative of fibrosis)	7 (9.2%)	26 (32.5%)	<0.001
Abnormal ALT (>40 U/L)	12 (15.8%)	28 (35.0%)	0.005
Hepatomegaly on Ultrasound	4 (5.3%)	9 (11.3%)	0.151
Fatty Liver Changes on Ultrasound	6 (7.9%)	15 (18.8%)	0.044

4.7 Impact of Antenatal Screening and Treatment Compliance on Maternal-Fetal Outcomes

This section assesses how the timing of the antenatal screening and antiviral therapy compliance impacted the neonatal and maternal outcome in HBV- and HCV-infected pregnancies. HBV-positive women who were early-screened (first trimester) showed a higher mean gestation age at birth than those last-screened

(38.5± 1.1 vs 37.6 ± 1.4 weeks, p = 0.016). Early screening was though not statistically significant associated with a reduced rate of low birth weight (12.8% vs 25.6%), admission of the newborn to the NICU (7.7% vs 18.6%), and postpartum hemorrhage (2.6% vs 9.3%). Vertical transmission did not occur in any of the early-screened group, whereas in the late-screened group, it was found in 4.7 per cent cases and though this result does not amount to statistical significance (p = 0.181).

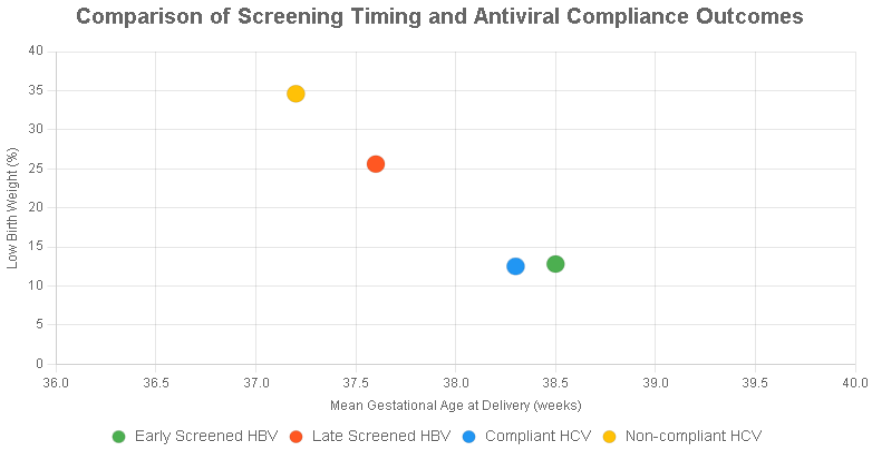

Figure 4.7: Association of Screening Timing and Antiviral Compliance with Outcomes in HBV and HCV-Infected Pregnant Women

Treatment-compliant women were found to fare much better across several parameters as compared to non-compliant HCV women. The amount of low birth weight and the NICU admissions in the compliant group were also lessened (12.5% vs 34.6%, p = 0.018, and 8.3% vs 26.9%, p = 0.049), as well as the rate of vertical transmission of transmission (2.1% vs 11.5%, p = 0.042). Also, higher levels of ALT (>80 U/L) at birth were more common in the non-compliant group (26.9% vs 6.3%, p = 0.009), which would indicate an excessiveness of disease activity and inflammatory processes in the liver related to not taking treatment.

These revelations strengthen the need to have screening and adherence to treatment of HBV on HCV to enhance maternal and perinatal health outcomes. This means that although not all of the associations were found to be statistically significant in the HBV cohort, there was an overall tendency that there might be benefits in terms of diagnosis and timely intervention.

Table 4.7. Association of Screening Timing and Antiviral Compliance with Outcomes in HBV and HCV-Infected Pregnant Women

Parameter	Early Screened HBV (n = 39)	Late Screened HBV (n = 43)	p-value	Compliant HCV (n = 48)	Non-compliant HCV (n = 26)	p-value
Mean Gestational Age at Delivery (wks)	38.5 ± 1.1	37.6 ± 1.4	0.016	38.3 ± 1.2	37.2 ± 1.5	0.007
Low Birth Weight (<2.5 kg)	5 (12.8%)	11 (25.6%)	0.148	6 (12.5%)	9 (34.6%)	0.018
Neonatal ICU Admissions	3 (7.7%)	8 (18.6%)	0.129	4 (8.3%)	7 (26.9%)	0.049
Vertical Transmission (PCR Positive)	0 (0%)	2 (4.7%)	0.181	1 (2.1%)	3 (11.5%)	0.042
PPH Occurrence	1 (2.6%)	4 (9.3%)	0.208	2 (4.2%)	3 (11.5%)	0.242
ALT > 80 U/L at Delivery	1 (2.6%)	6 (13.9%)	0.052	3 (6.3%)	7 (26.9%)	0.009

Discussion

As demonstrated by the findings in our prospective cohort of 156 women with viral hepatitis, liver enzymes and synthetic activities were worse in HCV-infected patients in comparison with the results of patients with HBV (Table 4.4). There was a significant increase in AST and ALT levels among the HCV-positive women as compared to HBV sample 62.9 ± 26.7 U/L; 59.2 ± 25.4 U/L respectively and p-values are 0.003 and 0.001. These are an indication of more severe hepatocellular inflammation in chronic HCV infection. Published evidence also shows that pregnancy patients are likely to experience an increase in the levels of aminotransferases following HCV infection, unlike the case with pregnant patients infected with HBV who tend to experience mild or normal activity unless there are flare-ups (Ahmad et al., 2021).

The total bilirubin and direct bilirubin count in HCV were significantly elevated (1.12 0.48 and 0.34± 0.14) as compared to the HBV (0.89± 0.42 and 0.28± 0.11) with p = 0.021 and 0.037. It is indicative of a subtly cholestatic aspect to HCV infected pregnancies. In spite of the fact that pregnancy may dilute the bilirubin to some degree, our results indicate toward the increased hepatic dysfunction among HCV patients.

Concentration of albumin was also lower in HCV group (3.45g/dL) compared to HBV (3.79g/dL; p<0.001) indicating a mild impaired production of albumin with long-term HCV infection. Nevertheless, the levels of LP did not significantly differ, 186.5 ± 72.1 IU/L in HBV and 179.3 ± 80.4 IU/L in HCV (p = 0.586) as is expected due to the normal placental output.

The differences in the trends as indicated are in line with what was previously recorded. A Lahore based study comparing among HBV and HCV infected women showed that the HCV posed higher levels of ALT and AST whereas HBVs mostly showed normal levels when compared to healthy pregnant controls (Ahmad et al., 2021). In terms of the international experience, the situation is also consistent, as, relative to an active chronic viral hepatitis in the states of other pregnancies, a more curious or stable biochemical activity is met with HBV than HCV infections (Floreani, 2013).

In addition, it has been found that pregnancy is relatively accompanied by a slight reduction in the levels of ALT/AST during the second and third trimester because one is in a state of physiological immune-modulating and haemodilution process especially amongst those patients who are HCV stable carriers. Chronic positive is also the possible indication of more active liver destruction or active virus replication (Hughes et al., 2017).

Our clinical findings indicate that pregnant women infected with HCV should be given more attention, such as frequent LFT testing, because of increased risks of hepatocellular damage and synthetic dysfunction. Increased transaminase levels and decreased albumin levels in this group can be a risk factor to complications in the perinatal period such as prematurity and intrauterine growth restriction. Even though HBV-positive women showed less severe enzyme perturbations, still, they should be observed closely especially when the viral loads are high or when they exhibit flaring.

Such data can justify individualized obstetric protocols: pregnancy in patients positive with HCV is recommended to have more extensive prenatal care and may also include collaboration between various specialists (hepatology-obstetrics), to identify and prevent risks in a timely manner. Conversely, stable liver profile/features in HBV-positive pregnancies can be considered with normal surveillance unless complications arise.

The result of this study shows that confirmed vertical transmission is significantly higher in the HCV infected group (13.8%) much more than the HBV (6.6%, p = 0.037) indicating the increased risk of perinatal infection linked to maternal HCV. This is in line with literature indicating how, in the event of no antiviral treatment or cesarean section, transmission of HCV can take place in up to 10 or 15 percent of pregnant couples- especially when mothers have excessive levels of HCV or when they have co-infections or complications of pregnancy (Hughes et al., 2017).

Although there were higher hospitable levels of neonatal ALT in the infants exposed to HCV (10.0 percent vs 5.3 percent), this was not of statistical significance (p = 0.112). Nevertheless, this pattern can also be interpreted as subclinical hepatic inflammation, and it confirms earlier findings of

transient hepatic enzyme abnormalities in infants delivered by HCV-positive patients (Terrault et al., 2021).

The other neonatal outcomes that were more prevalent (however, not significantly) in the HCV group are low birth weight, prematurity, and NICU stays. Still, these results can be discussed as clinically important. The high NICU admission (16.3 percent HCV vs 7.9 percent HBV) and low birth weight rates (18.8 percent HCV vs 13.2 percent HBV) are also significant and may be an accumulation of the effects of chronic inflammation and the impairment of the hepatic system on fetal development and stability.

Fortunately, both groups had low rates of loss (HBV: 85.5 percent, HCV: 82.5 percent) in a 12 months follow-up providing evidence of good post-natal follow-up. All of these observations further underline the necessity of regular neonatal screening, PCR management at birth and follow-up systems of childbearing mothers with infections (Faure-Bardon & Ville, 2021).

The examination of non-invasive hepatic fibrosis tests, such as APRI and FIB-4, indicated a higher fibrosis score in HCV infected women and thus reflected levels of fibrosis that were more advanced in the affected group. Further, almost a third of the HCV positive women had FIB-4 scores greater than or equal to 1.45 whereas only 9.2 percent of HBV women had such scores ($p < 0.001$). This confirms the earlier evidence stating that persistent HCV has a higher chance of developing to severe fibrosis levels, particularly among the patients of reproductive age who may not exhibit any symptoms (Sarkar et al., 2017).

Also, raised ALT levels were noted far more frequently in the HCV group (35.0 percent vs. 15.8 percent) which certainly confirms greater hepatocellular damage in HCV than in HBV during pregnancy. Remarkably, even though the liver inflammation was more pronounced in HCV-positive women, hepatomegaly and fatty liver were not as well distinguished as expected, with an observed significance related only to fatty liver ($p = 0.044$). This could possibly be representative of metabolic participation in chronic HCV infection since studies have already implicated HCV with hepatic steatosis (Chaudhari et al., 2021).

The combination of these findings shows that there is an increased risk of morbidity due to liver manifestation in HCV-infected pregnant women and therefore they should be observed more often (monitoring of hepatic functions, fibrosis, etc.) and their care should be multidisciplinary during pregnancy.

The data shows that early antenatal screening of HBV and strict tenancy of HCV treatment made a big difference in maternal and neonatal outcomes. In the infected group, early screening (first trimester) was associated with longer gestational length (38.5 ± 1.1 weeks vs. 37.6 ± 1.4 weeks, $p = 0.016$), and also tended to produce fewer adverse outcomes even though not significant in most indicators. It is important to note that vertical transmission was only noted in those screened late (4.7 percent), which points out to missed chances of providing timely antiviral prophylaxis (Cardenas et al., 2023).

In HCV, adherence to therapy resulted in a significantly improved outcome in several of the areas. Women who were compliant were older by the time of delivery ($p = 0.018$), they had fewer instances of low birth weight (12.5% vs 34.6%), fewer admissions in NICU (8.3% vs 26.9%), and a lower vertical rate (2.1% vs 11.5%). Also, higher ALT at delivery-which is an indicator of hepatic stress- was significantly higher in non-compliant women (26.9% vs 6.3, $p = 0.009$).

Such outcomes can be backed by the increasing number of professionals across the global medical community to agree that HCV management, including the consideration of pre-conceptual or lactation treatment, is a key part of ensuring that regional levels of maternal morbidity are minimized and the adverse potential of HCV in influencing the risk of perinatal transmission. In cases of HBV, WHO suggests that antiviral therapy be initiated in the second or third trimester of pregnancy in high-risk mothers when there is high viral load to reduce the risk of transmission (Lee et al., 2021).

Conclusion

This study is critical evidence, which can state that non-invasive imaging features, especially ultrasound-based elastography and magnetic resonance elastography can be employed safely and effectively in the assessment of hepatic inflammation and fibrosis

in women pregnant with HBV and HCV. The results have shown that HCV infection was linked with higher hepatic compromise evidenced by the large values of liver stiffness, high transaminases, and increased percentage of patients with significant fibrosis. These liver dysfunctions translated to unfavourable maternal fetal outcomes which included preterm birth, intrauterine fetal growth restriction, and admission of infants to the intensive care unit. Vertical transmission was also particularly more prevalent in mothers with HCV infection, and due to this, there is a need to perform increased perinatal monitoring and prevention. The research revealed the beneficial effect of having the screening and adhering to the treatment at an earlier stage of pregnancy: those women diagnosed and treated earlier had a lower number of complications, which supports general recommendations to perform a hepatitis screening at an early stage of pregnancy in all health facilities. The study also pointed out the need to correlate trimester-specific LSM reference values to meet changes in the physiology across the gestational period that alters the accuracy of images. Although these limitations are discussed in terms of single-center study design and incomplete imaging coverage, the study provides a formidable argument regarding the integration of non-invasive imaging into regular obstetrics care. These tools avoid the danger that is involved in biopsy and take to dynamic monitoring as well through the gestation period. To advance fibrosis detection and the estimation of risks in pregnant populations, future studies should be performed on multi-center trials and AI-integrated diagnostics algorithms to facilitate their results.

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