The Effects of Hepatitis Therapy and Virus Resistance on Pregnant Women: A Comprehensive Analysis
Ilham T. Qattan*1

ABSTRACT
This study aims to provide a comprehensive analysis of the effects of hepatitis therapy and virus resistance on pregnant women. Hepatitis, a liver condition that is often regarded as a viral infection, poses considerable risks during pregnancy for both the mother’s and baby’s health. In viral hepatitis (like hepatitis B or C), the risk of negative outcomes and liver damage increases dramatically for expecting women as well as for fetus health. In addition to antiviral therapy (considering the drug safety, efficacy, and resistance issue), vaccination and preventive measures are important components of the treatment process. The purpose of this manuscript is to critically examine the literature that is currently accessible to illuminate the most crucial aspects or elements and provide useful input into treatment strategy optimization for pregnant women afflicted with hepatitis. While remarkable advancements have been made, screening and diagnostic services demand improvements and illustrate the need for efficient measures to abridge the impact of this viral hepatitis on pregnant women and their newborn babies.

INTRODUCTION
A broad range of conditions, including heavy alcohol consumption, autoimmune diseases, medications, and toxins, can induce inflammation of the liver, which is known as hepatitis. On the other hand, viral hepatitis, which results from a viral infection, is the most common cause of hepatitis. Hepatitis is acute when it lasts less than six months and chronic when it persists longer. It may occur with limited or no symptoms but often leads to other diseases, such as anorexia (poor appetite), jaundice, and malaise (Aljumah et al., 2019). The most recent WHO global hepatitis report states that liver problems from all types of hepatitis viruses result in 1.34 million deaths annually (com, 2023). There are five known hepatitis viruses, A through E. The three most prevalent viral hepatitis kinds are hepatitis A, hepatitis B, and hepatitis C. Hepatitis D and E are the other forms of viral hepatitis that are less common (Mehta & Reddivari, 2022). Whereas Hepatitis D is considered a subgroup of hepatitis B due to its need for concurrent infection with hepatitis B. Pregnancy can impact all aspects of these viral agents due to distinct immunologic and physiological changes during and after gestation (Shata et al., 2022).
Hepatitis, a viral illness, has become a leading cause of fetal deaths during pregnancy and has an association with high-risk complications for the mother (Chilaka & Konje, 2021; Jaffe & Brown Jr, 2017; Seto et al., 2020). Viral hepatitis with the origin from pregnancy is a very difficult problem that would have better be dealt with since it may seriously harm the mother’s and fetus’ health. Acute progression is present in hepatitis A and hepatitis E, while the mortality risk and the high fetal deaths are high in hepatitis E. Further, hepatitis B and C have been tightly linked to being chronic, and yet women transmit the viruses to their unborn children (MTCT) (Terrault et al., 2021).
Pregnancy tends to worsen pre-existing viral disease conditions due to the numerous pregnancy-induced immigration, immunity-related, and gene-oriented changes. Just the same, hepatitis E causes fatality in about 26% of suspected cases among pregnant women (Berglov et al., 2019). Pregnancy can contribute to physiologic parameter alterations, giving physicians different treatment indications than the general population. Consequently, the picture of the safety and efficacy of drugs and vaccinations during pregnancy is constantly developing. It is still critically important to implement a preventive mechanism that cuts the levels of this transmission. Furthermore, to diagnose hepatitis different methods are being used namely, ICT, ELISA, CMIA and PCR (Rahaman et al., 2023).
This paper aims to facilitate a comprehensive examination of how pregnant women are affected by anti-hepatitis medicine and genetic resistance to the virus. Liver-damaging hepatitis, a virus that creates hazards for the mother as well as for the unborn child during pregnancy, is what poses these risks. Current antiviral therapy is an integral component of curing HCV, yet its downside problems, including poor efficiency, toxicity, and treatment resistance, must be agreed upon. This research aims to further clarify these crucial points by critically reviewing the literature and proposing recommendations to enhance the treatment of pregnant hepatitis patients.

LITERATURE REVIEW
Pregnant Women with Hepatitis
Viral hepatitis out of pregnancy has always been in

* Taibah University, Janadah Bin Umayyah Road, Tayba, Madinah 42353, Saudi Arabia
* Corresponding author’s e-mail: it.qattan54@outlook.com
Hepatitis A and E have severe consequences. The death rate ranges from 0.3% to 0.6%, with an estimated 1.5 million new cases reported annually. Efficient and secure vaccination prevents HAV infection (Chaudhry et al., 2015).

Diagnosis and Monitoring

People diagnosed with hepatitis should emergently seek monitoring. Diagnosing and monitoring of hepatitis include imaging and a number of blood tests. Furthermore, in pregnant women, the key blood tests used to diagnose and monitor hepatitis include Hepatitis antibody serology tests, liver function tests, and viral load assessment (Asafo-Agyei & Samant, 2020). A study regarding HBV infection stated that the antibodies HBeAg, anti-HBs, HBsAg, anti-HBe, and anti-HBc IgM and IgG are among the serological indicators of HBV infection. These markers aid in the diagnosis of HBV infection, comprehension of the progression of chronic hepatitis B (CHB), evaluation of the clinical stages, and tracking of antiviral treatment. The main marker, HBsAg, is at higher levels in CHB patients who test positive for HBeAg. Long-term immunity is provided by anti-HBs, which coexists with anti-HBe IgG. During acute infection, anti-HBe IgM and IgG emerge after HBsAg, and HBV DNA assays take the role of earlier indicators (Song, 2016).

Secondly, most commonly, abnormal liver function results in the third trimester (Mishra et al., 2016). In order to evaluate liver function and identify any abnormalities, liver function tests, or LFTs, are essential during pregnancy. They take albumin, bilirubin, and enzyme readings. Timely care and the reduction of problems depend on the accurate interpretation of LFT results. In order to protect pregnant women and their unborn children, these tests assist medical professionals in keeping an eye on liver health, spotting anomalies, and few pregnancies and HDV transmissions from mother to child (Sellier et al., 2018).

According to a study, there have been reports of vertical transmission of HAV and HEV from mother to child (Terrault et al., 2021). Hepatitis A and E have severe complications in pregnant women, which can be caused by drinking contaminated water. Additionally, the hepatitis A virus can lead to early labour, whereas HEV infection in the second or third trimester entails significant morbidity and death concerns (com, 2023).

A study evidenced that pregnant women had an 11.6% prevalence of the hepatitis E virus (HEV), with 11.4% testing positive for the anti-HEV IgG antibody, 0.1% for the anti-HEV IgM antibody, and 0.1% for both antibodies. HEV-IgG antibody-positive pregnant women are more likely to experience bad pregnancy outcomes, liver damage, and poor maternal and fetal outcomes. These unfavorable pregnancy outcomes are worsened by parity, age, and gravidity (Qian et al., 2023). Furthermore, studies have shown that the replication of the hepatitis E virus in the placenta is associated with maternal and fetal mortality with acute liver failure. The study also found that in HEV patients, receptors of estrogen ESR1α and ESR2β and estrogen itself have been identified as possible biomarkers predicting worse maternal and fetal health (Horvattis et al., 2019).
starting interventions. Furthermore, the interpretation of abnormal liver function tests (ALFTIs), which are essential for the diagnosis of liver disease, can be difficult during pregnancy because of hemodilution and physiological changes. Pregnant women's transaminases, especially ALT (Alanine Aminotransferase) and GGT (Gamma Glutamyl Transferase), are 20% lower than laboratory reference levels, while their alkaline phosphatase increases because of the placenta. (Daji et al., 2023).

HCV+ mothers don’t need to monitor transaminases during pregnancy; measuring liver enzymes at the start of pregnancy is adequate. A single pregnancy-related qualitative PCR test is recommended, but any liver disease staging should wait until after delivery. Furthermore, since there is currently no anti-HCV medication that can be given to expectant mothers to stop viral replication, a high maternal viral load is a significant but avoidable risk factor (Tovo et al., 2016).

At Ghent University Hospital, a study assessed three PCR assays and six serological assays to identify HEV in individuals who may have been infected. Using commercial ELISA and PCR assays, including in-house and commercial testing, they looked for HEV RNA and antibodies (IgM and IgG) specific to the virus. Across all ELISA assays, the frequency of HEV antibodies ranged from 5.7% to 14.3% for IgM and 15.7% to 20.0% for IgG. In clinical samples, most PCR findings were consistent; however, there were notable differences in 10 out of 16 external quality control samples (Cattoir et al., 2017). Another study concluded that the anti-HEV Ag-specific ELISA is less sensitive than HEV RNA real-time PCR. Yet, it is a valuable tool for distinguishing chronic from acute infection (Behrendt et al., 2016).

Furthermore, new research develops a method for identifying HBV perinatal transmission utilizing fast DNA extraction and recombinase polymerase amplification. The assay achieved 98.6% sensitivity and 88.2% specificity, with room for improvement in non-viremic patients. The study proposes that this approach be utilized in point-of-care testing to avoid HBV transmission. However, more validation on a larger cohort of HBV-positive plasma samples from pregnant women is required before in-field adoption (Mayran et al., 2022).

### Hepatitis Therapy and Medications in Pregnant Women

Most of the research has developed on treatment and therapy for hepatitis B and hepatitis C. Chronic Hepatitis B (CHB) has turned out to be a prominent health problem on a global scale, and the management of pregnant women with this disease is a necessity. Pregnant women will be running tests like hepatitis B surface antigen (HBsAg) and other tests. The management primarily focuses on the HBV infection stage rather than pregnancy since the latter state is hardly indicated. Antiviral treatment is intended mainly for indicated CHB patients and also for anti-vertical transmission purposes. Tenofovir should be taken during pregnancy. Use a combination of hepatitis B immunoglobulin and vaccination for all infants whose mothers are infected with CHB, insisting on no breastfeeding contraindications (Belopolskaya et al., 2021).

HCV is strongly associated with premature birth and cholestasis. Till now, there is no vaccine for hepatitis C, so the main focus is on the treatment. For the treatment of children with HCV transmitted through the mother, anti-HCV antibodies that pregnant women possess can be transmitted through the placenta to the fetus. The period of the baby’s serum can be detected in the same maternal antibodies for up to 13 months after birth. Diagnosed with antibody titer rise in the newborn serum does not mean they’re infected (Ragusa et al., 2020).

A study in Switzerland found that many pregnant women with HCV are unaware of their condition, and regular screening is not done. The Federal Office of Public Health and the Swiss Society of Obstetrics and Gynecology recommend HCV testing for high-risk women, including those who have used intravenous drugs, had HCV infection, received a solid organ transplant before 1992, received blood transfusions, or used clotting factor concentrate before 1987. Untrustworthy self-reporting of drug use during pregnancy is a significant obstacle to diagnosis (Aebi-Popp et al., 2016).

### Study Design and Methodology

#### Search Strategy

This literature review employed a systematic search strategy to identify relevant studies published in peer-reviewed journals. Electronic databases, including PubMed Google Scholar, PubMed, Science Direct, and Springer Link, were searched using predefined search terms related to HBV screening in pregnant women using keywords: hepatitis A, hepatitis B, hepatitis C, Hepatitis D, hepatitis E, pregnancy, viral resistance, treatment, hepatitis therapy, and diagnosis of hepatitis.

#### Inclusion and Exclusion Criteria

Articles were limited to those published in English from 2015 to 2024. This review includes only hepatitis-related articles, including therapeutic approaches to hepatitis in pregnant women. It excludes all those studies which do not include hepatitis in pregnant women. Studies published in journals where publishers do not offer a peer-reviewing policy were excluded, and only studies available in full-text format for the public view were included.

### RESULTS

The results of selected studies are presented in a table representing the author, years, published journal, title of the study objectives, and results.
<table>
<thead>
<tr>
<th>S. No</th>
<th>Author</th>
<th>Journal</th>
<th>Title</th>
<th>Objective</th>
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<tbody>
<tr>
<td>1.</td>
<td>(Qian et al., 2023)</td>
<td>Journal of Clinical Virology</td>
<td>Prevalence Of Hepatitis E Virus And Its Association With Adverse Pregnancy Outcomes In Pregnant Women In China</td>
<td>To investigate the prevalence of (HEV) infection among pregnant women and to assess the association between HEV infection, specifically the presence of anti-HEV IgG antibodies, and adverse pregnancy outcomes.</td>
<td>The existence of anti-HEV IgG antibodies has been linked to an increased risk of bad pregnancy outcomes, such as liver damage and poor mother and fetal health. Furthermore, the study found parity, age, and gravidity as factors that exacerbated the negative pregnancy outcomes linked with HEV infections.</td>
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<td>2.</td>
<td>(Song, 2016)</td>
<td>Annals of Translational Medicine</td>
<td>Diagnosis Of Hepatitis B</td>
<td>The study aimed to investigate the serological indicators of hepatitis B virus (HBV) infection and their involvement in the diagnosis, progression monitoring, and therapy evaluation of chronic hepatitis B.</td>
<td>The study found various serological indications of hepatitis B virus infection, including HBeAg, anti-HBs, HBsAg, anti-HBe, and anti-HBc IgM and IgG. The key marker, HBsAg, is present at high levels in chronic hepatitis B patients. Anti-HBs provide long-term protection, whereas anti-HBc IgM and IgG antibodies appear during acute infection. These findings advance our understanding of HBV infection and influence management options.</td>
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<td>3.</td>
<td>(Cattoir et al., 2017)</td>
<td>Archives Of Virology</td>
<td>Hepatitis E Virus Serology and PCR: Does The Methodology Matter?</td>
<td>The study aimed to compare the performance of six serological assays and three PCR assays in detecting Hepatitis E virus (HEV) genotype 3 in patients with clinically suspected HEV infection at Ghent University Hospital.</td>
<td>The study discovered variable prevalence rates of HEV antibodies, with IgM and IgG antibodies ranging from 5.7% to 20.0%. HEV RNA was detected using a commercial test and two optimized in-house real-time RT-PCR techniques. Most PCR findings were consistent. However, 10 of 16 external quality control samples exhibited significant differences in PCR assays. This emphasizes the importance of carefully interpreting serological and molecular HEV infection test data.</td>
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<td>4.</td>
<td>(Mayran et al., 2022)</td>
<td>Diagnostics</td>
<td>Rapid Diagnostic Test For Hepatitis B Virus Viral Load Based On Recombinase Polymerase Amplification Combined With A Lateral Flow Read-Out</td>
<td>This research aimed to develop a simple molecular method for detecting highly viremic pregnant women with Hepatitis B virus (HBV) infection, which is an important step in preventing perinatal transmission.</td>
<td>A study proposed a method for identifying HBV perinatal transmission utilizing fast DNA extraction and an isothermal recombinase polymerase amplification (RPA) technology. The approach was tested on plasma samples with different virus loads and genotypes. The assay had a sensitivity of 98.6%, indicating efficacy in detecting highly viremic individuals, and a specificity of 88.2%, indicating room for improvement in recognizing non-very viremic cases. The assay’s high overall performance suggests its potential for use in point-of-care testing.</td>
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5. (Aebi-Popp et al., 2016) Journal of Virus Eradication: Vertical Transmission of Hepatitis C: Towards Universal Antenatal Screening in The Era of New Direct Acting Antivirals (Daas)? Short Review And Analysis Of The Situation In Switzerland

The study aimed to determine the frequency of undetected Hepatitis C virus (HCV) infection among pregnant women in Switzerland, taking into account the lack of routine screening and the difficulties associated with self-reporting behaviors at high risk. Unreliable self-reporting of drug use during pregnancy appeared as a substantial hindrance to proper diagnosis. These findings highlight the significance of establishing more effective screening procedures and resolving self-reporting problems to improve the detection and management of HCV infection among pregnant women in Switzerland.

6. (Behrendt et al., 2016) The Journal of infectious diseases: Hepatitis E virus (HEV) ORF2 antigen levels differentiate between acute and chronic HEV infection.

The study aimed to evaluate the effectiveness of an ELISA-specific enzyme-linked immunosorbent assay in detecting HEV genotype 3 infections, comparing its sensitivity with real-time PCR and assessing its ability to differentiate between acute and chronic infections. Compared to real-time PCR, the anti-HEV Ag-ELISA showed lower sensitivity in detecting HEV infection but higher levels in chronically infected individuals. It also demonstrated high sensitivity and specificity in distinguishing acute and chronic HEV infections. Despite its less sensitive nature, it remains a valuable tool for HEV infection diagnosis.


The primary objective in treating pregnant women with Hepatitis B virus (HBV) infection is to prevent the virus from passing from mother to child. This includes carrying out essential examinations, such as the hepatitis B surface antigen (HBsAg), to determine the mother’s infection status and applying the related management practices. The management of infected pregnant women should involve carrying out relevant tests like HBsAg to determine the mother’s status. Management should focus on the stage of HBV infection rather than pregnancy itself, as pregnancy only marginally affects HBV progression. Antiviral treatment that contains tenofovir, for instance, should be prescribed for pregnant women with indicated chronic HBV infection to reduce the risk of vertical transmission. A combination of hepatitis B immunoglobulin and vaccination for every infant born to a chronic HBV carrier with the crucial point of close adherence to recommended breastfeeding practices to make transmission less likely.

DISCUSSION

This literature review concentrates on Hepatitis A, B, C, D, and E influences during pregnancy. It provides an extensive overview of the risks the mother and fetus share. It highlights the need for designing newer regimens for screening, diagnosing, and treating cases of hepatitis in women during pregnancy. The evidence shows that viral hepatitis is one of the main causes of fetal death during pregnancy, and the paper highlights the high-risk problems viral hepatitis poses to pregnant women. The paper looks at the different forms of viral hepatitis that appear throughout pregnancy, which include an acute disease progression in hepatitis A and E, a chronic disease form in hepatitis B and C, and the yet-to-be-described risks of preclampsia, gestational diabetes, and intrahepatic cholestasis. The review also briefly describes the difficulties in diagnosing and controlling viral hepatitis in pregnant women, the interpretation of liver function tests, and the impact of physiological changes during pregnancy.

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on diagnostic markers. Diagnosing and managing viral hepatitis in pregnancy has significant challenges as evidenced by many studies. Some physiological changes that occur during pregnancy include changes that involve liver function and hormones, and therefore, diagnostic test results may be affected. When it comes to the assessment of liver health, LFTs are essential though they may be affected by pregnancy’s normal physiological changes, thus presenting challenges for the distinction of pathological changes from normal fluctuations.

Besides, the fact that viral hepatitis interacts with the human body constantly, with periodically escalating and decreasing viral replication rates and immune responses, complicates matters even further. Particularly, pregnancy could change clinical characteristics in a patient, as well as the progression of the disease; therefore, diagnosis becomes problematic. Managing viral hepatitis in this population is also challenging due to the possible teratogenic effects of the antiviral agents and the potential consequences that coordination between the health of the mother and the fetus may have.

The issues that arise should be solved on the basis of a multidisciplinary approach through the cooperation between obstetricians, hepatologists, and specialists in infectious diseases; it will be possible to assess the management and prevent possible negative outcomes for both the mother and the fetus. The paper covers another aspect of the effects of hepatitis on fetal health, such as preterm delivery and the risk of newborn complications. Additionally, for the treatment of HEV, Ribavirin and interferon alpha are effective, but in pregnancy, the use of these agents is inhibited and is not suggested. However, ribavirin can be recommended for pregnant women infected with HEV in the last trimester due to its less teratogenic effects (Aslan & Balaban, 2020).

Furthermore, the study by Aniszewska et al. (2019) indicates the role of antiviral treatment in the course of hepatitis during the period of pregnancy, concerning both acute subtypes B and C. It stresses the involvement of tenofovir in pregnancy to minimize the risk of vertical transmission and birth immunoglobulin and vaccination in not transmitting hepatitis B to newborns. Besides this, the review is about the progress in diagnosing viral hepatitis, achieved by rapid DNA extraction and recombinase polymerase amplification. These appear useful in determining highly viremic and hepatitis B pregnant ladies.

Furthermore, the report by the researcher shows the importance of effective screening policies aimed at discovering HCV infection among pregnant women. It is worth noting that many infected individuals are only detected by diagnostic examinations, which signifies the importance of screening programs. Healthcare providers, including gynecologists, obstetricians, and other clinicians, are having a significant impact on the early detection and diagnosis of HCV in pregnant women. The research equally indicates that the forward increase or the dominance of intravenous drug use among pregnant women calls for special considerations regarding maternal and fetal health outcomes, further justifying the need for tailor-made solutions that address drug abuse during pregnancy (Aniszewska et al., 2019).

Moreover, it is of vital importance for the medical care provider to consider viral hepatitis among high-risk pregnancy women to avoid maternal and fetal complications that are linked with mother-to-child transmission. Holistic care of the mother requiring obstetrics, maternal-fetal medicine, hepatology, and neonatology is desired to ensure the best chances for both mother and child. It is recommended that pregnant women be tested for HBV and HCV as part of routine screening. Tenofovir Disoproxil Fumarate, Lopinavir, and Ritonavir with Antiviral Therapy may be required, while Lamivudine may be considered an option. Given the knowledge regarding the safety and efficacy of Direct-Acting Antivirals in HCV infection during pregnancy and Food and Drug Administration approval, the outcomes of clinical practices should be enhanced and improved (Sanghi & Lindenmeyer, 2021).

Alhussain et al. in his research studied about perinatal care and concluded that counselling on coping and stressor adaptation mechanisms should be provided to everyone during public health emergencies (Alhussain et al., 2023).

In conclusion, it is distinct that the diagnosis and management of viral hepatitis during pregnancy remain complicated due to the changes in physiological status. It is challenging to pinpoint what may be considered as a range of normal variations and what requires a special consideration of pathological changes affecting liver function tests, and their impact on the diagnostic markers. Thirdly, due to the high viral loads as well as the variability of the immune responses, diagnosis of viral hepatitis is not a very easy process.

CONCLUSION

To summarize, the hepatitis care of pregnant women is intricate, involving multiple obstacles and complexities, from diagnostic precision to treatment decisions. Though the literature review points out the already existing measures like diagnosis, monitoring, and therapy in different ways, shortcomings and unresolved issues still require further studies.

Limitations and Future Implications

The review on hepatitis management during pregnancy gives us a great range of information about therapeutic approaches, diagnosis, and monitoring. Nevertheless, a few barriers and topics have not been extensively explored. It is basically about therapeutic modalities and diagnostic methods, and it doesn’t touch upon aspects such as epidemiology and social impacts. One aspect that could limit data transferability from one region to another is the data regional variation. Publish bias is another issue, as only the studies published in English between 2015 and 2024 have been included in this review. Scientific research in this domain is challenging due to methodological
discrepancies across studies, making it hard to establish a solid, unified conclusion. Thus, longitudinal follow-up of fetal and mother outcomes is lacking. Still, more studies on genes that affect offense or susceptibility and treatment are required. Interventional studies that assess the effectiveness and safety of treatment modalities are, too, in short supply. Overcoming these constraints will provide us with a better insight into managing hepatic conditions in pregnancy and will lead to better outcomes for mothers and babies.

REFERENCES


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