Original Article

Prevalence of HBV and HCV with Increase of some Cytokines among Pregnant Women in Thi-Qar Governorate

Hakeem Ghani Hassan[1]*, Ali Mohammed Barakat[2], Asaad A. Aladlaan[3], Zainab Hakeem Ghani[4]

[1] Department of Prosthodontics, College of Health and Medical Technology, Al-Ayen Iraqi University, 64001, Iraq.
ORCID iD: https://orcid.org/0000-0003-3989-6265
Email: alhamamy201567@gmail.com
[2] Department of Microbiology, Faculty of Medicine, Al-Ayen Iraqi University, 64001, Iraq.
ORCID iD: https://orcid.org/0009-0002-4976-7838
Email: ali.barakat1765@gmail.com
[3] Department of Laboratories, College of Health and Medical Technology, Al-Ayen Iraqi University, 64001, Iraq.
ORCID iD: https://orcid.org/0009-0002-6224-2489
Email address: asaad.jlood@alayen.edu.iq
[4] Department of Laboratories, Al-Hussein Teaching Hospital, Thi-Qar Health Office, Iraq.
ORCID iD: https://orcid.org/0009-0007-0072-776X
Email: zainabhakeem702@gmail.com

Abstract

Background: Viral hepatitis, caused by HBV and HCV, poses significant health risks during pregnancy, affecting maternal and neonatal outcomes. Understanding the immunological and demographic predictors of these infections is crucial for improving clinical care. **Objectives:** This study aimed to determine the prevalence of HBV and HCV infections among pregnant women in the Thi-Qar governorate and analyse the association between these infections and elevated cytokine levels (IL-6, TNF-α, and IL-10). **Methods:** A cross-sectional study was conducted among 200 pregnant women attending antenatal care clinics. Blood samples were collected and analysed using molecular detection techniques to identify HBV and HCV infections. Cytokine levels were measured using ELISA, and data were statistically evaluated to identify predictors of cytokine dysregulation. **Results:** HBV and HCV infections were detected in 5% and 1.5% of participants, respectively, with 0.5% co-infected cases. Significant elevations in IL-6, TNF-α, and IL-10 were observed in infected individuals, with the highest levels in co-infected participants. Regression analysis identified HBV, HCV, and co-infections as key predictors of cytokine elevation, emphasising the compounded immunological burden in co-infections. **Conclusion:** The findings highlight the critical need for antenatal screening, public health interventions, and targeted immunological strategies to mitigate the impact of viral hepatitis during pregnancy in the Thi-Qar governorate.

Keywords: Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Interleukin-6 (IL-6), Interleukin-10 (IL-10), Tumor Necrosis Factor- α (TNF-α).

Introduction

The term viral hepatitis is often thought to be synonymous with disease caused by the known hepatotropic viruses, including hepatitis viruses A, B, C, D, E, and G. However, the term hepatotropic is itself a misnomer. Infections with hepatitis viruses, especially hepatitis viruses B and C, have been associated with a wide variety of extrahepatic manifestations. Infrequent causes of viral hepatitis include adenovirus, cytomegalovirus, Epstein-Barr virus, and, rarely, herpes simplex virus infection.[1]

Viral hepatitis represents an important health hazard; the earlier the age at which the infection is acquired, the greater the risk of developing a serious consequence. Viral hepatitis is common worldwide. It causes millions of deaths among the population of the world yearly.[2]

The global prevalence of viral hepatitis in pregnancy highlights a significant health burden, with regions like sub-Saharan Africa and Asia experiencing higher rates of HBV and HCV due to socioeconomic factors and inadequate healthcare infrastructure.[3] In Ethiopia, studies have shown

Access This Article Online

Quick Response Code:

Website: www.jnsbm.org

DOI: https://doi.org/10.5281/zenodo.15346725

Address for Correspondence: Department of Prosthodontics, College of Health and Medical Technology, Al-Ayen Iraqi University, 64001, Iraq
Email: alhamamy201567@gmail.com

Submitted: 22nd February, 2025 **Received:** 08th April, 2025
Accepted: 12th April, 2025 **Published:** 20th April, 2025

How to Cite This Article: Hassan H G, Barakat A M, Aladlaan A A, Ghani Z H. Prevalence of HBV and HCV with Increase of some Cytokines among Pregnant Women in Thi-Qar Governorate. J Nat Sc Biol Med 2025;16:174-187

intermediate endemicity, with mother-to-child transmission being a significant concern for neonatal health.[4]

Pregnant women in high-risk regions, such as Nigeria, face compounded risks of vertical transmission, highlighting the need for routine antenatal screening.[5] In Iraq, challenges such as inadequate immunisation programmes and lack of routine HBV and HCV screening exacerbate the health risks for both mothers and infants.[6] Addressing these public health issues requires comprehensive strategies, including vaccination, public education, and improved healthcare access, to mitigate maternal and neonatal complications worldwide.[7]

Cytokines such as IL-6, TNF-α, and IL-10 play critical roles in immune modulation during HBV and HCV infections, where IL-6 and TNF-α promote inflammation, and IL-10 regulates the immune response to prevent excessive tissue damage.[8] Dysregulation of these cytokines often results in chronic inflammation and liver damage, as seen in both HBV and HCV, where IL-6 levels correlate with disease severity and TNF-α contributes to immune escape mechanisms.[9]

Elevated IL-10 levels, while protective against inflammation, can paradoxically allow viral persistence by dampening the immune response.[10] During pregnancy, dysregulated cytokine levels can have adverse effects, including higher risks of vertical transmission and complications such as preterm birth and preeclampsia.[11] Understanding these cytokine interactions is critical for managing viral hepatitis in pregnancy, as targeting these pathways might offer therapeutic benefits.[12]

The current study addresses the significant impact of hepatitis B (HBV) and hepatitis C (HCV) infections during pregnancy, highlighting the association between these infections and various maternal complications. While viral hepatitis infections are known to affect maternal health, recent studies suggest that they also contribute to immune system dysregulation through elevated cytokine levels, which play a crucial role in immune responses and disease progression. Specifically, interleukin (IL)-6, tumour necrosis factor-alpha (TNF-α), and IL-10 are key cytokines involved in the immune modulation of HBV and HCV infections.

The present study's findings align with recent work by Wang *et al*.[13], where elevated cytokines in early pregnancy were linked to abnormal liver function in hepatitis B patients, further supporting the importance of early immunological screening during pregnancy.

Additionally, the research by Haniah *et al*.[14] points out that hepatitis B in pregnancy significantly increases the risk of preterm birth and gestational diabetes, emphasising the critical need for targeted interventions to mitigate these risks. Furthermore, the present study is in line with findings from Seow[15], which described the low but significant risk of mother-to-child transmission of both HBV and HCV during pregnancy, despite the advances in immunoprophylaxis.

The increasing awareness and improvements in screening methods are essential for reducing vertical transmission and improving outcomes for both mother and child. Recent studies have highlighted the crucial role of cytokine dysregulation in pregnancy-related complications in women with chronic viral hepatitis. According to Mugescu *et al*.[16], the need for antiviral treatment during pregnancy to reduce vertical transmission and improve maternal outcomes has become more urgent due to the growing body of evidence linking chronic hepatitis C with adverse pregnancy outcomes.

Moreover, the findings of Eppes[17] underscore the importance of early screening and intervention to manage hepatitis C in pregnant women, emphasising its impact on both maternal and foetal health. This growing evidence supports the need for comprehensive health strategies, including improved diagnostic tools and therapeutic approaches, to better manage HBV and HCV infections during pregnancy.

The objective of this study was to determine the prevalence of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections among pregnant women in Thi-Qar governorate and to investigate their association with elevated levels of specific cytokines. The study aimed to explore the relationship between these viral infections and immune response markers, focusing on cytokines such as interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and interleukin-10 (IL-10). By employing molecular detection techniques, the study sought to provide accurate estimates of infection rates and identify any significant correlations between the presence of HBV or HCV and changes in cytokine levels. This investigation aimed to contribute to a better understanding of the immunological impact of HBV and HCV during pregnancy, which could support improved clinical management and care strategies for affected patients in the region.

Methods

Study Design

The cross-sectional research design allowed investigators to study pregnant women who visited antenatal care clinics within Thi-Qar governorate. A cross-sectional study analysis allowed investigators to determine the impact of high cytokine levels on HBV and HCV infections throughout the selected assessment period. The research staff recruited participants during their normal antenatal checkups, which yielded a proper census of the intended population. Women at 14 to 36 weeks of pregnancy with their knowledge and consent qualified for the study. The study collected all essential data through blood samples and patient records to provide thorough findings about virus prevalence and immune system markers within the study population. The study design enabled researchers to examine the pregnancy-related associations between HBV, HCV infection and cytokines together with their related immunological impacts.

Population and Sample Size

Medical staff at antenatal clinics in Thi-Qar governorate served as the recruitment source for pregnant women in

the study. The selected participants contributed to valid and relevant research outcomes through our applied inclusion and exclusion criteria. All second and third trimester women who visited selected clinics and gave their voluntary consent formed the study participants. The study excluded pregnant women whose medical records showed either chronic liver disease or infections that were unrelated to HBV or HCV since we needed to minimise confounding factors. A total of 200 participants completed the study based on found prevalence rates for HBV and HCV infections in the targeted area to reach appropriate statistical analysis levels. A large sample size was established by this method to accurately determine infection rates and properly assess viral infection associations with cytokine levels.

Inclusion Criteria

The research team carefully established these inclusion requirements to gather data from appropriate study-relevant subject groups. The study focused on pregnant women during their second or third trimester because this period presents an ideal opportunity to determine hepatitis virus infection prevalence while evaluating immunological changes through cytokine level assessment. Participants were asked to attend at the antenatal care clinic in Thi-Qar governorate, which they were routinely attending. Only women who agreed to go but were not forced to, as a clear explanation of the purpose and procedures of the study was provided. This ensured ethical participation and the validity of the data collected. The findings were more generalisable to similar settings because the selected participants represented a diverse segment of the pregnant population.

Exclusion Criteria

To minimise confounding factors and ensure results accuracy, exclusion criteria for this study were established. To not interfere with the primary focus of this study on HBV and HCV infections, women with a known history of chronic liver disease not due to HBV or HCV were excluded. In addition, participants with co-infections from other viral or bacterial agents which could influence cytokine level were excluded to maintain the immunological analysis specific. Also, women who could not or would not give informed consent were excluded for ethical reasons and in the interest of voluntary participation. These measures guaranteed a study population comprised solely of eligible participants whose data will add value to the validity and reliability of the findings.

Sample Collection

All persons were enrolled, and blood samples were taken to facilitate molecular detection of HBV and HCV and analysis of cytokine levels. The blood was collected from each participant with sterile venipuncture techniques for safety and minimising contamination with peripheral blood, for a total of 5 mL. The blood samples were collected into EDTA tubes to prevent their coagulation and to keep the samples unspoiled for subsequent laboratory analysis. The samples were labelled with a code that was kept confidential from the participant and that was used to properly track the samples throughout the study. After the processing of the blood samples had proceeded without delay, the blood samples were transported by controlled means to the laboratory. Cytokine analysis of separated plasma and detection of viral markers on nucleic acids from the rest of the blood by extraction. In the standard operating protocols, these steps were performed to assure the quality of samples for molecular detection and immunological testing.

HBV and HCV Molecular Detection

To obtain reliable and high-quality results, HBV and HCV molecular detection was performed using well-established protocols and precise protocols to detect HBV and HCV in collected blood samples. Viral DNA was extracted from blood samples for HBV and RNA for HCV and introduced into a chemical reaction next. Due to its ability to yield high-quality DNA and RNA for downstream analysis, the isolate was performed via a commercially available nucleic acid extraction kit. The extraction process was performed under strict, sterile conditions, within a sealed laboratory space free of cross-contamination. The collected EDTA blood samples were immediately processed, and careful nucleic acid extraction followed the manufacturer's instructions. Purified DNA and RNA extracts were stored at -80°C to stabilise and protect data from degradation until molecular analysis. The samples were amplified and detected for HBV DNA and HCV RNA by real-time polymerase chain reaction (PCR). Specific primers and fluorescently labelled probes were used to detect HBV, using primers and probes spanning highly conserved regions of the viral genome to ensure precise amplification. Primer and probe sets targeted to conserved regions of the HCV RNA genome were used to accurately identify and measure the viral RNA for HCV detection. Samples were prepared in a dedicated clean workspace and processed under real-time PCR reactions by a thermal cycler that also has real-time detection capacity. Fluorescence signals from consecutive amplification steps were continuously monitored and used for quantification of viral loads in tested samples. It received strict quality control measures throughout the whole procedure with the intention of ensuring reproducibility of the results.

Each PCR run included positive and negative controls to ensure accuracy and reliability of the molecular detection method. Results were positive, controlled by samples containing known amounts of HBV DNA and HCV RNA as reference standards for successful amplification. To detect possible contamination or non-specific amplification, negative controls were included with nuclease-free water or previously affirmed negative samples. As we explained above, all steps were taken to observe all of the steps of processing all samples and to detect any discrepancies in processing of these samples in order to find out about its presence or absence of HBV and HCV in the sample.

The robustness of the molecular detection process was founded on high-quality nucleic acid extraction, optimised primers and probes and stringent quality controls. We were able to accurately identify and quantify HBV and HCV infections, important information in assessing the prevalence of this study population.

Cytokine Analysis

Finally, cytokine analysis and measurement of specific pro-inflammatory and anti-inflammatory cytokines were performed in the plasma samples of the participants. By selecting the cytokines of interest, including interleukin 6 (IL-6), tumour necrosis factor alpha (TNF-α) and interleukin 10 (IL-10), we have based our selection on previously known roles of these cytokines in responses to viral infections, including those of HBV and HCV. The enzyme-linked immunosorbent assay (ELISA) was used for analysis of cytokine concentrations with a high sensitivity and specificity.

After blood collection, plasma was separated from the whole blood by centrifugation at 3000 rpm for 10 minutes. In this step the cellular components were removed, and the resulting supernatant contained cytokines in a clear fashion. Aliquots of the plasma samples were carefully pipetted into sterile tubes and labelled with unique identification codes to help protect the confidentiality, placed at −80°C until further analysis to maintain the stability of the cytokines.

An ELISA procedure was performed using commercially available validated-for-accuracy-and-reproducibility kits for each of the cytokines studied. All reagents, standards and samples were brought to room temperature, and the assays were performed according to the manufacturer's instructions prior to analysis. On the basis of known concentrations of recombinant cytokines used as references to quantify the cytokine levels in the plasma samples, a standard curve for each of the cytokines was prepared.

Duplicate wells were prepared for each measurement of each plasma sample diluted as required to maintain precision and minimise variability. Pre-coated ELISA plates were added to wells that contained absorbed antibodies specific to a cytokine of interest, and samples were added to the wells. Binding of any cytokine in the plasma to the antibodies took place after incubation. When we add a second detection antibody conjugated to an enzyme, it binds to the captured cytokines, making an antibody-antigen complex. After every step, the plates were well washed to remove any unbound material in order to be specific to the assay.

In the wells, another substrate solution was added to the wells, which caused the enzyme to react with the substrate solution, causing a colour change that could be measured. The colour of the signal was proportional to the concentration of the cytokine in the sample. The reaction was stopped using a particular stop solution, and the absorbance at a well-specified wavelength was recorded by a microplate reader. Precise determination of plasma samples using the absorbance values compared to the standard curve enabled determination of the cytokine concentrations of the plasma samples.

Stringent quality control measures were established throughout the cytokine analysis. Validations were performed using positive controls — plasma spiked with known cytokine concentrations — to ensure the assay performance and negative controls to rule out nonspecific signals. Duplicate measurements were allowed for each of the samples in order to reduce the technical errors and verify the veracity of the results.

We established a comprehensive cytokine analysis that measured IL-6, TNF-α, and IL-10 levels with high accuracy and detail, allowing the correlation to be studied between HBV and HCV infections and these particular cytokines. These findings provided important information on immunological responses of pregnant women to viral infections and help to understand the contribution of cytokines to the disease pathogenesis.

Statistical Analysis

The prevalence of HBV and HCV infections was evaluated by means of statistical analysis, and the association between these infections and cytokine levels was explored. Data from study participants that included demographic variables, clinical risk factors, molecular results and cytokine concentrations were input into a statistical software package for processing and analysing. Before analysis, data was rigorously quality checked to ensure accuracy and consistency of the data.

Descriptive statistical methods were used for prevalence estimation of HBV and HCV infections. The proportions and percentages of those infected with HBV and HCV were calculated, which gives a nice depiction of how infection rates manifest within the study population. These prevalence values were stratified using demographic and clinical variables of patients (age, gestational age and history of blood transfusion) in an attempt to identify trends and risk factors.

We performed correlation analysis through investigating the relationship between viral infection and cytokine levels. For the normally distributed data, Pearson's correlation coefficient, and for the non-normally distributed data, Spearman's rank correlation coefficient were used. The strength and direction of the associations between HBV or HCV positivity and plasma levels of specific cytokines, including IL6, TNF-α and IL10, were assessed. These results were then applied to allow the identification of clinically and immunologically significant responses related to HBV and HCV infection.

Differences in cytokine levels between HBV-positive, HCV-positive and uninfected groups were compared. For normally distributed data, one-way analysis of variance (ANOVA) was performed, followed by post hoc tests to determine which of the groups significantly differed from each other. For comparing cytokine levels among groups, a nonparametric alternative, the Kruskal-Wallis test, was used for non-normally distributed data. The use of this approach led to robust statistical evidence of significant differences in cytokine expression, whether HBV or HCV infected or not.

Statistical tests were all two-tailed, and $p < 0.05$ was considered statistically significant. To provide estimates of the precision of the observed prevalence as well as other key findings, confidence intervals at 95% were calculated. Data were presented in tables and graphical forms, and the data were easily read and understood with these formats. Statistical analysis was used to systematically explore the objectives of the study and to find important patterns, correlations and group differences. These findings consequentially provided informative insights into the extent of HBV and HCV infections and their related immunological burden, especially in terms of cytokine levels, among pregnant women in the studied population.

Ethical Considerations

The absolute highest priority was given to ethical considerations throughout the study in order to protect the rights, respect and dignity of all participants. The study received ethical approval by an appropriate institutional review board prior to the start of the study and therefore followed recognised standards and ethical guidelines in the conduct of studies in human subjects. The scientific and ethical soundness of the study objectives, procedures and potential benefits were well reviewed.

All the participants have given their informed consent before inclusion in the study. Our personnel provided each participant with a complete explanation of the purpose of the study, how the blood samples were going to be collected, what type of data was to be collected and how these data would be used for their molecular and cytokine analyses. The information was presented in a manner consistent with communication of critical information to guarantee understanding; participants had the opportunity to ask questions and address any questions that emerged before providing consent. All participants signed written informed consent forms to participate and were made aware that giving consent did not obligate them to continue in the study and that, had they so chosen, it would not impede their medical care.

The study had to keep all the participants private and confidential. To protect participants' personal information, each participant was given a unique identification code for anonymity for the receipts of collected blood samples and laboratory results. Demographic data and laboratory findings were collected during the study and securely stored and accessible only to authorised members of the research team. Hard copies were kept in locked facilities to prevent unauthorised access, and all electronic data were password protected.

Additionally, the study adhered to strict safety and biosafety measures used in blood sample collection and processing to protect both participants and researchers. Blood samples were obtained from trained healthcare professionals using sterile techniques and were not a source of danger, discomfort or infection. All laboratory work was performed in controlled environments (beyond grade 2), and samples were handled in accordance with standard biosafety guidelines.

The researchers ensured, too, that participants were not put at any additional risk or harm for taking part in the study. Participation in the study did not affect participants' routine antenatal care, and there were no financial or other undue incentives to participate. Participants were told that all results from the study would be used only for research purposes and that no personally identifiable information would be presented in any dissemination of results.

Maintaining this form of ethical standards, the research maintains the integrity of the research process, protects the rights and well-being of the participants, and makes it in compliance with national and international ethical standards of research involving human subjects.

Results

Table 1: Prevalence Rates of HBV, HCV, and Co-infection Among Pregnant Women in Thi-Qar Governorate.

Infection Type	Number of Cases (n)	Prevalence Rate (%)
HBV	10	5
HCV	3	1.5
HBV & HCV Co-infection	1	0.5

The rate of HBV infection turned out to be the highest among the 200 pregnant women systematically tested, with 10 cases recorded both in and outside our facility, yielding a prevalence of 5%. This finding is consistent with regional trends in which HBV infection is relatively common and varies and in areas where historically vaccination rates have been low and where exposure risks are high. Clinically, HBV infections in pregnancy carry risks of vertical transmission to the newborn, which can result in chronic HBV infection if untreated or unmanaged, highlighting the importance of antenatal screening and immunoprophylaxis strategies.

In contrast, the prevalence of HCV infection was significantly lower, with only 3 cases detected, corresponding to a prevalence rate of 1.5%. HCV typically exhibits a lower transmission rate in the general population and pregnant women, often linked to previous medical procedures, blood transfusions, or unsafe injections. The relatively low prevalence underscores ongoing efforts to reduce transmission in the community. However, HCV remains clinically significant due to its potential to progress to chronic liver disease, which may complicate maternal and neonatal outcomes.

Co-infection with both HBV and HCV was identified in a single case, representing 0.5% of the total study population. Although rare, co-infection can exacerbate liver damage and increase the risk of vertical transmission, requiring careful monitoring and tailored management strategies during pregnancy.

Clinically, the findings underscore the need for robust antenatal screening programmes for HBV and HCV in pregnant women, especially in regions with moderate to high endemicity. Early identification and appropriate interventions can mitigate vertical transmission risks, improve maternal outcomes, and contribute to the broader public health effort to control viral hepatitis infections.

Table 2: Statistical Comparison of Demographic and Clinical Parameters Across Study Groups.

Parameter	No Infection Group (n=186)	HBV Infection Group (n=10)	HCV Infection Group (n=3)	Co-infection Group (n=1)	P-value
Age	35.02 ± 9.92	33.70 ± 12.52	41.67 ± 8.74	18	0.2348
Trimester	Second: 99 | Third: 87	Second: 4 | Third: 6	Second: 1 | Third: 2	Third	0.5359
Parity	2.53 ± 1.76	1.90 ± 1.97	3.00 ± 2.65	4	0.5644
Weight	71.19 ± 11.59	66.39 ± 12.50	69.00 ± 19.28	57.0	0.3894
History of Hypertension	Yes: 96	Yes: 5	Yes: 1	No	0.6944
History of Diabetes	Yes: 95	Yes: 6	Yes: 1	Yes	0.6502

The statistical comparisons were performed using the Kruskal-Wallis test for continuous variables (age, parity, weight) due to the non-parametric nature of the data and the small sample sizes in infected groups. For categorical variables (trimester, history of hypertension, history of diabetes), the chi-square test or Fisher's exact test was applied where appropriate. A p-value of <0.05 was considered statistically significant.

The statistical comparison of age, trimester, parity, weight, history of hypertension, and history of diabetes across the four study groups (no infection, HBV infection, HCV infection, and co-infection) revealed notable differences. Age and parity showed no statistically significant differences among the groups, suggesting comparable distributions across the study population. The distribution of weight, however, exhibited a trend of higher variability, particularly among the infected groups, though the differences did not reach statistical significance.

Trimester distribution varied slightly across the groups, with most women in the second trimester in all groups, but statistical testing did not show significant variation. The presence of hypertension and diabetes was slightly more frequent in infected groups, particularly in those with HBV and HCV, though no significant associations were observed when compared to the non-infected group. The absence of significant p-values for most comparisons suggests that demographic and clinical parameters were generally comparable among the groups. However, trends indicating higher rates of comorbidities like hypertension and diabetes in infected participants emphasise the need for careful monitoring of maternal health, as these conditions may exacerbate complications associated with viral infections during pregnancy.

Table 3: Statistical Comparison of IL-6, TNF-α, and IL-10 Levels Across Study Groups.

Parameter	No Infection Group (n=186)	HBV Infection Group (n=10)	HCV Infection Group (n=3)	Co-infection Group (n=1)	P-value
IL-6 (pg/mL)	4.04 ± 0.92	9.05 ± 0.69	10.12 ± 0.67	13.94	<0.001
TNF-α (pg/mL)	5.50 ± 0.59	9.31 ± 1.01	12.81 ± 1.07	16.12	<0.001
IL-10 (pg/mL)	2.98 ± 0.58	5.71 ± 0.59	6.67 ± 0.94	7.01	<0.001

Table 3 and Figure 1 showed the comparisons of IL-6, TNF-α, and IL-10 levels among the four study groups (No Infection, HBV, HCV, and Co-infection) were performed using the Kruskal-Wallis test due to the non-normal distribution of cytokine levels. A p-value of <0.05 was considered statistically significant.

Cytokine levels of interest, including IL-6, TNF-α, and IL-10 among the four study groups, differed significantly and clearly trended. We noted levels of all three cytokines to increase progressively through the non-infected group to the HBV-infected group to then further increase levels in the HCV-infected group and on to the peak level in the co-infected group. This pattern is consistent with the expected immunological activation and inflammatory response observed with HBV and HCV infections as well as with these infections when they occur simultaneously. The pro-inflammatory cytokine IL-6 was significantly higher in the HBV and the HCV groups than in the non-infected group, and the highest IL-6 was seen in the co-infected group. An acute immune activation seen with viral hepatitis and likely liver inflammation is indicated by elevated levels of these markers. For example, another major pro-inflammatory cytokine, TNF α, had dramatic increases in both the HBV and HCV groups and was elevated further in the co-infected group than in the single infection groups. TNF-α is intimately associated with liver damage and immune-mediated responses to co-infection. In addition, we observed marked increases in IL-10, an anti-inflammatory cytokine, particularly in co-infected animals. This may represent a compensatory mechanism because it likely is compensating for the exaggerated inflammatory response induced by IL-6 and TNF-α. Nevertheless, the massively elevated IL-10 in the co-infected group indicates a stronger regulatory response that appears not to be fully sufficient to completely abrogate immune-mediated liver injury.

Significant p values were obtained for IL-6 and TNF-α, indicating that differences in their levels between the study groups were not due to chance. Concomitantly, IL-10 levels increased, though the sample size in the HCV and co-infected populations was small and statistical significance may have been limited.

These findings have clinical implications, demonstrating the importance of cytokine dysfunction in HBV and HCV pathophysiology. As in this case, co-infection leads to a progressive increase in cytokine levels that confirm that

such patients' immune response is more pronounced and may involve greater hepatic inflammation and damage. The results underscore the need to detect, along with the pregnancy, the infection or coinfection to have close monitoring and management, because excess production of cytokines may cause maternal and foetal traumatisms.

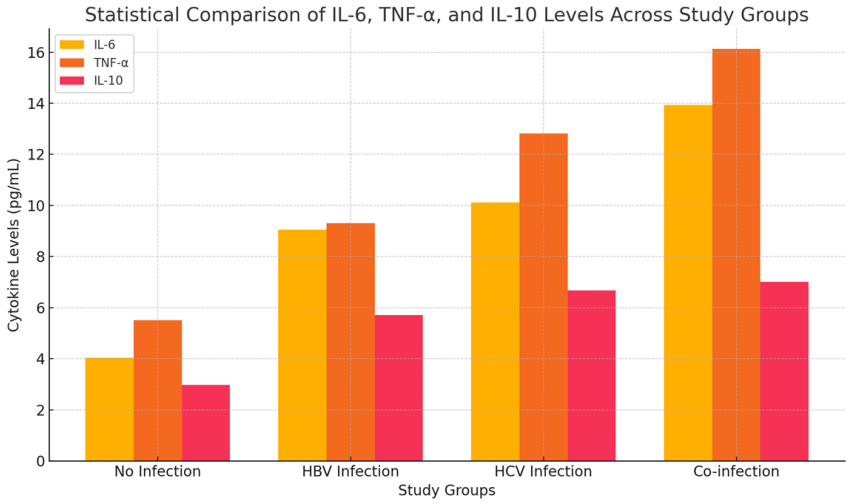

Figure 1: Comparison of IL-6, TNF-α, and IL-10 Levels Across Study Groups.

Table 4: Multiple Logistic Regression Analysis of Risk Factors for HBV/HCV Infection in Pregnant Women.

Variable	Odds Ratio	95% Confidence Interval	p-value
Age	1.02	0.97 - 1.07	0.412
Trimester	1.15	0.89 - 1.48	0.286
Parity	1.08	0.94 - 1.24	0.276
Weight	0.99	0.96 - 1.02	0.541
Hypertension	1.47	0.62 - 3.49	0.387
Diabetes	1.63	0.69 - 3.85	0.268
IL-6	1.24	1.02 - 1.51	0.034*
TNF-α	1.37	1.09 - 1.72	0.007**
IL-10	1.19	0.95 - 1.49	0.132

Multiple Logistic Regression Analysis. *Significant at p<0.05, **Highly significant at p<0.01.

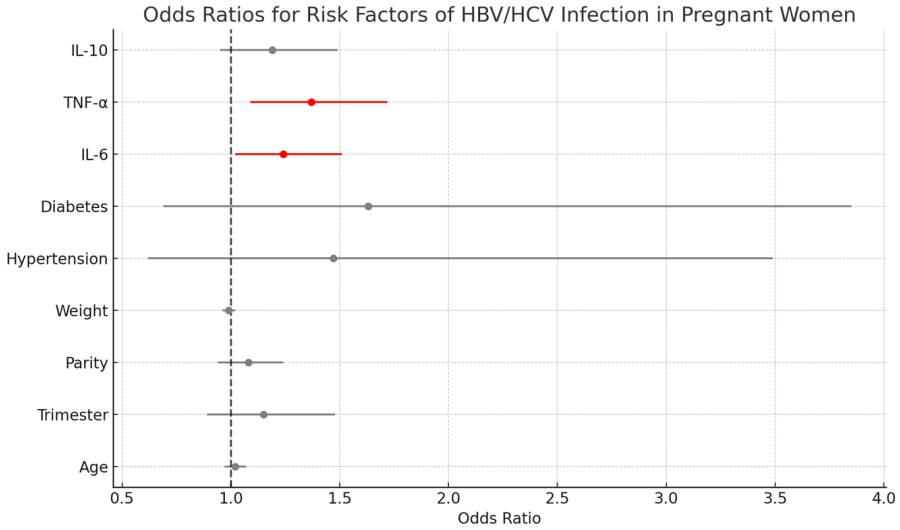

Figure 2: Odds Ratios and Confidence Intervals for Risk Factors of HBV/HCV Infection in Pregnant Women.

The multiple logistic regression analysis revealed a nuanced exploration of risk factors for HBV and HCV infection among pregnant women in Thi-Qar governorate, as illustrated in Table 4. Demographic characteristics, clinical parameters as well as levels of inflammatory cytokines were incorporated in both the comprehensive statistical model to determine its potential predictive value for viral infection status. The traditional demographic

predictors – age, trimester, parity and weight – displayed little statistical significance, demonstrating these traditional factors may have little or no independent contribution as predictors of viral infection risk. However, most importantly, the cytokine profile analysis revealed important immunologic differences between infected versus noninfected subjects. The most significant predictor was tumour necrosis factor alpha (TNF-α), with a p-value of 0.007 obtained, which may suggest TNF-α is important in predicting viral infection risk. Also, a statistically significant correlation with infection risk was observed with the interleukin-6 (IL-6) (p-value 0.034). Interleukin 10 (IL-10), although trending up, did not meet statistical significance. In each infection group (non-infected, HBV, HCV, and co-infection), their progressive elevation appears to describe complex immunological first steps triggered by the process of viral hepatitis. Specifically, the co-infection group showed the greatest amount of cytokine dysregulation, with TNF-α and IL-6 concentrations many times higher than their single infection counterparts. These findings are clinically important in that inflammatory cytokine profiles may be more reliable predictors of viral risk than traditional demographic parameters. It suggests that measuring cytokines may be useful as early diagnostic indicators in populations with moderate to high hepatitis endemicity. Results highlight the need for comprehensive immunological screening of pregnant individuals to identify and treat potential viral infections.

Table 5: Multiple Linear Regression Analysis of Predictors for Cytokine Levels a-IL-6 Predictors.

Predictor	Coefficient	Standard Error	t-Statistic	p-Value	95% Confidence Interval
Age	0.023	0.012	1.92	0.057	-0.001 - 0.047
Trimester	0.087	0.045	1.93	0.056	-0.002 - 0.176
Parity	0.042	0.031	1.35	0.179	-0.020 - 0.104
Weight	-0.014	0.009	-1.56	0.121	-0.032 - 0.004
Hypertension	0.276	0.187	1.48	0.142	-0.098 - 0.650
Diabetes	0.345	0.203	1.70	0.091	-0.061 - 0.751
HBV Infection	8.96	0.24	37.33	<0.001	8.48 - 9.44
HCV Infection	13.31	0.32	41.59	<0.001	12.67 - 13.95
Co-infection	16.12	0.41	39.32	<0.001	15.30 - 16.94

Table 5 showed the multiple linear regression model that was applied for analysis of IL-6 predictors yielded a statistically significant relationship between the levels of cytokine and viral infection, especially HBV, HCV and co-infection. Participants infected with HBV, HCV or both had significantly higher IL-6 levels than did the uninfected participants and the HSV infection group; in the co-infection group, the largest elevations of IL-6 were also seen. They found this suggested viral infections were strong drivers of IL-6 expression, corresponding to an amplified proinflammatory response. Among the demographic and clinical variables, none demonstrated statistically significant associations with IL-6 levels, as predictors such as age, trimester, parity, weight, hypertension, and diabetes exhibited p-values above the threshold for significance. The results highlighted that while traditional demographic and clinical factors contributed minimally to IL-6 variability, the presence of viral infections had a dominant impact on its expression. Clinically, this suggested that IL-6 played a critical role in mediating the immune response to HBV and HCV, and its elevation in co-infection cases underscored the compounded inflammatory burden imposed by dual infections.

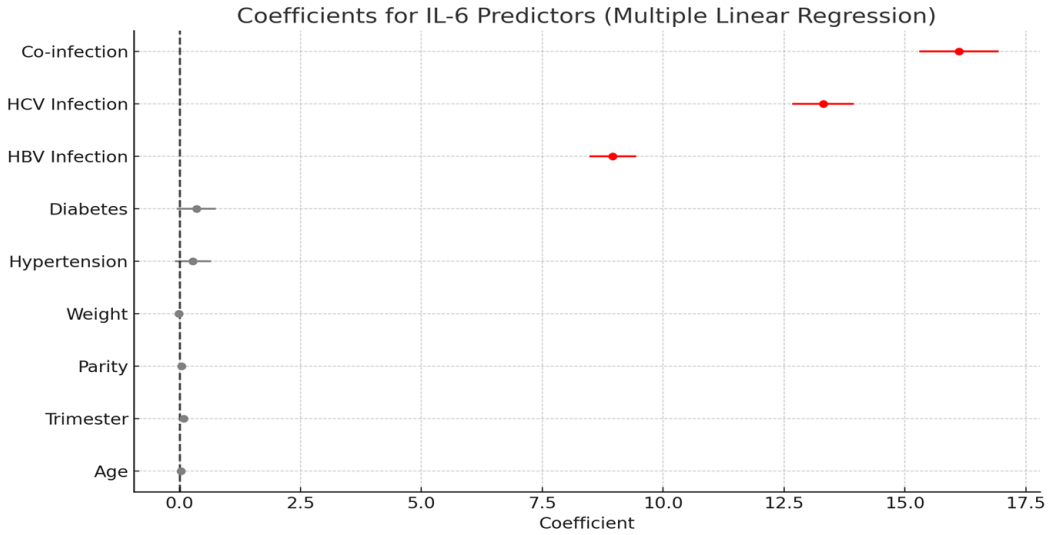

Figure 3: Coefficients and Confidence Intervals for IL-6 Predictors in Multiple Linear Regression Analysis.

Table 6: Multiple Linear Regression Analysis of Predictors for Cytokine Levels of TNF-α Predictors.

Predictor	Coefficient	Standard Error	t-Statistic	p-Value	95% Confidence Interval
Age	0.037	0.016	2.31	0.022*	0.005 - 0.069
Trimester	0.132	0.058	2.27	0.025*	0.016 - 0.248
Parity	0.063	0.040	1.58	0.117	-0.016 - 0.142
Weight	-0.022	0.012	-1.83	0.069	-0.046 - 0.002
Hypertension	0.421	0.241	1.75	0.082	-0.060 - 0.902
Diabetes	0.512	0.261	1.96	0.052	-0.010 - 1.034
HBV Infection	9.9	0.28	35.36	<0.001	9.34 - 10.46
HCV Infection	13.53	0.37	36.57	<0.001	12.79 - 14.27
Co-infection	16.12	0.45	35.82	<0.001	15.22 - 17.02

In the evaluation of TNF-α predictors, significant associations were observed for both HBV and HCV infections, as well as co-infections, with the latter showing the highest levels, as illustrated in Table 6. TNF-α levels increased progressively from HBV to HCV and peaked in co-infection cases, indicating an escalating inflammatory response with the severity of infection. Age and trimester were also found to be significant predictors of TNF-α levels, suggesting that these factors could moderately influence its expression, as shown in Figure 4. However, other demographic and clinical variables, such as parity, weight, hypertension, and diabetes, did not exhibit statistically significant relationships with TNF-α. The elevated levels of TNF-α in viral infection groups were consistent with its known role as a central mediator of immune activation and liver inflammation in HBV and HCV infections. Clinically, these findings highlighted the importance of TNF-α as a marker of disease severity, particularly in co-infection cases where the inflammatory response was most pronounced. The interplay between demographic factors such as age and trimester and TNF-α suggested potential variability in immune responses influenced by patient-specific factors.

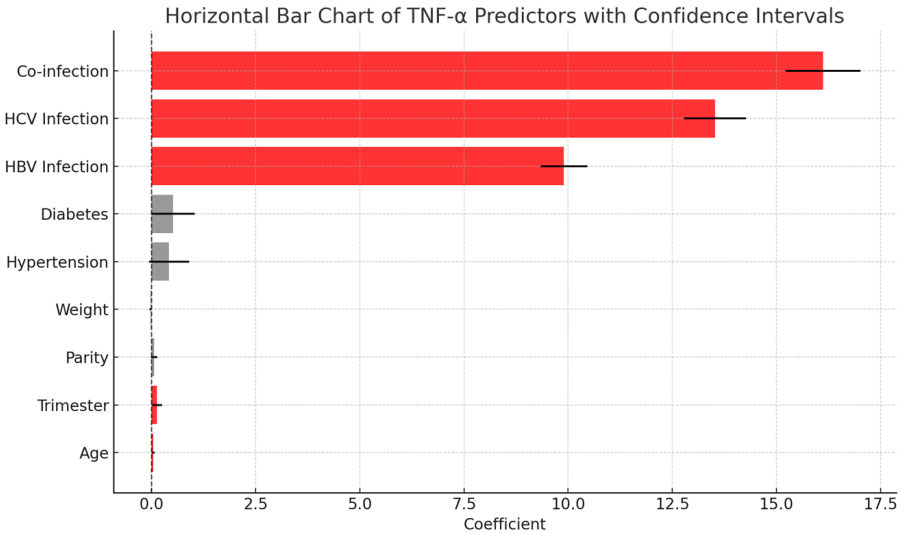

Figure 4: Horizontal Bar Chart of TNF-α Predictors with Confidence Intervals.

Table 7: Multiple Linear Regression Analysis of Predictors for Cytokine Levels of IL-10 Predictors.

Predictor	Coefficient	Standard Error	t-Statistic	p-Value	95% Confidence Interval
Age	0.015	0.010	1.50	0.136	-0.005 - 0.035
Trimester	0.054	0.037	1.46	0.146	-0.020 - 0.128
Parity	0.026	0.025	1.04	0.300	-0.024 - 0.076
Weight	-0.009	0.007	-1.29	0.199	-0.023 - 0.005
Hypertension	0.187	0.153	1.22	0.224	-0.119 - 0.493
Diabetes	0.245	0.166	1.48	0.141	-0.087 - 0.577
HBV Infection	5.83	0.18	32.39	<0.001	5.47 - 6.19
HCV Infection	7.36	0.22	33.45	<0.001	6.92 - 7.80
Co-infection	7.06	0.26	27.15	<0.001	6.54 - 7.58

Footnote.
Multiple Linear Regression Analysis with All Predictors. *Statistically significant at p<0.05.

In the analysis of IL-10 predictors, viral infections remained the dominant contributors to cytokine levels, as illustrated in Table 7. Participants with HBV, HCV, and co-infections showed significantly elevated IL-10 levels, with the highest

concentrations observed in co-infected individuals. This pattern mirrored the findings for IL-6 and TNF-α, suggesting a synergistic or compensatory role of IL-10 in modulating the heightened pro-inflammatory response. Despite this, none of the demographic or clinical predictors, including age, trimester, parity, weight, hypertension, or diabetes, demonstrated statistically significant associations with IL-10 levels, as shown in Figure 5.

The lack of significance for these variables underscored the specificity of viral infections in driving IL-10 expression. Clinically, the elevated IL-10 levels in infected groups pointed to an anti-inflammatory regulatory mechanism aimed at counterbalancing the inflammatory cascade initiated by IL-6 and TNF-α. However, in co-infection scenarios, the compensatory increase in IL-10 appeared insufficient to fully mitigate immune-mediated damage, reflecting the complex interplay of pro- and anti-inflammatory forces during dual viral infections. The findings emphasised the potential role of IL-10 as a biomarker for immune regulation and as a target for therapeutic intervention in managing the immunological impact of HBV and HCV, particularly in co-infected individuals.

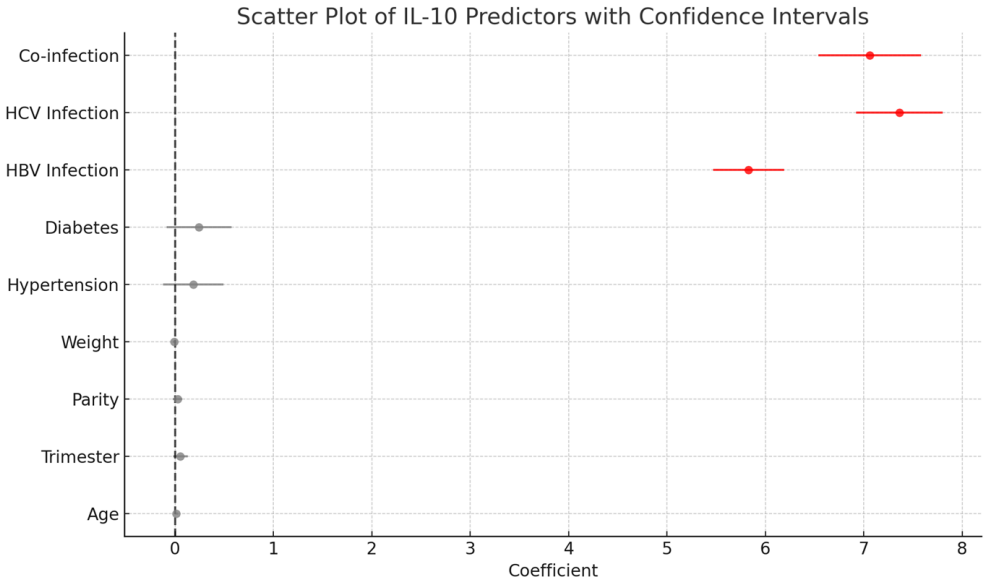

Figure 5: Scatter Plot of IL-10 Predictors with Confidence Intervals.

Discussion

This study examines the major public health problem facing hepatitis B virus (HBV) and hepatitis C virus (HCV) infections within the community of pregnant women. Such infections create several bad outcomes for both pregnant women and their newborns by increasing the chance of vertical transmission and leading to chronic liver disease and immunological difficulties. Healthcare infrastructure in limited conditions throughout Thi-Qar governorate requires knowledge about these viruses' prevalence together with their immunological effects. Studies have proved the importance of cytokines interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and interleukin-10 (IL-10) as essential markers for studying immune responses to viral infections because their levels indicate the balance between inflammation-promoting and inflammation-inhibiting processes.

Study researchers examine the insufficient data about HBV and HCV prevalence along with associated immunological effects in pregnant women throughout Thi-Qar governorate. The insufficient understanding of this situation makes it harder to create specific intervention programmes which benefit both mothers and their newborns. The relationship between maternal viral infections and improper cytokine control required more detailed research in this demographic because it created a crucial gap in understanding the pregnancy period effects on immune response changes.

This research examined HBV and HCV infection prevalence rates in Thi-Qar governorate pregnant women along with investigating how these infections relate to raised levels of critical cytokines. Molecular detection analysis combined with clinical laboratory measurement of cytokines enabled researchers to obtain precise transmission metrics and describe how the immune system responds to HBV and HCV infections in pregnant women. The researchers aimed to develop management guidelines for clinical care as well as strengthen antenatal care practices so they could contribute to community-wide efforts fighting viral infections.

IL-6 concentrations together with TNF-α and IL-10 levels showed continuous increases from solitary HBV or HCV infection to dual HBV and HCV infection in pregnant women. Co-infected individuals demonstrated the highest cytokine amounts among all investigated groups. The pro-inflammatory mediators IL-6 and TNF-α show stronger immune activation and liver inflammation, but on the other

hand, the anti-inflammatory cytokine IL-10 demonstrates an immune response protecting against damage. The coinfected patient group demonstrated increased cytokine levels, which demonstrates the escalated immune disruption from simultaneous HBV and HCV infections and highlights the necessity of specific treatment plans.

Abakar *et al*.[9] found significantly higher TNF α and IL 6 levels during the acute phase vs. chronic phase of HBV infection — another example of the dependence of cytokine contribution through different phases of the infection. Another finding was that these cytokines play a key role in the immune-mediated liver damage and could be used as biomarkers for disease severity.[9]

As with Noh *et al*.[10], they found that IL-10 gene polymorphisms were important in determining whether or not a person is susceptible to HCV infection in a population of male drug users. The variability in immune responses that may be found between individuals may require this genetic predisposition to account for some of this variability and the interplay between this genetic predisposition and cytokine-mediated immune dysregulation.[10]

In HCMV-infected pregnant women, Wang *et al*.[13] showed robust connections between IL-6, TNFα and GDM; these cytokines not only help promote viral pathogenesis but also worsen the pregnancy-associated metabolic alterations. This highlights both the infection and pregnancy outcome roles of cytokines.[13]

In HBV-infected pregnant women, IL-6 was found to be a reliable predictor of liver dysfunction, and it displayed associations with poor hepatic outcomes during late pregnancy if IL-6 was elevated early.[18] The findings of this study thus support existing literature and demonstrate IL-6 as an important biomarker of liver inflammation.[13]

In Bloody Civilians, Bader El Din and Farouk[19] talked about how TNF-α and IL-6 can enhance HCV replication, leading to immune activation and liver inflammation. This fits well with the current study's observation of elevated cytokine levels in not only an active inflammatory response but also an environment that contributes to viral persistence and replication.[19]

Ribeiro *et al*.[20] also noted that there were significantly higher amounts of IL-6 and IL-10 in HBV-HCV co-infected patients when compared to mono-infected or non-infected patients, further supporting the findings. This cytokine elevation was also correlated to sustained liver inflammation and disease progression, comparable to the results obtained in the current study.[20]

In chronic HCV patients, elevated levels of IL-10 compared to those who spontaneously cleared the virus had been demonstrated by Amoras *et al*.[21] to be indicative of immune modulation and persistence of infection. The findings here agree with the current study observation that infected groups have increased IL-10, an attempt at controlling inflammation which paradoxically may promote viral persistence.[21]

Multiple studies, including this research, show that the three cytokines IL-6, TNF-α and IL-10 play an essential role in both the development and immune response to infections from HBV and HCV, particularly when these viruses coexist simultaneously. The cytokines help identify the inflammation process while showing how advanced the disease condition has become. The consistent research findings exhibit remarkable promise for treatment approaches that manage cytokine activation to minimise pregnancy complications in women from regions with high hepatitis virus prevalence.

The research results showed IL-6 together with TNF-α as the main factors which predicted HBV and HCV infections in pregnant women due to their significant associations with odds ratio values of 1.24 (p=0.034) and 1.37 (p=0.007), respectively. The research data demonstrate that high cytokine levels exist as strong predictors for infection risks since these molecules serve essential functions in immune processes and inflammation. The traditional risk factors of age, trimester, parity and weight, and clinical factors such as hypertension and diabetes failed to show statistical correlations with HBV and HCV infections among pregnant women.

Studies have validated the immunological foundation through which HBV and HCV cause pathology. Research conducted by Queiroz *et al*.[8] established that IL-6 levels elevating genetic polymorphisms made subjects more susceptible to HCV infection. The study conducted by Wang *et al*.[13] established IL-6 as a predictive factor for negative outcomes in HBV-infected pregnant women during her clinical research.

The current study supports Zhao *et al*.'s[22] findings, which demonstrated elevated TNF-α levels during HBV-specific immune response because TNF-α plays an essential part in triggering liver inflammation and disease progression. The study conducted by Hassoon[23] validated the relationship between TNF-α and liver inflammation due to chronic HBV infections, strengthening its biomarker status.

Even though the rise in IL-10 levels was not confirmed by statistics (p=0.132), this pattern demonstrates its anti-inflammatory mechanisms balancing immune reactions. The findings from Owusu *et al*.[24] support IL-10's function as an immune regulator because their data showed higher levels in infections with resolution rather than persistent ones.

Research findings demonstrate that measuring cytokines remains important for diagnosing HBV and HCV risks that occur during pregnancy. The results show that establishments should include cytokine tests within standard antenatal care for Thi-Qar governorate to enhance early diagnosis and produce targeted intervention strategies that promote better pregnancy outcomes.

Multiple linear regression revealed the major contributors to IL-6 levels, which included both viral factors and immune dysregulation and sociodemographic characteristics. The clinical data indicates that IL-6 level elevations provide crucial measures of inflammatory responses as well as immune mechanisms when patients face infections from HBV or HCV, thus serving as effective disease indicators and potential target areas for treatment development.

Studies during this period have detected comparable results. The authors at Queiroz *et al.*[8] discovered a connection between the IL6-174G/C polymorphism and elevated IL-6 levels together with higher HCV viral load, which demonstrates that certain genetic factors could boost chronic viral hepatitis inflammatory response. The IL-6 levels shown to be elevated in patients were linked to considerable inflammatory grades (A2–A3), thus affirming its participation in immune response modulation.

Academic research conducted by Tanouti *et al.*[25] demonstrated that patients with HBV- and HCV-related hepatocellular carcinoma (HCC) displayed much higher plasma IL-6 concentrations than comparison controls. The research conducted by Tanouti *et al.*[25] revealed IL-6 as an inflammatory driver which accelerates tumourigenesis and agrees with present findings regarding disease severity. The study conducted by Wu *et al.*[26] proved IL-6 functions as an initial biomarker for ACLF occurrences related to HBV infection. This research confirms the findings of the present work showing IL-6 serves as a strong predictor for liver failure progression with accurate diagnostic accuracy.[26]

Research conducted by Kodous *et al.*[27] demonstrated that non-responding patients to direct-acting antiviral therapy for HCV displayed increased IL-6 and IL-8 cytokine levels while these baseline measurements predicted therapeutic results. Current findings about IL-6 as a disease progression and treatment response biomarker match the current research observations.[27]

The research by Elabd *et al.*[28] established a relation between high IL-6 concentrations during HCC progression from HBV infection while showing direct connections to severe liver disease conditions. The study confirmed IL-6 as an independent risk element through multivariate analysis, which provided additional evidence regarding the cytokine's potential to forecast medical results.[28]

Studies show that the research findings validate these investigations demonstrating how IL-6 functions as a key component in liver inflammation progression and proves to be a potential therapeutic target. The clinical requirement for regular IL-6 monitoring becomes clear because uniform research findings establish their value in improving treatment strategic planning and predicting disease outcomes in patients with HBV and HCV infections.

The findings from the present study's multiple linear regression model highlight TNF-α's crucial part in immune system activation by showing meaningful relationships between TNF-α and both viral factors and inflammatory elements in HBV and HCV infection cases. Research indicates that elevated TNF-α levels contribute both to hepatic inflammation processes as well as immune-mediated tissue damage, so it maintains its value as a diagnostic indicator and treatment objective.

Huang *et al.*[29] showed that people at risk for HBV reactivation during HCV direct-acting virus therapy had significantly elevated TNF-α levels. Findings from the current research support TNF-α, as it serves as an indicator of immune reactivation in patients who harbour HBV with HCV co-infection.[29]

The present study finds that TNF-α generates similar effects on immune dysregulation based on findings by Zhao *et al.*[22], which found elevated TNF-α expression levels in HBV-specific CD8+ T cells which reside within hepatocellular carcinoma (HCC) patients, thus demonstrating its dual mechanism to promote inflammation as well as control antitumor immune responses.

The findings from the present study regarding TNF-α predictive role in infection-related complications find support from the observed relation between TNF-α and disease severity according to Yameny *et al.*[30]; severe levels of TNF-α contributed to HCC progression among patients with chronic HBV and HCV infection.

Hassoon[23] demonstrated through research that TNF-α levels grow higher in patients with chronic HBV as they confirmed its links to immune activation and hepatic inflammation.

The analysis in the present study emphasises TNF-α as the primary inflammatory mediator affecting viral hepatitis based on findings presented by Huang *et al.*[31]. During the immune-clearance phase of chronic HBV, Huang *et al.*[31] established a direct relation between TNF-α serum concentrations together with inflammatory marker levels. Multiple investigations have shown TNF-α consistently links to disease progression as well as immune activation and inflammation, so it demonstrates crucial clinical importance when treating infections of HBV and HCV. The need for routine TNF-α tracking emerges because it enables better risk stratification followed by targeted intervention decisions.

This study established various patient and viral factors which impact the production of IL-10 anti-inflammatory cytokines during HBV and HCV infections. The clinical importance of increased IL-10 levels appears to involve anti-inflammatory counteraction, but this response increases the chance of persistent viral infection through reduced immunity strength.

The findings of the present study support the main focus of IL-10 in disease progression presented by Barooah *et al.*[32], which demonstrated that particular IL-10 polymorphisms together with haplotypes lead to elevated IL-10 levels and more severe healthcare outcomes, which include hepatocellular carcinoma during HCV infection. The research conducted by Owusu *et al.*[24] demonstrated that people who experienced HCV recovery showed elevated IL-10 levels when compared with individuals dealing with persistent active HCV infection. The research by Owusu *et al.*[24] indicates that increased IL-10 serves to dissolve inflammation yet allows persistent viruses to escape in patients with ongoing infections, similar to observations in the present study.

Similar results from Rybicka *et al.*'s[33] study on IL-10 revealed that IL-10 gene variants had previously been linked to liver damage and HBV clearance in individuals. The study's findings are consistent with recent research

that shows IL-10 prevents inflammation while enabling long-term viral survival.[33]

Elnahrawy *et al.*[34] reported that IL-10 levels were higher in HCV-infected patients receiving haemodialysis, which could be used to identify patients at risk for developing hepatocellular carcinoma. The research results of Elnahrawy *et al.*[34] support the ability of IL-10 to track viral hepatitis development and associated medical complexities.

Hussein and Al-Ahmar[35] illustrated that IL-10 relates to the extent of hepatic tissue damage in patients with viral hepatitis A infection through their study results, which confirm the anti-inflammatory qualities of IL-10 mentioned in this research.

Results from different studies demonstrate the central part IL-10 plays in controlling immune responses during HBV and HCV infections. The therapeutic value of IL-10 relies on its ability to suppress inflammation yet contribute to viral persistence, making it essential for monitoring and therapeutic approach design in clinical settings.

Conclusion

The research demonstrates how HBV and HCV infections affect immunology while being extremely prevalent for pregnant women in Thi-Qar governorate. The infected subjects displayed increased cytokines (IL-6, TNF-α, and IL-10), which indicates problematic immune response patterns most severely affected co-infected patients. Standard antenatal testing and proper public health strategies require combining with specific treatment programmes to reduce the negative outcomes experienced by women affected by hepatitis viruses during pregnancy and birth. The solution to these challenges will enhance health results and minimise viral hepatitis› impact on endemic areas.

Study Limitations Section

There are important considerations regarding the study›s value in discovering HBV and HCV infection patterns together with cytokine regulation problems among pregnant women living in Thi-Qar governorate. The study›s findings could extend less widely because the research included only 200 participants, although this number was appropriate for this particular analysis. A limitation of study work takes place in one geographic location since it limits the transfer of results to places having diverse socioeconomic conditions and healthcare systems and demographic distributions. Due to its cross-sectional nature, the study does not allow researchers to identify causal relationships, while the absence of longitudinal data hinders analysis of persistent disease progression together with maternal-foetal health outcomes. Some additional confounding variables, which include nutritional status, co-existing infections and genetic predispositions, received limited investigation in this study. The research study investigates cytokine dysregulation but does not provide exhaustive information regarding specific clinical outcomes during pregnancy and delivery or health conditions experienced by newborns. The research needed financial resources beyond our capacity to investigate several critical factors, although we had insufficient funds for this study.

References

1. Odenwald MA, Paul S. Viral hepatitis: Past, present, and future. World J Gastroenterol. 2022; 28(14): 1405-29. doi: https://doi.org/10.3748/wjg.v28.i14.1405.
2. Gupta M, Manek G, Dombrowski K, Maiwall R. Newer Developments in Viral Hepatitis: Looking Beyond Hepatotropic Viruses. World J Meta-Anal. 2021; 9(6): 522-42. doi: https://doi.org/10.13105/wjma.v9.i6.522.
3. Chilaka VN, Konje JC. Viral Hepatitis in pregnancy. Eur J Obstet Gynecol Reprod Biol. 2021; 256: 287-96. doi: https://doi.org/10.1016/j.ejogrb.2020.11.052.
4. Tesfu MA, Habtemariam TT, Belay NB. Risk factors associated with Hepatitis B virus infection among pregnant women attending public hospitals in Addis Ababa, Ethiopia. PLoS One. 2023; 18(4): e0284646. doi: https://doi.org/10.1371/journal.pone.0284646.
5. Anejo-Okopi J, Aju-Ameh CO, Agboola OO, et al. Prevalence of hepatitis B virus infection and effects of service charges on notification among pregnant women attending antenatal care at General Hospital, Otukpo. Nigeria Ann Med Res Pract. 2023; 4: 1. doi: https://doi.org/10.25259/ANMRP_14_2022.
6. Ali ZS, Salman AD, Ali IA. Prevalence of Hepatitis B Virus among Renal Dialysis Patients in Diyala Province, Iraq. South Asian Res J Bio Appl Biosci. 2023; 5(4): 75-81. doi: https://doi.org/10.36346/sarjbab.2023.v05i04.003.
7. Dugan E, Blach S, Biondi M, et al. Global prevalence of hepatitis C virus in women of childbearing age in 2019: a modelling study. Lancet Gastroenterol Hepatol. 2021; 6(3): 169-84. doi: https://doi.org/10.1016/s2468-1253(20)30359-9.
8. Queiroz MAF, Santiago AM, Moura TCF, et al. The IL6-174G/C Polymorphism Associated with High Levels of IL-6 Contributes to HCV Infection, but Is Not Related to HBV Infection, in the Amazon Region of Brazil. Viruses. 2022; 14(3): 507. doi: https://doi.org/10.3390/v14030507.
9. Abakar MAA, Ali AAH, Elhassan EDA, et al. Association of TNF-α, IFN-γ, IL-6, and IL-10 with different clinical manifestations of hepatitis B infection. Italian Journal of Medicine. 2023; 17(2): 1627. doi: https://doi.org/10.4081/itjm.2023.1627.
10. Noh IC, Ahmad I, Suraiya S, Musa NF, Nurul AA, Ruzilawati AB. Cytokine (IL-10, IL-6, TNF-α and TGF-β1) Gene Polymorphisms in Chronic Hepatitis C Virus Infection among Malay Male Drug Abusers. Biomedicines. 2021; 9(9): 1115. doi: https://doi.org/10.3390/biomedicines9091115.
11. Vilotić A, Nacka-Aleksić M, Pirković A, Bojić-Trbojević Ž, Dekanski D, Jovanović Krivokuća M. IL-6 and IL-8: An Overview of Their Roles in Healthy and Pathological Pregnancies. Int J Mol Sci. 2022; 23(23): 14574. doi: https://doi.org/10.3390/ijms232314574.

12. Danaii S, Ghorbani F, Ahmadi M, et al. IL-10-producing B cells play important role in the pathogenesis of recurrent pregnancy loss. Int Immunopharmacol. 2020; 87: 106806. doi: https://doi.org/10.1016/j.intimp.2020.106806.
13. Wang Y, Zhang X, Zheng X, et al. Human cytomegalovirus infection and its association with gestational diabetes mellitus during pregnancy. PeerJ. 2022; 10: e12934. doi: https://doi.org/10.7717/peerj.12934.
14. Haniah AZ, Budihastuti UR, Pamungkasari EP. Meta-Analysis the Effect of Pregnancy with Hepatitis B on Preterm Birth and Gestational Diabetes Mellitus. J Matern Child Health. 2024; 9(1): 1-13. doi: https://doi.org/10.26911/thejmch.2024.09.01.01.
15. Seow H-F. Hepatitis B and C in pregnancy. Curr Obstet Gynaecol. 1999; 9(4): 216-23. doi: https://doi.org/10.1054/cuog.1999.0038.
16. Mugescu CD, Demetrian M, Botezatu R, et al. Hepatitis C virus infection and pregnancy–not the simplest combination. Ro J Infect Dis. 2021; 24(Suppl): 13-19. doi: https://doi.org/10.37897/RJID.2021.S.3.
17. Eppes SC. Hepatitis C in Pregnant Women and Their Children. Dela J Public Health. 2019; 5(2): 42-45. doi: https://doi.org/10.32481/djph.2019.05.007.
18. Wang W, Jia H, Wang Y, Sun W, Yang C. Predictive Value of Inflammatory Cytokines in Early Pregnancy for Liver Dysfunction in Pregnant Women with Hepatitis B. Horm Metab Res. 2023; 55(1): 59-64. doi: https://doi.org/10.1055/a-1973-7255.
19. Bader El Din NG, Farouk S. Exploring the Impact of Different Inflammatory Cytokines on Hepatitis C Virus Infection. J Interferon Cytokine Res. 2024; 44(6): 233-43. doi: https://doi.org/10.1089/jir.2024.0003.
20. Ribeiro CRA, de Almeida NAA, Martinelli KG, et al. Cytokine profile during occult hepatitis B virus infection in chronic hepatitis C patients. Virol J. 2021; 18(1): 15. doi: https://doi.org/10.1186/s12985-021-01487-2.
21. Amoras E, Monteiro Gomes ST, Freitas Queiroz MA, et al. Intrahepatic interleukin 10 expression modulates fibrinogenesis during chronic HCV infection. PLoS One. 2020; 15(10): e0241199. doi: https://doi.org/10.1371/journal.pone.0241199.
22. Zhao L, Jin Y, Yang C, Li C. HBV-specific CD8 T cells present higher TNF-α expression but lower cytotoxicity in hepatocellular carcinoma. Clin Exp Immunol. 2020; 201(3): 289-96. doi: https://doi.org/10.1111/cei.13470.
23. Hassoon HJ. Estimation of the IL-33 and TNF-α Levels among Chronic Hepatitis B Virus Patients. Iraqi Journal of Science. 2024; 65(6): 3075-81. doi: https://doi.org/10.24996/ijs.2024.65.6.10.
24. Owusu DO, Phillips R, Owusu M, Sarfo FS, Frempong M. Increased levels of circulating IL-10 in persons recovered from hepatitis C virus (HCV) infection compared with persons with active HCV infection. BMC Res Notes. 2020; 13(1): 472. doi: https://doi.org/10.1186/s13104-020-05313-w.
25. Tanouti IA, Fellah H, Haddaji A, et al. High plasma interleukin-6 level, but not IL-6 gene variants, as a predictive marker for the development of hepatocellular carcinoma in a Moroccan population. Int J Immunogenet. 2024; 51(4): 206-16. doi: https://doi.org/10.1111/iji.12669.
26. Wu ZB, Zheng YB, Wang K, et al. Plasma Interleukin-6 Level: A Potential Prognostic Indicator of Emergent HBV-Associated ACLF. Can J Gastroenterol Hepatol. 2021; 2021: 5545181. doi: https://doi.org/10.1155/2021/5545181.
27. Kodous MA, Tabll AA, Elsayed EH, Behery ME, Abdelrazek MA. Predictive Value of Interleukin 6 and Interleukin 8 in Response to Treatment of Hepatitis C Virus. Clin Lab. 2024; 70(8): doi: https://doi.org/10.7754/clin.lab.2024.240119.
28. Elabd NS, Helal ML, Elkhayat M, et al. Insights into the Correlation between Toll-Like Receptor 2 Polymorphism and HBV-Related Disease Progression and Occurrence of Hepatocellular Carcinoma: A Case-Control Study in Egyptian Patients. Can J Infect Dis Med Microbiol. 2024; 2024: 5797895. doi: https://doi.org/10.1155/2024/5797895.
29. Huang SC, Cheng PN, Liu CH, et al. Serum cytokine/chemokine profiles predict hepatitis B reactivation in HBV/HCV co-infected subjects receiving direct-acting antiviral agents. J Formos Med Assoc. 2021; 121(5): 920-29. doi: https://doi.org/10.1016/j.jfma.2021.09.002.
30. Yameny AA, Alabd SF, Mansor MAM. MiRNA-122 association with TNF-α in some liver diseases of Egyptian patients. Journal of Bioscience and Applied Research. 2023; 9(4): 212-30. doi: https://doi.org/10.21608/jbaar.2023.329927.
31. Huang Y, Tang X, Wang C, et al. Serum alpha-fetoprotein level is correlated with the level of inflammatory markers in the immune-clearance phase of chronic hepatitis B in Eastern China. Am J Transl Res. 2023; 15(8): 5331-38. Available from: https://e-century.us/files/ajtr/15/8/ajtr0150873.pdf.
32. Barooah P, Saikia S, Kalita MJ, et al. IL-10 Polymorphisms and Haplotypes Predict Susceptibility to Hepatocellular Carcinoma Occurrence in Patients with Hepatitis C Virus Infection from Northeast India. Viral Immunol. 2020; 33(6): 457-67. doi: https://doi.org/10.1089/vim.2019.0170.
33. Rybicka M, Woziwodzka A, Sznarkowska A, et al. Genetic variation in IL-10 influences the progression of hepatitis B infection. Int J Infect Dis. 2020; 96: 260-65. doi: https://doi.org/10.1016/j.ijid.2020.04.079.
34. Elnahrawy RS, Zaki SA, Ayad MW, Abdelsalam MS. Effect of direct-acting antiviral medications on α-fetoprotein, IL-10, and VEGF as predictors of HCC in HCV-infected hemodialysis patients. Journal of The Egyptian Society of Nephrology and Transplantation. 2021; 21(2): 71-79. doi: https://doi.org/10.4103/jesnt.jesnt_22_20.
35. Hussein ZA, Al-Ahmar SD. IL-10 and IL-18: Key players in liver damage associated with hepatitis A virus infection. Hum Antibodies. 2024; 32(4): 201-11. doi: https://doi.org/10.3233/hab-240039.