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Assessment of Lipid and Blood Parameters among Patients Infected with Chronic Hepatitis C Virus: A Case - Control Study

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Abstract

Hepatitis C virus (HCV) infection is a blood-borne infection associated with high rates of morbidity and mortality, posing a serious global and Saudi Arabian public health concern. Globally, one million new infections occur each year, leading to severe consequences such as chronic inflammatory illness, cirrhosis, end-stage liver failure, and hepatocellular carcinoma. Additionally, HCV infection is linked to altered lipid and blood parameters, which are crucial in chronic hepatitis C (CHC) patients. This study aims to investigate the correlation of lipid and blood parameter irregularities among CHC patients at the Ministry of National Guard Health Affairs-Western Region (MNGHA-WR). In our case-control study, a total of 71 male and female patients diagnosed with CHC infection were enrolled from July 2014 to August 2021. Additionally, 142 sex- and age-unmatched non-HCV individuals were selected from the MNGHA-WR database. Medical records of patients and non-HCV individuals were analyzed to determine variations. Categorical variables were assessed using the Chi-square test, and numeric variables were analyzed using a t-test. A significant P value was considered to be < 0.05.There was a statistically significant decrease in the levels of total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), white blood cells (WBC), red blood cells (RBC), hemoglobin (Hgb), hematocrit (HCT), platelets (PLT), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV), and mean platelet volume (MPV) in CHC patients compared to non-HCV individuals ($P < 0.05$). This significant association persisted even after adjusting for age and gender, except for TC and TG, which showed a statistically insignificant relationship ($P > 0.05$). However, variations in lipid and blood parameters were observed in patients with CHC infection compared to non-HCV individuals. These findings underscore the intricate pathophysiologic relationships between the chronicity of the disease and these Parameters**.**

Keywords: Hepatitis C Virus; Chronic hepatitis C; Viral infection; Lipid Abnormalities; Hematologic Abnormalities; Hepatocellular Carcinoma.

1. Introduction

Hepatitis refers to the inflammation of the liver, which can be caused by toxic, metabolic, pharmacological, immune-mediated liver assaults, or viral infections [1].

Viral hepatitis is an infectious liver condition caused by viruses that actively replicate in the liver [2]. It is a significant public health concern and a leading cause of morbidity and mortality worldwide [3]. HCV is a major cause of chronic hepatitis, first identified in 1989 as non-A, non-B Hepatitis [4].

This virus belongs to the Flaviviridae family and Hepacivirus genus, with a single positive-stranded RNA genome of 9.6 Kb containing a single long open reading frame (ORF). Upon cleavage by host and viral proteases, this ORF encodes a polyprotein of approximately 3000 amino acids, giving rise to viral proteins [5].

In 15-45% of cases, HCV infection triggers both innate and adaptive immune responses that can clear the virus. However, failure to eliminate the virus can lead to persistent infection, often resulting in chronic progressive liver damage [6,7]. Patients with HCV may develop cirrhosis or hepatocellular carcinoma, even in the absence of symptoms for many years [8,9]. According to the World Health Organization (WHO), an estimated 50 million people worldwide are infected with chronic HCV, with 242,000 deaths attributed to HCV-related complications in 2022.

Additionally, in the Eastern Mediterranean Region of the WHO, around 12 million individuals are chronically infected [10]. Since 1990, HCV infection has been considered a reportable illness in Saudi Arabia. Regionally, the highest incidence of HCV cases was found in Alsharqiya, Taif, Jeddah, Makkah, and Riyadh [11, 12]. Additionally, up to 80% of HCV cases in Saudi Arabia go undiagnosed. Interestingly, 15% of HCV cases are identified through mandatory premarital screening. Saudi individuals diagnosed with HCV have a median age of 60 years [13, 14]. According to [15], blood transfusions, multiple

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medication injections, hemodialysis, and the reuse of unsanitary sterilized instruments are the primary reasons for the high prevalence of HCV. The consequences of an HCV infection are more severe and have broader systemic implications compared to other hepatitis virus infections [16].

Chronic HCV infection causes a complex systemic illness that extends beyond the liver, known as HCV extrahepatic manifestations (HCV-EHMs). Predicting the type and progression of these manifestations is challenging, as they have been reported in a significant number of cases. In some large cohort studies, up to 74% of patients experienced varying degrees of HCV-EHMs, ranging from mild to severe [17, 18].

Host lipids are essential for HCV persistence. Viral factors that interact with the host's immunological and metabolic systems influence the course of the disease. The relationship between HCV infection and hypobetalipoproteinemia, as well as the binding of HCV to lipoproteins in plasma and serum, has been studied. Reduced serum triglyceride (TG) levels have been previously reported in patients who tested positive for HCV antibody (anti-HCV). Lipids play a significant role in the HCV life cycle. In a minority of patients, severe triglyceride accumulation in hepatocytes presents as fatty liver [19, 20-24].

Moreover, HCV infection can lead to liver dysfunction and abnormalities in various hematological markers [25]. Although HCV primarily replicates in the liver, evidence suggests that it also replicates in peripheral blood cells leading to abnormal blood counts in patients with HCV infection [26-28].

Additionally, complete blood count (CBC) parameters have provided novel inflammatory biomarkers that are actively being investigated in many liver diseases [29, 30]. Due to persistent chronic inflammation, various hematological abnormalities, such as thrombocytopenia and other platelet indices, have been observed in patients with CHC [31-33]. Understanding the impact of blood and lipid parameters on the human body is essential for managing the disease and its consequences, especially since there is limited research on Saudi CHC patients, particularly in the western region.

Therefore, to investigate the association between specific lipid and blood parameter abnormalities in CHC patients at the Ministry of National Guard Health Affairs - Western Region (MNGHA-WR), we conducted a case-control study involving 71 CHC-infected patients and 142 age- and sex-matched non-HCV individuals.

2. Results

2.1. Demographic characteristics of CHC patients and non- HCV individuals

We studied 71 patients with CHC and 142 non-HCV individuals, as shown in Table 1. It was observed that the age and gender of CHC patients were significantly lower than those of the non-HCV individuals. The mean age of hepatitis C patients was 62.3 ± 13.73 years, while the non-HCV individuals were 70.3 ± 8.15 years ($P < 0.05$). Twenty-seven patients were males, and seventy-eight were non-HCV individuals. Forty-four patients were females, and sixty-four were non-HCV individuals. Consequently, there was a significant dominance of females in the CHC patients (61.97%), while there was a slight dominance of males in the non-HCV individuals (54.93%).

Table 1: Demographic characteristic of CHC patients versus the non- HCV individuals at NGHA - WR (Univariate analysis).

Parameters	**CHC patients (N =71)**	**Non-HCV individuals (N = 142)**	**P-value [2]**
	n (%)[1]	**n (%)**	
Age (years)*	62.3 ± 13.73	70.3 ± 8.15	<.0001
Gender			
Male (%)	27 (38.03)	78 (54.93)	0.02
Female (%)	44 (61.97)	64 (45.07)	

* mean ± SD "Standard deviation
[1] "n" sample size, % percentage
[2] Chi-square test for categorical variables, and t-test numeric variables

2.2. Lipid parameters in CHC patients

According to the study design, the laboratory investigations for CHC patients and non-HCV individuals were compared as shown in Table 2. The mean levels of TG, TC, and HDL were significantly lower among the CHC patients (1.24, 3.98, and 0.89, respectively) compared to the non-HCV individuals (1.37, 4.54, and 1.07, respectively) with a p-value of <0.05.

Table 2: Lipid parameters characteristics of CHC patients and non- HCV individuals at NGHA-WR.

Parameters	**CHC patients (N =71)**	**Non-HCV individuals (N = 142)**	**P-value [1]**
	Mean (range)	**Mean (range)**	
TG Mean (mmol/L)	1.24 (1.01, 1.47)	1.37 (1.27, 1.48)	<.0001
TC Mean (mmol/L)	3.98 (3.11, 4.85)	4.54 (4.33, 4.75)	<.0001
HDL Mean (mmol/L)	0.89 (0.78, 1.01)	1.07 (1.02, 1.11)	<.0001

[1] Chi-square test for categorical variables, and t-test numeric variables

2.3. Blood parameters in CHC patients

Statistical analysis revealed that the average white blood cell (WBC) and red blood cell (RBC) counts were significantly lower ($P < 0.05$) among CHC patients compared to non-HCV individuals (5.69 vs 7.39 and 4.04 vs 4.61, respectively). Furthermore, there was a statistically significant decrease ($P < 0.05$) in the levels of hemoglobin (Hgb) (9.43 vs 13.88), mean corpuscular hemoglobin concentration (MCHC) (26.92 vs 32.39), mean corpuscular hemoglobin (MCH) (23.40 vs 28.43), mean corpuscular volume (MCV) (72.30 vs 86.65), hematocrit (HCT) (31.25 vs 39.01), and mean platelet volume (MPV) (6.85 vs 8.31) among CHC patients compared to non-HCV individuals. Similarly, the platelet count was significantly lower ($P < 0.05$) in CHC patients compared to non-HCV individuals (232.61 vs 257.69) as shown in Table 3.

Table 3: Blood parameters characteristics of CHC patients and non- HCV individuals at NGHA - WR (Univariate analysis)

Parameters	**CHC patients (N =71)**	**Non-HCV individuals (N = 142)**	**P-value [1]**
	Mean(range)	**Mean(range)**	
WBC Mean ($\times 10^9$ /L)	5.69 (4.81, 6.58)	7.49 (6.74, 8.24)	0.02
RBC Mean (10^{12} /L)	4.04(3.15, 4.95)	4.61(4.49, 4.73)	0.03
Hgb Mean (g/dL)	9.43 (8.10, 10.76)	13.88 (12.15, 15.61)	<.0001
Hct Mean (%)	31.25 (27.42, 35.08)	39.01 (37.56, 40.47)	<.0001
PLT Mean ($\times 10^9$ /L)	232.61(210.55, 254.68)	257.69(242.46, 272.93)	0.005
MCHC Mean (g/dL)	26.92 (24.02, 29.83)	32.39 (32.17, 32.63)	<.0001
MCH Mean (Pg)	23.40 (20.81, 25.99)	28.43 (27.99, 28.87)	<.0001
MCV Mean (fl)	72.30 (64.29, 80.31)	86.65 (84.85, 88.46)	<.0001
MPV Mean (fl)	6.85(6.04, 7.66)	8.31(8.08, 8.54)	<.0001

[1] Chi-square test for categorical variables, and t-test numeric variables, fl=femtoliters

2.4. Multivariate analysis findings

The regression analysis shows that significant differences in lipid HDL and blood parameters (WBC, RBC, Hgb, HCT, PLT, MCHC, MCH, MCV, MPV) between CHC patients and non-HCV individuals, as identified in the bivariate analysis, remain significant at $P < 0.05$ after adjusting for age and gender as covariates (Table 4). However, TG and TC levels do not show a significant difference after adjusting for age and gender ($P > 0.05$) as shown in Figures 1 and

Table 4: Regression analysis for lipid and blood parameters comparison of CHC patients and non -HCV individuals at NGHA - WR (adjusted for age, gender)

Parameters	CHC patients vs non -HCV individuals		P-value CHC patients vs non - HCV individuals [1]
	Beta coefficient (β)	Standard error (SE)	
TG Mean	0.18	0.12	0.14
TC Mean	0.69	0.37	0.06
HDL Mean	0.19	0.05	0.001
WBC Mean	1.54	0.66	0.02
RBC Mean	0.76	0.35	0.03
Hgb Mean	5.19	1.41	0.0003
Hct Mean	8.89	1.82	<.0001
PLT Mean	40.04	14.11	0.005
MCHC Mean	6.37	1.10	<.0001
MCH Mean	5.63	1.03	<.0001
MCV Mean	15.78	3.33	<.0001
MPV Mean	1.58	0.35	<.0001

[1] ANCOVA used to estimate differences in covariances across patients with CHC and non -HCV individuals, adjusted for age and gender, and the kruskal wallis test for non-normal numeric variables.

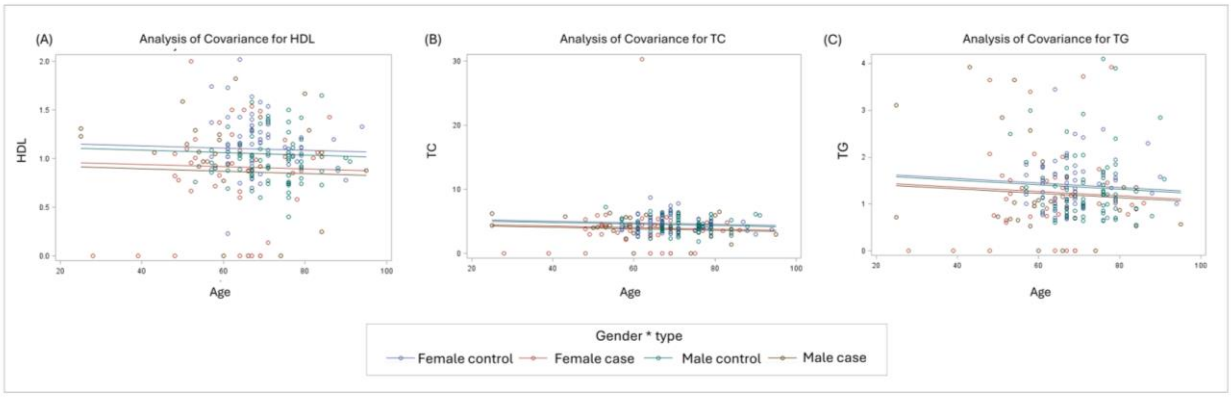

Figure 1: Comparison of Lipid Parameter Values Between CHC Patients and Non-HCV Individuals
The x-axis represents the age of the subjects, while the y-axis represents the lipid parameters. (A) Triglycerides (TG), (B) High-Density Lipoprotein (HDL), and (C) Total Cholesterol (TC) are displayed for both CHC (Chronic Hepatitis C) patients and non-HCV individuals

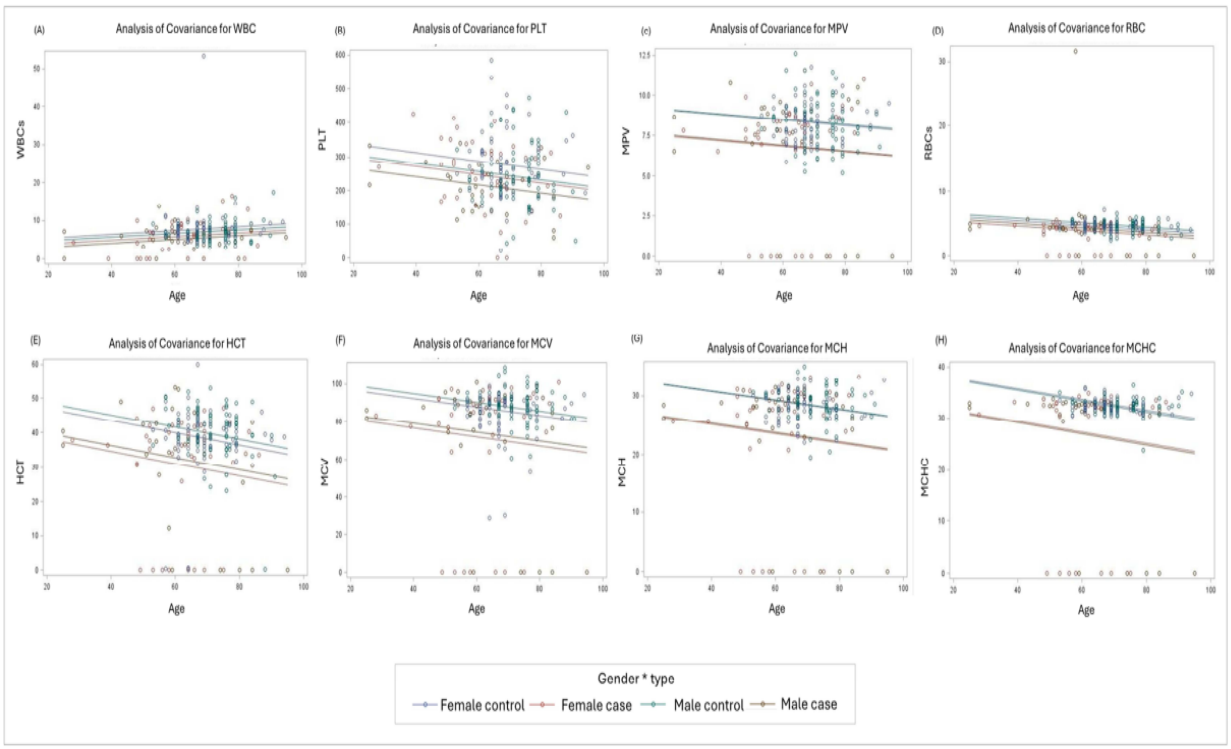

Figure 2: Comparison of Blood Parameter Values Between CHC Patients and Non-HCV Individuals
The x-axis represents the age of the subjects, while the y-axis represents the levels of various blood parameters. The figure displays the following parameters for both CHC (Chronic Hepatitis C) patients and non-HCV individuals: (A) White blood cell (WBC) count, (B) Platelet (PLT) count, (C) Mean platelet volume (MPV), (D) Red blood cell (RBC) count, (E) Hematocrit (HCT), (F) Mean corpuscular volume (MCV), (G) Mean corpuscular hemoglobin (MCH), and (H) Mean corpuscular hemoglobin concentration (MCHC**).**

3. Discussion

Lipids are essential components of biological membranes and serve as free molecules and metabolic regulators that play a crucial role in regulating cellular function and maintaining homeostasis in the body [34]. The liver is a key player in lipid metabolism, participating in both endogenous and exogenous lipid metabolism cycles, as well as lipid transport through the plasma [35]. However, metabolic syndrome (MetS) is a common complication among patients with chronic hepatitis C (CHC) [36]. In a case-control study, we found evidence that CHC infection was associated with lower levels of triglycerides (TG), total cholesterol (TC), and high-density lipoprotein (HDL) in 71 CHC-infected patients. We also observed a significant association ($P < 0.05$) between low HDL levels and disease chronicity. However, the low levels of TG and TC were not statistically significant among CHC patients compared to non-HCV individuals ($P > 0.05$). Previous studies [20, 37] have also reported an association between CHC infection and low TG, TC, and HDL levels. Additionally, a study by [38] demonstrated a lower TG level in HCV-infected individuals, consistent with our findings. Furthermore, our results align with the findings of [39], showing lower percentages of normal TC and HDL levels in CHC patients compared to non-HCV individuals. The TG levels in our study contradicted the results reported by [39]. The study found that the TG normal percentage was equal in patients and non-HCV individuals. In contrast, a study by [37] reported a higher level of HDL among CHC patients compared to non-HCV individuals, which contradicts our findings. There has been speculation about potential links between HCV infection and lipid parameters. All aspects of the HCV life cycle are closely connected to human lipid metabolism, as the virus relies on host cells to spread efficiently. When the virus enters the hepatocyte through lipoprotein cell receptors, it circulates as a lipid-rich particle. Additionally, it has been shown to enhance lipid biosynthesis and inhibit lipid breakdown, leading to a significant accumulation of fats within the cells, known as steatosis, and a marked decrease in blood cholesterol levels, known as hypocholesterolemia [40]. Research using heterologous expression systems has revealed that the HCV core protein interacts with a wide range of cellular proteins and regulates various host cell functions, such as gene transcription, apoptosis inhibition or promotion, cell signaling, and host immune suppression [41,42]. Furthermore, other HCV proteins, including nonstructural 2, nonstructural 4b, and nonstructural 5A, can also impact lipid metabolism by influencing the expression of lipogenic genes [43,44]. Studies have documented the binding of HCV to lipoproteins in plasma and established a connection between HCV infection and hypobetalipoproteinemia, a condition characterized by low levels of plasma lipoproteins [22-24, 45]. Additionally, HCV

infection has been linked to a unique lipid pattern with reduced serum cholesterol and TG levels in samples [46-48]. This dynamic alters lipid metabolism, especially as the disease progresses over time [49, 50]. These intriguing associations between CHC infection and lipid profile might be linked to the results of lipid parameters found in this study.

Prolonged liver illnesses also frequently result in the production of abnormal red blood cells and impact the functioning of membranes, which may have pathophysiologic implications. Many compounds and proteins necessary for the creation of blood are produced and stored by the liver. Furthermore, it supports the preservation of hemostasis [34, 51]. Infection with HCV produces liver dysfunction, which is associated with abnormalities in a variety of hematological markers [25]. Our findings showed a significant decline in the levels of WBC, RBC, PLT, Hgb, MCHC, and MCH among CHC patients compared with non-HCV individuals ($P < 0.05$). These results are in agreement with previous studies [25, 52-57].

The results of our study were contrary to some previous findings that reported high levels of WBC, RBC, Hgb, HCT, MCHC, MCV, and MPV among HCV-infected patients compared to non-HCV individuals. Several studies mentioned a statistically significant relationship ($P < 0.05$) [53, 55, 58-59]. Additionally, [30] observed an increase in MPV levels among CHC patients compared to non-HCV individuals, especially those with HCC. However, in our study, the MPV levels among CHC patients were lower than in non-HCV individuals. Furthermore, [60] analyzed hematological parameters, including total RBC count, Hgb, HCT, MCV, and MCHC levels, which did not show any statistically significant differences between HCV-infected patients and non-HCV individuals. In contrast, our study revealed significantly decreased levels of WBC, RBC, Hgb, HCT, MCHC, MCV, and MPV among CHC patients compared to non-HCV individuals. The hematopoietic system is one of the systems impacted by HCV infection. Therefore, the abnormalities in blood parameters were associated with extrahepatic manifestations, a common side effect of this infection [61, 62]. Previous studies indicate that thrombocytopenia, defined as a PLT level of less than 50,000 per microliter and often associated with viral infections, is a consequence of chronic liver disease. Several pathways have been proposed to explain thrombocytopenia, including: (1) transmission of intravascular coagulopathy [63], (2) virus-induced megakaryocyte mutation impairing thrombocytopoiesis [64], (3) direct interactions between the virus and platelets in the bloodstream leading to phagocytosis, platelet aggregation, release, and thrombocytosis, and (4) formation of an antigen-antibody complex that damages platelets or antiplatelet antibodies targeting platelet-specific antigens [65]. Additionally, mean platelet volume (MPV) is a commonly studied blood count measure in various liver diseases and has been associated with severe liver fibrosis and metabolic syndrome [66].

There are some limitations to the present study. Firstly, the fact that our study is focused on a single-center experience naturally restricts the broad applicability of the results. With only 71 CHC patients in the study population compared to 142 non-HCV individuals, the conclusions may not fully represent the entire hepatitis C community. Secondly, additional parameters are required to validate our findings. Lastly, grouping patients based on specific clinical characteristics could enhance our understanding of the relationship between these parameter irregularities and clinical presentation, as well as the progression and manifestation of the disease.

4. Experimental

4.1. Study design

The present retrospective study was conducted using a case-control study design at King Abdulaziz Medical City, Jeddah (KAMC-J), MNGHA, Saudi Arabia. The Medical Research and Ethics Committee of King Abdullah International Medical Research Center (KAIMRC) approved the study protocol under No. (SP19/498/J).

4.2. Study population

4.2.1. CHC infected patients

A total of 71 patients diagnosed with chronic hepatitis C (CHC) infection were regularly followed at the gastroenterology and infectious disease clinics from July 2014 to August 2021. The case-control study included adult males and females (>18 years of age) who tested positive for anti-HCV serology and had detectable HCV RNA. Inclusion criteria required patients to be treatment-naïve, have complete data, and not have co-infection with human immunodeficiency virus (HIV) or hepatitis B virus (HBV). Exclusion criteria comprised patients with incomplete data, co-infection with HBV or HIV, those who had received prior treatment, and patients outside the MNGHA.

4.2.2. Non-HCV individuals

A total of 142 individuals who were not infected with HCV and were unmatched in terms of sex and age were chosen from the MNGHA database. Subjects who tested positive for hepatitis B surface antigen (HBsAg), anti-HCV, or anti-HIV were excluded. To avoid duplication, a random selection method without replacement was employed to assign each non-HCV individual only once.

4.3. Demographic characteristics and clinical measurements

Based on the hospital's electronic system accessibility, we collected information on sex, age, triglyceride levels (TG < 1.70 mmol/L), total cholesterol (TC ≤ 5.18 mmol/L), high-density lipoprotein-cholesterol (HDL ≥ 1.55 mmol/L), white blood cell count (WBC 4-11×109 /L), red blood cell count (RBC 3.8~5.8×1012 /L), hemoglobin levels (Hgb 11.5~16.5 g/dL), platelet count (PLT 150-450 × 109 /L), mean corpuscular hemoglobin (MCH 27-32 Pg), mean corpuscular hemoglobin concentration (MCHC 32-36 g/dL), hematocrit (HCT 40~54%), mean corpuscular volume (MCV 76-96 FL), and mean platelet volume (MPV 8-12fl).

4.4. Sample size calculation

CHC cases were grouped with a control group consisting of individuals from the source population who do not have the outcome of interest (Hepatitis C infection). We conducted an unmatched case-control study with a case-control ratio of 1:2. Therefore, the minimum sample size required to detect a statistically significant effect is 71 CHC patients and 142 non-HCV individuals.

4.5. Statistical analysis

In univariate analysis, associations between demographics and lipid-blood irregularities characteristics were assessed among CHC patients and non-HCV individuals using the chi-square test for categorical data and t-test for numeric variables. Multivariate analyses, adjusted for age and gender, were conducted to compare differences between CHC patients and non-HCV individuals. Models were evaluated using analysis of covariance based on the nature of the outcome. Assumptions of a linear relationship between the dependent variable and the covariate, as well as homogeneity of regression slopes, were checked, and all models met the assumptions. P values were two-sided, and all confidence intervals were set at 95%. The analyses were performed using SAS statistical software version 9.4 (SAS Institute Inc., Cary, NC). All tests were two-sided, and a P-value < 0.05 was considered statistically significant.

5. Conclusions

Our results indicate variations in lipid and blood parameters among CHC patients compared to non-HCV individuals. In CHC patients, we observed low levels of total cholesterol, triglycerides, high-density lipoprotein, white blood cells, red blood cells, hemoglobin, hematocrit, platelet count, mean corpuscular hemoglobin concentration, mean corpuscular volume, and mean platelet volume. The statistically significant association persists even after adjusting for age and gender, while the total cholesterol and triglycerides show a statistically insignificant relationship. These findings highlight the complex pathophysiologic relationships between HCV infection and these parameters. Further investigation into blood and lipid parameters is warranted to identify at-risk populations, estimate the risk of comorbidities, and assess the efficacy of these parameters as potential biomarkers for predicting disease severity and stage. This is essential for a comprehensive understanding of how hepatitis C infection influences lipid and blood profiles and vice versa.

6. Abbreviations

anti-HCV, HCV antibody; ANCOVA, analysis of covariance; CBC, complete blood count; CHC, chronic hepatitis C; EHMs , extrahepatic manifestation; HCV, hepatitis C virus; HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen; HCC, hepatocellular carcinoma ; HDL, high-density lipoprotein-cholesterol; Hgb, hemoglobin; HCT, hematocrit; HIV, human immunodeficiency virus; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MPV, mean platelet volume; MetS, metabolic syndrome; OFR, open reading frame; PLT, platelet; RBC, red blood cell; TC, total cholesterol; TG, triglyceride; WBC, white blood cell.

7. Conflicts of interest

There are no conflicts to declare.

8. Formatting of funding sources

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9. Institutional Review Board Statement

The study protocol was approved by the Medical Research and Ethics Committee of King Abdullah International Medical Research Center, Jeddah, Saudi Arabia, under No. (SP19/498/J).

10. Author Contributions

Conceptualization, Noof Batook, Dhuha Alsharif and Abeer Alsofyani; Data curation, Noof Batook and Dhuha Alsharif; Funding acquisition, Alaa Karkashan; Supervision, Alaa Karkashan and Basma Abbas; Validation, Noof Batook; Writing – original draft, Noof Batook; Writing – review & editing, Dhuha Alsharif, Alaa Karkashan, Basma Abbas, Abeer Alsofyani and Roba Attar.

11. Data Availability Statement:

The data is not publicly available due to privacy and ethical restrictions.

12. Acknowledgments

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13. References and Bibliography

[1] Mazaheri S, Khazaei M, Moradi A, Raei R. Serum level of Helicobacter pylori antibody in stroke patients. Avicenna J Clin Med. 2020;26(4):206-212. https://doi.org/10.29252/ajcm.26.4.206

[2] Terrault NA, Lok AS, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. Hepatology. 2018;67(4):1560-1599. https://doi.org/10.1002/hep.29800.

[3] Rehermann B, Nascimbeni M. Immunology of hepatitis B virus and hepatitis C virus infection. Nat Rev Immunol. 2005;5(3):215-229. https://doi.org/10.1038/nri1573.

[4] Kuo G, Choo Q, Alter HJ, et al. An assay for circulating antibodies to a major etiologic virus of human non-A, non-B hepatitis. Science. 1989;244(4902):362-364. https://doi.org/10.1126/science.2496467.

[5] Fields BN, Knipe DM, Howley PM. Fields Virology. 5th ed. Wolters Kluwer Health/Lippincott Williams and Wilkins; 2007. https://doi.org/101201/9781003369349-13

[6] Rehermann B. Hepatitis C virus versus innate and adaptive immune responses: a tale of coevolution and coexistence. J Clin Invest. 2009;119(7):1745-1754. https://doi.org/10.1172/jci39133.

[7] Manns MP, McHutchison JG, Gordon SC, et al. Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial. Lancet. 2001;358(9286):958-965. https://doi.org/10.1016/s0140-6736(01)06102-5.

[8] Grattagliano I, Rossi A, Marconi E, Lapi F, Cricelli C. Determinants of HCV-related complications in Italian primary care patients. Liver Int. 2021;41(12):2857-2865. https://doi.org/10.1111/liv.15017 .

[9] Tada T, Toyoda H, Yasuda S, et al. Natural history of liver-related disease in patients with chronic hepatitis C virus infection: An analysis using a Markov chain model. J Med Virol. 2019;91(10):1837-1844. https://doi.org/10.1002/jmv.25533.

[10] World Health Organization: WHO. Hepatitis C. Available at: https://www.who.int/news-room/fact-sheets/detail/hepatitis-

[11] Hepatitis C cases in KSA. January 2024. Available at: https://od.data.gov.sa/Data/en/dataset/hepatitis-c-cases-in-ksa. Accessed [Jan;2024].

[12] Almajid A, Albarbari H, Bazroon A, et al. Epidemiological Perspectives: A Four-Year Insight Into Hepatitis C Surveillance in the Kingdom of Saudi Arabia. Cureus. 2024;16(1). https://doi.org/10.7759%2Fcureus.52646.

[13] Altraif I. Can hepatitis C virus be eliminated by 2030? Saudi Arabia as an example. Saudi Med J. 2018;39(8). https://doi.org/10.15537%2Fsmj.2018.8.22467 .

[14] Almosa FAM, Alnasser AHA, Al-Tawfiq JA. Distribution of hepatitis C virus (HCV) genotypes in a Saudi Arabian hospital during the 2015–2020 period. Le Infezioni in Medicina. 2021;29(3):450. https://doi.org/10.53854%2Fliim-2903-

[15] Hanafiah KM, Groeger J, Flaxman AD, Wiersma S. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. Hepatology. 2013;57(4):1333-1342. https://doi.org/10.1002/hep.26141.

[16] Desbois AC, Cacoub P. Diabetes mellitus, insulin resistance and hepatitis C virus infection: A contemporary review. World J Gastroenterol. 2017;23(9):1697. https://doi.org/10.3748%2Fwjg.v23.i9.1697 .

[17] Cacoub P, Gragnani L, Comarmond C, Zignego A. Extrahepatic Manifestations of Chronic Hepatitis C Virus Infection. Dig Liver Dis. 2014;46:S165–S173. https://doi.org/10.1016/j.dld.2014.10.005.

[18] Cacoub P, Poynard T, Ghillani P, et al. Extrahepatic manifestations of chronic hepatitis C. Arthritis Rheum. Official Journal of the American College of Rheumatology .1999;42(10):2204-2212. https://doi.org/10.1002/15290131(199910)42:10%3C2204::AID-ANR24%3E3.0.CO;2-D .

[19] Valkov I, Ivanova R, Alexiev A, Antonov K, Mateva L. Association of serum lipids with hepatic steatosis, stage of liver fibrosis and viral load in chronic hepatitis C. J Clin Diagn Res. 2017;11(8): OC15. https://doi.org/10.7860%2FJCDR%2F2017%2F28609.10459 .

[20] Dai C, Yeh M, Huang C, et al. Chronic hepatitis C infection is associated with insulin resistance and lipid profiles. J Gastroenterol Hepatol. 2015;30(5):879-884. https://doi.org/10.1111/jgh.12313 .

[21] Negro F. Abnormalities of lipid metabolism in hepatitis C virus infection. Gut. 2010;59(9):1279-1287. https://doi.org/10.1136/gut.2009.192732.

[22] Perlemuter G, Sabile A, Lettéron P, et al. Hepatitis C virus core protein inhibits microsomal triglyceride transfer protein activity and very llow-densitylipoprotein secretion: a model of viral-related steatosis. FASEB J. 2002;16(2):185-194. https://doi.org/10.1096/fj.01-0396com.

[23] Serfaty L, Andréani T, Giral P, et al. Hepatitis C virus induced hypobetalipoproteinemia: a possible mechanismfor steatosis in chronic hepatitis C. J Hepatol. 2001;34(3):428-434. https://doi.org/10.1016/s01688278(00)00036-2 .

[24] Monazahian M, Kippenberger S, Müller A, et al. Binding of human lipoproteins (low, very low, high densitylipoproteins) to recombinant envelope proteins of hepatitis C virus. Med Microbiol Immunol. 2000;188(4):177-184. https://doi.org/10.1007/s004300000032.

[25] Jalil AT, Dilfy SH, Karevskiy A, Najah N. Viral hepatitis in Dhi-Qar province: demographics and hematological characteristics of patients. Int J Pharm Res. 2020;12(01):326. https://doi.org/10.31838/ijpr/2020.12.01.326.

[26] Lerat H, Berby F, Trabaud M, et al. Specific detection of hepatitis C virus minus strand RNA in hematopoietic cells. J Clin Invest. 1996;97(3):845-851. https://doi.org/10.1172/jci118485.

[27] Nagamine T, Ohtuka T, Takehara K, Arai T, Takagi H, Mori M. Thrombocytopenia associated with hepatitis C viral infection. J Hepatol. 1996;24(2):135-140. https://doi.org/10.1016/s0168-8278(96)80021-3.

[28] Pawlotsky J, Bouvier M, Fromont P, et al. Hepatitis C virus infection and autoimmune thrombocytopenic purpura. J Hepatol. 1995;23(6):635-639. https://doi.org/10.1016/0168-8278(95)80027-1.

[29] Bilgin S, Aktas G, Koçak MZ, et al. Association between novel inflammatory markers derived from hemogram indices and metabolic parameters in type 2 diabetic men. Aging Male. 2019;23(5):923-927. https://doi.org/10.1080/13685538.2019.1632283.
[30] Omar MZ, Gouda MH, Elbehisy MM. Mean Platelet Volume and Mean Platelet Volume/Platelet Count Ratio as Diagnostic Markers for Hepatocellular Carcinoma in Chronic Hepatitis C Patients. Afro-Egyptian J Infect Endem Dis. 2018. https://doi.org/10.21608/aeji.2018.8731.
[31] Meng X, Wei G, Chang Q, et al. The platelet-to-lymphocyte ratio, superior to the neutrophil-to-lymphocyte ratio, correlates with hepatitis C virus infection. Int J Infect Dis. 2016;45:72-77. https://doi.org/10.1016/j.ijid.2016.02.025.
[32] Gîrleanu I, Trifan A, Sîngeap AM, Stoica OC, Cojocaru C, Stanciu C. Platelet indices and liver fibrosis evaluation in chronic hepatitis C. Med Surg J. 2016;120:55-61.
[33] Coşkun BDÖ, Dizdar OS, Başpınar O, Ortaköylüoğlu A. Usefulness of the Neutrophil-to-Lymphocyte Ratio and Platelet Morphologic Parameters in Predicting Hepatic Fibrosis in Chronic Hepatitis C Patients. PubMed. 2016;46(4):380-386.
[34] Behera BPA. A cross-sectional observational study of lipid profile of cirrhosis of liver patients in a teaching hospital in North Odisha, India. Int J Adv Med. 2020. https://doi.org/10.18203/2349-3933.ijam20201611.
[35] Mehboob F, Ranjha FA, Masud SH. Changes in serum lipid profile among patients suffering from chronic liver disease. Ann King Edward Med Univ. 2007;13(3):209. https://doi.org/10.21649/akemu.v13i3.113.
[36] Lavie M, Dubuisson J. Interplay between Hepatitis C Virus and Lipid Metabolism during Virus Entry and Assembly. Biochimie. 2017;141:62-69. https://doi.org/10.1016/j.biochi.2017.06.009.
[37] Hsu C, Liu C, Liu C, et al. Metabolic profiles in patients with chronic hepatitis C: a case–control study. Hepatol Int. 2008;2(2):250-257. https://doi.org/10.1007/s12072-008-9064-3.
[38] Jan CF, Chen CJ, Chiu Y, et al. A population-based study investigating the association between metabolic syndrome and hepatitis B/C infection (Keelung Community-Based Integrated Screening Study No. 10). Int J Obes. 2006;30(5):794-799. https://doi.org/10.1038/sj.ijo.0803204.
[39] Yazdansetad S, Nikoo HR, Azimi SM, Mohebbi A, Niazi M, Ajorloo M. Comparison of biomarkers between genotypes 1a and 3a in hepatitis C virus patients with control group. Biomed Res Ther. 2019;6(4):3121-3130. https://doi.org/10.15419/bmrat.v6i4.537.
[40] Elgretli W, Chen T, Kronfli N, Sebastiani G. Hepatitis C virus-lipid interplay: pathogenesis and clinical impact. Biomedicines. 2023;11(2):271. https://doi.org/10.3390%2Fbiomedicines11020271.
[41] Giannini C, Bréchot C. Hepatitis C virus biology. Cell Death Differ. 2003;10(S1):S27-S38. https://doi.org/10.1038/sj.cdd.4401121.
[42] McLauchlan J. Properties of the hepatitis C virus core protein: a structural protein that modulates cellular processes. J Viral Hepat. 2000;7(1):2-14. https://doi.org/10.1046/j.1365-2893.2000.00201.x.
[43] Kim K, Kim KH, Ha E, Park JY, Sakamoto N, Cheong J. Hepatitis C Virus NS5A Protein Increases Hepatic Lipid Accumulation via Induction of Activation and Expression of PPARgamma. FEBS Lett. 2009;583(17):2720-2726. https://doi.org/10.1016/j.febslet.2009.07.034.
[44] Oem J, Jackel-Cram C, Li YP, et al. Activation of sterol regulatory element-binding protein 1c and fatty acid synthase transcription by hepatitis C virus non-structural protein 2. J Gen Virol. 2008;89(5):1225-1230. https://doi.org/10.1099/vir.0.83491-0.
[45] Schonfeld G. The hypobetalipoproteinemias. Annu Rev Nutr. 1995;15(1):23-34. https://doi.org/10.1146/annurev.nu.15.070195.000323.
[46] Marzouk D, Sass J, Bakr I, et al. Metabolic and cardiovascular risk profiles and hepatitis C virus infection in rural Egypt. Gut. 2007;56(8):1105-1110. https://doi.org/10.1136/gut.2006.091983.
[47] Siagris D, Christofidou M, Theocharis G, et al. Serum lipid pattern in chronic hepatitis C: histological and virological correlations. J Viral Hepat. 2005;13(1):56-61. https://doi.org/10.1111/j.1365-2893.2005.00655.x.
[48] Fabris C, Federico E, Soardo G, Falleti E, Pirisi M. Blood lipids of patients with chronic hepatitis: differences related to viral etiology. Clin Chim Acta. 1997;261(2):159-165. https://doi.org/10.1016/s0009-8981(97)06532-7.
[49] Syed GH, Amako Y, Siddiqui A. Hepatitis C virus hijacks host lipid metabolism. Trends Endocrinol Metab. 2010;21(1):33-40. https://doi.org/10.1016/j.tem.2009.07.005.
[50] Felmlee DJ, Hafirassou ML, Lefèvre M, Baumert TF, Schuster C. Hepatitis C virus, cholesterol and lipoproteins—impact for the viral life cycle and pathogenesis of liver disease. Viruses. 2013;5(5):1292-1324. https://doi.org/10.3390/v5051292
[51] Fasola FA, Otegbayo JA, Abjah UMA, Ola SO. Hematological parameters in Nigerians with acute viral hepatitis. Niger J Gastroenterol Hepatol. 2009; 1:27-31.
[52] Dar MS, Gupta S, Gowhar O. Estimation of hematological parameters in patients with Hepatitis B and C. Int Arch Integr Med. 2019;6:76-80.
[53] Karabulut N, Ayyıldız H, Bayrak H, Kalaycı M. Evaluation of red cell distribution width in anti-HCV positive patients. Eur J Pharm Med Res. 2019; 6:161-164.
[54] Abdullah SM. Prevalence of hepatitis B and C virus infection and their co-relation with hematological and hepatic parameters in subjects undergoing premarital screening in the Jazan region, Kingdom of Saudi Arabia. Pak J Med Sci. 2018;34(2):263-267. https://doi.org/10.12669/pjms.342.14278.
[55] Demırcan F, Kılınç F, Gözel N, Şenateş BE, Şenateş E. Hepatit C enfeksiyonunda ortalama trombosit hacminin değerlendirilmesi. Viral Hepatitis Journal. 2014;20(1):11-14. https://doi.org/10.4274/vhd.65365.
[56] Asghar S, Zia MA, Jafri SA, Ahmed I, Amjad MA. Correlative study between biochemical and hematological parameters and hepatitis C prevalence in the premises of Faisalabad. Middle East J Sci Res. 2011;7:538-542.

[57] Alsaran K, Sabry A, Alghareeb AH, Sadoon GA. Effect of hepatitis C virus on hemoglobin and hematocrit levels in Saudi hemodialysis patients. Ren Fail. 2009;31(5):349-354. https://doi.org/10.1080/08860220902835855.
[58] Tsai MS, Lin KH, Lin KT, et al. Predictors for early identification of hepatitis C virus infection. BioMed Res Int. 2015;2015:1-7. https://doi.org/10.1155/2015/429290.
[59] Pürnak T, Ölmez Ş, Torun S, et al. Mean Platelet Volume Is Increased in Chronic Hepatitis C Patients with Advanced Fibrosis. Clin Res Hepatol Gastroenterol. 2013;37(1):41-46. https://doi.org/10.1016/j.clinre.2012.03.035.
[60] Mir SA, Alshehri B. Seroprevalence of hepatitis B and C viral infections in the premarital adult population of Al Majmaah, Saudi Arabia. Malawi Med J. 2021;33(3):221-225. https://doi.org/10.4314/mmj.v33i3.10.
[61] Zignego AL, Craxi A. Extrahepatic manifestations of hepatitis C virus infection. Clin Liver Dis. 2008;12(3):611-636. https://doi.org/10.1016/j.cld.2008.03.012.
[62] Sünbül, M. "HCV Enfeksiyonun epidemiyolojisi. Viral Hepatit 2007, 1." *Baskı. Ed., Tabak F, Balık İ, Tekeli E. İstanbul: Viral Hepatitle Savaşım Derneği* (2007): 208-19.
[63] Kitchens CS. Thrombocytopenia and thrombosis in disseminated intravascular coagulation (DIC). Hematology. 2009;2009(1):240-246. https://doi.org/10.1182/asheducation2009.1.240.
[64] Flaujac C, Boukour S, Cramer-Bordé E. Platelets and viruses: an ambivalent relationship. Cell Mol Life Sci. 2009;67(4):545-556. https://doi.org/10.1007/s00018-009-0209-x.
[65] Zahn A, Jennings NS, Ouwehand WH, Allain J. Hepatitis C Virus Interacts with Human Platelet Glycoprotein VI. J Gen Virol. 2006;87(8):2243-2251. https://doi.org/10.1099/vir.0.81826-0.
[66] Karaman H, Karakükçü Ç, Karaman A, et al. Mean Platelet Volume as a Fibrosis Marker in Patients with Chronic Hepatitis C. Turk J Med Sci. 2013. https://doi.org/10.3906/sag-1204-17.

الملخص العربى

عدوى فيروس التهاب الكبد الوبائي (ج) هي عدوى تنتقل عن طريق الدم وترتبط بارتفاع معدلات الإصابة بالأمراض والوفيات. ولا تزال الاصابة بالفيروس تمثل مشكلة خطيرة للصحة العامة العالمية والمملكة العربية السعودية، حيث تحدث مليون إصابة جديدة كل عام عالمياً. ترتبط الاصابة بالفيروس بحدوث عواقب وخيمة تتراوح من الأمراض الالتهابية المزمنة إلى تليف الكبد، فشل الكبد في المرحلة النهائية، وسرطان الخلايا الكبدية. علاوة على ذلك، فهو يرتبط بتغير معلمات الدهون والدم، والتي يتطلب تحديدها لدى المرضى المصابين بالتهاب الكبد الوبائي المزمن (ج). تهدف هذه الدراسة إلى التحقيق في العلاقة بين التباينات في بعض معلمات الدهون والدم لدى مرضى التهاب الكبد الوبائي المزمن (ج) في الشؤون الصحية بوزارة الحرس الوطني - المنطقة الغربية. في دراستنا للحالات والشواهد، تم تسجيل 71 مريضًا من الذكور والإناث الذين تم تشخيص إصابتهم بعدوى فيروس التهاب الكبد الوبائي (ج) في الفترة الزمنية من يوليو 2014 إلى أغسطس 2021. وفي موازاة ذلك، تم اختيار حوالي 142 فردًا من غير المصابين بفيروس التهاب الكبد الوبائي (ج) غير المتطابقين في الجنس والعمر من قاعدة البيانات الخاصة بالمستشفى. جُمعت السجلات الطبية للمشاركين في الدراسة من الأفراد المصابين بالفيروس والغير مصابين لتحديد التباين. تم تقييم المتغيرات الفئوية باستخدام اختبار مربع كاي للاستقلالية (Chi-square) بالإضافة لاختبار (T- test) للمتغيرات الرقمية. حيث تمثل القيم الأقل من($P < 0.05$) قيم ذو دلالة إحصائية. أظهرت هذه الدراسة انخفاض ذو دلالة إحصائية في اجمالي مستويات الكولسترول، الدهون الثلاثية، البروتين الدهني العالي الكثافة، كريات الدم البيضاء، كريات الدم الحمراء، الهيموجلوبين، حجم الكريات الحمراء المكدسة، الصفائح الدموية، متوسط تركيز الهيموجلوبين الجسيمي، متوسط الهيموجلوبين الجسيمي، متوسط حجم كريات الدم الحمراء، ومتوسط حجم الصفائح الدموية لدى المرضى المصابين بعدوى فيروس الالتهاب الكبدي (ج) المزمن مقارنة بالأفراد الغير مصابين بالفيروس ($P < 0.05$). حيث استمر ظهور الارتباط ذو الدلالة الإحصائية حتى بعد تثبيت العمر والجنس، باستثناء اجمالي مستويات الكوليسترول والدهون الثلاثية، واللتين أظهرتا علاقة غير ذات دلالة إحصائية ($P> 0.05$). ومع ذلك، لوحظ وجود تباين في معلمات الدهون والدم لدى المرضى المصابين بهذه العدوى الفيروسية عند مقارنتهم بالأفراد الغير مصابين. وتسلط هذه النتائج الضوء على العلاقات الفيزيولوجية المرضية المعقدة بين الحالة المزمنة للمرض وهذه المعلمات.