Online Journal of Biological Sciences

Original Research Paper

A Cross-Sectional Study of the Prevalence of Hepatitis C Virus Infection

[1,2]Omar Atrooz, [3]Rehab Thunibat and [4]Ihssan Atrooz

[1]Department of Medical Laboratory Sciences, Faculty of Applied Medical Sciences, Al-Ahliyya Amman University, Amman, Jordan
[2]Department of Biological Sciences, Mutah University, Mutah, Jordan
[3]Department of Central Lab, Al-Karak Health Directorate, Ministry of Health, Al-Karak, Jordan
[4]Department of Internal Medicine, Private Medicinal Clinic, Amman, Jordan

Article history
Received: 03-04-2024
Revised: 09-05-2024
Accepted: 25-05-2024

Corresponding Author:
Omar Atrooz
Department of Medical Laboratory Sciences, Faculty of Applied Medical Sciences, Al-Ahliyya Amman University, Amman, Jordan
Email: omihandd@gmail.com

Abstract: Liver pain is increased by hepatotropic viruses, such as the Hepatitis C Virus (HCV). This illness can progress to cirrhosis and hepatocellular cancer. This study aims to determine the prevalence of hepatitis C in the Southern Jordanian cities (Karak and Tafilah) as well as the correlations between alanine Aminotransferase (ALT), Aspartate aminotransferase (AST), age and gender in hepatitis C patients. Southern Jordanian cities of Karak and Tafilah hosted this cross-sectional study. Enzyme-linked immunosorbent Assay (ELISA), Polymerase Chain Reaction (PCR) and the automated chemical analyzer Cobas were used in this study. ELISA was conducted in two steps. HCV RNA genotype 1 was measured via PCR testing and the study included 100 HCV patients and 20 age-matched healthy controls. 2500 persons over the age of 18 participated in this study. Among the Jordanian participants in the study, HCV was the most common (1.7%). The findings demonstrate how widespread HCV infection was throughout the sample. The majority of affected persons are male and those who fall between the ages of 26 and 50 are most prone to get the ailment. The condition is associated with liver tests that measure ALT and AST. It has been demonstrated that in HCV patients, ALT and total protein levels increased while albumin levels decreased. Gender is negatively correlated with direct bilirubin, total protein and AST. There was a statistically significant difference between marital status and total bilirubin ($p = 0.007$). The findings indicated that there was a positive association with direct bilirubin, total bilirubin, Alkaline Phosphatase (ALP), AST and ALT and a negative correlation with albumin. ALP, ALT, ALB and AST showed positive relationships. The current study indicates that 1.7% of people in Jordan's Tafilah and Karak regions have HCV.

Keywords: Hepatitis C Virus, Liver Functional Tests, Enzyme-Linked Immunosorbent Test, PCR

Introduction

Because the hepatitis C virus affects 71 million individuals worldwide, hepatitis C is regarded as a global health issue (HCV). 399,000 people die from diseases per year (Thrift *et al*., 2017). Liver disease, such as cirrhosis, fibrosis and hepatocellular carcinoma, is the primary cause of morbidity and death from hepatitis C (Axley *et al*., 2018).

The RNA virus HCV possesses traits from multiple genetic variations. These genetic variants are separated into six genotypes based on 67-69% nucleotide sequence homology, according to Borgia *et al*. (2018). Nucleotide sequencing of HCV genotypes produced subgenotype variations of 20-25% (Mumtaz *et al*., 2020). These subgenotypes are given short English letters (e.g., 1a, 2c, 4d, etc.,) after genotyping. In clinical settings, the diagnosis of HCV genotype has a significant predictive value for predicting treatment success. This is particularly true for interferon-based treatments, as mounting data indicates that Direct-Acting Agents (DAA) may be treated with them (Martinez and Franco, 2020). Additionally, in the DAA age, subgenotype identification is probably going to become more significant. However, pan-genotyping approaches can be used to begin therapy

before the confirmation of the HCV genotype in certain circumstances (e.g., when genotyping is unavailable or prohibitively expensive) (Janiak *et al*., 2019). Rohaim *et al*. (2020) state that a reliable and efficient technique for identifying HCV genotype in clinical situations is direct hybridization and target detection of the HCV 5-Untranslated Region (5'UTR).

An estimated 400,000 fatalities globally. Globally, 71 million persons had HCV hepatitis in 2013 (Jefferies *et al*., 2018). Recent international studies show that the incidence of viremia (HCV RNA production) in HCV infection is less than 1% in many developing nations, including the United States (Schwander *et al*., 2022). However, the quality of transmission and incidence estimates differ across countries and regions. Bartenschlager *et al.* (2018); Morad *et al.* (2020); Pradat *et al*. (2018) state that there are higher rates in some Middle Eastern nations (Syria 3.0%), some African countries (Egypt 6.3%, Gabon 7.0%) and some Eastern European countries (Russia 3.3%, Latvia 2.2%). Its high frequency is observed in the Caucasus and Central Asian countries (Uzbekistan 4.3%, Georgia 4.2%), as well as in certain South and East Asian countries (Pakistan 3.8%, Mongolia 6.4%, Taiwan 2.1%). Sharing injectable supplies and medication combinations is currently the most common way that drugs are distributed in the US and other affluent nations. Immunization policies and additional health hazards in areas with greater rates of HCV infection than in wealthy nations.

Globally, there are discernible regional patterns in the frequency of HCV genotypes. Out of all HCV genotypes, genotype 1 is the most prevalent globally (46%), with genotypes 2 and 4 (12% each) and 3 (22%) following (Kazi *et al*., 2021; Sallam *et al*., 2020). Due to significant HCV reservoirs that date back to iatrogenic infections in the 1950s, genotype 4 is most common in the Middle East and North Africa (MENA) region among Egyptians (Wu *et al*., 2021). However, it indicates that several of the region's countries have a high genotype 1 prevalence (Qamar *et al*., 2021).

The most frequent causes of hepatitis C in the US are cirrhosis, hepatocellular cancer and liver transplantation. With hepatitis C, 80% of patient’s experience excruciating discomfort in the absence of symptoms. When symptoms do appear, they can include jaundice, exhaustion, nausea, vomiting and black urine, just like in other forms of hepatitis (Petruzziello, 2018). 75-85% of cases will go unreported if immunization is not received. One common sign of chronic hepatitis C is fatigue. Ten to twenty years following a chronic illness, 10-20% of individuals develop cirrhosis (Boerekamps *et al*., 2018).

According to Kwong *et al*. (2019), the two primary test types are IgG testing for HCV antibodies and nucleic acid amplification tests, which identify HCV RNA (viremia) in the blood. As of right now, there's no IgM test to detect a novel or dangerous infection. Seroconversion to anti-HCV occurs in about 70-75% of severe cases, which might result in viremia and persistent infection (Garvey *et al*., 2021). No IgM test can detect a recent or dangerous infection. Roughly 70-75% of individuals seroconvert to anti-HCV in severe situations, which might result in viremia and chronic illness (Garvey *et al*., 2021). HCV RNA testing should be done after a positive HCV antibody test to identify individuals with persistent HCV infection. The reason for this is that individuals with positive HCV antibodies are unable to differentiate between those who are infected and those who have had long-term therapy in the past but have either recovered or eradicated the virus (Cotter *et al*., 2019).

The study will be investigated to fill in the important knowledge gaps about HCV infection in Jordan. As far as we are aware, this study is the first to look into HCV infection in these areas. We anticipate that the results will refute the notion that Jordan has an exceptionally low prevalence of HCV infection and will emphasize the existence of core groups that actively engage in HCV acquisition and transmission. Further, Treating HCV infection in these primary categories with tailored therapies will be crucial if the WHO is to meet its 2030 targets. Given the high reported viremic rate, there is an immediate need to step up HCV treatment efforts, start using the HCV-TasP method as soon as the infection is identified and connect patients to DAA treatment. Thus, the goals were to determine the prevalence of hepatitis C in southern Jordan's Karak and Tafilah as well as the relationship between ALT, AST, age and gender in HCV patients.

The following sections on methodology results and discussion will examine these goals and offer insights. Finally, a synopsis of the overall results will be given.

Materials and Methods

The research was carried out in 2023. Initially, the study recruited 2500 individuals from the governorates of Karak and Tafilah in south Jordan. According to the size of the population, 100 HCV patients and 20 additional age-matched, healthy (Jordanian and non-Jordanian) individuals were selected. The HCV Patients group was selected at random from comprehensive health centers based on the presence of concomitant medical conditions. Dialysis patients, reviewers of examination work for government appointments, reviewers for the Department of Survey and Health of Expatriates and staff members from hospitals and health institutions who performed routine examinations to guarantee quality and dependability were among the HCV patients in the study. Gender, age groups and urban/rural areas were taken into account. Liver function tests were normal in healthy people and no concomitant diseases were present.

Data Gathering and Population Analysis

In the southern Jordanian regions of Karak and Tafilah, a cross-sectional survey was carried out between April and November of 2023. At the beginning of the study, 2,500 residents of the southern Jordanian governorates of Karak and Tafilah took part.

Population size: 20 age-matched healthy (Jordanian and non-Jordanian) volunteers and one hundred HCV patients. The HCV patient group is chosen by the health unit if they have additional medical conditions. Dialysis patients, government inspectors, expatriate research and ministry of health inspectors, hospital staff, hospitals that routinely inspect the disease and quality and dependability were not included in this study of hepatitis C patients. Age, gender and urban/rural status were used to create the groups. Liver function tests are normal in healthy persons and no concomitant illnesses are present.

Inclusion Criteria

Given that older age is linked to an increased risk for HCV, all patients who were seen on integrated therapy between April and November and who were tested for the virus for the first time were identified. A chronic HCV infection and aging-related processes may be the cause of HCV-associated liver disorders in infected individuals, such as cirrhosis and hepatocellular carcinoma. Includes those (blood donors, barbers, physicians, recent immigrants, etc.,) whose serum Antinuclear Antibodies (ANA) test positive for HCV viremia. Liver function tests are normal in healthy persons and no concomitant illnesses are present.

Exclusion Criteria

Those who declined to have their HIV and HCV tested were under the age of 18, were unable to participate in this study, or both were excluded.

Sample Size Calculation

The Epi-Info tool (centers for Disease Control and prevention, Atlanta, GA) was utilized to determine the sample size. A total of 2413 individuals were identified as participants, with a 95% confidence level. The sample size was raised to 2500 people to improve the research's efficacy. 100 of the samples that were examined came back positive for HCV. The equation number 1 (Eq. 1) were used to determine the sample size:

$$n = \frac{\lfloor DEFF * NP(1-p) \rfloor}{\left[\left(\frac{d2}{Z21-\frac{a}{2}} * (N-1) + p * (1-p)\right)\right]}$$

where:

- *DEFF* (Design Effect) = 1
- *N* (population) = 488800
- *p* (Hypothesized %) = 5% ±5
- *d* (tolerated margin of error) = 0.05; *Z* (level of confidence) =1.96
- α (Alpha) = 0.05
- *n* = 2413 increased to 2500 individual

Data Collection and Population Classification

To ensure data collection accuracy and prevent misunderstandings and biases, the researcher employed structured interview questions during in-person interviews. Demographic details like age, sex, gender, education level and location of residence (rural vs. urban) were requested in the survey. Every patient's medical history, including blood transfusions, surgeries, dental visits, unforeseen vaccines, cupping, jaundice in the family history and duration of hemodialysis, is appropriately documented.

Elisa Analysis

The analysis and determinations of anti-HCV were done by kit protocols (BioTek 4070569) of ELISA technique (ELISA model instrument: ELx 800^{TM}, Roche, Hitachi, Japan).

Specimen Collection and Preparation

Plasma or serum were utilized for this test. The serum or plasma was obtained from the clot or blood cells as soon as possible to avoid hemolysis. The specimen was frozen at $^{-}$20°C or below.

Automated Chemistry Analyzers

Variables and measurement analysis of T. protein, ALB, T.BIL, D.BIL, ALT, AST and ALP tests were done by an automated clinical chemistry analyzer, Cobas C311, Roche, Germany.

DNA Extraction, Target Amplification and PCR Test

All processes including DNA extraction, PCR amplification, sequencing and assembly were done according to the Kits protocols using Cobas® TaqMan® 48 analyzer.

Briefly, the steps of detection of RNA of HCV used whole blood samples by using the Real-Time (RT-PCR) method. Firstly, isolation of HCV-RNA in full automatic instrument (nucleic acid extraction) by magnetic bead method according to the Kit protocols (Nucleic acid isolation system model: Exm 3000 (Zybio), China). Secondly, the reverse transcription and PCR amplification in which HCV-RNA is prepared is reverse transcribed to generate complementary DNA (cDNA) in the RT-PCR reaction system and it is combined with specific primers and probes according to the conserved sequence of genes for PCR amplification as specified in the protocol (Applied Biosystem by Thermo fisher scientific quaint

studio TM, real-time PCR instrument A40425 (96-well, 0.2 mL block), Singapore). Finally, PCR amplification detection by fluorescent PCR instruments (thermo cycler) then the results are automatically saved after the reaction is ended.

Statistical Analysis

Version 26.0 of the Statistical Package for the Social Sciences (SPSS) was used to analyze the data. Mean, standard deviation (mean ± SD) and IQR were used for distributed numerical data. For analytical statistics, The Nonparametric data was analyzed using the Kruskal-Wallis analysis of variance test, the student t-test was used for normally distributed data and the Mann-Whitney U test was used for non-normally distributed data in comparison between groups. Further, the Pearson method was used for correlation and Multiple linear regression analysis was used to identify the relation between liver function tests and PCR results.

The probability of results was indicated as follows: $p>0.05$ was considered non-significant, $p<0.05$ was considered statistically significant and $p<0.001$ was considered highly significant.

Results

Prevalence of HCV Among the Studied Participants

In the current study, 2,500 people who were older than 18 were included. 1500 of them, or 60%, were Jordanians and the remaining 1000, or 40%, were not. Out of the 1500 Jordanians, 25 samples (1.7%) tested positive for HCV. Of the 1000 non-Jordanian participants, 75 (7.5%) obtained positive HCV findings. Consequently, 1.7% of the study's Jordanian participants had HCV. Table 1 shows how the participants were grouped and subgrouped. The following formula was employed to determine prevalence. The prevalence is calculated as the number of cases *100/total population.

Causes of the Prevalence of HCV Among Jordanian Patients

Table 2 revealed that hemodialysis (52%), followed by visits to private dental clinics (12%), was the most frequent source of HCV among patients in Jordan. Other common sources of infection are accidental needle sticks (8%), tattoos and piercings (8%) and acupuncture (8%). The least frequent conditions were blood transfusions (4%) and a family history of jaundice (4%).

Socio-Demographic Characteristics of the Control Group and HCV Patients

Two groups of 120 individuals each made up the study: The group of HCV patients consisted of one hundred patients, both Jordanian and non-Jordanian. The second group consisted of twenty age-matched, healthy Jordanians. The mean age of HCV patients was 37.73±8.909 years, whereas the mean age of controls was 35.6±9.96 years. The bulk of HCV patients (80%) and controls (65%) are reported to be between the ages of 26 and 50. Of HCV patients, 28% were female and 72% were male. Eleven percent of HCV patients lived in Al Tafelah, compared to eighty-nine percent in Al Karak. Most patients (80%) and controls (70%) were married. There was a statistically significant difference ($p = 0.028$) in the two groups' sexual preferences. There was no statistically significant difference ($p>0.05$) between the two groups based on demographic data (Table 3).

Liver Function Tests Among the Studied Groups

Direct bilirubin readings were 0.211±0.091 and 0.087±0.016 mg/dL in HCV patients and controls, respectively. Total bilirubin was measured and found to be 0.596±0.202 mg/dL in HCV patients and 0.364±0.095 mg/dL in controls. There was a statistically significant difference ($p<0.001$). After measurement, total protein levels in HCV patients were 7.88±0.43 g/dL and in control subjects 6.88±0.22 g/dL. Between the two groups, there was a statistically significant difference ($p<0.001$). The ALP levels of HCV patients were determined to be 103.79±26.79 U/L, while the control group's values were 81.85±4.1 U/L. There was a statistically significant difference ($p<0.001$). ALB values in HCV patients were 3.878±0.253 g/dL, lower than 4.24±0.18 g/dL in the control group. AST was greater in HCV patients (25.41±12.72 U/L) than in controls (10.75±1.65 U/L). The ALT of HCV patients was 37.18±12.29 U/L, which was higher than that of controls (11.35±2.34 U/L). This difference was statistically significant ($p<0.001$) when comparing the two groups. ALB levels have been shown to have decreased and total protein and ALT levels to have increased in HCV patients (Table 4).

Table 1: HCV prevalence in the subjects under study

Variable	Total	Jordanian	Non-Jordanian
Total participants	1000 (100%)	2500 (100%)	1500 (100%)
Negative	2400 (96%)	1475 (98.3%)	925 (92.5%)
HCV positive	100 (4%)	25 (1.7%)	75 (7.5%)
HCV p-value	<0.001	<0.001	<0.001

Data expressed as number (frequency). P-value: The difference between the study variables, p non-significant if >0.05, *P significant if <0.05, ** p highly significant if <0.001

Table 2: The current study's explanations for the rise in HCV prevalence among Jordanian patients

Causes	Number of patients (%) (n = 25)
Blood transfusion	1 (4%)
Private dental clinic visits	3 (12%)
Unintentional needle sticks	2 (8%)
Family history of jaundice	1 (4%)
Hemodialysis	13 (52%)
Barbers' visits	1 (4%)
Sharing of infection equipment	0
Tattoos and piercings	2 (8%)
Acupuncture	2 (8%)

Data expressed as number (frequency)

Table 3: Socio-demographic characteristics of the controls and HCV patients

Variable	Parameter	HCV patients (n = 100)	Control (n = 20)	χ^2	p-value
Age	Mean ± SD	37.73 ± 8.909	35.6 ± 9.96	2.950	0.229
	Median	38 (18-62)	36 (18-54)		
	18-25	11 (11%)	5 (25%)		
	26-50	80 (80%)	13 (65%)		
	>50	9 (9%)	2 (10%)		
Gender	Male	72 (72%)	19 (95%)	4.810	0.028*
	Female	28 (28%)	1 (5%)		
Place of residence	Al Karak	89 (89%)	20 (100%)	2.422	0.120
	Al Tafelah	11 (11%)	0 (0%)		
Marital status	Single	20 (20%)	6 (30%)	0.980	0.320
	Married	80 (80%)	14 (70%)		

Data expressed as Mean ± SD, number (frequency). P-value: The difference between the study variables, p non-significant if >0.05, *P significant if <0.05, **p highly significant if <0.001. χ^2: chi-square test. Min: Minimum, Max: Maximum, SD: Standard Deviation

Table 4: Liver function tests among controls and HCV patients

Variable	HCV patients parameter	Control (n = 100)	(n = 20)	Normal range	p-value
D. BIL (mg/dL)	Mean ± SD	0.211±0.091	0.087±0.016	0.0-0.25	<0.001**
	(Min - Max)	(0.1-0.54)	(0.06-0.12)		
T. BIL (mg/dL)	Mean ± SD	0.596±0.202	0.364±0.095	0.0-1.2	<0.001**
	(Min - Max)	(0.27-1.1)	(0.14-0.51)		
T. protein (g/dL)	Mean ± SD	7.88±0.43	6.88±0.22	6-8.3	<0.001**
	(Min - Max)	(7.1-8.7)	(6.5-7.2)		
ALP (U/L)	Mean ± SD	103.79±26.79	81.85±4.1	40-129	<0.001**
	(Min - Max)	(69-170)	(72-88)		
ALB (g/dL)	Mean ± SD	3.878±0.253	4.24±0.18	3.4-5.4	<0.001**
	(Min - Max)	(3.2-4.5)	(4-4.6)		
AST (U/L)	Mean ± SD	25.41±12.72	10.75±1.65	0.0-40	<0.001**
	(Min - Max)	(5-69)	(8-13)		
ALT (U/L)	Mean ± SD	37.18±12.29	11.35±2.34	0.0-41	<0.001**
	(Min - Max)	(18-94)	(8-18)		

Data expressed as Mean ± SD and median. Min: Minimum, Max: Maximum, SD: Standard Deviation. P-value: The difference between the study variables, p non-significant if >0.05, *P significant if <0.05, **p highly significant if <0.001

PCR Analysis of the Two Study Groups

The PCR result was 25281.81±697.95 IU/mL between 23900 and 26100 IU/mL in 11% of HCV patients. In all controls, the PCR result was negative (Table 5).

Age and T. protein levels showed a positive connection (r = 0.226) with a statistically significant difference (p = 0.024). Gender was negatively correlated with T. protein (r = -0.24, p = 0.016), D. BIL (r = -0.245, p = 0.014), ALP (r = -0.2, p = 0.046) and AST (r = -0.251, p = 0.012). T. BIL and marital status had a positive connection (r = 0.269) with a statistically significant difference (p = 0.007). The PCR tests and patient demographics did not significantly correlate (Table 6).

D.BIL exhibited a positive connection with T.BIL (r = 0.405, p<0.001), ALP (r = 0.44, p<0.001), AST (r = 0.43, p<0.001) and ALT (r = 0.35, p<0.001), whereas there was a negative association (r = -0.308, p<0.002) with ALB.ALP showed a negative connection (r = -0.289, p = 0.004) with ALB and a positive correlation (r = 0.306, p = 0.002) with ALT and AST. ALT and AST had a positive connection (r = 0.672, p<0.001) (Table 7).

Table 5: PCR test detection among the studied groups

Variable	Parameter	HCV patients (n = 100)	Control (n = 20)
PCR (IU/mL)	Positive	11 (11%)	0 (0%)
	Negative	89 (89%)	20 (100%)
	Mean ± SD	25281.81±697.95	-
	(Min-Max)	(23900-26100)	-

Data expressed as Mean ± SD, number (frequency). Min: Minimum, Max: Maximum, SD: Standard Deviation

Table 6: Correlation between HCV patients' demographics, liver function tests and PCR test

Variable	Parameter	D. BIL	T. BIL	T. protein	ALP	ALB	AST	ALT	PCR
Age									
	r-value	0.101	0.022	0.226*	-0.028	0.076	0.124	0.029	-0.050
	p-value	0.317	0.827	0.024	0.783	0.452	0.221	0.773	0.885
Gender									
	r-value	-.245*	-0.034	-.240*	-.200*	0.157	-.251*	-0.158	-0.183
	p-value	0.014	0.739	0.016	0.046	0.118	0.012	0.116	0.591
Place of residence									
	r-value	0.179	0.065	0.056	-0.062	-0.033	-0.069	-0.042	-0.040
	p-value	0.074	0.523	0.581	0.540	0.747	0.492	0.680	0.906
Marital status									
	r-value	0.172	0.269**	-0.029	0.020	0.085	0.105	0.063	-0.389
	p-value	0.087	0.007	0.778	0.847	0.399	0.298	0.536	0.237

Data expressed as p-value: The difference between the study variables, p non-significant if >0.05, *P significant if <0.05, **p highly significant if <0.001 and r-value: Pearson correlation

Table 7: Correlation between liver function and PCR tests among HCV patients

Variable	Parameter	D. BIL	T. BIL	ALP	ALB	AST	ALT
D. BIL	r-value	1	0.405**	.440**	-0.308**	0.430**	0.350**
	p-value		0.000	0.000	0.002	0.000	0.000
T. protein							
	r-value	0.183	-0.144	0.180	-0.125	0.181	0.167
	p-value	0.068	0.153	0.073	0.215	0.071	0.098
ALP							
	r-value		-0.009	1	-0.289**	0.306**	0.243*
	p-value		0.932		0.004	0.002	0.015
ALT							
	r-value		0.015		-0.143	0.672**	1
	p-value		0.879		0.156	0.000	
PCR (IU/ml)							
	r-value	-0.347	-0.293	-0.067	0.012	0.030	-0.054
	p-value	0.296	0.382	0.844	0.971	0.931	0.874

Data expressed as p-value: The difference between the study variables, p non-significant if >0.05, *P significant if <0.05, **p highly significant if <0.001 and r-value: Pearson correlation

Discussion

Hepatotropic viruses, such as hepatitis C, cause the liver to become increasingly inflamed and, if left untreated, can lead to cirrhosis and hepatocellular carcinoma. All infected people can recover if treated quickly. Unfortunately, a large number of patients with liver issues present later and remain asymptomatic (Ayoub *et al*., 2023). The World Health Organization (WHO) has unveiled a strategy to completely eradicate hepatitis C by 2030 in light of the financial and health costs associated with chronic infection. Early identification of HCV infection is crucial for the benefit of therapy (Hassanin *et al*., 2021).

The results of the current study show that 1.7% of Jordanian participants in southern Jordan have HCV. The number of HCV patients discovered in the most recent study by Abu-Dayyeh *et al*. (2023) to ascertain the prevalence of HCV among 28,798 visits to Jordan's bio-lab diagnostic laboratories was 5%. This prevalence level is 10 times higher than the expected prevalence of HCV Ab in the general population, which was previously reported by a meta-analysis to be only 0.3% (Chemaitelly *et al*., 2015).

Compared to Egypt and Pakistan, the two MENA countries most affected by HCV infection, the 19 MENA countries now have a chronic infection prevalence of less than or equal to 1%, which is much lower (Ayoub and Abu-Raddad, 2017; 2019). Other studies that also reveal declines in this regard tend to support the trend of reducing HCV infection incidence (Mahmud *et al*., 2022a-b).

According to the current study, hemodialysis (52%), followed by visits to private dental clinics (12%), was the most frequent source of HCV among patients in Jordan. Other common sources of infection are accidental needle sticks (8%), tattoos and piercings (8%) and acupuncture (8%). The least frequent conditions were blood transfusions (4%) and a family history of jaundice (4%).

Invasive dental operations, major surgeries, blood transfusions, pajamas (a traditional medical technique of cupping) and hemodialysis were among the exposures mentioned in a recent Jordanian study that included a sample of 48 individuals with chronic HCV infection (Fuentes *et al*., 2023). This is in line with data from the

Middle East and North Africa (MENA) region, where hemodialysis exposures, blood transfusions, chemotherapy, dental work and medical injections have all been linked to HCV infection (Ayoub *et al*., 2020; Chemaitelly *et al*., 2019). Eighty percent of the HCV patients in this study are between the ages of 26 and 50.

A recent study from Jordan confirmed the results of the current investigation and found that patients 50 years of age and older were the most infected age group (Abu-Dayyeh *et al*., 2023). A recent study found that 28% of HCV patients were female and 72% of patients were male. According to studies by Abu-Dayyeh *et al*. (2023), men were more likely than women to get HCV. This was consistent with their findings. This implies that a significant way of exposure for the research population may be injecting drugs. Male participation in this kind of behavior is significantly higher in the MENA region than female participation (Heijnen *et al*., 2016; Mumtaz *et al*., 2020).

The region most hit is Al Karak (89%) according to the current statistics. According to the study done by Abu-Dayyeh *et al*. (2023), there was a higher prevalence of HCV Ab outside of the governorate of Amman. It is uncertain whether the higher HCV prevalence in the Al-Karak governorate is linked to more frequent HCV healthcare-related exposures, which may indicate that those areas receive less advanced medical care (Abu-Dayyeh *et al*., 2023). Nevertheless, the cause of the greater HCV prevalence in that governorate is still unknown.

For HCV patients, reversal of the AST/ALT ratio is a crucial diagnostic and prognostic tool since it can be identified even in the absence of any other signs of cirrhotic alterations in the liver (Sheth *et al*., 1998). Throughout the past 20 years, a great deal of research has been done on the value and diagnostic potential of the AST/ALT ratio among individuals with CLD due to HCV (Sheth *et al*., 1998). According to Giannini research, the AST/ALT ratio in people with HCV-related CLD is correlated with both the histological phase and clinical assessment; a higher ratio is associated with more liver functional impairment (Giannini *et al*., 2003). Liver biopsy has drawbacks of its own while being the most reliable approach for diagnosing whether a patient develops cirrhosis from chronic hepatitis (Saadeh, 2001). Therefore, by using the AST/ALT ratio, the tedious process can be avoided.

The current study's findings corroborated those of Rahim *et al*. (2019) examination, which showed that in the early stages of the illness with little to no fibrosis, aminotransferase levels were higher. In more advanced stages of the disease, serum bilirubin, GGT, AST and ALP readings were increased, indicating potential liver issues. Except for ALT, these metrics increased with time as the patient's condition worsened (Rahim *et al*., 2019).

These results are in line with those of Hyder *et al*. (2013), who discovered that viral hepatitis is linked to elevated liver markers and cirrhosis and fibrosis symptoms. In contrast, ALT readings in our study are greater than AST levels at the onset of the disease. On the other hand, the results of Illis indicate that AST is higher than ALT (Illis, 1998). On the other hand, when the disease first manifests, ALT values in our investigation are higher than AST levels. However, the findings of Illis (1998) suggest that AST is greater than ALT. 2007 saw (Sulkowski *et al*., 2007) state that the utilization of AST and ALT is more important than biopsy in the early stages of the disease. Our findings suggest that non-invasive biochemical parameters are preferable to invasive biopsy techniques in the early stages of the disease, in line with earlier studies (Sulkowski *et al*., 2007).

Past studies have shown that viral infection can change liver enzyme levels (ALT, AST and ALP), which can be used as a measure of liver damage. When the liver is damaged, these enzymes, which are present in huge quantities there, are released into the bloodstream. These levels of enzymes can be used to test for possible liver damage when there is an HCV infection (Sugimoto *et al*., 2018). An association has been shown, according to data from epidemiological studies, between liver-related diseases and deaths and liver enzyme levels, particularly ALT and AST (Kunutsor *et al*., 2014). Reports state that the liver enzyme (ALT) levels of HCV patients increased (Hajarizadeh *et al*., 2016). A correlation between the progression of the HCV infection and the levels of ALT, AST and ALP was demonstrated by the results of a logistic regression analysis. As a result, these enzymes are important predictors of HCV infection. In our analysis, we found a strong correlation ($r = 0.739$, $p<0.001$) between the ALT and AST readings. Past studies have shown that these associations have not been found in a multitude of investigations (Haydon *et al*., 1998).

The results of the present investigation were in disagreement with those of Bacon (2004), who said that ALT levels in HCV patients are not a reliable measure of the severity of the disease or the necessity for treatment (Bacon, 2004). Evidence supporting the use of the AST profile as a useful, non-invasive marker of the progression of liver disease in clinical practice was presented by Yilmaz *et al*. (2011).

Bone complaints are among the well-known extrahepatic effects of chronic liver disease that elevate ALP. Reduced bone turnover and production are most likely the causes of the greater rate of bone loss associated with chronic liver disease (Abdallah *et al*., 2020).

Conclusion

The results of the investigation showed that the sample had a high frequency and incidence of HCV infection. According to a recent study, the prevalence of HCV is 1.7% in the southern region of Jordan. Hemodialysis accounted for 52% of HCV cases among Jordanian patients, with private dentistry clinic visits following at 12%. The most common sources of infection are accidental needle sticks (8%), tattoos and piercings (8%) and acupuncture (8%). The least frequent conditions were blood transfusions (4%) and a family history of jaundice (4%). Males were the most affected sex group and individuals between the ages of 26 and 50 were frequently infected. The infected population's liver test results showed a positive connection between ALT and AST. It has been shown that among HCV patients, there was a drop in ALB levels and an increase in total protein and ALT levels. These findings seem to refute the notion that HCV infection is extremely rare in Jordan and emphasize the existence of core groups that actively engage in HCV acquisition and transmission.

There are several restrictions on this study. First off, these assays may not have the best sensitivity and specificity, despite the fact that the study's protocols were based on reputable, well-liked and high-quality commercial platforms. Consequently, it is conceivable to obtain test results that are both mistakenly positive and falsely negative. In this inquiry, no request for a new sample for retesting, no use of a second high-quality assay for confirmatory testing and no final confirmation of the results by a reference laboratory were made. These rigorous methods significantly reduce the likelihood of inaccurate results and increase the validity of the study's findings.

Despite these limitations, the study looked at a large testing sample, which made it possible to do a range of analyses and come to a number of epidemiological findings. The study has closed significant knowledge gaps about HCV infection in Jordan.

Acknowledgment

The authors are thankful to all the associated personnel who contributed to this study by any means.

Funding Information

The authors have not received any financial support or funding to report.

Author's Contributions

Omar Atrooz: Supervised the research, designed the research plan, organized the study and prepared, revised and edited the article.

Rehab Thunibat: Participated in all experiments, coordinated the data analysis and contributed to the written of the manuscript.

Ihssan Atrooz: Participated in all experiments, coordinated the data analysis and the statistical analysis and formulated the ideas, research goals and aims.

Ethics

There are no ethical issues related to this study. Each participant gave their informed consent for the study and all data was handled with confidentiality. Random identification numbers were used to identify serum sample tubes and samples were transmitted to the lab without subject information, just a list of identifiers. The Ministry of health ethics committee gave its approval to this study.

References

Abdallah, N. M., Yousry, R., Abdel Hamid, F. F., EI-Rouby, M. N., & Abdel Fattah, S. M. (2020). Hepatitis C Patients with Progress of Disease Severity: Biochemical and Immunological studies. *Journal of Nuclear Technology in Applied Science*, *8*(1), 67–95. https://doi.org/10.21608/jntas.2020.24286.1019

Abu-Dayyeh, I., Chemaitelly, H., Ghunaim, M., Hasan, T., Abdelnour, A., & Abu-Raddad, L. J. (2023). Patterns and trends of hepatitis C virus infection in Jordan: an observational study. *Frontiers in Public Health*, *11*, 1280427. https://doi.org/10.3389/fpubh.2023.1280427

Axley, P., Ahmed, Z., Ravi, S., & Singal, A. K. (2018). Hepatitis C Virus and Hepatocellular Carcinoma: A Narrative Review. *Journal of Clinical and Translational Hepatology*, *6*(2), 1–6. https://doi.org/10.14218/jcth.2017.00067

Ayoub, H. H., & Abu-Raddad, L. J. (2019). Treatment as prevention for hepatitis C virus in Pakistan: mathematical modelling projections. *BMJ Open*, *9*(5), e026600. https://doi.org/10.1136/bmjopen-2018-026600

Ayoub, H. H., Chemaitelly, H., Kouyoumjian, S. P., & Abu-Raddad, L. J. (2020). Characterizing the historical role of parenteral antischistosomal therapy in hepatitis C virus transmission in Egypt. *International Journal of Epidemiology*, *49*(3), 798–809. https://doi.org/10.1093/ije/dyaa052

Ayoub, H. H., Mahmud, S., Chemaitelly, H., & Abu-Raddad, L. J. (2023). Treatment as prevention for hepatitis C virus in the Middle East and North Africa: a modeling study. *Frontiers in Public Health*, *11*, 1187786. https://doi.org/10.3389/fpubh.2023.1187786

Ayoub, H. H., & Abu-Raddad, L. J. (2017). Impact of treatment on hepatitis C virus transmission and incidence in Egypt: A case for treatment as prevention. *Journal of Viral Hepatitis*, *24*(6), 486–495. https://doi.org/10.1111/jvh.12671

Bacon, B. R. (2004). Chronic Hepatitis C and Normal ALT: Considerations for Treatment. *The American Journal of Gastroenterology*, *99*(9), 1706–1707. https://doi.org/10.1111/j.1572-0241.2004.40627.x

Bartenschlager, R., Baumert, T. F., Bukh, J., Houghton, M., Lemon, S. M., Lindenbach, B. D., Lohmann, V., Moradpour, D., Pietschmann, T., Rice, C. M., Thimme, R., & Wakita, T. (2018). Critical challenges and emerging opportunities in hepatitis C virus research in an era of potent antiviral therapy: Considerations for scientists and funding agencies. *Virus Research*, *248*, 53–62. https://doi.org/10.1016/j.virusres.2018.02.016

Boerekamps, A., van den Berk, G. E., Lauw, F. N., Leyten, E. M., van Kasteren, M. E., van Eeden, A., Posthouwer, D., Claassen, M. A., Dofferhoff, A. S., Verhagen, D. W. M., Bierman, W. F., Lettinga, K. D., Kroon, F. P., Delsing, C. E., Groeneveld, P. H., Soetekouw, R., Peters, E. J., Hullegie, S. J., Popping, S., … Rijnders, B. J. (2018). Declining Hepatitis C Virus (HCV) Incidence in Dutch Human Immunodeficiency Virus-Positive Men Who Have Sex with Men After Unrestricted Access to HCV Therapy. *Clinical Infectious Diseases*, *66*(9), 1360–1365. https://doi.org/10.1093/cid/cix1007

Borgia, S. M., Hedskog, C., Parhy, B., Hyland, R. H., Stamm, L. M., Brainard, D. M., Subramanian, M. G., McHutchison, J. G., Mo, H., Svarovskaia, E., & Shafran, S. D. (2018). Identification of a Novel Hepatitis C Virus Genotype from Punjab, India: Expanding Classification of Hepatitis C Virus into 8 Genotypes. *The Journal of Infectious Diseases*, *218*(11), 1722–1729. https://doi.org/10.1093/infdis/jiy401

Chemaitelly, H., Chaabna, K., & Abu-Raddad, L. J. (2015). The Epidemiology of Hepatitis C Virus in the Fertile Crescent: Systematic Review and Meta-Analysis. *PLOS ONE*, *10*(8), e0135281. https://doi.org/10.1371/journal.pone.0135281

Cotter, T. G., Paul, S., Sandıkçı, B., Couri, T., Bodzin, A. S., Little, E. C., Sundaram, V., & Charlton, M. (2019). Increasing Utilization and Excellent Initial Outcomes Following Liver Transplant of Hepatitis C Virus (HCV)-Viremic Donors into HCV-Negative Recipients: Outcomes Following Liver Transplant of HCV-Viremic Donors. *Hepatology*, *69*(6), 2381–2395. https://doi.org/10.1002/hep.30540

Fuentes, A., Abu-Dayyeh, I., de Salazar, A., Khasharmeh, R., Al-Shabatat, F., Jebrin, S., Chueca, N., Hamdan, F. M., Albtoush, Y., Al-Shaer, O. A., Rashid, M. M., AlMohsen, O., Al-Jbour, M., Abdelnour, A., & García, F. (2023). Molecular characterization of patients with chronic hepatitis C virus infection in Jordan: implications on response to direct-acting antiviral therapy. *International Journal of Infectious Diseases*, *135*, 63–66. https://doi.org/10.1016/j.ijid.2023.08.004

Garvey, L. J., Cooke, G. S., Smith, C., Stingone, C., Ghosh, I., Dakshina, S., Jain, L., Waters, L. J., Mahungu, T., Ferro, F., Sood, C., Freeman, C., Phillips, C., Dhairyawan, R., Burholt, R., Sharp, H., Ullah, S., Gilleece, Y., Brown, A., … Bhagani, S. (2021). Decline in Hepatitis C Virus (HCV) Incidence in Men Who Have Sex with Men Living with Human Immunodeficiency Virus: Progress to HCV Microelimination in the United Kingdom? *Clinical Infectious Diseases*, *72*(2), 233–238. https://doi.org/10.1093/cid/ciaa021

Giannini, E., Risso, D., Botta, F., Chiarbonello, B., Fasoli, A., Malfatti, F., Romagnoli, P., Testa, E., Ceppa, P., & Testa, R. (2003). Validity and Clinical Utility of the Aspartate Aminotransferase–Alanine Aminotransferase Ratio in Assessing Disease Severity and Prognosis in Patients with Hepatitis C Virus–Related Chronic Liver Disease. *Archives of Internal Medicine*, *163*(2), 218–224. https://doi.org/10.1001/archinte.163.2.218

Hajarizadeh, B., on behalf of the ATAHC Study Group, Lamoury, F. M., Feld, J. J., Amin, J., Keoshkerian, E., Matthews, G. V., Hellard, M., Dore, G. J., Lloyd, A. R., Grebely, J., & Applegate, T. L. (2016). Alanine aminotransferase, HCV RNA levels and pro-inflammatory and pro-fibrogenic cytokines/chemokines during acute hepatitis C virus infection. *Virology Journal*, *13*(1), 1–10. https://doi.org/10.1186/s12985-016-0482-x

Hassanin, A., Kamel, S., Waked, I., & Fort, M. (2021). Egypt's Ambitious Strategy to Eliminate Hepatitis C Virus: A Case Study. *Global Health: Science and Practice*, *9*(1), 187–200. https://doi.org/10.9745/ghsp-d-20-00234

Haydon, G. H., Jarvis, L. M., Blair, C. S., Simmonds, P., Harrison, D. J., Simpson, K. J., & Hayes, P. C. (1998). Clinical significance of intrahepatic hepatitis C virus levels in patients with chronic HCV infection. *Gut*, *42*(4), 570–575. https://doi.org/10.1136/gut.42.4.570

Heijnen, M., Mumtaz, G. R., & Abu-Raddad, L. J. (2016). Status of HIV and hepatitis C virus infections among prisoners in the Middle East and North Africa: review and synthesis. *Journal of the International AIDS Society*, *19*(1), 20873. https://doi.org/10.7448/ias.19.1.20873

Hyder, M. A., Hasan, M., & Mohieldein, A. H. (2013). Comparative levels of ALT, AST, ALP and GGT in liver-associated diseases. *European Journal of Experimental Biology*, *3*(2), 280–284.

Janiak, M., Perlejewski, K., Grabarczyk, P., Kubicka-Russel, D., Zagordi, O., Berak, H., Osuch, S., Pawełczyk, A., Bukowska-Ośko, I., Płoski, R., Laskus, T., & Caraballo Cortés, K. (2019). Hepatitis C virus (HCV) genotype 1b displays higher genetic variability of hypervariable region 1 (HVR1) than genotype 3. *Scientific Reports*, *9*(1), 12846. https://doi.org/10.1038/s41598-019-49258-y

Jefferies, M., Rauff, B., Rashid, H., Lam, T., & Rafiq, S. (2018). Update on global epidemiology of viral hepatitis and preventive strategies. *World Journal of Clinical Cases*, *6*(13), 589–599. https://doi.org/10.12998/wjcc.v6.i13.589

Kazi, A., Bano, S., Tunio, S. A., Mirjatt, A. N., Khushik, F. A., & Memon, F. S. (2021). Molecular epidemiology and viral load analysis of hepatitis C virus genotypes from Sindh, Pakistan. *Pure and Applied Biology*, *10*(2), 341–347. https://doi.org/10.19045/bspab.2021.100037

Kunutsor, S. K., Apekey, T. A., Seddoh, D., & Walley, J. (2014). Liver enzymes and risk of all-cause mortality in general populations: a systematic review and meta-analysis. *International Journal of Epidemiology*, *43*(1), 187–201. https://doi.org/10.1093/ije/dyt192

Kwong, A. J., Wall, A., Melcher, M., Wang, U., Ahmed, A., Subramanian, A., & Kwo, P. Y. (2019). Liver transplantation for hepatitis C virus (HCV) non-viremic recipients with HCV viremic donors. *American Journal of Transplantation*, *19*(5), 1380–1387. https://doi.org/10.1111/ajt.15162

Illis, L. S. (1998). Harrison's Principles of Internal Medicine 14th Ed. *Spinal Cord*, *36*(9), 665–665. https://doi.org/10.1038/sj.sc.3100671

Mahmud, S., Chemaitelly, H., Alaama, A. S., Hermez, J. G., & Abu-Raddad, L. (2022a). Hepatitis C virus among blood donors and general population in Middle East and North Africa: Meta-analyses and meta-regressions. *World Journal of Meta-Analysis*, *10*(1), 12–24. https://doi.org/10.13105/wjma.v10.i1.12

Mahmud, S., Chemaitelly, H., Alaama, A. S., Hermez, J. G., & Abu-Raddad, L. J. (2022b). Characterizing trends and associations for hepatitis C virus antibody prevalence in the Middle East and North Africa: meta-regression analyses. *Scientific Reports*, *12*(1), 20637. https://doi.org/10.1038/s41598-022-25086-5

Martinez, M. A., & Franco, S. (2020). Therapy Implications of Hepatitis C Virus Genetic Diversity. *Viruses*, *13*(1), 41. https://doi.org/10.3390/v13010041

Morad, W. S., Elsabaawy, M., & Allam, M. H. (2020). Social Awareness and Knowledge of Parenteral Viral Hepatitis (B and C) Among Residences of Menoufia Governorate, Egypt: A Questionnaire-Based Field Study. *American Journal of Infectious Diseases*, *16*(2), 60–72. https://doi.org/10.3844/ajidsp.2020.60.72

Mumtaz, S., Ahmed, J., Gul, A., Tariq, S. A., Siraj, S., & Sarwar, T. (2020). Genetic Diversity of Hepatitis C Virus Genotype 3a Based on Complete Core Protein in Peshawar, Pakistan. *Jundishapur Journal of Microbiology*, *13*(3), e98942. https://doi.org/10.5812/jjm.98942

Petruzziello, A. (2018). Epidemiology of Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) Related Hepatocellular Carcinoma. *The Open Virology Journal*, *12*(1), 26–32. https://doi.org/10.2174/1874357901812010026

Pradat, P., Virlogeux, V., & Trépo, E. (2018). Epidemiology and Elimination of HCV-Related Liver Disease. *Viruses*, *10*(10), 545. https://doi.org/10.3390/v10100545

Qamar, Z., Anwar, F., Ahmad, R., Haq, I., haq, M., Kashif Khan, A. M., Hussain, R., Abdullah, A., Shahzad, Z., Ahmad, I., Munir Malik, M. S., Kamran khan, M., & Khan, J. (2021). Prevalence of Hepatitis C virus and determination of its genotypes in subjects of Tehsil Daggar District Buner, KP, Pakistan. *Clinical Epidemiology and Global Health*, *12*, 100809. https://doi.org/10.1016/j.cegh.2021.100809

Rahim, A., Shafqat, T., Nazli, R., Lutfullah, G., Fatima, S., & Zubair, A. (2019). Noninvasive Parameters and Staging of Liver Fibrosis in Chronic Hepatitis C Patients. *Khyber Medical University Journal*, *11*(1), 26–31. https://doi.org/10.35845/kmuj.2019.18561

Rohaim, M. A., El Naggar, R. F., Abdelsabour, M. A., Mohamed, M. H. A., El-Sabagh, I. M., & Munir, M. (2020). Evolutionary Analysis of Infectious Bronchitis Virus Reveals Marked Genetic Diversity and Recombination Events. *Genes*, *11*(6), 605. https://doi.org/10.3390/genes11060605

Saadeh, S. (2001). The role of liver biopsy in chronic hepatitis C. *Hepatology*, *33*(1), 196–200. https://doi.org/10.1053/jhep.2001.20534

Sallam, M., Batarseh, R., Natsheh, A., Abbadi, J., Al-Fraihat, E., Yaseen, A., Kaddomi, D., Khamees, N., Mahafzah, A., & Şahin, G. Ö. (2020). An update on hepatitis C virus genotype distribution in Jordan: a 12-year retrospective study from a tertiary care teaching hospital in Amman. *BMC Infectious Diseases*, *20*(1), 1–11. https://doi.org/10.1186/s12879-019-4735-3

Schwander, B., Feldstein, J., Sulo, S., Gonzalez, L., ElShishiney, G., & Hassany, M. (2022). Pursuing Elimination of Hepatitis C in Egypt: Cost-Effectiveness and Economic Evaluation of a Country-Wide Program. *Infectious Diseases and Therapy*, *11*(3), 1193–1203. https://doi.org/10.1007/s40121-022-00631-x

Sheth, S. G., Flamm, S. L., Gordon, F. D., & Chopra, S. (1998). AST/ALT Ratio Predicts Cirrhosis in Patients with Chronic Hepatitis C Virus Infection. *American Journal of Gastroenterology*, *93*(1), 44–48. https://doi.org/10.1111/j.1572-0241.1998.044_c.x

Sugimoto, R., Iwasa, M., Hara, N., Tamai, Y., Yoshikawa, K., Ogura, S., Tanaka, H., Eguchi, A., Yamamoto, N., Kobayashi, Y., Hasegawa, H., & Takei, Y. (2018). Changes in liver function and body composition by direct-acting antiviral therapy for hepatitis C virus infection. *Hepatology Research*, *48*(5), 337–344. https://doi.org/10.1111/hepr.12999

Sulkowski, M. S., Mehta, S. H., Torbenson, M. S., Higgins, Y., Brinkley, S. C., de Oca, R. M., Moore, R. D., Afdhal, N. H., & Thomas, D. L. (2007). Rapid fibrosis progression among HIV/hepatitis C virus-co-infected adults. *AIDS*, *21*(16), 2209–2216. https://doi.org/10.1097/qad.0b013e3282f10de9

Thrift, A. P., El-Serag, H. B., & Kanwal, F. (2017). Global epidemiology and burden of HCV infection and HCV-related disease. *Nature Reviews Gastroenterology & Hepatology*, *14*(2), 122–132. https://doi.org/10.1038/nrgastro.2016.176

Wu, G. H.-M., Yang, W.-W., Liu, C.-L., Pwu, R.-F., Chien, R.-N., Lee, P.-C., Chen, S.-C., Chen, D.-S., & Lu, S.-N. (2021). The epidemiological profile of chronic hepatitis C with advanced hepatic fibrosis regarding virus genotype in Taiwan: A nationwide study. *Journal of the Formosan Medical Association*, *120*(7), 1444–1451. https://doi.org/10.1016/j.jfma.2021.01.005

Yilmaz, Y., Yonal, O., Kurt, R., Bayrak, M., Aktas, B., & Ozdogan, O. (2011). Noninvasive assessment of liver fibrosis with the aspartate transaminase to platelet ratio index (APRI): Usefulness in patients with chronic liver disease: APRI in chronic liver disease. *Hepatitis Monthly*, *11*(2), 103. PMID: 22087126