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BLOOD VISCOSITY AND GIT DISORDERS OF HCV PATIENTS

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Abstract: Background: Hepatitis C virus (HCV) infection is a blood-borne viral illness responsible for significant morbidity and mortality all over the world. The current study aims to determine the role of HCV in increasing blood viscosity that is accompanied by attacks and serious heart disorders, in addition to knowing the effect of this infection on irritations and disorders of the digestive system. **Methods**: The practical side included collecting blood samples from 50 HCV infected persons and 50 healthy persons as a control group. Laboratory and clinical tests were carried out at Al-Diwaniyah General Teaching Hospital, where HCV was determined by checking for antibodies using the ELISA test, while blood viscosity was determined by knowing the percentage of red blood cells (hemocrit) as part of the complete blood test. Gastrointestinal tract (GIT) diseases were diagnosed using gastroendoscopy and x-rays, in addition to investigations *Helicobacter pylori* (*H. pylori*). **Result**: ulcers and stomach acidity with colitis together (A,B,D) were in high rates in patients (58%) compared with healthy people (6%) and produced this is a clear statistical difference ($p<0.05$). Moreover, Blood viscosity increased (71.54%) with a rise titer of HCV in patients blood (18.38 logIU/mL) that associated with appearance of strong positive linear correlation ($r= 0.965$, $p= 0.004$). **In conclusion:** HCV leads to serious complications, especially the digestive system and circulation, and the risk of these disorders increases with the increased survival of the virus C in the patient's liver. Therefore, it is necessary to use appropriate treatments, especially effective modern treatments represented by Harvoni.

Keywords: **:** HCV, Blood viscosity, GIT Disorders, ELISA, Hemocrit, Ulcer

Introduction

Hepatitis C virus is a single-stranded RNA virus, which is a member of the family Flaviviridae. As a primarily hepatotropic virus, the main target of infection is hepatocytes, resulting in chronic inflammation in about 80% of infections. Chronic hepatitis C is known to lead to cirrhosis, end stage liver disease, and hepatocellular carcinoma [1,2]. It is, however, less known that chronic HCV infection leads to a series of systemic disorders and diseases that can often leave greater health consequences than the liver disease alone [3]. These disorders are commonly called extrahepatic manifestations of chronic hepatitis C and encompass a wide spectrum of conditions, from a clinically insignificant presence of different autoantibodies to vasculitis, skin disease, kidney damage, lymphoproliferative disorders, diabetes, various neurological and neuropsychiatric changes, and even

increased cardiovascular morbidity and mortality [4,5].The fact that the severity of these disorders does not necessarily correlate with the severity of hepatic disease is of great clinical significance because even in cases of mildly active chronic hepatitis, a considerable disruption of overall health and quality of life can occur [6,7,8]. On the other hand, numerous studies have shown that treatment of chronic HCV infection accomplishes the resolution of extrahepatic disease or greatly increases function of the affected organ and lowers accompanying morbidity and mortality risks [9,10,11]. The current study aims to detect the role of HCV in increasing blood viscosity that is accompanied by attacks and serious heart disorders, in addition to knowing the effect of this infection on irritations and disorders of the gastrointestinal tract. The basis of this work was our observation of these signs in HCV patients in Laboratories and medical care units, at the same time, we did not find enough studies to demonstrate this.

Methods

Study design and sample collection: in this case- control study, 50 blood samples were collected from hepatitis C patients present in the internal consultation at Al-Diwaniyah Teaching Hospital during the period from 2/2/2021 to 10/9/2021. The patients' ages ranged between 5 to 68 years, all patients belonged to the same race. All clinical and laboratory tests were performed in the same hospital.

The following values were adopted in collecting samples from patients:

1. Recording the age and gender of the patient
2. Non smokers
3. Do not use aspirin
4. Do not drink alcoholic beverages
5. Age >5 year
6. Do not suffer from familial hereditary blood diseases
7. Duration and type of treatment for HCV if present

Fifty blood samples were also collected from healthy individuals as a control group, their ages ranged from 5 to 70 years, and the following assessments were adopted in their selection:

1- They were recently examined for HCV and the result of the examination was negative for a virus
2- Non smokers
3- Do not take aspirin or alcohol
4- They do not suffer from genetic blood diseases

HCV identification: Serological tests for anti-hepatitis C were performed after the initial detection of the virus due to the urgent need to screen blood donors and prevent transmission. This was done in the Virology Laboratory of the Digestive Diseases Unit at Al-Diwaniyah Teaching Hospital. Anti-HCV is usually identified using ELISA. Human Anti-Hepatitis C Virus Antibody ELISA Kit (DEIA015) on TECAN analyzer were used in present detection. **Contents of** Kit include

- Microwell plate: 1 x 96 wells
- Conjugate: 2 x 7.5 mL
- Positive control: 1 x 1.0 mL
- Negative control: 1 x 1.0 mL
- Chromogen A: 1 x 8 mL
- Chromogen B: 1 x 8 mL
- Wash Solution(25X): 1 x 80 mL

- Stopping Solution: 1 x 7 mL
- Specimen Diluent: 1 x 20 mL

The current test was carried out according to the manufacturer's instructions and results detected depending on optical density.

Determine blood viscosity: in the current study, blood viscosity was determined based on the hematocrit (HCT) which is the volume fraction of red blood cells, which make up 99.9% of cellular elements and also known by several other names, in other words it is the volume percentage (vol%) of red blood cells (RBC) in the blood as part of a complete blood count. The measurement is based on the number and size of red blood cells. It is usually 40.7%-50.3% for males and 36.1%-44.3% for females.The examination is done automatically using a Ruby device/USA for complete blood count in hematology Lab.

Diagnosis of GIT disorders: clinical examination, X ray and Lab diagnosis were used for determine GIT disorders as following:

1. Diagnosis of peptic ulcer: in this research, blood , stool and breathing tests preform if the patient have peptic ulcer, or another disease (such as indigestion or irritation / irritation of the mucous layer of the stomach) whose symptoms are similar to those of peptic ulcers, in order to look for the presence of *H. pylori*. Blood test procedure depend on detection antibodies against *H. Pylori* in blood by using AimStep H. Pylori kit/AMAZON. The OneStep H. pylori Antigen Rapid Test is an in vitro qualitative immunochromatographic assay for the rapid detection of *H. pylori* antigens in human stool specimen by using Pylori Antigen Rapid Test Kit/ USA. In additional, Urea 13C Breath Test kit is based on secretion of much active urease by gastric H. pylori that can break down urea into ammonia and carbon dioxide (CO2).
2. Endoscopic biopsy: This procedure is done in the hospital or outpatient center throughout taking biopsy from stomach lining so done to visualized ulcer in duodenum and other parts of GIT. Endoscopic test is the most accurate way to detection *H pylori* infection throughout direct examination and culture.
3. Clinical examination and X ray Preformed by clinicians to detect colonic abnormalities and other GIT diseases.
4. Computed tomography (CT): use of CT to evaluate gastrointestinal diseases include CT angiography and multiphase CT angiography of the intestine. Multiphase CT is used primarily to evaluate stable patients who have had upper and lower endoscopy without identifying the source of the disease.

GIT disorders that identified in present HCV patients classified into groups as following:

A: stomach ulcer
B: stomach acidity
C: duodenal ulcer
D:colon irritation/colitis
E: non- GIT disorders

Statistical analysis : Statistical analysis was carried out using the SPSS program, and they were added to the Microsoft Excel 2010 program, where the result less than 0.05 was considered statically significant . Standard divination (SD) and Standard Error (SE) were also determined to know the distribution of the values in relation to the average values.The approximate percentage of gender and gastrointestinal disorders in HCV patients was determined. The Pearson correlation coefficient is used to measure the strength of a linear association between blood viscosity and the rate of virus that presence in the blood, where the value r = 1 means a perfect positive correlation and the value r = -1

means a perfect negative correlation

Results and Discussion

During the period of our study, the current results were based on 50 people infected with hepatitis C virus, whose ages ranged from 5 to 68 years, with an average age of 38.48+8.95 year, and a portion of these patients had received treatment, but they were not cured. The results of pathological analyzes were compared with the results of healthy individuals as a control group (not infected with HCV), their ages ranged from 5 to 70 years, with an average age of 39.77+12.31 as shown in Table 1.

On the other hand, the ongoing investigation showed that both sexes are exposed to the same risk of infection with this virus in close proportions, with no significant differences (P=0.830) appearing, as the infection rate was slightly higher in males 26 (52%) than females 24 (48%) as in Figure 1.

Table (1): compared age mean of studied groups

Age/years	Cases	Control	P value
Age range	**5-68**	**5-70**	
Mean ± SD	**38.48±8.95**	**39.77±12.31**	**0.812 [NS]**
SE	**1.27**	**1.74**	
Total number	**50**	**50**	
SD= Standard Deviation; SE= Standard Error, NS= Non Significant (P>0.05)			

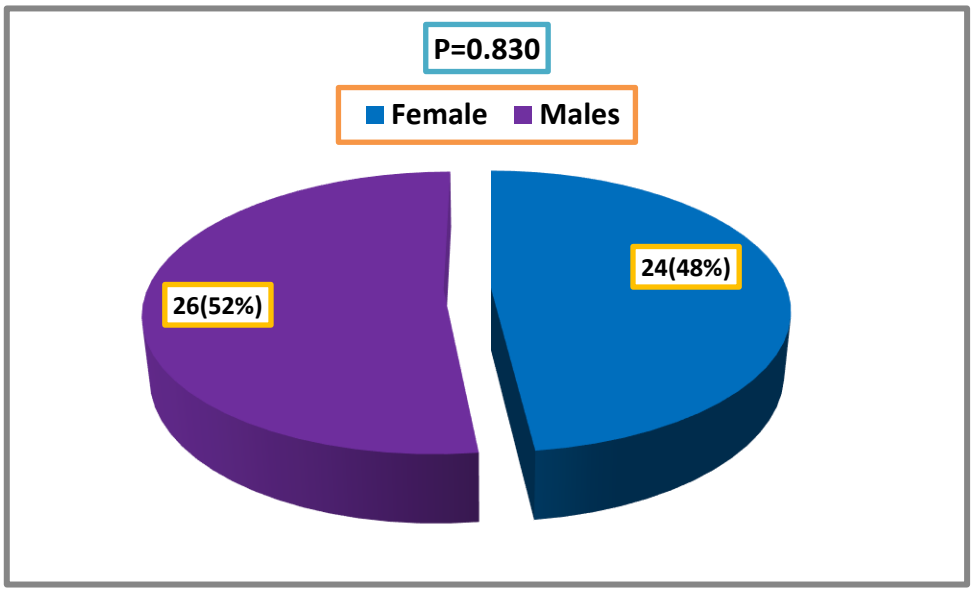

Figure (1): Distribution of HCV patients according to gender

We have divided the digestive disorders associated with hepatitis C infection into five groups, as indicated in the aforementioned practical part. Where the current results in Table 2 showed the incidence of primary disorders such as stomach ulcers (A), stomach acidity (B), intestinal ulcers (C) and colitis (D) in close proportions in patients (8%, 2%, 8% and 14% respectively) and healthy people (6%, 8%, 6% and 12%), while simultaneous digestive diseases such as ulcers and stomach acidity with colon disorders together (A,B,D) were in high rates in patients (58%) compared with healthy people (6%) and produced this is a clear statistical difference ($p<0.05$), as shown in Figure 2. Moreover, most of the healthy individuals in the control group (E) did not suffer from any problems or disorders in the digestive system compared with the HCV infected patients, and this also reflected statistical differences ($P<0.05$).

In any case, there were no significant differences when relying on the χ2 Test and Degree of Freedom to measure the statistical differences of the multiple groups, which is represented by comparing digestive disorders between healthy and patients (DF=6, χ2 =0.967, p=0.987).

Table (2): correlation between HCV and GIT disorders

GIT disorders	HCV Patients	Control	DF	χ2 test	P value
	N(%)	N(%)			
A	4 (8)	3 (6)	6	0.967	0.987 [NS]
B	1 (2)	4 (8)			
B,C	2 (4)	0 (0)			
C	4 (8)	3 (6)			
D	7 (14)	6 (12)			
A,B,D	29 (58)	3 (6)			
E	3 (6)	31 (62)			

χ2 test =chi-squared test, DF= degree of freedom, NS= Non Significant (p>0.05)

To assess the incidence of hepatitis C infection, the immunoassay ELISA available in most hospitals was used, where the results of all patients were positive, and all of them had been suffering from infection for more than a year, and a proportion of these patients had received the available treatment, but did not comply with recovery, as the Mean of antibodies it was higher in patients (18.38+ 3.44logIU/mL) compared with the control group (2.08+0.24logIU/mL) (p=0.0022), as shown in Table No. 2.

The nature of the viscosity of the blood of patients infected with hepatitis C has been observed since the period of our work in the field of hematology, where the viscosity was high and the color of the blood changed to dark red with the difficulty of obtaining the required amount of blood in a short period during the blood draw, and what was mentioned is a sign of individuals infected with hepatitis C compared with healthy individuals. This was confirmed by making a complete picture of the blood, specifically the hemocrit, which was high in patients (**71.54%)** compared to the healthy ones (41.11).

Table (2): evaluation serum levels of anti- HCV and blood viscosity in patients and control

Parameters	HCV Patients	Control	P value
Anti-HCV logIU/mL			
Range	8.11- 22	0.1 – 6.26	
Mean ±SD	18.38± 3.44	2.08±0.24	0.0022*
SE	0.486	0.0339	
Total number	50	50	
Blood viscosity (hematocrit %)			
Range	54.5 - 82	37.2 – 50.01	
Mean ±SD	71.54± 22.01	41.11± 9.77	0.0113*
SE	3.12	1.38	
Total number	50	50	

SD= Standard Deviation; SE= Standard Error, *= Significant (P<0.05)

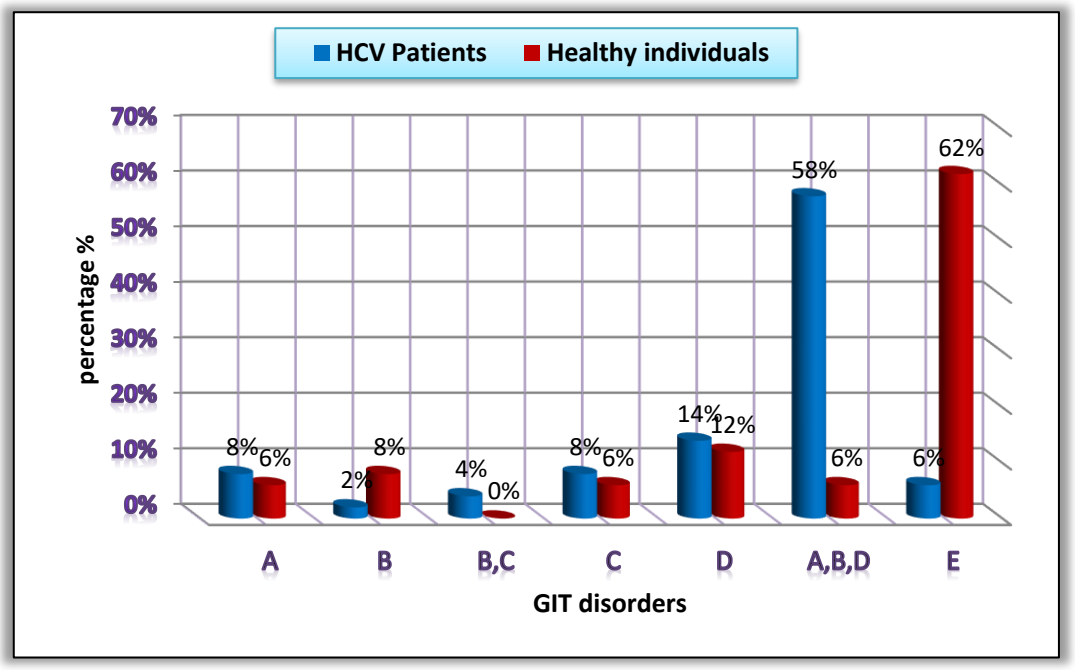

Figure (2): percentage of GIT disorders among patients and control

To find out the effect of liver disorders resulting from infection with the HCV on the blood, the two subjects were linked in a linear relationship with a comparison of the significant differences where the results showed that the increase in the proportion of Anti-HCV is associated with an increase in blood viscosity (r= 0.965, p= 0.004), as shown in Figure 3. On the other hand, figure (4) showed that an increase in the duration of infection with hepatitis coincided with an increase in blood viscosity, and this result culminated in a positive linear relationship between the period of infection and blood viscosity (r=0.786, p= 0.0061).

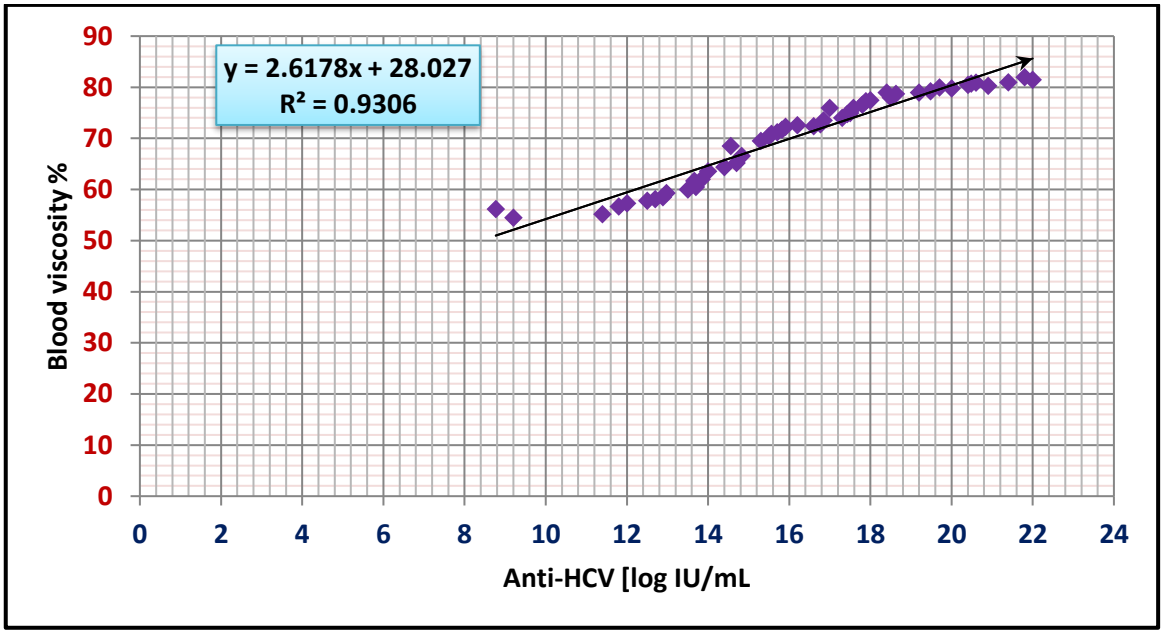

Figure (3): linear correlation between anti-HCV and blood viscosity (r= 0.965, p= 0.004)

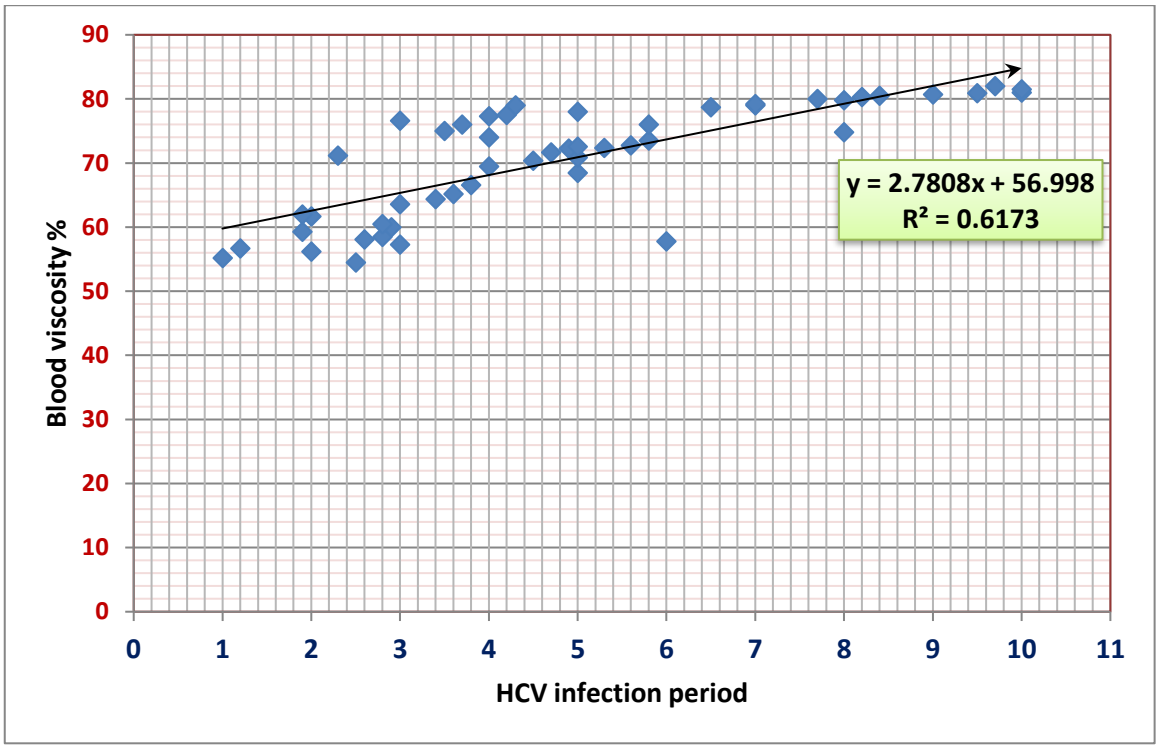

Figure (4): effects of HCV infection period on blood viscosity (r=0.786, p= 0.0061)

Discussion

The blood departing the stomach and intestines passes throughout the liver. The liver processes this blood and breaks down, balances, and creates the nutrients and also metabolizes drugs into forms that are easier to use for the rest of the body or that are nontoxic [12,13]. The liver plays a role in the production of clotting factors, as well as red blood cell production. These important functions of the liver can be disturbed or stopped if the liver is infected with a microbe or any other cause [14]. The most prominent infection that targets the functions of the liver is hepatitis C virus, which causes a defect in the functions mentioned above, which leads to an increase in hemocrit or causes disturbances in blood proteins, which increases its viscosity [15,16]. Perhaps explanation explains the increase in blood viscosity in patients with the HCV in the current study. So blood viscosity maybe enhanced by several direct actions of HCV on the clotting system, platelet aggregation, RBC count and altered anticoagulation [17].

Moreover, Asaduzzaman and his coworkers found that 79.2% and 87.5% male and 92.9% and 92.9% female HCV patients suffer from anemia and blood viscosity due to less hemoglobin content and less RBC count respectively [18]. Other research showed that hepatic iron overload is one of the pathophysiologic features of HCV-associated chronic liver disease, even though the level of hepatic iron content is not extremely high [19]. Anemia with iron overload is a condition of chronic HCV infection that impairs the normal transport of iron in cells. In this condition, red blood cells cannot access iron in the blood, so there are an increase blood viscosity and a decrease of red blood cell production. The red blood cells that are produced are abnormally small (microcytic) and pale (hypochromic) may be also rise blood viscosity[20]. In haematopoietic cells, HCV interferes with peripheral blood maturation and causes thrombocytopenia. Thrombocytopenia also occurs in HCV infection and in liver cirrhosis [21,22,23]. Notably, patients with liver fibrosis or cirrhosis have abnormally low serum thrombopoietin (TPO) levels since TPO is mostly produced by the liver before its release into the bloodstream [24,25]. Thrombopoietin is the main regulator of platelet production, and a feedback loop between circulating TPO and platelet mass has been reported. However, little is

known regarding platelet count (PLT) and TPO levels in apparently healthy people[26] .

On the other hand, our study in line with study of Alsaran *et al* [27]who found that complete picture of the blood, specifically the hemocrit, which was high in HCV patients compared to the healthy individuals but present study not compatible with study of Sabry *et al*.,[28] who studied 99 patients (70 HCV-positive and 29 HCV-negative); the result of this study showed comparable hemoglobin and hematocrit levels as well as the erythropoietin dose between the two groups (HCV-positive and HCV-negative). This deference between our results and those of Sabry *et al.* may be attributed to a difference in the HCV genotyping, or the period of patient follow-up [27].

In the current study, a high percentage of HCV patients appeared to suffer from several digestive disorders at the same time, including peptic ulcers resulting from bacterial infection, in addition to colitis and gastric acidity. Frankly, we did not find a study dealing with these diseases associated with hepatitis C.

The prevalence of peptic ulcer in patients with liver cirrhosis Is increased compared with that in the general population, suggesting that factors such as congestive gastropathy associated with portal hypertension, impaired mucus and bicarbonate secretion and reduced mucosal prostaglandin levels may increase the risk to develop a gastric lesion , stomach acidity and colitis [29,30]. Factors such as a reduced production of bile salts and the impairment of gastric mucosal defense due to The portal hypertensive gastropathy in HCV-associated cirrhotic patients may allow *H pylori* to be more aggressive in the stomach and duodenal bulb than in subjects without cirrhosis[31].Furthermore, results of El-Masry *et al* reflect a remarkable increase in *H. pylori* prevalence with advancing hepatic lesions, and the eradication treatment may prove beneficial in those patients with chronic hepatitis C [32].

In the present study, the *H. pylori* infection was investigated among patients with HCV with chronic active hepatitis and cirrhosis with different staging. The results revealed that this bacterial infection was significantly higher in the patient groups compared with the healthy control group. These results reflect high prevalence of *H. pylori* infection, and this may explain the frequent occurrence of gastro-duodenal ulcer in cirrhotic patients [33]. Furthermore, Ponzetto *et al.* proposed that *H. pylori* is implicated in the pathogenesis and progression of cirrhosis, particularly in HCV-infected individuals, and the involvement of *Helicobacter* spp in hepatocellular carcinoma seems highly possible [34]. In the end, it must be mentioned that the current study is the first study according to our knowledge that dealt with the effect of hepatitis C on peptic ulcers, colitis and gastric acidity. Therefore, we did not cover the pathological relationship accurately.

Conclusion

The current study showed that hepatitis C has a role in increasing blood viscosity, which increases with time also, most HCV patients suffer from several digestive disorders such as peptic ulcers and stomach acidity at the same time. We have done this work according to our observation of these pathological signs in patients with the hepatitis C, but we did not find sufficient studies to explain this. Therefore, it is important to find research in this regard, in addition to the necessity of treating HCV patients using the new treatment known as Harvoni.

Abbreviations	
Carbon dioxide	**CO2**
Degree of Freedom	**DF**
enzyme-linked immunosorbent assay	**ELISA**

Gastrointestinal tract	**GIT**
Helicobacter pylori	***H. pylori***
Hematocrit	**HCT**
Hepatitis C antibody	**Anti-HCV**
Hepatitis C virus	**HCV**
Platelet count	**PLT**
Red blood cells	**RBC**
Standard divination	**SD**
Standard Error	**SE**
The United States of America	**USA**
Thrombopoietin	**TPO**
X^2 test	**chi-squared test**

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