Significance of serum leptin and adiponectin levels in Egyptian patients with chronic hepatitis C virus associated hepatic steatosis and fibrosis

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Abstract

AIM: To study serum levels of leptin and adiponectin in patients with chronic hepatitis C virus infection genotype-4 (HCV-4) related steatosis and fibrosis.

METHODS: We prospectively studied 45 untreated men with chronic HCV-4, with proven steatosis (group I, 30 patients), and fibrosis (group II, 15 patients), on liver biopsy. In addition, 15 healthy men (group III), matched for age, and body mass index were included. However, we excluded another five patients with steatohepatitis, and six patients with cirrhosis. We measured total serum leptin and adiponectin levels, as potential predictors for liver steatosis and fibrosis. Also, a correlation between these adipokines and various clinical and laboratory data were evaluated. All subjects were selected from Tropical and Internal medicine departments, Menoufiya University Hospital, Menoufiya, Egypt, during the period from February 2010 to August 2011.

RESULTS: In group I, severity of hepatic steatosis was mild, moderate, and severe, in 19 patients (63.5%), 8 patients (26.5%), and 3 patients (10%), respectively. In contrast, in group II, hepatic fibrosis was found to be in stage 1, 2, and 3, in 6 patients (40%), in 6 patients (40%), and in 3 patients (20%), respectively. On comparing group I with group II, there was a significant decrease in serum adiponectin levels (131.4 ± 7.91 pg/mL vs 436 ± 9.75 pg/mL, P < 0.001), while there was no significant difference between both groups regarding serum leptin levels (34.69 ± 7.69 ng/mL vs 35.17 ± 1.06 ng/mL, P > 0.05). However, in the same group, when compared with group III, there was a significant increase in serum leptin levels (34.69 ± 7.69 ng/mL vs 10.69 ± 0.84 ng/mL, P < 0.001), while there was a significant decrease in serum adiponectin levels (131.4 ± 7.91 pg/mL vs 342.4 ± 44.48 pg/mL, P < 0.001). In contrast, in group II, when compared with group III, there was a significant increase in serum leptin and adiponectin levels (35.17 ± 1.06 ng/mL vs 10.69 ± 0.84 ng/mL, P < 0.001, and 436 ± 9.75 pg/mL vs 342.4 ± 44.48 pg/mL, P < 0.05, respectively), while there was no significant difference between both groups regarding serum creatinine (0.83 ± 0.34 vs 0.89 ± 0.24, P > 0.05). On the other hand, serum leptin was not correlated with serum adiponectin in group I, and in group II (r = 0.09, P > 0.05, and r = -0.1, P > 0.05, respectively). However, serum adiponectin was significantly negatively correlated with serum aspartate transaminase in group I, but no correlation detected in group II (r = -0.39, P > 0.05, and r = -0.03, P > 0.05).

CONCLUSION: In male patients with chronic HCV-4, serum adiponectin levels are elevated in hepatic fibro-
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Korah TE et al. Adipokines in hepatic steatosis and fibrosis

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Key words: Leptin; Adiponectin; Hepatitis C virus; Hepatic steatosis; Hepatic fibrosis

INTRODUCTION

Leptin and adiponectin are the main metabolic products of adipose tissue. The former is expressed also in the stomach, placenta and mammary gland, while the latter is also secreted by hepatocytes[1,2].

Currently, there is an increasing interest in the role of these adipokines in the development of hepatic steatosis, and fibrosis, particularly in patients with nonalcoholic fatty liver disease (NAFLD) and chronic hepatitis C virus (HCV) infection[3].

Chronic HCV genotype-4 (HCV-4) is known to be endemic in Egypt, Central Africa and in the Middle East[4]. However, several recent studies carried out in Europe have indicated changes in genotype distribution and have underlined the increasing prevalence of HCV-4[5,6].

There are controversial data about the relationship between serum leptin levels and HCV-related steatosis[7,8].

The role of leptin in hepatic fibrosis is also less clear[9]. Moreover, the levels of adiponectin in patients with different stages of liver diseases, particularly in those with NAFLD and chronic HCV (especially genotype 4) infection, have been partly unraveled[10,11].

Therefore, the aim of this study was to measure serum leptin and adiponectin levels, as potential predictors of liver steatosis and fibrosis, for use in clinical practice, in patients with chronic HCV-4 infection, associated steatosis and fibrosis. Moreover, a correlation between these adipokines and different clinical and laboratory data were evaluated.

MATERIALS AND METHODS

Patients and study design

A total of 45 (30 with hepatic steatosis, and 15 with hepatic fibrosis) untreated Egyptian male patients with chronic HCV-4, who had undergone liver biopsy, were prospectively included in this study. We excluded another five patients with steatohepatitis, and six patients with cirrhosis, on liver biopsy. Patients were selected from Tropical and Internal medicine departments, Menoufiya University Hospital, Egypt, during the period from February 2010 to August 2011.

In addition, a control group comprised 15 healthy males matched for age and body mass index (BMI), from the same hospital. They were considered healthy on the basis of history, physical examination and laboratory tests. None received any medication and had normal liver enzymes and no clinical, laboratory or imaging evidence of liver disease.

We excluded all female patients, those with chronic HCV non-genotype 4, steatohepatitis or cirrhosis on liver biopsy, other causes of chronic liver disease (hepatitis B virus infection, alcoholism, Wilson’s disease, haemochromatosis, and autoimmune hepatitis), seropositivity for anti-human immunodeficiency virus, evidence of cirrhosis or hepatocellular carcinoma, decompensated liver disease (evidence of ascites, variceal bleeding, or hepatic encephalopathy), history of heart failure, diabetes mellitus, thyroid diseases, abnormal renal function, obesity (i.e., BMI ≥ 30), previous treatment with metformin, a thiazolidinedione, or interferon-based antiviral therapy, and use of drugs known to induce liver steatosis (corticosteroids, amiodarone, tamoxifen, valproic acid) within the last 6 mo.

Chronic HCV was defined as a positive serological test for HCV by at least a fourth-generation enzyme-linked immunosorbent assay (ELISA), positive HCV RNA results by polymerase chain reaction assay and compatible liver biopsy[12].

Clinical and laboratory data

A complete medical history was taken and physical examination carried out in all patients and controls. BMI was calculated according to the following equation: BMI = weight (in kilograms)/height² (in meters). Overweight was defined as a BMI of 25-29.9 kg/m², and obesity was defined as a BMI ≥ 30 kg/m²[13].

Laboratory investigations included: liver function tests (serum aspartate transaminase (AST), alanine transaminase (ALT), prothrombin activity, serum proteins and albumin, total serum bilirubin and alkaline phosphatase (ALP)) kidney function tests (serum urea and creatinine), total serum leptin and adiponectin levels.

Sample collection and assay

After gaining the consent of all subjects studied, 10 mL of venous blood was withdrawn from all subjects after fasting for at least 10 h. 1.8 mL whole blood was added to 0.2 mL sodium citrate, then centrifuged at 4000 g for 5 min, then plasma was used for measuring prothrombin concentration using Fibrinometer II instrument of Behring, Germany Using Sysmex K-21, Japan.

7 mL of venous blood was transferred slowly into a plain tube, allowed to clot, and then centrifuged for ten minutes. The clear supernatant was separated in several aliquots, kept frozen at -20 °C, until analysis of the fol-
lowing: kinetic determination of ALT and AST[13], serum total bilirubin by a timed endpoint Diazo method[14], serum albumin, using a method of enhanced specificity of bromcresol purple for albumin[15], serum ALP activity by a kinetic method using a 2-amino-2-methyl-1-propa-nol buffer[16], serum total protein by using the modified method of Biuret reaction[17], colorimetric kinetic determination of serum creatinine, and colorimetric determination of serum urea[18].

**Leptin and adiponectin assay**

Serum leptin levels were determined by a solid phase ELISA based on the sandwich principle. The microlitre wells were coated with a monoclonal antibody directed towards a unique antigenic site on the leptin molecule. An aliquot of patient sample containing endogenous leptin was incubated in the coated well with a specific rabbit anti-leptin antibody. A sandwich complex was formed. After incubation the unbound material was washed off and anti-rabbit peroxidase conjugate was added for detection of bound leptin, the substrate solution was added and the intensity of color obtained was proportional to the concentration of leptin in the patient sample. (BioSource Europe S.A. 8 B-1400 Nivelles Belgium)[19]. For leptin, the intra-assay coefficient of variation (CV) was 6.91%, while inter-assay CV was 8.66%.

Regarding serum adiponectin levels, they were estimated by Human Adiponectin ELISA kits. This assay employed an antibody specific for human adiponectin coated on a 96-well plate. Standards, samples and biotinylated anti-human adiponectin were pipetted into the wells. Then, adiponectin was captured by the antibody immobilized to the wells and by the biotinylated adiponectin-specific detection antibody. After washing away unbound biotinylated antibody, horse radish peroxidase-conjugated streptavidin was pipetted into the wells. The wells were washed again. Following this second wash step, tetramethylbenzidine substrate solution was added to the wells, resulting in color development proportional to the amount of adiponectin bound. The Stop Solution changed the color from blue to yellow, and the intensity of the color was measured at 450 nm (FIN-00790 Helsinki, Finland)[20]. For adiponectin, the intra-assay CV was > 10%, while inter-assay CV was < 12%.

The study was approved by the Ethical Committee of our hospital. All patients and control subjects gave their verbal informed consent, and consented to the use of clinical data and serum for research purposes.

**Liver histological assessment**

The degree of hepatic fibrosis was assessed according to the modified Knodell scoring system[21]. Steatosis was identified and graded according to the histopathological criteria described by Burnt et al[22]. Based on the percentage of hepatocytes containing fat droplets, steatosis was graded as mild (< 33% of hepatocytes affected), moderate (33%-66% of hepatocytes affected) and severe (> 66% of hepatocytes affected)[23].

**Statistical analysis**

Results were collected, tabulated and statistically analyzed using an IBM personal computer and statistical package SPSS version 16 (SPSS Inc. Chicago, Illinois, United States). Student’s t test was used for comparison between two groups having quantitative variables. Analysis of variance (F) test was used for comparison among three groups having quantitative variables. Pearson correlation (r) was used to detect association between quantitative variables. χ² test to compare the qualitative data between different groups. A P-value of < 0.05 was considered statistically significant.

**RESULTS**

In group I, severity of hepatic steatosis was mild, moderate, and severe, in 19 patients (63.5%), 8 patients (26.5%), and 3 patients (10%), respectively. In contrast, in group II, hepatic fibrosis was found to be in stage 1, 2, and 3, in 6 patients (40%), in 6 patients (40%), and in 3 patients (20%), respectively.

Table 1 shows the clinical and laboratory data of patients and controls studied. There was no significant difference between all groups studied regarding age and BMI (P > 0.05). In group I, when compared with group II, there was a significant increase in serum AST, prothrombin activity (PT), and albumin (P < 0.001), while, there was a significant decrease in serum total bilirubin, and serum adiponectin (P < 0.001, for each). There was no significant difference, between both groups regarding serum ALT, proteins, ALP, blood urea, serum creatinine, and leptin levels (P > 0.05). In contrast, for group I, when compared with group III, there was a significant increase in serum AST, ALT, total bilirubin, ALP, blood urea, and serum leptin levels (P < 0.001, 0.001, 0.001, 0.001, 0.001, 0.005, 0.001, respectively), while, there was a significant decrease in serum PT, proteins, and serum adiponectin (P < 0.001, for each). There was no significant difference, between both groups regarding serum albumin, and serum creatinine levels (P > 0.05). Finally, in group II, when compared with group III, there was a significant increase in serum AST, ALT, total bilirubin, ALP, blood urea, serum leptin and adiponectin levels (P < 0.001, 0.001, 0.001, 0.001, 0.001, 0.005, 0.001, 0.005, respectively), while, there was a significant decrease in serum PT, proteins, and albumin (P < 0.001, for each). There was no significant difference, between both groups regarding serum creatinine (P > 0.05).

Table 2 shows the correlation between serum leptin and other parameters in the patients studied. In group I, there was a significant negative correlation between serum leptin levels, and serum AST, ALT, albumin, ALP, and creatinine (r = -0.78, -0.39, -0.37, -0.70, -0.38, and P < 0.001, 0.05, 0.05, 0.001, 0.001, 0.05, respectively). However, there was a significant positive correlation with BMI, as well as serum total bilirubin (r = 0.43, 0.64, and P < 0.05, P < 0.001, respectively). There was no significant correlation detected with age, PT, serum

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proteins, blood urea, and serum adiponectin \((r = -0.24, 0.11, -0.28, -0.25, 0.09, \text{and } P > 0.05 \text{ for each})\). In group II, there was a significant negative correlation between serum leptin levels, and age, serum AST, albumin, and ALP \((r = -0.77, -0.99, -0.80, \text{and } -0.95, \text{and } P < 0.001 \text{ for each})\). However, there was a significant positive correlation with BMI, PT, serum total bilirubin, blood urea, and serum creatinine \((r = 0.94, 0.93, 0.98, 0.95, 0.97, \text{and } P < 0.001 \text{ for each})\). There was no significant correlation detected with ALT, serum AST, PT, total bilirubin, ALP, blood urea, and serum creatinine \((r = -0.45, 0.03, -0.46, 0.09, 0.41, -0.39, -0.35, \text{and } P > 0.05 \text{ for each})\).

Table 3 shows the correlation between serum adiponectin and other parameters in the patients studied. In group I, there was a significant negative correlation between serum adiponectin levels, and AST \((r = -0.39, \text{and } P < 0.05)\). However, there was no significant correlation with all other parameters studied \((P > 0.05, \text{for each})\). In group II, there was a significant negative correlation between serum adiponectin levels, and age \((r = -0.55, \text{and } P < 0.05)\). However, there was a significant positive correlation with serum ALT, proteins, and albumin \((r = 0.91, 0.95, 0.68 \text{ and } P < 0.001 \text{ for each})\). There was no significant correlation detected with BMI, serum AST, PT, total bilirubin, ALP, blood urea, and serum creatinine \((r = -0.45, 0.03, -0.46, 0.09, 0.41, -0.39, -0.35, \text{and } P > 0.05 \text{ for each})\).

### DISCUSSION

The behavior of leptin concentrations in the course of liver disease due to HCV infection is still under investigation\textsuperscript{[24-28]}. The relationship between leptin and hepatic fibrosis is controversial. Studies in vitro have clearly demonstrated a role in profibrogenic responses within the liver\textsuperscript{[24,25]}\textsuperscript{[27-28]}. However, human studies describing the role of leptin in fibrosis are less convincing\textsuperscript{[26-28]}. We found that serum leptin levels were significantly associated with fibrosis in patients with chronic HCV-4 infection. This is in agreement with many previous studies\textsuperscript{[23,29,30]}\textsuperscript{[27-28]}. In contrast, several other studies have shown

| Table 1  Clinical and laboratory data of patients studied and controls (mean ± SD) |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Parameter                        | Group I \((n = 30)\) | Group II \((n = 15)\) | Group III \((n = 15)\) | \(F\) test | \(P\) value |
| Age (yr)                         | 39.87 ± 6.1     | 38.20 ± 6.09    | 39.40 ± 4.56    | 0.52   | \(P > 0.05\) NS |
| BMI (kg/m\(^2\))                 | 29.33 ± 1.92    | 28.20 ± 3.05    | 27.73 ± 1.62    | 1.71   | \(P > 0.05\) NS |
| ALT (U/L)                        | 42.40 ± 23.03   | 39.00 ± 8.7     | 27.00 ± 5.35    | 32.63  | \(P1 < 0.001\) |
| Total bilirubin (mg/dL)          | 1.30 ± 0.92     | 1.90 ± 0.97     | 0.53 ± 0.35     | 20.85  | \(P1 < 0.001\) |
| ALP (U/L)                        | 7.21 ± 3.99     | 4.30 ± 1.08     | 2.4 ± 0.82      | 24.97  | \(P1 < 0.05\) |
| Creatinine (mg/dL)               | 1.10 ± 0.36     | 0.83 ± 0.34     | 0.89 ± 0.24     | 3.77   | \(P1 < 0.05\) |
| Leptin (mg/mL)                   | 34.69 ± 7.69    | 35.17 ± 1.06    | 10.69 ± 0.84    | 107.28 | \(P1 < 0.05\) |
| Adiponectin (pg/mL)              | 131.40 ± 7.91   | 436.00 ± 9.75   | 342.40 ± 44.48  | 374.77 | \(P1 < 0.001\) |

\[1\] Significant. Group I: Patients with hepatic steatosis; Group II: Patients with hepatic fibrosis; Group III: Controls. \(P1\): Comparison between group I and group II; \(P2\): Comparison between group I and group III; \(P3\): Comparison between group II and group III. NS: Non significant; BMI: Body mass index; AST: Aspartate transaminase; ALT: Alanine transaminase; PT: Prothrombin activity; ALP: Alkaline phosphatase.
no association between serum leptin and fibrosis in HCV infection\[^{31-33}\]. The reason for this discrepancy is not clear. It is possible that leptin levels intrahepatically, rather than in the serum, are more important determinants of hepatic fibrosis\[^{40}\].

Meanwhile, we found that serum leptin was increased in patients with steatosis. In line with our work, patients with NAFLD\[^{8,26}\] and alcoholic liver disease have increased levels of circulating leptin in their bodies\[^{34}\].

In the present study, we observed that serum leptin levels correlated with BMI in our overweight HCV-4 patients. This is in accordance with Myers RP, study\[^{9}\].

Hepatic steatosis is defined as excessive lipid accumulation within the hepatocyte cytoplasm. The prevalence of steatosis among different HCV genotypes is quite variable\[^{8,26}\].

In the current study, hepatic steatosis was detected in about half of our patients with chronic HCV-4 associated steatosis, with predominance of mild steatosis in 63.5\% of them. These findings are in accordance with other, similar, studies conducted by El-Zayadi et al\[^{8,26}\], and Tsiochatzis et al\[^{35}\]. The mechanisms underlying the development of parenchymal steatosis in HCV infection are not precisely known\[^{36}\].

Regarding serum adiponectin, we found that it was significantly elevated in patients with HCV-4 associated hepatic fibrosis versus controls. This coincides with other studies\[^{40,41,42}\].

In contrast, the results of our study indicate that serum adiponectin was decreased with the presence of steatosis in patients with chronic HCV-4 infection. This is in accordance with other studies conducted in patients with HCV-4\[^{38}\] and HCV of different genotypes\[^{43}\]. However, Tiftikci et al\[^{43}\], found an increase in serum adiponectin levels in patients (about 57\% were females) with HCV (mostly with genotype 1). Also, Kara et al\[^{44}\], found that serum adiponectin levels in HCV genotype 1 were similar to healthy control subjects. This difference might be due to the effect of gender and different HCV genotypes. In addition, circulating adiponectin concentrations may also be affected by renal clearance, as adiponectin levels are elevated in states characterized

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Table 2. Correlation between serum leptin and other parameters in patients studied

| Parameter          | Group I (n = 30) |         | Group II (n = 15) |         |
|--------------------|-----------------|---------|------------------|---------|
| Age (yr)           | -0.24           | > 0.05 NS | -0.77            | < 0.001¹ |
| BMI (kg/m²)        | 0.43            | < 0.05⁴ | 0.94             | < 0.001¹ |
| AST (U/L)          | -0.78           | < 0.001¹ | -0.99            | < 0.001¹ |
| ALT (U/L)          | -0.39           | < 0.05⁴ | -0.51            | > 0.05 NS |
| PT (%)             | 0.11            | > 0.05 NS | 0.93             | < 0.001¹ |
| Protein (gm/dL)    | -0.28           | > 0.05 NS | -0.39            | > 0.05 NS |
| Albumin (gm/dL)    | -0.37           | < 0.05⁴ | -0.80            | < 0.001¹ |
| Total bilirubin (mg/dL) | 0.64       | < 0.001¹ | 0.98             | < 0.001¹ |
| ALP (U/L)          | -0.70           | < 0.001¹ | -0.95            | < 0.001¹ |
| Urea (mg/dL)       | -0.25           | > 0.05 NS | 0.95             | < 0.001¹ |
| Creatinine (mg/dL) | -0.38           | < 0.05⁴ | 0.97             | < 0.001¹ |
| Adiponectin (pg/mL)| 0.09            | > 0.05 NS | -0.10            | > 0.05 NS |

¹Significant. Group I: Patients with hepatic steatosis; Group II: Patients with hepatic fibrosis. NS: Non significant; BMI: Body mass index; AST: Aspartate transaminase; ALT: Alanine aminotransferase; PT: Prothrombin activity; ALP: Alkaline phosphatase.

Table 3. Correlation between serum adiponectin and other parameters in patients studied

| Parameter          | Group I (n = 30) |         | Group II (n = 15) |         |
|--------------------|-----------------|---------|------------------|---------|
| Age (yr)           | -0.09           | > 0.05 NS | -0.55            | < 0.05⁴ |
| BMI (kg/m²)        | -0.24           | > 0.05 NS | -0.45            | > 0.05 NS |
| AST (U/L)          | -0.39           | < 0.05⁴ | 0.03             | > 0.05 NS |
| ALT (U/L)          | -0.15           | > 0.05 NS | 0.91             | < 0.001¹ |
| PT (%)             | -0.35           | > 0.05 NS | -0.46            | > 0.05 NS |
| Protein (gm/dL)    | -0.09           | > 0.05 NS | 0.95             | < 0.001¹ |
| Albumin (gm/dL)    | -0.17           | > 0.05 NS | 0.68             | < 0.001¹ |
| TBilirubin (mg/dL) | -0.16           | > 0.05 NS | 0.09             | > 0.05 NS |
| ALP (U/L)          | 0.04            | > 0.05 NS | 0.41             | > 0.05 NS |
| Urea (mg/dL)       | -0.08           | > 0.05 NS | -0.39            | > 0.05 NS |
| Creatinine (mg/dL) | -0.10           | > 0.05 NS | -0.35            | > 0.05 NS |

¹Significant. Group I: Patients with hepatic steatosis; Group II: Patients with hepatic fibrosis. NS: Non significant; BMI: Body mass index; AST: Aspartate transaminase; ALT: Alanine aminotransferase; PT: Prothrombin activity; ALP: Alkaline phosphatase.
by impaired renal function, such as macroalbuminuria. We include only male patients in our study for two reasons: firstly, it is known that serum leptin and adiponectin levels are higher in females than males; secondly, to avoid the confirmed negative role of menopause on steatosis, and the potential benefit of hormone replacement therapy on hepatic fibrosis in HCV patients.

In conclusion, serum leptin levels were elevated in male patients with both HCV-4 related hepatic steatosis and fibrosis, so it has a poor predictive value for either alone. In contrast, serum adiponectin levels were elevated in those patients with hepatic fibrosis, but decreased in hepatic steatosis, therefore, hypoadiponectinemia is a good predictor of hepatic steatosis in those patients.

Identification of individuals with hepatic fibrosis in chronic HCV-4 may be important for a number of reasons. Firstly, it can decrease the need for liver biopsy in those patients. Secondly, pharmacological treatments are currently being evaluated in NAFLD, but if successful agents are found it will be important to have identified a target population that can potentially be treated. Finally, once fibrosis is identified it may increase the imperative for patients to implement major lifestyle changes and clinicians to monitor the response to intervention.

On the other hand, serum adiponectin can be considered as a non-invasive marker for hepatic steatosis, and might decrease the need for liver biopsy in patients with chronic HCV-4 infection. Also, therapy to increase circulating adiponectin concentration, such as overweight reduction or thiazolidinediones, might represent a novel strategy to improve steatosis in those patients.

Limitations of the present study include the small sample size studied, which consisted of Egyptian male patients with chronic HCV-4, and thus, applicability to other populations requires further work and, the lack of data related to serum HCV load, which may not significantly impact the results. Indeed, HCV quantity is not an independent predictor of pathology. Finally, we measured total serum leptin levels (which is composed of free and protein-bound components) and total serum adiponectin levels (which is composed of three forms); so, we cannot exclude the beneficial role(s) for measurement of these specific components for each one.

COMMENTS

Background
Leptin and adiponectin are the main metabolic products of adipose tissue. Recently, there is an increasing interest in the role of these adipokines in the development of hepatic steatosis and fibrosis, particularly in patients with nonalcoholic fatty liver disease (NAFLD) and chronic hepatitis C virus (HCV) infection. Chronic HCV genotype-4 (HCV-4) is known to be endemic in Egypt, Central Africa, Middle East, and recently, increasing in Europe. The role of leptin in hepatic steatosis and fibrosis is not clear. Moreover, the levels of adiponectin in patients with different stages of liver diseases, particularly in those with NAFLD and chronic HCV (especially genotype-4) infection, has been partly unraveled. Hence, the aim of this study was to measure serum leptin and adiponectin levels, as potential predictors of liver steatosis and fibrosis, for use in clinical practice.

Research frontiers
Liver biopsy is still the standard method for evaluation of liver steatosis and fibrosis. However, it is an invasive procedure and may carry some complications. So, authors tried to discover a simple blood test to measure a substance that can address liver steatosis and fibrosis.

Innovations and breakthroughs
Many noninvasive methods for the evaluation of liver fibrosis and steatosis, in patients with HCV-4, have been proposed, but none are easy nor simple methods. The present study shows that estimation of serum adiponectin in patients may potentially be used for identification of hepatic steatosis and fibrosis.

Applications
Diagnosis of hepatic fibrosis in chronic HCV-4 is important because it can decrease the need for liver biopsy. Also, pharmacological treatments are currently being evaluated in NAFLD. Furthermore, once fibrosis is identified it may increase the imperative for patients to implement major lifestyle changes. In contrast, serum adiponectin can be considered as a non-invasive marker for hepatic steatosis, and might decrease the need for liver biopsy in patients with chronic HCV-4 infection. Also, therapy to increase circulating adiponectin concentration, such as overweight reduction or thiazolidinediones, might represent a novel strategy to improve steatosis in those patients.

Terminology
Serum leptin and adiponectin are produced mainly by adipose tissue. However, recently, it was found that they may have an important role in NAFLD and HCV.

Peer review
This study focuses on the potential use of serum adiponectin in identification of liver steatosis and fibrosis in people with HCV-4. Although this study is primary, but avoiding liver biopsy through estimation of these substances in the serum is promising. So, this study may be interesting for the readers, particularly those with HCV.

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