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# Is dietary glycemic load associated with liver fibrosis in hepatitis C?

Juliana Paula Bruch[1,2], Bruna Cherubini Alves[1,2], Laura Alencastro de Azevedo[1,] Mário Reis Álvares-da-Silva[1,3,4] and Valesca Dall'Alba[1,2,5,6]

[1]Post Graduate Program: Ciências em Gastroenterologia e Hepatologia. School of Medicine. Universidade Federal do Rio Grande do Sul (UFRGS). [2]Centre for Studies in Food and Nutrition (CESAN). Hospital de Clínicas de Porto Alegre, UFRGS. [3]Department of Internal Medicine. School of Medicine, UFRGS. [4]Gastroenterology Division. Hospital de Clínicas de Porto Alegre, UFRGS. [5]Department of Nutrition. School of Medicine, UFRGS. [6]Nutrition Division. Hospital de Clínicas de Porto Alegre, UFRGS. Porto Alegre, Brazil

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Correspondence: Juliana Paula Bruch. Post Graduate Program: Ciências em Gastroenterologia e Hepatologia. School of Medicine. Universidade Federal do Rio Grande do Sul (UFRGS). Ramiro Barcelos 2400. Santana, Porto Alegre, RS, Brazil. Zip code: 90035-003

e-mail: julianabruch@gmail.com

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## ABSTRACT

**Introduction:** Occidental diet and metabolic profile seems to increase hepatic fibrosis (HF) in patients with chronic hepatitis C virus (HCV) infection, but there is scarce information about the diet components and their role in this setting.

**Objectives:** This study aims to evaluate the dietary intake, metabolic profile, presence of metabolic syndrome (MetS) and cardiovascular risk in patients with chronic HCV infection according to the presence of fibrosis.

**Methods:** Cross-sectional study which 58 patients with HCV infection without active antiviral therapy and non-cirrhotic were assessed. All patients were subjected to clinical, laboratorial and dietary evaluation, and classified according to the METAVIR score. Patients were divided as the presence of hepatic fibrosis.

**Results:** In this sample, fifty-five percent of patients were females, the average age was 51.6 ± 9.7 years, and 79.3% were carriers of HCV genotype 1. Patients with HF presented higher energy, and fat intake as well as higher glycemic load of meals in comparison to those without HF. Patients with HF presented higher systolic and diastolic arterial pressure and higher levels of insulin.

**Conclusions:** In conclusion, patients with HF had higher total daily energy and total fat intakes, and worse metabolic profile, characterized by a higher insulin resistance and blood pressure.

**Key words:** Diet. Glycemic load. Liver fibrosis. Chronic hepatitis C. Nutrition.



**RESUMEN**

**Introducción:** en pacientes infectados crónicamente por el virus de la hepatitis C (VHC), la dieta occidental y el perfil metabólico parecen aumentar la fibrosis hepática (FH), sin embargo existe poca información sobre los componentes de la dieta y su papel en este contexto.

**Objetivos:** evaluar la ingesta dietética, el perfil metabólico, la presencia de síndrome metabólico (SAT) y el riesgo cardiovascular en pacientes con VHC crónico según la presencia de fibrosis.

**Métodos:** estudio transversal en el que se evaluaron 58 pacientes con VHC sin terapia antiviral activa ni cirrótica. Todos los pacientes fueron sometidos a evaluación clínica, de laboratorio y dietética, y fueron clasificados según la puntuación METAVIR. Los pacientes se dividieron según la presencia de FH.

**Resultados:** en esta muestra el 55% de los pacientes eran mujeres, con edad promedio de 51,6 ± 9,7 años, siendo el 79,3% portadores del genotipo 1 del VHC. Los alimentos de los pacientes con FH presentaron una mayor proporción de energía y grasa, así como mayor carga glucémica en

comparación con las personas sin FH. Los pacientes con circunferencia de la cintura presentaron mayor presión arterial sistólica y diastólica y mayores niveles de insulina.

**Conclusión:** en conclusión, los pacientes con FH presentaron un consumo mayor de energía y grasas diario total, y peor perfil metabólico, caracterizado por mayor resistencia a la insulina y presión arterial.

**Palabras clave:** Dieta. Carga glicémica. Fibrosis hepática. Hepatitis C crónica. Nutrición.



**INTRODUCTION**

The hepatitis C virus infection (HCV) is a serious global public health problem, with a high social and economic impact, since chronic HCV infection is closely related to liver fibrosis, cirrhosis and also to the risk of hepatocellular carcinoma. Furthermore, HCV has notable metabolic consequences, with glycemic and lipid disturbances and may be associated to cardiovascular risk (1,2).

The hepatic fibrosis (HF) is characterized by the accumulation of scar tissue in response to persistent chronic hepatic injury. A number of factors can influence HCV fibrosis progression such as: age over 40 years old, male gender, hepatic steatosis, insulin resistance (IR), immunosuppression, and necroinflammatory activity, among others (3). Moreover, even with the new potent direct antiviral drugs, a weight greater than 75kg and advanced fibrosis continue to be negative factors for a sustained virological response (3).

Metabolic syndrome (MetS), that includes glucose abnormalities, central obesity, dyslipidemia and hypertension, is a common disorder resulting from diabetes and obesity epidemic worldwide. There is a close relationship between HCV infection and MetS, and individual components of MetS are independent predictors of mortality in patients with chronic liver disease, including those infected with HCV (4).

The adoption of a healthier lifestyle, with regular physical activity, diets with normal fat content, and maximum of 10% of saturated fats, seems to improve the metabolic profile, and even prevent hepatic steatosis and non-alcoholic steatohepatitis (5). Beyond that, diet components such as carbohydrates, lipids, polyunsaturated fatty acids, and also alcohol consumption were described as independent factors of liver damage (6).

There is scarce information about the role of the diet profile on HF in chronic HCV infected patients. Therefore, this study aimed to evaluate dietary intake, metabolic profile, presence of MetS and cardiovascular risk in these patients in accordance with the presence of fibrosis.

## MATERIALS AND METHODS

This cross-sectional study was conducted in adult patients (more than 18 years-old), chronically infected by HCV, genotypes 1, 2 or 3, all of them attending the Gastroenterology Division's outpatient clinic at Hospital de Clínicas de Porto Alegre (HCPA), Brazil, from October 2013 to July 2014. The study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human patients were approved by the HCPA Research Ethics Committee, number 13-0281. Written informed consent was obtained from all patients.

HCV infection was confirmed by anti-HCV ELISA 3 and by the detection of viral RNA through real-time polymerase chain reaction (HCV RNA PCR). A liver biopsy was performed in every patient up to one year before inclusion in the study. Only specimens with more than 10 portal spaces were considered. The samples were analyzed by the same experienced pathologist, without the knowledge of individual details of each case. The samples were classified accordingly to the METAVIR score: F0 = absence of fibrosis; F1 = portal fibrosis without septum; F2 = portal fibrosis with rare septum; F3 = numerous septum without cirrhosis; and F4 = cirrhosis (7). Patients with alcohol intake (over 10 g of ethanol/day) (8), cirrhosis, hepatocellular carcinoma or other malignant tumors, as well as those coinfected with HIV or hepatitis B virus, transplant recipients, pregnant women and those undergoing any active antiviral were not included. Patients were separated into two groups according to METAVIR score: Group absence of fibrosis (score = F0) and Group HF (scores F1 to F3).



### Dietary assessment

The patient's usual diet was assessed by 3-day-diet-record (two non-consecutive weekdays and one-weekend day). Records were analyzed using the Nutribase 2007 software (Clinical Nutritional Manager v.7.14; Cybersoft Phoenix, AZ, USA) (9). Data intake from nutrients were expressed in crude amounts (g/day, mg/day mcg/day or IU/day) or in grams per kilogram of body weight. The data relating to food consumption were obtained throughout the study during different seasons.

The type and content of dietary fibers was estimated according to the data provided in the CRC Handbook of Dietary Fiber in Human Nutrition (10). In the present study, the fibers were classified into two major groups depending on their solubility in water.

The 24-h glycemic index (GI) was estimated by the weighted GI value of each consumed food at 24-h and expressed as percentage. The values of the GI and available carbohydrates of each food were obtained and glucose was used as the reference food (11). Dietary glycemic load was calculated as the product of dietary GI and total carbohydrate intake divided by 100.

**Anthropometric measurements**

The body weight and height of patients (without shoes or coats) were obtained using an anthropometric scale, with measurements recorded to the nearest 100 g for weight and to the nearest 0.1 cm for height. Body mass index (BMI) was calculated as weight (kilograms) divided by height (meters) square. The waist circumference was measured at the midpoint between the last rib and the iliac crest) by the World Health Organization (WHO) (12); flexible, non-stretch fiberglass tape measure was used for measurements.

**Laboratory measurements**

Blood samples were obtained after a 12-h fast, between seven and fifteen days after inclusion in the study: the following tests were then performed: aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyl transpeptidase (GGT), ferritin, triglycerides and total cholesterol, cholesterol HDL, C-reactive protein (CRP), insulin, serum glucose, cholesterol LDL – calculated by the Friedewald formula: Cholesterol LDL = cholesterol total – (cholesterol-HDL – TG ÷ 5). The estimated insulin resistance (IR) was calculated by the HOMA-IR by the following formula: HOMA = fasting insulin (µU/ml) X fasting glycaemia (mmol/l)/22.5.



**Cardiovascular risk assessment**

Cardiovascular risk was assessed by calculating the Framingham score (13), which predicts a 10-year risk of suffering a cardiovascular event on the basis of the following factors: age, total cholesterol, HDL cholesterol, systolic arterial blood pressure and presence/absence of diabetes mellitus and smoking.

**Metabolic syndrome**

The criteria for the clinical diagnosis of the MetS according to the Consensus (14) definition are the following: presence of 3 or more of these factors: waist circumference ≥ 94 cm for men and ≥ 80 cm for women, arterial blood pressure ≥ 130/85 mmHg or taking medications for blood pressure, triglycerides ≥ 150 mg/dl or taking fibrates, HDL cholesterol < 40 mg/dl for men and < 50 mg/dl for

women or taking pharmacological therapy, and fasting glucose ≥ 100 mg/dl or a diagnosis of diabetes.

**Leptin**

Serum leptin levels were determined by a solid phase ELISA based on the sandwich principle (BioSource), accordingly with the manufacturer instructions.

**Sample size**

Sample size calculation was based on the results from the study conducted by Petit et al. (15), that compared BMI and insulin among HCV infected patients with and without non-alcoholic fatty liver disease (NAFLD). It was calculated a sample size assuming a power of 80%, and an alpha of 5%.

**Statistical analysis**

The results were expressed as an average ± SD for the quantitative variables, and as frequencies and percentages for the qualitative variables. The evaluations of the differences between the quantitative variables were analyzed with the Student´s t test or Mann-Whitney U test. For the qualitative variables, the chi square test ($\chi^2$) or where appropriate, the Fisher exact test was used. Results were considered statistically significant with values of $p < 0.05$.



**RESULTS**

**Demographic data**

Fifty-eight patients with chronic HCV infection were analyzed. Almost half of participants (46.6%) are classified as lower middle class, 39.7% have studied up to middle school and most of them (70.7%) live in urban area.

**Clinical assessment**

Thirty-nine patients (67.2%) presented distinct levels of fibrosis. F1 (37.9%), F2 (27.6%) and F3 (1.7%). There was a predominance of females in the two groups, with the average age being similar between them. Significantly, higher values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were observed in the group of patients with fibrosis. Regarding the investigation of alcohol consumption, 8.6% of patients reported occasional consumption, equivalent to 2 drinks per week, while the remaining patients reported not use any type of

alcoholic beverage. The complete description of clinical characteristics of patients is presented in table I.

**Laboratorial measurements**

The HF group showed significantly higher levels of glycaemia, insulin, HOMA-IR, ferritin and, hemoglobin. The other laboratory measurements (hematocrit, total cholesterol, HDL, LDL, triglycerides, AST, ALT and GGT) did not differ statistically between the groups (Table I). When the increase of HOMA_IR is observed, there is also an increase in Ferritin levels between the patients in the sample, 3.18 (0.48-12.40) and 317.10 (28.90-881.91), respectively ($p = 0.05$). Eighteen Patients with HF (46.2%) have MetS, however there was no statistical difference between the groups.

The leptin serum levels did not differ between chronic HCV infected patients with and without fibrosis, though women and men had different levels: 28.5 (15.8-33.1) *versus* 7.2 (5.1-9.3), as well as eutrophic and overweight/obesity patients: 7.2 (4.4-11.7) *versus* 22.8 (8.3-31.4), respectively, with $p < 0.001$ for all.

**Dietary intake x hepatic fibrosis**

The patients with HF presented a significantly higher total daily energy and fat (g/kg/day) intakes. The glycemic load of meals was also higher in this group of patients. The other components of diet (carbohydrate, protein, cholesterol, fiber, calcium, zinc, iron, folic acid, niacin, thiamine, vitamin A, vitamin C, vitamin B6, vitamin B12 and vitamin D) did not show significant differences between the groups (Table II).

**Assessment of hepatic steatosis**

Additionally, hepatic steatosis was evaluated in 54. In only eight cases (13.8% of samples) steatosis was found: minimal (0 to 5%) in five, and mild (5 to 33%) in three. No patient in the study had diagnostic criteria for non-alcoholic steatohepatitis.

**DISCUSSION**

In the present study, an increased total energy and fat intakes among chronic HCV infected patients was observed, this consumption being especially evident in patients with HF. Fioravante et al. (16) described similar findings in relation to diet; however, the authors did not evaluate differences as to the presence of HF. Another research (5) also assessed patients with chronic HCV

infection, however, the patients included in their study presented a significant alcohol consumption, about 40 g of ethanol/day, while, in our study most of patients did not consume any alcohol.

As for the glycemic load of the meals, which translates as the product of the GI and the total carbohydrate consumed, it was observed that in the HF group, it was greater. Meals with a high glycemic load give a reduced level of fullness and are usually associated with an excessive ingestion of food, which may contribute to an increase in body fat and a higher IR (17). In contrast, meals with a low glycemic load can improve IR, since smaller quantities of insulin are required, as well as promoting smaller variations in glycemia (18,19). To the best of our knowledge, this is the first study who analyzed the glycemic load in HCV infected patients. Balanced food intake may modulate the severity of NAFLD development. The association between a high intake of saturated fat, low fiber intake and high intake of fructose leads to a more serious manifestation of NAFLD (20). The role of fructose intake is associated with the development IR, fatty liver, and hepatic damage in experimental studies, and a clinical study confirmed that a diet rich in fructose-sweetened beverages was also associated with increased insulin resistance (21,22).

Although we show a greater intake of calories and fats by the patients with fibrosis, differences in relation to body weight in the groups of patients were not observed, considering that the measured weight was liquid and ascites free. Moreover, we can infer that components of diet have a more important role than weight in the process of liver disease.

Since patients with fibrosis evaluated in this study presented higher serum glucose and insulin levels Fibrosis itself seems to be important to the relationship with IR and type 2 diabetes mellitus (19). Hui et al. (23) described higher HOMA-IR levels, in patients carrying chronic hepatitis C, without fibrosis (degree of F0) compared to patients with fibrosis (F1-F3) and to healthy individuals, alerting to the fact that even in the early stages of disease, the IR may be present. Moreover, a meta-analysis of more than 2,700 patients indicated that the IR reduces the rates of sustained virological response in patients treated with pegylated interferon and ribavirin regardless of genotype (24).

In this study, increased levels of ferritin in patients with fibrosis were also found, similar to the findings of Petta et al. (25). For the analysis of pathology, we can tell our patients had iron storage related liver disease. Hyperferritinemia thus is probably related to chronic inflammation, secondary to hepatitis C, not to excess iron. Other authors demonstrated increased ferritin levels in hepatitis C (1).

Insulin resistance is a recognized extrahepatic manifestation of hepatitis C, as the virus promotes the secretion of soluble mediators that act on glucose homeostasis (extrahepatic insulin resistance) and also has direct interference with insulin signaling (intravenous insulin resistance-hepatic) (26). In the present study, there was a relationship between insulin resistance and the presence of fibrosis, which suggests that some additional factor may be associated. Whether this factor is caloric intake, systemic inflammation or even both, there is no way to define. The fact is that as there is increased HOMA-IR increases ferritin, an acute phase marker, and suggesting increased inflammation. This ratio, however, was not maintained when inflammation was assessed by C-reactive protein. Perhaps this question deserves to be better explored in studies designed for this purpose, with a control group not infected by virus C.

The overall prevalence of hypertension in the patients studied was almost 40%, being that the patients with hepatic fibrosis presented higher average values of systolic blood pressure and diastolic blood pressure. The systemic arterial blood pressure is a factor in the metabolic syndrome, which in turn correlates to a faster evolution of fibrosis in patients with hepatitis C (27). In general, the pressure levels are associated with body weight, not evident in our study.

MetS was detected in almost half patients with HF, but it was not found significant difference according to the presence of liver fibrosis, as well as, it was not found in a cohort of 10,383 patients with HCV infection (28). Studies have shown that there is a strong association between metabolic disorders and liver disease caused by chronic hepatitis C. This association tends to lead to worse prognosis. Patients with both comorbidities had lower treatment response against HCV and faster progression to cirrhosis and hepatocarcinoma compared to those chronic HCV infected patients without MetS (29).

Behavioral factors are involved in the pathogenesis of NAFLD, therefore, an increased dietary intake, especially an elevated intake of total energy and fat, can be considered as risk factors for disease progression (30); besides the fact that HCV infection *per se* can be responsible for glucose metabolism and lipid profile disorders (31). It has been demonstrated that an increased in the fat intake is also associated to a greater incidence of cirrhosis and liver cancer, by induction of hepatic steatosis and fibrosis (32), once the excess calories in the diet are stored principally as triglycerides, which accumulate in the liver (33). On the other hand, dietary interventions in the management of patients with NAFLD demonstrated that a diet low in carbohydrates (20 g/day) (34), energy restriction and adoption of a Mediterranean style diet (6) were effective in promoting the reduction of hepatic triglycerides, contributing significantly to the reduction of hepatic steatosis and improvement of insulin sensitivity.

Despite an increased fat intake shown in this study, increased rates of steatosis were not found. The low rate of steatosis (13.8%) can be explained in part by the fact that most included patients were infected by genotype 1, and not by genotype 3, that is recognized as being more steatogenic (35). Although finding low steatosis prevalence on the sample, patients with HF were related to dietary and metabolic factors, so it is suggested that steatosis itself should not be the only factor associated with increased development of fibrosis. Inflammation could be an independent factor.

In our study, leptin levels were analyzed, however it was not find any association with the presence of HF. Similar findings were shown by Muzzi et al. (36) that evaluated the leptin levels in 221 patients with hepatitis C, however, there were no differences as to the plasma leptin levels, irrespectively of the presence/absence of steatosis and/or fibrosis. The role of leptin is still controversial, with studies suggesting that this hormone promotes hepatic steatosis and steatohepatitis, and others showing that leptin levels correlate with steatosis, but not with inflammation and fibrosis (37).

Regarding waist circumference, most males showed higher values than recommended. Abdominal fat, irrespective of total fat volume, is an independent predictive factor of fat buildup in hepatocytes, with a crucial role in the pathogenesis of NAFLD. Lipid stocks can reach toxic levels, increasing oxidative stress, with formation of free radicals, mitochondrial damage, inflammation and even fibrosis (38). Furthermore, obesity and, more specifically, intra-abdominal fat, is positively associated with IR and MetS, both related with faster progression to fibrosis in patients with HCV (39). This study found a high prevalence of MetS in the sample. This can be justified because of the hepatitis C virus is associated with IR, an important feature of MetS and present in many of these patients, both (Mets and IR) play a role in the progression of HCV (40).

Although it was found high prevalence of elevated cardiovascular risk in this study, there was no significant difference between patients with and without fibrosis. Indeed, 70% of the patients assessed in this study exhibited moderate or high risk of suffering a cardiovascular event within 10 years, similar to results reported for diabetic patients and patients with metabolic syndrome (41).

**Strengths and limitations**

Possible limitations of this study are related to unintentional predominance of patients with genotype 1, this fact limits the generalization of our results to patients with other genotypes. Furthermore, regarding data from dietary intake, food records were obtained throughout the study and not in a single season, but as the patients were evenly distributed in the months of the study, we believe that this fact has not affected the results.

Another restriction that could preclude generalization of our data is associated with the number of participants, however it was reached the planned sample size calculation. Patients were carefully selected to avoid confounding factors (especially alcohol intake, cirrhosis and active antiviral treatment); especially this last item was a difficult obstacle along the data collection, since most of the patients attending the Gastroenterology Division's outpatient clinic were using antiviral drugs and could not be included. On the other hand, these factors strengthened data obtained by relating the diet with liver fibrosis. The strong point of this work is the dietary evaluation and it relationship with HF; until now there was not another study that had evaluated the glycemic load meals of these patients. Our data could prove of great value for taking the decision to adopt more specific interventions for HCV patients, especially with emphasis on energy and lipid restrictions, and also on carbohydrates type, considering the glycemic index and glycemic load.

**CONCLUSIONS**

In conclusion, patients with HF presented elevated total daily energy and total fat intakes, a higher glycemic load of meals, as well as a worse metabolic profile, with higher rates of insulin resistance and increased pressure levels, when compared to patients without fibrosis. These metabolic alterations associated to chronic infection by HCV tend to worsen the prognosis of liver disease, reinforcing the need for early diagnosis and treatment of the disease, including dietary management of patients to minimize morbidity and mortality.



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**Table I**. Clinical and laboratory characteristics of chronic HCV infected patients in accordance with the presence of hepatic fibrosis

| | *Absence HF* | *Presence HF* | *p-value* |
|---|---|---|---|
| Gender (female) | 13 (68.4%) | 19 (48.7%) | 0.157[b] |
| Ethnicity (Caucasian) | 15 (78.9%) | 31 (79.5%) | 0.795[b] |
| Age (years) | 47.8 ± 12.3 | 53.4 ± 7.6 | 0.079[a] |
| *Genotype* | | | 0.078[a] |
| 1 | 14 (77.8%) | 32 (82.1%) | |

| | | | |
|---|---|---|---|
| 2 | 0 (0.0%) | 1 (2.6%) | |
| 3 | 4 (22.2%) | 6 (15.4%) | |
| *Physical activity* | | | 0.198[b] |
| Sedentary/irregularly active | 11 (57.9%) | 22 (56.5%) | |
| Economic classification (B2)[d] | 7 (36.8%) | 9 (23.1%) | 0.673[b] |
| SBP (mmHg)[e] | 129.5 ± 17.7 | 140.1 ± 18.9 | 0.046[a] |
| DBP (mmHg)[f] | 78.0 ± 8.2 | 84.8 ± 10.7 | 0.010[a] |
| *Framingham Score*[g] | | | 0.114 [b] |
| High risk (> 10%) | 6 (31.6%) | 23 (59.0%) | |
| *High waist circunference* | | | 0.137 [b] |
| Female | 6 (18.8%) | 11 (42.3%) | |
| Metabolic syndrome | 4 (21.1%) | 18 (46.2%) | 0.087[b] |
| Body mass index (kg/m$^2$) | 26.8 ± 2.1 | 27.5 ± 4.6 | 0.440[a] |
| Glucose (mg/dL) | 86 (82-9) | 94 (89-102) | 0.001[c] |
| Insulin (µUI/mL) | 10.7 (8.2-14.7) | 15.3 (10.2-26.0) | 0.009[c] |
| HOMA_IR | 2.18 (1.6-3.3) | 3.4 (2.4-6.4) | 0.002[c] |
| Ferritin (µg/mL) | 143.8 ± 33.0 | 378.8 ± 200.1 | 0.009[a] |
| Albumin (g/dL) | 4.2 (4.1-4.4) | 4.4 (4.2-4.5) | 0.021[c] |
| Hematocrit (g/dL) | 40.6 (38.8-41.5) | 42.8 (39.3-45.8) | 0.050[c] |
| Hemoglobin (g/dL) | 13.9 (13.2-14.7) | 14.8 (13.9-15.8) | 0.031[c] |
| Triglycerides (mg/dL) | 87 (63-101) | 97 (75-122) | 0.097[c] |
| Cholesterol Total (mg/dL) | 166.0 ± 25.3 | 165.1 ± 26.9 | 0.901[a] |
| HDL-cholesterol (mg/dL) | 48.5 ± 12.6 | 43.0 ± 10.2 | 0.083[a] |
| LDL-cholesterol (mg/dL) | 100.0 ± 23.8 | 99.8 ± 26.0 | 0.977[a] |
| CRP (mg/L)[h] | 4 (4-4) | 4 (4-4) | 0.541[c] |
| AST (U/L)[i] | 39 (29-55) | 45 (35-74) | 0.125[c] |
| ALT (U/L)[j] | 46 (32-74) | 56 (39-104) | 0.074[c] |
| Gama GT (U/L)[k] | 59.9 ± 13.7 | 77.5 ± 12.4 | 0.158[a] |

[a] t Test.; [b]$\chi^2$; [c]Mann-Whitney; [d]Brazil Economic Classification Criteria (ABEP, 2008); [E]Systolic blood pressure; [f]Disastolic blood pressure; [g]Cardiovascular disease risk estimate, percentage in 10 years, calculated according to Framingham study, 2008; [h]C-reactive protein; [i]Aspartate aminotransferase; [j]Alanine aminotransferase; [k]Gama glutamyl transpeptidase; [l]Hepatic fibrosis.

**Table II**. Daily intake of nutrients of chronic HCV patients in accordance with the presence of hepatic fibrosis

| | *Absence HF*[c] *n = 19* | *Presence HF n = 39* | *p-value* |
|---|---|---|---|
| Energy (Kcal/kg/day) | 28.8 ± 7.9 | 34.6 ± 11.2 | 0.048[a] |
| Carbohydrates (g/kg) | 3.2 (2.6-3.8) | 3.7 (2.6-5.0) | 0.187[b] |
| Proteins (g/kg) | 1.2 (0.9-1.7) | 1.3 (0.9-1.9) | 0.588[b] |
| Lipids (g/kg) | 1.1 (0.8-1.3) | 1.4 (1.0-1.9) | 0.010[b] |
| Cholesterol (mg) | 264.7 (149.9-367.2) | 272.3 (173.3-358.6) | 0.909[b] |
| Total Fiber (g/day) | 12.6 (9.7-15.8) | 15.5 (10.7-21.4) | 0.221[b] |
| Soluble Fiber (g/day) | 3.7 (3.3-5.8) | 5.2 (3.4-6.5) | 0.221[b] |
| Insoluble Fiber (g/day) | 8.9 (6.5-11.4) | 10.2 (7.3-14.7) | 0.282[b] |
| Glycemic Load (g) | 181.0 (140.5-223.4) | 221.9 (168.9-307.8) | 0.046[b] |
| Glycemic Index (%) | 61.1 (56.9-62.5) | 61.0 (57.2-64.3) | 0.740[b] |
| Calcium (mg) | 694.57 ± 288.14 | 714.63 ± 323.75 | 0.820[a] |
| Zinc (mg) | 12.74 ± 5.39 | 14.38 ± 6.47 | 0.346[a] |
| Iron (mg) | 13.90 ± 5.49 | 15.00 ± 4.96 | 0.446[a] |
| Folic Acid (mcg) | 166.11 ± 94.06 | 156.23 ± 78.07 | 0.674[a] |
| Niacin (mg) | 21.81 ± 7.93 | 24.54 ± 9.92 | 0.300[a] |
| Thiamine (mg) | 1.64 ± 0.84 | 1.70 ± 0.61 | 0.746[a] |
| Vitamin C (mg) | 10.91 (41.77-146.98) | 94.94 (42.10-173.93) | 0.270[b] |
| Vitamin A (IU) | 4370.43 (2146.27-7427.93) | 3853.70 (2088.92-8217.622) | 0.987[b] |
| Vitamin B6 (mg) | 1.65 ± 0.63 | 1.80 ± 0.7 | 0.440[a] |
| Vitamin B12 (mcg) | 4.07 (2.84-5.88) | 3.59 (3.05-5.58) | 0.866[b] |
| Vitamin D (IU) | 13.33 (0-84) | 44.00 (0- 74.66) | 0.371[b] |

[a]t Test, [b]Mann-Whitney; [c]Hepatic fibrosis.