Research Article

iMedPub Journals
http://www.imedpub.com/

Journal of Nutraceuticals and Food Science

2016
Vol.1 No.1:7

Overweight and Liver Disease: A New Paradigm

Serafim MGC, Leite IA, Freire MBS, Araújo LW, Araújo-Neto J, Santos JCF and Moura FA

Faculty of Nutrition, Universidade Federal de Alagoas

Corresponding author: Fabiana Andréa Moura, Faculade de Nutrição Universidade Federal de Alagoas, Campus A. C. Simões, Avenida Lourival Melo Mota, s/n, Tabuleiro dos Martins, 57072-970 Maceió, AL, Brazil. Tel: 5582988871468; E-mail: fabianamoura_al@hotmail.com

Received: November 02, 2015; **Accepted:** March 23, 2016; **Published:** March 25, 2016

Citation: Serafim MGC, Overweight and Liver Disease: A New Paradigm. 2016;1: 1.

Abstract

Introduction: The progression of hepatic disorders such as alcoholic liver disease (ALD) or viral hepatitis B/C (VHB/VHC) usually depends on the nutritional status of an individual. In the past, malnutrition commonly induced the progression of these hepatic disorders. However, due to a worldwide increase in the prevalence of nonalcoholic fatty liver disease (NAFLD) and its developed forms, as well as nonalcoholic steatohepatitis (NASH), these fatty liver diseases become one of the main causes of liver fibrosis or liver cirrhosis. It may then be possible that fat accumulation rather than malnutrition also develops the severity of ALD or VHB/VHC.

Objective: The aim of the present study was to identify the clinical, nutritional and socio-economical profiles of patients with liver disease under nutritional monitoring at the University Hospital Nutrition and Hepatology Outpatient clinic, Alagoas/Brazil.

Methods: Cross-sectional study that collected demographics, socio-economics, life style habits, anthropometrics and clinical data using a questionnaire. The study protocol was approved by the ethical review committee.

Results: Of the 17 patients studied, most of them were adults (70.5%) and male (76.4%). The major liver disease etiology was VHC (35.2%), followed by VHB (17.6%) and then ALD (11.7%). Among the clinical complications associated with liver disease, gastrointestinal bleeding (35.3%) and ascites and/or edema (35.3%) stood out. Despite several patients showing ascites/edema at the time of anthropometric measure, overweightness/obesity was detected in 63.6% (by body mass index) and 33.3% (by mid-upper arm circumference) of the patients, while undernutrition (25.0%) was determined only by mid-upper arm circumference.

Study limitation: Small sample size was the main study limitation.

Conclusion: Despite the limitations of this study, a high frequency of overweight/obesity among patients with liver disease was observed, which presents a challenge to health care professionals, who will need to adapt to a new paradigm regards malnutrition and under nutrition among hepatic patients.

Keywords: Liver disease; Viral hepatitis C; Viral hepatitis C; Overweight; NAFLD

Introduction

Hepatic disorders are a group of diseases, which affect both function, and metabolism of the liver in different ways and in the degree of gravity. Chronic hepatitis presents, generally, a long evolution time and may develop into hepatic cirrhosis (HC) and hepatocellular carcinoma (HCC). Among the causes of chronic hepatitis, alcohol, Viral Hepatitis C (VHC), Viral Hepatitis B (VHB) and Nonalcoholic Fatty Liver Disease (NAFLD) stands out. In the western world, the prevalence of hepatic disorders is considered high, and ranges from 2.8% for VHC [1] and roughly 30% for VHB [2].

On the other hand, hepatic disorders due to alcohol is considered responsible for 3.8% of all global deaths and 4.6% of global disability-adjusted life-years [3], while for NAFLD, the median prevalence is estimated at 20-30% for the general population, and 70%-90% in obese or diabetic patients [4]. In Brazil, the estimated prevalence is between 1 to 2% for VHC [5] and 7.4% for VHB [6]. For epidemiological data regarding alcohol intake and alcoholliver disease (ALD) there is no consensus. Portugal et al. estimated that alcohol was responsible for 3% of disability adjusted life years, indicating an abusive intake of this substance in Brazil [7]. Although there is no precise data regards the prevalence of NAFLD, 51% of the adult population in Brazil are overweight [8], such that the prevalence of NAFLD including simple steatosis and its aggressive form, nonalcoholic steatohepatitis (NASH) may be considered high in this country [9].

It is known that regardless of the etiology of liver disease, nutritional status undergoes important changes, both at the level of macro and micronutrients [10]. Malnutrition is prevalent in individuals with chronic liver disease and occurs as a result of inadequate nutrient intake, altered metabolism, and malabsorbtion [11]. In addition, common clinical complications from liver damage, such as ascites, esophageal varices, hepatic encephalopathy and others, contribute to nutritional disorders [12]. However, in the last year, an increase in overweight and

obesity in the world population, considered a consequence of several changes, such as food intake and sedentary lifestyle [13], fetal programming (consequence of under nutrition during pregnancy) [14], genetic disorders [15], and others [16-18] has called much attention to itself.

In this context, there has been an increase in the number of disorders associated with obesity and fat accumulation in the liver. Lipid accumulation in liver tissue is closely related to oxidative stress and Comentado [FM5]: Modifed according to Reviewer 2 consequent inflammation [9], and both complications may stimulate liver disease progression, independent of etiology [19-21]. Considering the above, the objectives of the present study were to identify the clinical and nutritional profiles of hepatic patients who sought (spontaneously or by referral from another health professional) nutritional monitoring at the University Hospital Nutrition and Hepatology Outpatient clinic in Alagoas, Brazil.

Methods

Study design, sample and ethical procedures

This was a cross-sectional study conducted with patients treated at the Nutrition and Hepatology Outpatient clinic in the Professor Alberto Antunes University Hospital (Alagoas/Brazil), from 09/2014 to 04/2015. This outpatient clinic was specific to patients with liver disease preferentially, but not exclusively. Patients who were older than 18 years and who showed liver disease of any etiology were included in the study. This study followed resolution n°196/96 of the National Health Council and was approved by the ethics committee at the Universidade Federal de Alagoas (n577.359/2014).

Demographics, socio-economic status, life habits and clinical variables

Data was collected for characterization of the patients life: birth date; marital status (currently unmarried - single/separated/divorced; currently married; and widowed); and total number of family members. Regards schooling, the number of years of education was considered (<4 yrs - Illiterate or functional illiterate; 4 yrs - primary completed; 5 to 8 yrs – completed junior high school; 11 yrs – completed high school, university, or higher). Occupational designations included formal (professional or government employees), informal (manual laborers, farmers), retired or government benefit and unemployed (not in the labor force, housewife or student). Income such as monthly family income and monthly per-capta income (according to minimum wage) was recorded.

In addition, information on life habits such as smoking and alcohol intake was collected. These variables were specifically characterized as ex-smoker/ex-drinker (if the habit had been confirmed as stopped), smoker/drinker (if the patient smoke or consumed any amount of cigarettes or alcoholic drinks, respectively), or non-smoker/drinker (if the patient did not have the habit of smoking or drinking, respectively). Besides etiology of liver disease, data was also collected for clinical complications after a nutritional consult, such as hepatic encephalopathy, gastrointestinal bleeding (upper or lower), jaundice, ascites, edema and hospitalizations.

Anthropometric variables

The patients' weight, height, and arm circumference were measured by trained professionals (Nutrition student and professor) with individuals in the orthostatic position and wearing light clothing. Body weight was determined using a Filizzola® electronic scale with a maximum tare of 150 kg and a precision of 100 g. Height was determined with the individual in an orthostatic position with the aid of a fixed stadiometer consisting of a non-extendable 2 m measuring tape divided into 0.1 cm divisions. Mid-upper arm circumference was determined at a medial point on the right arm using a non-extendable tape divided into 0.1 cm divisions. Body Mass Index (BMI) was calculated by the quotient of the body weight (kg) and the square of the height (m^2).

Adult patient (18-59yrs) nutritional status was classified as recommended by the WHO as follows [22]: thin (BMI, 18.5 kg/m^2); normal (BMI between 18.5 and 24.9 kg/m^2); overweight (BMI between 25 and 29.9 kg/m^2) and obese (BMI ≥ 30.0 kg/m^2). Elderly patient (>60yrs) nutritional status was classified as recommended by the WHO as follows [23]: thin (BMI, 22.0 kg/m^2); normal (BMI between 22.0 and 26.9 kg/m^2); overweight (BMI ≥ 27.0 kg/m2). For mid-upper arm circumference classification Frisancho standards were utilized as follows [24]: severe malnutrition (% adequacy <70); moderate malnutrition (% adequacy between 70 and 80); mild malnutrition (% adequacy between 80 and 89.9); normal (% adequacy between 90 and 109.9); overweight (% adequacy between 110 and 119.9); and obesity (% adequacy ≥110). If the patient showed ascites and/or edema in the legs or arms at the time of the interview, the BMI and/or arm circumference were not considered as a determinant of nutritional status.

Statistical analysis

The data was entered into Excel® and analyzed with the aid of SPSS 21.0 software (SPSS Inc., Chicago, IL, USA). Frequency was expressed as “n(%)” and the numeric results as “mean ± SD”.

Results

Of the 17 patients evaluated most of them (n=13; 76.4%) were male and of medium of age, ± 27.5yrs (51.8%). The general characteristics of the study population are presented in **Table 1.**

Most of the patients studied were adult (n=12; 70.5%), were currently married (n=13; 76.4%), finished primary or high school (n=12; 70.5%) and had a monthly per capita income between 1-2 minimum wage (n=12; 70.5%).

In **Table 1**, we may also observe that most of the patients consumed alcoholic drinks or were ex-drinkers (n=13; 76.5%).

Table 1 Socio-economic, Demographic and Life habits of Patients treated at the ambulatory of Nutrition and Hepatology of a University Hospital from Alagoas, Brazil

Sex		N(%)
	Male	13(76·4%)
	Female	04(23·5%)
Schooling		
	Illiterate	04(23·5%)
	<4y	05(29·4%)
	4-8y	07(41·1%)
	More than 11y	01(5·9%)
Occupation		
	Formal	03(17·6%)
	Unformal	08(47·1%)
	Retired or government benefit	05(29·4%)
	Did not answered	01(5·9%)
Number of family members		
	1	04(23·5%)
	3-Feb	08(47·1%)
	>3	01(5·9%)
	Did not answered	04(23·5%)
Family income (minimum wage*)		
	<1	02(28·5%)
	2-Jan	05(29·4%)
	>2	09(52·9%)
	No RENDA	01(5·9%)
Monthly Per capita Income		
	<1	04(23·5%)
	2-Jan	05(29·4%)
	>2	04(23·5%)
	No RENDA	01(5·9%)
Smoke		
	Smoker	01(5·9%)
	ex-smoker	06(35·3%)
	no smoker	10(58·8%)
Alcohol intake		
	Drinker	03(17·6%)
	Ex-drinker	10(58·8%)
	No drinker	04(23·5%)

***US$ 272,18 (2014); US$ 261,91 (2015)**

Table 2 shows the clinical evaluation of the patients studied. We can observed that most patients had liver disease caused by VHC (n=6; 35.2%) and VHB (n=3; 16.6%).

Several clinical complications were related, the most common one being gastrointestinal bleeding (n=6; 35.2%) and ascites and/or edema (n=6; 35.2%). It is worth noting the high number of hospitalizations due to liver disease (n=7; 41.1%).

Table 2 Clinical characterization of patients treated at the ambulatory of Nutrition and Hepatology of a University Hospital from Alagoas, Brazil

	N(%)
Liver Disease Etiology	
Hepatitis C virus	06(35·3%)
Hepatitis B virus	03(17·6%)
Alcohol	02(28·5%)
Schistosomiasis	01(5·9%)
Hepatic Steatois	02(28·5%)
Autoimmune	01(5·9%)
MISTA	02(28·5%)
Clinical complications	
Gastrointestinal bleeding	06(35·3%)
Hepatic encephalopathy	01(5·9%)
Jaundice	02(28·5%)
Ascites and/or edema	06(35·3%)
None	02(28·5%)
Hospitalization	
Yes	07(41·1%)
No	10(58·8%)

Table 3 shows the anthropometric evaluation of the patients studied. It is worth noting the high number of patients who were not evaluated by BMI (n=7; 63.6%) and arm circumference (n=6; 35.3) because they had ascites and/or edema (in the legs or arms) at the time of the anthropometric evaluation. Among the patients whose BMI could be measured, a high frequency of overweight/obesity was observed, independent of the age group: adult (n=4; 57.1%) and elderly (n=3; 75.0%).

However, compared to BMI, arm circumference indicated different frequencies in relation to nutritional status. According to this parameter, both under nutrition (n=3; 25.0%) and overweight (n=4; 33.3%) had a similar frequency, while a

normal nutritional status was seen in most of the participants (n=5; 41.7%).

Table 3 Anthropometrics measures of Patients treated at the ambulatory of Nutrition and Hepatology of a University Hospital from Alagoas, Brazil, Number of patients who could have anthropometric parameter measured

	N(%)
BMI	**11(64·7%)***
Adult	07(63·6%)*
Normal	03(27·3%)
Overweigh	01(14·3%)
Obesity	03(27·3%)
Older	04(80·0%)*
Normal	01(25·0%)
Overweigh	03(75·0%)
Mid-upper arm circumference	**12(70·6%)***
Under nutrition	03(25·0%)
Normal	05(41·7%)
Overweigh	03(25·0%)
Obesity	01(8·3%)

Discussion

In the present study, an elevated frequency of viral hepatitis among the patients studied was observed. According to Lim et al., VHC and alcohol intake are major etiologies responsible for HC in the world [25], and are also the first and second cause, respectively, for liver transplants [26]. Among the main complications associated with liver disease, gastrointestinal bleeding and hydric retention (ascites and edema) stand out, which are both closely related to portal hypertension [27], which is derived from structural changes caused by liver fibrosis, and that occur independent of liver disease etiology [28]. Portal hypertension is defined as a pathologic increase in portal vein pressure compared to inferior vena cava pressure, with a gradient Comentado [FM6]: Adjusted according to Reviewer 2 greater than 5 mmHg [29] and causes the development of varices in the gastrointestinal tract, especially in the esophagus and stomach [30]. Bleeding varices are very common (5-15%) [29] and show elevated mortality levels (20%) among patients with liver diseases [31]. On the other hand, ascites and edema were as frequently seen as gastrointestinal bleeding in our patients. Ascites is considered the more common complication of cirrhosis. It is believed that ~60% of patients with compensated cirrhosis develop ascites within 10 years during the course of their disease [32]. It is closely associated with long-term mortality in cirrhotic patients, especially among malnourished patients [33]. Despite that the number of participants in our study was insufficient to carry out a statistical analysis between groups regards prevalence of nutritional status according to liver disease etiology, we did observe a higher frequency of overweight and obesity than undernutrition, which were similar to the results identified by Menta et al. studying patients with VHB and VHC [34]. Our results confirm that there is a nutritional transition that it is occurring in the western world, including Brazil. Reis and Cople studying cirrhotic patients with a previous history of alcohol intake, in Rio de Janeiro/Brazil, found some degree of malnutrition in 96% of the subjects evaluated [35]. Similar to our study, Reis and Cople also used anthropometric measures to diagnose nutritional status. However, the limitation of these measures is known, due to the presence of edema and/or ascites during the course of liver disease. Nunes et al. compared different methods of nutritional assessment for classification of malnutrition in cirrhotic patients and concluded that anthropometric methods (triceps skinfold thickness and mid-upper arm circumference) were less sensitive in identifying malnutrition. According to these authors, the best parameter for nutritional assessment in cirrhotic patients was the hand grip strength measurement using a dynamometer, which identified 58.8% malnutrition among the cirrhotic subjects studied [36]. However, a dynamometer is not a common piece of equipment found in nutritional outpatient clinics or hospital environments. As such anthropometry is the technique more commonly utilized among health care professionals. VHC and VHB are associated with several systemic disorders, besides liver damage, especially diseases that show RI, such as diabetes mellitus [37] and HS [38], and are critical factors in the development of NASH and the progression of liver fibrosis to cirrhosis and related complications [34]. It is believed that 50-73% and 13% of patients infected with VHC [39] and VHB [38], respectively, have HS or NASH. In this context, the high frequency of overweight and obesity found in this study may be associated with an increase in the risk of the onset of disorders associated with lipid metabolism, such as HS and NASH, increasing considerably, the risk of morbidity and mortality associated with liver damage.

According to our results, it is possible to conclude that the main etiology of liver disease among the patients studied was viral Hepatitis (VHC and VHB), most of whom had some clinical complication such as gastrointestinal bleeding or ascites and/or edema and almost half of these had been hospitalized due to liver complications. It is important to note the elevated frequency of overweight and obesity both in adult individuals as well as elderly patients, and that this may be closely associated with the risk of HS or NASH. The low number of individuals identified with malnutrition using anthropometric measures, shows us a new paradigm for health care professionals. Patients with liver disorders and who are overweight may not, necessarily, have an appropriate balance of micronutrients. Thus, research on dietary habits and biochemical profiles will allow health care professional to conduct a more comprehensive diagnosis of their patients and thus understand that malnutrition may come masked as overweight.

There are some limitations of our study that should be considered. Firstly, the small number of patients in this study that made it impossible to use statistical analysis and make

This article is available from: ${articleDOI}

comparisons between different groups, such as age, sex and etiology. Secondly, the limited use of anthropometric measures due to the presence of water retention abnormalities such as ascites and/or edema, that made a nutritional status diagnosis more difficult. Thirdly, there was no clinical data including blood chemical analyses related to the severity of liver cirrhosis. Never the less, the data obtained in this study does contribute a further understanding to the clinical and anthropometric profiles of hepatic patients from Alagoas, Brazil.

Acknowledgements

This study was supported by Hospital Universitário Professor Alberto Antunes (HUPAA/UFAL-Brazil).

References

1. Mohd HK, Groeger J, Flaxman AD, Wiersma STB (2013) Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. Hepatology 57: 1333-1342.
2. McMahon BJ (2010) Natural history of chronic hepatitis B. Clinics in liver disease 14: 381-396.
3. Rehm J, Mathers C, Popova S, Thavorncharoensap M, Teerawattananon Y, et al. (2009) Global burden of disease and injury and economic cost attributable to alcohol use and alcoholuse disorders. Lancet 373: 2223-2233.
4. Vernon G, Baranova A, Younossi ZM (2011) Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. Aliment Pharmacol Ther 34 : 274-285.
5. Gottschall CB, Pereira TG, Rabito EI, Alvares D (2015) Nutritional Status and Dietary Intake in Non-Cirrhotic Adult Chronic Hepatitis C patients. Arq Gastroenterol 52: 204-209.
6. http://www.aids.gov.br/sites/default/files/anexos/publicacao/2010/50071/estudo_prevalencia_hepatites_pdf_26830.pdf.
7. Portugal FB, Campos MR, Carvalho JRD, Flor LS, Schramm JM, et al. (2015) Disease burden in Brazil: an investigation into alcohol and non-viral cirrhosis. Ciencia & saude coletiva 20: 491-501.
8. http://www.brasil.gov.br/saude/2014/04/brasil-estabiliza-taxas-de-sobrepeso-e-obesidade.
9. Santos JCDF, Valentim IB, Araújo ORPD, Ataide TDR, Goulart MOF (2013) Development of nonalcoholic hepatopathy: contributions of oxidative stress and advanced glycation end products. International journal of molecular sciences 14: 19846-19866.
10. Moriwaki H, Miwa Y, Tajika M, Kato M, Fukushima H, et al. (2004) Branched-chain amino acids as a protein- and energy-source in liver cirrhosis. Biochem Biophys Res Commun 313: 405-409.
11. Hasse JM, DiCecco SR (2015) Enteral nutrition in chronic liver disease: Translating evidence into practice. Nutr Clin Pract 30: 474-487.
12. Harrison PM (2015) Management of patients with decompensated cirrhosis. Clinical medicine 15: 201-203.
13. Gadiraju TV, Patel Y, Gaziano JM, Djousse L (2015) Fried food consumption and cardiovascular health: A review of current evidence. Nutrients 7: 8424-8430.
14. Ferreira HS, Moura FA, Cabral CR, Florencio TM, Vieira RC, et al. (2009) Short stature of mothers from an area endemic for undernutrition is associated with obesity, hypertension and stunted children: a population-based study in the semi-arid region of Alagoas, Northeast Brazil. Br J Nutr 101: 1239-1245.
15. Chesi A, Grant SF (2015) The genetics of pediatric obesity, TEM.
16. Moreno-Indias I, Cardona F, Tinahones FJ, Queipo-Ortuno MI (2014) Impact of the gut microbiota on the development of obesity and type 2 diabetes mellitus. Front Microbiol 5: 90.
17. Valsamakis G, Kyriazi EL, Mouslech Z, Siristatidis C, Mastorakos G (2015) Effect of maternal obesity on pregnancy outcomes and long-term metabolic consequences. Hormones 14: 345-357.
18. Kawicka A, Regulska IB, Regulska IB (2015) Metabolic disorders and nutritional status in autoimmune thyroid diseases. Postepy Hig Med Dosw 69: 80-90.
19. Ansari MHK, Omrani MD, Kheradmand F (2015) Oxidative stress response in patients infected by diverse hepatitis C virus genotypes. Hepatitis monthly 15: e22069.
20. Dikici I, Mehmetoglu I, Dikici N, Bitirgen M, Kurban S (2005) Investigation of oxidative stress and some antioxidants in patients with acute and chronic viral hepatitis B and the effect of interferon-alpha treatment. Clin Biochem 38: 1141-1144.
21. Grasselli E, Compalati AD, Voci A, Vecchione G, Ragazzoni M, et al. (2014) Altered oxidative stress/antioxidant status in blood of alcoholic subjects is associated with alcoholic liver disease. Drug and alcohol dependence 143: 112-119.
22. Organization WH (1995) Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. World Health Organization technical report series 854: 1-452.
23. Lipschitz DA (1994) Screening for nutritional status in the elderly. Prim Care 21: 55-67.
24. Frisancho AR (1974) Triceps skin fold and upper arm muscle size norms for assessment of nutrition status. Am J Clin Nutr 27: 1052-1058.
25. Lim YS, Kim WR (2008) The global impact of hepatic fibrosis and end-stage liver disease CLD 12: 733-746.
26. Parolin MB, Zaina FE, Lopes RW (2002) Nutritional therapy in liver transplantation. Arq Gastroenterol 39: 114-122.
27. Ripoll C, Groszmann R, Garcia-Tsao G, Grace N, Burroughs A, et al. (2007) Hepatic venous pressure gradient predicts clinical decompensation in patients with compensated cirrhosis. Gastroenterology 133: 481-488.
28. Poordad FF (2015) Presentation and complications associated with cirrhosis of the liver. Current medical research and opinion 31: 925-937.
29. Luigiano C, Iabichino G, Judica A, Virgilio C, Peta V, et al. (2015) Role of endoscopy in management of gastrointestinal complications of portal hypertension. World journal of gastrointestinal endoscopy 7: 1-12.
30. Amico GD, Garcia-Tsao G, Pagliaro L (2006) Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. J Hepatol 44: 217-231.

31. Amico GD, Franchis RD (2003) Cooperative study of upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. Hepatology 38: 599-612.

32. Gines P, Quintero E, Arroyo V, Teres J, Bruguera M, et al. (1987) Compensated cirrhosis: natural history and prognostic factors. Hepatology 7: 122-128.

33. Kim TY, Kim MY, Sohn JH, Kim SM, Ryu JA, et al. (2014) Sarcopenia as a useful predictor for long-term mortality in cirrhotic patients with ascites. Journal of Korean medical science. 29: 1253-1259.

34. Menta PL, Correia MI, Vidigal PV, Silva LD, Teixeira R (2015) Nutrition status of patients with chronic hepatitis B or C. Nutr Clin Pract 30: 290-296.

35. Reis NT, Cople CDS (1998) Acompanhamento Nutricional de cirróticos com história pregressa de alcoolismo. Revistra de Nutrição de Campinas 11: 10.

36. Nunes FF, Fernandes SA, Bertoline CM, Rabito EI, Gottschall CBA (2012) Avaliação nutricional do paciente cirrótico: comparação entre diversos métodos. Scientia Medica 22: 6.

37. Musleh UK, Ali AMA, Sidra A, Syed MUH, Syeda J, et al. (2014) Frequency of diabetes in hepatitis. International Journal of Collaborative Research on Internal Medicine & Public Health 6: 9.

38. Pais R, Rusu E, Zilisteanu D, Circiumaru A, Micu L, et al. (2015) Prevalence of steatosis and insulin resistance in patients with chronic hepatitis B compared with chronic hepatitis C and non-alcoholic fatty liver disease. European journal of internal medicine 26: 30-36.

39. Negro F, Sanyal AJ (2009) Hepatitis C virus, steatosis and lipid abnormalities: clinical and pathogenic data. Liver Int 29: 26-37.