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**NONALCOHOLIC FATTY LIVER DISEASE (NAFLD): RISK FACTORS AND SEVERITY**

**DOENÇA HEPÁTICA GORDUROSA NÃO ALCÓOLICA: CHANCES E RISCOS DE GRAVIDADE.**

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**ABSTRACT - Objective:** To evaluate the relationship between sociodemographic, biochemical and anthropometric variables and the risk factors and severity of NAFLD in patients who underwent abdominal ultrasonography at reference centers in Aracaju, Sergipe, Northeast of Brazil. **Materials and Methods:** This is a descriptive study based on an analytical and quantitative approach. It was conducted through the use of abdominal ultrasonography with a convex, dynamic 3.75 MHz transducer. Hepatic steatosis was diagnosed and classified in degrees. In patients with NAFLD, sociodemographic, biochemical and anthropometric factors were analyzed. SPSS® 22.0 software was used for statistical analysis and  $p < 0.05$  was adopted as the significance level. **Results:** A total of 800 individuals were evaluated and the steatosis prevalence was found to be 29.1% (233 patients). In relation to steatosis classification, 119 had grade 1 (51.0%); 94 were grade 2 (40.4%); and 20, grade 3 (8.6%). There was statistical significance with weight, waist measurement, hip measurement, AST, ALT, GGT, Blood Glucose, triglycerides,

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insulin, HOMA-IR and the NAFLD degrees. Elevated levels of triglycerides and low levels of LDL in patients with NAFLD increase the risks of finding the disease in advanced grades (2 and 3). **Conclusion:** The results suggest that elevated levels of triglycerides and low levels of LDL in patients with NAFLD is associated with elevated grades of steatosis on US. These metabolic variables may contribute to the selection of patients who would benefit from the investigation of steatosis or steatohepatitis through more invasive methods.

**Keywords:** Nonalcoholic fatty liver disease (NAFLD); Triglycerides; Low density lipoprotein (LDL); Steatosis. Ultrasonography.

**RESUMO - Objetivos:** Avaliar a relação das variáveis sociodemográficas, bioquímicas e antropométricas com o risco de gravidade da esteatose hepática não alcoólica (DHGNA) em pacientes submetidos à ultrassonografia abdominal em serviços de referência em Aracaju, Sergipe, Nordeste do Brasil. **Materiais e Métodos:** Estudo prospectivo, com abordagem analítica e quantitativa, realizado através de ultrassonografia abdominal com transdutor convexo, dinâmico e com 3,75 MHz. Os pacientes foram diagnosticados e classificados conforme os graus (1, 2 ou 3) de esteatose hepática. Após isso, nos pacientes diagnosticados foram analisados fatores sociodemográficos, bioquímicos e antropométricos. Foi considerado nível de significância  $p < 0,05$  e utilizado o programa estatístico SPSS® 22.0. **Resultados:** Foram avaliados 800 indivíduos, desses 233 (29,1%) foram diagnosticados com DHGNA. Quanto ao grau classificação, 119 tinham grau 1 (51,0%), 94 grau 2 (40,4%) e 20 grau 3 (8,6%). Após análise, pôde-se perceber associação estatisticamente significativa entre peso, circunferência da cintura, circunferência do quadril, LDL, triglicérides e os graus de DHGNA. **Conclusão:** Pôde-se demonstrar, após uma regressão logística, que um aumento dos triglicérides e uma diminuição do LDL em pacientes com esteatose hepática elevam as chances, e consequentemente o risco, de se encontrar graus mais avançados da doença, podendo sugerir que essas variáveis metabólicas contribuam para seleção de pacientes que necessitem realização de investigação diagnóstica através de métodos invasivos como a biópsia hepática.

**Palavras-chave:** Esteatose hepática não alcoólica (DHGNA); Triglicérides; Lipoproteína de baixa intensidade(LDL); Esteatose; Ultrassonografia.



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### INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) comprises a spectrum of pathologies that range from simple steatosis to steatohepatitis with or without fibrosis to cirrhosis. This disease is defined as an accumulation of lipids in hepatocytes that exceeds 5% of the total liver weight, in the absence of viral hepatitis, alcohol consumption and metabolic disease (LANKARANI et al., 2013; ZAMORA-ALVIZO et al., 2013). Several classes of lipids can accumulate in the liver; however, triglycerides are the most commonly identified in fatty infiltration (COTRIM et al., 2016).

NAFLD is one of this century's pandemics, with an estimated prevalence of approximately one billion worldwide (LOOMBA; SANYALA, 2013; BIRERDINC; YOUNOSSI, 2015). It is the most common reason for referral to hepatology services and the most common form of chronic liver disease. Similar to a true public health problem, its occurrence is due to changes in lifestyle, alimentation, and sedentariness (HYOGO; CHAYAMA; YAMAGISHI, 2014).

Simple steatosis is the most benign state of the NAFLD spectrum. Steatohepatitis is an aggressive form of steatosis with the ability to evolve into cirrhosis and hepatocellular carcinoma, secondary to parenchymal inflammation and fibrosis (MACHADO; CORTEZ-PINTO, 2014). Obesity, sedentariness, improper eating habits and genetic factors are involved in the etiology of disease, although the causes are indeterminate (PANG et al., 2015). NAFLD is intimately linked to diabetes mellitus, dyslipidemia, and metabolic syndrome, and NAFLD is associated with high homeostasis model Assessment (HOMA) values (CAVALCANTE et al., 2015; LI et al., 2015).

It is estimated by ultrasonography that the NAFLD prevalence in the general population ranges from 20 to 40% (WILLIAMS et al., 2011). According to some studies, individuals who with combined diabetes, obesity, dyslipidemia and metabolic syndromes show steatosis rates that range from 57.5 to 74% (SCHILD; SANTOS; ALVES, 2013). The NAFLD prevalence, measured by serum levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), is lower, varying between 7 and 11% (DYSON; ANSTEE; MCPHERSON, 2014). Hepatic biopsy, despite being expensive and invasive with a risk of bleeding to the patient, is the gold standard in diagnosis (FIERBINTEANU-BRATICEVICI et al., 2010).

Due to the difficulties and risks inherent in liver biopsy, ultrasonography is gaining acceptance as a noninvasive, low-cost alternative. It provides 83 to 94% sensitivity and 84 to 100% specificity in the detection of fatty liver infiltration in non-obese patients, depending on the degree of severity (ALMEIDA et al., 2008).



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The pathophysiology of NAFLD results from an imbalance between hepatic fatty acid uptake, lipogenesis, beta oxidation and transport via VLDL particles. Several studies have shown the importance of adipose tissue lipolysis in the development of hepatic steatosis (KAWANO; COHEN, 2013).

The objective of this research is to evaluate the relationship between sociodemographic variables (age, education level, income, sedentariness, smoking status and civil status), biochemical variables (aspartate aminotransferase (AST), Alanine Aminotransferase (ALT), Gamma-Glutamyltransferase (GGT), blood glucose, total cholesterol, low density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, insulin and Homeostasis Model Assessment (HOMA) and anthropometric variables (weight, height, body mass index, waist circumference, hip circumference, waist to hip ratio, and fat percentage) and the risk factors and severity of Nonalcoholic fatty liver disease (NAFLD) in patients who underwent abdominal ultrasonography at reference centers in Aracaju, Sergipe, Northeast of Brazil.

## MATERIALS AND METHODS

This is a descriptive study with an analytical and quantitative approach. The data were collected in four clinics in the city of Aracaju, SE, Brazil, from July 2013 to July 2014, with approval of the Committee for Ethics in Research of Tiradentes University (under No. 010513R). Abdominal US scans were performed with a convex, 3.75 MHz dynamic transducer (with continuous and automatic imaging), and each device used in the study was similar in terms of technology and image quality. A total of 800 subjects were assessed by the same physician.

The present study included both male and female patients aged between 18 and 60 years whose alcohol consumption was < 40 g/day. The following exclusion criteria were adopted: patients with hepatocarcinoma, other malignant tumors, cirrhosis, previous hepatopathies or cognitive deficiency.

Patients were prepared appropriately for the examination by fasting for six hours and taking an antifatulence agent, and an informed consent has been obtained, according to consent form attached to paper. During the US, evaluation of the parenchymal texture allowed NAFLD to be classified within grades, as follows: 0 – normal echogenicity; 1 – mild steatosis, with visualization of fine echoes from the liver parenchyma, normal visualization of the diaphragm and intrahepatic vessels; 2 – moderate steatosis, with diffuse increase in fine echoes, impaired visualization of intrahepatic vessels and



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diaphragm; and 3 – severe steatosis, with significant increase in fine echoes, with impaired or absent visualization of intrahepatic vessels (SAADEH et al., 2002).

The groups defined by the degree of NAFLD present on ultrasonography were compared to the following variables: age, education level, income, sedentariness, smoking status, civil status, weight, height, body mass index, waist circumference, hip circumference, waist to hip ratio, fat percentage, AST, ALT, GGT, blood glucose, total cholesterol, LDL, HDL, triglycerides, insulin and HOMA-IR.

Numerical variables were observed for the distribution of normality using the Shapiro-Wilk test. As a normality was not met, these data were known by the median and its quartiles. The categorical variables were presented by means of absolute and relative frequency. Median values and contingency tables were analyzed with Kruskal-Wallis and Pearson's chi-squared tests, respectively.

Two groups were created for the logistic regression. One group of patients with grade 1 hepatic steatosis were compared to a second group of patients with grade 2 or 3 hepatic steatosis. The logistic regression was performed stepwise forward. IBM SPSS Statistics for Windows version 22.0 (Armonk, New York, Unites States) was used for statistical analysis, adopting  $p < 0.05$  as the significance level.

## RESULTS

A total of 800 individuals (561 women and 239 men) were evaluated. Of these, 233 (29.1%) patients were diagnosed with NAFLD. In regard to grades, 119 patients had grade 1 NAFLD (51.0%), 94 presented with grade 2 (40.4%) and 20 presented with grade 3 (8.6%).

The group was subdivided into grade 1, grade 2 and grade 3 based on the ultrasonography classification criteria of fatty hepatic infiltration. In relation to numerical sociodemographic and anthropometric variables, weight, waist measurement, hip measurement showed significant statistical association with the degree of NAFLD. These results are demonstrated in table 1.



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**Table 1.** Sociodemographic and anthropometric numeric variables.

|        | Steatosis degree | Percentiles |        |        | N  | P     |
|--------|------------------|-------------|--------|--------|----|-------|
|        |                  | 25          | 50     | 75     |    |       |
| Weight | Grade 1          | 65.85       | 76.00  | 88.60  | 65 | 0,026 |
|        | Grade 2          | 69.28       | 80.90  | 91.53  | 54 |       |
|        | Grade 3          | 78.28       | 101.70 | 123.03 | 8  |       |
| WC     | Grade 1          | 90.00       | 99.00  | 104.00 | 63 | 0,006 |
|        | Grade 2          | 93.75       | 100.40 | 109.00 | 50 |       |
|        | Grade 3          | 103.25      | 112.00 | 127.65 | 8  |       |
| HC     | Grade 1          | 97.35       | 102.55 | 108.25 | 54 | 0,023 |
|        | Grade 2          | 98.78       | 104.00 | 114.90 | 44 |       |
|        | Grade 3          | 103.53      | 120.90 | 127.25 | 6  |       |

P: Level of significance, WC: Waist Circumference; HC: Hip Circumference.

The numerical biochemical variables and insulin resistance that were verified to have a significant statistical association with the degree of fatty liver among AST, ALT, GGT, blood glucose, triglycerides, insulin and HOMA-IR are shown in table 2.



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**Table 2.** Biochemical and insulin resistance numeric variables.

|               | Steatosis grade | Percent |        |        | N  | P      |
|---------------|-----------------|---------|--------|--------|----|--------|
|               |                 | 25      | 50     | 75     |    |        |
| AST           | Grade 1         | 16.00   | 19.00  | 23.00  | 68 | <0,001 |
|               | Grade 2         | 18.00   | 23.00  | 31.25  | 58 |        |
|               | Grade 3         | 24.00   | 28.00  | 40.00  | 9  |        |
| ALT           | Grade 1         | 17.00   | 24.00  | 28.50  | 69 | 0,001  |
|               | Grade 2         | 20.75   | 29.50  | 44.00  | 58 |        |
|               | Grade 3         | 28.50   | 45.00  | 73.00  | 9  |        |
| GGT           | Grade 1         | 21.50   | 34.00  | 55.50  | 65 | 0,034  |
|               | Grade 2         | 28.50   | 39.50  | 62.00  | 56 |        |
|               | Grade 3         | 45.25   | 57.00  | 80.25  | 6  |        |
| Blood Glucose | Grade 1         | 83.00   | 90.50  | 99.75  | 68 | <0,001 |
|               | Grade 2         | 89.00   | 96.00  | 108.00 | 55 |        |
|               | Grade 3         | 100.50  | 114.00 | 143.00 | 9  |        |
| Triglycerides | Grade 1         | 101.00  | 128.00 | 168.00 | 71 | 0,001  |
|               | Grade 2         | 112.50  | 176.00 | 230.00 | 61 |        |
|               | Grade 3         | 136.00  | 258.00 | 376.00 | 9  |        |
| Insulin       | Grade 1         | 7.90    | 9.95   | 14.38  | 40 | 0,004  |
|               | Grade 2         | 9.73    | 11.55  | 17.78  | 36 |        |
|               | Grade 3         | 14.10   | 27.20  | 53.10  | 6  |        |
| HOMA-IR       | Grade 1         | 1.91    | 2.27   | 3.53   | 37 | 0,007  |
|               | Grade 2         | 2.05    | 2.63   | 5.23   | 35 |        |
|               | Grade 3         | 4.20    | 6.98   | 27.20  | 5  |        |

P: Level of significance, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, GGT: Gama-Glutamyltransferase, HOMA-IR: Homeostatic model assessment.

The categorical variables that showed a significant statistical association with liver steatosis were sex and income. This is demonstrated in table 3.



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**Table 3.** Categorical variables.

| Variables |                     | Classification Grades |         |         | P     |
|-----------|---------------------|-----------------------|---------|---------|-------|
|           |                     | Grade 1               | Grade 2 | Grade 3 |       |
| Sex       | Female              | 87                    | 57      | 9       | 0.021 |
|           | Male                | 32                    | 37      | 11      |       |
| Income    | Up to 1.5 wages     | 54                    | 52      | 4       | 0.006 |
|           | 1,5 to 4,5 wages    | 56                    | 29      | 14      |       |
|           | More than 4.5 wages | 7                     | 12      | 2       |       |

P: Level of significance.

Table 4 displays the final model generated for regression, relating isolated modifications in each variable to an increased chance of finding more advanced degrees of disease.

**Table 4.** Logistic regression.

| Variables     | B      | E. P. | P      | Exp (B) |
|---------------|--------|-------|--------|---------|
| LDL           | -0.011 | 0.006 | 0.053  | 0.989   |
| Triglycerides | 0.012  | 0.003 | <0,001 | 1.012   |
| Constant      | -0.415 | 0.833 | 0.618  | 0.660   |

n = 136

B: Parameter of the equation for each variable and the constant of the model generated, E. P.: Standard error (of B), Exp (B): OR, P: Level of significance, LDL: Low density lipoprotein.





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Based on the logistic regression table (table 4), it was possible to estimate the chance ( $\hat{O}$ ) and probability or risk that a patient with hepatic steatosis has more advanced disease.

$$\hat{O} = e^{0,415 + 0,011 * LDL + 0,012 * triglicerideos}$$
$$\hat{P} = \frac{\hat{O}}{1 + \hat{O}}$$

## DISCUSSION

Influenced by genetic, environmental and metabolic factors, NAFLD is among the most common chronic non-communicable diseases in the modern world (LANKARANI et al., 2013). Estimations of the prevalence of hepatic steatosis vary widely and depend largely on the method used to calculate its value. However, by ultrasonography, the prevalence of hepatic steatosis ranges from 20 to 40% in industrialized countries (WILLIAMS et al., 2011; LAZO et al., 2013). Asian countries have a lower prevalence ranging from 15 to 30%, as in Iran, where was found a prevalence of 21.5% (LANKARANI et al., 2013; WONG, 2013). In the present study, the prevalence found was 29.1% in agreement with the literature.

Excessive fat deposition in the liver may occur due to an increase in fatty acid (FA) supply of adipose tissue, an increase in the synthesis of the FAs, an increase in dietary fat, a decrease in beta-oxidation of FAs, decrease in the export of very low density lipoprotein particles (VLDL) or the combination of these factors. It is estimated that 60% of the accumulated triglycerides in the liver are derived from adipose tissue fatty acids, 30% are the result of lipogenesis and 10% of the diet (KAWANO; COHEN, 2013; RESS; KASER, 2016).

Under normal conditions, the liver does not serve as a fat deposit and the concentration of hepatic triglycerides is low. However, there is a considerable flow of triglycerides and FAs in and out of the liver in response to food and fasting. FAs are absorbed by the small intestine, transformed into triglycerides and stored in the liver. In the excess of carbohydrates, a new production of FAs in the liver occurs through the process of lipogenesis (KAWANO; COHEN, 2013; RESS; KASER, 2016).

Analysis of the logistic regression model for patients with NAFLD reveals that high triglycerides are a disease marker. Each additional point leads to an increase of 1.2%



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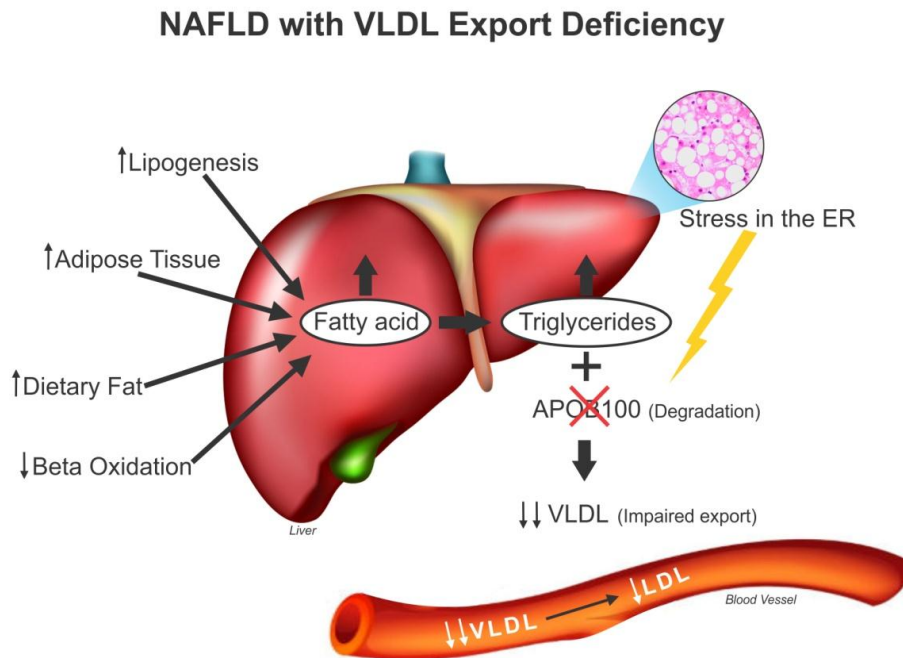
in the risk of finding the most advanced degrees of NAFLD. This is explained by the fact that triglyceride is the most prevalent class of lipid stored in the liver (FONTACER; ROZMAN, 2011).

VLDLs are formed when triglycerides are linked with apolipoprotein B100 (apoB 100) through the action of the microsomal triglyceride transfer protein (MTP). Fatty acid accumulation in the liver can lead to chronic stress of the endoplasmic reticulum of hepatocytes that results in increased degradation of ApoB100, decreasing the liver's ability to export triglycerides in the form of VLDL and potentially worsening steatosis (COREY; COHEN, 2015).

The present study evidences this fact, since in patients with NAFLD, it was also possible to observe that each additional point of LDL leads to a decrease of 1.1% in the chance of finding more severe forms of the disease. A portion of liver-excreted VLDLs, rich in triglycerides, gives rise to IDLs, which are rapidly removed from the plasma and further continuation of the catabolic process results in LDLs formation. In cases of more severe hepatic steatosis with evident insulin resistance, in addition to the decrease in the export of VLDL, the lipoprotein lipase that is activated by insulin has little effect on the VLDL particles, resulting in decreased fatty acid release, reduced LDL levels and hypertriglyceridemia (NOVAKOVIĆ et al., 2013; XAVIER et al., 2013). This is shown in figure 1.



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**Figure 1.** NAFLD with VLDL Export Deficiency.

Although there is a large association of patients with NAFLD and heart disease, patients with more advanced degrees of fatty liver disease presented lower levels of LDL, the most atherogenic lipoprotein, in this study. An explanation for this is that there are additional factors for the development of atherogenic disease, such as high levels of triglycerides and low levels of HDL-C. This result shows the need for additional studies to prove if in the case of NAFLD with VLDL export deficiency, the profile of systemic lipoproteins favors a good cardiac prognosis (MIKOLASEVIC et al., 2016).

## CONCLUSIONS

This study of ultrasound diagnosis in different degrees of hepatic steatosis presents a method that is noninvasive, faster, inexpensive and easily accessible. By associating this method with biochemical, anthropometric and sociodemographic



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measures by logistic regression, it was possible to demonstrate that the elevation of serum triglycerides and decrement of serum LDL in patients with fatty liver increase the risk of finding disease in advanced grades. This may suggest selection criteria for patients in need of diagnostic investigation requiring more invasive methods, such as hepatic biopsy.

**REFERENCES**

ALMEIDA, A. M. et al. Fatty liver disease in severe obese patients: Diagnostic value of abdominal ultrasound. **World Journal of Gastroenterology**, v. 14, n. 9, 1415-1418, 2008.

BIRERDINC, A.; YOUNOSSI, Z. Can NASH lipidome provide insight into the pathogenesis of obesity-related non-alcoholic fatty liver disease? **Journal of Hepatology**, v. 62, n. 4, p. 761-762, 2015.

CAVALCANTE, L. N. et al. Genetic ancestry analysis in non-alcoholic fatty liver disease patients from Brazil and Portugal. **World Journal of Hepatology**, v. 7, n. 10, p. 1433-1438, 2015.

COREY, K. E.; COHEN, D. E. Lipid and lipoprotein metabolism in liver disease. In: GROOT, L. J. et al. Endotext. South Dartmouth: MDText.com, 2015.

COTRIM, H. P. et al. Nonalcoholic fatty liver disease Brazilian society of hepatology consensus. **Arquivos de Gastroenterologia**, São Paulo, v. 53, n. 2, p. 118-122, 2016.

DYSON, J. K.; ANSTEE, Q. M.; MCPHERSON, S. Non-alcoholic fatty liver disease: a practical approach to diagnosis and staging. **Frontline Gastroenterology**, v. 5, n. 3, p. 211, 218, 2014.

FIERBINTEANU-BRATICEVICI, C. et al. Noninvasive investigations for non alcoholic fatty liver disease and liver fibrosis. **World Journal of Gastroenterology**, v. 16, n. 38, p. 4784-4791, 2010.

FONTACER, K.; ROZMAN, D. Nonalcoholic fatty liver disease: focus on lipoprotein and lipid deregulation. **Journal of Lipids**, v. 2011, p. 1-14, 2011.



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HYOGO, H.; CHAYAMA, K.; YAMAGISHI, S. Nonalcoholic fatty liver disease and cardiovascular disease. **Current Pharmaceutical Design**, v. 20, n. 14, p. 2403-2411, 2014.

KAWANO, Y.; COHEN, D. E. Mechanisms of hepatic triglyceride accumulation in non-alcoholic fatty liver disease. **Journal of Gastroenterology**, v. 48, n. 4, p. 434-441, 2013.

LANKARANI, K. B. et al. Non alcoholic fatty liver disease in southern Iran: a population based study. **Hepatitis Monthly**, v. 13, n. 5, p. 1-7, 2013.

LAZO, M. et al. Prevalence of Nonalcoholic Fatty Liver Disease in the United States: The Third National Health and Nutrition Examination Survey, 1988–1994. **American Journal of Epidemiology**, v. 178, n. 1, p. 38-45, 2013.

LI, W. et al. Comparison of effects of obesity and non-alcoholic fatty liver disease on incidence of type 2 diabetes mellitus. **World Journal of Gastroenterology**, v. 21, n. 32, p. 9607-9613, 2015.

LOOMBA, R.; SANYALA, J. The global NAFLD epidemic. **Nature Reviews Gastroenterology & Hepatology**, v. 10, n. 11, p. 868-690, 2013.

MACHADO, M. V.; CORTEZ-PINTO, H. Non-alcoholic fatty liver disease: What the clinician needs to know. **World Journal of Gastroenterology**, v. 20, n. 36, p. 12956-12980, 2014.

MIKOLASEVIC, I. et al. Nonalcoholic fatty liver disease - A multisystem disease? **World Journal of Gastroenterology**, v. 22, n. 43, p. 9488-9505, 2016.

NOVAKOVIĆ, T. et al. Cardiovascular disease risk factors in patients with non-alcoholic fatty liver disease. **Medicinski Pregled**, v. 66, n. 1, p. 24-31, 2013.

PANG, Q. et al. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. **World Journal of Gastroenterology**, v. 21, n. 5, p. 1650-1662, 2015.



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RESS, C.; KASER, S. Mechanisms of intrahepatic triglyceride accumulation. **World Journal of Gastroenterology**, v. 22, n. 4, p. 1664-1673, 2016.

SAADEH, S. et al. The utility of radiological imaging in nonalcoholic fatty liver disease. **Gastroenterology**, v. 123, n. 3, p. 745-750, 2002.

SCHILD, Z.; SANTOS, L. N.; ALVES, M. K. Doença hepática gordurosa não alcoólica e sua relação com síndrome metabólica no pré-operatório de pacientes submetidos à cirurgia bariátrica. **Revista da Associação Médica Brasileira**, v. 59, n. 2, p. 155-160, 2013.

WILLIAMS, C. D. et al. Prevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy: a prospective study. **Gastroenterology**, v. 140, n. 1, p. 124-131, 2011.

WONG, V. W. Nonalcoholic fatty liver disease in Asia: a story of growth. **Journal of Gastroenterology and Hepatology**, v. 28, n. 1, p. 18-23, 2013.

XAVIER, H. T. et al. V Diretriz brasileira de dislipidemias e prevenção da aterosclerose. **Arquivos Brasileiros de Cardiologia**, v. 101, n. 4, p. 1-20, 2013.

ZAMORA-ALVIZO, E. L. et al. Prevalence of Non-alcoholic Steatohepatitis in Patients with Metabolic Syndrome. **Atención Familiar**, v. 20, n. 1, p. 16-20, 2013.



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Tables

**Table 1.** Sociodemographic and anthropometric numeric variables.

|        | Steatosis degree | Percentiles |        |        | N  | P     |
|--------|------------------|-------------|--------|--------|----|-------|
|        |                  | 25          | 50     | 75     |    |       |
| Weight | Grade 1          | 65.85       | 76.00  | 88.60  | 65 | 0,026 |
|        | Grade 2          | 69.28       | 80.90  | 91.53  | 54 |       |
|        | Grade 3          | 78.28       | 101.70 | 123.03 | 8  |       |
| WC     | Grade 1          | 90.00       | 99.00  | 104.00 | 63 | 0,006 |
|        | Grade 2          | 93.75       | 100.40 | 109.00 | 50 |       |
|        | Grade 3          | 103.25      | 112.00 | 127.65 | 8  |       |
| HC     | Grade 1          | 97.35       | 102.55 | 108.25 | 54 | 0,023 |
|        | Grade 2          | 98.78       | 104.00 | 114.90 | 44 |       |
|        | Grade 3          | 103.53      | 120.90 | 127.25 | 6  |       |

P: Level of significance, WC: Waist Circumference; HC: Hip Circumference.



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**Table 2.** Biochemical and insulin resistance numeric variables.

|               | Steatosis grade | Percent |        |        | N  | P      |
|---------------|-----------------|---------|--------|--------|----|--------|
|               |                 | 25      | 50     | 75     |    |        |
| AST           | Grade 1         | 16.00   | 19.00  | 23.00  | 68 | <0,001 |
|               | Grade 2         | 18.00   | 23.00  | 31.25  | 58 |        |
|               | Grade 3         | 24.00   | 28.00  | 40.00  | 9  |        |
| ALT           | Grade 1         | 17.00   | 24.00  | 28.50  | 69 | 0,001  |
|               | Grade 2         | 20.75   | 29.50  | 44.00  | 58 |        |
|               | Grade 3         | 28.50   | 45.00  | 73.00  | 9  |        |
| GGT           | Grade 1         | 21.50   | 34.00  | 55.50  | 65 | 0,034  |
|               | Grade 2         | 28.50   | 39.50  | 62.00  | 56 |        |
|               | Grade 3         | 45.25   | 57.00  | 80.25  | 6  |        |
| Blood Glucose | Grade 1         | 83.00   | 90.50  | 99.75  | 68 | <0,001 |
|               | Grade 2         | 89.00   | 96.00  | 108.00 | 55 |        |
|               | Grade 3         | 100.50  | 114.00 | 143.00 | 9  |        |
| Triglycerides | Grade 1         | 101.00  | 128.00 | 168.00 | 71 | 0,001  |
|               | Grade 2         | 112.50  | 176.00 | 230.00 | 61 |        |
|               | Grade 3         | 136.00  | 258.00 | 376.00 | 9  |        |
| Insulin       | Grade 1         | 7.90    | 9.95   | 14.38  | 40 | 0,004  |
|               | Grade 2         | 9.73    | 11.55  | 17.78  | 36 |        |
|               | Grade 3         | 14.10   | 27.20  | 53.10  | 6  |        |
| HOMA-IR       | Grade 1         | 1.91    | 2.27   | 3.53   | 37 | 0,007  |
|               | Grade 2         | 2.05    | 2.63   | 5.23   | 35 |        |
|               | Grade 3         | 4.20    | 6.98   | 27.20  | 5  |        |

P: Level of significance, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, GGT: Gama-Glutamyltransferase, HOMA-IR: Homeostatic model assessment.





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**Table 3.** Categorical variables.

| Variables |                     | Classification Grades |         |         | P     |
|-----------|---------------------|-----------------------|---------|---------|-------|
|           |                     | Grade 1               | Grade 2 | Grade 3 |       |
| Sex       | Female              | 87                    | 57      | 9       | 0.021 |
|           | Male                | 32                    | 37      | 11      |       |
| Income    | Up to 1.5 wages     | 54                    | 52      | 4       | 0.006 |
|           | 1,5 to 4,5 wages    | 56                    | 29      | 14      |       |
|           | More than 4.5 wages | 7                     | 12      | 2       |       |

P: Level of significance.

**Table 4.** Logistic regression.

| Variables     | B      | E. P. | P      | Exp (B) |
|---------------|--------|-------|--------|---------|
| LDL           | -0.011 | 0.006 | 0.053  | 0.989   |
| Triglycerides | 0.012  | 0.003 | <0,001 | 1.012   |
| Constant      | -0.415 | 0.833 | 0.618  | 0.660   |

n = 136

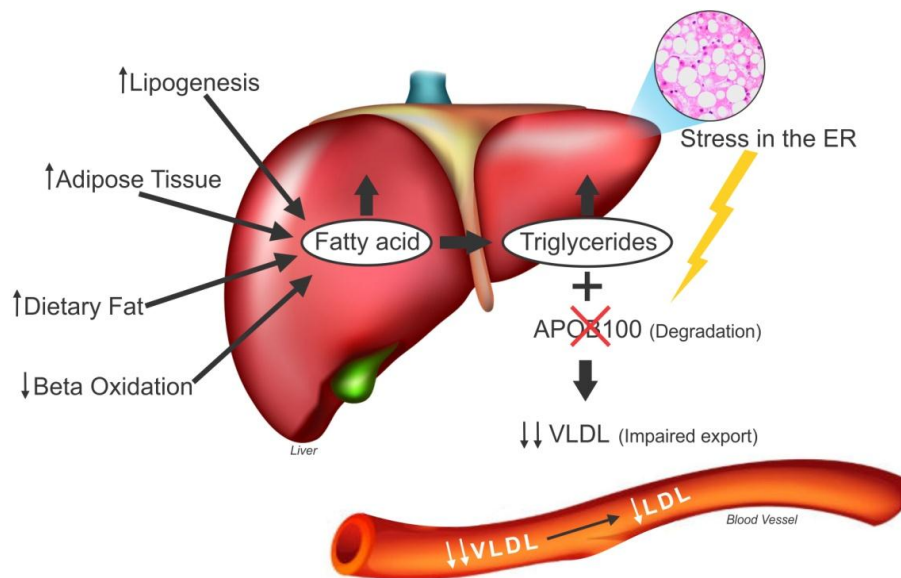
B: Parameter of the equation for each variable and the constant of the model generated, E. P.: Standard error (of B), Exp (B): OR, P: Level of significance, LDL: Low density lipoprotein.



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**Figure**

**NAFLD with VLDL Export Deficiency**



**Figure 1.** NAFLD with VLDL Export Deficiency.

