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Original article

Nonalcoholic fatty liver disease and its association with metabolic syndrome in the preoperative period in patients undergoing bariatric surgery☆

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A B S T R A C T

Objective: To investigate the association between nonalcoholic fatty liver disease (NAFLD) and metabolic syndrome (MS) in the preoperative period in patients undergoing bariatric surgery.

Methods: A total of 68 medical records of patients from a center for advanced treatment of obesity in the city of Caxias do Sul, state of Rio Grande do Sul, Brazil, were reviewed. The variables analyzed were gender, age, biochemical parameters (fasting glucose, HDL-cholesterol and triglycerides), abdominal ultrasound, blood pressure, and anthropometric data (weight, height, waist circumference, and body mass index [BMI]). The diagnosis of NAFLD was obtained by abdominal ultrasonography; the diagnosis of of MS was obtained according to the protocol described by the National Cholesterol Education Program's Adult Treatment Panel III, updated by the American Heart Association; and the National Heart, Lung, and Blood Institute.

Results: 72.1% (n = 49) of the sample consisted of females, and the mean age for the sample was 37.57 ± 10.29 years. The mean weight was 123.14 ± 25.40 kg, mean height was 1.67 ± 0.09 m, and mean BMI was 56.24 ± 9.30 kg/ m². A total of 60% (n = 27) of patients with MS (p = 0.008), 63.4% (n = 26) of patients with hypertension (p = 0.013), and 66.7% (n = 18) of patients with altered glucose levels (p = 0.028) were diagnosed with NAFLD.

Conclusion: The results of this study showed that the diagnosis of MS, as well as the presence of disorders associated with this syndrome (obesity, hypertension, and high blood glucose levels) are strongly associated with the presence of NAFLD.

Doença hepática gordurosa não alcoólica e sua relação com a síndrome metabólica no pré-operatório de pacientes submetidos à cirurgia bariátrica

Palavras-chave:
Esteatose hepática
Obesidade

R E S U M O

Objetivo: Verificar a relação entre a doença hepática gordurosa não alcoólica (DHGNA) e síndrome metabólica (SM) no período pré-operatório de pacientes submetidos à cirurgia bariátrica.

☆Study conducted at Centro de Tratamento Avançado da Obesidade (CENTROBESI), Caxias do Sul, RS, Brazil

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Síndrome metabólica
Cirurgia bariátrica

Métodos: Foram revisados 68 prontuários de pacientes de um centro de tratamento avançado da obesidade da cidade de Caxias do Sul – RS. As variáveis estudadas foram gênero, idade, parâmetros bioquímicos (nível de glicose em jejum, colesterol HDL e triglicerídeos), ultrassonografia abdominal, pressão arterial e antropometria (peso, estatura, circunferência abdominal e índice de massa corporal [IMC]). O diagnóstico da DHGNA foi obtido pela ultrassonografia abdominal e o da SM através do protocolo descrito pelo National Cholesterol Education Program's Adult Treatment Panel III, atualizado pela American Heart Association; e a National Heart, Lung, and Blood Institute.
Resultados: 72,1% (n = 49) da amostra foi composta pelo gênero feminino e a média de idade encontrada na população foi de 37,57±10,29 anos. A média de peso entre eles foi de 123,14±25,40 kg, a altura de 1,67±0,09 m e o valor médio de IMC de 56,24±9,30 kg/m^2. Apresentaram diagnóstico de DHGNA 60% (n = 27) dos pacientes portadores de SM (p = 0,008), 63,4% (n = 26) dos pacientes portadores de hipertensão arterial (p = 0,013) e 66,7% (n = 18) dos pacientes que apresentaram níveis glicêmicos alterados (p = 0,028).
Conclusão: Os resultados do presente estudo mostraram que o diagnóstico de SM, bem como a presença das desordens associadas a esta (obesidade, hipertensão arterial e elevação nos níveis glicêmicos) estão fortemente relacionadas à presença da DHGNA.

Introduction

Considered a major public health problem, obesity has been increasing its prevalence at an alarming rate in recent years. Changes in the lifestyle and education of the population, which has become more sedentary and has acquired inadequate eating habits, have been identified as the main causes of this increase.[1,2] In Brazil, according to the Household Budget Survey (HBS), conducted in 2008 and 2009, 50.1% of men and 48% of women are overweight.[3] Another study performed by the Surveillance of Risk Factors and Protection for Chronic Diseases through Telephone Interviews (Vigilância de Fatores de Risco e Proteção para Doenças Crônicas por Inquérito Telefônico – VIGITEL) in 2011 showed that 15.8% of the Brazilian adult population is obese.[4] Along with the increase in obesity, the prevalence of chronic diseases has also grown. Among them, nonalcoholic fatty liver disease (NAFLD)[5,6] and the metabolic syndrome (MS) must be highlighted.[7]

NAFLD is a condition defined by an abnormal clinico-pathological accumulation of triglycerides in hepatocytes, exceeding 5% of the liver weight.[8] It has different stages, ranging from simple accumulation (NAFLD) to accumulation with inflammation (non-alcoholic steatohepatitis [NASH]), and can progress to fibrosis, cirrhosis, or hepatocellular carcinoma.[5]

It is estimated that NAFLD affects 10% to 24% of the population in many countries worldwide. This prevalence grows alarmingly in the obese population, reaching 57.5% to 74%.[9]

NAFLD is strongly associated with insulin resistance, diabetes mellitus type II, obesity, and dyslipidemia.[10] It is more common among men and its prevalence increases with age.[11]

Its diagnosis requires the exclusion of alcoholic liver disease (ALD) and viral hepatitis,[12] and can be attained by abdominal ultrasound, a noninvasive, inexpensive and easily accessible method that can detect NASH levels as mild, moderate, or severe, with a sensitivity of 60% to 94% and specificity of 88% to 95%.[13-15]

MS is defined as a complex disorder represented by a set of cardiovascular risk factors that are typically associated with insulin resistance and central adiposity.[7] Among the main factors contributing to its occurrence are genetic predisposition, inadequate diet, and physical inactivity.[16,17] Although not part of the diagnostic criteria of MS, NAFLD is frequently associated with this disorder.[7]

Therapeutic treatment for NAFLD involves weight loss through dietary changes, associated or not to physical exercise, or bariatric surgery.[6] Body weight reduction through bariatric surgery leads to an improvement in patients' biochemical and histological profiles, as well as in steatosis and inflammation in patients with NAFLD.[6] Thus, the present study aimed to investigate the relationship between NAFLD and metabolic syndrome in the preoperative period in patients undergoing bariatric surgery.

Methods

This was a retrospective cross-sectional study that reviewed the medical records of patients from a center of advanced treatment of obesity in the city of Caxias do Sul, state of Rio Grande do Sul, Brazil. The study was approved by the Research Ethics Committee of Faculdade Nossa Senhora de Fátima.

The sample consisted of 199 medical records of obese patients who underwent bariatric surgery between 2008 and April, 2012. Of these, 68 records met the inclusion criteria, which were patients of both genders, aged ≥ 20 years, who had abdominal ultrasonography. All patients had a body mass index (BMI) ≥ 40 kg/m², or ≥ 35 kg/m² associated with one or more comorbidities (hypertension, dyslipidemia, or altered glucose levels). None of these patients had alcohol consumption > 20 g of ethanol per day or had a positive diagnosis of viral hepatitis.

The studied variables were gender, age, biochemical parameters (fasting glucose, HDL-cholesterol, and triglycerides), abdominal ultrasound, blood pressure, and anthropometrics (weight, height, waist circumference, and BMI).

Grade II obesity was considered in patients with BMI 35.0-39.9 kg/m², and grade III obesity in those with BMI ≥ 40.0 kg/m².[18] NAFLD diagnosis was obtained through abdominal ultrasonography, which classifies NASH as mild (slight diffuse increase of fine echoes in the hepatic parenchyma, with normal visualization of the diaphragm and intrahepatic vessel walls), moderate (moderate diffuse increase of fine echoes with slight difficulty in visualization of the vascular wall and diaphragm), or severe (significant increase of fine echoes with poor visualization of the diaphragm, vascular walls, and posterior segments of the right lobe, which could increase liver volume).[19]

The diagnosis of MS was attained using the protocol described by the National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III, 2001), updated by the American Heart Association, and the National Heart, Lung, and Blood Institute (AHA / NHLBI, 2005), which considers that the patient has MS when three or more risk factors described below are associated: high waist circumference (≥ 102 cm for men and ≥ 88 cm for women), high triglycerides (≥ 150 mg/dL or specific treatment), reduced HDL cholesterol (< 40 mg/dL for men and < 50 mg/dL for women, or specific treatment), high blood pressure (≥ 130 / ≥ 85 mmHg, or drug treatment for hypertension), elevated fasting glucose (≥ 100 mg/dL, or recently diagnosed diabetes mellitus type II).[20-22]

Data were entered in duplicate into a Microsoft Excel 2007® spreadsheet and were analyzed using Stata software, version 11.0. Analyses of data consistency were initially conducted, followed by descriptive analyses. The associations of the outcome "NAFLD" with the "MS" exposure and other explanatory variables were tested using the chi-squared test and linear association, and prevalence ratios with their respective 95% confidence intervals (95% CI) were calculated.

Results

The medical records of 68 patients were evaluated, of which 72.1% (n = 49) were of female patients; the mean age of the sample was 37.57 ± 10.29 years.

The study population had a mean weight of 123.14 ± 25.40 kg, mean height of 1.67 ± 0.09 m, and a mean BMI of 56.24 ± 9.30 kg/m². Considering the classification of BMI,[18] 35.3% (n = 24) patients were identified as having grade II obesity, and 64.7% (n = 44) as grade III obesity.

NASH, diagnosed by abdominal ultrasonography, was present in 50% (n = 34) of patients; 20.3% (n = 14) presented mild NASH, 17.4% (n = 12), moderate, and 11.6% (n = 8) severe. The disease was more prevalent among male patients (52.6%), but no statistical significance was found between genders. Regarding age range, a linear trend was observed, where there was an increase in the prevalence of the outcome with increasing age, which was not statistically significant (p = 0.673), as shown in Figure 1.

MS was present in 66.2% (n = 45) of studied patients. Among the criteria for this diagnosis, 60.3% (n = 41) had hypertension, 39.7% (n = 27) had altered glucose levels, 100% (n = 68) had high waist circumference, 57.4% (n = 39) had hypertriglyceridemia, and 45.6% (n = 31) had reduced HDL cholesterol levels.

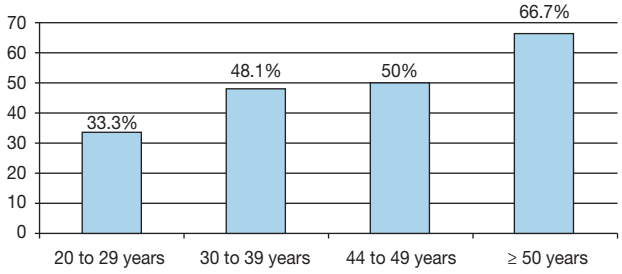

Fig. 1 – Prevalence of nonalcoholic fatty liver disease in obese patients submitted to bariatric surgery by age (p = 0.673).

The population studied had mean glucose level of 106.94 ± 32.84 mg/dL and mean waist circumference of 121.06 ± 16.67 cm. Mean triglyceride levels were 196.09 ± 119.73 mg/dL, and mean HDL cholesterol was 49.51 ± 11.92 mg/dL. Blood pressure classification followed the diagnosis of hypertension that was already established in the patients' charts.

Table 1 shows that among the 41 (60.3%) patients with hypertension, 26 (63.4%) had a diagnosis of NASH, showing an increased risk for developing the disease in the presence of hypertension (p = 0.002).

The presence of altered glucose levels in patients also showed to be statistically associated with increased prevalence of NASH (p = 0.015). For this variable, it was found that among the 27 (39.7%) patients with altered glucose levels, 18 (66.7%) had a diagnosis of NASH.

The study demonstrated that among the 39 (57.4%) patients with hypertriglyceridemia, 20 (51.3%) had a diagnosis of NASH. A statistically significant result was not observed between the variable and the outcome (p = 0.598), but it showed that patients with hypertriglyceridemia have an 8% higher risk of developing the outcome when compared to those who do not have this alteration.

Patients that had inadequate levels of HDL-cholesterol had a higher prevalence of NASH (58.1%) when compared with patients with adequate HDL levels (40.5%). The difference between the prevalences showed no statistical significance (p = 0.150), but showed that patients who have adequate levels of HDL cholesterol are 72% less likely to develop the outcome, as compared to those who have inadequate HDL levels.

When analyzing the variable of greatest interest for this study, it was found that the presence of MS was statistically associated with the development of NASH (p = 0.008). It was observed that among the 66.2% (n = 45) patients with MS, 60% (n = 27) were diagnosed with NASH by abdominal ultrasonography. When separated into the NASH classification of mild, moderate, and severe, it was found that 100% of patients diagnosed with moderate NASH, 83.3% of patients with severe NASH, and 61.54% of patients with mild NASH were diagnosed with MS.

Table 1 – Sample distribution according to patients' demographic and health variables and prevalence of hepatic steatosis in patients undergoing bariatric surgery performed in Caxias do Sul, Rio Grande do Sul, Brazil, 2012 (n = 68).

	Frequency	Prevalence		PR
	n (%)	Steatosis	p-value	(CI)
*Gender**			0.673	
Female	49 (72.1)	46.9		1
Male	19 (27.9)	52.9		1.09 (0.62-1.92)
*Age range**			0.395	
20-29	15 (22.1)	33.3		1
30-39	27 (39.7)	48.1		1.43 (0.56-3.64)
40-49	14 (20.6)	50.0		1.62 (0.61-4.31)
≥ 50 years	12 (17.6)	66.7		2.16 (0.86-5.41)
*BMI**			0.858	
Grade II obesity	24 (35.3)	50.0		
Grade III obesity	44 (64.7)	47.7		
*Arterial hypertension**			0.002	
Yes	41 (60.3)	63.4		1
No	27 (39.7)	25.9		0.41 (0.20-0.83)
*Altered glycemia**			0.015	
Yes	27 (39.7)	66.7		1
No	41 (60.9)	36.6		0.56 (0.33-0.93)
*Hypertriglyceridemia**			0.598	
Yes	39 (57.4)	51.3		1
No	29 (42.6)	44.8		0.92 (0.45-1.57)
*HDL cholesterol classification**			0.150	
Adequate	37 (54.4)	40.5		1
Inadequate	31 (45.6)	58.1		1.28 (0.76-2.16)
*Metabolic syndrome**			0.008	
Yes	45 (66.2)	60.0		1
No	23 (33.8)	26.1		0.44 (0.21-0.93)

CI, confidence interval; BMI, body mass index; HDL, high density lipoprotein.
*p-value per Pearson's chi-square test.

Discussion

Obesity has become a major public health problem in both developed and developing countries.[1] Currently, studies show that obesity has been identified as a significant risk factor for the increase in non-transmissible chronic diseases, among them, NAFLD and MS.[5-7]

It is estimated that NAFLD affects 57.5% to 74% of the obese population in several countries worldwide,[9] and this prevalence has alarmingly increased in patients undergoing bariatric surgery, ranging from 84% to 96%.[23] Unlike what has been suggested by Clark et al.,[23] the present study showed that 50% of patients undergoing bariatric surgery have NAFLD.

The findings regarding age and gender of the study population are very close to those found in a study conducted in Brazil involving 1,280 patients, in which the mean age of patients with NAFLD was 49.8 (± 13.59) years and of which 53.3% were males.[11]

Regarding the diagnosis of NAFLD, a liver biopsy is still considered the gold standard, but it is a costly, invasive method associated with a low, but significant risk for patients who undergo this procedure.[24] For this reason, the use of an imaging test such as abdominal ultrasonography to screen for NAFLD is a good method, as it has low cost when compared to others, is noninvasive, and is available in almost all centers. The abdominal ultrasound, a method used in this study, is used to detect NASH levels as mild, moderate, or severe, having good sensitivity and specificity.[13-15] It is noteworthy that no imaging test can distinguish NASH from NAFLD, or define the severity of liver disorders. The method that can make this distinction, and also assess the degree of fibrosis, excluding other causes of liver disease and determining disease prognosis is liver biopsy, but for the reasons already mentioned, in clinical practice this procedure is only indicated for patients with higher likelihood of liver fibrosis.[25,26]

Although it is not part of the diagnostic criteria, NAFLD is often associated with MS.[7] Authors have shown that over 90% of patients with NAFLD had at least one of the parameters related to the diagnosis of MS, and approximately 33% had the syndrome.[27] A study of 69 patients aiming to describe this association demonstrated an even higher prevalence, concluding that MS was three times more common in the group who had NAFLD diagnosed by abdominal ultrasonography than the group with no evidence of NAFLD.[28] This is in accordance with the results found in the present study, which demonstrated that 60% of patients with MS have NAFLD. These findings suggest that NAFLD can be described as the liver manifestation of metabolic syndrome.[27,29]

Diabetes mellitus affects approximately 12 million people in Brazil.[30] NAFLD has been strongly associated with patients that have increased glucose levels, with a prevalence of

62%.[31] In the present study, the prevalence was 66.7%, which is very similar to the aforementioned. A study of 100 patients with diabetes mellitus type II showed a 49% incidence of NAFLD,[32] while a second study diagnosed NAFLD in 42% of such patients,[33] confirming that the increase in blood glucose is a strong risk factor for NAFLD.

Arterial hypertension has also been shown to be a common finding in patients with NAFLD.[34] Cotrim et al.[11] reported that 64% of patients with NAFLD were hypertensive, a prevalence that is consistent with that found in this study.

Dyslipidemia is a disorder that is often associated with the diagnosis of NASH.[10] A study of 304 patients with a NAFLD diagnosis reported that 64% had hypertriglyceridemia, and 30% to 42% of cases had decreased HDL-cholesterol levels.[27] These results differ from those found in the present study, which showed a lower prevalence of hypertriglyceridemia and a higher prevalence of altered levels of HDL cholesterol. These differences in results may have been due to the fact that the sample population of this study consisted of an insufficient number of patients.

Conclusion

The present study showed that both the presence of MS and the disorders associated with it (obesity, hypertension, and high blood glucose levels) are strongly associated with the presence of NAFLD. Results suggest that NAFLD can be considered the hepatic manifestation of MS.

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Conflict of interest

All authors declare to have no conflict of interest.

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