Review Article
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Non-alcoholic hepatic steatosis and its relation with metabolic syndrome

Abstract

Objective: The aim of this study is to investigate the relationship between Non-Alcoholic Hepatic Steatosis (NASH) and Metabolic Syndrome (MS).

Bibliographic review: NASH is a common liver condition in western industrialized countries, affecting individuals who do not consume alcohol. The pathogenesis of NASH involves environmental, genetic, and gut microbiota factors, and there is a strong association between NASH and MS, a condition that increases the risk of cardiovascular disease and type 2 diabetes. The relationship between NASH and MS is complex, with both sharing features such as obesity, insulin resistance and inflammation. The study analyzed 13 articles and found a strong association between NASH and MS. Patients with NASH often have features of MS, including type 2 diabetes, obesity, and hypertension. Furthermore, the presence of MS is related to a higher risk of liver disease progression. The relationship between these conditions appears to be driven by factors such as elevated glucose, insulin resistance and increased visceral fat.

Final considerations: NASH and MS are conditions that pose significant public health challenges, especially in developed countries. The prevention and control of these conditions are closely linked to the promotion of lifestyle changes, including a healthy diet and physical exercise. These changes can have a positive impact on the incidence and progression of both NASH and MS, improving quality of life and reducing the risks associated with these pathological conditions. In addition, the importance of considering genetics and other individual factors in the evaluation and management of these multifactorial conditions is highlighted.

Keywords: metabolic syndrome, obesity, non-alcoholic fatty liver disease

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Abbreviations: NASH, non-alcoholic fatty liver disease; MS, metabolic syndrome

Introduction

Non-alcoholic fatty liver disease (NASH) is the most common liver condition in Western industrialized nations, affecting people who do not drink alcohol.[1] Non-alcoholic liver disease management guidelines in the United States define NASH as steatosis with ≥5% fat infiltration on imaging or histology and without the use of alcohol, drugs, or the presence of virus-induced steatosis.[2] The pathogenesis of NASH involves multiple factors characterized by the simultaneous occurrence of events involving a complex interaction between environmental factors, patient genetics and intestinal microbiota. This interaction may promote steatosis or progressive liver damage.[3]

NASH and Metabolic Syndrome (MetS) have a close connection, and patients with NASH generally present one or more elements of MetS.[1] MetS, also known as insulin resistance syndrome, is characterized as a set of risk factors for cardiovascular diseases (CVD) and type 2 diabetes mellitus (DM2), which are more commonly identified together than in isolation.[2,3] It has been proven that adults who have MS have twice the chance of developing CVD in the next five to ten years, when compared to adults without MS, thus making it a significant challenge for public health worldwide.[4] Therefore, it is a clinical condition that, in addition to the excessive accumulation of adipose tissue (manifested by increased waist circumference and/or body mass index), also includes hypertension, insulin resistance and dyslipidemia.[5]

Its pathophysiology is complex and not entirely clear, but abdominal adiposity and insulin resistance are considered central elements for its development.[1,4] Data reveal complex interactions between internal factors, such as genetic backgrounds, and external factors, such as physical activity and diet.[5] Inflammation can also be an important contributing factor to metabolic dysfunction, as it presents a chronic pro-inflammatory state with elevation of inflammatory cytokines (such as tumor necrosis factor-α and interleukin-6) and acute-phase reactants (such as protein C-reactive and fibrinogen).[3,4] Data show that inflammatory cytokines associated with MS stimulate insulin resistance in adipose, muscle and liver tissue.[6]

NASH is considered a component of metabolic syndrome, as both are related to similar metabolic changes.[4] Currently, the diagnostic criteria for MetS is the coincidence of three or more of the following factors: high abdominal circumference (≥102cm in men and ≥88cm in women) or body mass index (BMI) > 30 kg/m²; elevated triglycerides (≥150 mg/dL or 1.7 mmol/L) or treatment for elevated triglycerides; low-density lipoprotein (LDL) cholesterol (<40 mg/dL or 1.03 mmol/L in men and <50 mg/dL or 1.3 mmol/L in women) or treatment for low HDL cholesterol; arterial hypertension (systolic ≥130 mmHg and diastolic ≥85 mmHg) or treatment for systemic arterial hypertension; and elevated fasting blood glucose (≥100 mg/dL) or treatment for type 2 diabetes.[7]

Therefore, NASH may contribute to the development of other conditions associated with the metabolic syndrome, such as type 2 diabetes, cardiovascular disease and chronic kidney disease. Therefore, this review aims to establish the relationship between NASH and the development of MS.

Material and methods

The study was produced from bibliographic reviews in the databases Sicentific Eletronic Library Online (Scielo), National Library of Medicine (PUBMED), Latin American and Caribbean Literature in helth Science Direct- Elsevier and in the Mais Collection. Thus, in order to develop the work, steps were established for the execution of the article, these being the definition of the theme, listing its inclusion and exclusion criteria, the search for assertive information with specific criteria, guided in relation to the theme, as well as the analysis and interpretation of the results obtained for the production of the article. It should be noted that the preparation of the review was limited to the theme of non-alcoholic fatty liver disease and its relationship with the metabolic syndrome, using articles and books published in Portuguese and English, given its international notoriety.

It is important to highlight that this article did not require approval by the research ethics committee (CEP), as it is a review study (Resolution No. 510 of April 2016 of the Local Committee).

Results and discussion

A total of 167 articles were found in the databases, of which 13 met the inclusion criteria, according to the title, abstract reading, population, study period and adequacy to the searched theme. Thus, the systematization of the analyzed materials allowed observing that the Metabolic Syndrome has a significant relationship with Non-Alcoholic Hepatic Steatosis, also called Non-Alcoholic Fatty Liver Disease (NAFLD).

According to Rector et al.[12], about 90% of patients with NAFLD have one or more features of the Metabolic Syndrome, and approximately 33% have the complete syndrome. Furthermore, according to Hamaguchi et al.,[4] in addition to MS increasing the risk of developing NAFLD by 4 to 8 times, it is also associated with less regression of liver disease.

In a cross-sectional study, patients with Non-Alcoholic Fatty Liver Disease, from the Gastroenterology Service of the Hospital das Clínicas, Faculty of Medicine, University of São Paulo (HC-FMUSP), between January 2009 and August 2012 were evaluated. 360 patients were followed, from which only 207 were selected. Inclusion criteria were: patient with NAFLD aged between 18 and 75 years, of both sexes, liver biopsy compatible with NAFLD and signed informed consent.[7,8]

Exclusion criteria were other causes of chronic liver disease and refusal to collaborate with the research. Thus, in this study, it was observed that the most advanced degrees of fibrosis occur in patients diagnosed with DM (66.9% vs 37.5%; p= 0.007), in addition to being more obese (32.3% vd 29%; p=0.003). It was also observed that the serum levels of glucose and insulin increased significantly, according to the presence of Non-Alcoholic Hepatic Steatosis (NASH). The frequency of MS was higher in patients with NASH (82.4% vs 62.5%; p= 0.03).[9]

Furthermore, according to a study conducted by Chaves et al.,[2] a significant association was identified between the diagnosis of MetS and non-alcoholic hepatic steatosis (NASH) ($\chi 2 = 6.84$; $p = 0.01$).[2,3] Regarding the diagnostic components of MetS, it was found a positive and significant association between HDL-c, which is high-density cholesterol ($p = 0.05$), waist circumference ($p < 0.05$) and arterial hypertension ($\chi 2 = 4.195$; $p = 0.041$) with NASH. The HOMA-IR index ($p < 0.001$) also showed a positive association with liver disease.[10]

The results of this study demonstrated the relationship between NASH and a set of risk factors that represent a complex disorder of modern civilization, MS.[5] Therefore, MS was associated with NASH through the following variables: positive diagnosis of type 2 DM, presence of obesity, high serum levels of glucose and insulin, high HDL-c, waist circumference with high adipose tissue, individuals conditioned individuals with high blood pressure and high HOMA-IR index scores.[6,7] Moreover, when risk factors are positive and increased, they are also indicators of more advanced degrees of fibrosis.[8,9]

It is inferred that the presence of MS increases the probability of a patient being affected by NASH rather than simple steatosis, due to the excess circulation of fats in the blood. Therefore, an individual's lifestyle is a crucial factor to prevent MS and, consequently, the progression of NASH.[3,4,6]

In this way, it directs itself to a questioning about the growing picture of NASH in children and adolescents, due to childhood obesity, which is considered a worldwide epidemic by the World Health Organization (WHO).[1,3] This scenario is fostered by a refusal to adopt or maintain healthy eating habits and a lack of regular physical activity. Children with obesity are 75% more likely to become obese adolescents, and 89% of obese adolescents may become obese adults.[11,12]

Considering that both NASH and MS are multifactorial conditions, which include environmental factors together with genes, it should be noted that in this study, priority was given to the clinical characteristics observed in patients, with no exploration and analysis of the frequencies of genetic manifestations or of the genes affected in these pathologies.[13]

Conclusion

Metabolic syndrome and (NASH) are constantly increasing nowadays, especially in developed countries, which constitute a significant challenge to public health. The pathogenesis of NASH occurs as a multifactorial disease that is interrelated with environmental, genetic, and intestinal microbiota factors, in addition to being closely related to the Metabolic Syndrome and obesity, as well as other metabolic components, such as dyslipidemia, hyperinsulinemia, and insulin resistance.

Therefore, it is necessary to encourage changes in lifestyle, changes in eating habits and physical activity, which are primarily recommended for health promotion and prevention. Thus, it can be seen that changes in these patterns can significantly influence their incidence, thereby improving the quality of life, which may reduce the occurrence and progression of both pathological conditions.

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Conflicts of interest

The authors declare no conflicts of interest.

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