Causes of erectile dysfunction in non-alcoholic fatty liver disease

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Abstract

Background and Aim: Erectile dysfunction (ED) is an important and commonly seen disorder in patients with non-alcoholic fatty liver disease (NAFLD). The objective of this study was to assess the rate of ED and its causes in a group of NAFLD patients.

Materials and Methods: The International Index of Erectile Function questionnaire (IIEF-5) was used to evaluate the presence, causes, and severity of ED. Participants with an IIEF-5 score of <22 who agreed to undergo a urological evaluation were referred to a urologist for further assessment.

Results: A total of 136 NAFLD patients were enrolled in the study. According to the IIEF-5, 68 (50.0%) patients had ED. Multivariate analysis indicated that older age, obesity, and hypertension were associated with ED. Seventeen patients had multiple etiological factors for ED. Psychogenic ED was identified in 19 patients (39.6%), vasculogenic ED in 35 patients (72.9%), drug-related ED in 3 patients (6.3%), and neurogenic ED in 6 patients (12.5%).

Conclusion: ED is frequently seen in NAFLD patients, which may, at least in part, be due to common risk factors. Vasculogenic dysfunction is the most common single source of ED in NAFLD patients. Nonetheless, all potential etiologies should be carefully investigated, with special attention given to psychogenic factors, since they may be more frequent and relevant than expected.

Keywords: Erectile dysfunction; fatty liver; International Index of Erectile Function; non-alcoholic fatty liver disease.

Introduction

Non-alcoholic fatty liver disease (NAFLD) is characterized by fat deposition in hepatocytes (>5% of liver weight) without a history of significant alcohol consumption or concurrent chronic liver disease.

Materials and Methods

The study was approved by the Marmara University Ethics Committee on December 2, 2016 (Study ID: 09.2016.593). The research was conducted in compliance with good clinical practice and the principles of the Declaration of Helsinki. All of the patients provided written, informed consent to participate.

Patients diagnosed with NAFLD between 2017 and 2018 at a single gastroenterology outpatient clinic were included in the study. Patients with cirrhosis were excluded. The diagnosis of NAFLD was established with evidence of hepatic steatosis observed using transabdominal ultrasonography in the absence of secondary causes of hepatic fat accumulation, such as significant alcohol consumption (≥30 g/day for men and ≥20 g/day for women), long-term use of steatogenic medication, monogenic hereditary disorders, viral or autoimmune hepatitis, hereditary hemochromatosis, or alpha 1-antitrypsin deficiency.
A detailed medical history was recorded and a physical examination was performed for all of the study patients. Clinical and laboratory data and anthropometric measurements were collected retrospectively from the hospital’s electronic database. Following a 12-hour fasting period, serum values of aspartate aminotransferase, alanine aminotransferase, platelet, albumin, total cholesterol, high-density lipoprotein, low-density lipoprotein cholesterol, triglycerides, plasma glucose concentration, and insulin level were measured as a part of routine follow-up tests for NAFLD patients and recorded. The body mass index (BMI) was calculated using the formula of the individual’s weight in kilograms divided by height in meters squared. Waist circumference was measured at the midpoint between the lower costal border and the iliac crest at the end of normal expiration, and hip circumference was measured at the maximum circumference around the buttocks.

ED was assessed using the International Index of Erectile Function questionnaire (IIEF-5). All of the participants completed the IIEF-5 questionnaire under the supervision of a physician. The total score of the questionnaire ranges from 5 to 25, and scores >21 were classified as the absence of ED. Participants with a score of <22 and who agreed to undergo a urological evaluation were referred to see a urologist (TES). A urogenital physical examination was performed and a urological medical history was recorded. The etiology of ED was evaluated and the pathophysiology was classified as vasculogenic, neurogenic, anatomical/structural, drug-induced, or mixed ED.

Normally distributed data were expressed as the mean±SD, and non-normally distributed data were presented as the median value. Variables were compared using an independent t-test or the Mann-Whitney U test according to the normality of distribution. A multivariate logistic regression model was used to assess the factors that contributed to ED. A p value of <0.05 was considered statistically significant.

## Results

A total of 136 patients with NAFLD were enrolled in this study. The mean age was 45.64±1.55 years. The gender orientation of all of the study participants was heterosexual. According to the IIEF-5, 68 (50.0%) patients had ED. In the group, 120 (88.2%) patients were married, 14 (10.3%) patients had a BMI between 18.5 kg/m² and 24.9 kg/m², 36 (26.5%) had a diagnosis of hypertension, 97 (71.3%) were smokers, and 72 (52.9%) had a fasting glucose level of ≥100 mg/dL or a prior diagnosis of diabetes mellitus (Table 1).

Multivariate analysis revealed that older age, obesity, and hypertension were associated with ED in NAFLD patients (p=0.003, 0.026, and 0.003, respectively) (Table 2).
Erectile dysfunction in NAFLD

The Marmara University Clinical Research [19–21] found that older age, obesity, and hypertension were associated with ED in patients with NAFLD. In the current research, Hasanain et al. [6] reported that obesity and hypertension were found to be associated with ED in our NAFLD cohort. Vascularogenic disorder was the most common etiology of ED in the group, which is similar to results for the general population. To the best of our knowledge, this is the first study to evaluate the underlying etiologies of ED in patients with NAFLD.

In an earlier study conducted by our team, the frequency of ED was 67.5% in patients with biopsy-proven NAFLD.[13] In the current research, ultrasound was used to screen for NAFLD and returned a lower rate of ED. This was likely due to the severity or stage of disease; in the previous cohort, there was a prominent nonalcoholic steatohepatitis (NASH) dominance, which is a more advanced stage of hepatic steatosis with inflammation. The lack of liver biopsy results precluded the calculation of the prevalence of NASH rates in the present study, which may be relevant to the interpretation of the findings. The rate of ED was 45.8% in a hospital-based study of 192 consecutive male patients that used radiological methods, rather than liver biopsy, to diagnose NAFLD.[11] That is to say, the modality used to detect NAFLD may have contributed to the differences between studies. The frequency of ED can be projected to be somewhere between 45% and 67% among patients with NAFLD.

The reported ED rates in NAFLD patients are far higher than that of the general population, which has been reported to be 18.4% among males over 20 years of age in the United States.[10] This may be related to common metabolic risk factors for NAFLD and ED, such as obesity and diabetes mellitus.[18–21] Given the significant proportion of patients with NAFLD suffering from ED, efforts to understand the causes and to find novel therapeutic approaches could have a substantial impact on the quality of life of this patient group.

Hasanain et al.[11] found that older age, obesity, and hypertension were significantly more frequent in patients with NAFLD and ED, but multivariate analysis yielded only age as a variable associated with ED. We found that obesity and hypertension were also associated with ED in patients with NAFLD, in addition to age. These factors are associated both with NAFLD and ED; the combination and potential interaction merits clarification in future studies.

To our knowledge, this is the first study to examine the underlying etiologies of ED in NAFLD patients. We found that 39.5% of the NAFLD patients had multiple etiologies of ED. The most common etiology in our study group was a vascularogenic disorder, which was probably linked to obesity, diabetes, or atherosclerosis. Notably, psychogenic ED was found in 39.6% of the NAFLD cases; thus, psychological disorders must also be evaluated carefully in NAFLD patients with concomitant ED.

Limitations of this research include the fact that it was a single-center study conducted with a small number of patients. Also, since this was a cross-sectional study, only the causes of ED in consecutive NAFLD patients who were diagnosed with ED were analyzed; the response to ED treatment was not evaluated. Future studies to examine the long-term results of ED treatment in NAFLD patients and the potential influence on the progress of NAFLD are warranted. In addition, a detailed endocrinological evaluation would add value to the findings of the present study.

In conclusion, ED is common in patients with NAFLD, and may be related to common risk factors. Vascularogenic ED is the most common single cause of ED in patients with NAFLD; however, all possible etiologies should be carefully assessed, and special attention should be given to psychogenic ED, since it has been detected in a non-negligible percentage of patients with NAFLD.

Discussion

The findings of the present study are a valuable contribution to the currently limited literature regarding the relationship between NAFLD and ED. The IIEF-5 questionnaire results indicated that there was an ED frequency of 50% among consecutive patients with NAFLD seen at a single tertiary center. As in the general population, older age, obesity, and hypertension were found to be associated with ED in our NAFLD cohort. Vascularogenic disorder was the most common etiology of ED in the group, which is similar to results for the general population. To the best of our knowledge, this is the first study to evaluate the underlying etiologies of ED in patients with NAFLD.

Table 3. Distribution of mixed ED etiologies in NAFLD patients

| Etiology             | Vasculogenic ED | Psychogenic ED | Neurogenic ED | Drug-related ED |
|----------------------|-----------------|----------------|---------------|----------------|
| Vasculogenic ED (n=35)| 8               | 5              | 3             |
| Psychogenic ED (n=16)| 8               | 1              | 0             |
| Neurogenic ED (n=6)  | 5               | 1              | 0             |
| Drug-related ED (n=3)| 3               | 0              | 0             |

The prevalence of NASH rates in the present study, which may be related to common metabolic risk factors for NAFLD and ED, such as obesity and diabetes mellitus.[18–21] Given the significant proportion of patients with NAFLD suffering from ED, efforts to understand the causes and to find novel therapeutic approaches could have a substantial impact on the quality of life of this patient group.

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