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Prevalence of Non-Alcoholic Fatty Liver Disease in Morbidly Obese Patients Undergoing Sleeve Bariatric Surgery in Iran and Association With Other Comorbid Conditions

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Background: Nonalcoholic fatty liver disease (NAFLD) is one of the most common causes of chronic liver disease including simple steatosis to nonalcoholic steatohepatitis (NASH). NASH could progress to cirrhosis and liver cancer. The prevalence of NAFLD is increasing by increasing the prevalence of obesity.
Objectives: This study was designed to determine the prevalence of NASH in morbidly obese patients undergoing sleeve bariatric surgery and its correlation with other comorbidities.
Patients and Methods: In this analytical cross-sectional study, 114 morbidly obese patients undergoing sleeve gastrectomy were selected. Liver ultrasonography was performed for all patients before surgery and NAFLD existence and its grade was determined by hyperechoic texture and fatty infiltration. The liver enzymes and lipid profile were also measured. Prevalence of NAFLD in these patients and its correlation with other comorbid conditions (e.g. diabetes mellitus, hyperlipidemia, hypertension, hypothyroidism and ischemic heart disease) were evaluated by SPSS software version 18.
Results: One hundred fourteen patients with a mean age of 33.96 ± 9.92 years and mean BMI of 43.61 ± 5.77 kg/m^2 were enrolled (48 males and 66 females). The prevalence of NAFLD was 16.7%. NAFLD existence was associated with systolic blood pressure, hyperlipidemia, hemoglobin, hematocrit, triglyceride, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase and potassium ($P < 0.05$).
Conclusions: According to high prevalence of NAFLD in morbidly obese patients undergoing sleeve gastrectomy in Iran, we suggest using gold standard diagnostic method to determine the exact NAFLD prevalence and evaluation of impact of sleeve surgery on NAFLD in short and long term follow-up periods.

Keywords: Non-alcoholic Fatty Liver Disease; Bariatric Surgery; Morbid Obesity; Prevalence

1. Background

Nonalcoholic fatty liver disease (NAFLD) is one of the most common causes of chronic liver disease in western countries characterized by accumulation of fat in liver cells in the absence of excessive alcohol consumption (1, 2). It includes simple steatosis, which can progress to nonalcoholic steatohepatitis (NASH). NASH can progress to cirrhosis and liver cancer. With increasing the prevalence of obesity, the impact and prevalence of NAFLD is increasing, thus in the coming decades, NASH would be the most common cause of advanced liver disease (3). Studies have shown that liver-related mortality in patients with nonalcoholic fatty liver was higher in patients with NASH than those without it (4). Many risk factors are involved in increased prevalence of fatty liver. According to previous studies, central obesity, type II diabetes, hyperlipidemia and hypertension are some of known risk factors of NAFLD (5). Prevalence of overweight and obesity is increasing and takes the place of smoking as the leading cause of preventable morbidity and mortality (6). The American Medical Association considered obesity as a disease. Obesity leads to fat deposition in nonadipose tissues called ectopic fat. The liver is one of these tissues and obesity is a major risk factor of NAFLD (7). The prevalence of NAFLD in obese individuals has been reported between 60% and 90% (8) and the mean prevalence of NASH has been reported 33% with a range of 10% to 56% (9). Weight loss is possible by lifestyle changes (behavior therapy) or bariatric surgery. Bariatric surgery is becoming popular with the increasing prevalence of obesity. There is increasing evidence

showing that weight loss after bariatric surgery can be helpful for patients with NASH (10). This improvement is associated with a reduction in metabolic parameters and the levels of inflammatory mediators (11). Sleeve gastrectomy also known as the vertical gastrectomy, is a newer bariatric procedure for the treatment of obesity and its related diseases. The sleeve operation is excision of the lateral aspect of the stomach, leaving a reduced tubular stomach (12-14). Although the American Society for Metabolic and Bariatric Surgery (ASMBS) and the American College of Surgeons (ACS) approved the safety of sleeve gastrectomy (15, 16), patients candidates for sleeve gastrectomy have better conditions in comparison of patients candidates for other bariatric methods in Iran (12, 13).

2. Objectives

This study was designed to determine the prevalence of NAFLD in morbidly obese patients undergoing sleeve bariatric surgery in Iran and association of NAFLD existence with other comorbid conditions.

3. Patients and Methods

This was an analytical cross-sectional study approved by Baqiyatallah University of Medical Sciences Ethics Committee (No.32-3, on meeting 2013-07-26). The sample size was calculated using sample size formula [$n = Z_{1-\alpha/2} \times P(1-P) / d^2$]. One hundred and fourteen morbidly obese patients undergoing sleeve gastrectomy by a single surgeon in Baqiyatallah hospital in April 2013 to September 2014 were included. Patients were enrolled using simple random sampling method. Non-morbid obese patients and those with other indications for sleeve gastrectomy were not included. Liver ultrasonography was performed for all patients before the operation. NAFLD was diagnosed and its grade was determined using abdominal ultra-sonography by seeing hyperechoic texture or a bright liver and fatty infiltration and liver enzymes (17, 18). All sonographies were performed by two expert sonographists in Baqiyatallah Hospital sonography ward and inter observers reliability of variables did not have any significant difference. Prevalence of NAFLD and its association with other comorbid conditions (e.g. diabetes mellitus, hyperlipidemia, hypertension, hypothyroidism and ischemic heart disease) were evaluated. Patients with known alcohol consumption, having a mean corpuscular volume of red cells > 100 fl, and those with chronic hepatic disease were excluded from the study.

3.1. Statistical Analysis

Data was analyzed using statistical package for social sciences (SPSS) version 18 (SPSS Inc. Chicago, IL, USA) for windows. Data was reported using mean ± SD, number and percentage. Patients with and without NAFLD were compared together using independent sample T-test, Mann-Whitney U test (in case of non-normal distribution variables) and Chi square test. Normal distribution of variables was approved by one-sample Kolmogorov-Smirnov test.

4. Results

One hundred and fourteen patients with a mean age of 33.96 ± 9.92 years were included (48 males and 66 females). The prevalence of NAFLD was 16.7% (9 patients grade one, 4 patients grade two and 6 patients grade three). The mean BMI was 43.61 ± 5.77 kg/m^2. Fifty patients (43.9%) had diabetes mellitus, 39 patients (34.2%) hyperlipidemia, 47 patients (41.2%) hypertension, 24 patients (21.1%) hypothyroidism and 17 patients (14.9%) ischemic heart disease. Comparison of characteristics, comorbid conditions and laboratory findings of patients with or without NAFLD are shown in Table 1. Comparison of comorbid conditions prevalence in patients with and without NAFLD is shown in Figure 1. The mean BMI was 43.21 ± 4.09 kg/m^2 in patients with NAFLD and 43.7 ± 6.09 kg/m^2 in patients without it (P = 0.759). The mean BMI was 44.23 ± 6.88 kg/m^2 in patients with diabetes and 43.15 ± 4.77 kg/m^2 in those without it (P = 0.383). The mean BMI was 43.53 ± 4.8 kg/m^2 in patients with hypertension and 43.67 ± 6.41 kg/m^2 in those without it (P = 0.912). The mean BMI was 44.23 ± 5.89 kg/m^2 in patients with hyperlipidemia and 43.26 ± 5.72 kg/m^2 in those without it (P = 0.444). The mean BMI was 44.08 ± 5.95 kg/m^2 in patients with hypothyroidism and 43.46 ± 5.75 kg/m^2 in those without it (P = 0.668). The mean BMI was 46.61 ± 4.83 kg/m^2 in patients with ischemic heart disease and 43.11 ± 5.79 kg/m^2 in patients without it (P = 0.042).

5. Discussion

The prevalence of NAFLD among patients undergoing sleeve surgery was 16.7%, which is higher than the value reported in Harnois et al. study (19). Although some previous studies reported a higher prevalence, general prevalence of NAFLD in patients undergoing bariatric surgery was reported between 2.6% and 91% (20-25). The gold standard to diagnose and grading NAFLD and NASH is liver biopsy (18, 26). However, due to its invasive nature, is not performed routinely for NAFLD screening in Iran (18). However, age, gender, BMI and other risk factors may be involved in the dispute. Fatty liver prevalence increases with age, while patients undergoing sleeve surgery in this study were younger than previous studies, and their mean age was 34 years. In this study, no significant differences were observed between obese patients with and without NAFLD regarding age, gender, weight, height, body mass index, diabetes, hypertension, cardiovascular disease and hypothyroidism, but this difference was significant for hyperlipidemia. Some of these findings are consistent with previous studies and some are inconsistent with previous studies (Table 2). It is recommended

Table 1. Characteristics and Laboratory Data of Patients With and Without Non-Alcoholic Fatty Liver Disease [a,b]

Variables	NAFLD (+) (n = 19)	NAFLD (-) (n = 95)	Total (n = 114)	P Value
Age, y	36.58 ± 8.52	33.41 ± 10.15	33.96 ± 9.92	0.208
Male gender	10 (52.6)	38 (40)	48 (42.1)	0.309
Weight, kg	129.13 ± 28.74	121.86 ± 24.06	123.16 ± 24.93	0.293
Height, cm	171.88 ± 16.56	166.74 ± 12.4	167.66 ± 13.27	0.162
Body Mass Index, kg/m^2	43.21 ± 4.09	43.7 ± 6.09	43.61 ± 5.77	0.759
Systolic Blood Pressure, mmHg	125.32 ± 12.04	117.85 ± 12.28	119.12 ± 12.51	0.017
Diastolic Blood Pressure, mmHg	75.0 ± 9.72	72.22 ± 8.71	72.69 ± 8.91	0.216
Diabetes Mellitus	7 (36.8)	43 (45.3)	50 (43.9)	0.499
Hyperlipidemia	14 (73.7)	25 (26.3)	39 (34.2)	< 0.001
Hypertension	10 (52.6)	37 (38.9)	47 (41.2)	0.269
Hypothyroidism	2 (10.5)	22 (23.2)	24 (21.1)	0.335
Ischemic Heart Disease	5 (26.3)	12 (12.6)	17 (14.9)	0.157
Hospital Stay, days	1.21 ± 0.54	2.17 ± 1.41	2.01 ± 1.37	0.004
White Blood Cell, $10^3/mm^3$	10.53 ± 3.12	10.18 ± 3.4	10.24 ± 3.34	0.699
Red Blood Cell, $10^6/mm^3$	5.03 ± 0.73	4.74 ± 0.47	4.79 ± 0.53	0.050
Hemoglobin, mg/dL	14.26 ± 2.45	13.15 ± 1.49	13.31 ± 1.7	0.018
Hematocrit	42.57 ± 6.27	39.38 ± 4.41	39.86 ± 4.83	0.018
Platelet	237.59 ± 44.3	262.77 ± 61.63	258.44 ± 59.59	0.113
Fasting Blood Sugar, mg/dL	99.58 ± 24.53	119.32 ± 46.27	116.03 ± 43.95	0.074
BUN, mg/dL	12.56 ± 3.01	14.08 ± 3.83	13.77 ± 3.71	0.146
Creatinine, mg/dL	0.931 ± 0.22	0.896 ± 0.13	0.902 ± 0.15	0.395
Triglyceride, mg/dL	185.09 ± 73.31	136.39 ± 51.15	143.73 ± 57.19	0.008
Total Cholesterol, mg/dL	164.79 ± 22.48	168.31 ± 41.68	167.48 ± 37.95	0.726
HDL, mg/dL	42.94 ± 11.85	48.32 ± 11.98	47.15 ± 12.09	0.087
LDL, mg/dL	127.29 ± 35.56	118.23 ± 30.43	120.21 ± 31.63	0.272
Alanine Aminotransferase, U/L	54.16 ± 49.58	23.07 ± 5.77	32.02 ± 30.09	< 0.001
Aspartate Aminotransferase, U/L	65.84 ± 23.72	45.61 ± 12.23	51.44 ± 22.08	< 0.001
Alkaline Phosphatase	181.21 ± 59.68	94.0 ± 58.86	119.11 ± 70.86	< 0.001
Sodium, mEq/L	137.42 ± 3.4	135.9 ± 4.37	136.19 ± 4.22	0.267
Potassium, mEq/L	4.18 ± 0.3	3.94 ± 0.4	3.98 ± 0.39	0.048

[a] Abbreviations: NAFLD, Nonalcoholic fatty liver disease; BUN, Blood urea nitrogen; HDL, High density lipoprotein; LDL, Low density lipoprotein.
[b] Data are presented as mean ± standard deviation or No. (%).

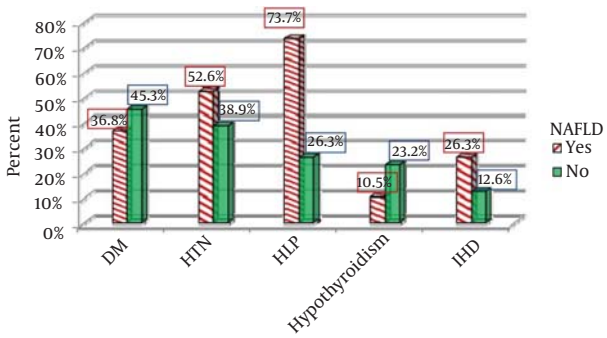

Figure 1. The Prevalence of Diabetes Mellitus (DM), Hypertension (HTN), Hyperlipidemia (HLP), Hypothyroidism and Ischemic Heart Disease (IHD) in Patients With and Without Non-Alcoholic Fatty Liver Disease (NAFLD).

to perform diagnostic gold standard (liver biopsy during the operation) to determine the exact prevalence of NAFLD and NASH in patients undergoing sleeve surgery. It is also recommended to assess the impact of sleeve surgery on fatty liver in short-term and long-term in further investigations. A high prevalence of diabetes, hyperlipidemia, hypertension and hypothyroidism was observed in these patients; thus, it is recommended to examine the effects of surgery in controlling comorbid conditions in short-term and long-term.

Ultrasound method was used in our study, which is a routine method for NAFLD screening in Iran and it was one of the limitations of the present study. Another limitation was the small sample size, because of small number of bariatric surgery with sleeve method in Iran and prospective structure of our study. We selected patients undergoing sleeve bariatric surgeries because of special conditions of these patients compared to other bariatric methods (e.g. younger age).

Table 2. Comparison of Our Study With Previous Studies Showing NAFLD and NASH Prevalence and Association With Other Comorbid Conditions [a]

Study, Year	BMI	Mean Age	Male, %	Sample Size	Kind of Surgery	Diagnostic Method	NAFLD/ NASH Prevalence, %	Related Factors	Not-Related Factors
Spaulding et al. (23), 2003	51	Not clear	16	48	Roux-en-Y gastric bypass (RYGBP)	Biopsy	56	DM, Abnormal LFT	Central Obesity, Gender, HLP, HTN
Moretto et al. (22), 2003	48.1	36.1	24.7	77	Bariatric Surgery (undefined)	Biopsy	2.6 NASH, 83.1 Steatosis	HLP, DM	BMI
Boza et al. (27), 2005	42	40	38	127	Bariatric Surgery (undefined)	Biopsy	26	Female, Type 2 DM, HDL, AST, ALT, Insulin resistance, Metabolic syndrome	BMI, Age, HTN, Chol, LDL, TG
Harnois et al. (19), 2006	45.7	38	8	92	Laparoscopic Gastric Bypass/ Laparoscopic gastric band	Biopsy	9.8	BMI, Chol, TG	Gender, Age, Waist/ Hip Ratio, DM, HTN, FBS, ALT, AST
Feijo et al. (28), 2013	44.2	38.4	27	60	Gastric bypass	Biopsy	66.7	γGT	Age, Gender, DM, BMI, Waist, HDL, TG, Uric Acid, LFT, Ferritin
Holterman et al. (29), 2013									
Adolescents	52	16	21	24	Gastric Banding	Biopsy	87.5	Not clear	Not clear
Adults	51	38	12.5	24	Gastric Banding	Biopsy	50	Not clear	Not clear
Present study	43.6	34	42.1	114	Sleeve Bariatric Surgery	Sonography	16.7	SBP, HLP, Hgb, Hct, TG, LFT, Potassium	Age, Gender, Weight, Height, BMI, DBP, DM, HTN, Hypothyroidism, IHD, WBC, RBC, Plt, FBS, BUN, Cr, Chol, HDL, LDL, Na

[a] abbreviations: BMI, Body mass index; NAFLD, Nonalcoholic fatty liver disease; NASH, Nonalcoholic steatohepatitis; DM, Diabetes Mellitus; LFT, liver function test; HLP, Hyperlipidemia; HTN, Hypertension; HDL, High density lipoprotein; AST, Aspartate aminotransferases; ALT; Alanine aminotransferase; FBS, Fasting blood sugar; SBP, Systolic blood pressure; Hgb, Hemoglobin; Hct, Hematocrit; TG, Triglyceride; DBP, Diastolic blood pressure; IHD, Ischemic Heart Disease; WBC, White blood cell; RBC, Red blood cell; Plt, Platelet; BUN, Blood urea nitrogen; Cr, Creatinine; LDL, Low density lipoprotein; Na, Sodium.

This is the first study reporting the prevalence of NAFLD in patients undergoing sleeve gastrectomy in Iran. Despite using ultrasonography instead of gold standard (liver biopsy) for diagnosis of NAFLD, our study showed an almost high prevalence of NAFLD in morbidly obese patients undergoing sleeve gastrectomy in Iran. We suggest using the gold standard diagnostic method (liver biopsy) to determine the exact NAFLD prevalence and evaluate the impact of sleeve surgery on NAFLD in short and long term follow-up.

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Authors' Contributions

Study concept and design: Hamidreza Karimi-Sari. Collecting data: Hamidreza Karimi-Sari, Shahriar Najafizadeh-Sari, Mohammad Hosein Mir-Jalili and Fardin Dolatimehr. Administrative, technical and material supports: Seyed Morteza Mosavi-Naeini. Statistical analysis: Hamidreza Karimi-Sari and Fardin Dolatimehr. Drafting of the manuscript: Mahdi Ramezani-Binabaj and Hamidreza Karimi-Sari. Critical revision of the manuscript for important intellectual content: Seyed Morteza Mousavi-Naeini and Mahdi Ramezani-Binabaj.

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