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Liver Function Tests and Ultrasonography Findings in Iranian Morbid Obese Patients Undergoing Bariatric Surgery

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Abstract

Background: Obesity, a major risk factor for fatty liver disease, is increasing worldwide. Morbid obese patients have a higher prevalence of fatty liver disease in addition to more severe complications, and high prevalence of abnormal liver function tests (LFTs). The aim of this study is to determine the pattern of LFT and liver ultrasonography of morbid obese Iranian patients undergoing bariatric surgery.

Methods: The study population included 308 morbid obese patients who were candidates for Laparoscopic Roux-en-Y Gastric Bypass surgery. Body mass index (BMI), age, gender, weight, height, blood tests including alanine transaminase (ALT), aspartate transaminase (AST), direct bilirubin (Bil D), total bilirubin (Bil T), and liver ultrasound reports were recorded for all of the patients. Patients with alcohol intake or hepatitis or human immunodeficiency virus (HIV) were excluded from the study. The data were entered and analyzed using SPSS-16. The chi-square, ANOVA and Independent-sample t- test used in the study analysis.

Results: Data analyses showed that alkaline phosphatase (ALKP) is the most elevated serum enzyme in morbid obese patients 26 (87.6%). ALT, AST, bilirubin total and bilirubin direct were more than upper normal range in 70 (24.1%), 80 (26%), 2 (1.5%) and 15 (11.4%) in all patients, respectively. Ultrasonography of the liver showed that fatty liver disease occurred in approximately 280 (91%) of our patients. In our study, the only liver enzyme that had significant difference with fatty liver and normal groups was AST (P: 0.027). The patients were divided into three groups on the basis of the BMI: BMI of 35 - 40 kg/m^2, 40 - 50 kg/m^2, and above 50 kg/m^2. There is not any significant difference between the mean of ALKP, ALT, AST, bilirubin (direct and total) serum level and fatty liver in these three groups.

Conclusions: The prevalence of abnormal LFTs in Iranian morbid obese patients is in high status especially the level of ALKP. Liver ultrasonography has high sensitivity for the fatty liver in morbid obese patients but LFTs rise only in few patients with fatty liver.

Keywords: Bariatric Surgery, Liver Function Tests, Morbid Obesity, Ultrasonography

1. Background

Obesity is an increasing condition around the world which can develop enormous risks affecting different organs that cause low quality of life and vast economic burden for health care systems (1, 2) and it has been doubled in the last 20 years (3). There are some risk factors like genetics, behavioral, psychological, and lifestyle changes which can increase its prevalence (4, 5). It may also be associated with diabetes, hypertension, dyslipidemia, asthma, arthritis, and liver disease (1). Obesity can be categorized into 3 minor categories: mild-moderate (BMI 30 - 39.9 kg/m^2), morbid (BMI 40 - 49.9 kg/m^2), and super (BMI >50 kg/m^2) (6). Studies show that the prevalence of obesity is 21.5% in Iranian adults (>18 yrs) (7).

This pathologic condition is the most common cause of nonalcoholic fatty liver disease (NAFLD) (8), which can be defined as the presence of steatosis and necroinflammation on liver biopsy. The entire spectrum of fatty liver has been termed as NAFLD and covers the gamut from simple fatty infiltration to cirrhosis. When inflammatory changes occur with or without fibrosis, the disease becomes nonalcoholic steatohepatitis (NASH) afterwards, which can lead to fibrosis and cirrhosis (9, 10). The worldwide prevalence of NAFLD among adult has been estimated to range from 10% to 24%; and occurs as high as 57.5% to 74% in obese adults. The correlation of obesity and different features of metabolic syndrome depicts high risk of developing NAFLD in obese patients (11, 12). The best treatment for NAFLD is life style modification, such as weight reduction (13, 14).

There are some noninvasive imaging techniques, which can investigate the liver, such as ultrasound (US),

magnetic resonance imaging (MRI), and computed tomography (CT) and some liver enzyme tests, such as alaninaminotransaminas (ALT), aspartate aminotransaminase (AST), ammaglutamyltranspeptidase (GTT), and alkaline phosphatase (ALKP) which can reflect hepatic cell function and can also be used as a valuable diagnostic test in hepatic cell dysfunctions such as NAFLD (15). But, they cannot differentiate the degrees of NAFLD (benign steatosis against NASH (16); they only distinguish whether the fatty liver exists or not. So, liver biopsy is still the gold standard for diagnose and staging the NAFLD (17).

Despite the high prevalence of obesity and the increasing trend of overweightness in Iran (18), regarding its correlation with NAFLD, we have not gathered valid data indicating the prevalence of liver function abnormalities in asymptomatic morbid obese patients undergoing bariatric surgery.

2. Objectives

The purpose of our study was to evaluate the prevalence of liver cell dysfunction by means of liver function tests (LFTs) and ultrasonography in morbid obese Iranian patients undergoing bariatric surgery.

3. Methods

This retrospective study, based on the data extracted from national obesity surgery database of the obesity center of Rasul-e-Akram hospital, Tehran, Iran is composed of 308 morbid obese patients, who were candidates for Laparoscopic Roux-en-Y gastric bypass (LRYGB) surgery, which has been done by a united surgical team, since June 2009 to August 2012.

Inclusion criteria were all candidates for bariatric surgery (BMI $\geq$ 40 solely or BMI > 35 with related comorbidities). BMI, age, gender, weight, height, blood tests including ALT, AST, direct bilirubin, total bilirubin and liver ultrasound reports were recorded. All blood tests were done in Rasoul-e-Akram laboratory with the same standards and normal ranges, which are in compliance with internationally accepted figures for laboratory tests. In our study, Fatty liver disease was defined as >50% hepatocytes with fat droplets. Available laboratory data were reviewed for serologic and liver function tests to exclude viral hepatitis and other potential causes of liver disease.

3.1. Exclusion Criteria Included

history of alcohol consumption, medications that might have adverse effects on the liver (hepatotoxicity), known hepatitis B or C viral infection, Wilson's disease, autoimmune hepatitis, hemochromatosis, alpha-1 antitrypsin disease or other known liver disease, and previous jejunoileal bypass.

The study was approved by the ethical committee of Iran University of Medical Sciences (code: IR.IUMS.rec.1390.16285) and is in accordance with guidelines laid down by the latest version of Helsinki Declaration. The informed consent for liver biopsy was not obtained from all patients; therefore the liver biopsy has not been used as an available test to investigate fatty liver in this study.

3.2. Statistics

The data were entered and analyzed using SPSS-16. The chi-square or Fisher exact test was used to compare the prevalence of fatty liver in the three groups. Analysis of variance (ANOVA) was used to compare the mean of quantitative data between the three groups of BMI and also Independent-sample t-test was used for comparing the mean of quantitative data between two gender groups or normal and fatty liver groups. P value less than 0.05 was accepted as statistically significant. The quantitative data were expressed as mean $\pm$ standard deviation (SD) or median with interquartile range (IQR); frequency was used for the qualitative data.

4. Results

308 candidates for LRYGB surgery between June 2009 and August 2012 were included in this study. The subjects were divided into three categories on the basis of their BMI: 39 subjects (12.7%) had a BMI in range of 35 - 40 kg/m^2 (group A), 215 (69.8%) in range of 40 - 50 kg/m^2 (group B) and 54 subjects (17.5%) above 50 kg/m^2 (group C). Table 1 summarizes the demographic as well as liver function test results of the study population based on gender. The abdomen ultrasonography study showed that 280 (90.9%) patients had positive evidence for fatty liver disease. Patients who were diagnosed to have NAFLD had a wide spectrum of liver involvement. In addition, gender showed no significant association with ultrasound study's result (P = 0.780) (Table 1).

Table 2 compares the demographic and clinical characteristics of different BMI groups. Although, NAFLD was most frequent in those with a BMI greater than 50 kg/m^2, it did not reach the threshold for statistical significance (P = 0.125). In addition, we did not observe a significant association between liver function test results (including AST, ALT, ALKP, direct and total bilirubin levels) and BMI categories (P > 0.05).

In general, 80 patients (26%) had an abnormal AST level. Also, these values for the levels of ALT, ALKP, Total Bil and

Table 1. Demographic and Clinical Characteristics of the Study Participant Based on Gender[a]

Variables	Total Population n = 308	Female, n = 262	Male, n = 46	P Value[b]
Age, y	39.42 ± 9.51	39.81 ± 9.55	37.15 ± 9.07	0.08
Weight, kg	121.47 ± 19.22	117.67 ± 16.49	141.46 ± 21.52	0.009
Height, cm	163.93 ± 8.53	161.86 ± 6.23	176.86 ± 8.39	< 0.001
BMI, kg/m^2	45.12 ± 5.55	45.12 ± 5.62	45.10 ± 5.21	0.595
Fatty liver	280 (90.9)	237 (90.5)	43 (93.5)	0.780
AST,IU/L: median (IQR)	21 (15 - 27)	20 (15 - 26)	25 (19 - 37.5)	< 0.001
ALT,IU/L: median (IQR)	22 (4 - 172)	20 (16 - 30)	37.5 (29.75 - 76.50)	< 0.001
ALKP,IU/L	183.99 ± 59.77	184.84 ± 59.77	179.07 ± 60.21	0.555
Bil D, mg/dL: median (IQR)	0.20 (0.1 - 0.2)	0.2 (0.1 - 0.21)	0.2 (0.2 - 0.22)	0.219
Bil T, mg/dL	0.6 (0.5 - 0.81)	0.63 ± 0.26	0.6 (0.5 - 0.9)	0.181

Abbreviations: ALKP, alkaline phosphatase; Bil D, direct bilirubin; Bil T, total bilirubin.
[a]Values are expressed as No. (%) or mean ± SD.
[b]P values represent the differences between female and male groups

Table 2. Demographic and Clinical Characteristics of Participants Based on BMI[a]

Variables	BMI, Kg/M^2			
	Group A (35 ≤ BMI < 40)	Group B (40 ≤ BMI < 50)	Group c (BMI ≥ 50)	P Value[b]
No. (%)	39 (13)	215 (70)	54 (17)	
Age, y	39.72 ± 9.17	39.28 ± 9.81	39.74 ± 8.86	0.930
Female gender	34 (87.2)	182 (84.7)	46 (85.2)	0.920
AST, IU/L	20.87 ± 6.74	21(15 - 28)	19.5 (15 - 28.25)	0.724
ALT, IU/L: median (IQR)	21 (17-30)	23 (17 - 35)	21 (16 - 35)	0.419
ALKP, IU/L	182.89 ± 48.52	181.03 ± 60.96	196.42 ± 61.09	0/245
Bil D, mg/dL	0.2 (0.1-0.3)	0.2 (0.1 - 0.3)	0.18 ± 0.06	0.310
Bil T, mg/dL	0.65 ± 0.31	0.60 (0.5- 0.8)	0.69 ± 0.17	0.680
NAFLD	35 (89.7)	192 (89.3)	53 (98.1)	0.125

Abbreviations: AST, aspartate transaminase; ALT, alanine transaminase; ALKP, alkaline phosphatase; Bil D, direct bilirubin; Bil T, total bilirubin; NAFLD, nonalcoholic fatty liver disease.
[a]Values are expressed as No. (%) or mean ± SD.
[b]P values represent the differences between the three groups.

Direct Bil were 70 (24.1%), 261 (87.6%), 15 (11.4%) and 4 (3.1%), respectively. There were no significant difference between groups of BMI and the frequency of high level of these tests (for all of them P > 0.05) (Table 3).

Table 4 presents the comparison of the age and liver function test between patients with and without NAFLD.

The age variable showed no significant difference between the healthy and fatty liver groups (P > 0.05). The mean of AST levels in fatty liver cases was significantly higher than in normal subjects, but the mean of ALT, ALKP, Bil D and Bil T levels showed no difference between the two groups (for all of them P > 0.05).

5. Discussion

The incidence of non-alcoholic fatty liver disease is increasing among individuals with obesity.

In this study, we evaluated the pre-operative liver function tests and abdominal ultrasonography findings of morbid obese patients undergoing bariatric surgery. In addition, we evaluated the potential association between demographic and LFT findings with different BMI categories.

The prevalence of abnormal liver function test results in asymptomatic healthy adults is estimated to be 7% - 9% (19). In several studies on morbid obese patients going for weight reduction surgery, this prevalence has been raised

Table 3. The Frequency of Higher Than Normal Level of Liver Function Tests

Variables	BMI			
	Group A (35 ≤ BMI < 40)	Group B (40 ≤ BMI < 50)	Group C (BMI ≥ 50)	P Value
AST	6 (15.4)	58 (27)	16 (29.6)	0.521
ALT	5 (12.8)	52 (26.1)	13 (24.5)	0.449
ALT	31 (88)	184 (87.6)	46 (86.8)	0.973
Bil D	2 (15.4)	13 (14.6)	0	0.083
Bil T	0	2 (2.3)	0	0.259
NAFLD	35 (89.7)	192 (89.3)	53 (98.1)	0.125

Abbreviations: AST, aspartate transaminase; ALT, alanine transaminase; ALKP, alkaline phosphatase; Bil D, direct bilirubin; Bil T, total bilirubin; NAFLD, nonalcoholic fatty liver disease.

Table 4. Comparison of Characteristics Between Patients With and Without NAFLD

Variables	Patients With NAFLD, n = 280	Patients Without NAFLD n = 28	P Value
Age: mean± SD	38.04 ± 10.26	39.55 ± 9.44	0.422
AST: median (IQR)	21 (16 - 28)	16.50(14 - 22.75)	0.027[a]
ALT: median (IQR)	22 (17- 36)	19 (15 - 29)	0.189
ALKP: mean± SD	183.07 ± 59.34	193.62 ± 64.51	0.391
Bil D: median (IQR)	0.2 (0.1- 0.21)	0.15(0.1 - 0.27)	0.615
Bil T: median (IQR)	0.6 (0.5 - 0.8)	0.85(0.72 - 1)	0.118

Abbreviations: NAFLD, nonalcoholic fatty liver disease; AST, aspartate transaminase; ALT, alanine transaminase; ALKP, alkaline phosphatase; Bil D, direct bilirubin; Bil T, total bilirubin.
[a]Significant difference between two groups P < 0.05.

to 19% - 24% (20, 21). But, our study demonstrated a higher prevalence than the previous ones. We found that 87.6% of our patients had elevated ALKP as the most elevated liver enzyme in our survey. The incidence of other abnormal LFTs in our study was 26% for AST and 24% for ALT. In other studies, the most elevated liver enzymes were ALT, AST, and ALKP, respectively (22-24).

The analysis of our results showed that both ALT and AST have strong relationship with gender (P < 00.1). But, for ALKP we did not observe a significant correlation. Wolf et al. (25) also showed a positive association between elevated levels of ALT and AST with male gender; however the ALKP level was similar in male and female morbid obese patients. A recent study (26) did not find a significant association between gender and ALT and AST levels. (P value of 0.25 and 0.16, respectively).

The serum level of total bilirubin in our patients was in normal range (0.65 ± 0.31 mg/dL) with the normal range of 0.3 to 1.0 mg/dL. Boza et al. (27) also announced that in their morbid obese patients, the pre-operative serum level of total bilirubin was 0.5 ± 0.3.

In our study, the incidence of fatty liver in male patients was more than female, but there were no significant differences in its frequency between male and female. Other investigators have, likewise, showed that the incidence of fatty liver is more likely in male patients than females (24, 26, 27). Some articles believe that the correlation between the incidence of fatty liver and male gender maybe a result of their generally greater abdominal visceral fat mass (25).

Fatty liver disease occurred in approximately 91% of our patients. Although the prevalence of NAFLD is increasing in the developed countries and it has been estimated that more than half of individuals with obesity have NAFLD (28-31), we observed a much higher frequency of NAFLD in our population of obese patients. In the current study, the only liver enzyme that had significant difference with fatty liver and normal groups was AST (P value: 0.027). We did not observe a significant difference between patients with and without NAFLD in terms of age, ALT, ALKP, total bilirubin, and direct bilirubin.

We acknowledge that this study includes a number of weaknesses. A great limitation of this study is the use of abdominal ultrasonography for detection of patients with NAFLD as the liver biopsy data were not available for all patients. The lack of liver biopsy results to confirm the diagnosis and identify the grade of hepatic damage is a further weakness of this study. Moreover, we recognize that there are various factors, e.g. gamma-glutamyltranspeptidase that might have a significant association with NAFLD frequency and intensity that were not measured in this study.

5.1. Conclusion

We observed much higher frequency of abnormal LFT levels, in particular ALKP level, in Iranian obese patients in

comparison with the results of similar investigations. LFTs (AST and ALT) are usually resistant to liver changes and do not elevate in patients with NAFLD. Prospective studies of obese patients with liver biopsy are warranted to further evaluate the correlation between NAFLD grade and serum LFT levels.

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Footnotes

Authors' Contribution: Study concept and design: Amir Hossein Faghihi, Arezou Hashemzadeh and Abdolreza Pazouki; acquisition of data: Pejman Mansouri, Somayyeh Mokhber and Abdolreza Pazouki; analysis and interpretation of data: Amir Hossein Faghihi and Abdolreza Pazouki; drafting of the manuscript: Amir Hossein Faghihi, Somayyeh Mokhber, Arezou Hashemzadeh, Pejman Mansouri and Abdolreza Pazouki; critical revision of the manuscript for important intellectual content: Amir Hossein Faghihi and Abdolreza Pazouki; statistical analysis: Pejman Mansouri and Amir Hossein Faghihi; administrative, technical, and material support: Amir Hossein Faghihi, Somayyeh Mokhber, Arezou Hashemzadeh, Pejman Mansouri and Abdolreza Pazouki; study supervision: Amir Hossein Faghihi, Somayyeh Mokhber, Arezou Hashemzadeh, Pejman Mansouri and Abdolreza Pazouki.

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