ORIGINAL ARTICLE

OUTCOMES OF BARIATRIC SURGERY IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD): A PROSPECTIVE OBSERVATIONAL STUDY

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Background: The prevalence of non-alcoholic fatty liver disease (NAFLD) has significantly. increased due to the obesity pandemic. Reducing body weight by 5 to 10% in obese patients can improve all aspects of NAFLD. Objective of the study was to determine the outcomes of Bariatric Surgery in patients with Non-Alcoholic Fatty Liver Disease in terms of effect on liver enzymes and fibrosis level. **Methods**: This prospective observational study was carried out from August 2021 to July 2022.Patients undergoing laparoscopic sleeve gastrectomy (LSG) with a diagnosis of non-alcoholic fatty liver disease confirmed through clinical findings, elevated liver enzymes evident by laboratory testing along with ultrasound were included. Preoperative data was gathered including demographics and Laboratory tests included HbA1c, lipid profile, fasting glucose, and liver function tests (ALT, AST, and GGT). The NAFLD fibrosis score (FIB-4) Index). De Ritis ratio (AST/ALT), and the AST to platelet ratio index (APRI) were among the serum marker scores that were evaluated post-surgery at different follow ups of 3, 6, and 12 and 18 months. **Results:** A total of 922 (90%) patients had non-alcoholic fatty liver disease (NAFLD). Majority of the patients 765 (83%) patients showed continued improvement in steatosis at eighteen months post-surgery evident by ultrasound while 51 (37%) patients with F2 fibrosis and 165 (60%) of those with F1 fibrosis demonstrated lower fibrosis stage at 1 year following surgery. From a preoperative value of 1.2±0.5 to 0.6±0.2 at one year and then to 0.5±0.2 at eighteen months after surgery, the AST/ALT ratio gradually decreased. **Conclusion:** It has been concluded that bariatric surgery helps individuals with non-alcoholic fatty liver disease by improving their liver enzyme profiles and slowing the progression of fibrosis. These results provide evidence to bariatric surgery's status as a safe and successful treatment for non-alcoholic fatty liver disease.

Keywords: Bariatric Surgery; Management; Non-Alcoholic Fatty Liver Disease (NAFLD); Sleeve gastrectomy

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INTRODUCTION

The prevalence of obesity has increased within the last 20 years worldwide and is rapidly becoming a global health concern.[1] The pandemic of obesity has led to a large increase in the prevalence of non-alcoholic fatty liver disease (NAFLD). Twenty five to thirty percent of the general population and 50–90% of obese individuals are affected by NAFLD.[2] The estimated prevalence in Pakistan varies from 14–47%.[3] A recent analysis projects that by 2030, the prevalence of non-alcoholic fatty liver disease will continue to climb, accompanied by a notable increase in liver-related mortality and hepatocellular carcinoma (HCC).[4] Non-alcoholic fatty liver disease, the hepatic manifestation of metabolic syndrome, is directly linked to abdominal obesity, a condition marked by an enlarged waist circumference, insulin resistance, abnormal lipid metabolism, and persistent inflammation.[5] NAFLD typically progresses to simple steatosis, fibrosis, and non-alcoholic steatohepatitis (NASH). Patients with histologic non-alcoholic steatohepatitis (NASHLD) comprise a subgroup which is more vulnerable to hepatocellular carcinoma (HCC) (five per thousand persons per years), excess liver-related mortality (eleven per thousand person per year), advanced liver illness (sixty-eight per 1000 persons per years), and liver transplantation (a highly selected group of patients).[6] The fatty liver disease and steatohepatitis have been the most quickly expanding liver transplant indications during the past 20 years, according to statistics from the registry of liver transplant. Furthermore, the most common reason for liver transplant owing to causes other than the infection among adult Americans at this time is NAFLD.[7]

A significant body of research demonstrates the robust association between NASH and dietary adjustments, physical activity, and weight loss. It has been demonstrated that reducing body weight by 5 to 10% in obese patients can improve all aspects of non-alcoholic steatosis (NASH), including inflammation and fibrosis.[8] Individuals suffering from progressive steatohepatitis (bridging cirrhosis and fibrosis), initial stages of steatohepatitis with an increased chances of developing the disease, and active NASH with strong necro-inflammatory activity are recommended to get pharmaceutical therapy.[9] However, changing the lifestyle of an obese patient can be difficult and rarely has the desired effect along with use of medications.[10]

Several obesity-related disorders, including type 2 diabetes, hypertension, dyslipidaemia, and obstructive sleep apnoea, are treated and managed by bariatric surgery, in addition to producing a large, long-term weight loss.[11,12] Hepatic fat deposits may decrease due to the weight loss surgery's substantial metabolic adjustments involving the release of adipokines and incretins, and reduction of chronic inflammation.[13] Bariatric surgery is categorized as a desirable therapeutic approach in treating NAFLD.[14]

The aim of this study was to evaluate the outcomes of bariatric surgery in the management of Non-alcoholic fatty liver disease in terms of effect on liver enzymes and fibrosis level.

MATERIAL AND METHODS

Over the course of one year, this prospective study was carried out at a tertiary care centre in Peshawar from August 2021 to July 2022. Following the hospital's review board's approval, patient data was gathered and informed consent from the participants. Convenience sampling technique was used. Patients undergoing laparoscopic sleeve gastrectomy (LSG) with a diagnosis of non-alcoholic fatty liver disease confirmed through clinical findings, elevated liver enzymes evident by laboratory testing along with ultrasound were included in the study. Liver disease caused by viruses, autoimmune disorders, or alcoholism were excluded. Elevated ALT/AST levels, an AST/ALT ratio close to or greater than 1, clinical signs of hepatic inflammation, and ultrasound-confirmed hepatic steatosis were used to distinguish Non-alcoholic steatohepatitis NASH from NAFLD.

Preoperative data, which included medical history and comorbidities along with demographic data like age, sex, and BMI, were gathered one month prior to surgery. Laboratory tests included HbA1c, lipid profile, fasting glucose, and liver function tests (ALT, AST). Following surgery, patients were reassessed on 3, 6,12 months and 18 months follow up period. Measurements of the changes in liver fibrosis stage, improvement in steatosis along with laboratory tests, were among the outcome's measures used in the study.

The FIB-4 Index, a validated non-invasive scoring system designed to correlate with Ishak fibrosis stages, was used to assess fibrosis. Three stages of fibrosis severity are distinguished by the FIB-4 score: mild fibrosis (0–2), moderate fibrosis (3–4), and severe fibrosis/cirrhosis (5–6). The patient's age, AST, ALT, and platelet count were used to create this index. Among the serum marker scores that were assessed were the AST to platelet ratio index (APRI), the De Ritis ratio (AST/ALT), and the NAFLD fibrosis score.

We performed the statistical analysis using SPSS version 26. To ascertain the frequency and percentages for the categorical variable, descriptive statistics were incorporated while mean and standard deviations were reported for numerical data. To determine the normality of the data, Shapiro Wilk test was used. Wilcoxon signed rank tests were used to compare changes in liver stiffness and other parameters between different time periods.

RESULT

During the study period, 1024 bariatric surgeries were conducted out of which 922 (90%) of the patients had a diagnosis of Non-Alcoholic Fatty Liver Disease (NAFLD). The patient group had a mean age of 42.5±11.3 years, with 572 females (62%) and 350 males (38%). Sleeve Gastrectomy was the technique used for all procedures (SG). Prior to surgery, the average BMI recorded was 46.2±8.1 kg/m². Following evaluation of the preoperative phases of liver fibrosis, 599 (65%) of the 922 individuals with NAFLD had mild fibrosis (F0-F1), 184 (20%) had moderate fibrosis (F2), and 139 (15%) had severe fibrosis (F3-F4, cirrhosis), according to fibrosis staging using the FIB-4 index.

BMI was assessed at four follow-up periods following surgery: three months, six months, a year, and eighteen months. At 42.8±7.6 kg/m² at 3 months (p<0.001), 39.5±7.2 kg/m² at 6 months (p<0.001), 35.8±6.9 kg/m² at 1 year (p<0.001), and 33.2±6.5 kg/m² at 18 months (p<0.001) using pair t test. The preoperative mean BMI of 46.2±8.1 kg/m² declined considerably with time. (Table-1)

A total of 765 (83%) patients showed continued improvement in steatosis at eighteen months post-surgery while 51 (37%) patients with severe fibrosis and 110 (60%) of those with moderate fibrosis demonstrated lower fibrosis stage at 1 year following surgery. By the 18-month mark, there had been notable improvements in liver health, with both the moderate and severe fibrosis groups showing considerable declines in fibrosis stages. (Table-2)

Significant postoperative improvements were seen in the laboratory values using repeated measure Anova. At three months (p<0.001), six months (p<0.001), one year (p<0.001) and eighteen months (*p*<0.001), the AST/ALT ratio dropped from a preoperative value of 1.2±0.5 to 0.5±0.2 at 18 months. A preoperative value of 2.3±1.2 was replaced with 1.8±1.1 at 3 months (*p*<0.001), 1.4±1.0 at 6 months (*p*<0.001), 1.0±0.8 at 1 year (*p*<0.001), and 0.6±0.6 at 18 months (*p*<0.001) for the NAFLD fibrosis score. Significant improvement was also evident in the APRI score, which dropped from 1.5±0.6 preoperatively to 1.2±0.5 at 3 months (*p*<0.001), 0.9±0.4 at 6 months (*p*<0.001), 0.6±0.3 at 1 year (*p*<0.001), and 0.3 at the end of the procedure.

Table-1: Follow-up and weight reduction

Follow-Up Interval	Mean BMI (kg/m²)	*p*-value
Preoperative	46.2±8.1	-
3 months	42.8±7.6	< 0.001
6 months	39.5±7.2	< 0.001
1 year	35.8±6.9	< 0.001
18 months	33.2±6.5	< 0.001

Table-2: Postoperative liver health improvements

Follow-Up Interval	Improvement in Liver Steatosis	Decreased Fibrosis Stages from moderate to no fibrosis	Decreased Fibrosis Stages from severe to moderate
3 months	553 (60%)	46 (25%)	24 (17%)
6 months	664 (72%)	74 (40%)	35 (25%)
1 year	728 (79%)	110 (60%)	51 (37%)
18 months	765 (83%)	129 (70%)	108 (78%)

Table-3: **Laboratory parameters and fibrosis scores**

Follow-Up Interval	AST/ALT Ratio	NAFLD Fibrosis Score	APRI Score
Preoperative	1.2±0.5	2.3±1.2	1.5±0.6
3 months	0.9±0.4	1.8±1.1	1.2±0.5
6 months	0.8±0.3	1.4±1.0	0.9±0.4
1 year	0.6±0.2	1.0±0.8	0.6±0.3
18 months	0.5±0.2	0.6±0.6	0.3±0.2
P value (overall)	<0.001	<0.001	<0.001

DISCUSSION

The current study evaluated the outcomes of bariatric surgery more particularly, sleeve gastrectomy, impact in the management of NAFLD. Our results validate the significance of bariatric surgery in the management of NAFLD by showing improvements in both weight loss and liver function after surgery.

In our study, NAFLD was found in 922(90%) of patients undergoing sleeve gastrectomy. This prevalence is consistent with findings of a review carried out by Mummadi *et al* that reported the prevalence to be 85–95% in morbidly obese patients while 70% in only obese patients.[15] However, another study showed a comparable less prevalence rate (59%) of non-alcoholic fatty liver.[16] The high prevalence observed in all studies is consistent, highlighting the important role that bariatric surgery plays in treating obesity and related liver diseases. This further emphasizes the need for focused preoperative evaluation and individualized postoperative treatment to achieve the best possible outcomes for liver health.
Significant improvements in liver health were seen in this study after surgery; at three months, 533 (60%) of patients showed improvements in hepatic steatosis, and by eighteen months, 765 (83%) of patients had shown similar changes. Furthermore, at eighteen months, 129 (70%) of patients with moderate fibrosis had a notable decrease in the amount of liver fat and were classified as improved to mild stage. These results are consistent with recent systematic review conducted in 2022, who showed a noteworthy reduction in fibrosis and remission of NAFLD following surgery. The systematic review constituted a total of thirty-seven studies the results of which illustrated that following bariatric surgery, on average 56% of patients had better steatosis resolution, proven by biopsy; 45% had resolution of inflammation while 25% showed considerable improvements in fibrosis. The mean NAFLD activity ratings were dramatically reduced by bariatric surgery.[17] Similarly in accordance with our study, a systematic review was conducted to determine the outcomes of NAFLD after bariatric surgery, The study noted improvements in liver function and histology. Their study results showed that Steatosis (50.2 and 95%CI of 35.5–65.0), fibrosis (11.9 and 95%CI of 7.4–16.3%), hepatocyte ballooning (67.7 and 95%CI of 56.9–78.5), and lobular inflammation (50.7 and 95%CI of 26.6–74.8%) associated with NAFLD were significantly decreased after bariatric surgery. A decrease in liver enzyme levels were also reported to be linked to surgery, with statistically significant decreases in ALT (11.36 u/l, 95%CI 8.36–14.39), AST (3.91 u/l, 95%CI

2.23–5.59), ALP (10.55 u/l, 95%CI 4.40–16.70), and gamma-GT (18.39 u/l, 95%CI 12.62–24.16). The results showed a considerable degree of heterogeneity.[18] The benefits of weight loss and the metabolic adjustments brought on by bariatric surgery are demonstrated by the steady improvements in liver health observed in several studies. Surgical techniques, postoperative care, and disease stage at diagnosis can all affect differences in carcinoma outcomes.

Both fibrosis stages and laboratory markers showed notable surgical improvements. At 18 months, the preoperative AST/ALT ratio of 1.2 was decreased to 0.5, suggesting better liver function. At 18 months, the preoperative NAFLD fibrosis score dropped from 2.3 to 0.6, while the postoperative APRI score dropped from 1.5 to 0.3. These findings are consistent with earlier research, including that conducted by Felix Nickel and colleagues, the findings of which demonstrated that twelve months following surgery, TG, AST, ALT, and GGT fell dramatically and exhibited notable improvements. After surgery, the mean liver stiffness in patients decreased from 12.9±10.4 kPa to 7.1±3.7 kPa while stage of fibrosis decreased from F3 to F1.The study also reported that after 12 months, there was a considerable improvement in the absolute values of the AST/ALT ratio, NAFLD fibrosis score, APRI score, and BARD score while the APRI score had already improved significantly after one month.[19] While differences in patient demographics and surgical methods may be the cause of any discrepancies seen in other research, the continuous decline in fibrosis scores highlights the efficacy of bariatric surgery in correcting liver damage. These results support the idea that bariatric surgery can greatly enhance the liver health of NAFLD patients.

Through a number of methods, bariatric surgery, in particular sleeve gastrectomy (SG), helps regulate laboratory markers, cancer, fibrosis, and non-alcoholic fatty liver disease (NAFLD). According to Jastrzębska-Mierzyńska M, SG first causes a large reduction in body weight, which lowers the amount of fat in the liver and enhances liver function by improving AST/ALT ratios and fibrosis scores.[20] Furthermore, losing weight reduces insulin resistance, which plays a crucial role in the aetiology of non-alcoholic fatty liver disease (NAFLD).[21] Additionally, SG influences gut hormones, increasing GLP-1 and PYY levels that improve insulin sensitivity and aid in weight loss.[22] Moreover, SG lowers oxidative stress and pro-inflammatory cytokines, both of which contribute to the development of NAFLD and fibrosis . Additionally, research indicates that by lowering the underlying inflammatory and metabolic factors that encourage carcinogenesis, bariatric surgery can stop the progression of liver.[23] These combined effects highlight the diverse advantages of SG in liver health management, which are corroborated by several research findings.[24]

There are a few limitations that needs to be noted. First off, the fact that only one Center participated in the study could restrict how broadly the results can be applied. Furthermore, even with its length, the follow-up period might not have captured long-term effects and possible complications later. It was also challenging to credit all the observed gains to SG without taking other possible contributing factors into account because the study lacked a control group. To validate these results, multi-centre trials with extended follow-up durations should be the focus of future research. A more thorough understanding would also be possible by include control groups and investigating the effects of various bariatric operations on liver health. Examining the molecular processes that underlie the noted advancements may also provide information on focused treatments for NAFLD and associated illnesses.

CONCLUSION

It has been concluded that bariatric surgery helps individuals with non-alcoholic fatty liver disease by improving their liver enzyme profiles and slowing the progression of fibrosis. These results provide evidence to bariatric surgery's status as a safe and successful treatment for NAFLD.

AUTHORS' CONTRIBUTION

MA, AHS: Study Design, Methodology, and Paper Writing. MA, WA: Data Calculation and Data Analysis. AHS, MA: Interpretation of Results. WA, MA: Statistical Analysis. MA, AHS: Literature Review. AHS, MA: Literature Review and Quality Insurer

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