ORIGINAL ARTICLE

Rising in level of liver biomarkers after different types of bariatric surgery; is there any concern?

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Background: Previous studies indicated that metabolic and bariatric surgery (MBS) is a well-known procedure for considerable and sustainable weight loss. While the studies showed that MBS may unfavorably influence and stimulate hepatic dysfunction by raising the aspartate aminotransferase (AST) and alanine aminotransferase (ALT). It is not yet clear whether the ALT and AST alterations following MBS are transient or it is permanently dangerous for liver function. Thus, we aimed to compare the metabolic effect of three MBS methods on liver function status. **Materials and Methods:** In this retrospective cohort study, we focused on adults who underwent MBS without a history of liver disorders. The trends of liver function enzymes and albumin levels from the baseline to 3, 6, and 12 months postsurgery were explored for all patients with complete data using multiple binary logistic regressions. **Results:** The study involved 1378 participants who completed all of the measurements, with 366 (26.56%) undergoing sleeve gastrectomy (SG), 772 (56.02%) undergoing one-anastomosis gastric bypass (OAGB), and 240 (17.41%) undergoing Roux-en-Y gastric bypass (RYGB). While there were no significant differences in the levels of AST, ALT, and albumin between the three surgical methods at baseline, the effect of bariatric procedures on the AST and ALT levels went through completely differed across time. Furthermore, each bariatric technique had a different trend of the levels of AST and ALT. The trend of the levels of AST and ALT of RYGB and OAGB reached a stable level after 12 months of surgery. On the other hand, the stability time of the AST and ALT levels for SG was observed at 6 months, and the reduction was significantly higher than other methods. **Conclusion:** Our findings suggest that the increasing trend of the AST and ALT levels and the stimulation of the liver function postoperatively were transient. The changes in the AST and ALT trend also reached a stable level after 12 months postoperative.

Key words: Bariatric surgical procedures, liver diseases, liver function test

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INTRODUCTION

Metabolic and bariatric surgery (MBS) has superior effects in both efficacy and durability in combating obesity and improvement of obesity-associated comorbidities, when lifestyle and nutritional modifications and anti-obesity medications have been faced to failure in individuals with severe obesity.[1,2] However, it has been reported that MBSs may not always reverse pathological liver conditions, and there is even some evidence showing a worsening of liver function, particularly following hypoabsorptive bariatric surgeries.[3-5] Furthermore, a noteworthy transient increase in the levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) has been revealed in the early stages following One-Anastomosis Gastric Bypass (OAGB), as compared to sleeve gastrectomy (SG).[6,7] Similar findings have been observed 1 year after surgery for Roux-en-Y gastric bypass (RYGB) compared to SG.[8] In other studies, SG has shown greater improvements in hepatic enzyme levels and resolution of nonalcoholic

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fatty liver disease (NAFLD) compared to RYGB.[9] This suggests that the metabolic effects on liver function after surgery depend on the type of surgical procedure performed.[3] Postoperative liver dysfunction after bariatric surgery may occur through several mechanisms described in the literature. Rapid weight loss increases free fatty acid mobilization from adipose tissue, which can accumulate in the liver and cause hepatotoxicity and stress. In addition, Bariatric procedures, especially those with a malabsorptive component (e.g. OAGB, RYGB), alter bile acid metabolism and gut-liver signaling, impacting hepatic function, and probably due to the increase in pro-inflammatory cytokines at the time of surgery as well. Furthermore, small intestinal bacterial overgrowth (SIBO) (caused by the presence of a blind loop with decreased motility and then gut microbiota alterations) can increase gut permeability through the production of hepatotoxic macromolecules, leading to bacterial translocation and liver inflammation. This worsening of hepatic histology postrestrictive and combined procedures is also probably related to low-normal serum albumin, uncontrolled diarrhea, low intake of alcohol, and menopausal status.

Chronic protein malnutrition after bariatric procedures, leading to malabsorption, as well as SIBO, seems to be an underlying mechanism involved in increased liver enzyme levels.

However, it is still unclear by which mechanism MBS can influence liver function load.[7] As a result, the precise impact of bariatric surgeries on liver conditions continues to be a subject of controversy.

To the best of our knowledge, there is a lack of comprehensive global data in this field. Specifically, detailed trends in AST and ALT levels and an analysis of important factors, such as the types of surgical operations, are often missing.[10] Further medium to long-term studies are needed to reach a comprehensive consensus.

The current study provided an opportunity to determine whether the AST and ALT alterations following MBS are transient or permanently dangerous for liver function. This retrospective cohort project aims to provide an update on the ongoing debate regarding liver function in obese patients undergoing RYGB, SG, and OAGB, from the preoperative stage to 1-year postsurgery, spanning from 2009 to 2023.

MATERIALS AND METHODS

Study design and participants

The present retrospective and high-volume center of excellence cohort study was conducted at the obesity clinic at Rasoul Akram Hospital, designated as a Center of Excellence by the European Branch of the International Federation for the Surgery of Obesity at Iran University of Medical Sciences, Tehran, Iran. The patients who had undergone bariatric surgery and were referred for severe obesity management from the whole country participated in this study between 2009 and January 2023.

All eligible participants were adults at age 18 or older who had undergone one of the bariatric procedures, such as RYGB, OAGB, or SG. The patients with no previous history of alcohol intake or other causes of hepatic disorders were recruited into this study.

In addition, all data from the preoperation appointment and the 3-, 6-, and 12-month follow-ups for each eligible participant must be recorded and accessible. Finally, all individuals had such items, including a history of medication intake in the previous 2 months, especially nonsteroidal anti-inflammatory drugs, antibiotics, use of anti-secretory medication, and levothyroxine, were excluded. In addition, individuals who had experienced abdominal surgery or a second bariatric procedure and had a pregnancy after undergoing obesity surgery were not included in this study.

The sonographic scoring system utilized to assess steatosis severity categorized findings as follows: Grade 0 (normal) when liver echogenicity appeared normal; Grade I (slight) when there was a diffuse increase in liver parenchymal echogenicity with intact visualization of the diaphragm and intrahepatic vessels; Grade II (moderate) when a moderate diffuse elevation in hepatic echogenicity was noted, accompanied by compromised visualization of intrahepatic vessels and the diaphragm; Grade III (severe) denoted a marked increase in echogenicity, with diminished penetration of the posterior segment of the right hepatic lobe and poor visualization of hepatic vessels and the diaphragm.[11]

All essential participant data were collected by a multidisciplinary team of experts during preoperative and postoperative follow-ups and recorded in the database.[12,13] The protocol for this cohort project was approved by the Medical Ethics Committee of the Research Council at our university.

Data collection

Sociodemographic information and the presence of any concurrent diseases for all patients were obtained from the mentioned database by a qualified specialist.[14] Simultaneously, data on lifestyle factors, including smoking and alcohol consumption history, drug abuse, as well as fatty liver grade and comorbidities such as dyslipidemia, diabetes, hypertension, and hypothyroidism, were collected.

Anthropometric indices, which included body weight, height, and body mass index (BMI), were measured by trained medical staff. BMI was calculated as weight in kilograms divided by height squared (kg/m²). According to the World Health Organization criteria, severe obesity was defined as a BMI ≥ 40, or a BMI ≥ 35 in conjunction with underlying risk factors.[15]

For all participants, biochemistry laboratory tests were conducted following an overnight fast of at least 12 h. These tests included routine items such as ferritin, platelet count, Vitamin D, lipid profile, fasting blood sugar, AST and ALT, and Albumin levels. These tests were performed at various intervals, including the preoperative stage, and at 3, 6, and 12 months during the postoperative follow-up period.

To accurately interpret an abnormal result, it is essential to consider the reference ranges specific to that particular test. The normal reference ranges for adults in a given hospital are found below in Table A.[16]

In addition to the above information, the medications used by the patient over the past 2 months, including lipid-lowering, antihypertensive, and antidiabetic medications, were recorded in the chart.

Statistical methods

This study comprised all participants who underwent laboratory measurements at baseline and at 3, 6, and 12 months after surgery. Initially, the normality of the measured values for ALT, AST, and Albumin was assessed using the Shapiro–Wilk test. In addition, we modeled the changes in measurements as the fold increased relative to the baseline values.

For each time point, 3-, 6-, and 12-month postsurgery, the values of ALT, AST, and Albumin were summarized using medians and the 5th and 95th percentiles. This approach allowed us to precisely describe the central tendency of each measure (the median) and to identify the range in which 90% of the sample values fell (from the 5th to the 95th percentile). Furthermore, we presented the 5th, 50th, and 95th percentiles for fold increases in measurements relative to the baseline at these time points.

Table A: Normal adult reference ranges for selected biochemical variables

Variable	Male	Female
Serum albumin (g/dL)	3.3–5.0	3.3–5.0
Serum ALP (units/L)	45–115	30–100
Serum ALT (units/L)	29–33	19–25
Serum AST (units/L)	10–40	9–32

ALP=Alkaline phosphatase; ALT=Alanine aminotransferase; AST=Aspartate aminotransferase

To assess the odds of a two-fold increase in ALT and AST levels, the value of each liver biomarker (ALT and AST) at each time point was divided by its baseline value. If the change represented at least a two-fold increase, it was coded as 1; otherwise, it was coded as 0. The odds of a two-fold increase in ALT and AST at 3, 6, and 12 months after surgery were estimated. Therefore, we performed separate logistic regression analyses for each time point.

The analysis was adjusted for covariates, including sex, age, baseline Type 2 Diabetes Mellitus (T2DM) status, and the percentage total weight loss (%TWL) achieved after surgery. %TWL was measured using the formula: 100% × ([postsurgery BMI-presurgery BMI] ÷ presurgery) BMI postoperatively.[14,17]

To compare the distribution of continuous variables across different types of surgical procedures, the Kruskal–Wallis rank sum test was used. Pearson's Chi-squared test was used to measure categorical variables. The significance level for all analyses was set at 0.05. All statistical analyses and data visualizations were performed using base stats and ggplot2 packages of R software, version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Figure 1 presents the flow diagram of subject participation, summarizing the selection and enrollment process for the study cohort. Table 1 presents the baseline characteristics of the 1378 participants enrolled in this study, categorized by the type of surgery. Of the participants, 366 (26.56%) underwent SG, 772 (56.02%) underwent OAGB, and 240 (17.41%) underwent RYGB. The average age of the participants ranged between 36 and 42 years, with a mean BMI of 42.1–44.4 kg/m². The Shapiro–Wilk test indicated that the study variables did not adhere to a normal distribution. Therefore, we presented summary data as medians along with other percentiles.

Statistically significant differences in the levels of ALT ($P < 0.001$) and Albumin ($P = 0.006$) between the three surgical techniques at baseline were observed. However, there were no significant differences between the three procedures in terms of the baseline values of the AST to ALT ratio and AST levels.

Table 2 provided significant insights into AST and ALT trends during the follow-up period. Initially, there were no statistically significant differences in AST and ALT levels among the surgical methods. However, SG exhibited higher levels compared to the other two methods. In the first 3 months postsurgery, SG showed a more pronounced

Table 1: Baseline characteristics of participants by type of surgery

Characteristic	SG (*N*=366[a])	OAGB (*N*=772[a])	RYGB (*N*=240[a])	*P*[b]
Demographics				
Age	36 (29–44)	42 (34–50)	41 (34–49)	<0.001
Education				
Diploma or less	168 (46)	488 (63)	139 (58)	<0.001
Undergraduate	150 (41)	219 (28)	80 (33)	
Postgraduate	48 (13)	65 (8.4)	21 (8.8)	
Job				
Unemployed	201 (55)	527 (68)	180 (75)	<0.001
Employee	165 (45)	245 (32)	60 (25)	
Marital				
Divorced/widow	12 (3.3)	41 (5.3)	13 (5.4)	<0.001
Single	101 (28)	111 (14)	31 (13)	
Married	253 (69)	620 (80)	196 (82)	
Sex (male)	81 (22)	162 (21)	19 (7.9)	<0.001
BMI baseline	42.1 (40.1–46.4)	44.4 (41.4–49.2)	42.5 (40.3–45.4)	<0.001
BMI baseline categories				
35–40	85 (23)	100 (13)	53 (22)	<0.001
40–50	242 (66)	497 (64)	169 (70)	
>50	39 (11)	175 (23)	18 (7.5)	
Dyslipidemia	25 (17–38)	24 (18–35)	22 (15–33)	<0.001
Hypothyroidism	55 (27–103)	57 (30–107)	43 (21–80)	0.015
HTN	279 (228–325)	274 (234–320)	275 (235–318)	<0.001
T2DM	23 (6.3)	156 (20)	29 (12)	<0.001
Para-clinics				
TC	184 (164–207)	189 (164–212)	191 (167–218)	0.2
HDL	44 (38–51)	45 (39–52)	46 (40–52)	0.11
LDL	110 (90–128)	110 (90–130)	114 (95–134)	0.2
TG	139 (107–181)	144 (110–195)	144 (102–199)	0.4
FBS	21 (16–29)	21 (17–29)	20 (16–27)	<0.001
Albumin	96 (90–105)	100 (92–114)	98 (90–112)	0.006
AST	25 (17–38)	24 (18–35)	22 (15–33)	0.2
ALT	178 (146–215)	185 (147–224)	179 (137–213)	0.042
ALP	184 (164–207)	189 (164–212)	191 (167–218)	0.093
AST/ALT	0.83 (0.68–1.05)	0.86 (0.69–1.08)	0.88 (0.72–1.13)	0.053
Vitamin-D3	4.40 (4.20–4.60)	4.40 (4.10–4.60)	4.30 (4.04–4.56)	0.032
Ferritin	24 (16–33)	27 (18–37)	25 (16–35)	<0.001
PLT	21 (16–29)	21 (17–29)	20 (16–27)	>0.9
Normal sonography	34/365 (9.3)	54/763 (7.1)	30/219 (14)	0.009
Fatty liver grade				
I	94/298 (32)	188/651 (29)	72/185 (39)	0.092
II	139/298 (47)	310/651 (48)	82/185 (44)	
III	65/298 (22)	153/651 (24)	31/185 (17)	

[a]Median (IQR); *n/N* (%), [b]Kruskal–Wallis rank sum test. Pearson's Chi-squared test. BMI=Body Mass Index; FBS=Fasting blood sugar; TC=Total cholesterol; PLT=Platelets; ALP=*Alkaline Phosphatase*; AST=Aspartate aminotransferase; ALT=Alanine aminotransferase; SG=Sleeve gastrectomy; OAGB=One-anastomosis gastric bypass; RYGB=Roux-en-Y gastric bypass; HDL=High-density lipoprotein; LDL=Low-density lipoprotein; IQR=Interquartile range, T2DM=Type 2 diabetic mellitus; HTN=Hypertension

reduction in AST and ALT levels, while OAGB showed a slight increase. SG also continued to show the greatest reduction in AST and ALT levels at both the 6-month and 1-year marks after the operation.

In the "Proportion" section of Table 2, values below 1 indicate a decrease from baseline, while values above 1 indicate an increase. Regarding AST values 1-year postsurgery, over 95% of individuals across all surgical methods had values within the normal range. For ALT levels, more than 95% of SG patients exhibited values within the normal range, but for OAGB and RYGB, the 95th percentiles were 42 and 39.05, respectively, indicating elevations beyond the normal range. Albumin levels remained relatively stable across follow-up periods for all surgical approaches.

Analysis of the AST ratio in the first 3 months postsurgery showed that SG had an average ratio of 0.92, signifying an 8% reduction in AST levels for 50% of patients. In OAGB, the average ratio was 1.05, indicating that 5% of individuals experienced a more than 5% increase in AST. RYGB surgery exhibited a median ratio of 1, indicating an equal distribution of AST level changes. During the subsequent 3 months, all three surgery types exhibited a reduction in AST levels, with SG demonstrating the highest reduction. A similar pattern was observed in ALT levels over the corresponding time intervals, albumin with a more pronounced decline compared to AST.

In Table 3, the odds ratio (OR) for AST elevation during the initial 3 months was twice as high in OAGB compared to SG, but balanced out during the subsequent 6 months. Over the 12-month postoperative period, the likelihood of AST increases in OAGB remained more than double that of SG. In addition, the OR for elevated ALT levels 1-year postoperative was twice as high in OAGB compared to SG.

Furthermore, women were 76% more likely than men to experience the AST and ALT levels increase, particularly in terms of the type of surgery. For every 1% increase in %TWL, the odds of ALT elevation 1 year after surgery increased by 7%, even when controlling for other variables, including the type of surgery.

Figure 2 provides a visual representation of the data, showing that approximately 95% of individuals fell within a range marked by a red line. The median values of AST, ALT, and Albumin across all three surgical types highlight that the most pronounced elevation in ALT and AST levels occurred during the initial 3–6 months of postoperative monitoring, primarily in SG and mini-bypass surgery. Notably, RYGB surgery did not exhibit significant increases in the AST and ALT levels.

These findings underscore the dynamic changes in the AST and ALT levels following different bariatric surgeries and the importance of considering both surgical type and patient characteristics in the postoperative management of liver health.

DISCUSSION

The investigation into the AST and ALT trends following various bariatric-metabolic surgeries offers valuable insights

Table 2: Comparison of liver enzyme/protein levels and proportional changes from baseline after bariatric surgery: A comparison across 3 surgical types

Surgery	Time	Observed values			Proportion to the baseline		
		AST	ALT	Albumin	AST	ALT	Albumin
SG	Baseline	21 (13–48)	25 (12–74)	4.4 (3.82–5)	-	-	-
OAGB	Baseline	21 (12–50)	24 (11–73)	4.39 (3.7–5)	-	-	-
RYGB	Baseline	20 (12–52)	22 (12–70.1)	4.3 (3.7–5)	-	-	-
SG	3 months	19 (11.25–38.75)	20 (10–48.75)	4.4 (3.8–5.1)	0.92 (0.47–1.78)	0.79 (0.33–1.96)	1 (0.86–1.17)
OAGB	3 months	22.7 (13–46)	23 (11–60)	4.3 (3.7–5)	1.05 (0.46–2.14)	0.92 (0.36–2.33)	1 (0.83–1.14)
RYGB	3 months	20 (12.95–41.05)	21 (10.95–50)	4.3 (3.8–4.9)	1 (0.44–2.21)	0.86 (0.36–2.5)	1 (0.84–1.19)
SG	6 months	16 (10–29.75)	14 (8–32)	4.4 (3.9–5)	0.79 (0.38–1.49)	0.6 (0.21–1.35)	1 (0.86–1.17)
OAGB	6 months	18 (12–35)	17 (10–38)	4.3 (3.7–4.9)	0.88 (0.36–1.68)	0.7 (0.27–1.67)	0.98 (0.83–1.16)
RYGB	6 months	17 (11–30.15)	15 (9–30.05)	4.2 (3.8–4.81)	0.89 (0.36–1.53)	0.69 (0.24–1.53)	1 (0.81–1.19)
SG	1 year	16 (11–27)	14 (9–29)	4.4 (3.8–5)	0.77 (0.38–1.62)	0.58 (0.23–1.49)	0.99 (0.83–1.17)
OAGB	1 year	20 (12–36.45)	19 (11–42)	4.2 (3.7–4.9)	0.95 (0.36–2)	0.83 (0.24–2.12)	0.98 (0.81–1.15)
RYGB	1 year	19 (12–34)	19 (10–39.05)	4.2 (3.7–4.81)	0.93 (0.39–1.76)	0.84 (0.29–1.91)	0.98 (0.8–1.2)

The values in the table are median (percentile 5–percentile 95). AST=Aspartate aminotransferase; ALT=Alanine aminotransferase; SG=Sleeve gastrectomy; OAGB=One-anastomosis gastric bypass; RYGB=Roux-en-Y gastric bypass

Table 3: Exploring factors affecting the increase (at least doubling) of liver enzymes by logistic regression

Variables	AST			ALT		
	3 months	6 months	1 year	3 months	6 months	1 year
Surgery (reference: SG)						
OAGB	2.08 (1.07–4.02)	1.39 (0.53–3.61)	2.57 (1.05–6.26)	1.65 (0.94–2.90)	1.38 (0.57–3.37)	2.25 (1.02–4.97)
RYGB	1.89 (0.87–4.11)	0.67 (0.16–2.73)	0.85 (0.24–3.09)	1.70 (0.88–3.30)	0.79 (0.23–2.77)	1.48 (0.56–3.94)
Sex (reference: Female)						
Male	0.24 (0.08–0.67)	0.42 (0.12–1.42)	0.75 (0.33–1.73)	0.23 (0.09–0.57)	0.53 (0.18–1.55)	0.28 (0.10–0.79)
Age (years)	0.99 (0.97–1.02)	0.97 (0.96–1.03)	1.03 (1.00–1.07)	0.99 (0.97–1.01)	0.99 (0.96–1.03)	1.02 (0.99–1.05)
T2DM (reference: No)						
Yes	0.66 (0.31–1.38)	2.59 (1.08–6.25)	0.87 (0.40–1.91)	0.95 (0.51–1.77)	1.75 (0.73–4.20)	0.85 (0.39–1.83)
TWL (%)	0.97 (0.91–1.04)	1.04 (0.96–1.13)	1.03 (0.98–1.08)	0.97 (0.92–1.03)	1.02 (0.95–1.11)	1.07 (1.03–1.12)

The results are reported as OR (95% CI), and the bolded values indicate statistically significant ORs at $P<0.05$. AST=Aspartate aminotransferase; ALT=Alanine aminotransferase; SG=Sleeve gastrectomy; OAGB=One-anastomosis gastric bypass; RYGB=Roux-en-Y gastric bypass; T2DM=Type 2 diabetic mellitus; TWL=Total weight loss; OR=Odds ratio; CI=Confidence interval

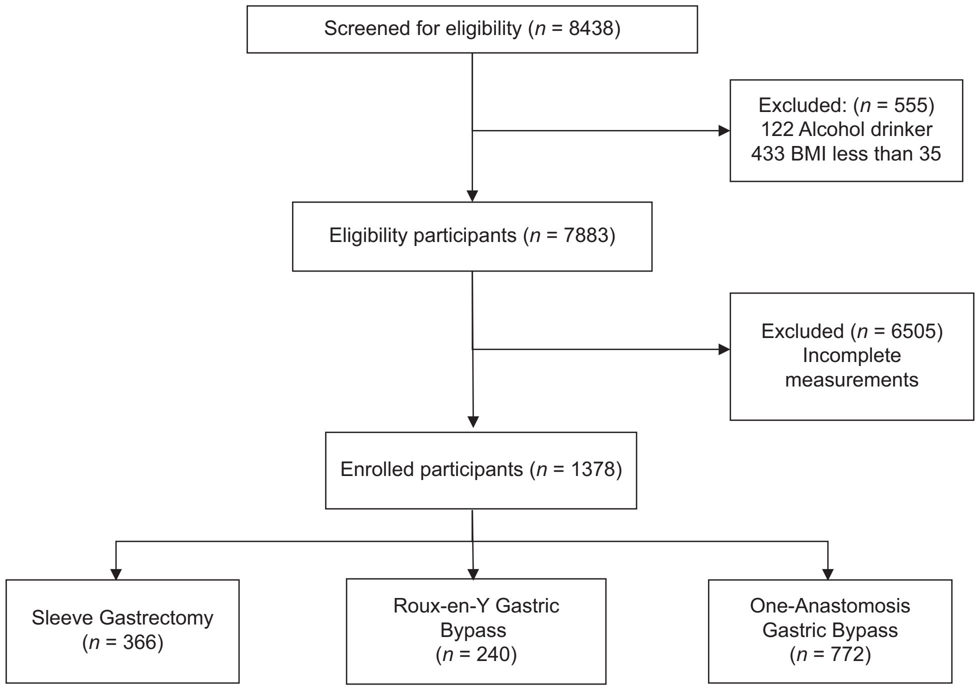

Figure 1: Flow diagram of subject participation

into their effects on liver health. The main finding of this study was the higher AST and ALT values in SG compared to other surgical methods.

In this study, the median values of AST, ALT, and Albumin across all three surgical types emphasize that the most pronounced elevation of ALT and AST trends occurred during the initial 3–6 months of postoperative monitoring, primarily in SG and OAGB. RYGB surgery did not exhibit significant increases in the AST and ALT levels. These graphical trends align with the findings of previous studies, which illustrated that RYGB stands out as one of the most effective bariatric surgical procedures when it comes to its positive impact on NAFLD, nonalcoholic steatohepatitis (NASH), and fibrosis. This effectiveness is notably higher compared to SG and laparoscopic adjustable gastric banding, likely due to its more pronounced metabolic effects. As mentioned, RYGB is technically a combination procedure, while SG is a restrictive method. Thus, it seems that weight loss alone is not the only important factor; the hypoabsorptive nature of bypass surgeries may also be more effective in promoting liver function recovery.[3] However, within the initial 6-month postsurgery, SG patients exhibited a more pronounced reduction in the AST and ALT levels, indicative of early improvement in liver function. This observation is consistent with the findings of Hirt *et al*. and Groth *et al*. studies, that reported a similar amelioration in the AST and ALT profiles, including ALT and AST, after SG.[18,19] Furthermore, the sustained decrease in the AST and ALT levels among SG patients at the 6-month are in line with the results of Groth *et al*.'s study, further supporting the notion of SG's substantial and lasting impact on liver health. This sustained improvement is evidenced by the amelioration of the AST and ALT profiles over a 6-month follow-up period (AST 22.0 vs. 16.0, P < 0.001, and ALT 27.5 vs. 19.0, P < 0.001), with no statistical differences noted regarding gender.[19]

This study revealed that at the 1-year postoperation, the AST and ALT values decreased once again for SG, while all three surgical types maintained values within the normal range. This aligns with the results of a study by Głuszyńska *et al*., which emphasized the overall safety of SG concerning liver function. They reported a statistically significant reduction in AST and ALT serum activity even at 6 months and 1 year postsurgery.[20] It's crucial to emphasize that maintaining the AST and ALT values within the normal range is a primary objective of bariatric surgery, potentially linked to changes in hepatic fat content and an increase in hepatic fatty acid oxidation, as supported by the literature.[3] The elevation of the AST and ALT signifies a risk of progressing to fibrosis and ultimately, end-stage liver disease, which is associated with a higher risk of all-cause mortality.[20,21] Interestingly, our findings revealed that over 95% of individuals who underwent all three surgical methods had AST values within the normal range 1 year after surgery. However, the elevation of ALT and AST levels beyond the normal range in OAGB and RYGB patients suggests a nuanced effect that may warrant further investigation. In addition, the odds of AST and ALT increase in OAGB remained more than double that of SG over the 12-month postoperative period, indicating a sustained effect. These findings reinforce

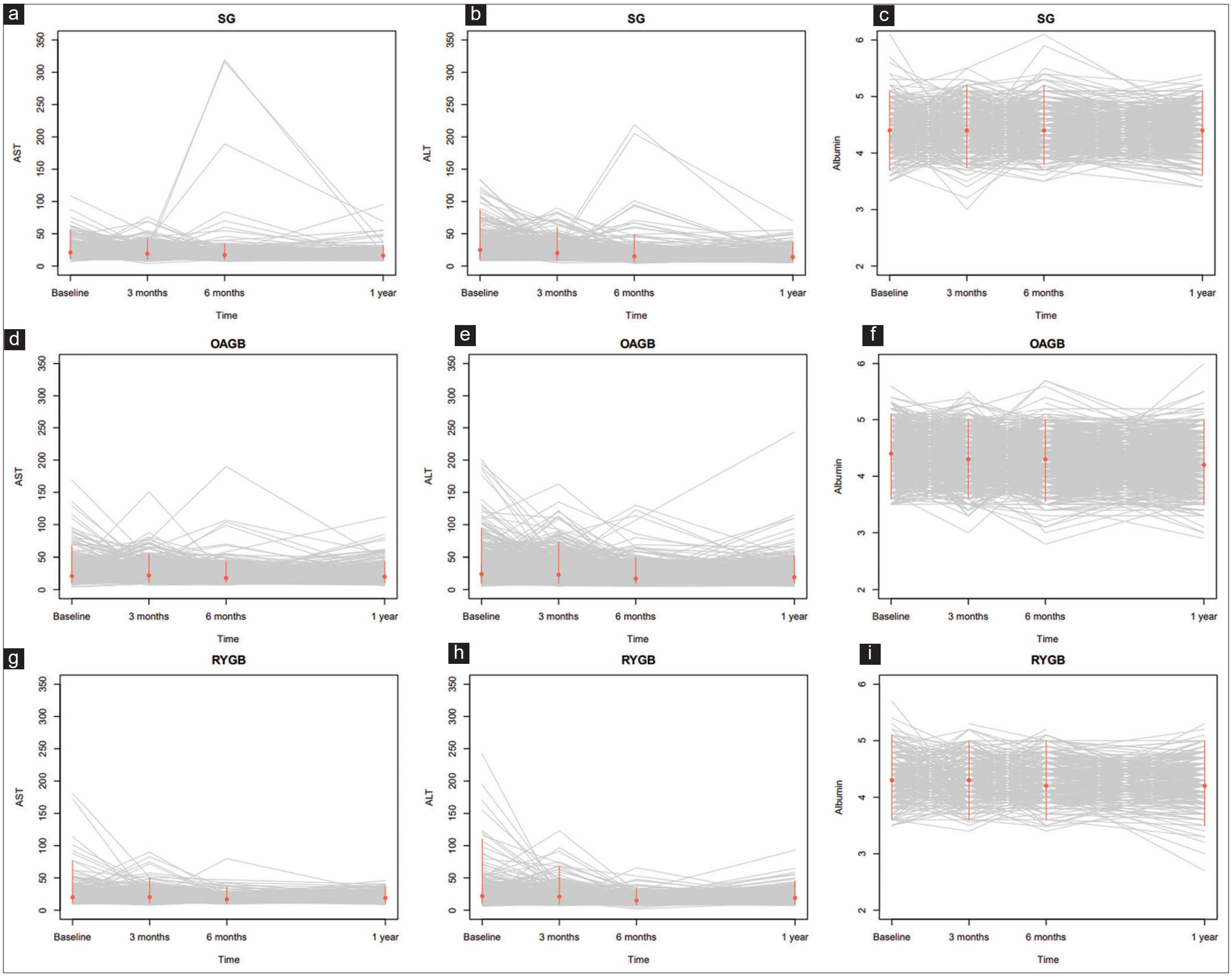

Figure 2: Changes in liver enzymes and albumin in the 1st year after surgery according to three common types of surgery. (a–c) Sleeve gastrectomy (SG): AST, ALT, and albumin, (d–f) One-anastomosis gastric bypass (OAGB): AST, ALT, and albumin, (g–i) Roux-en-Y gastric bypass (RYGB): AST, ALT, and albumin. The vertical red lines at each time point indicate the 95% confidence intervals for the mean

the idea that different surgical approaches have distinct effects on changes in the AST and ALT. Froylich *et al*. reported a worsening of fibrosis in OAGB patients, and Nikai *et al*. detected the presence of steatosis.[22,23] Recent data suggest that hypo-absorptive procedures remarkably change enterohepatic circulation and bile acid metabolism, which may contribute to liver function fluctuations.[3,4] This hypothesis aligns with the observation that acute liver failure after bariatric surgery has, so far, been observed only after bypass procedures.[24,25] Nevertheless, further research is warranted to elucidate these differences comprehensively.[26]

Our results showed that female patients had a 76% higher likelihood of AST and ALT elevations compared to males. This observation suggested that sex hormones influence hepatic fat metabolism and inflammation.[21,27] In addition, women have been shown to have a higher prevalence of hepatic failure after bariatric surgery, particularly in cases of rapid weight loss.[28]

This gender-specific effect aligns with our prior systematic review in 2019, which also highlighted the role of gender in AST and ALT changes following bariatric surgery.[27] In addition, 90% of hepatic failure cases involve females.[27] It is conceivable that more women undergo bariatric surgery, as evidenced by the consistent female-to-male distribution of 80% to 20% reported annually between 1998 and 2010 among bariatric surgery patients. Similarly, our participants exhibited a female-to-male distribution of 78% to 22%.[28] Furthermore, it is noteworthy that NAFLD appeared to have a higher prevalence among men, with 50 individuals affected. This gender disparity may be linked to the protective influence of female sex hormones, which have the capacity to direct fatty acids towards the production of ketone bodies rather than low-density lipoproteins or TG, potentially reducing the risk of hepatic fibrogenesis. This effect was substantiated by the presence of more severe steatosis and fibrosing NASH in postmenopausal women, although the menopausal status had not been evaluated as a studied outcome in that systematic review.[27]

We also observed a 7% increase in the odds of ALT elevation per 1% increase in %TWL. This suggests that patients experiencing extreme weight loss may be at greater risk for hepatic stress. Similar findings have been reported in other studies, where severe caloric restriction and lipid mobilization were associated with transient liver enzyme elevation.[29] Although our study excluded patients with known liver disease, prior research indicates that individuals with preoperative insulin resistance, NAFLD, or metabolic syndrome are at greater risk for liver dysfunction postsurgery.[20] As these patients may already have compromised liver function, postoperative liver enzyme monitoring should be prioritized in this subgroup.[25]

Dong *et al*. suggested that the alterations in the microbiome resulting from bariatric surgery can influence weight loss and the development of NAFLD.[29] In this context, elevations in the AST and ALT levels can also result from the proliferation of intestinal bacteria, which can produce harmful substances that may damage the liver. These harmful molecules are transported to the liver through the portal vein. In livers that are susceptible and subject to dietary challenges, this process can lead to liver damage.[6] In the largest cohort, it has demonstrated a strong gut microbiota modulation following SG and LRYGB by increasing Proteobacteria species. *Escherichia coli* and *Klebsiella pneumoniae* but the increase was considerably stronger after LRYGB.[30] There was also a rise in *Akkermansia muciniphila* count, known to be negatively related to inflammation, in patients after SG or RYGB.[30] In a recent study conducted by Kaniel *et al*., it has been shown a significant declining in gut microbial profile diversity after 6 months postoperative OAGB.[31] Even a remarkable decrease in Firmicutes count and a rise in Bacteroidota were seen at 12 months postoperative OAGB in another study.[31] This phenomenon can be associated with the distinct anatomical alterations and physiological variations resulting from OAGB versus RYGB. Moreover, there are several contributors, such as diet, gender, and age, influencing gut microbiota changes post-RYGB and OAGB that need to comprehensively analyzed over extensive periods. The practical implications of our findings suggest that specific patient populations require closer monitoring of liver function postbariatric surgery. OAGB patients exhibited the highest odds of AST and ALT elevation, particularly within the first 12 months postsurgery, emphasizing the need for extended liver enzyme surveillance in this group. In addition, women were significantly more likely than men to experience AST and ALT increases, which may be attributed to sex-specific metabolic adaptations following bariatric surgery. Another critical factor was %TWL, with a 7% increased likelihood of ALT elevation per 1% increase in TWL, reinforcing concerns about rapid weight loss and hepatic stress. Furthermore, patients with preexisting metabolic conditions such as T2DM exhibited a higher likelihood of transient ALT elevations, suggesting that underlying insulin resistance may contribute to liver function fluctuations. Based on these insights, we recommend that clinicians tailor postoperative monitoring schedules, prioritizing more frequent liver function assessments for OAGB patients, women, individuals with rapid weight loss, and those with metabolic disorders. To the best of our knowledge, no previous studies have included a sample size as large as the current study. We have addressed this gap and compared similar prior studies to improve upon some of their limitations. Those studies have focused on histopathological examination findings, resulting in smaller sample sizes. We chose a different approach to include a larger sample size based on routine follow-ups. However, we acknowledge that exploring the liver enzyme levels, which are common in clinical practice, may provide more useful insights. Our study included a prolonged follow-up period after MBS. Furthermore, we had the opportunity to compare trends in the hepatic enzyme values across three distinct bariatric techniques, as well as might control for other potential confounders, such as the exact timing of rapid weight loss, dietary adherence, and variations in supplementation.

However, we acknowledge that this study has its own limitations. For example, the aim of our study was to estimate the odds of a two-fold increase in ALT and AST at individual follow-up points (3, 6, and 12 months after surgery). Therefore, methods capable of accounting for within-subject correlation over the entire follow-up period were not applied. Although relative risk is generally preferred for retrospective cohort studies, ORs were reported in this study because separate logistic regression analyses were performed for each time point. Another important limitation of this study is the absence of comprehensive histopathological and advanced imaging assessments, including liver histology, magnetic resonance elastography, and controlled attenuation parameter on FibroScan. Liver biopsy data were also not available, as these procedures are invasive and not routinely employed for hepatic monitoring in bariatric patients. Nevertheless, this limitation is unlikely to have substantially influenced our findings, as all participants underwent regular pre-and postoperative liver function testing.

CONCLUSION

We found that liver enzyme trends following bariatric surgery differed by surgical type, sex, and metabolic status. While AST and ALT levels initially increased postoperatively, their trends stabilized after 6 months in SG patients and after 12 months in RYGB and OAGB patients. Based on these findings, OAGB patients, women, individuals with rapid weight loss, and those with preexisting metabolic disorders like T2DM may require more frequent liver function monitoring beyond standard follow-up schedules. Future research should explore long-term hepatic outcomes beyond 1 year to further refine postbariatric surgery monitoring protocols.

Ethics and consent

This study was approved by the research ethics committee (Ethics number: IR. IUMS. REC.1401.684). Written informed consent form was received from all patients at the time of first registry in our database for any possible anonymous usage from their data.

Informed consent

Written informed consent form was received from all patients at the time of the first registry in our database for any possible anonymous usage of their data.

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Conflicts of interest

There are no conflicts of interest.

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