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Estimate the Effect of Age Pre and Post Sleeve Gastrectomy on Liver Functions

Conflict of interest: nothing to declare.
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Abstract

Introduction. The obesity is markedly increasing in low-income and middle-income countries. Bariatric surgery has proven to be effective in treating obesity and its related diseases. The liver is the largest intracorporeal organ in the human body and plays a predominant role in several pivotal functions to maintain normal physiological activities.
Purpose. To demonstrate the effect of age on patients pre and post sleeve gastrectomy on liver functions.
Materials and methods. This study was conducted at Al-Basrah metabolic and Bariatric Surgery Centre, Iraq, from December 2021 to March 2022, on 52 patients with morbid obesity treated by sleeve gastrectomy. Patients were divided into three age categories and two groups according to the periods of their operation. The first group was collected before the operation, the second group was collected after six months of the operation.
Results. There is a significant reduction in BMI after 6 months in first and second categories of age, there was significant lower in ALT and ALP after 6 months in first and second categories of age. Regarding AST there is only significant reduction in the second category and there is a significant increase in INR in the first category.
Conclusion. The excess weight loss tended to increase with decreasing age, AST, ALT, ALP this enzyme levels before and after the surgery can provide insights into liver function and potential liver-related effects of the procedure and age have effect on INR level.
Keyword: sleeve gastrectomy, liver functions, bariatric surgery, middle-income countries, obesity, AST, ALT, INR

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Оценка влияния возраста пациентов на показатели функции печени до и после рукавной гастрэктомии

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Информированное согласие: от всех пациентов были получены информированные согласия, анонимность сохранялась в течение всего исследования.
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Резюме

Введение. В странах с низким и средним уровнем дохода наблюдается заметный рост числа людей с ожирением. Бариатрическая хирургия доказала свою эффективность в лечении ожирения и связанных с ним заболеваний. Печень является крупнейшим внутриполостным органом человеческого тела и играет первостепенную роль в выполнении ряда важнейших функций по поддержанию нормальной жизнедеятельности организма.
Цель. Изучение влияния возраста пациентов на функции печени до и после рукавной гастрэктомии.
Материалы и методы. Данное исследование проводилось в Центре метаболической и бариатрической хирургии Аль-Басра, Ирак, с декабря 2021 г. по март 2022 г. В исследовании участвовали 52 пациента с патологическим ожирением, которые подверглись рукавной гастрэктомии. Пациенты были разделены на три возрастные категории и две группы согласно срокам проведения операции. Первая группа была сформирована до операции, вторая – через 6 месяцев после операции.
Результаты. Отмечено достоверное снижение ИМТ через 6 месяцев в первой и второй возрастных категориях, достоверное снижение уровней АЛТ и АЛП через 6 месяцев в первой и второй возрастных категориях. Что касается АСТ, то достоверное снижение отмечено только у пациентов второй категории, а достоверное повышение МНО – у пациентов первой категории.
Заключение. Выявлена следующая закономерность: потеря избыточного веса была выше у лиц более молодого возраста. Уровни АСТ, АЛТ, АЛП до и после операции позволяют оценить функцию печени и потенциальные последствия оперативного вмешательства для ее функционирования; возраст пациента влияет на показатели МНО.
Ключевые слова: рукавная гастрэктомия, функциональные показатели печени, бариатрическая хирургия, страны со средним уровнем дохода, ожирение, АСТ, АЛТ, МНО

■ INTRODUCTION

Obesity is a condition characterized by an excessive accumulation of fat in the body [1], to the extent that it may impact one's health [2]. Obesity is a major public health issue all around the world [3]. The prevalence of obesity is also markedly increasing in low-income and middle-income countries [4]. Therefore, if these trends continue, by 2025, the global prevalence of obesity will reach 18% in men and >21% in women, with severe obesity surpassing 6% and 9%, respectively [5]. Therefore, Bariatric surgery has proven to be effective in treating obesity and its related diseases [6]. Sleeve gastrectomy, is a surgical weight-loss procedure in which the stomach is reduced to about 15% of its original size, by the surgical removal of a large portion of the stomach, following the major curve. The open edges are then attached together to leave the stomach shaped more like a tube, or a sleeve, with a banana shape [7].

The liver is the largest intracorporeal organ in the human body and plays a predominant role in several pivotal functions to maintain normal physiological activities [8]. An organ as complex as the liver can experience a range of problems including fatty liver disease, hepatitis, cirrhosis, hepatocellular carcinoma and cholangiocarcinoma [9]. It is an organ considered as the most significant organ for detoxification and protein synthesis, both of which are facilitated by a number of enzymes. Therefore, analyse liver health is represented by estimating the enzymes that released from liver cells and proteins that created by the liver and released into the blood stream [10]. The most common tests of liver function include total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) [11]. Whereas, bilirubin is the break down product of haemoglobin produced within the reticuloendothelial system, emitted in unconjugated (indirect bilirubin) (BilIND) form which enters into the liver, converted to conjugated (direct bilirubin) (Bili D) forms bilirubin mono and diglucuronides by the enzyme UDP-glucuronyl transferase [12].

As AST can be rise in diseases affecting other organs, involve acute haemolytic anaemia, pancreatitis, myocardial infarction, burns, muscular skeletal diseases and acute kidney injury. Thus, ALT is more specific for liver inflammation and disease than AST. In addition to that, clearance of serum aminotransferases involves catabolism by the reticuloendothelial system, and in that assessment, is comparable to the clearance of other serum proteins. AST is consumption more rapidly than ALT, and the major site of clearance is the hepatic sinusoidal cell [13]. At the same time, alkaline phosphatase is important enzyme in the subject, which represents a group of isoenzymes created by liver, kidneys, bones, placenta and small intestine [14]. The serum Alkaline phosphatase (ALP) level signifies the total quantities of isoenzymes that are released from the specialized tissues into the blood stream and its major function is thought facilitate transport across cell membranes and assistance in metabolism [15]. Prothrombin time (PT/INR) whereas the PT is a measure of the integrity of the extrinsic and final common pathways of the procoagulant cascade. The PT represents the time, in seconds, for patient plasma to clot after the addition of calcium and an activator of the extrinsic pathway (thromboplastin). Thus, deficiencies or inhibitors of clotting factors within the extrinsic and final common pathways result in prolongation of the PT and the INR is a mathematical conversion of a patient's PT that accounts for the sensitivity of the thromboplastin used in a given laboratory by factoring in the international sensitivity index (ISI) value supplied by its manufacturer [16].

The two laboratory tests are used to evaluate coagulation disorders where the PT test measures the time it takes for blood to clot in response to prothrombin, a clotting factor, activation, and the PTT test measures the time it takes for blood to clot in response to clotting factor activation [17].

The International Normalised Ratio (INR) is calculated as follows: INR = (patient PT/MNPT) ISI, in which MNPT is the geometric mean of the PT of at least 20 healthy subjects of both sexes tested at the performing laboratory. Since its introduction, INR has reduced the interlaboratory variations in PT results [18]. A number of researchers including Meyer et al., and Donaldson et al. they suggested that liver enzymes abnormalities have relationship with obesity, hormone therapy or autoimmunity [19, 20].

Some studies show that bariatric surgery causes the changes in intestinal anatomy and metabolism may precipitate severe hepatic complications under certain circumstances [21].

Liver-related complications or adverse outcomes following BS suggest that we should pay attention to the evaluation of liver status after surgery [22, 23]. Bariatric surgery (BS) can improve the adverse metabolic status and hepatocellular pathological status of nonalcoholic fatty liver disease (NAFLD) [24, 25]. Several clinical studies have shown that bariatric surgery has an important positive impact on the liver, with improvements of liver enzymes and liver histology [26, 27].

Patient's age is a crucial determinant for many medical interventions, including the results of Bariatric surgery. Differences in energy requirements, psychological condition as well as physiopathological and behavioral hypothesis may explain the association between age and weight loss after bariatric treatment. No upper age limit for bariatric surgery was recommended by the consensus panel. At the time of publication, it was felt that insufficient data was available to make a recommendation for or against surgery in the adolescent population. However, multiple studies have now shown bariatric surgery to be safe in both extremes of age [28]. The results of sleeve gastrectomy may differ depending on patient's age, a few reported studies suggest that younger patients may achieve more satisfactory weight loss results. However, these studies were carried out for a shorter followup, and as it is known, long-term observation is crucial to analyse the effects of BS [29].

■ PURPOSE OF THE STUDY

To demonstrate the effect of age on patients pre and post sleeve gastrectomy on liver functions.

■ MATERIALS AND METHODS

Study Population

This is a prospective study will be carried out on 52 patients with morbid obesity by sleeve gastrectomy, with age about 18–59 years for about 10-months duration at Al-Basra metabolic and Bariatric Surgery Center Iraq, the southern part of Iraq. All patient will be subjected to questioner including: age, sex, marital state BMI, chronic disease, drugs history. Blood sample will be drawn at preoperative time, and sex months after surgery, for LFT, PT, PTT, INR.

Required data that were collected by the researcher depend on a direct interview with patients before the operation and being admitted to the study, using the questionnaire, which includes data on items such as age, sex, height, weight and geographical area.

Exclusion criteria are diabetes, cardiomyopathy, chronic liver disease, liver cirrhosis and chronic hepatitis (hepatitis B and hepatitis C), also drugs that cause abnormal liver enzymes or prolong PT and INR like statin or warfarin and alcoholic drinker.

Patient's weight was measured while they were standing without shoes using the same scale for all patients (Detecto, model 339, physician scale with height rod eye level, max. 180 kg ± 0.1 kg, Philippine).

Study Design

Patients were divided into three age groups and two groups according to the periods of their operation. The first group was collected before the operation, the second group was collected after six months of the operation. BMI was calculated as Body Mass Index = Weight (kg) / height (m2).

Blood samples

A total (3.5 ml) of blood will draw from the patient preoperational and post operation and subdivided to (2 ml) of whole blood for PT (prothrombin time) and INR (international normalized ratio), and (1.5 ml) serum for liver function teste (LFT) include:

a. Total serum bilirubin both direct and indirect.
b. Liver enzymes (ALT alanine transaminase and AST aspartate aminotransferase).
c. Alkaline phosphatase.

■ RESULTS

As shown in table (1) there is significant reduction in BMI after 6 months in first and second categories of age, although there is reduction in BMI in the third category but it is statistically not significant.

Table 2 shown no significant in bilirubin after six months in all categories of age.

In Table (3) we found that there was significant reduction in ALT and ALP after 6 months in first and second categories of age, although there is reduction in ALT and ALP in the third category but it is statistically not significant. Regarding AST there is only significant reduction in the second category.

Table (4) shown only significant increase in INR in the first category, while not significantly increase in the second and third categories and there are no significant changes in the other parameters.

Table 1
Comparison between (G1) and (G3) according to the Age, regarding the BMI

Variables	Age Groups					
	15–30 years		31–45 years		46–60 years	
	Mean±SD	Median (Min.–Max.)	Mean±SD	Median (Min.–Max.)	Mean±SD	Median (Min.–Max.)
BMI before	44.5411± 5.94901	44.0800 (35.43–55.16)	46.9378± 11.15499	43.2500 (37.66–79.04)	44.4444± 8.54185	44.0600 (31.48–58.94)
BMI after six months	32.2711± 6.21078	31.1400 (22.53–45.17)	33.5360± 5.56526	33.2600 (24.49–42.15)	31.5600± 3.74276	33.0300 (26.57–35.94)
P-value	**0.001**		**0.0001**		0.08	

Table 2
Comparison between (G1) and (G3) according to the Age, regarding the TSB, Bili D, and Bili IND

Variables	Age Groups					
	15–30 years		31–45 years		46–60 years	
	Mean±SD	Median (Min.–Max.)	Mean±SD	Median (Min.–Max.)	Mean±SD	Median (Min.–Max.)
TSB before	0.8326± 0.35258	0.7200 (0.50–2.10)	0.8343± 0.41630	0.7000 (0.28–22.2)	0.7456± 0.24419	0.7200 (0.45–1.28)
TSB after six months	0.7239± 0.37234	0.6400 (0.35–1.81)	0.7515± 0.31035	0.6600 (0.38–1.67)	0.7080± 0.302	0.6500 (0.36–1.20)
P-value	0.327		0.455		0.893	
Bili D before	0.2826± 0.16776	0.2400 (0.10–0.60)	0.2913± 0.16821	0.2700 (0.10–0.68)	0.2256± 0.18467	0.1700 (0.05–0.65)
Bili D after six months	0.2839± 0.20371	0.1800 (0.11–0.90)	0.2525± 0.12443	0.2250 (0.11–0.62)	0.3200± 0.23622	0.2000 (0.14–0.70)
P-value	0.925		0.349		0.715	
Bili IND before	0.5495± 0.37064	0.5200 (0.17–0.199)	0.5430± 0.37986	0.4800 (0.12–1.94)	0.5167± 0.08078	0.5400 (0.40–0.64)
Bili IND after six months	0.4389± 0.27101	0.4000 (0.18–1.31)	2.2820± 7.93970	0.5050 (0.18–36.00)	0.3880± 0.16634	0.5000 (0.16–0.51)
P-value	0.240		0.970		0.138	

Table 3
Comparison between (G1) and (G3) according to the Age, regarding the AST, ALT, and ALP

Variables	Age Groups					
	15–30 years		31–45 years		46–60 years	
	Mean±SD	Median (Min.–Max.)	Mean±SD	Median (Min.–Max.)	Mean±SD	Median (Min.–Max.)
AST before	29.00± 8.869	28.00 (17–51)	38.43± 42.442	31.00 (15–229)	26.67± 8.031	28.00 (14–37)
AST after six months	23.72± 9.815	22.00 (14–42)	22.90± 7.181	21.50 (11–38)	28.20± 7.225	30.00 (18–36)
P-value	0.150		**0.012**		0.343	
ALT before	35.00± 16.826	28.00 (16–85)	41.13± 43.686	36.00 (12–236)	28.44± 10.442	30.00 (13–39)
ALT after six months	19.50± 8.920	18.00 (11–44)	18.55± 4.419	18.50 (10–29)	22.40± 9.370	19.00 (12–35)
P-value	**0.002**		**0.000**		0.416	
ALP before	200.74± 48.415	202.00 (109–301)	198.43± 58.920	194.00 (100–337)	211.22± 37.745	229.00 (146–262)
ALP after six months	114.61± 64.392	79.00 (60–240)	130.75± 57.117	115.50 (63–250)	160.80± 58.410	194.00 (68–205)
P-value	**0.003**		**0.0001**		0.500	

Table 4
Comparison between (G1) and (G3) according to the Age, regarding the PT, PTT, and INR

Variables	Age Groups					
	15–30 years		31–45 years		46–60 years	
	Mean±SD	Median (Min.–Max.)	Mean±SD	Median (Min.–Max.)	Mean±SD	Median (Min.–Max.)
PT before	14.1474± 3.81858	13.4000 (11.70–29.30)	14.5352± 4.84620	13.4000 (8.11–29.70)	13.6333± 1.02225	13.7000 (12.00–15.20)
PT after six months	14.9856± 5.80677	14.3500 (2.14–34.70)	15.4900± 4.18480	14.6500 (12.10–32.10)	14.5800± 2.59557	14.1000 (12.30–18.80)
P-value	0.113		0.079		0.686	
PTT before	32.5842± 7.11144	31.4000 (24.90–58.00)	33.6130± 9.18563	33.6130 (23.20–68.80)	33.8478± 4.54833	32.7000 (28.00–41.10)
PTT after six months	32.7278± 5.77365	31.8500 (26.30–52.40)	32.8600± 5.10649	30.6000 (26.90–48.60)	30.4000± 2.73313	31.3000 (25.60–32.10)
P-value	0.777		0.881		0.225	
INR before	1.2226± 0.34297	1.1600 (0.90–2.55)	1.2822± 0.43453	1.1500 (0.96–2.68)	1.1844± 0.08777	1.1900 (1.04–1.33)
INR after six months	1.3944± 0.45358	1.2650 (1.15–3.16)	1.3765± .38617	1.2800 (1.08–2.91)	1.2700±.35010	1.2300 (0.36–1.20)
P-value	**0.006**		0.073		0.686	

■ DISCUSSION

In this study when compare between the level BMI according to the age, the present study found that there is significant difference (P=0.001, P=0.001) between patients before and after 6 months of surgery through the first and second age categories and that is in agreement with [30] who said that younger age is associated with better weight loss. In our study there is reduction in the body weight in third category but not statistically significant. It may be due to the fact that elderly patients exercised less and had more comorbidities. The excess weight loss tended to increase with decreasing age, probably resulting from stricter adherence of younger patients to exercise programs and diet changes advised by dieticians. Other reasons that older patients with higher BMI are unable to get as close to a BMI 24.9 could include excess this agreement with [31, 32].

So, when compare the level of AST according to the age, we found that there is a statistically significant lower in patients second category of age (P=0.012) and not statistically significant lower in patients first and third categories of age between patients before and after 6 months of surgery.

This disagreement with [33]. Changes in this enzyme levels before and after the surgery can provide insights into liver function and potential liver-related effects of the procedure.

AST is a liver enzyme that plays a vital role in various metabolic processes, including protein metabolism. SG which involves the removal of a significant portion of the stomach, leading to changes in gastrointestinal anatomy and metabolic processes, therefore comparing AST values between different age groups before and after sleeve gastrectomy can help researchers and healthcare professionals understand how age influences liver function and the impact of the surgery on different age categories. This needs further studies and research.

Moreover, the current study showed that there is a significant reduction in first and second age categories in ALT level (P=0.002, 0.000) respectively. Similar results were

reported previous study Venâncio F.A. et al. whose said that serum liver enzymes such as AST and ALT are biomarkers of liver function and injury. An increase in the serum levels of these enzymes is associated with hepatocyte injury and inflammation [34]. The increase of serum liver transaminases observed in RYGB operation, suggests worsening of hepatic function in these patients. Although most studies have reported beneficial effects of BS on liver function, including a reversal of pathological liver changes [35] some studies found an increased risk of progressive liver dysfunction and worsening of inflammation and fibrosis following RYGB [35, 36]. This fact might be partially attributed to the malabsorption that occurs after RYGB [37], and in SG there is no malabsorption. On the other hand, the significant decrease of serum liver transaminases observed in the SG group is consistent with previous reports [38].

Moreover, the current study showed that there is a significant reduction in first and second age categories in ALP level (P=0.003, 0.000) respectively.

This is supported by the fact that a significantly lower level of serum Parathyroid hormone after SG, ALP which is the marker of bone resorption is decreased [39].

In this study when compare between the level INR according to the age, we found that there is significant difference (P=0.006) between patients before and after 6 months of surgery through the first age category only, and that is similarly with [40] whose said that age have effect on INR level. This is might be due to the metabolic alterations can influence the coagulation cascade and clotting factors, leading to changes in INR [41], because the metabolism slows with age due to loss of muscle tissue, but also due to hormonal and neurological changes.

The prevalence of obesity is dramatically rising at present, making it a public health issue [42]. The liver is one of the largest lymphoid organs in the human body. A primary line of defence, it modulates the inflammatory response in autoimmune diseases [43, 44].

■ CONCLUSION

The excess weight loss tended to increase with decreasing age. AST, ALT, ALP this enzyme levels before and after the surgery can provide insights into liver function and potential liver-related effects of the procedure and age have effect on INR level.

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