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EFFECT OF CHOLECYSTECTOMY ON SERUM LIPID PROFILE PRE AND POST OPERATION

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ABSTRACT

Background: The objective of this study was to examine changes in body mass index (BMI). and to determine the changes in lipid profile parameters in three stages: preoperative, postoperative and long periods for cholecystectomy. **Methods:** Blood samples were collected from two groups of females (Women who will undergo their cholecystectomy as well as women who have been undergoing from cholecystectomy for a long time) with a total number of 128 women and 64 control females at AL-Hussein Teaching Hospital in Thi-Qar Governorate. from November 2017 to May 2018. Serum was separated by centrifugation and lipid profile (TC, TG, HDL, LDL, VLDL) were measured. The data were analyzed using SPSS. **Results:** Levels of BMI was significantly increased in all patient groups in comparison with control groups ($p \leq 0.05$). It was found significant differences in BMI between each of post (short and long terms) groups ($p \leq 0.05$). And the levels of serum TC, TG, LDL and VLDL were significantly increased in all patient groups in comparison with control groups ($p \leq 0.05$). It was found no significant differences in the concentration of serum TC, TG, LDL and VLDL between each of post (short and long terms) groups ($p \leq 0.05$). Also it was found significant differences in the concentration of serum TC, TG, LDL and VLDL between each of post (short and long terms) and control groups ($p \leq 0.05$). While levels of serum HDL was significantly decreased in all patient groups in comparison with control groups ($p \leq 0.05$). It was found no significant differences in the concentration of serum HDL between each of post (short and long terms) groups ($p \leq 0.05$). Also it was found a significant difference in the concentration of serum HDL between each of post (short and long terms) and control groups ($p \leq 0.05$). **Conclusion:** May be patients at risk of continuing to obesity as well as changes in some serum lipid profiles, long-term follow-up of these patients should be considered. The best solution is keeping a healthy diet and lifestyle after cholecystectomy. Follow-up long after the surgery may therefore be necessary to facilitate additional healthcare interventions.

KEYWORDS: Body mass index, cholecystectomy, lipid profile.

INTRODUCTION

The gallbladder is a small, thin-walled green sac[1], lies on the underside of the liver in the main liver scissura at the junction of the right and left lobes of the liver.[2] The Choledocholithiasis is defined as a presence or formation of gallstones in the common bile duct (CBD).[3] The basis for which is the impaired metabolism of cholesterol, bilirubin and bile acids, which is characterized by the formation of gallstones in the hepatic bile duct, common bile duct.[4] The prevalence of cholecystitis is approximately of 13% to 19% in Thi -Qar during the period between 2012-2017. Most cases are asymptomatic, as gallstones are usually discovered incidentally during routine imaging for other abdominal conditions. Although small stones can be spontaneously eliminated to the duodenum through the ampulla of Vater, the narrow termination of the bile duct frequently leads to the impaction of stones.[5] Gallstones and diseases of the biliary tract affect more than 10% of the adult population.[6] which can be caused by either primary stones that originated from the bile duct or by secondary stones that migrated from the gallbladder, and can lead to obstructive jaundice, cholangitis, or pancreatitis[3], can be lethal. Moreover, surgery to remove the gallbladder in these patients, in an attempt to relieve the symptoms, gives variable results.[6]

Laparoscopic surgery is a surgical technique in which operations in the abdomen are performed through small incisions in the abdominal.[7] Today, more than 90% of cholecystectomies are performed laparoscopically. The procedure has been found to be superior to open cholecystectomy with less morbidity and mortality.[8] Currently, CO2 is usually used for insufflation due to its low cost, non-flammability, chemical stability.[9] Cholecystectomy increased during two years past to approximately of 13% to 17% in Thi –Qar. The CO2 pneumoperitoneum causes an increase in intra-abdominal

pressure with a consecutive elevation of the diaphragm which can result in hyperventilation[10] when the laparoscopic procedure is completed, abdominal deflation is performed this reduces the intra-abdominal pressure and increases splanchnic perfusion.[11]

Cholecystectomy has long been considered as a safe procedure, while secondary effects have been overlooked[12] where the gallbladder is a 'controller' operating in concert with key pathways governing metabolic homeostasis.[13] Thus, several pathophysiological and clinical changes are anticipated after cholecystectomy procedure associated with loss of reservoir-concentrating function of the gallbladder.[14,15] The intestine will act as the major bile acid reservoir and bile acid synthesis will show a twofold increase.[16] Different studies in mice and humans showed that cholecystectomy increased the enterohepatic recirculation rates of bile acids, in particular during fasting.[17] Accelerated intestinal recycling is associated with increased secretion rates of bile acids and cholesterol in bile, after cholecystectomy. Therefore, although the bile acid pool is not enlarged, fat is digested and absorbed normally in cholecystectomized patients.[18] In keeping with an increased exposure of the bile acid pool to intestinal bacteria as a result of a more rapid enterohepatic circulation, cholecystectomy also increases bacterial deconjugation and dehydroxylation of bile acids, and thereby the proportion of secondary bile acids.[19,20] Despite conflicting results, there is agreement about the increased incidence of colon cancer after cholecystectomy Secondary bile acids, known to have a role in colon cancer promotion, have been considered responsible since cholecystectomized patients have high proportions of Secondary bile acids in their bile acids pool.[21]

Gallstones are formed as a result of impaired metabolic regulation of human body. Biliary cholesterol hypersecretion is the main cause for biliary cholesterol supersaturation and bile stasis also plays an additional role. Impaired lipid homeostasis can give rise to cholesterol hypersecretion from biliary canaliculi.[22] Cholesterol is one of the key components for production of bile acids, steroid hormones, and Vitamin D. On one hand small quantities of cholesterol are important and necessary, on the other hand high levels of cholesterol can damage arteries and are potentially linked to diseases such as those associated with the cardiovascular system (heart disease).[23]

Female sex hormones (Estrogens) lowers cholesterol levels. Increased cholesterol level due to bile calculi and ducts. In patients with gallstones, dietary cholesterol increases biliary cholesterol secretion. In addition to environmental factors such as high-caloric and cholesterol-rich diets, genetic factors play an important role in cholesterol hyper secretion and gallstone formation.[24] Triglycerides are not soluble in water and thus cannot directly enter the bloodstream, which is mostly water. Within the small intestines, bile salts surround the monoglycerides and fatty acids to form micelles. The non–water-soluble fat particles (e.g., fatty acids, monoglycerides) are found in the middle of the packaged micelle, whereas the hydrophilic part faces outward. This structure allows the products of lipid digestion to travel to the brush border membrane. Once there, fats are absorbed into the epithelial cells of the intestine. Bile is absorbed and transported by the portal vein to the liver for reuse; this process is called enterohepatic circulation. Monoglycerides and fatty acids that made it into the intestinal cells via micelle transport are now recon- structed to form triglycerides again.[25] Most lipids, such as triglycerides, are nonpolar and therefore very hydrophobic molecules. They do not dissolve in water. To be transported in watery blood, such molecules first must be made more water-soluble by combining them with proteins produced by the liver and intestine to form are lipoproteins spherical particles with an outer shell of proteins, phospholipids, and cholesterol molecules surrounding an inner core of triglycerides and other lipids Lipoproteins are categorized and named mainly according to their density, which varies with the ratio of lipids (which have a low density) to proteins (which have a high density). From largest and lightest to smallest and heaviest, the four major classes of lipoproteins are chylomicrons, very-low-density lipoproteins (VLDLs), low-density lipoproteins (LDLs), and high-density lipoproteins (HDLs).[26] The lipid profile or lipid panel is a pattern of lipids in the blood, which is also a group of blood tests used to assess the risk of developing cardiovascular disease or to monitor treatment effect.[27] Hypertriglyceridemia and a low HDL are associated with gallstones.[28] It is not surprising that obese patients who have hypertriglyceridemia and a low HDL are at higher risk for developing stones.[29]

The aim of this study was to determine their propensity for weight gain, and to determine the changes in serum lipid levels (serum TG, total cholesterol, HDL, VLDL, and LDL) preoperative and postoperative cholecystectomy and compared with control group. As well as comparison between short and long term after cholecystectomy.

SUBJECTS AND METHODS

This study has been conducted at AL-Hussein Teaching Hospital in Thi-Qar, Biochemistry Laboratory in College of Science, at the period between 10/11/2017 to 5/5/2018. It included (192) women, (64) control and (64) patients before operation and 24 hr after operation and (64) long term for a period ranging from 3 months to 3 years, their ages were between 20 -69 years. Those patients were diagnosed by specialist doctors as uncomplicated, symptomatic gallstones (cholelithiasis), who underwent elective laparoscopic cholecystectomy. Patients with respiratory, hepatic, cardiovascular (ischemic heart disease and hypertension), diabetes were excluded from this study. Patients were weighed and

measured and their BMI was then calculated using the formula — weight in kilograms/height in meters squared.

Blood Sampling

Five ml of blood vein puncture were drawn from each fasting patient and control. the sample left at room temperature for 10 minutes to clotted then centrifuged for at 3000 rpm for 10min, the serum samples were separated and stored at (-20ºC) for later measurement of biochemical parameters, unless used immediately.

Determination of Serum lipid profile

The estimation of lipid profile includes the total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL), high density lipoprotein (HDL) and very low density lipoprotein (VLDL).[30,31] Total cholesterol (TC), triglyceride (TG), and high density lipoprotein (HDL) were estimated spectrophotometrecaly by using special kit for each one from Biolabo company, while the very low density lipoprotein (VLDL) and low density lipoprotein (LDL) were determined through different equations as following: -

VLDL = TG / 5.[32]

LDL= TC – (HDL + VLDL).[32]

Statistical analysis

Statistical analysis was done using the software SPSS version 17.0; the results were expressed as mean ± standard deviations (mean ± SD). One-way ANOVA was used to compare parameters in different studied groups. P-values ($P \leq 0.05$) were considered statistically significant.

RESULT

In this study, we estimated the levels of BMI and lipid profile, Women patients and comparison between short and long term after cholecystectomy and also with compared with control group. Levels of BMI showed a significant increase in all patient groups in comparison with control groups ($p \leq 0.05$). Table 1, figure 1 shows a significant increase in BMI in the group post long terms in comparison with control group ($p \leq 0.05$). It was found significant differences in BMI between each of post (short and long terms) groups ($p \leq 0.05$). And the levels of serum TC, TG, LDL and VLDL were showed significant increase in all patient groups in comparison with control groups ($p \leq 0.05$). Table 2,3,4 and 5 shows a significant increase in the concentration of serum TC, TG, LDL and VLDL in the groups pre and each of post (short and long terms) groups in comparison with control group ($p \leq 0.05$). It was found no significant differences in the concentration of serum TC, TG, LDL and VLDL between each of post (short and long terms) groups ($p \leq 0.05$). Also it was found significant differences in the concentration of serum TC, TG, LDL and VLDL between each of post (short and long terms) groups and control group ($p \leq 0.05$). While levels of serum HDL showed a significant decrease in all patient groups in comparison with control groups ($p \leq 0.05$). Table 6 show a significant decrease in the concentration of serum HDL in the groups pre and post (short and long terms) in comparison with control group ($p \leq 0.05$). It was found no significant differences in the concentration of serum HDL between each of post (short and long terms) groups ($p \leq 0.05$). Also it was found a significant difference in the concentration of serum HDL between each of post (short and long terms) groups and control group ($p \leq 0.05$). Also it was found a significant difference in the concentration of serum HDL between control (A and B) groups ($p \leq 0.05$).

Table 1: Body mass index in all studies groups.

Group of Age	NO.	BMI (Kg/m^2)			
		Con	Pre	Post	
				Short term	long term
A: (20-45)	37	24.00±5.93^{c,A}	31.98±7.05^{b,A}	31.98±7.05^{b,A}	35.09±7.44^{a,A}
B: (46-69)	27	25.03±5.54^{c,A}	32.10±7.53^{b,A}	32.10±7.53^{b,A}	34.88±7.56^{a,A}

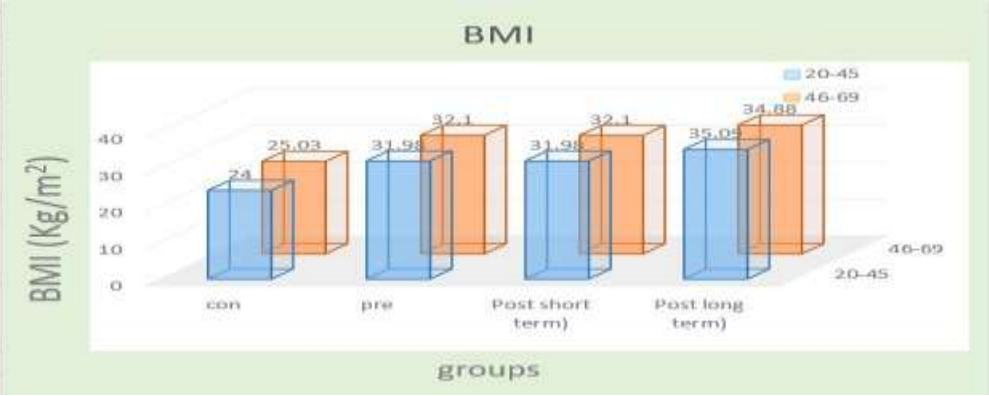

Figure 1: BMI for studies groups.

Table 2: Concentration of serum Total Cholesterol in all studies groups.

Group of Age	NO.	TC (mg/dL)				
		Con	pre	Post		Lsd
				Short term	Long term	
A: (20-45)	37	159.32±26.32^{c,B}	200.03±33.23^{a,B}	185.15±31.08^{b,B}	178.32±28.30^{b,B}	8.75
B: (46-69)	27	169.23±9.86^{c,A}	236.27±18.85^{a,A}	224.27±24.32^{b,A}	219.04±22.83^{b,A}	8.62
LSD		5.83	7.93	8.19	7.54	

NO: The number of each class, Con: control groups, pre: patient preoperative group at least of 20 min, post (short term): 24 hr after operation, post (short term): postoperative long term for a period ranging from 3 months to 3 years, non-identical superscript (a,b orc …etc). were considered significantly differences (P≤ 0.05) to compare horizontally, and with non-identical superscript (A, B or C…etc.) were considered significantly differences (P ≤ 0.05) to compare vertically. LSD: Low significantly differences.

This table shows significant increase in the concentration of serum Ch the groups B in comparison with A group (p≤0.05).

Table 3: Concentration of serum Triglyceride in all studies groups.

Group of Age	NO.	TG (mg/dL)				
		Con	Pre	Post		Lsd
				Short term	Long term	
A: (20-45)	37	125.18±22.92^{c,A}	176.18±32.33^{a,A}	166.32±35.55^{b,A}	158.17±23.15^{b,A}	8.51
B: (46-69)	27	120.25±20.03^{c,A}	180.15±32.16^{a,A}	170.18±33.15^{a,A}	155.23±21.39^{b,A}	11.94
LSD		6.32	6.36	10.08	9.46	

Legend as in table 1

This table shows no significant differences in the concentration of serum TG between A and B groups (p≤0.05).

Table 4: Concentration of serum High Density Lipoprotein in all studies groups.

Group of Age	NO.	HDL (mg/dL)				
		Con	Pre	Post		Lsd
				Short term	Long term	
A: (20-45)	37	58.26±6.38^{a,A}	40.03±5.52^{c,A}	48.09±4.98^{b,A}	47.33±4.73^{b,A}	1.59
B: (46-69)	27	55.28±5.97^{a,B}	39.08±5.33^{c,A}	47.23±5.01^{b,A}	46.53±4.86^{b,A}	2.31
LSD		1.81	1.59	1.47	1.41	

Legend as in table 1

This table shows no significant differences in the concentration of serum HDL between pre and post (short and long terms) groups (p≤0.05).

Table 5: Concentration of serum Low Density Lipoprotein in all studies groups.

Group of Age	NO.	LDL (mg/dL)				
		Con	Pre	Post		Lsd
				Short term	Long term	
A: (20-45)	37	76.02±11.71^{c,B}	124.76±20.73^{a,B}	103.80±21.13^{b,B}	99.36±25.35^{b,B}	5.97
B: (46-69)	27	89.90±15.50^{c,A}	161.14±23.33^{a,A}	143.03±20.21^{b,A}	141.45±27.33^{b,A}	6.46
LSD		4.03	6.48	6.07	7.73	

Legend as in table 1
This table shows significant increase in the concentration of serum LDL the groups B in comparison with A group ($p \leq 0.05$).

Table 6: Concentration of serum Very Low Density Lipoprotein in all studies groups.

Group of Age	NO.	VLDL (mg/dL)				
		Con	pre	Post		Lsd
				Short term	Long term	
A: (20-45)	37	$25.04 \pm 5.02^{c,A}$	$35.24 \pm 5.89^{a,A}$	$33.26 \pm 6.44^{b,A}$	$31.63 \pm 4.34^{b,A}$	1.61
B: (46-69)	27	$24.05 \pm 4.33^{c,A}$	$36.05 \pm 5.57^{a,A}$	$34.04 \pm 4.37^{a,A}$	$31.06 \pm 4.55^{b,A}$	2.06
LSD		1.38	1.68	1.61	1.30	

Legend as in table 1
This table shows no significant differences in the concentration of serum VLDL between A and B groups ($p \leq 0.05$).

DISCUSSION

Obesity is a major risk factor for gallstones, especially in women.[33] A risk factor for the development of recurrent stones may be overweight or obesity and associated dietary pattern. However, the mechanisms for this effect are still unclear.[34] Even moderately overweight increases the risk for developing gallstones. The most likely reason is that the amount of bile salts in bile is reduced, resulting in more cholesterol.[35] For many, cholecystectomy is the only promise of relief from all their gallbladder pain and trouble. This makes the procedure one of the most frequently performed surgeries. Deciding to have it was even made easier with the development of laparoscopic cholecystectomy. Due to its less invasive nature, healing time and recovery is much quicker, with most patients out of the hospital and back to their normal lives in no time. The successful and permanent relief of symptoms by cholecystectomy however allows patients to resume their prior eating habits. Indeed, they are often encouraged to do so. This may facilitate gluttony. It is therefore highly likely that patients who start eating large quantities of fatty foods after their operations will gain weight, but this is not an automatic result of the procedure. Metabolic and hormonal factors may theoretically play a role in different patterns of weight gain found in those undergoing biliary as opposed to non-biliary surgery.[36]

Gallstone disease is one of the most common and most expensive conditions to treat of all digestive disorders requiring admission to hospital.[37] Most Cholecystitis are made up of cholesterol, calcium carbonate calcium bilirubinate, or a mixture of these. Gallstones are believed to form, when the concentration of cholesterol exceeded that which can be held in mixed micelles solution with bile acids and phospholipids.[38]

Patients with gallstones may have defects resulting in the production of abnormally supersaturated bile because of an increase in the secretory rate of biliary cholesterol or decrease in the secretory rate of biliary bile salts, lecithin and phospholipids. Changes in the concentration of one of the key promoters of crystallization, consumption of a high calorie diet is more common and is clearly an important factor in the formation of cholesterol gallstones.

It is apparent therefore that a large number of lipid parameters are involved and had been implicated in the pathogenesis of cholelithiasis. Abnormalities in lipids and apoliproteins metabolism may, however, arise from a combination of various factors such as excess dietary cholesterol/fat, obesity, diabetes and genetic factors. A number of studies have implicated HDL, VLDL and lipoprotein, diabetes mellitus, polycystic ovarian syndrome (POS), etc. were implicated in patients with cholelithiasis.[39] The lipolysis rate is known to accelerate in response to many types of general anesthesia, due to the increase in catecholamine production.

The per-operative glucose infusion given to patients is associated with acceleration of the lipolytic rate.[40] Our results showed a significant decrease in total cholesterol, TG, VLDL, and LDL cholesterol at long term after surgery relative to preoperative levels. that showed plasma total and LDL cholesterol levels were significantly reduced in cholecystectomy patients three days, one month and one year after the operation[41], but our results of after 24 hours and of 3 months to 3 years, however, significant reductions in total cholesterol at various times after cholecystectomy were reported. These results can be explained by the fact that BA and phospholipids' secretion rates significantly increase after cholecystectomy. The significant reduction in LDL cholesterol seen in gallstone patients at intervals after the operation can be explained by the increase in BAs and phospholipids secretion rate after cholecystectomy, as well as the up-regulation of LDL-ApoB receptors, which leads to the increased up-take of LDL cholesterol particles into hepatocytes. Inside the hepatocytes, LDL cholesterol particles bind to lysosomes, leading to the delivery of more cholesterol into the intracellular cholesterol pool. Therefore, bile synthesis using serum cholesterol as a precursor in this condition will cause LDL cholesterol to steadily reduce after

cholecystectomy.[40] Roda et al., evaluated that the lowering of cholesterol in post cholescystectomy period due to a more rapid circulation of the bile acid pool in fasting cholecystectomised patients leading to improved solubility of cholesterol in bile.[42] Cholecystectomy causes redistribution of bile acid pool in the enterohepatic circulation and increases the frequency of cycling. This exert negative feedback on bile acid synthesis and cause reduction in pool size and hence exerts effect on lipid profile decreasing total cholesterol and LDL cholesterol levels.[43]

CONCLUSION

In the field of gastroenterology, the changes in the profile of some serum lipids following cholecystectomy remain an issue raises controversy. patients who start eating large quantities of fatty foods after their operations will gain weight. A physical activity together with a tailored nutritional planning for each patient could help to reduce postsurgical complications following cholecystectomy and minimize symptoms, and a long-lasting educational program to change erroneous eating habits, Follow-up long after the surgery may therefore be necessary to facilitate additional healthcare interventions.

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