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Clinical Study For Serum Lipid Profile And Lipid Peroxidation In Patients With Gallstones In Thi-Qar Governorate - Iraq

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ABSTRACT

Objective: A **gallstone** (also called **cholelithiasis**) is a crystalline concretion formed within the gallbladder by accretion of bile components. These calculi are formed in the gallbladder but may distally pass into other parts of the biliary tract such as the cystic duct, common bile duct, pancreatic duct or the ampulla of Vater. Rarely, in cases of severe inflammation, gallstones may erode through the gallbladder into adherent bowel potentially causing an obstruction termed gallstone ileus. The study was designed to determine and compare the levels of lipid profile, and MDA in gallstones diseases and healthy individuals. **Material and Methods:** Blood lipid profile and malondialdehyde levels were determined in 50 gallstones Disease and 40 healthy subjects . **Results:**The levels of serum malondialdehyde and biochemical markers of body lipid profile (serum TCH,TG,LDL,VLDL) were showing significant increase in gallstones disease patients as compared to control group whereas the levels of HDL showed a significant decrease in gallstones disease patients in comparison to control subjects($P \leq 0.01$).. However we compared all measurement parameters for all groups according to type of disease.

Conclusion: In gallstones Disease, we finding a significant elevation in the levels of cholesterol and triglyceride during gallstones disease.

-Gallstones disease can effect on lipoproteins levels (high LDL, low HDL, and high VLDL. The increase in lipid peroxidation in gallstones disease, the increase in cholesterol, TG, LDL,VLDL . In gallstones disease lipid peroxidation can clearly occur.

Keywords: gallstones disease , gallbladder , lipid profile and Malondialdehyde.

INTRODUCTION

A gallstone (also called cholelithiasis) is a crystalline concretion formed within the gallbladder by accretion of bile components. These calculi are formed in the gallbladder but may distally pass into other parts of the biliary tract such as the cystic duct, common bile duct, pancreatic duct or the ampulla of Vater. Rarely, in cases of severe inflammation, gallstones may erode through the gallbladder into adherent bowel potentially causing an obstruction termed gallstone ileus.[1] Presence of gallstones in the gallbladder may lead to acute cholecystitis.[2] Factors increasing hepatic secretion of biliary cholesterol (obesity, aging, medications, oral contraceptives, oestrogen, and progesterone), oversaturation of bile with cholesterol, impaired gallbladder motility, and an increase in nucleating factors contribute to the formation of cholesterol gallstones. [3],[4] gallstones can be divided into the following types: Cholesterol stones :Cholesterol stones vary from light yellow to dark green or brown and are oval, between 2 and 3 cm long, each often having a tiny, dark, central spot. To be classified as such, they must be at least 80% cholesterol by weight (or 70%, according to the Japanese- classification system).[5] Pigment stones :Pigment stones are small and dark and comprise bilirubin and calcium salts that are found in bile. They contain less than 20% of cholesterol (or 30%, according to the Japanese-classification system).[5] Mixed stones: Mixed gallstones typically contain 20–80% cholesterol (or 30–70%, according to the Japanese- classification system).[5] Cholesterol is water insoluble lipid, and is taken in mixed micelles and vesicles. Micelles are aggregates of phospholipids, bile salts, and cholesterol, and vesicles are closed spherical bilayers of phospholipids with associated cholesterol. There are three stages of gallstone formation, super saturation, nucleation and aggregation. [6] These changes in bile composition are closely related to the disorders of lipid metabolism in liver. However, during the formation of cholesterol gallstones, different links in the disturbance of lipoprotein cholesterol metabolism. [7]Triglycerides are fatty acid esters of glycerol, each containing three different fatty acids [8].Lipoproteins are complex aggregates of lipids and proteins that render the lipids compatible with the aqueous environment of body fluids(HDL ,LDL, VLDL,chylomicrons). [9] Reactive oxygen species degrade polyunsaturated lipids, forming malondialdehyde. This compound is a reactive aldehyde and is one of the many reactive electrophile species that cause toxic stress in cells and form covalent protein adducts referred to as advanced lipoxidation end-products, in analogy to advanced glycation end-products. The production of this aldehyde is used as a biomarker to measure the level of oxidative stress in an organism. [10] Malondialdehyde is a potent stimulator of mucin secretion by cultured gallbladderepithelialcells. [11],[12]

MATERIAL AND METHODS

This study conducted at AL-Hussein Teaching Hospital, especially in the surgery unit ,Biochemistry Laboratory, and specialist clinics. It included (90) subjects, control(40) and patients(50) including:(30 female, 20male).

A bout (5mL)of blood samples of gallstones patients and controls were taken and allowed to clot at room temperature in empty disposable tubes centrifuge to separate it in the centrifuge at 3000 rotor per minute (rpm)for 10min,the serum samples were separated and stored at (-20^{o}C) until analyzed Lipid Profile and malondialdehyde.

Serum cholesterol(TCH) was analyzed by enzymatic colorimetric method by UV/VIS spectrophotometer, Japanusing kits supplied by Spinreact, Spain .

Serum triglyceride (TG) was analyzed by enzymatic colorimetric method by UV/VIS spectrophotometer, Japanusing kits supplied by Biolabo, France.

Serum high density lipoprotein (HDL) was analyzed by enzymatic colorimetric method by UV/VIS spectrophotometer, Japanusing kits supplied by Biomerieux, France**.** Serum low density lipoprotein (LDL) is calculated through the following equation LDL = Total Cholesterol – (HDL + VLDL) Serum very low density lipoprotein (VLDL) is calculated through the following equation: VLDL = Triglyceride/5 Serum Malondialdehyde (MDA) was measured as thiobarbituric acid (TBA) activity by using the colorimetric method recommended, MDA level of the plasma was measured according to a modified method of Fong *et al* [13]. The results were expressed as mean ± standard deviations (mean ± SD). One way ANOVA-test was used to compare parameters in different studied groups. P-values ($P \leq 0.01$) were considered statistically significant.

RESULTS

In this work we determined the effect of this disease on lipid profile (**TCH**),(**TG**), (**HDL**),(**LDL**) ,(**VLDL**) and determined it effect on oxidation state by measurement lipid peroxidation and determined its effect on the concentrations of lipid peroxidation marker (***MDA***) .

The levels of biochemical markers of body lipid profile(serum TCH, TG, LDL,VLDL) and malondialdehyde were showing significant increase in gallstones disease patients as compared to control group whereas the levels of HDL showed a significant decrease in gallstones disease patients in comparison to control subjects.

Table(1):-Serum Lipid Profile concentrations of (control) and (gallstones patients)groups.

Group	n	TC mmol/L	TG mmol/L	HDL mmol/L	LDL mmol/L	VLDL mmol/L
control	40	3.11±0.48[a]	1.19±0.25[a]	1.45±0.29[a]	1.56±0.91[b]	0.38±0.10[a]
gallstones	50	6.41±1.20[b]	2.02±0.41[b]	0.96±0.13[b]	4.59±1.09[a]	0.40±0.12[b]

* Each value represents mean ± SD values with non-identical superscript (a , b or c …etc.) were considered significantly differences ($P \leq 0.01$).

Table(2):-Serum Malondialdehyde concentrations in patients with gall stones.

Group	N	MDA concentration (nmol/mL) mean± SD
control	40	46.98±18.55[b]
gallstones	50	163.65± 43.21[a]

- Legend as in table (1)

DISCUSSION

Gall stone disease is one of the most common and most expensive conditions to treat of all digestive disorders requiring admission to hospital[14] . All gallstones found during cholecystectomy, cholesterol

gallstones account for 80-90%[15]. Cholesterol gallstones are primarily made up of cholesterol crystals (70%) which are held together in an organic matrix of glycoproteins, calcium salts, and bile pigments. They could be present either singly or multiply, in various sizes, shapes and surfaces.[16] The mean serum total cholesterol, serum triglycerides was high in gall stone patient but not significant, compared to control group.[17] This suggests a positive association between gallstone disease and serum cholesterol and triacylglycerol levels. In the study, LDL cholesterol was significantly high in the case than the control group. Considerable study found a positive association between gallstone disease and increased levels of

serum triglycerides, LDL cholesterol and decreased HDL cholesterol.[18] This suggests that changes in serum lipid profile are a possible consequence of the presence of gallstones, especially through biliary obstruction. In present study, because only few gallstone patients had experienced symptoms of biliary obstruction in the past (jaundice, pale stools, or dark urine), it is believed that only few of them would have had cholestasis at the time of the study. Nevertheless, more subtle changes in lipid profile as a consequence of the presence of gallstones cannot be excluded.[19] All major classes of biomolecules are affected by free radicals, but the most sensitive molecules are lipids, Oxidative stress plays a role in the occurrence of several diseases. Oxidative stress requires either increased reactive oxygen species formation or decreased antioxidant defence mechanisms.[20] In this study, we found that lipid peroxidation is increased in gallbladder bile of patients with cholesterol gallstones [21]

CONCLUSION

-In gallstones Disease, we found a significant elevation in the levels of cholesterol and triglyceride during gallstones disease .
-Gallstones disease can effect on lipoproteins levels (high LDL, low HDL, and high VLDL).

- In gallstones disease lipid peroxidation can clearly occur.

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دراسة سريرية لنمط الدهون والأكسدة الفوقية للدهون في المرضى المصابين بحصى المرارة في محافظة ذي قار – العراق

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الهدف: حصى المرارة (تسمى أيضًا حصى الصفراء) هي عبارة عن شكل بلوري يتكون داخل المرارة عن طريق تراكم مكونات الصفراء. وتتكون هذه الحصيات في المرارة ولكنها قد تنتقل إلى أجزاء أخرى من القناة الصفراوية مثل القناة الكيسية أو القناة الصفراوية المشتركة أو قناة البنكرياس أو أمبولة فاتر. نادرًا ، في حالات الالتهاب الشديدة ، قد تتآكل الحصى الصفراوية من خلال المرارة إلى أمعاء ملتصقة يحتمل أن تسبب انسدادًا. تم تصميم الدراسة لتحديد ومقارنة مستويات الدهون في الجسم ، و MDA في مرضى حصى المرارة والأشخاص الأصحاء.
المواد وطرق العمل: تم تحديد مستوى الدهون في الدم ومستويات MDA في 50مريض مصاب بحصى في المرارة و 40 شخص من الاشخاص الاصحاء . **النتائج**: كانت مستويات المالونديالديهيد في الدم والعلامات البيوكيميائية لنمط الدهون في الجسم (TCH، TG، LDL، VLDL) تظهر زيادة كبيرة في مرضى حصى المرارة بالمقارنة مع مجموعة السيطرة في حين أن مستويات HDL أظهرت انخفاض كبير في مرضى حصى المرارة بالمقارنة مع الاشخاص الاصحاء . ($P \leq 0.01$) ومع ذلك ،قورنت جميع مقاييس القياس لجميع المجاميع وفقًا لنوع المرض.

الاستنتاج : في مرض حصى المرارة ، نجد ارتفاعًا ملحوظًا في مستويات الكوليسترول والدهون الثلاثية أثناء مرض حصى المرارة. يمكن أن تؤثر هذه الامراض على مستويات البروتينات الدهنية (LDL عالي ، HDL منخفض ، و VLDL عالي). الزيادة في الاكسدة الفوقية للدهون في مرض حصى المرارة ، الزيادة في الكوليسترول ، TG، LDL، VLDL. في مرض حصى المرارة الاكسدة الفوقية للدهون يمكن أن تحدث بوضوح.

الكلمات المفتاحية: مرض حصى المرارة ، المرارة ، نمط الدهون والمالونديالديهايد.