

Lipid Profile and Fasting Blood Sugar Analysis in Patients with Cholelithiasis

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Abstract

Cholelithiasis is one of the commonest surgical problems and one of the most common gastrointestinal diseases throughout the world but its pathogenesis remains unclear. Many theories have been proposed forward to explain the mechanism of stone formation. It is not fully clear if symptomatic gallstone disease is associated with a specific pattern of some biochemical abnormalities, as lipid profile and fasting blood sugar in serum of patients.

This study was designed to estimate lipid profile and fasting blood sugar in the sera of patients with cholelithiasis in comparison with normal individuals (control).

In this study, 104(male=16, female=88) were symptomatic gallstone patients (aged 42.79 ± 12.18 years), and 38(male=6 and female=32) were apparently healthy controls (aged 40.03 ± 7.47 years).

Blood samples were collected from symptomatic gallstones patients before their cholecystectomy operation. Over night fasting, blood samples were collected from all subjects to evaluate serum lipid profile: Total cholesterol (TC), triglyceride (TG), high density lipoprotein-cholesterol (HDL-c), low density lipoprotein-cholesterol (LDL-c), very low density lipoprotein-cholesterol (VLDL-c) and fasting serum glucose (FSG). There was a significant increase ($P < 0.05$) in serum: TC, TG, LDL-c, VLDL-c and FSG of patients with cholelithiasis compared to the apparently healthy controls. The study also showed that there was a significant decrease ($P < 0.05$) in serum HDL-c in gallstone patients compared to control.

In conclusion, cholelithiasis was associated with lipid profile and fasting serum glucose abnormality that be the cause or the effect of gallstone formation. These findings should be taken into consideration while treating gallstone patients.

Key words: Gallstones, Cholesterol, Cholecystectomy.

تحليل صيغة الدهون ومستوى سكر الدم الصائم عند المرضى والمصابين بحصى المرارة رجاء نعمة امين الاطرقجي* ، محمد عباس ظاهر**¹ و ابتهال نوري سعيد**

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**فرع العلوم المختبرية السريرية ، كلية الصيدلة ، جامعة بغداد ، بغداد ،العراق .

الخلاصة

يعد مرض حصى الصفراء أحد المشاكل الجراحية الشائعة واحدا من امراض الجهاز الهضمي الاكثر شيوعا حول العالم لكن امراضه يكتنفها بعض الغموض . وقد وضعت الكثير من النظريات لتوضيح آلية تشكل الحصى . انه من غير المعروف بشكل واضح ارتباط مرض حصى الصفراء بنمط معين لبعض التغيرات الكيميائية الحيوية مثل مستويات شحوم الدم و سكر الدم في حالة الصيام في مصل دم المرضى. وقد تم تصميم هذه الدراسة لمعرفة مستويات الشحوم و سكر الدم في حالة الصيام في مصل المرضى الذين يعانون من حصى الصفراء مقارنة مع الاشخاص الاصحاء (مجموعة السيطرة).

اشترك في هذه الدراسة مئة واربعة (88 انثى و 16 ذكور) يمثلون مجموعة المرضى معدل اعم ارمهم 42.79 ± 12.18 سنة ، وثمانية وثلاثون (32 انثى و 6 ذكور) يمثلون مجموعة السيطرة معدل اعمارهم 40.03 ± 7.47 سنة.

عينات الدم تم جمعها من مرضى حصى الصفراء قبل عملية استئصال المرارة. عينات الدم تم سحبها من المرضى والاصحاء بعد الصوم ليلا لقياس شواكل شحوم المصل: الكوليسترول الكلي (TC) ، الدهون الثلاثية (TG) ، البروتين الشحمي ذو الكثافة العالية المرتبط بالكوليسترول (HDL-C) ، البروتين الشحمي ذو الكثافة الوائنة المرتبط بالكوليسترول (LDL-C) ، البروتين الشحمي ذو الكثافة الوائنة جدا المرتبط بالكوليسترول (VLDL-C) ، وسكر الدم في حالة الصيام (FSG).

وجدت زيادة معنوية ($P < 0.05$) في مصل الدم: الكوليسترول الكلي والدهون الثلاثية وكوليسترول البروتين الشحمي ذو الكثافة الوائنة وكوليسترول البروتين الشحمي ذو الكثافة الوائنة جدا و سكر الدم في حالة الصيام في المرضى الذين يعانون من حصى المرارة مقارنة بالاصحاء. كما اظهرت الدراسة وجود انخفاض معنوي ($p < 0.05$) في مصل الدم لكوليسترول البروتين الشحمي ذو الكثافة العالية في نفس المرضى مقارنة بالاصحاء. نستنتج ان مرض حصى المرارة مرتبط بتغير مستويات شحوم الدم و سكر الدم في حالة الصيام التي قد تكون ناتجة او مسببة لتكوين الحصى. لذا ينبغي أن تؤخذ هذه النتائج بعين الاعتبار أثناء علاج مرضى حصى المرارة.

الكلمات المفتاحية: حصى المرارة ، كوليسترول ، استئصال المرارة.

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Introduction

The presence of stones in the gallbladder is referred to as cholelithiasis (from the Greek: chol, "bile" + lith-, "stone" + iasis-, "process")⁽¹⁾. Cholelithiasis or Gallstone disease (GD), is one of the most prevalent gastrointestinal diseases, with a substantial burden to health care systems⁽²⁾. Gallstones (GS) are abnormal masses of a solid mixture of cholesterol crystals, mucin, calcium bilirubinate, and proteins that have affected people for centuries⁽³⁾.

Gallstone formation is multifactorial, and known risk factors are advancing age, female gender, genetics- ethnicity, obesity, rapid weight loss, diet, drugs, and activity⁽⁴⁾.

The association of gallbladder (GB) stone disease with metabolic abnormalities such as diabetes, dyslipidemia, obesity, and hyperinsulinemia has supported the hypothesis that GB stone formation is a type of metabolic syndrome^(5,6). Gallstones are classified as cholesterol, pigmented or mixed stones based on their chemical composition^(7,8).

The role of serum lipid in the etiology of cholelithiasis is very important and particularly in cholesterol gallstones in which serum lipid profile are altered which is suggestive of metabolic syndrome. Research suggests that metabolic syndrome is a risk factor for gallstones⁽⁹⁾. Low levels of high-density lipoprotein cholesterol (HDL-c) and high triglycerides are associated with gallstone disease⁽¹⁰⁾. Cholecystectomy is the standard and definitive treatment for symptomatic gallbladder stones and can be performed regardless of the type, number, and size of the stones^(11,12). It is effective and safe, with low rates of complications (14%) and mortality (0.17%). For cholesterol gallstones, current medical treatment includes: litholytic therapy (stone dissolution) by oral bile acid litholysis with chenodeoxycholic acid and/or ursodeoxycholic acid (UDCA)^(13,14), and lithotripsy (stone shattering)⁽¹⁵⁾. The aim of our study is to evaluate the biochemical changes in some serum parameters (lipid profile and fasting serum glucose) in gallstone patients compared to controls.

Subjects and Methods

The study was carried out on patients with clinical and imaging features confirming symptomatic cholelithiasis admitted to Imam AL-Hussein Medical City, Safer AL-Hussein Surgical Center and Maitham AL-Tammar Surgical Hospital in Karbala City from February to October 2013. Patients with symptomatic gallstones had a history of (pain

located in the epigastrium and/or right upper quadrant; recurrent symptoms occurring at different intervals; and episodes lasting 30 minutes or more. The pain may present with one or more of the following: associated nausea and vomiting; radiating to the back and/or right infrascapular region; and causing one to awaken from sleep in the middle of the night⁽¹⁶⁾, an abdominal ultrasonography is the standard diagnostic test for gallstone detection⁽¹⁷⁾. A total number of 104 patients were included in this study, among which 88 females and 16 males in age group ranged between 18-75 years with a mean \pm SD (42.79 \pm 12.18). These were compared with 38 (age and sex matched) healthy controls (32 females, 6 males), with mean age \pm SD (40.03 \pm 7.47). The patients were selected not have liver cirrhosis, viral hepatitis, renal failure, thyroid disease, asthma and diabetes mellitus nor Pancreatitis and Gallbladder cancer nor those taking anti-hyperlipidemic drugs that may interfere with the data obtained.

Samples collection

After an overnight fasting, 5 milliliters venous blood samples were collected from patients before laparoscopic cholecystectomy and from healthy volunteers in plain tubes. After allowing the blood to clot at room temperature for about 30 minutes, blood samples were centrifuged at 5000 rpm for about 5 minutes to obtain serum. The serum samples were stored at -20 °C until analysis was performed.

Biochemical assay methods

Biochemical assay was done at Imam AL-Hussein Medical City, laboratory department using ARCHITECT plus, Abbott4000, Automated auto-analyzer. The assay was include: serum total cholesterol⁽¹⁸⁾, serum triglyceride⁽¹⁹⁾, serum high density lipoprotein-cholesterol⁽²⁰⁾, serum low density lipoprotein-cholesterol and very low density lipoprotein-cholesterol were calculated using Friedewald formula⁽²¹⁾, and serum glucose level⁽²²⁾.

Statistical analysis

The following statistical data analysis approaches were done through the Statistical Package for Social Sciences (SPSS 17) and Excel application were used in order to analyze and assess the results of the study⁽²³⁾:

- Statistical tables.
- Mean value and standard deviation (SD).
- Bivariate comparisons were examined for parameters using pearson rank correlation coefficients (r).

- Graphical presentation.
- Student's *t*-test was used to examine the degree of significance. P values less than 0.05 was considered significant.

Results

Table (1) and figures (1), (2) and (3) showed that the levels of total cholesterol, LDL, VLDL, TG, and fasting serum glucose were significantly higher ($p < 0.05$), while the levels of HDL were significantly lower ($p < 0.05$) in the sera of gallstone patients in comparison with healthy control group.

Table (1): Serum lipid profile and Fasting serum glucose in gallstone patients and controls.

Parameters/ (mg/dl) mean \pm SD	Patients N=104	Controls N=38	P- value
Total cholesterol	197.64 \pm 49.68	178.78 \pm 37.60	<0.05
TG	180.006 \pm 50.00	159.71 \pm 25.12	
HDL	46.78 \pm 11.062	52.59 \pm 8.53	
LDL	115.76 \pm 37.694	97.24 \pm 21.015	
VLDL	36.83 \pm 17.82	30.20 \pm 7.82	
FSG	112.73 \pm 25.53	101.88 \pm 28.50	

Data are expressed as mean \pm SD (standard deviation), N=number of patients or controls. TG: triglyceride, HDL: high density lipoprotein, LDL: low density lipoprotein, VLDL: very low density lipoprotein and FBS: fasting serum glucose. P < 0.05 : significant.

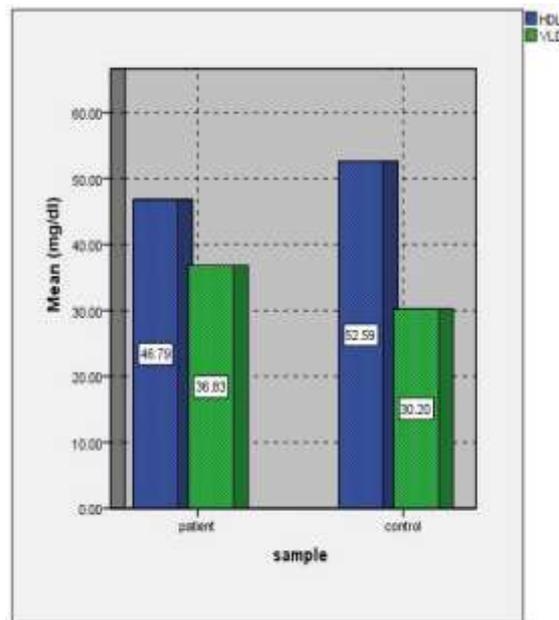


Figure 2: Mean serum high density lipoprotein (HDL) and very low density lipoprotein (VLDL) in patients with cholelithiasis and healthy controls (milligram per deciliter).

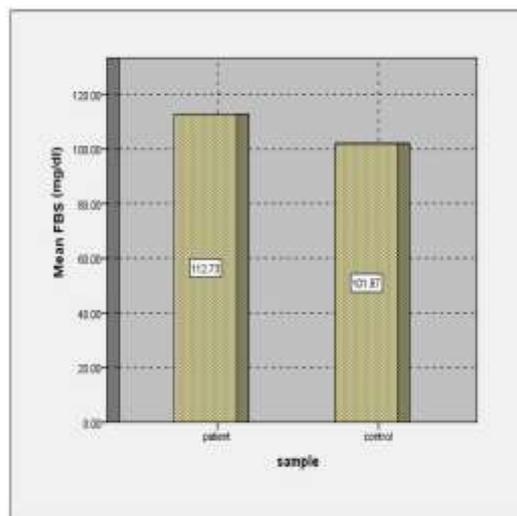


Figure 3: Mean of serum fasting blood sugar (FBS) in patients with cholelithiasis and healthy controls (milligram per deciliter).

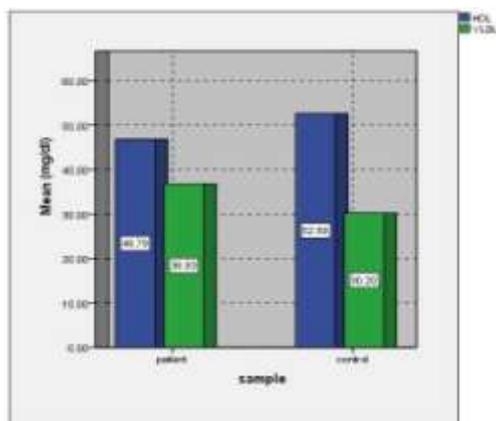


Figure 1: Mean serum total cholesterol (cholesterol), triglyceride (TG) and low density lipoprotein (LDL) in patients with cholelithiasis and healthy controls (milligram per deciliter).

Table (2): Pearson rank correlations between parameters.

Parameters (mg/dl)	T. cholesterol	TG	HDL	LDL	VLDL	FBS
T. cholesterol	1	.323** .000	.127 .140	.760** .000	.427** .000	-.030- .725
TG	.323** .000	1	.060 .489	.123 .155	.532** .000	.123 .153
HDL	.127	.060 .489	1	-.012- .894	-.006- .944	-.044- .610
LDL	.760** .000	.123 .155	-.012- .894	1	.243** .004	-.023- .786
VLDL	.427** .000	.532** .000	-.006- .944	.243** .004	1	.067 .440
FBS	-.030- .725	.123 .153	-.044- .610	-.023- .786	.067 .440	1

*Significant at P <0.05 and ** high significant at P <0.01

Table (2) showed that there were positive correlations between:

- serum total cholesterol and TG ($r=0.323$, $P<0.05$), serum total cholesterol and LDL ($r=0.76$, $P<0.05$), and serum total cholesterol and VLDL ($r=0.42$, $P<0.05$).
- serum TG and VLDL ($r=0.53$, $P<0.05$).
- serum LDL and VLDL ($r=0.24$, $P<0.05$).

Discussion

The present study observe low serum HDL levels and high serum triglyceride, total cholesterol and LDL levels in patients with cholelithiasis which is in agreement with other studies^(24,25), Virupaksha HS *et al*⁽¹⁰⁾, Channa NA *et al*, found that lipids elevation in cholelithiasis, seems to play a major contributing role in the pathogenesis of gallstones in females of up to 45 years age⁽²⁵⁾. The elevation of serum total cholesterol and TG levels in patients may be due to: Gallstone patients have abnormal secretory mechanism for bile acids and phospholipids, decrease bile acids and phospholipids (which solubilize cholesterol in the bile) will increase cholesterol precipitation⁽²⁶⁾, and some of gallstone patients may present with metabolic syndrome which is a cluster of symptoms such as glucose intolerance, high total cholesterol, hyperinsulinemia, increased VLDL and/or total cholesterol, decrease HDL and hypertension who indicate that the metabolic syndrome is one of the risk factors for

gallstone disease⁽²⁷⁾. Previous study described a decrease in HDL in gallstone patients, and there will be a return to the normal condition after gallstone removal⁽²⁸⁾. The high LDL was seen in gallstone patients in this study either due to abnormal secretory function and/or prolonged high fatty diet and agree with Zhao *et al*⁽²⁶⁾, and down regulation of LDL-ApoB receptors by inhibition of LDL-ApoB receptor gene expression⁽²⁹⁾. Hyperlipidemia are strong risk factors in cholelithiasis as estimated previously⁽³⁰⁾. Life style and dietary modification are effective measures for the prevention of cholelithiasis⁽³¹⁾. The previous observation indicate that medications used to treat dyslipidemia may be of value in the prevention and treatment of cholelithiasis⁽³²⁾. There was significant positive correlation ($r=0.53$, $P<0.05$) between serum VLDL and TG in patients with cholelithiasis in the present study. Cholelithiasis is associated with hypertriglyceridemia^(10,33).

Hypertriglyceridemia is associated with decreased HDL-cholesterol (HDL-c) and increased small dense LDL⁽³⁴⁾. LDL particles are formed as VLDL lipoproteins lose triglyceride through the action of lipoprotein lipase and they become smaller and denser (fewer fat molecules with same protein transport shell), containing a higher proportion of cholesterol esters^(35,36). A positive correlation ($r=0.32$, $P<0.05$) between serum

triglyceride and serum total cholesterol in patients with cholelithiasis was observed in the present study, which is in agreement with the other study demonstrated that there was a significant positive correlation between total cholesterol and TG levels⁽³⁷⁾.

In present study, fasting serum glucose (FSG) was significantly higher ($p < 0.05$) in gallstone patients compared to healthy controls, in agreement with other studies performed by Simona Tîrziu, *et al.*⁽³⁸⁾ and Jindal N, *et al.*⁽³⁹⁾ "they reported that fasting glucose levels were significantly increased in gallstone patients as compared to controls". Gallstone disease appeared strongly associated with fasting glycemia⁽⁴⁰⁾. There was a positive correlation between prevalence of gallstone with higher fasting glucose. The possible mechanisms for this association may be as follows: hyperglycemia inhibits bile secretion from the liver and disturbs gallbladder contraction⁽⁴¹⁾. Gallstone disease appears to be strongly associated with metabolic syndrome, and the more the components of metabolic syndrome, the higher the prevalence of gallstone disease, and elevated fasting blood glucose is one of component of metabolic syndrome that associated with gallstone disease⁽⁴²⁾.

Conclusions

Gallstone disease is associated with some biochemical abnormalities (elevation of total cholesterol, triglyceride, LDL, VLDL, fasting serum glucose level and decrease in HDL level compared to control) that may be the cause or the result of gallstone formation.

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