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Assessment of Serum Lipids Profile in Sudanese Patients with Cholelithiasis

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Abstract: Gallstones disease is one of the most prevalent gastrointestinal diseases with a substantial burden to healthcare systems that is supposed to increase in ageing populations at risk. Gallstones disease is one of the major surgical problems in the Sudanese population. The aim of this study was to measure serum lipids profile in Gall stone diseases, and also to evaluate the risk and demographic factors.This study was case control hospital bases study, and conducted in Khartoum teaching hospital and Ibin Sina hospital, Khartoum state. During Oct 2008 to Oct 2009. 65 Sudanese patients with gall stones which are confirmed by abdominal ultrasound scanner and underwent cholecystectomy and 50 healthy persons as a control group (matched age sex)have been studied. Serum of fasting total cholesterol, triglycerides, HDL-cholesterol and LDL-cholesterol were measured using spectrophotometric methods. Results revealed that the high incidence of gallstones was more frequently among females(83.9%) relatives to males(16.1%)giving female to male ratio 4.9:1.The most affected age groups were 51-60 years (32.31%) and 41-50 years (30.77%).The majority of patients 34 (52.31%) were obese and their body mass index(BMI) 25-30.Comparison of serum lipid profile between patients and controls groups showed that the levels of serum total cholesterol and LDL-C in patients were slightly higher than that of the control group but there was no significant variation in total Cholesterol and LDL-C ($p>0.05$) . Furthermore, It is found that there is Highly significant difference between patients and controls groups in serum triacylglycerol and HDL-C($p<0.05$) . Serum total cholesterol level of patients with CS was high compared to that of other types of patients, while the level of serum HDL-C was low of patients CS. Pigment stone (PS) was found to be the commonest comprising, followed by mixed stone and cholesterol stone. Biochemical analysis of serum lipid profile between patients and controls groups revealed significantly increase of serum triacylglycerol and HDL-C levels. Serum total cholesterol level of patients type one was high compared to that of two types of patients, while the level of serum HDL-C was low of patients type one.

Keywords: Gallstone disease, cholecystectomy, Lipid profile, Cholesterol, Sudanese.

INTRODUCTION

Cholelithiasis is the gallstone disease (GSD) where stones are formed in the gallbladder[1]. Analogous stones also occur in intra hepatic and extra hepatic[2].The principal function of the gallbladder is to store and concentrate bile[3]**.** Concentration of bile by active absorption of water, sodium chloride and bicarbonate by the mucous membrane of the gall bladder. The hepatic bile that enters the gall bladder becomes concentrated 5–10 times, with a corresponding increase in the proportion of bile salts, bile pigments, cholesterol and calcium. The third function of the gall bladder is the secretion of mucus– approximately 20 ml is produced per day[4]. Gallstone disease (GSD) is a worldwide disease and it remains to be one of the most common health problems leading to surgical intervention [5]. Gallbladder stone disease is one of the major surgical problems in the Sudanese population and it accounts for many hospital admissions and surgical interventions[6]. Gallstones are a common clinical finding in the Western populations [7] with an estimated prevalence of 10% to 15% in white adults, leading to significant morbidity, mortality, and considerable health care costs[8]. Gallstones are common, and are estimated to be present in20–30% of people in developed countries. Only 20–30% of these people will develop problems related to their stones[9]. In contrast the low incidence occur in sub-Saharan black Africans (<5%) [8,10]. They have been described as the disease of fat, fertile, forty, female[11]. More than 80% of gallstone carriers are unaware of their gallbladder disease, but about 1–2% per year of patients develop complications and need surgery[12].The accepted current classification recognized three main types of gall stones. cholesterol, combined, and pigment type[13]. In general, most of the gall stones are made predominately of cholesterol. About 6% only are pure cholesterol stones, and 15% are pigment stones that comprise mainly calcium bilirubinate with less than 10% cholesterol, but most of them are mixed stones. About 15 to 19% of cholesterol stones are mixed stones, and 50% of pigment stones contain enough calcium to

confer rationality[14]. Gallstone formation is multifactorial, including constitutional and environmental factors .Some factors, such as diet, activity, rapid weight loss, and obesity, are modifiable, whereas others (e g, age, female gender, genetics, and ethnicity) cannot change [8]. Other theories related the disease to geographical, ethnic and dietary factors [15]. Etiology of gall stones is probably multifactorial. The implicated factors are: metabolic, infection and bile stasis[16]. The formation of cholesterol gall stones involves: super saturation of bile with cholesterol, incomplete transfer of cholesterol from biliary vesicles to bile salt micelles, formation of abnormal high cholesterol containing biliary vesicles, aggregation and fusion of unstable vesicles, cholesterol crystallization, nucleating and anti-nucleating factors, biliary sludge formation and stone growth[17]. Pathogenesis of black pigment stones is due to: hemolysis, e.g. hereditary spherocytosis, sickle cell anemia, thalassemia and malaria, in which bilirubin production is increased[18]. Brown pigment stones occur only in the biliary system mainly in the intra or extra hepatic duct. Their pathogenesis may due to stasis**[**19] and infection, by gram-negative bacteria [20]. The aim of this study was to measure serumlipids profile in Gall stone diseases, and also to evaluate the risk and demographic factors.

MATERIALS AND METHODS

Study populations:

This study was case control hospital bases study, and conducted in Khartoum teaching hospital and Ibin Sina hospital, Khartoum state. During Oct 2008 to Oct 2009. 65 Sudanese patients with gall stones which are confirmed by abdominal ultrasound scanner and underwent cholecystectomy and 50 healthy persons as a control group (matched age sex) have been studied. who were free from signs and symptoms of gallstone disease, liver disease, lipid disorders, diabetes mellitus and hypertension as a control group matched for age and sex with patients group.

Sampling and Data collections:

The datas were collected using a questionnaire, A questionnaire will be constructed sated in an attempt to collect the necessary information about the subjects, i.e. sex, age, body weight, number of pregnancies.

Overnight fasting blood samples were collected from each individual (patients and controlgroups) to determine the level of the following biochemical parameters: { serum Total cholesterol, triacylglycerol, high density lipoprotein cholesterol (HDL-C),low density lipoprotein cholesterol (LDL-C). allparameters were analyzed by spectrophotometric methods, using kits supplied by Bio Systems S.A. company (Spain). serum Total cholesterol was estimated by method as per reported by[21]whereas, the method used for the estimation triglycerideswas described by [22]. High density lipoprotein cholesterol(HDL-C) and Low density lipoprotein cholesterol(LDL-C) were determined by method according to[23,24]. Gallstones from 65 patients [11 men and 54 women] of cholelithiasis were collected after cholecystectomy. The stones were divided into 3 groups depending upon their colors according to methods of [25]the various physical parameters of stones such as number, shape, size and texture were noted

Statistical analysis:

Results were expressed mean ± SEM. Students t test was used to compare the data between patients and control groups and between the patients distributed in different groups, also analysis of variance (ANOVA) was used for comparison between the different age groups using SPSS computer package version 20. At 95% confidence level of p. value <0.05 was considered statistically significant.

RESULTS:

Table-1: Incidence of different types of gallstones in relation to age in patients with symptomatic calcular cholecystitis in the studied groups (n=65)

Age group (years)	**Cholesterol stones (CS)**		**Mixed stones (MS)**		**Pigment stones (PS)**		**Total**
	Male	Female	Male	Female	Male	Female	
< 30	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.54%)	0 (0.0%)	4 (6.15%)	**5 (7.69%)**
31-40	0 (0.0%)	1 (1.54%)	0 (0.0%)	4 (6.15%)	0 (0.0%)	5 (7.69%)	**10 (15.38%)**
41-50	0 (0.0%)	4 (6.15%)	0 (0.0%)	4 (6.15%)	1 (1.54%)	11 (16.92%)	**20 (30.77%)***
51-60	0 (0.0%)	5 (7.69%)	4 (6.15%)	4 (6.15%)	1 (1.54%)	7 (10.77%)	**21 (32.31%)***
>60	0 (0.0%)	1 (1.54%)	1 (1.54%)	1 (1.54%)	4 (6.15%)	2 (3.11%)	**9 (13.85%)**
Total	**0 (0.0%)**	**11 (16.92%)**	**5 (7.69%)**	**14 (21.54%)**	**6 (9.23%)**	**29 (44.62%)**	**65 (100%)**

Table-2: Distribution of the participants according to their body mass index.

B MI	No. of patients (Male)	No. of patients (Female)	**Total**	No. of control (male)	No. of control (female)	**Total**
Underweight(<18.5)	3(4.62%)	4(3.3%)	**7(6.55%)**	1 (2%)	6 (2%)	**7 (14%)**
normal(18.5 to24.9)	0(0%)	18 (33.3%)	**18 (33.3%)**	7 (14%)	23 (32%)	**30 (60%)***
obese(25 to 30)	7(6.55%)	27(33.3%)	**34 (52.31%)***	0 (0%)	9 (12%)	**9 (18%)**
over weight (30to 40)	1(1.4%)	5 (7.69%)	**6 (9.23%)**	0 (0%)	4 (8%)	**4 (8%)**
Extreme over weight (above 40)	0 (0%)	0 (0%)	**0 (0%)**	0 (0%)	0 (0%)	**0 (0%)**
Total	**11 (16.9%)**	**54 (83.1%)**	**65 (100%)**	**8 (16%)**	**42 (84%)**	**50(100%)**

Table-3: Distribution of the participants by their number pregnancies .

subject	**No. of pregnancy (0)**	**No. of pregnancy (1-3)**	**No. of pregnancy (4-6)**	**No. of pregnancy (7-10)**	**No. of pregnancy >10**	**Total**
patients	2(3.11%)	9(13.8%)	12(18.5%)	28(43.17%)*	3(4.6%)	**54(83.1%)**
controls	3(6%)	16(23%)	12(24%)	10(20%)	1(2%)	**42 (84%)**

Table-4: values of some lipid profile parameters in gallstones patients and control group.

subject	No.	Cholesterol (mg/dl) [Mean ±SED]	TG (mg/dl) [Mean ±SED]	HDL-c (mg/dl) [Mean ±SED]	LDL-c (mg/dl) [Mean ±SED]
Patients	65	202.86±4.99	171.92±7.65*	31.31±3.90*	160.43±5.87
Control	50	157.91±4.10	76.84±4.89	76.72±4.87	124.96±4.70
Probability		0.122	0.013	0.011	0.157

*Significant difference at P<0.05**Highly significant difference at P< 0.001

Table-5 :Mean concentration values of some serum lipid profile parameters of the patients (Male and Female).

Group	No.	Cholesterol (mg/dl) [Mean ±SED]	TG (mg/dl) [Mean ±SED]	HDL-c (mg/dl) [Mean ±SED]	LDL-c (mg/dl) [Mean ±SED]
Male	11	180.80±11.83	182.00±18.70	32.76±9.56	172.82±4.29
Female	54	207.35±5.34	169.87±8.44	31.02±4.32	157.91±6.45
Probability		0.450	0.557	0.869	0.345

*Significant difference at P< 0.05**Highly significant difference at P< 0.001

Table-6: Concentration [Mean ±SED] of some serum lipid profile parameters of the patients with deferent age groups.

Age group	**No.**	**Cholesterol (mg/dl) [Mean ±SED]**	**TG (mg/dl) [Mean ±SED]**	**HDL-c (mg/dl) [Mean ±SED]**	**LDL-c (mg/dl) [Mean ±SED]**
< 30	5	182.76±16.16	163.02±27.89	24.00±14.04	143.00. ±21.14
31-40	10	185.77±11.43	170.82±19.72	27.23±9.93	145.10±14.95
41-50	20	201.26±8.08	155.84±13.95	43.00±7.02	157.00±10.57
51-60	21	228.59±7.89*A	184.34±13.61	27.92±6.85	176.276±10.31
> 60	9	176.53±12.05*A	184.87±20.79	21.86±10.48	157.78±15.75
total	**65**	**202.86±4.99**	**171.92±7.65**	**31.31±3.90**	**124.96±4.70**

*Significant difference at P< 0.05**Highly significant difference at P< 0.001

Table-7:Mean concentration values of some serum lipid profile parameters of the three types of patients

Type of patients	No.	Cholesterol (mg/dl) [Mean ±SED]	TG (mg/dl) [Mean ±SED]	HDL-c (mg/dl) [Mean ±SED]	LDL-c (mg/dl) [Mean ±SED]
Type one	11	227.35±11.81	164.90±18.60	23.00±9.41	177.64±13.99
Type two	19	202.00±8.98	157.74±14.152	41.32±7.162	171.21±10.65
Type three	35	195.63±6.62	181.83±10.43	28.50±5.28	149.17±7.85
Probability		0.072	0.397	0.360	0.257

*Significant difference at P< 0.05

**Highly significant difference at P< 0.001

DISCUSSION:

65 Sudanese patients were participated into this study 54(83.1%) females and 11(16.9%) males, their mean age was 45.7years (ranged between 27 to 76 years), with female to male ratio of 4.9:1. These findings were in agreement with [25] who found that the ratio of female to male were 5:1.Apossible explanation for the high incidence of gallstones in female may be attributed to the fact that endogenous and exogenous estrogens (giving as oral contraceptive pills or hormone replacement therapy) induce propel of chenodeoxycholic acid and increase total bile acid pool, with consequent saturation .Also progesterone causes smooth muscle relaxation and impairs emptying of gall bladder, [26] on the other hand women with gallstones are more likely to have had cholecystectomy than men with gallstones[27]. The majority of patients were from the age groups 51-60 and 41-50 years, 21(32.31%) and 20 (30.77%) patients respectively, while it was rare in patients < 30 and elderly patients > 60 years. These results were in partial agreement with [28] who reported that the high incidence of gallstones found in age group31-50 years (64 patients (68.08%)), while it was rare in patients < 30 and elderly patients > 70 years.

Probably the explanation for the higher prevalence of gallstones in these age groups is that, with increasing age biliary cholesterol saturation increases, due to a decline in the activity of cholesterol 7á hydroxylase, the rate limiting enzyme for bile acid synthesis[16]. In the elderly, bile acid synthesis is reduced, biliary cholesterol output is increased and cholesterol saturation of bile increases, and that is true both in men and women[17]. Deoxycholic acid proportion in bile increases with age through enhanced 7á de hydroxylation of the primary bile acids by the intestinal bacteria. In addition, increasing age allows the cumulative lithogenic action of more risk factors[27]. On the other hand the low incidence of gallstone disease over the age of 60 might be due to partly the fact that old people are poor candidate for surgery and anesthesia in addition to lesser easy access of medical assistance to this age group[25].

Stones were classified into 3 groups depending upon their colors: pale yellow and whitish stones as cholesterol calculi, black and blackish brown as pigment calculi and brownish yellow or greenish with laminated features as mixed calculi. The results demonstrated that the percentage of the of gallstones were 53.85% as pigment stones, 29.23% mixed and 16.92% as cholesterol stone .The results also showed that Cholesterol stones were not found in males and in young aged (< 30 years) in female ,mix and pigment stones were not found in age groups(< 30 and 31-40years) in male but present in age groups(31-40 years) in female .mix stones also they were not found in males in groups(41-50 years) (Table 1). These results were in agreement with [29] who considered that the most common type of gallstone in Sudanese patients was The pigment calculi 48 (51.07%) followed by mixed stone (31.9%) and then cholesterol type (17%) . Similarly pigment gallstone remains the major component of gallstones in Libya[30]. The patients with gallstones under study were also classified to four groups depended on their body mass index(BMI :kg/m2) (Table 2).

Result revealed that the highest percentage(52.31%) of gall stones was found in the patient who had body mass index(25-30).these result indicated that the high incidence of gallstones was found in obese persons. In the control group (60%) had a normal body mass index. These results were in agreement with[27,31] who stated that obesity is an important risk factor for gallstone disease, more so for women than for men. It raises the risk of cholesterol gallstones by increasing biliary secretion of cholesterol, as a result of an increase in HMG CoA reductase activity[27]. In this study table (3) showed the distribution of the participants by their parity.

It was clear that the higher percentage of gallstones disease 43.17% was found among the married multiparous women with (7-10) pregnancies. Meanwhile the lower percentage 3.11% was found among unmarried women, seem to be in accordance with the findings of other investigators who had reported a positive association of parity with gallstone disease in females [32], during pregnancy the most likely mechanism is an increased secretion of cholesterol caused by the hormonal changes during pregnancy. Interestingly, sludge and gallstones formed during pregnancy frequently dissolve after delivery[33]. In this study the levels of serum some serum lipid profile ; total cholesterol, triglycerides, high density lipoprotein cholesterol, and low density lipoprotein cholesterol where measured in patients and control group.

The mean concentration values[Mean ±SED] of serum some serum lipid profile represented in(table (4). Comparison of serum lipid profile between patients and controls groups showed that the levels of serum total cholesterol and LDL-C in patients were slightly higher than that of the control group but there was no significant variation in total Cholesterol and LDL-C ($p>0.05$) between patients and controls groups. Furthermore, It is found that there is Highly significant difference between patients and controls groups in serum triacylglycerol and HDL-C($p<0.01$) These results were in partial agreement with [25,34], who reported that gall stone disease were associated with elevated level of triacylglycerol. Whish might be attributed to obesity. Comparison for serum lipid profile between male and female in patients group as indicated in (Table 5) showed no significant difference ($p>0.05$) between the two groups.

Among age groups patients, there was a no significant variation in serum lipid profile except for the total Cholesterol, which were significantly raised in age group 51-60years ($p<0.05$.(Table 6)

Classification of gallstones was carried out according to the criteria suggested by [25]which based on their colors, according to these classification, the patients with gallstones were classified in to three types : Type one :patients with CS, Type two: patients with MS and Type three: patients with PS. Table (7) revealed the Mean concentration values (mg/dl) of serum Total cholesterol, triacylglycerol (HDL-C), (LDL-C in the three types patients with gallstones. The highest Total cholesterol level was observed for patients type one but no significant difference ($p>0.05$)in serum total cholesterol level between the three types of patients. The explanation of the high concentration levels of serum cholesterol in patients type one in the present study suggests that serum lipids do play just as big a role in the pathogenesis of cholesterol gallstones.

The data presented in (table 7) also indicated that the lowest level of HDL-C was found in patients type one however level of HDL-C showed that no significant difference ($p>0.05$) between the three types of patients.

CONCLUSION

The gallbladder stones diseases are one of most frequent causes of morbidity and surgical operation in Sudan. They are major diseases causing public health problem, their complication are serious and fatal (e.g. acute pancreatitis), their management is cost. This study considered that the incidence of gallstones diseases among Sudanese was not rare, as indicated of biliary operation in hospitals. Forty, fertile, fatty female are most predisposing factors, Pigment stone (PS) was found to be the commonest comprising, followed by mixed stone and cholesterol stone. Serum lipid profile between patients and controls groups revealed significantly increase of serum triacylglycerol and HDL-C levels. Serum total cholesterol level of patients type one was high compared to that of two types of patients, while the level of serum HDL-C was low of patients type one.

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