Cerrahi Sanatlar Dergisi
Journal of Surgical Arts
ISSN: 1308-0709
2016 Vol:9 No: 2

Original study

Dyslipidemia and gall stone disease; A search for their causal relationship.

DİSLİPİDEMİ VE SAFRATAŞI HASTALIĞI; OLAĞAN İLİŞKİLERİYLE İLGİLİ BİR ÇALIŞMA.

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J Surg Arts (Cer San D), 2016(2):67-70.

ABSTRACT

The study was conducted with the aim of exploring any possible relationship between gall stone disease and lipid profile.

Patients of any age or gender admitted for cholecystectomy due to gall stones (n=100) were kept in the study group while those admitted for reasons other than gall stone disease (n=100) were included as controls. Patients with history of intake of any hypolipidemic agents and diabetics were excluded. The patients of both the groups were divided into 3 different age groups which were further sub-divided into male and female. Thorough medical histories of the patients were taken and estimation of serum lipid profile was done.

The study group (with gall stone disease) was found to have significantly high value of serum triglycerides ($p < 0.05$) in all age groups in both genders. Total cholesterol and serum LDL was found to be higher in males > 20 years. A definite inverse relationship between serum high density lipoprotein and gall stone was also noted in both genders above 20 years of age.

In this study high serum triglycerides, total cholesterol, serum LDL and low serum HDL are shown to be significantly related to gall stone disease.

Key words: Cholecystectomy, dyslipidemia, gall stone disease, lipid profile, lifestyle, triglycerides.

ÖZET

Bu çalışmada safrataşları ve dislipidemi ararsında bir ilişkinin olup olmadığı araştırılmıştır.

Safrataşı nedeniyle hastaneye müracaat eden 100 kişi ile başka nedenlerle hastaneye gelen ve safrataşı tesbit edilen 100 hasta çalışmaya alınmıştır. Lipid azaltıcı ilaç kullanan hastalar çalışmaya alınmadı. Hastalar 3 farklı yaş grubuna ve erkek kadın olarak bir diğer alt gruba tanımlandılar.

Çalışma grubunda (Safra taşı şikayeti ile gelen hastalar) bulunan bütün alt grup hastalarda serum trigliserid değerleri anlamlı derecede yüksek bulundu (<0.05). Total kolesterol ve serum LDL seviyesi 20 yaş üstü erkeklerde yüksek bulundu. Her iki cinste ve 20 yaş üstü hastalarda yüksek serum HDL ve safr taşı hastalığı arasında ters bir ilişki saptandı.

Bu çalışmada, yüksek serum trigliserid, total kolesterol ve serum LDL, düşük serum HDL değerleri ile safra taşı varlığı arasında kuvvetli bir ilişki olduğu ortaya konmuştur.

Anahtar kelimeler: Kolesistektomi, dislipidemi, safrataşı hastalığı, lipid profili, yaşam tarzı, trigliserid.

INTRODUCTION

Gall stones are amongst the most common gastrointestinal illness. The overall prevalence of the disease is up to 10% (1) of the general population. It may require hospital admission and even surgical treatment in the form of cholecystectomy. The disease

cholelithiasis was first described in 1507 by a pathologist, Antonio Benivenius (2). Since then observers are trying to find out the causes and the mechanisms of stone formation in the gall bladder. Unfortunately as yet it is incompletely and insufficiently understood.

The only definitive treatment available now a days is surgical removal of the gall bladder (cholecystectomy), which has potential complications like post cholecystectomy syndrome thereby further adding to the morbidity of the patient. The change in diet and life style in the last few decades has changed the demography of many diseases worldwide. The alteration in lipid profile has been shown to be linked to various diseases like atherosclerosis, coronary heart disease, metabolic syndromes etc. Hence it is one of the widely studied parameter in the modern medical science. However, the available current literatures are unable to establish any definite relationship between the serum lipid and gall stone disease. Some studies generally agree that gall stone disease is not associated with total cholesterol (CH-T) (3-8) or low density lipoprotein (LDL) cholesterol (4). Decreased high density lipoprotein (HDL) cholesterol was associated with occurrence of gall stones in two studies (4, 8) but in another study (3) no such association was found. Plasma triglyceride is found positively correlated with gall stone diseases (3, 4, 7, 8).

There is lot of variation in opinion in the available literatures about lipid profile and gall stone disease. So the current study was undertaken to explore any possible relationship between gall stone disease and lipid profile of a patient.

MATERIAL AND METHOD

This retrospective observational study was conducted during the period from March 2010 to February 2011 in the Department of General Surgery at Calcutta National Medical College, Kolkata. The institutional ethical committee clearance was taken. Patients of any age and gender admitted in the surgical ward for undergoing cholecystectomy were selected and kept in study group (n=100). While those admitted for problems unrelated to gall bladder were placed in control group (n=100). Patients of either sex in both the groups were further divided according to age into 3 categories i.e., < 20 years, 20-40 years & > 40 years respectively. Patients with history of intake of any hypolipidemic agents or diabetics were excluded from both the groups. All patients were informed about the risks and benefits of the study and written informed consent was taken. History of each patients included in the study were thoroughly documented and estimation as lipid profile i.e., Total Cholesterol (CH-T), Triglycerides (TGs), Low Density Lipoprotein (LDL), High Density lipoprotein (HDL), Very Low Density Lipoprotein (VLDL)) done.

The results of lipid profile of the each patient was entered in excel sheet. The mean, standard deviation, standard error of mean was calculated for each parameter. And finally the values were compared within the two study groups by applying the student "t" test and were interpreted statistically using the software Graph pad Instant version 3. A "p" value < 0.05 was considered to be statistically significant.

RESULTS

The distribution of lipid profile amongst different age groups of both the genders has been shown in the table I. In the study group 66% of the patients were female where as in the control group they were 50% of the cases. Gall stone disease was twice common in females than male (M/ F: 1/1.94). The disease was more common in age group of >40 years. Males showed higher values of total cholesterol, serum LDL, serum VLDL, while values of serum TGs & serum HDL were higher in females. We found statistically significant relationship between serum TG and gall stone diseases in all age groups in both genders in study arm. The values of serum cholesterol were statistically significant in age groups 20-40 years in both genders while only in males in age > 40 years. HDL cholesterol values were low in all age groups except age < 20 years. Serum level of VLDL was found to have no relationship with gall stone disease in any age groups. A significantly higher LDL levels were found in both the genders of >40 years of age and in males of age 20-40 yrs whereas no such association was found in both the genders < 20 years (Table 1).

DISCUSSION

The formation of gall stones has been attributed to factors like metabolic, infective and stasis. Observers have investigated and put up a number of hypothesis on how metabolic factors can lead to the formation of gallstones (cholesterol stones in particular). The metabolic theory for the production of gallstone was first conceived by Aschoff (9) (1909). He was of the opinion that metabolic increase in the biliary cholesterol as a result of the dietary variations or hypercholesterolemia may be responsible for aseptic cholesterol stones. Moynihan(10) (1925) was of the opinion that solitary cholesterol stone was not caused by infection but resulted due to the condition of hypercholesterolemia. He suggested that the diagnosis of such a stone might be made by the estimation of the cholesterol. Sherlock (11) (1963) was not certain that whether hypercholesterolemia played any role in the production of the gallstones. But she opined that increased amount of biliary cholesterol or decreased amount of bile salts due to any reason might be responsible for the formation of gallstones. The major understanding to the formation of stones came from the concept of physico-chemical properties of the lipid in the bile pursued by Admirend and Small(12) in (1968). They demonstrated that the solubility of cholesterol in bile could be described by the molar concentration of cholesterol, bile salts and lecithin. If the concentration of bile salts and lecithin falls below a critical level, cholesterol precipitates from bile. Den-

besten L (13) (1973) found that an increase in dietary cholesterol causes bile to become more saturated hence causing precipitation as cholesterol stones. Thornton et. al. (14) in a study showed that the bile cholesterol saturation index is negatively correlated with plasma HDL cholesterol and positively correlated with both plasma triglycerides and LDL cholesterol. Indian researchers like Aulakh R et al, Mohan H et al (15) clearly ruled out any relationship between the lipid profile and gall stone disease while others like Saraya A, Irshad M et al (16) had established a positive relationship between the two.

Table 1: Distribution of lipid profile according to age and gender.

Lipid Profile (mg%)	<20 years				20-40 years				>40 years			
	Male		Female		Male		Female		Male		Female	
	Study Mean ±SD N=3	Control Mean ±SD N=4	Study Mean ±SD) N=7	Control Mean ±SD N=5	Study Mean ±SD N=12	Control Mean ±SD N=18	Study Mean ±SD N=23	Control Mean ±SD N=17	Study Mean ±SD N=19	Control Mean ±SD N=28	Study Mean ±SD N=36	Control Mean ±SD N=28
CH (T)	152±16.0	146 ±13.8	102.2 ±19.6	97.8 ±12.8	171.1 ±17.1	150.9 ±12.4	133.8 ±17.5	120.8 ±15.4	186.7 ±25.3	157 ±16.3	151.1 ±20.7	145.3 ±17.3
	P=0.6364		P=0.6661		**P=0.0008**		**P=0.0194**		**P=0.0001**		P=0.1885	
TG	104 ± 21.0	64.5 ±10.7	107.1 ±20.0	64.8 ±10.8	122.1 ±20.0	72 ±14.3	171.7 ±23.5	73.8 ±18.8	133.4 ±25.8	76.6 ±14.9	179.3 ±24.2	80.6 ±17.0
	P=0.0221		**P=0.0016**		**P=0.0001**		**P=0.0001**		**P=0.0001**		**P=0.0001**	
HDL	33.6 ±2.5	37.5 ±1.2	34.8 ±2.7	36 ±2.5	21.2 ±1.7	39.7 ±0.8	30 ±1.0	34.4 ±1.5	21 ±1.8	41.3 ±1.2	32.6 ±1.0	34.2 ±1.4
	P=0.0443		P=0.4862		**P=0.001**		P=0.0001		P=0.0001		P=0.0001	
LDL	90.3 ±12	77 ± 9.9	81.7 ±10.6	80.2 ±10.2	94.7 ±12.1	74.1 ±10.4	82.3 ±12.3	79 ± 11.9	102 ±11.4	85.3 ±15.7	91.1 ±10.2	81.3 ±10.8
	P=0.189		P=0.814		**P=0.001**		P=0.4045		**P=0.0003**		**P=0.0004**	
VLDL	18.6 ±5.0	19 ± 3.9	18 ±4	18 ± 3.5	21.3± 5.6	21.3 ±4.8	20.4 ± 4.5	19.5 ±5.5	22.5 ±4.6	21.6 ±5.1	22.3 ±4.7	21 ± 5.2
	P=0.924		P=1.04		P=0.9772		P=0.4045		P=0.526		P=0.3056	

CH(T)=Total plasma cholesterol, TG=Triglycerides, HDL= High density lipoproteins LDL= low density lipoproteins, VLDL= very low density lipoproteins. P= P value
Values of "p" in bold indicates statistically significant values i.e. p<5%

The findings of our study bore resemblance in some parameters to some previous studies while differed from others. Levels of serum TGs in our was significantly higher in both males and females in all age groups unlike Aulakh R et al(15), while similar findings were reported by Saraya A et al (16), Thijs C et al (17) & Jorgenson et al (18). Serum VLDL levels on the contrary were found to be statistically insignificant in all age groups like Saraya A et al(16) and Thijs C et al(17). Total cholesterol levels were significantly higher in both the genders in the age groups 20-40 years and only in males > 40 years. These values were similar to study conducted by Naseem et al (19) while researchers like Thijs C (17) and Jorgensen (18) found no relationship. We found significantly lower values of HDL in comparison with the control group except for the female patients < 20 years. Jorgenson (18) also found a definite inverse relationship between the two on the other hand Saraya A(16) found it to be insignificant. A significant higher LDL levels were found in both the genders of > 40 years of age and in males of age 20-40 years whereas no such association was found in both the genders <20 years. This is in contrary to the findings of study conducted by Saraya A et al (16), Thijs C et al (17) and Aulakh R et al (15).

This is the first study of its type in the tertiary centre in Eastern India. It is able to show relationship between dyslipidemia and formation of gall stones unlike some others which clearly ruled it out. The main limitation in the study was its smaller sample size. The serum lipid profile obtained in the study may differ from other populations, which can be attributed to the local food habits. A larger multi-institutional study would surely be more conclusive. The present study widens our knowledge regarding serum lipid being a factor contributing to the formation of gall stone disease. Further research in the molecular level for the same can be done for the etiopathogenesis of the disease.

Gall stone formation may be attributed to dyslipidemia. Serum lipid profile especially high serum triglycerides can indicate the patients at risk of gall stone diseases. Regular lipid estimation as a routine investigation can be advocated in age > 20 years and more so after 40 yrs of age. If dyslipidemia is identified, life style modification and or medical management should be started.

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