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Association of non-clinical characteristics and lipid profile with gall bladder stone patients; a case control study

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Abstract :

Increased incidence of cholelithiasis has been reported among female with advancing of age. Age, gender, race, obesity, diabetes, dietary factors and parity have all been identified as significant risk factors for the development of gallstones. Cholelithiasis is frequently associated with carcinoma gallbladder up to 40%-100% patients and is the most common associated factor independent of age or sex. A case control study. was carried out in 160 subjects (case n=80, control n=80). A detail questioner has been filled for non-clinical characteristics. Lipid profile has been done with the help of spectrophotometer by using the commercially available kit. In the present study we found the significant association of postmenopausal women, use of contraceptive pills and high parity with the gall bladder stone disease in comparison of control group. The level of total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL), very low density lipoprotein (VLDL)were significantly (p<0.001)higher in study group in comparison of control group. However, high density lipoprotein(HDL) cholesterol serum levels were found significantly(p<0.001)lower in cases in comparison of controls.Our study revealed that gall bladder stone patients have increased level of total cholesterol, triglycerides, low density lipoprotein, and very low density lipoprotein.

Keywords : Gall bladder stone, Lipid profile, Contraceptive, High parity.

Introduction:

These days the world is bearing an assortment of non-communicable diseases. Gallstone disease is a major health problem worldwide, particularly in adult population. Its occurrence has been found to be at least 6% in the adult population of Northern India (1).Gallstone disease (cholelithiasis) has been reported among female with advancing of age and a spurt in it has been noted recently (2).Age, gender, race, obesity, diabetes, dietary factors and parity have all been identified as significant risk factors for the development of gallstones (3-4).The pathogenesis of cholesterol gallstones is known to be multifactorial with the key factors includingcholesterol supersaturated bile, nucleation and growth of cholesterol monohydrate crystals and altered biliary motility. In addition, epidemiologic evidence, particularly ethnic differences, suggests the importance of genetic factors that affect susceptibility to gallstone formation and gallbladder disease (5). Cholesterol is water insoluble lipid, and it is digested in intestine after micelles formation. Micelles are aggregates of phospholipids, bile salts, and cholesterol, and vesicles are closed spherical bilayers of phospholipids with associated cholesterol (6). Cholelithiasis is frequently associated with carcinoma gallbladder in up to 40%-100% patients and is the most common associated factor independent of age or sex (7). The risk of carcinoma gall bladder in patients with gall stones may be increased 4 to 7 times (8) and patients with gallstones more than 3cm in diameter have a much higher risk (9). Hypercholesterolemia is common finding in adults and pure cholesterol gallstones are more common as compared to other types of gallstones (10). The risk factors for the development of cholelithiasis include repeated pregnancy, use of contraceptive pills, a family history of gall stones, serum lipids, dietary factors, chronic liver disease and possibly major abdominal surgery (11).This study was carried out with an objective to evaluate the association of contraceptive use, menstrual status, parity and lipid profile with gall bladder stone patients and control in north Indian population.

Material and Methods:

The present study was approved by the institutional ethics committee of King George's Medical University, UP, Lucknow India. This present case control study was carried out in the department of physiology with the collaboration of General surgery, King George's Medical University, UP, Lucknow, India. After obtaining the informed consent total N=160subjects were selected for the study in which N = 80(male=10, female=70) case group and N= 80(male=11, female=69) control group. Subjects between the age group of 20 to 50 years were included in the study on the basis of well define inclusion and exclusion criteria. 3 ml blood sample was collected from each participant and the serum has been separated. A detail questioner has been filled for non-clinical characteristics such as contraceptive use, menstrual status and parity. Lipid profile has been done with the help of spectrophotometer by using the commercially available kit.(Microlab 300, Merck) on the same day of sample collection. Low density lipoprotein and Very low density lipoprotein was calculated by the Friedewald Formula [LDL= TC-(HDL+ VLDL) and VLDL = TG/5] (12). All the statistical analyses were carried out by using SPSS 16.0

version (Chicago, Inc. USA).We used chi-square test for analysis of categorical data and student t test for non-categorical data.

Result:

In present study we have found majority of the patients were females in comparison of male in both study and control group (p<0.8149). Postmenopausal women had more significant (p<0.001) relation in gallstone patient in comparison of control subjects. The significant association (p<0.001) were found in case with oral contraceptive user. The female subjects with high parity were also significantly (p<0.002) associated with gall bladder stone (Table1).

Table 1: Distribution of Gender, Menstrual status, Contraceptive User and parity in Case and Control

	Gall Bladder Stone (n=80)	Control (n=80)	(χ^2) P value	OR (CI 95%)
Gender				
Male	10 (12.5%)	11 (13.7%)		
Female	70 (87.5%)	69 (86.3%)	0.8149	0.896 (0.357-2.246)
Menstrual status	N=70	N=69		
Premenopausal	17 (24.3%)	42 (60.9%)		
Postmenopausal	53 (75.7%)	27 (39.1%)	0.001*	0.206 (0.099-0.427)
Contraceptive user	N=70	N=69		
Yes	52 (74.3%)	26 (37.7%)		
No	18 (25.7%)	43 (62.3%)	0.001*	4.778 (2.316-9.858)
Parity (Childbirth)	N=70	N=69		
More than 3 children	42 (60%)	23 (33.3%)		
Less than 3 children	28 (40%)	46 (66.7%)	0.002*	3.00 (1.501-5.996)

P value- <0.005* (statistically significant), OR- Odd Ratio, CI- Confidence Interval (95%)

The comparison of lipid level between case and control shows the level of total cholesterol, triglyceride, low density lipoprotein, very low density lipoproteinwere significantly (p<0.0001) higher in patients compared with controls. However, high-density lipoprotein was significantly (p<0.0001) higher among controls in comparison of gall bladder stonepatients(Table 2).

Table 2: Comparison of lipid profile in study and control group

S.no.	Variable	Gall Bladder Stone (n=80)	Control (n=80)	P Value
1.	TC (mg/dl)	192.46±57.22	157.27±40.91	0.001*
2.	TG (mg/dl)	177.50±91.81	125.35±74.67	0.001*
3.	HDL (mg/dl)	26.84±8.82	32.97±11.05	0.001*
4.	LDL(mg/dl)	130.11±53.25	99.22±37.60	0.001*
5.	VLDL(mg/dl)	35.50±18.36	25.07±14.93	0.001*

P value- <0.005* (statistically significant)

Discussion:

Gallstones are a major cause of morbidity worldwide.The larger occurrence of gallstones in elderlyfemale is frequently reported in literature(13). This affinity was also reported in the present study,as most of the patients were women in comparison of men. In general, women are probably at increased risk because estrogen stimulates the liver to remove more cholesterol from blood and divert it into the bile. An increased risk of gallbladder stone was seen with Postmenopausal status, because use of hormone replacement therapy (HRT) has more risk for gallstones. The finding was consistent with an earlier report, which suggests that the premenopausal status probably had a protective role in the development of gallbladder stone. The underlying mechanism for the familial tendency of gallstone disease may be related to genetic susceptibility or shared lifestyle or metabolic factors. Although the present association appeared independent risk factors for gallstones, such as lifestyle factors, diet, and some time genetic factors. In the present data, the high parity was also significantly associated with gall bladder stone disease and the finding was consistent with our previous report as well as some others (14-16). It is proposed that the lithogenicity of bile increases in pregnancy due to the effect of estrogen and progesterone hormones, predisposing to gallstone formation and probably gallbladder carcinoma (17).

The majority of studies have evaluated that the gall bladder stonehas positive associationwithincreased triglyceride, total cholesterol, low density lipoprotein and very low density lipoprotein concentration. In this study, the similar observation was found between lipid profile concentration and gall bladder stone subjects in comparison of controls. Several epidemiologic studies have linked that the high serum triglyceride and low high density lipoproteinserum cholesterol due to(increased activity of 3-hydroxy-3-methyl glutaryl-CoA reductase) associated with gallstone for mation (18-19).Lower high density lipoprotein increases biliary cholesterol secretion there by raising the level of cholesterol precipitation and gallstone formation. Women are more

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prone for gallbladder stone formation than men, because of oral contraceptive user, high parity and hormone replacement therapy. In general gallbladder stone formation is more common, those having altered lipid profile. Therefore strategies can be made to improve nutrition and lifestyle which may have an influential consequence on a series of pathological conditions that signify a major source of morbidity and mortality in our society due to gallbladder stones and carcinoma.

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