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ESTIMATION OF SERUM LIPID PROFILE IN CHOLELITHIASIS PATIENTS

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ABSTRACT

Gallstones happen to be the most prevalent among varied pathologies affecting the biliary system. Gall bladder takes precedence over all other sites in the biliary system in formation of stone, owing to its physiological function of concentration of bile. There has been a significant increase in incidence of cholelithiasis in the world including India. The prevalence of gallstones is increasing due to the changes in dietary pattern. A fat, fertile, flatulent, female, fifty is the classical sufferer from symptomatic gallstones. The present study was conducted to estimate the serum cholesterol and Triglycerides levels in the gallstone patients. 50 healthy clinically normal subjects of age group between 20 – 60 yrs are selected as controls.50 patients of age group 20-60 yrs from gastroenterology department who have been diagnosed as having cholelithiasis by imaging namely ultrasound abdomen, CT abdomen, MRCP are selected as study group. Serum lipid profile was estimated using standard methods. HDL levels were decreased in cholelithiasis patients whereas Total cholesterol, LDL levels, triglycerides were elevated but were not significant. The study concluded that there was a significant decrease in HDL levels and significant increase in triglycerides levels in cholelithiasis patients when compared to the control group.

INTRODUCTION

Food we eat has a significant effect on our health**.** ***Hippocrates***, the Greek physician known as father of medicine, recognized the value of nutrition and the power to enhance health when he declared "you should let food be your medicine and medicine be your food".A diet may be defined as the kind of food on which a person or group lives. The dietary patterns vary widely in different parts of the world. A balanced diet is defined as one which contains a variety of food in such quantities and proportions that the need for energy, amino acids, vitamins, minerals, fats, carbohydrate and other nutrients is adequately met for maintaining health, vitality and general well being and also makes a small provision for extra nutrients to withstand short duration of leanness. Eating habits have been considerably changed in this modern society compared to the early days. Eating habits, for example eating in between meals, preference to sweets, refined foods and fats are established very early in life. The compositions of the diet, the periodicity with which it is eaten and the amount of energy derived from it are all relevant to the etiology of obesity and various diseases.

The diet containing more energy than needed may lead to prolonged postprandial hyperlipidemia and to deposition of triglycerides in the adipose tissue resulting in obesity. This has led to the development of various diseases. One such common disease is formation of gallstones or cholelithiasis. The current major focus of nutrition research, both epidemiological and experimental, is how our diets and even specific food or nutrients in our diets affect our health, primarily as related to the development of chronic diseases. One such disease is cholesterol gallstones whose prevalence is very high depending on dietary patterns and ethnic background. Dietary risk factors have been implicated in the development of gallstones.

Gallstones have been found since antiquity. They were found in autopsy studies of Egyptian mummies. And today, gallstone disease is a common problem in developed as well as developing countries. Gallstone disease thus represents a major health problem. It is found to be the chief cause of admission in the hospital for gastrointestinal problems (Russo *et al.*, 2004).

Being overweight or obese may increase the chances of having gallstones, especially in females. Researchers have found that people who are obese may produce high levels of cholesterol. This may produce bile having more cholesterol than it cannot dissolve. When this happens, gallstones can be formed.(Ov and Sudheer, 2007)

Of varied pathologies affecting the biliary system, gallstones happen to be the most prevalent. Gall bladder takes precedence over all other sites in the biliary system in formation of stone, owing to its Physiological function of concentration of bile. Gallstones disease has been identified as one of the diseases of civilization and modern affluent lifestyles of Nations (Sama *et al.*, 1990) There has been a significant increase in incidence of cholelithiasis in the world including India. The prevalence of gallstones is increasing due to the changes in dietary pattern (Sama *et al.*, 1990). A fat, fertile, flatulent, female, fifty is the classical sufferer from symptomatic gallstones (Williams and Ronan O'Connell, 2013). It is seen that cholelithiasis occurs in both sexes, quite often at a much earlier age, even in childhood, and it is also more common in old age. Gallstones are formed because of abnormal bile constituents. When bile is saturated or supersaturated with cholesterol or bile

salts when reduced results in gallstones formation. Gallstones are divided into cholesterol stones, pigment stones and mixed stones.

Of this, cholesterol gallstones are the commonest stone which results from too much cholesterol in bile which constitutes about 80% of the total. The Pathogenesis of cholesterol gallstones is an altered lipid metabolism. The prevalence of gallstones continues to rise with age and higher in women than men. This may be due to an increase in cholesterol content in the bile due to the effect of oestrogen (Bowen *et al.*, 1992)(Diehl, 1991). Cholesterol gallstones in man are associated with abnormalities in the relative concentration of major biliary lipids like cholesterol and phospholipids.

Gallstone disease has been found to be in great incidence in females with advancing age groups and a spurt in it has been found recently. It has been identified as one of the diseases of civilization and modern affluent lifestyles of the developed nations. There is a greater incidence in the occurrence of gallstones in the world including India. The risk factors for the occurrence or formation of gallstones include obesity, Diabetes mellitus (DM), smoking, plasma lipids, dietary factors, chronic liver disease and possibly major abdominal surgery .(Kosters *et al.*, 2003)

It was suggested that the person with increased triglyceride and decreased HDL cholesterol levels were more prone for the development of gallstones (Aulakh *et al.*, 2007). Since serum lipids have a role as risk factor in the development of gallstones, present study was conducted to estimate the serum cholesterol and Triglycerides levels in the gallstone patients and control group subjects

MATERIALS AND METHODS

Ethical clearance was obtained from the institutional ethical committee before the study was started

STUDY DESIGN:

Control group**:** 50 healthy clinically normal subjects of age group between 20 – 60 yrs are selected as controls.

Study group**:** 50 patients of age group 20-60 yrs from gastroenterology department who have been diagnosed as having cholelithiasis by imaging namely ultrasound abdomen, CT abdomen, MRCP are selected as study group.

Inclusion Criteria:

Cholelithiasis patients of age group between 20 – 60 yrs.

Clinically healthy individuals without cholelithiasis and other diseases between 20-60 yrs.

Exclusion **Criteria:**

Patients with diabetes mellitus, hypertension, haemolytic anaemia and metabolic disorders like Wilson disease.

RESULTS AND DISCUSSION

Serum Lipid Profile:

Total cholesterol **in cholelithiasis patients**

There is no significant change in the total cholesterol levels of cholelithiasis patients when compared with control subjects (p value 0.465) (Fig 1).

HDL cholesterol **in cholelithiasis patients**

There is a significant decrease in the HDL cholesterol levels of cholelithiasis patients (case) when compared to the control subjects (p value 0.00) (Fig 2).

LDL cholesterol in cholelithiasis patients

There is no significant change in the LDL cholesterol levels of cholelithiasis patients when compared with control group subjects (p value 0.073) (Fig 3).

VLDL cholesterol in **cholelithiasis patients**

There is no significant change in the VLDL cholesterol levels of cholelithiasis patients when compared with control subjects (p value 0.244) (Fig 4).

Triglycerides in cholelithiasis **patients**

There is a significant increase in the triglycerides levels of cholelithiasis patients when it is compared to the normal control group subjects (p value 0.000) (Fig 5).

Out of 50 cholelithiasis patients, 32 cholelithiasis patients were female and 18 cholelithiasis patients were male. This shows that female gender are more prone for the development of cholelithiasis (Fig 6).

There is a great need to have a study on cholelithiasis and the factors that attribute to its development because of greater incidence of gallstone and its varying presentation in recent years in India.

There are many factors that favor the formation of gallstones. The first among those is cholesterol hypersecretion, which may occur in conditions of advancing age groups, obesity, hyperlipidemia, medications and marked weight reduction. The study over 30 yrs ago showed that nearly half of the patients with cholelithiasis have lipid disorders (Bell *et al.*, 1973).

The purpose of this study was to investigate the serum lipid profile in cholelithiasis patients and to find out the contribution of serum lipids in the development of gallstones or cholelithiasis. And this is done by investigating serum lipid profile in gallstone patients and comparing it with serum lipid profile of control subjects.

Cholelithiasis or gallstones has become a major cause of morbidity and mortality throughout the world including India. There is a recent rise in the occurrence of gallstones development and there are many factors that attribute to the development of gallstones. One such factor is the change in the dietary patterns and lifestyle (Prakash and Lal, 2006). The most common type among gallstones is cholesterol gallstone that is either pure cholesterol stones or those having cholesterol as the major chemical constituents.

The greater incidence of gallstones was found among older persons as per the study by (Kay, Jørgensen and Schultz-Larsen, 1992)(Jørgensen, Kay and Schultz-Larsen, 1990), in older person and in obese individuals (Misciagna *et al.*, 1994). A number of epidemiologic studies have linked obesity, type II diabetes, high triglyceride levels and low HDL cholesterol levels to Gallstone formation (Amigo *et al.*, 2000).

The prevalence of gallstones differs widely from one country to another. The prevalence of gallstones in India is estimated to be 4%. And its occurrence varies even between North and South India due to the variation in the dietary habits. North Indians have 7 times higher preponderance in the development of gallstones when compared to the south Indians (Rakesh tendon, 2003).

Increase in gallstone development is mainly attributed to the Westernization and change in socio economic status. The female: male ratio in gallstone formation is about 2: 1 and the risk factor in females that is attributed to its formation includes child bearing, oestrogen replacement therapy and oral contraceptive use.

Gallstones were found to be more common in females who develop the disease especially in their 5^{th} decade. And they are found to be present with

the complaints of pain in the abdomen as the principal or major complaint. The most common investigation is ultrasonography which reveals the presence of stones in the gallbladder (Prakash and Lal, 2006).

Females are more prone for the development of gallstones. Some studies suggest the factor that contributes to its development is female sex hormones. According to the study by Shaffer, 2006, female sex hormones have a role to play especially in the age between 20 and 30 yrs.(Shaffer, 2006)

Another study on Oestrogen receptors and cholesterol biosynthesis suggests that female hormone oestrogen has a role in stimulating HMG-Co-A reductase enzyme which causes increased production of cholesterol and hence places female gender to be under increased risk of supersaturation. Hence this suggests the link between oestrogen and gallstones. ((Hulley *et al.*, 1999),

In the present study also, females were found to be more in number compared to males which also suggests that female gender is a risk factor for gallstone formation and this is comparable to the study by Heaton. (Heaton *et al.*, 1991). Out of 50 selected cholelithiasis patients, 32 were found to be females and only 18 were males. The cause might be due to the hormone that is oestrogen in females might place the female gender to be a risk factor. The study by Heaton shows that the risk factors involved in the cholesterol gallstone are age, female gender and parity.

Cavallini, Messa, Mangin, 1987 suggested that cholelithiasis patients >40 yrs had high cholesterol, normal triglycerides levels and also both these components were elevated in an another Indian study ((Aulakh *et al.*, 2007)

Diets rich in saturated fatty acids also are found to increase the risk of gallstone formation whereas diets with substituted mono or polyunsaturated fatty acids reduce the risk of gallstone formation. (Jonnalagadda, Trautwein and Hayes, 1995)

Gallstones formation is notably higher in obese patients and also in those who lose weight rapidly. Increased biliary cholesterol saturation occurs in fasting and this occurs more in obese persons. Even moderately overweight people are more prone to have risk of developing gallstone disease. Obesity in turn is related to increased food containing high levels of cholesterol. Obesity reduces gallbladder emptying which leads to development of gallstones. Obesity is thus a well known risk factor for the development of cholelithiasis. It also does this by acting primarily by increasing the synthesis of cholesterol, thereby causing biliary cholesterol secretion and supersaturation of cholesterol (Hayes, Livingston and Trautwein, 1992).

Drugs that lower cholesterol actually increase the cholesterol levels in the bile resulting in gallstone formation. Excess oestrogen from pregnancy, hormone replacement therapy and contraceptive pills are found to increase the cholesterol secretion in the bile and they also favour the decreased gallbladder motility hence leading to the gallstone formation.

Gallbladder movement is decreased in fasting favouring the bile supersaturation or oversaturation with cholesterol which leads to the formation of gallstones.

Low fibre diets, diets containing high cholesterol content and diets rich in starchy foods contribute as a risk factor in the development of gallstones. Dietary soluble fibre Psyllium inhibits cholesterol gallstone formation by reducing biliary cholesterol saturation index (Schwesinger *et al.*, 1999)).

Gallstone occurs in great preponderance in patients having hyperlipidaemia. Virupaksha et al., 2011 observed in their studies that serum lipids namely serum total cholesterol, LDL cholesterol, serum triglycerides levels were significantly elevated in both female and male cholelithiasis patients when compared to controls. Serum HDL cholesterol levels were decreased significantly in female cholelithiasis patients, but the decrease was not found to be significant in male patients as per their studies. This is in comparison with present study where only triglycerides levels and HDL levels have a significant change in cholelithiasis patients and there is no significant elevation of total cholesterol, LDL, VLDL levels when compared to control groups. Hence our study also suggests the possible association between lipid profile and cholelithiasis. And hence hyperlipidemia also plays a risk factor role in cholelithiasis formation.

Cholesterol levels in serum of cholelithiasis patients were decreased and triglycerides levels in serum of cholelithiasis patients were considerably elevated when compared to the control group subjects.(Thijs, Knipschild and Brombacher, 1990). This study is highly in consistent with our study which also suggests the significant elevation in triglycerides level and significant decrease in HDL cholesterol levels.(Thijs, Knipschild and Brombacher, 1990)

Pettiti et al. (Petitti, Friedman and Klatsky, 1981) observed that there was elevation of triglycerides levels and decrease in HDL Cholesterol levels in patients with cholelithiasis and thus it shows a positive association between serum triglycerides levels, serum HDL levels and cholelithiasis. This study is also highly in link with our study.

In the present study conducted, females were found to be more in number compared to males which suggests that female gender is a risk factor for gallstone formation and this is comparable to the study by Heaton, et al., 1991. The study by Heaton shows that the risk factors involved in the cholesterol gallstone are age, female gender and parity.

Some investigators found that there is a positive relationship between gallstones and increase in serum triglycerides levels and LDL cholesterol levels. And this also shows the decrease in HDL levels (Naseem aslam channa, et al., 2010). But as per our study there was no significant elevation of LDL cholesterol levels. This study is consistent with the present study with reference to elevation of serum triglycerides levels and HDL levels in cholelithiasis patients alone. This shows that hyperlipidaemia and obesity may affect cholesterol saturation in the bile. And our study has shown that there was no significant change or increase in total cholesterol levels in serum of cholelithiasis patients. Also there was no change in serum LDL cholesterol levels in serum of cholelithiasis patients when the levels were compared to the serum lipid levels of normal control group subjects. Also there was no significant increase in VLDL levels in serum compared to the normal control subjects. This is in link with Thijs, et al (Thijs, Knipschild and Brombacher, 1990) and Petitti, et al studies (Petitti, Friedman and Klatsky, 1981).

So as per our study there is a possible association between HDL levels, triglycerides levels and cholelithiasis patients. And female gender seems to be a risk factor in the development of cholelithiasis patients.

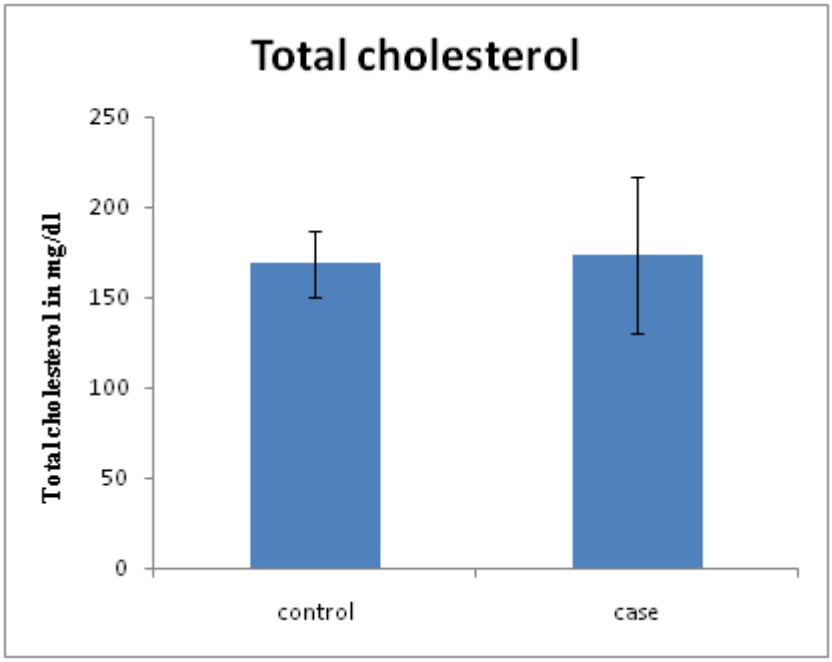

Fig 1: Graph represents the Total cholesterol of control and cholelithiasis patients. Unpaired T test was done. There was no significant change in the total cholesterol levels of cholelithiasis patients when compared with control subjects (p value 0.465).

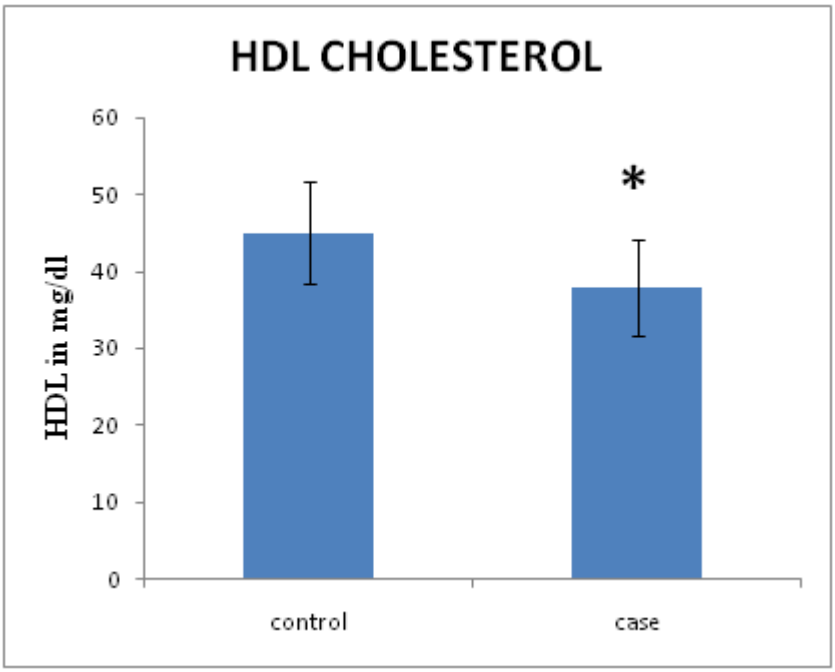

Fig 2: Graph represents the HDL of control and cholelithiasis patients. Unpaired T test was done, There was a significant decrease in the HDL cholesterol levels of cholelithiasis patients (case) when compared to the control subjects (p value 0.00). * indicatessignificance compared with control subjects.

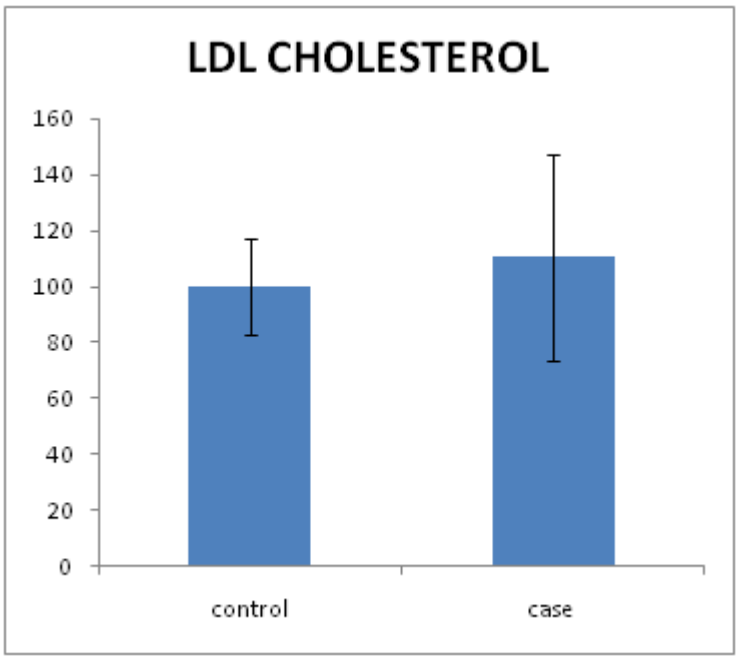

Fig 3 Graph represents the LDL of control and cholelithiasis patients. Unpaired T test was done, There was no significant change in the LDL cholesterol levels of cholelithiasis patients when compared with control group subjects (p value 0.073).

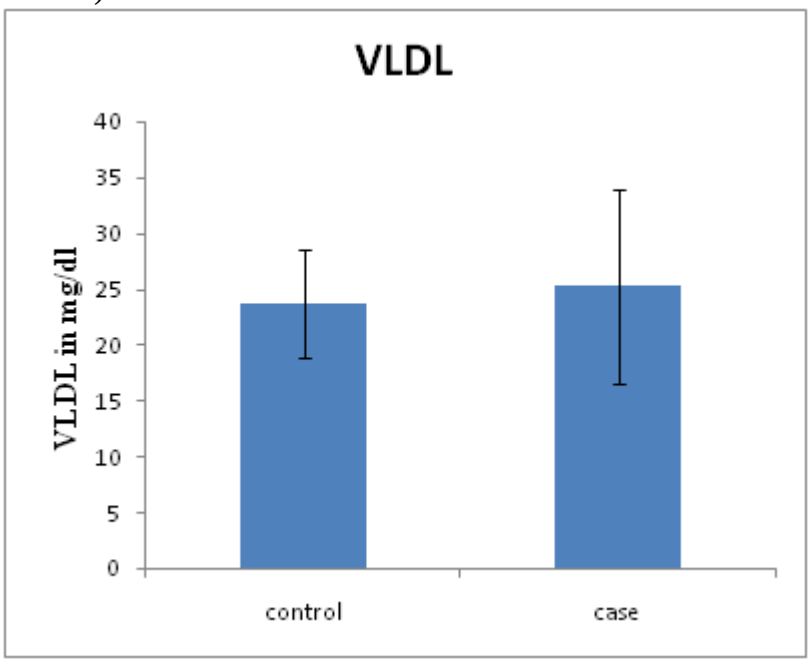

Fig 4: Graph represents the VLDL of control and cholelithiasis patients. Unpaired T test was done, There was no significant change in the VLDL cholesterol levels of cholelithiasis patients when compared with control subjects (p value 0.244).

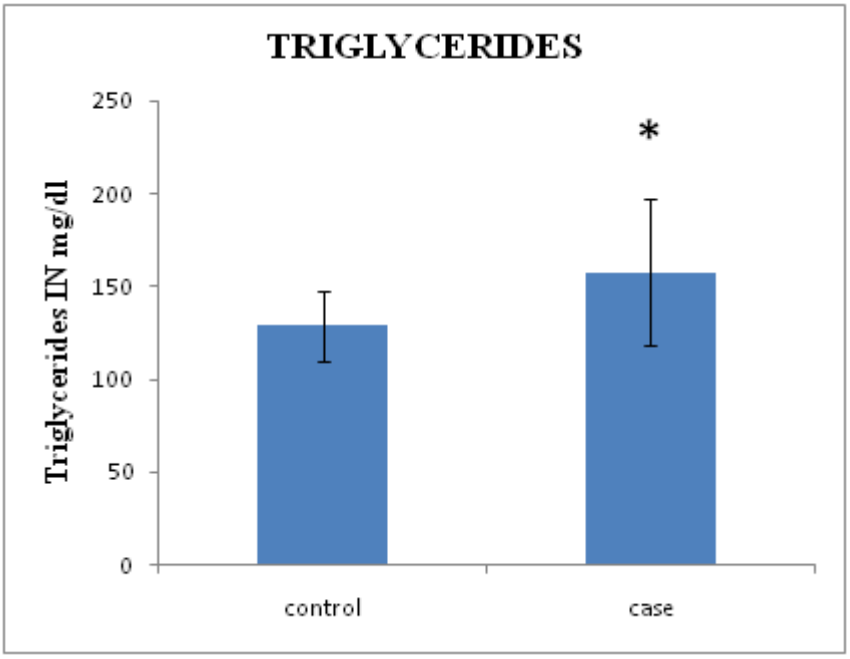

Fig 5: Graph represents the Triglycerides of control and cholelithiasis patients. Unpaired T test was done, There was a significant increase in the triglycerides levels of cholelithiasis patients when it is compared to the normal control group subjects (p value 0.000). * indicatessignificance compared with control subjects.

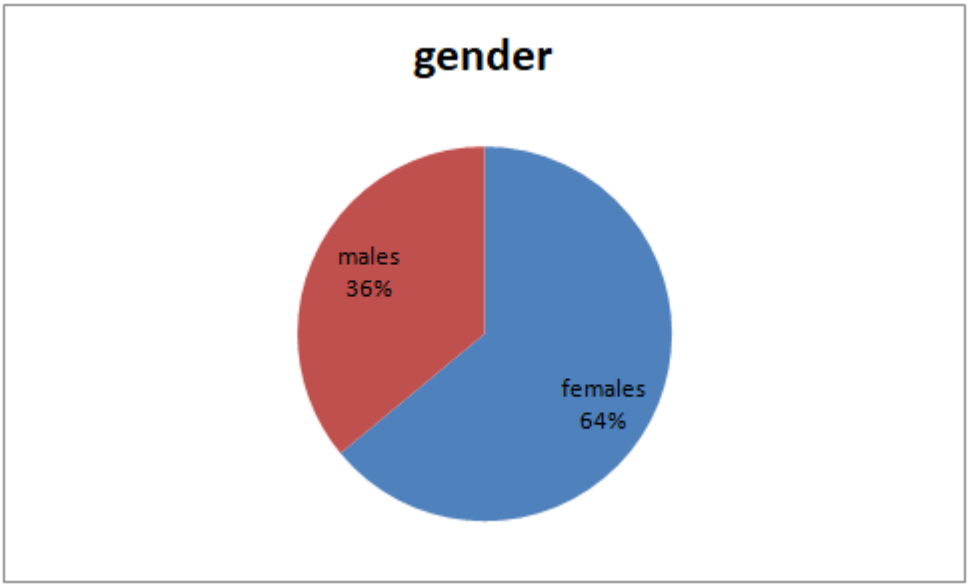

Fig 6: pie chart represents gender distribution in the study group. 36% were males (red) and 64% were females (blue)

CONCLUSION

Thus the study showed that cholelithiasis patients are found to have significant elevated levels of triglycerides in the serum, showing positive relationship with the development of cholelithiasis and that there was a significant decrease in the levels of serum HDL cholesterol in cholelithiasis patients when compared to control subjects. There was elevation of total cholesterol and LDL levels but the increase was statistically not significant.

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