Original Research Article

Comparative study of serum cholesterol, bilirubin, calcium and phosphorous in different types of gallstones, age and sex

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Abstract

Aims and Objective: To study the variables, i.e., Serum cholesterol, bilirubin, calcium and phosphorous in relation to age and sex in gallstone diseases. **Study design:** Cross-sectional observational study, Place and duration of study, Mamata Medical College and General Hospital, Khammam from October 2017 to September 2019**. Materials and methods:** Patients in whom the presence of gallstones was confirmed by ultrasound abdomen were included in this study. A series of 50 patients were compiled for the present study during this time, after obtaining clearance from ethical committee. **Results:** In the present study, mean age of the study group was 44.4 years, ranging from 17 to 76 years. The commonest age group in the study was middle 31-50 years, followed by 51-60 years. Among 50 cases, 41 (82%) were females and 9 (18%) were males with male to female ratio of 1:4.5. Representing the majority of the study population were females. Out of these 3 cases two were pigmented, one was cholesterol stone. But Chi-square statistic at 0.866 with P value of 0.64. Out of 41 female patients in the present study, 10 had a history of OCP use at some point in their life. Among them 5, 4, 1 patients had pigment, cholesterol and mixed stones. Mean serum bilirubin value was more among pigmented stone group (1.069 mg/dl) as compared to mixed (0.850 mg/dl) and cholesterol group (0.6 mg/dl). Mean serum calcium value was more among pigmented stone group (8.962 mg/dl) as compared to mixed (8.6 mg/dl) and cholesterol group (8.627 mg/dl).Serum phosphorous value was more among pigmented stone group (4.041 mg/dl) as compared to mixed (3.790 mg/dl) and cholesterol group (3.382 mg/dl). **Conclusion:** On the basis of the above observations, it is possible to say that pigment gallstone patients have high serum bilirubin, calcium and phosphate levels and the type of gallstone doesn't depend on age, sex, BMI status and OCP usage.

Keywords: Gallstone,Bilirubin,Cholesterol,Calcium,Phosphorous.

Introduction

Gallstones are one of the most common problems associated with the gallbladder, affecting millions of people throughout the world[1]. Studies have shown that Indian females shoulders the burden of 10-22 % of the worldwide prevalence of gallstones among females. Gallstones are the commonest associated risk factor with Gallbladder cancer, and appear to occur at a younger age in India. The problem of high incidence of gallstones with a rising rate of Gallbladder cancer is a uniquely Indian problem[2].

Gallbladder disease today is a common problem: 20 to 25 million Americans harbour gallstones, representing 10% to 15% of the adult population. Northern India has one of the highest reported incidence of gallbladder cancer (GBC) in the World. The highest incidence rates of GBC in the world are 21.5/100 000 in females in Delhi. Gallstones were said to play a major role in gallbladder cancer[3].

Major elements involved in the formation of human gallstones are cholesterol, bile pigment and calcium[4]. Analysis of chemical composition of gallstones can provide a significant reference to the treatment and prevention of their reoccurrence[5]. Quantitative analysis of the principal constituents of gallstones, such as total cholesterol, bilirubin, inorganic phosphate and calcium is well known6. However, there is not much data available on the correlation between bile and serum levels of these constituents in this patient population[4].

The purpose of this study is to identify whether the serum levels of different variables decides the type of gallstone and to study variables distribution among gallstone patients. If there are any significant results, researchers can try to target that variable while formulating a newer specific technique to treat gallstones.

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Aims and objectives

- To study the variables, i.e., Serum cholesterol, bilirubin, calcium and phosphorous in relation to age and sex in gallstone diseases.

Materials and methods

The present study was a cross-sectional observational study, which was conducted on patients presenting with gallstone disease in Mamata General Hospital, Khammam from October 2016 to September 2018. Patients in whom the presence of gallstones was confirmed by ultrasound abdomen were included in this study. A series of 50 patients were compiled for the present study during this time, after obtaining clearance from ethical committee.

Inclusion criteria

- Patients in whom the presence of gallstones was confirmed by ultrasound abdomen.
- Patients who have undergone cholecystectomy for the same.
- Patients who were ready to participate in the study.

Exclusion criteria

- Acalculous Cholecystitis.
- Patients with obstructive Jaundice.
- Patients not fit for cholecystectomy.
- Patients who refused cholecystectomy.
- Patients who were not ready to give informed written consent for the study

An elaborate study of these cases with regard to patient's details, including history, examination findings, routine and special investigations, type of surgery, type of stone and the number of stones, were done.

In history details regarding the presenting complaints, duration, past history, family history of gallstone disease, haemolytic disorder history and OCP use were noted. A thorough clinical examination was done and the findings noted. The patients were subjected to an ultrasound examination of the abdomen and the presence of cholelithiasis confirmed by it, associated acute or chronic cholecystitis was also noted. Patients who did not have cholelithiasis on USG were excluded from the study.

All these patients were subjected to quantitative analysis of:-

a. Serum total cholesterol - Based on enzymatic calorimetric determination employing cholesterol esterase and cholesterol oxidase,

b. Serum bilirubin - Based on Bichromatic method,

c. Serum phosphate by the calorimetric method, and

d. Serum calcium by modified OCPC (O-Cresolphthaleincomplexone) kit method

All these patients were subjected to routine preoperative investigations and underwent either open or laparoscopic cholecystectomy. These patients after cholecystectomy and retrieval of stones, were divided into three groups based on the morphology of gallstones into

i. Cholesterol stones – solitary/multiple, oval, large, granular surface, yellow white.

ii. Pigment stones – multiple, small, jet black, mulberry shaped.

iii. Mixed stones – multiple, multifaceted, brown, variable size

Observations and results

Age group

In the present study, mean age of the study group was 44.4 years, ranging from 17 to 76 years. The commonest age group in the study was middle 31-50 years, followed by 51-60 years age group as depicted in table

Age Group	Frequence	Percentage of Cases
<20	2	4
21-30	4	8
31-40	15	30
41-50	16	32
51-60	9	18
61-70	2	4
71-80	2	4
TOTAL	50	100

Mean age of patients in cholesterol stone group (45.36 years) was more than pigment and mixed stone group as depicted in table 3. However, this difference was statistically not significant (P value=0.9).

Type Of Stone	Frequency N=50	Mean Age In Years
Pigment	29	44.34
Cholesterol	11	45.36
Mixed	10	43.90
Total	50	44.48

Sex distribution

In the present study, among 50 cases, 41 (82%) were females and 9 (18%) were males with male to female ratio of 1:4.5. Representing the majority of the study population were females as depicted in table

Sex	Frequency (n-50)	Percentage of cases
Female	41	82
Male	9	18
Total	50	100

Serum levels of variables

Mean serum cholesterol value was 156.1 mg/dl, ranging from 96 to 223 mg/dl. Mean serum bilirubin value was 0.922 mg/dl, ranging from 0.4 to 2.4 mg/dl. Mean serum calcium value was 8.81 mg/dl, ranging from 7.3 to 10.3 mg/dl. Mean serum phosphorous value was 3.846 mg/dl, ranging from 2.8 to 12.6 mg/dl.

	Serum cholesterolmg/dl	Serum Bilirubin	Serum Calcium	Serum Phosphorous
Mean	156.10	0.922	8.816	3.846
Median	163	0.850	8.800	3.700
Standard Deviation	31.14	0.379	0.7388	1.3293

Serum cholesterol

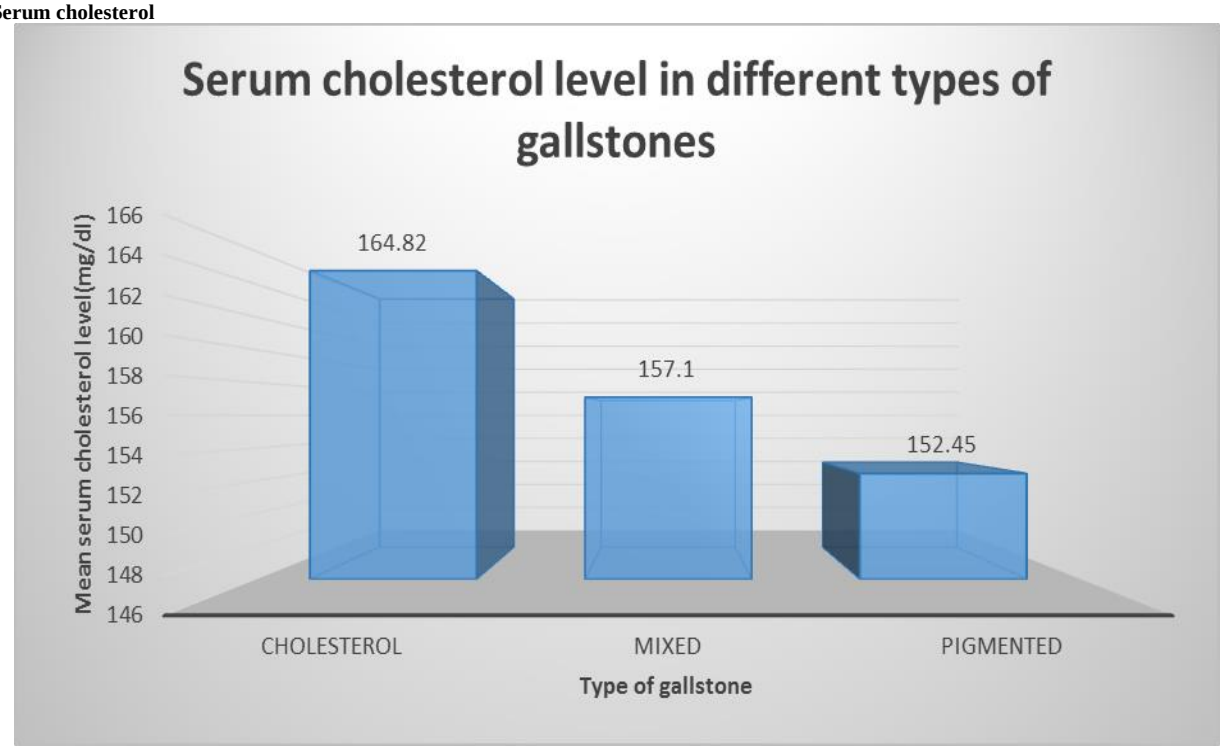
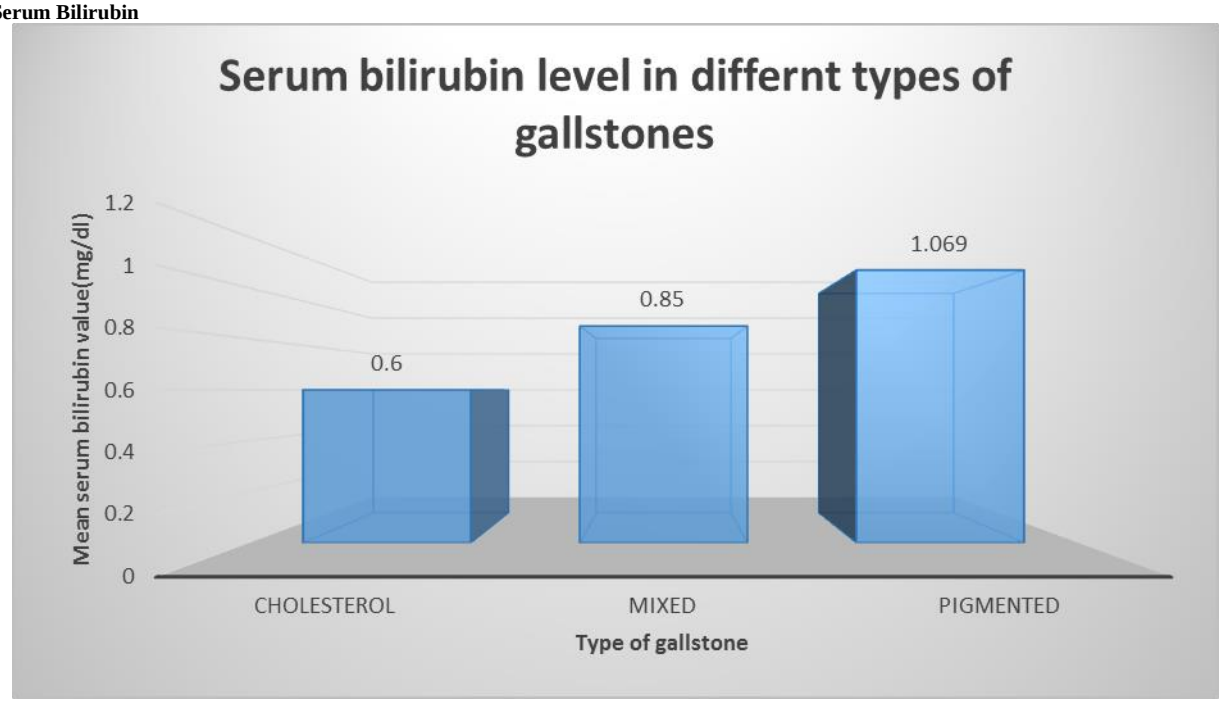
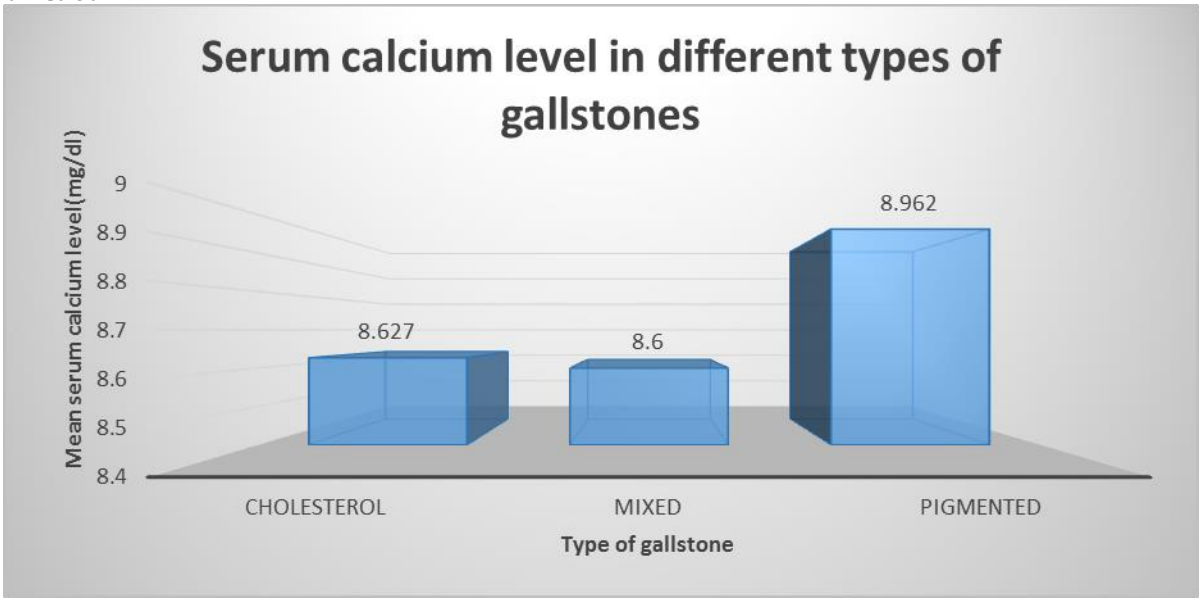


Fig.8: Mean serum cholesterol level in different types of gallstones

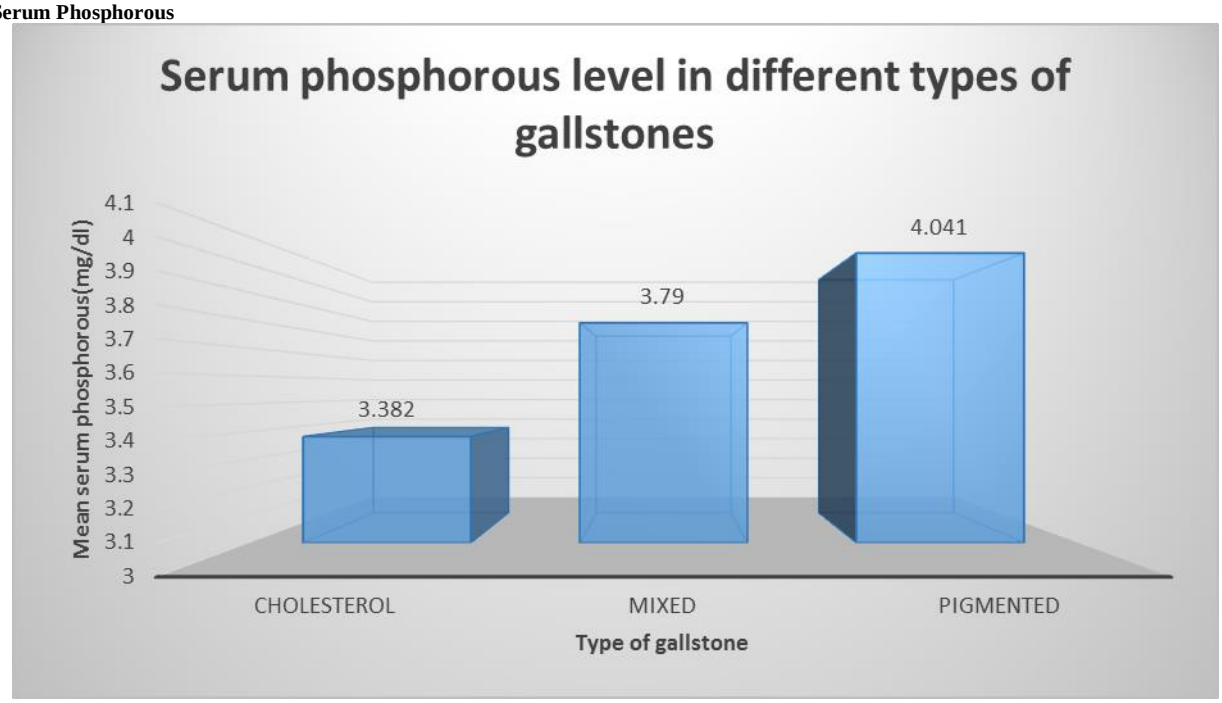
Serum Bilirubin



Serum Calcium



Serum Phosphorous



Comparison of serum values based on gender

Mean serum cholesterol value was more among females (156.27 mg/dl) as compared to males (155.33 mg/dl). However, this difference was not found to be statistically significant on unpaired T test (P value >0.05).

Mean serum bilirubin value was more among females (0.973 mg/dl) as compared to males (0.689 mg/dl). This difference was found to be statistically significant on unpaired T test (P value <0.05).

Mean serum calcium value was more among males (8.989 mg/dl) as compared to females (8.778 mg/dl). However, this difference was not found to be statistically significant on unpaired T test (P value >0.05).

Mean serum phosphorous value was more among females (3.876 mg/dl) as compared to males (3.711 mg/dl). However, this difference was not found to be statistically significant on unpaired T test (P value >0.05).

Variables	Sex	Number of cases(n)	Mean	Standard deviation	T Test	P Value
s.cholesterol	M- F-	9 41	155.33 156.27	35.253 30.655	0.081	0.936
s. bilirubin	M-	9	0.689	0.2088	2.107	0.04

	F-	41	0.973	0.3905		
s.calcium	M-	9	8.989	0.7897	0.772	0.444
	F-	41	8.778	0.7320		
s.phosphorous	M-	9	3.711	0.5207	0.333	0.740
	F-	41	3.876	1.4510		

Discussion

Gallstone disease remains one of the major causes of abdominal morbidity and mortality throughout the world. Gallstone disease is a chronic recurrent hepatobiliary disease due to impaired metabolism of cholesterol, bilirubin and bile acids, which is characterised by the formation of gallstones in the hepatic bile duct, common bile duct or gallbladder. Asian populations (5-20%) suffer from gallstones with lowest frequencies being in Black Americans[37].In India too, the gallstone disease is relatively common with an overall prevalence in the order of 10-20 per cent.

There is a clear North-South divide (commoner in the North) in the burden of gallbladder diseases in India, a phenomenon which is poorly understood.

Cholecystectomy is currently considered the "gold standard" for the treatment of gallstone disease. Cholecystectomy is one of the most commonly performed abdominal surgical procedures. Laparoscopic cholecystectomy has now replaced open cholecystectomy as first-choice treatment[39].

Age group distribution

Mean age of cases in this study was 44.4 years, ranging from 17 to 76 years. Most common age group in this study was middle age i.e., 31-50 years followed by 51-60 years. Which was consistent with other studies conducted by BansalA et al47, Jenna P et al[37]. Where as in studies conducted by Kafia SM et al[48], Karlatti SS et al[49] most common age group was 41-60 years which was about 10years older than the present study[48, 49]. The mean age of cases in Nakeeb A et al[50] study was 58.2 years.

The frequency of gallstones increases with age, escalating markedly after age 40 to become 4 to 10 times more likely in older individuals. The stone type also changes with age: initially being composed predominantly of cholesterol (corresponding to an increased cholesterol secretion into and saturation of bile) but in late life tending to be black pigment stones. Further, symptoms and complications increase with age, leading to more frequent cholecystectomies.

Majority of the study population was females 82% (41 cases) while males constituted only 18% (9 cases) with male to female ratio of 1:4.5. Study by Das B et al[40] has observed a male to female ratio of 1:3.8. In Shareef KM et al[48] study male to female ratio was 1:7.3. In Parambil SM et al[51] and Bansal A et al[47] study male to female ratio was 1:2.1 and 1.8 respectively. Nath K et al[2] observed a ratio of 1:1.5.

In present study out 50 cases, Most common type of stone was pigmented stone seen in 29 cases (58%) followed by cholesterol stones in 22%(11) and mixed variety in 20%(10) cases. In Western countries, gallstones are composed primarily of cholesterol.

Mean serum cholesterol value in the present study was 156.1 mg/dl, which was about same value as in other studies by Aulakh R et al78, Weerakoon W et al[79], Bwtazoo H et al[80]. Mean serum cholesterol in females (156.2mg/dl) was more than males (155.3mg/dl) which was in accordance with study conducted by Cavallini A et al.

Mean serum total bilirubin in the present study was 0.922mg/dl. Mean serum bilirubin value was more among females (0.973 mg/dl) as compared to males (0.689 mg/dl). This difference was found to be statistically significant on unpaired T test (P value = 0.04). From this in the present study, female cases had more serum bilirubin than males. This difference in the present study can be attributed to use of OCP in 10 cases among 41 female cases.

Mean serum calcium value in the present study was 8.81 mg/dl. Mean serum calcium value was more among pigmented stone group (8.962 mg/dl) as compared to mixed (8.6 mg/dl) and cholesterol group (8.627 mg/dl). However, this difference was not found to be statistically significant on ANOVA test (P value >0.05).

Mean serum calcium value was more among males (8.989 mg/dl) as compared to females (8.778 mg/dl). However, this difference was not found to be statistically significant on unpaired T test (P value >0.05).

Mean serum phosphorous value in the present study was 3.846 mg/dl. Mean serum phosphorous value was more among females (3.876 mg/dl) as compared to males (3.711 mg/dl). However, this difference was not found to be statistically significant on unpaired T test (P value >0.05). Mean serum phosphorous value was more among pigmented stone group (4.041 mg/dl) as compared to mixed (3.790 mg/dl) and cholesterol group (3.382 mg/dl). However, this difference was not found to be statistically significant on ANOVA test (P value >0.05).

In Shareef KM et al[5] study, Inorganic phosphate in serum was moderately correlated to that in cholesterol and mixed gallstones with significant negative correlation in case of pigment stones. In contrast, Nath k et al[2] observed no significant correlation between inorganic phosphate levels in serum with cholesterol, mixed or pigment stones.

Conclusion

On the basis of the above observations, it is possible to say that pigment gallstone patients have high serum bilirubin, calcium and phosphate levels and the type of gallstone doesn't depend on age, sex, BMI status and OCP usage.

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