

## Original Research Article

# Evaluation of changes in serum lipid profile and fasting blood glucose levels in patients with gall stone disease before and after cholecystectomy

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**Received:** 05 February 2020

**Revised:** 26 February 2020

**Accepted:** 27 February 2020

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## ABSTRACT

**Background:** There is paucity of information regarding the effects of cholecystectomy on serum lipid profile parameters and blood glucose levels in the patients of cholelithiasis. Therefore, this study was undertaken to compare some serum lipid parameters and blood glucose levels in patients of cholelithiasis and effect of cholecystectomy on the same.

**Methods:** The study was conducted on 50 patients of cholelithiasis who were admitted in Surgery department, MLN Medical College over a period of one year and were planned for cholecystectomy. Complete lipid profile (which included total cholesterol, triglycerides, high density lipoproteins (HDL) cholesterol, low density lipoproteins (LDL), very low density lipoproteins (VLDL) and atherogenic index) and fasting blood glucose was evaluated pre-operatively and post-operatively on the 3rd, 7th and further after 1 month of cholecystectomy.

**Results:** Out of 50 patients, maximum of 38% were in their 4th decade with females constituting 82% of total. There was significant elevation in fasting blood glucose and HDL cholesterol on 3rd, 7th and 30th day post-cholecystectomy as compared to pre-operative values ( $p$  value $<0.0001$ ). Triglyceride and VLDL cholesterol elevated on 3rd and 7th day but it significantly decreased one-month post-cholecystectomy as compared to pre-operative levels ( $p$  value $<0.0001$ ). However, LDL, total cholesterol and atherogenic index significantly decreased on 3rd, 7th and 30th day post-cholecystectomy.

**Conclusions:** Cholelithiasis is an important cause associated with significant pathological changes in many lipid profile parameters, which will return towards normal after cholecystectomy. This normalization will be a time dependent phenomenon with long term beneficial effects.

**Keywords:** Cholecystectomy, Lipid profile, Blood glucose

## INTRODUCTION

Gallstone disease is one of the most prevalent gastrointestinal diseases with worldwide distribution and with a substantial burden to health-care delivery system. Gall stones continue to be one of the major health problems in the world today, although the exact number

of patients is unknown, because there are no signs and symptoms related to the disease when there are no complications. The majority of the patients are diagnosed incidentally.<sup>1</sup> However, some patients come with acute complication of gall stones.<sup>2</sup> Gall stones are classified into three main types: cholesterol, pigment or mixed stones. Cholesterol stones contain 51% to 99% pure

cholesterol and mixed stones contain cholesterol plus calcium salts, bile acids, phospholipids and bile pigments.<sup>3</sup> In about 70% to 80% patients gall stones are of mixed type. Pure cholesterol stones are rare (10%). Pigment stones contain less than 30% cholesterol and are classified as either black or brown stones.<sup>4</sup>

Gall stones are associated with metabolic syndrome, which is defined as a cluster of multiple cardiovascular risk factors including central obesity, elevated fasting plasma glucose, high blood pressure, lower high density lipoprotein-cholesterol (HDL-C) and higher serum triglyceride (TG) levels.<sup>5</sup> Super saturation of bile in cholesterol is the most significant factor.<sup>6</sup>

The secretion of cholesterol supersaturated lithogenic bile, bile acids pool, concentration and the type of phospholipids favouring cholesterol precipitation, gallbladder dysmotility aiding aggregation of cholesterol crystals and delayed large bowel transit times favouring reabsorption of deoxy-cholic acid, resection of ileum depleting the acid pool have all been implicated in gallstone formation.<sup>7</sup>

The prevalence of gall stones continues to rise with age, and it is higher in women (2-3 times) than men. This may be due to the increase of cholesterol content in the bile by the effect of estrogen.<sup>4</sup> Oestrogen or oral contraceptives can increase secretion of cholesterol and decrease bile acids rendering super saturation of bile and increased lithogenicity.<sup>8</sup>

Gall stones association has been most consistently found with high levels triglycerides and low HDL whereas, it is inconsistent with low density lipoprotein (LDL) and total cholesterol levels.<sup>9</sup> Gall bladder disease is more common in patients with hyperlipidemia type IV.

Evidences from 30 years ago showed that about half of patients with gallstones will have an abnormal lipid profile that would lead to increase in the risk of coronary heart disease and stroke.<sup>10-15</sup> However, there is a paucity of information regarding the effects of cholecystectomy on serum lipid profile parameters and blood glucose levels in the patients with gallstone disease (GSD) in Northern India specially eastern Uttar Pradesh as earlier studies were carried out in other parts of the country. Therefore, this study was undertaken to compare some serum lipid parameters including total cholesterol (TC), HDL-C, LDL-cholesterol (LDL-C), TG level, atherogenic index (AI) and blood glucose levels in patients of GSD and effect of cholecystectomy on the same.

### ***Aims and objectives***

Aim of our study was to assess the serum lipid profile and blood glucose levels in patients of gall stone disease in eastern Uttar Pradesh and to evaluate the effect of cholecystectomy on these parameters.

## **METHODS**

The proposed study was carried out in P.G. Department of surgery, S.R.N. Hospital associated with M.L.N Medical College, Allahabad from September 2018 to September 2019 after approval from the ethical committee and after obtaining written and informed consent either from patient or their legal heir.

The study was conducted on the patients of gall stone disease who were admitted in the department of Surgery, SRNH, MLN medical college between September 2018 to September 2019 who will be undergoing cholecystectomy.

Patients were evaluated and their complete biodata was recorded after taking detailed history. The diagnosis was made on the basis of clinical picture, supported by ultrasonography and confirmed pre-operatively. The confirmation of cholelithiasis was done by ultrasonography.

### ***Inclusion criteria***

All the patients of gall stone disease between 20 to 60 years of age undergoing cholecystectomy.

### ***Exclusion criteria***

The patients suffering from the condition which are known to alter lipid levels and serum glucose levels such as patients with renal failure, nephrotic syndrome, pancreatitis, cardiac failure, morbid obesity, hypothyroidism, sickle cell disease, hemoglobinopathies and pregnancy were excluded. Patients who were on lipid lowering agents and anti-diabetic drugs, who were unable to understand and give consent and who did not comply with the study procedures till the end of the study were also excluded from the study.

Complete lipid profile (which included total serum cholesterol, serum triglycerides HDL cholesterol, LDL cholesterol, VLDL cholesterol and atherogenic index) and fasting blood glucose levels was evaluated pre-operatively (on the day of operation) and post-operatively on the 3<sup>rd</sup> day, 7<sup>th</sup> day and further after 1 month of cholecystectomy. Blood samples were collected from all subjects in this study by an antecubital venipuncture. A sample of (3 ml) blood was taken from every patient, and was divided into 2 portions: a portion of (0.5 ml) blood was taken in a fluoride tube for glucose estimation which was measured at once by standard kit method. The remaining blood (2.5 ml) was allowed to clot in the plain tube and the serum was separated after centrifugation at 3000 rpm for 3 minutes, which was then used for lipid profile estimation.

Serum fasting glucose and serum lipid profile parameters such as serum triglycerides, total serum cholesterol, HDL cholesterol was estimated by enzymatic method using

autoanalyzer.

LDL cholesterol was calculated by Friedewald's formula<sup>16</sup>

$$LDL = \text{Total cholesterol} - \text{HDL cholesterol} + \frac{\text{Serum Triglyceride}}{5}$$

VLDL was calculated by

$$VLDL = \frac{\text{Serum Triglyceride}}{5}$$

Atherogenic index was calculated by the following equation

$$AI = \frac{\text{Total Serum cholesterol}}{\text{HDL cholesterol}}$$

**Statistical analysis**

Results were tabulated, analyzed and subjected to statistical analysis using SPSS version 20. Two-sided paired t-test was used to compare changes in fasting blood glucose and lipid profile parameters from pre-operative levels to 3<sup>rd</sup> day post cholecystectomy, one-week post-cholecystectomy and one-month post cholecystectomy levels. At 95% confidence (p<0.05) was considered as statistically significant.

**RESULTS**

Total of 50 patients who had gall stone disease and were planned for elective cholecystectomy were included in this observational study which took place in Department of Surgery, MLN Medical College, Allahabad over a period of 1 year, between September 2018 to September 2019. All the patients underwent elective laparoscopic cholecystectomy.

Patients were followed up for a duration of 1 month. Those patients who were not able to comply with the study duration were excluded from the study. Fasting blood glucose, lipid profile parameters such as serum triglyceride, total cholesterol, HDL cholesterol, LDL cholesterol, VLDL cholesterol and atherogenic index were obtained from the patients on the day of cholecystectomy (pre-operative value), 3<sup>rd</sup> post-operative day, 7<sup>th</sup> post-operative day and 30<sup>th</sup> post-operative day.

In Table 1, out of 50 patients who participated in the study majority of the patients are in their 4<sup>th</sup> decade i.e. between 31-40 years of age group, followed by in the 5<sup>th</sup> decade and then in the 3<sup>rd</sup> decade with percentage total of 38%, 32% and 24% respectively. Least number of patients were of age group between 51-60 years. Only 6% patients fell in this group.

Table 2, shows that only 18% (09) patients who presented with gall stone disease that were included in our study were male while the rest 82% (41) were females.

**Table 1: Distribution on the basis of age of patients.**

Age of patients (years)	Number of patients (n=50)	Percentage N (%)
20-30	12	24
31-40	19	38
41-50	16	32
51-60	03	6

**Table 2: Distribution on the basis of sex of patients.**

Sex	Number of patients (n=50)	Percentage N (%)
Male	9	18
Female	41	82

**Table 3: Distribution on the basis of signs and symptoms.**

Symptoms	Number of patients (n=50)	Percentage N (%)
Pain in right hypochondrium	42	84
Nausea and vomiting	28	56
Dyspepsia	19	38
Murphy's sign	46	92

In Table 3, out of 50 patients included in our study 42 patients had a history of pain in right hypochondrium i.e. 84%, whereas 28 patients (56%) had the complaint of nausea and vomiting. The least common presenting complaint was dyspepsia, noted only in 19 (38%) patients. Murphy's sign was present in 46 out of 50 patients in our study i.e. in 92% of patients participating in study.

**Table 4: Pre-cholecystectomy deranged lipid profile values.**

Parameters	Number of patients (n=50)	Percentage N (%)
Serum triglyceride level (>150 mg/dl)	43	86
Total cholesterol (>200 mg/dl)	38	76
HDL cholesterol (<40 mg/dl)	21	42
LDL cholesterol (>130 mg/dl)	33	66

In Table 4, shows that in our study on comparing pre-cholecystectomy values of lipid profiles parameters with reference values taken from ATP III NCEP guidelines, it was found that 38 patients (76%) had total cholesterol above 200 mg/dl before cholecystectomy and 33 patients (66%) had LDL cholesterol above 130 mg/dl.<sup>17</sup> Whereas, 21 patients (42%) had their HDL cholesterol below 40

mg/dl before cholecystectomy. This shows the deranged pre-cholecystectomy lipid profile in patients of cholelithiasis. In Table 5, fasting blood glucose (FBS) found to be increased on 3<sup>rd</sup>, 7<sup>th</sup>, 30<sup>th</sup> post-operative day as compared to pre-operative values and was found to be highly statistically significant in each case.

In Table 6, serum triglycerides were significantly increased on 3<sup>rd</sup> and 7<sup>th</sup> post-operative day but there was statistically significant decrease on 30<sup>th</sup> post-operative day as compared to pre-operative values and was found

highly statistically significant. Serum HDL was found to significantly increase on 3<sup>rd</sup>, 7<sup>th</sup>, 30<sup>th</sup> day as compared to pre-operative values. Total cholesterol and serum LDL were found to significantly decrease on 3<sup>rd</sup>, 7<sup>th</sup>, 30<sup>th</sup> day as compared to pre-operative values. Serum VLDL was found to increase significantly on 3<sup>rd</sup> day and 7<sup>th</sup> day but there was a significant decrease on 30<sup>th</sup> day as compared to pre-operative values. Atherogenic index was found to significantly decrease on 3<sup>rd</sup>, 7<sup>th</sup>, 30<sup>th</sup> post-operative day as compared to pre-operative values (p value<0.0001).

**Table 5: Pre-operative and post-operative fasting blood glucose levels.**

	Pre-operative (mg/dl)	3rd post-operative day (mg/dl)	7th post-operative day (mg/dl)	30th post-operative day (mg/dl)	P value (in each comparison)
<b>FBS</b>	64.10±8.997	79.31±8.82	92.18±8.57	97.96±6.06	<0.0001

**Table 6: Pre-operative and post-operative serum triglyceride estimation.**

	Pre-operative (mg/dl)	3rd post-operative day (mg/dl)	7th post-operative day (mg/dl)	30th post-operative day (mg/dl)	P value (in each comparison)
<b>Serum TG</b>	175.45±24.19	179.44±24.00	183.04±24.15	144.00±18.92	<0.0001
<b>Total cholesterol</b>	217.29±24.50	206.95±23.10	199.89±22.63	187.45±20.71	<0.0001
<b>HDL-C</b>	44.09±8.88	51.99±8.97	59.73±8.97	68.65±7.99	<0.0001
<b>LDL-C</b>	138.11±21.82	119.07±20.68	103.56±19.56	90.00±17.76	<0.0001
<b>VLDL-C</b>	35.09±4.84	35.89±4.80	36.61±4.83	28.80±3.76	<0.0001
<b>AI</b>	5.08±0.97	4.07±0.72	3.40±0.52	2.75±0.34	<0.0001

## DISCUSSION

In our observational study, total of 50 patients who were the diagnosed cases of cholelithiasis and planned for cholecystectomy were included. Patients were followed up for a duration of 1 month and serum fasting blood glucose, and various lipid profile parameters were studied before and after cholecystectomy.

In our study out of total 50 patients, majority of patients who presented with gall stone disease were in between 31-40 years of age group i.e. 38% patients were in their 4<sup>th</sup> decade. 32% patients were in 5<sup>th</sup> decade and 27% were in 3<sup>rd</sup> decade. While in a study conducted by Jindal et al they found that high incidence of GSD was seen in middle age group (41-50 years) i.e. in the 5<sup>th</sup> decade.<sup>18</sup>

### *Fasting blood glucose evaluation*

In our study, a low fasting blood glucose is seen in the patients before cholecystectomy with mean value of 64.10±8.997. It was found that 3 days after cholecystectomy fasting blood glucose was increased as compared to pre-op values. Also, one-week post-cholecystectomy fasting blood glucose was again found to be increased on comparing with the pre-op values. In both of the instances this difference was found to be

highly statistically significant (p<0.0001). This may be due to the effect of the catabolic phase of surgical trauma that leads to the increase of serum concentration of adrenaline and noradrenalin.

After 1 month of cholecystectomy, the Fasting blood glucose was still high, with mean value of 97.96±6.06. This was found highly significant as compared to pre-op values (p<0.0001). This high blood glucose seen in gall stone patients after 1 month of cholecystectomy may be due to the complications that are associated with the surgical intervention or the return of the patients to the normal life style and administration of large amount of fatty diet or high carbohydrates diet. This significant increase in fasting blood glucose after cholecystectomy is in accordance with study by Ahmed et al.<sup>19</sup> In their study they also found an increasing trend in fasting blood glucose levels on 7<sup>th</sup> and 30<sup>th</sup> day post-cholecystectomy.

### *Serum lipid profile parameters evaluation*

#### *Serum triglyceride*

In the present study, mean concentrations of pre-cholecystectomy serum triglyceride, Total cholesterol, LDL cholesterol, and atherogenic index are found to be higher and that of HDL-C are found to be lower in

patients of cholelithiasis as compared to normal reference values. Similar finding has been seen in the studies done by Ahmed et al, Devaki et al, Chapman et al, and Olokoba.<sup>19-22</sup> In our study, mean level of serum triglyceride before cholecystectomy was  $175.45 \pm 24.19$ . This mean concentration is higher than normal reference value of triglyceride (normal triglyceride  $<150$  mg/dl).<sup>17</sup>

Our study showed that there was an increase in triglyceride levels 3 days and one-week post-cholecystectomy when compared with that before operation. This increase in triglyceride on both post-op intervals was found highly statistically significant ( $p < 0.0001$  in both the cases). But there was reduction in triglyceride levels in gall stone patients after 1 month of cholecystectomy when compared with that before operation. This decrease in triglyceride after 1 month was also found to be highly statistically significant when compared with pre-operative levels ( $p < 0.0001$ ). The decrease in triglyceride level that is seen after 1 month of cholecystectomy may be due to; an increase in the bile acids and phospholipids secretion rate.

#### *Total cholesterol*

In our conducted study, mean total cholesterol level before cholecystectomy was  $217.29 \pm 24.50$ . This high level of total cholesterol in pre-operative phase is in agreement with results of others where they also defined a high total cholesterol in gall stone patients before cholecystectomy.<sup>23-24</sup>

In our study, there was decrease in total cholesterol levels on 3<sup>rd</sup> day, 7<sup>th</sup> day and 1 month after cholecystectomy when compared with pre-operative values. This decrease was found highly statistically significant ( $p$  value in each comparison  $< 0.0001$ ). This finding is in accordance with study done by Jindal et al, and Ahmed et al where they have concluded that serum concentrations of total cholesterol were significantly reduced in patients after cholecystectomy at 1 week interval and 1 month thereafter.<sup>18,19</sup>

#### *HDL cholesterol*

In our study, mean HDL cholesterol before cholecystectomy was  $44.09 \pm 8.88$  (normal HDL-C  $> 60$ , according to ATP III NCEP classification).<sup>17</sup> This reduced HDL-C in pre-cholecystectomy patients agrees with studies done by Ahmed et al, who described a decrease in HDL-C in gall stone patients before operation.<sup>19</sup> In our study, post-cholecystectomy HDL cholesterol was found to increase successively on 3<sup>rd</sup> day, 7<sup>th</sup> day and 30<sup>th</sup> day after cholecystectomy when compared with pre-cholecystectomy values.

#### *LDL cholesterol*

In our study, LDL cholesterol before cholecystectomy was  $138.11 \pm 21.82$ . The high LDL Cholesterol that was

seen in gall stone patients before operation may be due to abnormal secretory function.<sup>25</sup> In our study, post-cholecystectomy there was decrease in LDL cholesterol levels on 3<sup>rd</sup> day, 7<sup>th</sup> day and 1 month after operation when compared with pre-operative values. This highly significant reduction in the LDL-C ( $p < 0.0001$ ) after cholecystectomy when compared with that before operation is in accordance with Ahmed et al and Jindal et al.<sup>18-19</sup> The significant reduction in LDL-C that was seen in gall stone patients on 3<sup>rd</sup> day post-operative, 7<sup>th</sup> day post-operative and 30<sup>th</sup> day post-operative can be accounted to the increase in bile acids and phospholipids secretion rate after cholecystectomy.

#### *VLDL cholesterol*

In our study, VLDL cholesterol before cholecystectomy was  $35.09 \pm 4.84$ . Post cholecystectomy on 3<sup>rd</sup> and 7<sup>th</sup> day there was an increase in VLDL cholesterol levels as compared to pre-operative values. But one-month post-cholecystectomy VLDL cholesterol level was decreased with mean value of  $28.80 \pm 3.79$ . This decrease was found highly statistically significant ( $p$  value  $< 0.0001$ ) on comparing with pre-operative values. This finding is in contrast with studies done by Gill et al where they found no significant difference in VLDL cholesterol after 1 week and 1 month of cholecystectomy.<sup>26</sup>

#### *Atherogenic index*

Atherogenic index is ratio of total cholesterol to HDL cholesterol. In our study, mean atherogenic index prior to cholecystectomy was  $5.08 \pm 0.97$ . Before cholecystectomy, atherogenic index was higher in gall stone patients.

The reduction in the atherogenic index on 3<sup>rd</sup> day, 1 week and 1 month after cholecystectomy when compared with that before operation was seen in our study. This decrease was found as highly significant ( $p < 0.0001$  in each case). This finding of our study in terms of atherogenic index is in agreement with studies done by Ahmed et al.<sup>19</sup>

## **CONCLUSION**

In our study it is clearly evident that fasting blood glucose levels increased and serum triglyceride, total cholesterol, HDL-C, LDL-C, VLDL-C level and atherogenic index decreased significantly one month post-cholecystectomy. Hence, it would be appropriate to conclude that cholelithiasis is an important cause which is associated with significant pathological changes in many lipid profile parameters, which will return towards normal after cholecystectomy. This normalization will be a time dependent phenomenon with long term beneficial effects.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Kumar R, Singh V, Ahmad S, Singh M, Singh A, Rai N et al. Evaluation of changes in serum lipid profile and fasting blood glucose levels in patients with gall stone disease before and after cholecystectomy. *Int Surg J* 2020;7:1089-94.