



**RESEARCH ARTICLE**

**Correlation of Surgical and Conservative Management of Cholelithiasis & its Varying Complications by Clinical Pharmacists in a South Indian Tertiary Care Teaching Hospital**

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**ABSTRACT**

Cholelithiasis (Gall stone) is most frequent disorders of biliary tract, Cholelithiasis complications includes; Acute Cholecystitis, Choledocholithiasis & Cholangitis, Acute Pancreatitis and Intestinal Obstruction. These complication managed by surgical procedures or conservative methods. Laparoscopic Cholecystectomy is choice of procedure for shorter length of stay & faster convalescence period. Conservative method includes; oral dissolution therapy (Ursodeoxycholic acid for less than 5mm stone) and broad spectrum antibiotics with analgesics. Study was aimed to correlate the management approach for cholelithiasis & its varying complications by surgical procedure or conservative methods, to observe Cholelithiasis prevalence and to establish a pharmaceutical care plan. A prospective observational study conducted between September 2016 and February 2017 in the in-patient department of General Surgery, Gandhi Medical College and Hospital, Secunderabad. Patient data were documented in a structured format according to inclusion criteria. ANOVA statistical methods were performed for final outcome. In 104 cases, 67% were Cholelithiasis, 17% Choledocholithiasis and 13% Acute Cholecystitis. Study demonstrates female predominance, surgical and conservative management was 67% and 33% respectively. Laparoscopic Cholecystectomy (94%) was most preferred surgical procedure and Metronidazole & Ceftriaxone mostly prescribed antibiotics along with analgesic Tramadol. Hyoscine was commonly prescribed anti-spasmodic but Ursodeoxycholic acid prescription was minimal. Majority of stone size observed was within 10mm and maximum patient were obese or overweight. Management depends upon factors like; surgeon's choice, stone size & pre-existing conditions. Clinical pharmacist can provide pharmaceutical care through counseling and education for obese patients to prevent recurrence. Overall management was satisfactory as nearly all patients got cured with negligible number of mortality or morbidity.

**KEYWORDS**

Cholelithiasis, Surgical management, Conservative management, Clinical Pharmacist

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**INTRODUCTION**

Cholelithiasis is the presence or formation of gall stones which is the most common disorder of the biliary tract. Gallstones are classified into cholesterol and pigment stones, although the majorities are of mixed composition<sup>1</sup>. According to the III National Health and Nutrition Examination Survey (NHANES III);

the overall prevalence of gall stones in women is 16.6% compared to 7.9% in men. Gall stones are less frequent in India compared to other countries<sup>2</sup>. Common Risk Factors are classified as modifiable and non-modifiable. Modifiable risk include; obesity, metabolic syndrome, diabetes mellitus, dyslipidemia, reduced physical activity, rapid weight loss, diet, total parenteral nutrition (TPN), underlying diseases (e.g., Cirrhosis, Crohn's disease, Hypothyroidism), drugs (eg. Ceftriaxone, Octreotide, Thiazide diuretics), female sex hormones, smoking, dietary factors and BMI. Whereas non-modifiable are; family history, genetic predisposition, ethnic background, age and female gender. In female; estrogen increases cholesterol secretion and diminish bile salt secretion, while the progestin act by reducing bile salt secretion and impairing gall bladder emptying leading to stasis. Women are almost twice as likely as men to form gallstones. The risk factors for female includes; oral contraceptive and estrogen replacement therapy<sup>3</sup>. There are three types of gallstones, these include: - (1) Cholesterol stones which contain at least 90% cholesterol, (2) Pigment stones either brown or black which contain at least 90% bilirubin and (3) Mixed composition stones which contain varying proportions of cholesterol, bilirubin and other substances such as calcium carbonate, calcium phosphate and calcium palmitate<sup>4,5</sup>.

Various complications of Cholelithiasis are; Acute Cholecystitis, Choledocholithiasis & Cholangitis, Acute Pancreatitis and Intestinal Obstruction (Gallstone ileus)<sup>6</sup>. Generally, patients with gallstones remain asymptomatic, which are called “**silent stones**” and may not require treatment. Patients with symptomatic Cholelithiasis have often right hypochondrium and epigastric pain with nausea and vomiting<sup>7,8</sup>. Abdominal ultrasonography (USG) is inexpensive and highly sensitive test to diagnose gallstones. Endoscopic Retrograde Cholangio-Pancreatography (ERCP) and Magnetic Resonance Cholangio-Pancreatography (MRCP) are more accurate than USG in diagnosing thickened bile ducts.

White Blood Cell count (WBC), Total, Serum Bilirubin (TSB), Serum Aspartate Transferase (AST), Serum Alanine Transferase (ALT), Alkaline Phosphatase (ALP), Serum Amylase and Lipase are usually elevated in Gallbladder Diseases (GBD)<sup>9</sup>.

### **Management Approach of Varying Complications of Cholelithiasis**

Among various complications of cholelithiasis, Acute Cholecystitis is surgically managed by Laparoscopic Cholecystectomy and conservatively managed with Ursodeoxycholic acid, Intravenous 2<sup>nd</sup> and 3<sup>rd</sup> generation cephalosporins (Cefaperazone 1 to 2 cm) intravenously for 12 hours, Metronidazole 500mg for 6 hours, Analgesic and Antispasmodics. Choledocholithiasis and Cholangitis; surgically managed with Endoscopic Sphincterotomy and Stone Extraction and conservatively managed with Antibiotics. Acute Pancreatitis is surgically managed with Laparoscopic Cholecystectomy and ERCP. Intestinal obstruction is surgically managed with Enterolithotomy/Laparoscopic Cholecystectomy. Both Acute Pancreatitis and Intestinal Obstruction are generally not managed conservatively<sup>10</sup>.

In Special Cases like Pregnancy; Cholelithiasis is generally managed with Meperidine prescribed to relieve pain rather than NSAIDs as they are contraindicated. Ursodeoxycholic acid (Category B) safety and effectiveness for treating gallstones during pregnancy has not evaluated by US-Food and Drug Administration<sup>11</sup>.

### **Diet in Cholelithiasis**

Healthy dietary pattern includes high amounts of vegetables and fruits, low fat dairy products, vegetable oil, nuts, whole grains, legumes, fruit juices, fish and low intake of salt. Unhealthy dietary pattern such as high intake of solid fat, red meat and egg increases the risk of GBD stones<sup>12</sup>.

## **MATERIALS AND METHODS**

This prospective observational study was

conducted between September 2016 and February 2017 in the inpatient units of Department of General Surgery, Gandhi Medical College and Hospital, Secunderabad. Permission for the study was obtained from the Institutional Ethical Committee, CMR College of Pharmacy and permission from Department Head was also obtained. A structured case documentation form was prepared for documentation of study cases. Cases were identified and observed on a daily basis upon visiting various in-patient units. Out of a total of 158 cases observed, 104 cases were selected and documented during the study period, according to inclusion criteria of age 18-80yrs of both genders diagnosed as Cholelithiasis and its varying complications with/without comorbidities. HIV positive case, cases without complete information and if the patient dies during the hospitalization were excluded from the study. Collected data were analyzed and incorporate on a regular manner in various parameters to interpret. Interpreted data, then further analyzed statistically to get the final result.

### Statistical Analysis

Data were statistically analyzed to obtain the result by using ANOVA in Graph Pad Software. TUKEY- KRAMER one way ANOVA was used to analyze variable data in multiple parameters. P value <0.001 was considered as statistically significant & denotes as \*\*\*.<sup>13</sup>

## RESULTS

A total number of 158 cases were observed in the department of General Surgery during the study period. Out of total observed cases, 54 were excluded as in 30 cases, data were misplaced, in 21 cases the patient absconded from hospital and in 3 cases patient died during the course of treatment.

Finally a total of 104 cases was included during the study period, according to the inclusion criteria. Data were obtained from the collected cases based on various parameters. The final outcome was interpreted and analyzed to

acquire the result. This study has revealed that a high number of Female 77 (74%) with age group of 41-50yrs were predominant in developing gallstones [Table-1].

Highest number of cases was observed as Cholelithiasis alone 70 (67.31%) and among its complications; Choledocholithiasis 18 (17.31%) was observed [Table-2].

Cholelithiasis and its varying complications were mostly managed surgically 69 (67.3%) and also with conservative method 35 (32.7%) [Table-3].

Among 126 drugs used for conservative method, 8 types of Antibiotics 59 (46.83%) and 3 types of Analgesics 25 (19.84%) were used. Distribution of various prescribed medication for the management of Cholelithiasis was found in the following manner; Buscopan (Hyoscine) 25 (19.84%) followed by Metronidazole 18 (14.3%), Ceftriaxone 15 (11.9%), Tramadol 12 (9.52%), Paracetamol 9 (7.14%), Vitamin K 8 (6.35%), Amikacin 6 (4.76%), Cefotaxime 5 (3.98%), Ursodeoxycholic Acid 5 (3.98%), Diclofenac 4 (3.17%), Piperacillin + Tazobactam 4 (3.17%), Amoxicillin + Clavulanate 4 (3.17%), Ciprofloxacin 4 (3.17%), Ondansteron 4 (3.17%) and Ofloxacin 3 (2.38%) [Table-4].

From the observed cases it was found that maximum numbers fall into the category of overweight 42 (40.38%) as per BMI scale, followed by obese 26 (25%) and normal 36 (34.62%) [Table-5].

Cases with stone size  $\leq$  10mm were predominantly 67 (64.42%), followed by 11-15mm 30 (28.85%) and >15mm 7 (6.73%) [Table-6].

ALP values were found to be higher than the normal in maximum number of cases 71 (68.2%) [Table-7].

This study found that the majority of cases were managed surgically whereas conservative management were also chosen for 1/3<sup>rd</sup> of the cases [Table-8].

Table 1: Patient Demographics in collected cases (n=104)

S. No.	Demographics	Number with Percentage (%)
<b>Gender</b>		
1.	Female	77(74%)
2.	Male	27(26%)
<b>Age</b>		
1.	≤ 20	06 (5.77%)
2.	21-30	18 (17.31%)
3.	31-40	21 (20.20%)
4.	41-50	24 (23.07%)
5.	51-60	18 (17.31%)
6.	61-70	15 (14.42%)
7.	>70	02 (1.92%)

Table 2: Diagnosis wise distribution of collected cases (n=104)

S. No.	Varying Diagnosis	Number of cases with Percentage (%)	Statistical significance
1.	Cholelithiasis	70 (67.31%)	<b>SEM-0.084</b> <b>SD-0.86</b> <b>P-value- &lt;0.0001***</b>
2.	Choledocholithiasis and Cholangitis	18 (17.31%)	
3.	Acute Cholecystitis	13 (12.50%)	
4.	Acute Pancreatitis	2 (1.92%)	
5.	Intestinal obstruction	1 (0.96%)	

Table 3: Distribution of Management Procedure (n=104)

S. No.	Procedure for management	Number of cases with Percentage (%)
1.	Surgical method	69 (67.30%)
2.	Conservative method	35 (32.70%)

Table 4: Distribution of various drugs according to Pharmacological Class prescribed in conservative management (n=126)

S. No.	Drugs with Pharmacological Class	Frequency with Percentage (%)
<b>1. Antibiotics (n=59)</b>		
i.	Metronidazole	18 (14.30%)
ii.	Ceftriaxone	15 (11.90%)
iii.	Amikacin	06 (4.76%)
iv.	Cefotaxime	05 (3.98%)
v.	Piperacillin+Tazobactam	04 (3.17%)
vi.	Amoxicillin+Clavulanate	04 (3.17%)
vii.	Ciprofloxacin	04 (3.17)
viii.	Ofloxacin	03 (2.38%)
<b>2. Analgesics (n=25)</b>		
i.	Tramadol	12 (9.52%)
ii.	Paracetamol	09 (7.14%)
iii.	Diclofenac	04 (3.17%)
<b>3. Antispasmodics (n=25)</b>		
i.	Hyoscine	25 (19.84%)
<b>4. Haemostatic agent (n=08)</b>		
i.	Vitamin K	08 (6.35%)
<b>5. Anticholelithic agent (n=05)</b>		
i.	Ursodeoxycholic Acid	05 (3.98%)
<b>6. Antiemetic (n=04)</b>		
i.	Ondansetron	04 (3.17)

Table 5: Distribution of Body Mass Index (BMI) (n=104)

S. No.	BMI	Number of cases with Percentage (%)	Statistical significance
1.	Obese	26 (25%)	SD- 0.77 SEM- 0.075 P-value <0.0001***
2.	Over weight	42 (40.38%)	
3.	Normal	36 (34.62%)	

Table 6: Distribution of gallstone size (n=104)

S. No.	Stone Size	Number of cases with Percentage (%)	Statistical significance
1.	≤10mm	67 (64.42%)	SD- 0.618 SEM- 0.060 P-value <0.0001***
2.	11-15mm	30 (28.85%)	
3.	>15mm	07 (6.73%)	

Table 7: Distribution of Alkaline Phosphatase level (ALP) values (n=104)

S. No.	ALP Value (Normal:40-141 IU/L)	Number of cases with Percentage (%)
1.	High	71 (68.20%)
2.	Normal	33 (31.80%)

Table 8: Distribution of Management in Cholelithiasis & its varying complication

S. No.	Varying Diagnosis	Total No. Of cases	Cases managed surgically (n=70)	Cases managed conservatively (n=34)
			Number of cases with Percentage (%)	Number of cases with Percentage (%)
1.	Cholelithiasis	70	53 (75.71%)	17 (24.29%)
2.	Choledocholithiasis & Cholangitis	18	11 (61.11%)	07 (38.89%)
3.	Acute Cholecystitis	13	05 (38.46%)	08 (61.54)
4.	Acute Pancreatitis	2	-	02 (100%)
5.	Intestinal Obstruction	1	01 (100%)	-

Table 9: Distribution of Past Medical History (n=104)

SI No	Various Past medical history	Frequency	Percentage (%)
1.	Nil significant	30	28.85
2.	Hypertension	22	21.15
3.	Diabetes Mellitus	13	12.50
4.	Tubectomy/ Hysterectomy	13	12.50
5.	Hypothyroidism	05	4.80
6.	LSCS	05	4.80
7.	Jaundice	04	3.84
8.	Appendectomy	03	2.90
9.	Menopause	03	2.90
10.	Previous ERCP	02	1.92
11.	Asthma	02	1.92
12.	Hernia	02	1.92

Table 10: Distribution of Length of stay (LOS) (n=104)

SI No	Length of stay	No of Cases	Percentage (%)	Statistical Significance
1.	<15 Days	72	69.20	<b>SD- 0.610</b> <b>SEM- 0.059</b> <b>P-value &lt;0.0001***</b>
2.	16-30Days	25	24.10	
3.	>30 Days	07	6.70	

Past medical history of cases shows that Hypertension was predominantly higher in 22 (21.15%) cases followed by Diabetes Mellitus, Tubectomy & Hysterectomy 13 (12.5%), Hypothyroidism & LSCS 5 (4.8%), Jaundice 4 (3.84%), Appendectomy & Menopause 3 (2.9%), Previous ERCP, and Asthma & Hernia 2 (1.92%). As well as without any significant past medical history was also found in 30 (28.85%) cases [Table-9].

As LOS concern, 15days LOS was observed in 72 (69.2%) cases, followed by 16-30days LOS in 25 (24.1%) cases and more than 30days LOS in 7cases (6.7%) [Table-10].

Statistically, there was no significance among age and gender group as well as in various prescribed medication group & in past medical history distribution.

## **DISCUSSION**

Incidence of 158 cases of Cholelithiasis for a period of six months only in the In-patient dept. Of General Surgery represents quite high in prevalence, similar incidence were also reported in previous studies by Attili AF<sup>14</sup>. In the present study, we correlated the surgical and conservative management of Cholelithiasis & its varying complications with standard or recommended guidelines and found that rational treatment was provided to patients in maximum cases. It was also found that equal distribution of Cholelithiasis was present among all age groups (18-80yrs) and slightly higher prevalence rate in 41-50yrs of age group and the same was reported by Kharga B 2016<sup>15</sup>. Multiple studies have demonstrated that Diabetes mellitus is one among the major risk factors for development of gallstones and the same was observed in our study where almost 13% of the cases were present with Diabetes mellitus as a past medical history, Pagliarulo M 2004, Pacchioni M 2000<sup>16,17</sup>. Moreover, this particular condition significantly increases the length of hospital stay (LOS) when compared with non-diabetics, Aldaqal SM 2012<sup>18</sup>. From the present study, we found that 9 cases of recurrent Cholelithiasis, which is due to failure

of timely surgical follow up that leads to re-admission. Similar findings were also reported by Williams TP 2015<sup>19</sup>.

From our study, we observed that Acute Cholecystitis was managed with broad spectrum antibiotics for 4-6weeks which is a recommended therapy and the same was also reported by Oliveira Junior SA 2016<sup>20</sup>. We observed that almost all cases were managed with Laparoscopic Cholecystectomy whenever the choice of surgical method of management was considered. This is mainly due to shorter length of stay and faster convalescence period than Open Cholecystectomy. A similar report was published by Abraham S 2014<sup>21</sup>. Out of total collected cases only a single case of surgical site infection (SSI) was present in the Laparoscopic Cholecystectomy procedure which ultimately enhances better patient management with this procedure. A similar trend was previously described by Ismat U 2013<sup>22</sup>. In this study, LOS of maximum cases were less than 2 weeks, but simultaneously LOS of the few cases where more than a month also including pre-operative and post-operative factors such as Hypertension, Diabetes Mellitus, Non elective status and improper WBC count. The same was reported by the previous study conducted by Ivatury SJ 2011<sup>23</sup>.

We observed that the majority of cases are with improper BMI value with either obese or overweight, which is considered as one of the major risk factors for gallstone developers. This is mainly due to Carbohydrate rich food habit and lack of physical exercise especially in Female population. Similar finding was also reported previously by Sachdeva S 2011<sup>24</sup>. Clinical Pharmacist can play a major role in this particular area by providing appropriate knowledge and information focusing about the relation between BMI & Gallstones development which may help in reducing this particular condition in the society, Jordan MA 2015<sup>25</sup>. In contrast to previous statement, even cases with normal BMI has also developed Gallstones. Thus a conclusive judgment cannot be confirmed in the role of BMI to form

Gallstones. Same was also reported by Attili AF 1995<sup>14</sup>.

Diabetes mellitus and unfitting lifestyle adds a major contribution to the development of Cholelithiasis which confers increase of health care cost for longer duration. A tight glycemic & BMI control can help to reduce the incidence of Cholelithiasis ultimately providing better economic and health support to the society, similar outcome regarding Diabetes mellitus & BMI and its implication towards gallstone was reported by Stinton ML 2012<sup>26</sup>.

## CONCLUSION

Cholelithiasis management requires an adequate and appropriate approach for better treatment outcome. However the choice of surgical procedure or to go with conservative management entirely depends upon various factors, namely; Surgeon, Stone size and preexisting medical conditions. As lifestyle and diet were found to be one of the significant contributing factors for the development of gallstone. A timely and suitable tactic with proper pharmaceutical care can control the situation without further complications. The overall correlation of Cholelithiasis management by surgical and conservative method was quite satisfactory as the majority of cases got relieved with a negligible number of morbidity and mortality.

## LIMITATIONS

This study was conducted for a period of 6 months, which is very less to establish any marvel for a common disease with a high prevalence rate. Moreover, only one department and in-patient units were selected for the study which leads to a restricted number of the patient as patients were also present in other department and also in the outpatient department. This study can be further extended with the inclusion of multiple departments by inclusion of larger sample size with longer follow-up. Along with this multi-center observational data for a particular region/zone will deliver a clear outcome about the disease.

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## CONFLICT OF INTEREST

None

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Nil

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