

## Research Article

# A Cross Sectional Study on Gallstone Disease and its Risk Factors in a Tertiary Care Hospital of South India

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• Gallstone disease (GSD); South india; Cholecystectomy; Cholecystitis

**Abstract**

This study aims to evaluate the epidemiology and risk factors of Gallstone disease (GSD) in South India population. Medical records of 124 patients diagnosed with GSD between October 2012 to May 2015 were reviewed retrospectively. Mean age of the GSD patients was  $44.56 \pm 14.9$  years. Patients with gallstones were higher in women than in men. The male-to-female ratio of GSD patients was 1:1.4. Ninety Nine (80%) patients with gallstones underwent cholecystectomy. In our analysis, none of the risk factors (Diabetes mellitus, Coronary Artery Disease, Multiparity, Cholecystitis, Cholecystectomy, Non-veg diet) on occurrence of gallstones has been statistically significant. This study shows that increasing age and female gender are higher chance of gallstone formation compared to the others. Even though variations in risk factors for GSD, our study did not find any unique and different risk factor among the population of South India as compared to the other countries.

**INTRODUCTION**

The presence of one or more stones in the gallbladder (Cholelithiasis) and its associated complications such as cholecystitis, pancreatitis and cholangitis represents a major problem for health care systems worldwide [1]. Irrespective of being either single or multiple, gallstones have various sizes and are reported to be a principal cause of inpatient admissions for gastrointestinal disorders. Gallstone disease (GSD) is a common disorder among patients presenting with abdominal discomfort such as epigastric pain, nausea, vomiting and loss of appetite [2]. While most of the GSD patients are asymptomatic, some (approximately 20%) become symptomatic after ten years of follow up [3]. Ultrasonography is recognized as the gold standard for diagnosing GSD [4]. Gallstone formation is multifactorial and several etiologic factors have been identified for GSD which are categorized as modifiable and unmodifiable causes, competing to lithogenesis [5]. The risk factors which are closely related to cholelithiasis are gender, race, age, obesity, dislipidemia, usage of contraceptives, diabetes mellitus and alcohol consumption [6-8]. Recognition of the rate of cholelithiasis and consequently its risk factors in different societies will aid the clinicians in the management of this disease, as the risk factors of gallstone formation are not the same in different parts of the world [9]. It has been reported in studies that changes in lifestyle and trend towards high energy diets have major influence on gallstone prevalence [10]. Therefore, knowledge about the epidemiology of this disease is indispensable for diagnostic and therapeutic strategies.

Existence of heterogeneity has been observed with regard to prevalence of GSD in different parts of the world. Westerners tend to have higher prevalence than Asians. 60 - 70% of Native Americans and proportionately small number individuals of mixed Hispanic/Native American background are being affected by Cholelithiasis. The estimated prevalence of GSD in Western countries is more than 10% [9]. The prevalence of GSD in Asian countries is approximately 10%, while in Africans this rate is less than 5%. Several studies from Middle Eastern countries have reported a prevalence rate of 4% -12% for GSD [11-13].

An association between increasing age and increased prevalence of gallstones has been shown in many epidemiological studies. Authors claim reduced bile acid synthesis as underlying cause for increased cholesterol saturation in the elderly people which ultimately contribute to gallstone formation [14]. Pregnancy also has been detected as a major risk factor for GSD. Decreased gallbladder motility during the third trimester of pregnancy favors the growth of stones in pregnant women [15]. An increased HMGC<sub>o</sub>A reductase activity contributes to the risk of cholesterol gallstones by increasing biliary cholesterol secretion, proving obesity as an important risk factor for GSD. Lifestyle and dietary factors plays a pivotal role in gallstone pathogenesis, leading to the progressive increase in the prevalence rate of gallstones during this century [5].

In India, the prevalence of GSD varies in different regions. Higher prevalence of gallstones has been reported in North compared to South Indians by the previous studies [16,17].

This cross-sectional study aimed to assess the risk factor for the burden of GSD among the patients attending tertiary care hospital of south India.

## MATERIALS AND METHODS

### Study participants

A retrospective cross-sectional study was conducted at Rajiv Gandhi Government General hospital, Chennai from October 2012 to May 2015. Patients with diagnosis of Cholelithiasis were included in the study. The study was approved by the institutional ethical committee.

### Clinical assessment

Data was collected from all the participants including demographic characteristics like age, gender, literacy, occupation, religion, family size. Lifestyle variables and dietary pattern (vegetarian/non-vegetarian) were also recorded. Height and body weight were measured and body mass index (BMI) was calculated by dividing weight (kg) by square of height (m<sup>2</sup>).

The diagnosis of GSD was ascertained by ultrasonography or having a medical history of cholecystectomy for GSD. History of diabetes, Coronary Artery Disease (CAD), parity (nulliparous/primiparous/multiparous), Cholecystitis (inflammation of gall bladder), Cholecystectomy, number of gallstones (single/multiple), laboratory values (lipid profile) was retrieved from case sheets.

### Statistical analysis

Data was analysed using SPSS Version 20. Demographic characteristics were analyzed using chi-square test for categorical variables and independent t test for continuous variables. Categorical values less than five were assessed by Fisher's exact test. Independent influence of potential risk factors was analyzed for its association with gallstones.

## RESULTS

A total of 124 subjects data were analysed in this study. The demographic characteristics of subjects were reported in Table 1. Fifty one (41%) was male and seventy three (59%) were female (Figure 1). Mean age of the study participants was 44.56 ± 14.9 years. Out of 124, 78 (63%) were diabetic (Figure 2) and 15 (12%) were having coronary artery disease (Figure 3). Cholecystitis was observed in one hundred and eight cases (87%) (Figure 4). Ninety nine participants (80%) had undergone cholecystectomy because of gallstones. Of the 73 females, 81% were multiparous and 11% were nulliparous (Figure 5). On analyzing the dietary pattern of participants it was found that 85% of them were non-vegetarians and 15% were vegetarians (Figure 6). The frequency of participants with multiple gallstones were higher (85%) compared with those who had single gallstone (15%) (Figure7). Cholecystectomy was done for the 80% patients (Figure 8).

Table 2 represents the distribution of GSD in different age groups. In the 30-39 year age group, the proportion of patients with gallstones was twice higher in women than in men. The highest percentage of participants having gallstones (47.6%) belongs to age group 30-49. Female gender predominance was observed with overall ratio of Male: Female is 1:1.4.

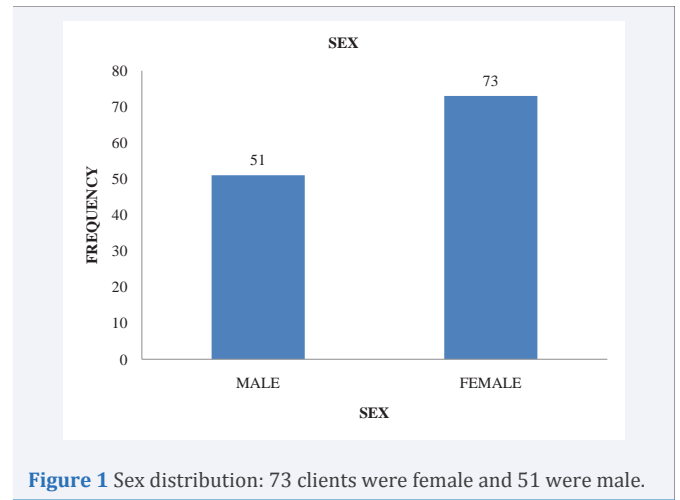


Figure 1 Sex distribution: 73 clients were female and 51 were male.

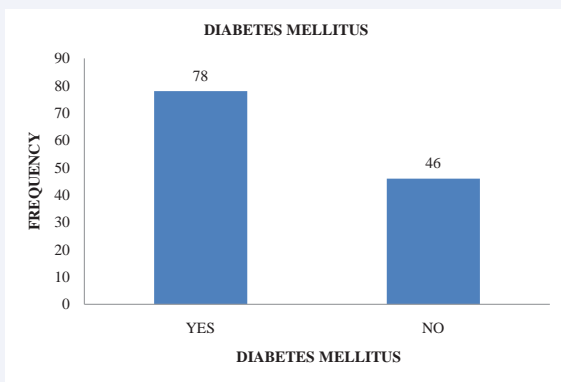
Table 1: Characteristics of the study subjects.	
Characteristics	Study subjects 124
Male	51 (41)
Female	73 (59)
BMI (Kg/cm <sup>2</sup> )	30.2 ± 3.04
Multiparity	59 (81)
Diabetes	78 (63)
CAD	15 (12)
TCH (mg/dL)	177.5 ± 24.4
TG (mg/dL)	191.6 ± 28.5
HDL-C (mg/dL)	39.6 ± 3.2
LDL-C (mg/dL)	99.6 ± 21
TBL (mg/dL)	1.0 ± 0.5
Cholecystitis	108 (87)
Cholecystectomy	99 (80)
Vegetarians	18 (14.5)
Mixed diet	106 (85.5)
Multiple stones	105 (85)
Single stones	19 (15)

Data shown as number (%) or mean ± SD  
**Abbreviations:** BMI: Body Mass Index; CAD: Coronary Artery Disease; TCH: Total Cholesterol; TG: Triglyceride; HDL-C: High Density Lipoprotein Cholesterol; LDL-C: Low Density Lipoprotein Cholesterol; TBL: Total Bilirubin Level

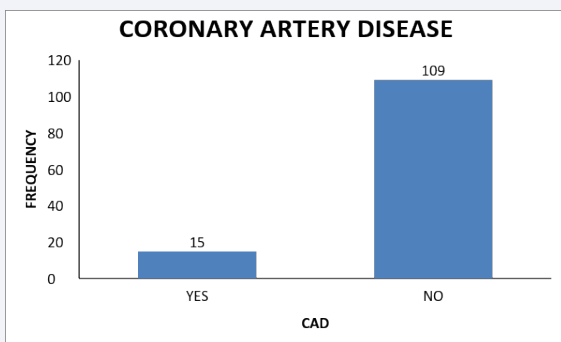
The influence of various risk factors (Diabetes mellitus, Coronary Artery Disease, Multiparity, Cholecystitis, Cholecystectomy, Non-veg diet) on occurrence of gallstones has been depicted in Table 3, Table 4. To our surprise, none of the risk factors were related to gallstone disease.

## DISCUSSION

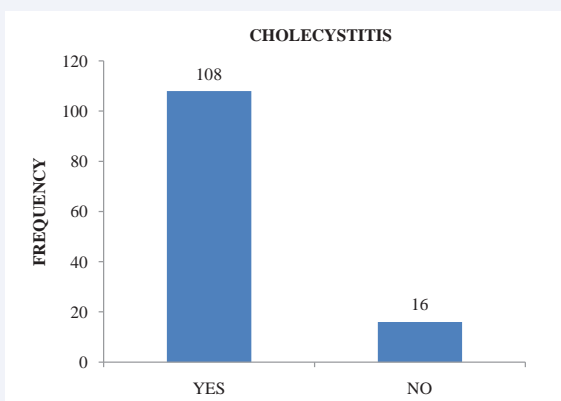
This study aimed to evaluate the epidemiology and risk factors of gallstone disease amidst population of Southern India in order to gain profound knowledge on demographic information of GSD in this region. Numerous studies have been carried out on the prevalence of cholelithiasis in several regions from USA, Southern



**Figure 2** History of Diabetes- 78 patients had a history of diabetes mellitus.



**Figure 3** History of Coronary Artery Disease: 15 patients had a history of coronary artery disease.

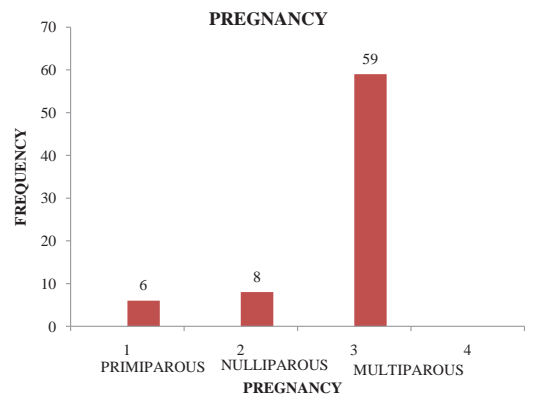


**Figure 4** Cholecystitis-108 patients were having cholecystitis.

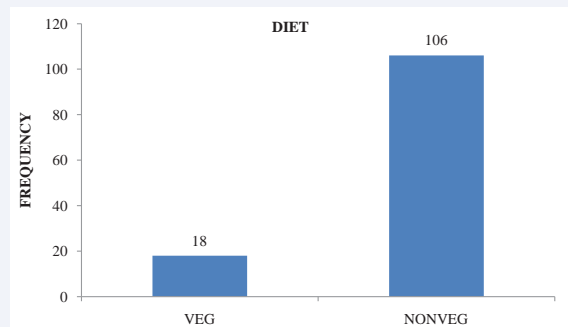
and Northern Europe and Asia, with a prevalence ranging from 5.9% to 21.9% [18,19]. Though western diet, obesity, sedentary life style can be attributed as common factors for growing prevalence of gallstone, the differences in composition of gallstone indicates that the etiology of cholelithiasis is different in Asian and western countries. According to the results of this study, the most commonly involved age group for cholelithiasis (47.6%) was found to be 30-49 years with a female predisposition (Male : Female = 1:1.4). In concordance, a study from Kathmandu

reported the similar age group (30-39 years) as having higher gallstone prevalence [20]. Moreover women belonging to 30-39 year age group had twice higher gallstone prevalence compared with men in our study. In accordance with our finding, a study from Argentina also reported gallstone prevalence twice higher in women belonging to same age group [21]. The prevalence ratio of GSD in male and female participants in the present study was 1:1.4 which was similar to another study carried out in Chennai (Stanley Medical college Hospital) [22]. It is intriguing that Liu et al., found a higher incidence of cholelithiasis in males than in females below 50 years of age in Chinese population [23] which was opposing our study report. These differences may be related to the diets and lifestyles of various regions. Thus it's evident from above comparisons that age is a major contributing factor in the pathogenesis of cholelithiasis (the older the person, the greater prevalence of cholelithiasis) besides female gender. This may be due to longer time exposure of subjects to gallstone risk factors. In women, gallstone formation often occurs during the fertile years. The plausible explanation speculated by authors for increased gallstone formation in women was increased cholesterol saturation in bile by the female sex hormone [24].

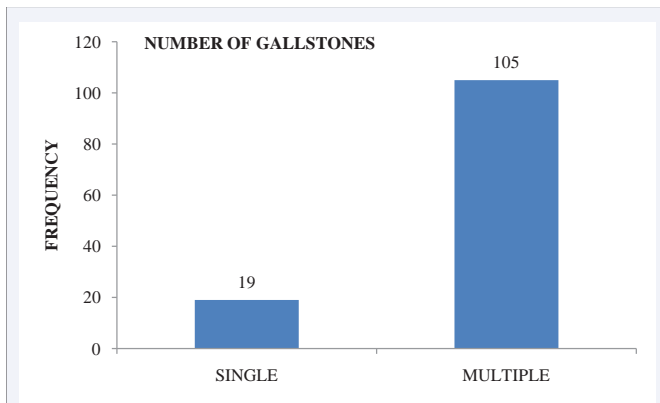
Pregnancy is an important pathogenic factor for GSD. In our study 81% women were multiparous and 11% women were nulliparous. Another study also reported that multiparous females had a higher prevalence of GSD than nulliparous ones [25], supporting our finding.



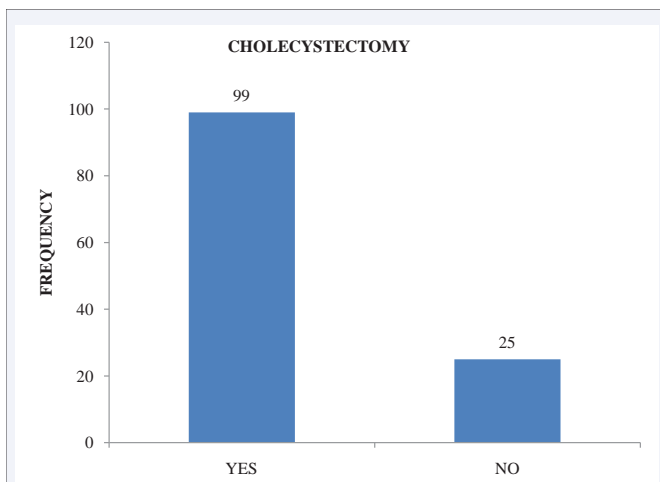
**Figure 5** Parity frequency- 59 women were multiparous and 8 were nulliparous.



**Figure 6** Type of diet: 106 subjects were non vegetarians and 18 were vegetarians.



**Figure 7** Number of Gallstones: 105 patients had multiple stones and single stone were present in only 19 clients.



**Figure 8** Cholecystectomy frequency: Cholecystectomy was done for 99 subjects.

Conflicting reports pertaining to role of diabetes in gallstone pathogenesis is preventing the authors from confirming the association between diabetes mellitus and the gallstones. In the present study 63% of subjects had history of diabetes mellitus. A previous study from North India observed higher incidence of gallstones among diabetic patients than the general population [26]. However there are also studies which failed to prove diabetes mellitus as a risk factor for gallstone disease [27]. Possible mechanisms of diabetes mellitus in gallstone formation

are easy cholesterol super saturation in bile; reduced ejection fraction of the gall bladder and increased volume of gall bladder in fasting phase among diabetic patients [27].

In our study 85% of the clients were found to follow non-veg dietary pattern. Non vegetarianism did not emerge as an association for gallstone in a study carried out in Chennai [22]. Nevertheless studies reporting association between type of diet and GSD are scarce and more studies are needed to verify the correlation between type of diet and GSD. Obesity, hyperlipidemia including low serum levels of high density lipoprotein, high serum triglyceride levels were identified as strong independent risk factors for cholelithiasis [28]. We also observed high serum levels of triglycerides and total cholesterol in our participants, endorsing the pivotal role of dislipidemia in gallstone pathogenesis. Identification of risk factors for cholelithiasis is a vital part in preventing the formation of gallstones and reducing cholelithiasis-related illness.

## CONCLUSIONS

In our study we proved that increasing age and female gender are universal risk factors for GSD. Besides, multiparity, non-veg dietary pattern, diabetes mellitus and hyperlipidemia were observed as important factors contributing to gallstone formation. These findings emphasize the importance of environmental factors in gallstone formation. Many studies concerning gallstone risk factors have been conducted in western societies and developed Asian countries. According to these studies, age, sex, race, obesity and metabolic syndrome are important factors in the development of gallstone disease [29,30]. Thus preventive measures like changes in lifestyle and diet should be undertaken to eliminate these risk factors and prevent gallstone formation.

The limitation in the present study was the small sample size resulting in lack of association for risk factors of cholelithiasis including diabetes mellitus, coronary artery disease, multiparity and cholecystitis in multivariate analysis. Further, the relationship between chronic kidney disease and cholelithiasis was not assessed in our study as the data couldn't be retrieved from the case sheets.

## ACKNOWLEDGEMENTS

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**Table 2:** Distribution of age group and sex among the patients with GSD.

Age group	Male N(%)	Female N(%)	Total N(%)
Below 30	9 (18)	11 (15)	20 (16.1)
30 - 39	8 (16)	22 (30)	30 (24.2)
40 - 49	15 (29)	14 (19)	29 (23.4)
50 - 59	5 (10)	15 (21)	20 (16.1)
60 and above	14 (27)	11 (15)	25 (20.2)
Total	51 (41)	73 (59)	124 (100)

About 24% of them belong to age group of 30-39 years. 73 female patients and 51 male patients show a female gender predominance with ratio of (M: F = 1:1.4)

**Table 3:** Distribution of various factors among patients with Single and multiple gall stones.

S. No	Risk factors	Cholelithiasis		P- Value	Significance
		Single stone (n = 19)	Multiple stones (n = 105)		
1	Diabetes Mellitus	14 (74%)	64 (61%)	1.1	NS
2	Coronary Artery Disease	2 (10.5%)	13 (12.4%)	0.1	NS
3	Multiparous	7 (78%)	52 (81%)	2.0	NS
4	Cholecystitis	17 (89%)	90 (86%)	1.0	NS
5	Cholecystectomy	16 (84%)	83 (79%)	0.2	NS
6	Non-vegetarians	14 (74%)	92 (88%)	2.5	NS

No association existed between any of the risk factors analyzed and cholelithiasis.

**Table 4:** Distribution of various factors among patients with acute cholecystitis and Gallstone Biliary Disease.

S. No	Risk factors	Gallstone Biliary Disease (n = 5)	Acute cholecystitis (n = 119)	P - Value	Significance
1	Diabetes Mellitus	3 (60%)	75 (63%)	0.01	NS
2	Coronary Artery Disease	0 (0)	15 (13%)	0.7	NS
3	Multiparous	1 (20%)	58 (49%)	4.0	NS
4	Cholecystitis	5 (100%)	102 (86%)	0.8	NS
5	Cholecystectomy	4 (80%)	95 (80%)	0.0	NS
6	Non-vegetarians	4 (80%)	102 (86%)	0.1	NS

No association existed between any of the risk factors analyzed and acute cholecystitis.

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