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## Research Article

# A PROSPECTIVE STUDY COMPARING THE CLINICOBIOCHEMICAL PROFILE IN OBESE AND NON OBESE SUBJECTS WITH GALL STONE DISEASE

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### ABSTRACT

Gallstones represent a sizeable problem for the health care system in both developed and developing countries alike. It results from a complex interaction of genetic and environmental factors. Obesity, female gender, increasing age, multiparity, rapid weight loss, pregnancy, use of oral contraceptives, high fat diet are among the many risk factors associated with gall stone disease. The study was conducted on 120 patients with clinical features suggestive of cholecystitis and cholelithiasis confirmed by ultrasonogram and who underwent cholecystectomy. Study groups were divided into obese and non-obese subjects on the basis of their Body Mass Index (BMI). A detailed history, clinical examination and investigation of the patients admitted with features suggestive of cholecystitis and cholelithiasis was taken and compared between the obese and the non obese. Out of the 120 subjects 46 (38%) were obese. F:M=3.2:1. Obese patients had higher cholesterol, TG and LDL levels with more number of subjects following a non vegetarian diet. Cholesterol stones were the most common. Obese patients develop gall stones at a relatively early age with more troublesome symptoms and greater complication rates. Higher levels of total cholesterol, triglycerides and LDL cholesterol seen in the obese are associated with higher incidence of gall stone disease. Obese patients also seem to be having a greater risk of developing into malignancy.

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## INTRODUCTION

Gallstones have been recognized as a major health problem since ancient times. They have been found even during the autopsies of Egyptian mummies. (Berci G, 2004; Tiderington E *et al.*, 2016). A Greek physician, Alexander Trallianus, first described gallstones in the fifth century and they continue to be a major health problem in today's world as well. Gallstones represent a sizeable problem for the health care system in both developed and developing countries alike. (Burkitt DP *et al.*, 1975; Stinton LM *et al.*; 2012) It is a leading cause for hospital admissions related to gastrointestinal problems. (Shaheen NJ *et al.*, 2006) It results from a complex interaction of genetic and environmental factors.

With an overall prevalence of 10% to 15% in developed countries, geographic-specific prevalence is from 0% to 10% in Africa and up to 60% to 70% in certain populations, such as Pima Indians; this likely reflects combined differences in

environmental, dietary, and genetic factors. (Shaffer EA, 2006) Obesity, female gender, increasing age, multiparity, rapid weight loss, pregnancy, use of oral contraceptives, high fat diet are among the many risk factors associated with gall stone disease. (Trotman BW *et al.*, 1980; Paumgartner G *et al.*, 1989; Madden AM *et al.*, 2017; Donovan JM *et al.*, 1991; Gaby A.R, 2009; Einarsson K *et al.*, 1985; Valdivieso V *et al.*, 1993; Yang H *et al.*, 1992; Pixley F *et al*, 1985; Aulakh R *et al.*, 2007; Banim PJ *et al.*, 2011; Bennion L.J *et al.*, 1978; De Santis A *et al*, 1997)

The prevalence of cholesterol gallstones is increased in obese persons. The risk is especially high in those with the higher body mass index. Weight loss further increases the risk of gallstones. About one-third of the stones are symptomatic. The increased prevalence of stones is mostly due to supersaturation of bile with cholesterol, because of an increased synthesis by the liver and secretion into bile. Saturation is further increased

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during weight loss. (Festi D *et al.*, 1998; Erlinger S, 2000; Everhart JE, 1993)

Although there have been multiple studies proving obesity to be associated with gall stone, yet not much literature can be found comparing the obese and the non obese subjects with gall stones in terms of their clinical and biochemical profile.

**MATERIAL AND METHOD**

This is a single centre based study conducted on 120 patients admitted with clinical features suggestive of cholecystitis and cholelithiasis confirmed by ultrasonogram and who underwent cholecystectomy. Subjects undergoing laparotomy for other purpose served as control group. Symptomatic patients having gall stones who were willing to be a part of the study and willing for regular follow up were counted in the inclusion criteria.

Study groups included patients divided into obese and non-obese subjects on the basis of their Body Mass Index (BMI). A BMI of 30.0 or more in male and in female indicates obesity.

A detailed history, clinical examination and investigation of the patients admitted with features suggestive of cholecystitis and cholelithiasis was taken and compared between the obese and the non obese. Special emphasis was given to age, sex, BMI, marital status, parity status, dietary habits, alcohol intake, smoking habits and family history. Blood investigations included complete blood count, liver function test, lipid profile and thyroid function test.

The bile was sent for culture and the stones were analysed by Fourier transform infrared (FTIR) spectroscopic method for their chemical composition.

In some of the obese patients, cholecystectomy was performed along with some other bariatric procedure they were undergoing. 5 of them underwent sleeve gastrectomy, 2 had a mini gastric bypass and 3 had a gastric bypass procedure.

**RESULT**

In the present study 120 subjects with gall stone disease who underwent cholecystectomy were included and 120 control subjects who underwent laparotomy for different reasons were taken. Out of the 120 subjects 46 (38%) were obese while 74 (62%) were non obese. Overall 30-39 years was the age group most affected (28%), Obese subjects presented at a slightly younger age (average age of presentation 39.4 years) than the non obese group (average age of presentation 43 years).

Among the 120 subjects analyzed, 28 were males and 92 were females (F:M= 3.2:1). 10 out of the 28 males were obese (36%) whereas 36 out of the 92 females were obese (39%).

Cholesterol stones were found to be the most common type of gall stone (82% overall) both in obese and non obese groups (87% and 78% respectively). Next most common were mixed stones (15% overall) with 6 obese subjects (13%) and 12 non obese subjects (16%) having mixed stones. Least common were pigment stones (3% overall). 4 non obese subjects (6%) had pigment stones while none of the obese subjects had pigment stones.

Serum lipid profile was compared, average Total cholesterol was found to be highest in obese subjects (171.2 mg/dL)

followed by non obese subjects (153.4 mg/dL) and lowest in control subjects (121.4 mg/dL). Similar trend was followed in the levels of triglycerides with obese subjects having an average of 121.6 mg/dL, non obese subjects as 91.4 mg/dL and control subjects as 85.6 mg/dL. HDL levels were found to be the highest in non obese subjects with gall stone disease (39.9 mg/dL) and lowest in obese subjects (37.8 mg/dL). LDL followed a similar trend like total cholesterol with the highest average LDL in obese subjects (128.3 mg/dL) followed by non obese (114.6 mg/dL) and lowest in control subjects (104.5 mg/dL).

Among the 120 subjects analyzed 70 (58%) were non vegetarians while 50 (42%) were vegetarians. Subjects with cholesterol stones were mostly non vegetarians (61%). Slight predisposition was seen in vegetarians for mixed stones (56%) while pigment stones did not show any such relation (50% each). Most of the obese subjects (80%) followed a non vegetarian diet while more than half (55%) the non obese had a vegetarian diet.

Mostly the subjects were euthyroid (77%). Out of the 24 (20%) hypothyroid patients, 16 (67%) were obese and 8 (33%) were non obese. Only 4 (3%) patients were hyperthyroid with 2 each obese and non obese.

**Table 1** Percentage Incidence of Gall Stone Disease in Obese and Non Obese In Different Age Groups

Age Group (Years)	Obese Patients		Non obese patients		Total	
	No.	%	No.	%	No.	%
10-19	0	0	4	5	4	3
20-29	6	13	14	19	20	17
30-39	22	48	12	16	34	28
40-49	4	9	18	24	22	18
50-59	12	26	8	12	20	17
60-69	2	4	18	24	20	17
	46		74		120	100

**Table 2** Gallstone Composition in Obese and Non Obese Patients with Gallstone Disease

Types of gall stone	Obese		Non obese		Total	
	No.	%	No.	%	No.	%
Cholesterol	40	87	58	78	98	82
Pigment	0	0	4	6	4	3
Mixed	6	13	12	16	18	15

**Table 3** Serum Lipid Profile In Obese, Non Obese and Control Subjects

Parameter	Obese	Non obese	Control
Total Cholesterol (mg/dL)	171.2 ± 39.2	153.4 ± 29.3	121.4 ± 31.7
Triglycerides (mg/dL)	121.6 ± 66.2	91.4 ± 64.3	85.6 ± 42.1
HDL (mg/dL)	37.8 ± 4.5	39.9 ± 5.2	39.7 ± 5.9
LDL (mg/dL)	128.3 ± 45.1	114.6 ± 32.9	104.5 ± 30.1

**Table 4** Relation of Thyroid Status With Gall Stone Disease

Subject	Value of TSH (in uIU/mL)					
	<0.35		0.35-5.5		>5.5	
	No.	%	No.	%	No.	%
Obese	2	50	28	30	16	67
Non obese	2	50	64	70	8	33
Total	4		92		24	

**Table 5** Dietary Comparison between Obese And Non Obese Subjects With Gall Stone Disease

Subject	Dietary habit
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	Vegetarian		Non vegetarian	
	No.	%	No.	%
Obese	9	20	37	80
Non obese	41	55	33	45
Total	50		70	

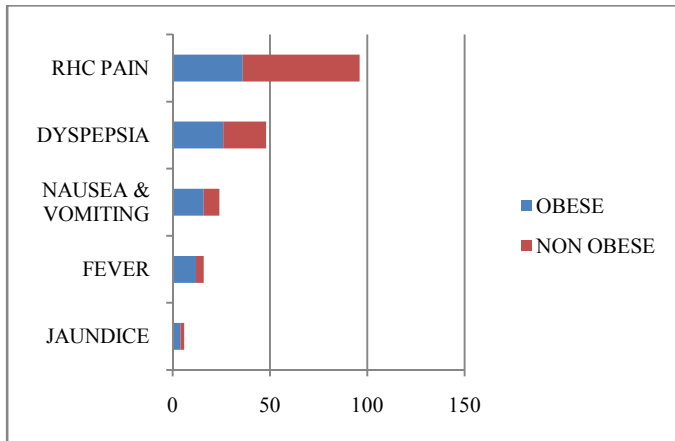


Fig 1 Frequency of Clinical Features in Obese and Non Obese Subjects

## DISCUSSION

Obesity is a well-established major risk factor for the development of gallstones. The association with simple obesity is important in females; in males it is mostly associated with intraabdominal (central) obesity and metabolic syndrome. (Trotman BW *et al.*, 1980; Maclure KM *et al.*, 1989; Tsai CJ *et al.*, 2004; Liddle RA *et al.*, 1989; Stampfer M.J *et al.*, 1992) Obesity also appears to be a risk factor in the development of gallstones in childhood and adolescence. (Kratzer W *et al.*, 2010) In the present study, out of the 120 subjects 46 (38%) were obese while 74 (62%) were non obese. Our study shows slightly early occurrence of gall stone disease in obese subjects as compared to non obese subjects. Also, there is a wide range of distribution of patients ranging from 18 to 69 years sparing only the early teens and childhood. This is consistent with the finding of previous studies stating that the incidence of gallstones increases with age across all ethnic groups, and it is very low among infants and children. (Einarsson K *et al.*, 1985; Chen CY *et al.*, 1998)

In the present study the female to male ratio was found to be 3.2:1 which is consistent with similar studies in the past. (Sleisenger MH *et al.*, 1989; Nakeeb A *et al.*, 2002) Increased levels of the hormone estrogen, as a result of pregnancy or hormone therapy, or the use of combined (estrogen-containing) forms of hormonal contraception, may increase cholesterol levels in bile and also decrease gallbladder movement, resulting in gallstone formation. (Valdivieso V *et al.*, 1993) ( $p < 0.05$ )

Cholesterol stones were found to be the most common type of gall stones (82%) in the present study followed by mixed (15%) and pigment (3%) stones. This is in contrast to the studies conducted earlier stating mixed gall stones to be the most common in India. (Karlatti SS *et al.*, 2016) Studies in the western world have found cholesterol stones to be the most common there, similar to the results found in the present study. (Njeze GE, 2013) This could be explained by the progressive westernization of the diet of the North Indians with increase in protein and fat intake. Obese subjects had higher incidence of cholesterol stones as compared to the non obese

ones, probably due to the high fat diet and high cholesterol status of the obese patients.

Literature has shown insignificant difference in the level of serum total cholesterol in patients with gall stones as compared to control. However in the present study, it is observed that serum total cholesterol in obese subjects ( $171.2 \pm 39.2$  mg/dL) and non obese subjects ( $153.4 \pm 29.3$ ) is significantly higher than the control group ( $121.4 \pm 31.7$  mg/dL). A similar trend is observed in levels of LDL-cholesterol and triglycerides with the mean value being highest in obese subjects and lowest in control subjects. These findings suggest that the level of lipoproteins has a direct relation with the incidence of gall stones. Obese patients have a higher total cholesterol, LDL-cholesterol and triglyceride levels indicating the ill effects of metabolic syndrome generally associated with such patients, and hence a higher incidence of gall stones. ( $p < 0.05$ )

The role of diet in the pathogenesis of gallstones is controversial. In the present study the subjects with gall stone disease more commonly followed a non vegetarian diet (58%). The difference was more so in subjects with cholesterol stones in which 61% patients followed a non vegetarian diet. Subjects with mixed and pigment stones had similar incidences in vegetarians and non vegetarians. These findings show an association between cholesterol stones and a non vegetarian diet which contains more of protein and fat and less of fiber. Hence high fiber diet seems to be protective against cholesterol stones. ( $p < 0.05$ )

On relating thyroid status with the incidence of gall stone, the present study found that hypothyroid state rather than hyperthyroid state was more often associated with gall stone disease. Although most subjects were euthyroid, the association of raised TSH with gall stone disease was significant, especially in obese subjects. ( $p < 0.05$ )

It has been shown that significant associations with a family history of gallstones were seen for all first-degree relatives, including parents, siblings, and offspring, but not spouses. (Hsing AW *et al.*, 2007; Sarin S.K *et al.*, 1995) In our study 30 out of 120 (25%) subjects gave history of gall stone disease in their family. ( $p < 0.05$ ) The incidence was slightly higher in males with 29% of male subjects giving family history as compared to 24% females who gave a positive family history.

Most patients with gall stone have no symptoms. (Madden AM *et al.*, 2017; Friedman GD, 1993) These gall stones are called "silent stones" and may not require treatment. Most of these patients hence do not even present to the hospital. In the present study, all the patients had some symptom troublesome enough to warrant a visit to the hospital. The most common symptom was upper abdomen pain (in 80% subjects) either in the right hypochondrium or the epigastrium or both. This was common for both obese and non obese subjects. The next most common symptom was flatulent dyspepsia which was present in 40% subjects most often at night. Obese subjects were more affected than non obese. Other symptoms like nausea and vomiting, early satiety, fever and jaundice were also more common in obese subjects. Moreover, it was observed that localization of pain was more difficult in the obese making the clinical diagnosis more difficult. Hence gall stone disease in obese people is associated with more troublesome symptoms and greater complications due to gall stones. ( $p < 0.05$ )

## CONCLUSION

Cholelithiasis is a common health problem affecting a wide range of age group of both the sexes with a high incidence in the obese people. Females in the middle age group are more commonly affected. Obese patients develop gall stones at a relatively early age with more troublesome symptoms and greater complication rates. Higher levels of total cholesterol, triglycerides and LDL cholesterol seen in the obese are associated with higher incidence of gall stone disease while HDL cholesterol seems to play a protective role. Other risk factors that seem to have a causal association with gall stones are hypothyroidism, non vegetarian diet, pregnancy and early puerperium, intake of alcohol, smoking and usage of oral contraceptive pills. Obese patients seem to have higher complication rates and higher risk of developing into malignancy

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