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Epidemiological Study of Gallstone in Cuddalore District

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Abstract: Gallstone disease is common in developing as well as developed countries. The exact mechanism of stone formation is not yet understood clearly. An attempt has been made to clarify such problem. This is a case-control study with gallstone disease in Cuddalore district of Tamilnadu, the study population consists of 124 cases and 50 controls residing in the same region. Data were collected through standard questionnaire during the period between May 2007 and June 2009 (25 months) and the results were compiled and interpreted. The investigation suggests that mixed stones are predominant in the selected study area. The significant associations (BMI, beverage consumption, pregnancy, socio-economic status, and food habit) between control and patients groups were found.
Key words: epidemiology, gallstone, gallbladder disease, Cuddalore.

Introduction

Gallbladder stones affect a significant percentage of the population in many countries throughout the world and they remain the major cause of abdominal morbidity.[1-2] The Gallstone affects more than 20 million Americans and 800, 000 patients are hospitalized every year,[3] resulting in gallbladder surgery one of the most common operations with direct cost of more than $2 billion.[4] Although many studies on calculi have been undertaken hitherto, most of them are dealt with etiological or clinical problems and with all those studies, no perfect explanation in the field has been made. Gallstones are primarily composed of cholesterol. Human gallstones may be generally classified into three types (1) cholesterol stones, (2) black pigment or calcium bilirubinate stones, and (3) brown pigment or pure pigment stones.[5-13] Its classification was proposed at the National Institutes of Health International Gallstone Workshop.[14] Although, other types such as combined (cholesterol and pigment) are also found.[8-10] Gallstones are composed of a mixture of hard-to-separate substances of different chemical natures, mainly cholesterol with admixture of higher fatty acids, bile acids, phospholipids, bilirubin, protein, etc.[15] The major elements involved in the formation of gallstones are cholesterol, bile pigment and calcium,[16] altered hepatic bile composition, biliary glycoprotein, infection, age, genetic, sex, estrogen, dietary factors, geographical prevalence and cirrhosis of the liver.[17] Multiple gallstones were found in mummified Egyptian priests also.[18] Mixed and pigment gallstones are common in Southern India whereas cholesterol gallstone in Northern India.[19-20] Nowadays gallstones are prevalent in south India. Most gallstone patients are asymptomatic.

Cholesterol stones occur much more frequently in the patients in the United States, and bilirubin stones in those in China, while Japanese fall in intermediate position.[21] Factor affecting the formation of brown-pigment gallstones are not yet understood. Calcium bilirubinate and protein are the main components of this kind of stones. Early comparisons showed considerably higher prevalence of gallbladder disease (GBD) in developed countries than in underdeveloped countries.[22]

To determine the association of gallstone disease with epidemiological factors such as age, sex, body-mass-index (BMI), socio economic status, marital status, number of pregnancy, heredity, educational level, history of gallstone disease, food habit, stone type, stone color, residing area, type of beverage consumption (tea/coffee/milk/combination) and type of drinking water, have been studied and compared with normal people those residing the same region.

Subject and methods

The randomly selected 124 symptomatic patients from Cuddalore district are involved in this study. Controls are in the same area and have not previous history of abdominal pain or the symptoms of gallstone. The printed form of questionnaire was used. Some of the relevant information about the patients was obtained from medical case history. The various physical parameters of stones such as number, type of stone etc., were noted.

Diagnosis of gallstone disease

The diagnosis of gallstone disease was verified, based on their medical records showing either a history of cholecystectomy or a diagnosis of gallstone disease, based on cholecystectomy or ultrasound investigation. All patients fasted at least eight hours before the examination.

Questionnaire

Patients with gallstone underwent assessment of their dietary habit using semi-quantitative questionnaire. Details of the questionnaire included age, sex, height, weight, BMI, marital status, number of pregnancy, smoking habit, colour of the stone, stone type (single/multiple), food habit, stone weight, family socio-economic status, educational status, ethnic group, residing area (urban/rural), previous history of gallstone and heredity of gallstone disease, women were questioned regarding number of pregnancies. BMI was calculated by the relation weight divided by square of height in meters. These details were obtained by medical officers working the respective hospitals and prior to study consent was obtained from all study subjects. The study protocol was approved by institutional review board. The controls were volunteers, similar socio-economic and demographic characteristics. The volunteers were from the same demographic region with no history of gallstone disease. The method of interviewing was carefully standardized so that the required information could be obtained and interpreted in a uniform way. Partially filled in questionnaire from the participants were excluded from this study. The same questionnaire was used for both cases and controls. The study period was between May 2007 and June 2009 (25 months).

Statistical analysis

Paired sample *t* test and Pearson correlation were calculated between age and BMI of the patients with black, brown and mixed stone separately and as a whole. Skewness is nothing but studies of asymmetry. Skewness was studied for age, BMI and stone weight in each group (black, brown and mixed). Chi square tests were performed between control and gallstone patients as a whole and as well as group wise (black,

brown and mixed). While calculated value is less that the tabulated value, null hypothesis may be accepted at 5% significance and we may conclude that there is no significance difference in the sampling technique. The results are expressed as mean ± standard deviation (SD). Statistical analyses were performed using Microsoft Excel 2007.

Results and Discussion

The study included 124 patients 55 male (48.47 ± 13.87years), range (9 - 83); 69 female (38.12 ± 9.91 years), range (12 - 60), control male (41.62 ± 11.81years), range (27-65); female (40.36 ± 10.55years), range (17-68). Table 1 shows the abstract of the questionnaire.

There is a high prevalence of gallstone disease in western countries as a consequence of genetic, biochemical and environmental factors. Animal and clinical studies have explored the importance of dietary elements. Demographic and socio-economic characteristics were similar between the two groups. In the present study, an individual with BMI > 23 Kg/m^2 considered a case of obesity. Excessive energy intake is thought to increase the risk for gallstones because of its relationship to obesity,[23] women with a BMI greater than 32 Kg/m^2 have a six fold higher risk of developing gallstone disease than those with a BMI less than 22 Kg/m^2. In the present study average BMI (23.65 ± 2.64 Kg/m^2) of women patients is greater than average value (23.48 ± 2.28 Kg/m^2) of men patients. The obese subjects exhibit an increased biliary secretion of cholesterol from the liver, which produces bile supersaturated with cholesterol and induces precipitation of cholesterol monohydrate (ChM) microcrystal that grows, agglomerates, and forms macroscopic stones.[24]

The BMI of 68 (54.84%) patients was greater than 23. Higher BMI and use of tamarind are risk factors in the formation of gallstone in Southern India;[19] and they also found that demographic characteristic and social customs did not contribute to pigment gallstone formation.[25] There are several reports describing north-south differences in the type of gallstone in India till date.[26-27] Difference in diet pattern may be responsible for different types of gallstones. Stones were classified visually by naked eye. If doubt arises, Fourier Transform Infrared (FTIR) spectrum will be recorded, the details analysis was discussed in our previous study.[28] The patients' average age, in the cases of mixed stone, black stone and brown stone are 43.32 ±13.43, 43.21±12.86, and 41.86±12.39 respectively. Pigment stones were more prevalent in the elderly people, but were present throughout all age groups[29] and were associated with biliary infection.[30] Gallstones are uncommon in infants

and children,[31] it is closely agreed with our results and shown in Fig 1.

Generally, gender is a predominant risk factor. In the present study, gallstone prevalence in men (44.35%) and in women (55.65%) patients i.e. women have a greater risk of gallstone disease than men at all ages. These are confirmed by many studies with a range of female-to-male ratio of 1.2:1, which is very low 10:1 for pima Indians[32] and 2-3:1 in European women.[33]

In the United States, cholesterol stones account for 70% to 95% of adults and brown pigment stones for most of the remainder;[34] but in the present study 56% of adult patients had mixed stones, and the remainder had black and pigmented stones. Out of 124 patients, 43 had solitary stones, while the rest had multiple stones. Mixed stones are bigger in size, compared to pigment stones, this is similar to earlier report in Calcutta.[35] Approximately one-third (34.67%) of the gallstone patients were admitted during April to June, and it is furnished in Fig 2.

Multiple stones were found in 81 (65.32%) cases and solitary stones were found in the remaining cases. Sixty three patients' stone weight was within one gram, in 18 (14.51%) cases within 1-2 gm, only 9 (7.26%) had the stone weight more than two grams. The rest of the patients' details are not available. Sixty eight (53.84%) patients in this region drink the tap water, 45 (36.29%) patients drink mineral water and the remaining patients drink bore-well water. Among the patients, 42 (33.87%) patients, 23 (18.55%) patients, 41 (33.06%) patients and 18 (14.52%) patients used to drink tea, coffee, both tea and coffee, milk respectively. The average age of the female patients is 38.12 ± 9.91 years, for male patient 48.30 ± 13.87 years, these are agreeing with earlier reports. In fact, only a very few men were smokers in either of the two groups. Smoking was not reported among any female patients in these studies and hence women were excluded from the analysis. Most of the study cases and controls were residing in urban (75% and 65%). Many of the cases and controls family (70.97% and 70%) belong to middle socio-economic status. Economic status was classified by total month income (less than Rs. 4,000 –poor; between Rs. 4,000-12,000 –middle; greater than Rs. 12,000 - rich). Approximately 80% of the cases and controls were literate. Here we refer to literate, who read their mother language. There is no association between educational status and gallstone diseases.

One hundred and thirteen (91.13%) of the 124 cases were married as against 42 (84%) of controls. 11 (8.87%) cases affected by gallstone disease previously, 93-95% of cases and control i.e. equal proposition among them was not of hereditary gallstone. Stone types (black, brown and mixed) are approximately distributed between both sexes equally. Among the women patients 43.48 % had two pregnancies in his lifetime. A maiden attempt (stone weight, stone type and drinking water) has been included in the epidemiology study. Skewness was studied for age, BMI and stone weight in each stone group (black, brown and mixed). Age of black stone and BMI of brown stones were in left skewness remaining were right skewness. Our results were in general agreement with some data in the reported literature,[21,36] but also either partially or totally in disagreement with others' report.[37-42]

Conclusion

To the best of our knowledge there is no previously published report relevant to epidemiology of gallstone diseases in the present study area. In conclusion, pure cholesterol stones are uncommon and mixed stones are predominantly present in the study area. Patients with mixed stone have highest average BMI. The average age of brown pigmented stone patients is less compared to other stone patients. Gallstone formation is a multifactorial disease that can be influenced both positively and negatively by diet. The strongest studies, on the importance of diet and gallstone disease in humans, are epidemiological; and more intervention studies in humans are needed to clarify the biological processes involved in this interesting associations. Some of the major reported risk factors for cholesterol gallstones are not applicable for gallstone formation in the present study area.

This study may have a few limitations while retrieving and weighing the entire gallstone during operations, some data were not included. Here we found a positive association between gallstone disease and smoking habit, socio-economic status, pregnancy, beverage consumption, BMI, type of water used to drink. Gallstone associations are difficult owing to the complexity of evaluating one dietary component isolated from all the others, which also vary according to the season, while gallstone generally requires months or years to develop. So this is somewhat difficult to characterize and associate with gallstones. For any individual some risk factors are unalterable, such as advancing age, being female and ethnicity. Other factors such as obesity, smoking habit, beverage consumption, food habit etc., can be modified; due to change in westernized food, low fibre and high-fat may lead to formation of gallstone disease. Reducing the detriments such as high fat intake, calorie, decrease fibre, caffeinated coffee may useful to reduce the risk of gallstone formation. In the light of the present study, we believe that the investigation of the gallstones and risk factors is difficult task; however it could be minimized by controlling such risk factors.

Table 1 Gallstone prevalence and control

Parameters	Controls (n=50)	black (n=14)	Brown (n=51)	Mixed (n=59)
Sex		NS	NS	NS
Male	22	5	22	28
Female	28	9	29	31
Age (years)		S	NS	S
Male	41.62 ± 11.81	49.20 ± 17.64	45.36 ± 13.79	50.79 ± 13.30
Female	40.36 ± 10.55	39.89 ± 8.84	39.21 ± 10.71	36.58 ± 9.50
Age group				
0-20	3	0	4	1
21-40	17	6	17	26
41-60	28	6	28	26
61-80	2	2	2	5
above 80	0	0	0	1
		S	S	S
Smoking habit				
non smokers	40	1	46	52
Smokers	10	13	5	7
		NS	S	S
Food habit				
Vegetarian	20	5	12	35
non-veg	30	9	39	24
		S	S	S
Socio economic status				
Poor	10	2	37	6
Middle	35	11	7	40
Rich	5	1	7	13
		S	NS	NS
Educational status				
Literate	45	11	46	51
Illiterate	5	3	5	8
		NS	S	S
Residing area				
Rural	17	4	12	15
Urban	33	10	39	44
Heredity of GS disease				
Yes	3	0	3	5
No	47	14	48	54
		S	NS	S
Marital status				
Married	42	13	45	55
Unmarried	8	1	6	4
		S	S	S
Pregnancy (for women only)				
Un married	0	0	3	1
None	5	0	1	3
One	5	2	5	5
Two	12	3	14	16
Three	3	1	5	4
Above 3	3	3	1	2
		S	S	S
Beverage consumption				
Tea	22	2	12	28
Coffee	13	6	9	10
Both	15	4	23	12
Milk	-	2	7	9
Stone weight				
NA	-	2	16	16
less than 1 gm	-	9	25	29
1—2	-	2	7	9
above 2	-	1	3	5
Stone type				
Solitary	-	2	7	34
Multiple	-	12	44	25

Drinking water		s	s	s
Tap water	25	6	30	32
Mineral water	10	7	19	19
Bore well	15	1	2	8
BMI		s	s	s
>23	37	6	33	17
<23	13	8	18	42

[NS] –Not significant, [S] - Significant at $p<0.05$
Chi-square test for comparisons between control and stone groups
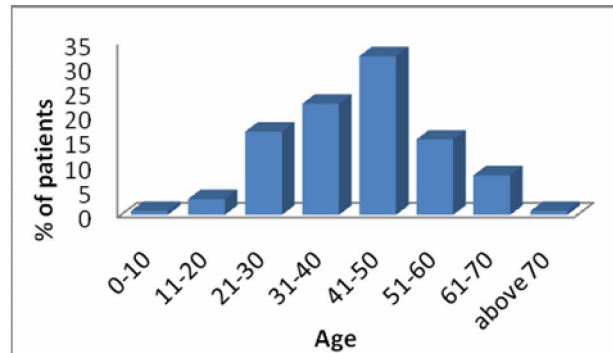GS- gallstone disease , NA –not available
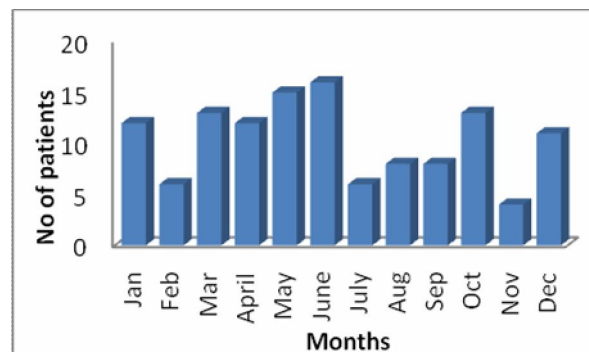

Fig. 1 Patient's details (age group wise)

Fig. 2 Admission frequency of gallstone Patients in the hospitals

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