

Diabetes Mellitus and other Lifestyle Risk Factors for Cholelithiasis: A Case Control Study

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ABSTRACT

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Background: Gallstone disease (GSD) and its complications are major global public health issues, and it remains a common cause of surgical intervention, contributing substantially to health care costs. This study is to estimate the risk of diabetes and life style risk factors responsible for cholelithiasis (gallstone).

Materials & Methods: This was a case control study, 137 cases were recruited from cholelithiasis patients (proven by sonography) admitted in the surgical wards of Government Medical College, Trivandrum from June to December 2009. Sex-matched controls (n = 274) comprising of patients admitted for other morbidities and sonographically negative for gallstones were simultaneously recruited from the same wards.

Results: People with diabetes mellitus have 2.37 times increased chance of developing cholelithiasis. The chance of getting cholelithiasis was found to be 2.7448 times higher in age group of 50 years or more, with odds ratio of 2.7448. It was found that those with sedentary lifestyle have almost double the chance of developing cholelithiasis compared to non-sedentary, odds ratio of 1.8985.

Conclusion: It has been found in this study that in Type 2 diabetes, sedentary physical activity, increasing age, over-weight and obesity were the risk factors for the development of cholelithiasis. Regular exercise with maintenance of healthy body weight with good diabetes control can help in delaying or preventing the development of cholelithiasis.

Keywords: Cholelithiasis, Gallstone, Gall bladder, Gallstone disease

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INTRODUCTION

Gallstone disease (GSD) and its complications are major global public health issues, and it remains a common cause of surgical intervention, contributing substantially to health care costs.^{1,2} Gallstone disease is common, >700,000 cholecystectomies and costs approximately 6.5 billion dollars annually in the U.S itself. In developed countries, at least 10% of white adults harbor cholesterol gallstones; women have twice the risk, and age further increases the prevalence in both sexes. The prevalence of gallstones in adults in developed countries is 10%-15%.³ Gallstones reach epidemic proportions in the North and South American Indian populations, accompanied by an increased risk for gallbladder cancer. In contrast, the rate in sub-Saharan Africa and Asia is quite low.³ The burden of disease is epidemic in American Indians (60-70%), and a corresponding decrease occurs in Hispanics of mixed Indian origin.⁴

The traditional risk factors for gallstone disease (GSD) are the four 'F's- 'female, fat, forty and fertile'. But age, multiparity and cigarette smoking are now additional risk factors in Western countries, where cholesterol is the leading component of gallstones.⁵ Previous studies have detected age, female gender, family history of gallstone, pregnancy, diabetes, and obesity as risk factors for GSD.^{6,7} Among the aged senior citizens, individuals with old age, lower serum high-density lipoprotein level, diabetes and glucose intolerance are at high risk for developing GSD.⁸

There were few studies from developing countries, like India which establishes the association of various risk factors for cholelithiasis. The objective of this study was to investigate the association of diabetes mellitus and various lifestyle risk factors responsible for cholelithiasis, such as food habit, hyperlipidaemia, over-weight and obesity among adult patients of more than 35 years.

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MATERIALS AND METHODS

In the present case control study, 137 cases were recruited from cholelithiasis patients (proven by sonography) admitted in the surgical wards of Government Medical College, Trivandrum from June to December 2009. Their clinical presentations were noted from the records. Sex-matched controls (n = 274) comprising of patients admitted for other morbidities and sonographically negative for gallstones were simultaneously recruited from the same wards. Patients above the age of 35 years were included as both cases and control. Patients who were diagnosed to have any gall bladder and pancreatic diseases were excluded from the control group.

Tools for data collection were interview, clinical examination (including anthropometry), and investigations (estimation of fasting blood sugar and serum lipids). Anthropometric indices (weight, height and body mass index) were calculated for all cases and controls. Physical activity was gauged as non-sedentary and sedentary. In non-sedentary, both moderate to vigorous physical activities were included. Moderate physical activity includes moderate indulgence per day of 60 min or more in activities such as brisk walking/ domestic chores/carrying or moving loads up to 20 kg, and vigorous includes running/cycling/swimming/ carrying or moving loads above 20kg. Anything short of moderate physical activity was considered sedentary.

The ethical consent was obtained from Institutional Ethical committee, and consents were taken from cases and control subjects. The data entry was done by using EpiInfo, and analysis was done by using SPSS 10. The risk of developing gallstones was estimated by using odds ratio 95% confidence interval (CI).

RESULTS

Out of the 137 cases 36% of them belong to 55 to 64 years age group, and 25% belong to 45 to 54 years age group, while in 274 controls, age is distributed almost uniform (**Table 1**).

The chance of getting cholelithiasis was found to be 2.7448 times higher in age group of 50 years or more, with odds ratio of 2.7448 (CI, 1.7767 to 4.2404). When age advances, 50 years and above is a risk factor for cholelithiasis (**Table 2**).

All patients during the study period diagnosed as cholelithiasis were included in this study as cases, and among this, the majority 76% of the patients were females.

Table 1. Age distribution of cases and controls

Date	T3 ng/dl N=(62-179)	T4 µg/dl N=(4.5-12.5)
35 - 44	25 17.00%	72 24.00%
45 - 54	38 25.00%	78 26.00%
55 - 64	54 36.00%	78 26.00%
> 65	33 22.00%	72 24.00%

Chi square= 6.093, P value = 0.1

Table 2. Age as a risk factor in Cholelithiasis

Age group (years)	Cases	Control
≥ 50	113	158
< 50	37	142

Odds Ratio= 2.7448 (CI, 1.7767 to 4.2404)

Table 3. Gender-wise distribution of cases and control

Gender	Case	Control
55 - 64	36 24.00%	72 24.00%
> 65	114 76.00%	228 76.00%

Table 4. Diabetes Mellitus as a risk factor for cholelithiasis

Diabetes Mellitus	Case	Control
Present	60	66
Absent	90	234

Odds ratio =2.3636 (CI, 1.544 to 3.6184), Chi-Square = 16.071 (P-value = 0.00006)

Table 5. Physical activity as a risk factor for Cholelithiasis

Physical activity	Case	Control
Sedentary	113	185
Non-sedentary	37	115

Chi square = 8.3 (P= 0.0039), Odds ratio =1.8985 (CI, 1.2249 to 2.9424)

The statistical significance of gender as risk factor cannot be established because sex matching was done with control group (**Table 3**).

People with diabetes mellitus have 2.37 times increased chance of developing cholelithiasis, with odds ratio of 2.3636 (CI, 1.544 to 3.6184). There was a significant difference between people with diabetes and non-diabetic in developing cholelithiasis with P-value of <0.0001 (**Table 4**).

Physical activity is a risk factor for cholelithiasis, as it was found that those with sedentary lifestyle have

Table 6. Food habit as a risk factor for Cholelithiasis		
Food habit	Case	Control
Non-vegetarian	127	252
Vegetarian	23	48

Odds ratio: 1.0518 (CI, 0.6124 to 1.8064)

Table 7. Hyperlipidaemia as a risk factor for Cholelithiasis		
Hyperlipidaemia	Case	Control
Yes	57	21
No	93	279

Odds ratio = 8.1429 (CI, 4.6857 to 14.1509), Chi-Square = 67.067 (P-value, <0.0001)

Table 8. Overweight and Obesity as risk factor for Cholelithiasis		
Body Mass Index	Case	Control
≥ 25	90	33
18-25	60	267

Odds ratio = 12.1364 (7.4548 to 19.758), Chi-Square = 120.883 (P-value <0.0001)

almost doubled the chance of developing cholelithiasis compared to non-sedentary, odds ratio of 1.8985 (CI, 1.2249 to 2.9424). The relation was found to be statistically significant, with Chi-square value of 8.3 (P=0.0039) (Table 5).

There is no difference between Vegetarian and Non-vegetarian food habit in the development of cholelithiasis, with odds ratio of 1.0518 (CI, 0.6124 to 1.8064). Majority of population in cases and control were non-vegetarians (Table 6).

This study shows that hyperlipidaemia patients have 8 times higher risk of developing cholelithiasis, odds ratio = 8.1429 (CI, 4.6857 to 14.1509). The association of hyperlipidaemia and development of cholelithiasis was found to be highly significant, P-value, < 0.0001 (Table 7).

Overweight and obesity persons were 12 times higher risk for developing cholelithiasis when compared to person with normal weight category, Odds ratio = 12.1364 (7.4548 to 19.758). The relation between overweight and obesity with development of cholelithiasis was found to be highly significant, P-value <0.0001 (Table 8).

DISCUSSION

This study aims to evaluate various risk factors for the development of gallstone disease among adult popu-

lation, above the age of 35 years. Increasing age has been universally regarded as a significant risk factor for cholelithiasis. The long-term exposure to chronic environmental factors may account for the increased relative risk.⁶ This study also show that there is 2.73 times more chance for cholelithiasis among persons above 50 years of age. The risk of gallstone disease is greater in women than in men at all ages in the majority of studies.³ In this study, gender as risk factor for cholelithiasis was not accounted because of the sex matching done during selection of controls.

It has been studied that mild-to-moderate intense physical activity plays a protective role against cholelithiasis.⁹ Our study also demonstrated physical activity, in terms of sedentary life style as a risk factor for the development of cholelithiasis. It was found that those with sedentary lifestyle have almost doubled the chance of developing cholelithiasis, Odds ratio of 1.8985 (CI, 1.2249 to 2.9424).

Studies show that diabetes mellitus is associated with cholelithiasis, and the association has been linked to increased cholesterol saturation in gallbladder bile.¹⁰ The study conducted by De Santis A et al also shows diabetes was more frequent in subjects with gallstone disease than in the control group, even according to sex (In men: OR, 2.03; 95% CI, 0.99-4.2 and in women: OR, 3.85; 95% CI, 1.4-10.6) (11). Our study also shows people with diabetes mellitus having 2.37 times increased chance of developing cholelithiasis, with odds ratio of 2.3636 (CI, 1.544 to 3.6184). Possible mechanisms of DM in gallstone formation are: easy cholesterol supersaturation in bile; reduced ejection fraction of the gallbladder and increased volume of the gallbladder in fasting phase among DM patients.¹² A study by Unisa, et al. in rural areas of India, reported a prevalence of 6.2% for gallstone disease that was associated with increased age, diabetes, unsafe water use and water pollution with metal elements.¹³

The study by Shih-Chang Hung et al demonstrated that hyperlipidaemia and obesity are the strong risk factors for the development of cholelithiasis.¹⁴ Our study also demonstrated strong association between hyperlipidaemia and cholelithiasis. Overall, these findings point to a likely benefit of life style modification as effective measures for the prevention of cholelithiasis. In addition, they support previous observations indicating that medications used to treat dyslipidemia may be of value in the prevention and treatment of cholelithiasis.¹⁵

Most of the studies demonstrated a positive independent association of new gallstone disease with body mass index (BMI) irrespective of sex.^{13,14} The present study also shows a strong association with BMI, with 12 times increased risk of cholelithiasis for those with BMI > 25 compared to other group with BMI < 25. It has been estimated that about 25% of morbidly obese subjects suffer from gallstone disease. The possible mechanism of association between obesity and gallstones increases cholesterol synthesis in the liver and cholesterol-supersaturated bile in obese subjects which consequently multiplies their risk of gallstone formation.¹⁸

CONCLUSION

It has been found in this study that Type 2 diabetes, sedentary physical activity, increasing age, over-weight and obesity were the risk factors responsible for the development of cholelithiasis. Regular exercise with maintenance of healthy body weight with good diabetes control can help in delaying or preventing the development of cholelithiasis. Hyperlipidaemia was found to be one of the most important risks in the pathogenesis of cholelithiasis, and the early detection and control of it may help in preventing the development of cholelithiasis.

END NOTE

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Conflict of Interest: None declared

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