ORIGINAL ARTICLE

Risk factors associated with gallstone disease

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Abstract

Background: Gallstone disease is one of the most common abdominal conditions for which patients are admitted in surgical wards of hospitals. **Aim & Objective**: The study was conducted to understand the association between behavioral and personal factors and gall stone disease among study subjects. Settings & Design: a case-control study conducted in a tertiary care hospital of New Delhi. **Material & Methods**: 120 each of cases and controls of over 20 years, matched for age and sex were recruited in the study. Data collection was done on a self-designed pretested "interview schedule." Statistical analysis: The observations have been described in terms of mean and standard deviation for continuous data. To measure the strength of association simple Odd's Ratio (OR) was calculated and McNemar's test was used for matched pair analysis. Binary logistic regression was used for multivariate analysis to find out different correlates and analyses the independent effects of these correlates on GSD. **Results**: weight (59.20±9.57), height (159.67±6.25), BMI (23.20±3.15), waist circumference (75.79±7.07) and W/H ratio (0.80±0.06) were significantly higher [as seen by applying student t test] in cases as compared to controls 54.84±7.02, 156.58±4.93, 21.95±2.81, 73.49±6.09 and 0.77±0.05 respectively. High parity [OR-5.75, 95% CI 1.99-16.63] had the strongest association followed by high W/H ratio [OR-5.25, 95% CI 1.80-15.29], sedentary physical activity [OR-4.75, 95% CI 2.22-10.18], smoking [OR-3.4, 95% CI 1.25-9.21], consumption of smokeless tobacco [OR-2.36, 95% CI 1.17-4.78] and high BMI [OR-1.71, 95% CI1.03-2.83]. **Conclusion**: High parity, High W/H ratio, Physical inactivity, Current smoking, Smokeless tobacco and high BMI were found to be risk factors for the development of gallstone disease.

Keywords

Case-Control Study; Gallstone Disease; Personal and Behavioural Risk Factors;

Introduction

Gallstone disease (GSD) is defined as the presence of one or more stones in the gallbladder and they occurred commonly in the western world and mostly asymptomatic. High prevalence was reported in North America, Scandinavia and other Northern European countries, but low in sub-Sahara Africa and Asia (1,2). This represents a significant burden for healthcare systems worldwide and is one of the most common disorders among patients presenting to

emergency rooms with abdominal discomfort (3). Once considered a disease of the western world and the affluent, gallstones have increasingly become major cause of abdominal morbidity in developing countries (4). In a study in north India the occurrence of gallstones was found to be at least 6.12% in the adult population. However, India being a diverse country, taking an overall average may not reflect true situation in the population that consist of diverse ethnic groups and various socio-economic groups (5). Potential risk factors for the development of gall stones are obesity, sedentary life style, geriatric age group and female gender (6). Several behavioural factors like physical inactivity, tobacco and alcohol consumption and some personal factors (weight, height, Waist Circumference, Hip Circumference and parity) also determine the prevalence of GSD. The study was conducted to understand the association between behavioral and personal factors and gallstone disease among study subjects.

A case-control study was conducted in tertiary care hospital; Smt Sucheta Kripalani Hospital (SSKH), New Delhi. Sample size was calculated based on prevalence of obesity in India among males and females which is 12.1% and 16% respectively (7). Assuming prevalence of obesity in India as 14% among general population and 30% in patient with gallstones, at confidence limit of 95% and power of 80%, equal number of cases and controls were calculated for the sample size using Fleiss formula, without the correction factor (8). 104 was the calculated sample size. Considering non-response of 10%, 116 cases and 116 controls were needed to be recruited in the study. In the study 120 each of cases and controls were included in the final analysis (Figure 1).

Sampling: Study subjects were selected from outpatient department (OPD) of general surgery of the hospital. **Cases:** Every consecutive confirmed case of gallstone disease presenting in the OPD during the study period was enrolled until the sample size was met. **Inclusion criteria**: cases of gallstone disease above 20 years of age, its diagnosis confirmed by ultra-sonography. **Controls:** Every consecutive patient presenting to surgical OPD and diagnosed negative for gall stones by ultrasonography until the sample size was met. Controls were matched for age and sex. **Inclusion criteria**: Patients attending surgery OPD above 20 year of age and found negative for gallstone disease on ultrasonography.

Data Collection: Data of 120 cases and 120 controls matched for age and sex was collected. Data collection was done on a self-designed pretested "interview schedule," with special focus on behavioral risk factors like tobacco use, alcohol consumption & physical inactivity. For the purpose of study; current smoker were defined as those who have smoked in last 1 year and current alcoholics were defined as those who had consumed alcohol in last 1 year. Assessment of physical activity was done on the basis of activity performed during a typical day at work place, travel and in leisure time. Physical activity was categorized as moderate (indulgence per day of 60 min or more in activities such as brisk walking/domestic chores/carrying or moving loads up to 20kg) and vigorous (running/cycling/swimming/ carrying or moving loads above 20kg) (9). Personal factors like parity and anthropometric indices (weight, height, Body Mass Index, waist-hip circumference, waist-hip ratio) (10) were calculated for all cases and controls. Cut-off for BMI > 23 kg/m2, W/H ratio > 0.80 for females and > 0.90 for males and parity ≥ 3 were used for analysis. Anthropometric measurements were recorded using standard methods and instruments which were used for measurement were standardized. Clinical presentations, ultra-sonography findings & final diagnosis were recorded from individual records. Data Management and Statistical Analysis: data was recorded in MS Excel and Epi info 7 software was used for statistical analysis. Observations have been described in terms of mean, range and standard deviation for continuous data and in terms of percentages/proportions for categorical data. To measure the strength of association simple Odds Ratio (OR) was calculated and McNemar's test was used for matched pair analysis. Independent Student's't' test was used to study the group difference for quantitative variables. Binary logistic regression was used for multivariate analysis to find out different correlates and analyses the independent effects of these correlates on GSD. Ethical Considerations: Ethical approval for this study was provided by the institutional ethical committee of Lady Hardinge Medical College and Associated Hospitals (letter no. LHMC/ECHR/2014/180). Also the informed consent was obtained from each of the study subject.

Results

Total of 120 cases and 120 controls were included in final analysis. Table 1 shows the age and sex wise distribution of study subjects. Most of the study subjects (65.8%) were more than 40 years. The maximum proportion of the study subjects belonged to the age group of 51-65 years, followed by 41-50 years. Majority of study subjects were females.

Table 2 shows that mean age of cases was higher as compared to controls. Among females, cases had significantly higher parity than controls. In anthropometric indices weight, height, BMI, waist circumference and W/H ratio were significantly higher in cases as compared to controls.

Univariate Odds ratio was calculated to know the association of the different risk factors enumerated with the occurrence of gall stone disease. Table 3 shows univariate Odds ratio for unmatched pairs, except for alcohol consumption, all the other risk factors enumerated had a statistically significant association with the occurrence of gallstone diseases among the study subjects. In this study the strength of association was found to be maximum for sedentary physical activity (p value=000) followed by high parity (p value=002), high W/H ratio (p value=005), consumption of smokeless tobacco (p value=009), high BMI (p value=028) and smoking (p value=034).

We also analysed the findings using matched pair analysis to undermine the effects of confounders. The findings suggest that association was found to be maximum for high parity (p value=000) followed by high W/H ratio (P value=000), sedentary physical activity (p value=000), smoking (p value=010) consumption of smokeless tobacco (p value=014) and high BMI (p value=035) (Table 4).

We further analysed selected variables by using multivariate binary logistic regression to adjust confounders and it was found that all the selected variables increases the risk of development of GSD except for alcohol consumption (Adjusted OR=0.968) but only physical inactivity statistically significantly associated with GSD (p value=0.002) (Table 5)

Discussion

The factors found to be associated with the development of gall stone disease were high waist-hip ratio, high parity, physical inactivity, tobacco consumption and high BMI in present study. Multiparous females had a significantly higher association with GSD; reason for such finding in this study may be due to pregnancy favours gallstone formation through the hormonal influences on bile composition i.e. increased biliary cholesterol secretion, decreased and unbalanced bile acid pool, this finding was supported by studies conducted by other researcher (9,11,12,13).

We found current smoking was a risk factor for GSD, this finding had also been corroborated by several authors (11,14). Reason for such finding in this study may be because smoking is associated with low plasma high density lipoprotein (HDL) cholesterol concentrations, a risk factor for gallstones. It also depresses prostaglandin synthesis and mucus production in the gallbladder. Other studies showed that smoking was not significantly associated with GSD (15,16,17). There are not many studies addressing the association between consumption of smokeless tobacco with GSD, some studies showed no association (17,18), but we found it was significantly associated with GSD. Alcohol consumption was not significantly associated with the gallstones, this has been corroborated by several other researchers (11,12,19), Whereas, Some experimental studies had suggested the protective effect of alcohol against gallstone formation (15,17,18).

Obesity is one of important risk factor for the development of GSD, which can be expressed as high BMI or W/H ratio. In present study, BMI (>23 kg/m2) and high W/H ratio were strongly associated with gallstones, reason for such finding may be because obesity increases cholesterol synthesis, biliary cholesterol secretion and cholesterol super saturation. There were several studies supporting these findings (9,20,21,22,23). Sedentary lifestyle or physical inactivity was also strongly associated with the development of gallstones in present study; this has been corroborated by Sachdeva *et al.* (9)

We further analysed data by using multivariate binary logistic regression for some selected variables to find the independent effect of these risk factors on GSD, which shows physical inactivity increases the risk of gallstones nearly fourfold (adjusted OR=3.7) followed by high W/H ratio which increases the risk of GSD development twice (adjusted OR=2.05). High parity (adjusted OR=1.49), high BMI (adjusted OR=1.49), smokeless tobacco consumption (adjusted OR=1.55) and smoking (adjusted OR=1.06) also favours gallstones formation

Conclusion

High parity, High W/H ratio, Physical inactivity, Current smoking, Smokeless tobacco and high BMI were found to be risk factors for the development of GSD as shown by matched pair analysis. All these behavior and personal risk factors are potentially modifiable by primary prevention. Special emphasis should be given to promote physical activity [as the physical activity might modify other risk factors i.e. W/H ratio and BMI]. We should provide health education to community and masses regarding the benefits of physical activity and also making them aware about the recommended levels of daily physical activity. Attention should also be focused on avoidance of substance use. These strategies might be helpful in reducing the prevalence of gall stone diseases.

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Tables

TABLE 1 DISTRIBUTION OF SUBJECTS ACCORDING TO AGE AND GENDER

Variable		Cases N (%)	Controls N (%)
Age group (in completed years)	20-30	14 (11.7)	14 (11.7)
	31-40	27 (22.5)	27 (22.5)
	41-50	36 (30)	36 (30)
	51-65	43 (35.8)	43 (35.8)
	Total	120 (100)	120 (100)
Gender	Male	37 (30.8)	37 (30.8)
	Female	83 (69.2)	83 (69.2)
	Total	120 (100)	120 (100)

TABLE 2 COMPARING CHARACTERISTICS OF THE STUDY SUBJECTS USING INDEPENDENT STUDENT'S 'T' TEST

Variable	Case Mean ±SD*	Control Mean ±SD*	p value
Age (In completed years)	45.74±11.6	44.2±10.9	-
Parity (N-83)	3.22±1.40	2.69±1.31	0.011
Weight (Kilograms)	59.20±9.57	54.84±7.02	0.000
Height (Centimeters)	159.67±6.25	156.58±4.93	0.000
BMI†	23.20±3.15	21.95±2.81	0.001
WC‡ (Centimeters)	75.79±7.07	73.49±6.09	0.007
W/H§ Ratio	0.80±0.06	0.77±0.05	0.000

*Standard Deviation, †Body Mass Index, ‡Waist Circumference, §Waist/Hip Ratio

TABLE 3 UNIVARIATE ANALYSIS OF PERSONAL AND BEHAVIORAL RISK FACTORS AMONG STUDY SUBJECTS

Variable	Cases(120)	Controls(120)	OR* (95%CI) †	p value
Parity (n=83) (>=3)	62	43	2.75 (1.43-5.29)	0.002
Smoking (Current)	25	13	2.17 (1.05-4.47)	0.034
Smokeless tobacco (Current)	31	16	2.26 (1.16-4.41)	0.009
Alcohol (Current)	24	28	0.82 (0.44-1.52)	0.518
Physical activity (Sedentary)	74	44	2.78 (1.65-4.69)	0.000
BMI‡ (> 23 kg/m2)	68	51	1.77 (1.06-2.95)	0.028
W/H§ Ratio (High)	31	14	2.64 (1.32-5.26)	0.005

*Odds Ratio, † 95% Confidence Interval, ‡Body Mass Index, §Waist/Hip Ratio

TABLE 4 UNIVARIATE MATCHED PAIR ANALYSIS OF PERSONAL AND BEHAVIORAL RISK FACTORS AMONG STUDY SUBJECTS USING MCNEMAR'S TEST

Cases		Controls		OR* (95%CI) †	p value
		Present	Absent		
Parity (N-83]	>=3	39	23	5.75 (1.99-16.63)	0.000
	<3	4	17		
Smoking	Yes	8	17	3.4 (1.25-9.21)	0.010

(Current)	No	5	90		
Smokeless tobacco (Current)	Yes	5	26	2.36 (1.17-4.78)	0.014
	No	11	78		
Alcohol (Current)	Yes	10	14	0.78 (0.39-1.56)	0.479
	No	18	78		
Physical activity	Sedentary	36	38	4.75 (2.22-10.18)	0.000
	Mod/vigorous	8	38		
BMI‡ (> 23 kg/m2)	>= 23 kg/m2	27	41	1.71 (1.03-2.83)	0.035
	< 23 kg/m2	24	28		
W/H§ Ratio	High	10	21	5.25 (1.80-15.29)	0.000
	Normal	4	85		

*Odds Ratio, † 95% Confidence Interval, ‡Body Mass Index, §Waist/Hip Ratio

TABLE 5 MULTIVARIATE LOGISTIC REGRESSION ANALYSIS OF SELECTED VARIABLES WITH GSD AMONG STUDY SUBJECTS

Variable	Coefficient B	Adjusted OR*	95% CI†		p value
			Lower	Upper	
Parity	.397	1.488	.619	3.574	.374
BMI‡	.405	1.499	.747	3.006	.254
W/H§ Ratio	.719	2.052	.838	5.023	.115
Physical inactivity	1.308	3.699	1.599	8.558	.002
Smoking	.060	1.061	.206	5.480	.943
Tobacco	.440	1.552	.597	4.039	.367
Alcohol	-.033	.968	.243	3.863	.963

*Odds Ratio, † 95% Confidence Interval, ‡Body Mass Index, §Waist/Hip Ratio

Figures

FIGURE 1 SELECTION OF STUDY SUBJECTS