

## Original Research Article

# Gender specific variation in risk factors of gallstone disease among adult patients

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## ABSTRACT

**Background:** Gallstone disease (GSD) is a common gastrointestinal disease diagnosed in patients presented with abdominal pain. The present study was aimed to find the association between demographic, personal, behavioural and dietary factors and GSD by gender among adult population for suggesting specific gender wise intervention to control GSD.

**Methods:** Case-control study was conducted in 120 cases and same number of controls. Data was collected on a self-designed pretested "interview schedule". To measure the strength of association OR was calculated by matched pair analysis using McNemar's test.

**Results:** Among 120 study subjects, 83 cases were females and 37 were males. Strength of association was found to be significantly higher for family h/o GSD in females (OR=8), physical inactivity (OR=8), waist-hip ratio (OR=4.2), calorie intake more than recommended dietary allowance (RDA) (OR=2.09), and diabetes (OR=4) as compare to males OR=3, OR=2.8, OR=2.5, OR=1.43, OR=2.33 respectively.

**Conclusions:** Family h/o GSD, physical inactivity, high waist-hip ratio, calorie and fat intake more than RDA, protein intake less than RDA, hypertension and diabetes were found to be potential risk factors for the development of GSD in females. Consumption of smokeless tobacco, physical inactivity, non-vegetarian diet and intake of fats more than RDA were risk factors for GSD in males.

**Keywords:** Gallstone disease, Behavioural and dietary risk factors, Case control study, Matched pair analysis

## INTRODUCTION

Gallstone disease (GSD) is a common gastrointestinal disease diagnosed in patients presented with abdominal pain.<sup>1</sup> Prevalence of GSD among adult population ranges from 6% to 9% in India.<sup>2,3</sup> Potential risk factors for the development of gallstone disease are geriatric age, female gender, family history, obesity, physical inactivity, tobacco consumption and co morbidities. In female subjects high parity and intake of oral contraceptive pills

also increases the risk of gallstone disease. Among the dietary factors; type of diet, intake of calories, fats and proteins are potential risk factors of GSD, as all of these dietary factors affects the cholesterol saturation of bile.<sup>1,4-7</sup> Gender differences have been seen in the prevalence of gallstones, some other author also compared gender wise variation in association of various risk factors with gallstone disease, but none of them had compared all the known risk factors.<sup>2-5,7-10</sup> The present study was therefore aimed to find the association between demographic,

personal, behavioural and dietary factors and GSD by gender among adult patients for suggesting specific gender wise intervention to control GSD.

## METHODS

Case-control study was conducted from January 2013 to December 2013 among subjects attending outpatient department (OPD) of general surgery in Smt Sucheta Kripalani Hospital (SSKH), a tertiary care hospital of North India. We have enrolled all the subjects from surgical OPD two days in a week. Finally we have recruited 120 cases and same number of controls in the study. Cases were defined as ultrasonography confirmed case of gallstone disease aged 20 years or more presented in the OPD. We have excluded seriously ill patients and patients who did not give consent. Controls were defined as patients above 20 year of age presented to surgical OPD and diagnosed negative for gallstones by ultrasonography. We have matched the control for age and sex. Pregnant females, diagnosed cases of other hepatobiliary disease and renal stones were excluded. Data collection for both cases and controls was done on a self-designed pretested "interview schedule" which assessed the socio-demographic profile, personal history, medical history and co-morbidities, physical examination including anthropometry and dietary intakes. Modified Kuppaswamy's scale was used to calculate Socio-economic status (SES). Dietary assessment was done by using the 24 hour recall method and food frequency questionnaire as a cross-check, and calculations for nutrient intake were done using Indian Council of Medical Research (ICMR) standards.<sup>11</sup> For the purpose of study; current smokers and current smokeless tobacco users were defined as those who have smoked or consumed smokeless tobacco in last 1 year, respectively. 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 and anthropometric indices; weight, height, body mass index (BMI), waist and hip circumference, waist-hip ratio (WHR) were calculated for all cases and controls using standard definitions.<sup>4</sup> Cut-off for BMI > 23 kg/m<sup>2</sup>, W/H ratio > 0.80 for females and > 0.90 for males were used for analysis. Anthropometric measurements were recorded using standard methods and instruments.<sup>12</sup>

### Data management and statistical analysis

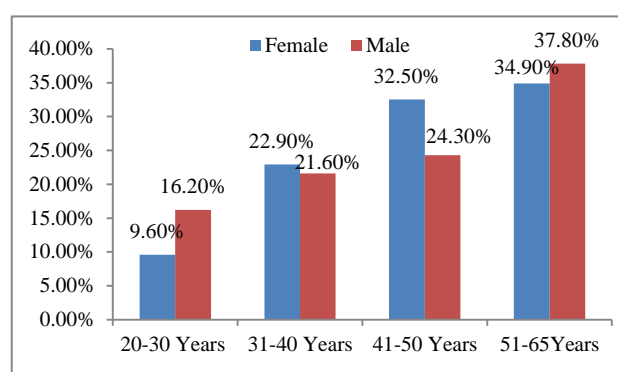
Data was recorded in MS Excel and Epi info 7 software was used for statistical analysis. Observations have been described in terms of mean and standard deviation for continuous data and in terms of percentages/proportions for categorical data; to measure the strength of association odd's ratio (OR) was calculated by matched pair analysis using McNemar's test.

## Ethical approval

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 written consent was obtained from each of the study subject.

## RESULTS

120 cases and same number of age and sex matched controls were included in the study. Among the study subjects, 83 cases were females and 37 were males. Proportion of cases in 31-40 and 41-50 age groups is higher in females as compare to males, whereas proportion of cases in 20-30 and 51-65 age groups is higher in males as compare to females (Figure 1).



**Figure 1: Age and gender wise distribution of cases.** Females=83, Males=37.

Comparison of basic characteristics of study subjects by gender showed that there were statistical significant difference in the mean value of body mass index and waist circumference in cases as compared to control group in males; whereas no statistical difference is seen in females. Mean daily protein intake is statistically lower in cases as compare to controls in females; no statistical difference is seen in males. Mean value of waist hip ratio, mean daily calories and fats intake are statistically higher in cases as compare to controls in females as well as males (Table 1).

Matched pair analysis of demographic factors shows that literacy and SES were not significantly associated with the development of GSD neither in females nor in males. Strength of association was found to be significantly higher for family h/o GSD in females (OR=8) as compare to males (OR=3). Smoking, consumption of smokeless tobacco and alcohol were not significantly associated with GSD in females, whereas smokeless tobacco found to be significantly associated with development of GSD in males. Sedentary lifestyle, high BMI and high W/H ratio were significantly associated with GSD in females, whereas in males only sedentary lifestyle was significantly associated with development of GSD (Table 2).

**Table 1: Comparison of basic characteristics of study subjects by gender.**

Variable	Female (N=83 Pairs)				Male (N=37 Pairs)			
	Case Mean± SD*	Control Mean± SD*	t-value	P value	Case Mean± SD*	Control Mean± SD*	t-value	P value
Age (years)	46.0±11.46	43.41±9.77	-	-	45.19±12.09	45.81±12.86	-	-
BMI <sup>†</sup> (kg/m <sup>2</sup> )	22.84±2.9	22.06±2.94	1.72	0.088	23.84±3.62	21.87±2.55	2.70	0.009
WC <sup>‡</sup> (centimeters)	74.07±05.56	73.10±5.66	1.12	0.264	79.49±8.67	74.54±6.92	2.71	0.008
W/H <sup>§</sup> ratio	0.80±0.06	0.78±0.06	2.35	0.020	0.79±0.07	0.75±0.03	2.74	0.008
Calorie intake (kcal <sup>¶</sup> )	2046±312	1875±365	3.25	0.001	2535±287	2298±391	2.97	0.004
Fat intake (gm <sup>#</sup> )	29.75±6.17	27.24±5.27	2.81	0.006	37.34±5	33.7±4.85	3.21	0.002
Protein intake (gm)	50.75±7.84	54.19±9.72	-2.51	0.013	54.11±5.47	55.27±8.24	-0.72	0.477

Standard deviation\*, body mass index<sup>†</sup>, waist circumference<sup>‡</sup>, waist hip ratio<sup>§</sup>, kilo calories<sup>¶</sup>, gram<sup>#</sup>

**Table 2: Matched pair analysis of demographic and behavioral risk factors of GSD by gender.**

Variable	Female (n=83 pairs)			Male (n=37 pairs)		
	Cases	Controls	OR* (95%CI) <sup>†</sup>	Cases	Controls	OR* (95%CI) <sup>†</sup>
<b>Literacy</b>	Illiterate	Literate	0.5 (0.24-1.03)	Illiterate	Literate	1.4 (0.44-4.41)
	37	11		22	7	
	Literate			5	3	
<b>SES<sup>‡</sup></b>	Lower	Upper and middle	0.7 (0.34-1.48)	Lower	Upper and middle	0.89 (0.34-2.30)
	32	17		6	8	
	Upper and middle	22		9	14	
<b>Family h/o GSD<sup>§</sup></b>	Yes	No	8 (1.00-63.95)	Yes	No	3 (0.31-28.84)
	1	8		1	3	
	No	73		1	32	
<b>Smoking</b>	Yes	No	2.5 (0.49-12.88)	Yes	No	0.33 (0.07-1.65)
	1	5		15	2	
	No	75		6	14	
<b>Smokeless tobacco</b>	Yes	No	1.57 (0.61-4.05)	Yes	No	3.25 (1.06-9.97)
	5	11		1	13	
	No	60		4	19	
<b>Alcohol</b>	Yes	No	0.8 (0.25-2.73)	Yes	No	0.93 (0.44-1.97)
	0	5		7	13	
	No	72		14	3	
<b>Physical activity</b>	Sedentary	Mod/vigorous	8 (2.41-26.57)	Sedentary	Mod/vigorous	2.8 (1.01-7.77)
	31	24		5	14	
	Mod/vigorous	25		5	13	
<b>BMI<sup>¶</sup></b>	≥23 kg/m <sup>2</sup>	<23 kg/m <sup>2</sup>	1.75 (0.95-3.23)	≥23 kg/m <sup>2</sup>	<23 kg/m <sup>2</sup>	2 (0.81-4.95)
	24	28		6	14	
	<23 kg/m <sup>2</sup>	15		7	10	
<b>W/H<sup>#</sup> ratio</b>	High	Normal	4.2 (1.58-11.14)	High	Normal	2.5 (0.48-12.88)
	6	21		0	5	
	Normal	51		2	30	

Odds ratio\*, 95% confidence interval<sup>†</sup>, socio-economic status<sup>‡</sup>, gallstone disease<sup>§</sup>, body mass index<sup>¶</sup>, waist/hip ratio<sup>#</sup>

Table 3 showed that non vegetarian diet was not significantly associated with GSD in females, whereas association of GSD with non-vegetarian diet was significant in males. High calories, high fats and low protein intake were significantly associated with GSD in females, whereas daily high fats intake was more strongly associated with GSD in males (OR=4.33) as compare to

females (OR=1.88), daily intake of high calories and low proteins were not associated with GSD in males. Among the comorbidities hypertension and diabetes were significantly associated with GSD, but no association was found with hyperlipidemia and GSD in females; whereas none of the comorbidities were significantly associated with GSD in males.

**Table 3: Matched pair analysis of dietary and co-morbidities risk factors of GSD by gender.**

Variable	Female (n=83 pairs)		OR* (95%CI) <sup>†</sup>	Male (n=37 pairs)		OR* (95%CI) <sup>†</sup>
Cases	Controls			Controls		
<b>Diet</b>	Non vegetarian	Vegetarian		Non vegetarian	Vegetarian	
Non vegetarian	13	26	1.63	10	14	2.8
Vegetarian	16	28	(0.87-3.03)	5	8	(1.01-7.77)
<b>Calorie</b>	>RDA <sup>‡</sup>	<RDA		>RDA <sup>‡</sup>	≤RDA	
>RDA <sup>‡</sup>	12	23	2.09	2	10	1.43
≤RDA	11	37	(1.02-4.29)	7	18	(0.54-3.75)
<b>Fat</b>	>RDA <sup>‡</sup>	≤RDA		>RDA <sup>‡</sup>	≤RDA	
>RDA	24	30	1.88	7	13	4.33
≤RDA	16	28	(1.02-3.44)	3	14	(1.24-15.21)
<b>Protein</b>	≤RDA	>RDA		≤RDA	>RDA	
≤RDA	55	16	3.2	22	9	1.8
>RDA	5	7	(1.17-8.73)	5	1	(0.60-5.37)
<b>Hypertension</b>	Yes	No		Yes	No	
Yes	4	23	2.09	2	7	1.4
No	11	45	(1.02-4.29)	5	23	(0.44-4.41)
<b>Diabetes</b>	Yes	No		Yes	No	
Yes	2	12	4	1	7	2.33
No	3	66	(1.13-14.17)	3	26	(0.60-9.02)
<b>Hyperlipidemia</b>	Yes	No		Yes	No	
Yes	1	5	2.5	0	3	3
No	2	75	(0.48-12.88)	1	33	(0.31-28.84)

Odds ratio\*, 95% confidence interval<sup>†</sup>, recommended daily allowance<sup>‡</sup>, green leafy vegetables<sup>§</sup>

## DISCUSSION

Many researchers showed that gender has a role in the occurrence of GSD; in present study we have analyzed risk factors of GSD according to gender. We have found that among the demographic risk factors literacy and SES had no role in the occurrence of GSD in males as well as females; whereas some studies showed higher SES had significantly associated with the development of GSD.<sup>13,14</sup> Family h/o GDS strongly and significantly associated with development of GDS in females; whereas no significant association was seen in males, this has been corroborated by several authors.<sup>15,16</sup> Smoking had no significant association with the development of GSD in females as well as males, a same finding was found by Duque et al whereas Figueiredo et al found significant association between smoking and GSD in females as well as males.<sup>17,18</sup> Smokeless tobacco had no significant association with GSD in females, a same finding was seen by Al-Kayatt et al, but in males it was significantly associated with the development of GSD.<sup>15</sup> Consumption of alcohol found to be inversely associated with GSD in females as well as males but it was statistically insignificant, this has been corroborated with other studies, whereas some studies showed that alcohol not associated with GSD in males and inversely associated in females.<sup>18-20</sup> Sedentary life style was found to be significant risk factor for the development of GSD in both the sexes, this has been corroborated with other

studies, whereas Sun et al found no significant association neither in females nor in males.<sup>4,6,7,18</sup> High BMI and high waist hip ratio were significantly associated with development of GSD in females same results were seen in other studies; but in males we have found no association, whereas as several studies found significant association.<sup>7-9,21-23</sup> Intake of calories and fats more than recommended dietary allowance (RDA) and intake of protein less than RDA were found to be significantly associated with GSD in females, whereas in males only intake of fats more than RDA was significantly associated with GSD, this has been corroborated with other studies.<sup>4,15</sup> Type of diet was not significantly associated with GSD In females, whereas non vegetarian diet was found to be risk factor for GSD in males.<sup>6,24</sup> Among the co-morbidities we have found that only hypertension and diabetes mellitus were significantly associated with GSD in females same findings were seen in other studies, whereas in males none of the co-morbidities were significantly associated with GSD.<sup>7,8,18,23</sup>

## CONCLUSION

Family h/o GSD, physical inactivity, high W/H ratio, calorie and fat intake more than RDA, protein intake less than RDA, hypertension and diabetes were found to be potential risk factors for the development of GSD in females. Consumption of smokeless tobacco, physical

inactivity, non-vegetarian diet and intake of fats more than RDA were risk factors for GSD in males.

Most of these risk factors are modifiable by simply changing the lifestyle and dietary habits. Physicians are advised to screen females with family history of GSD, hypertension or diabetes for gallstone disease. Males should be advised to consume vegetarian diet with recommended fats. For females we should promote diet with recommended calories and fats. Special emphasis should be given to promote physical activity in the community as it will modify other potential risk factors also.

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