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A STUDY ON THE PREVALENCE OF GALLBLADDER DISEASE AND ITS ASSOCIATED FACTORS IN A TERTIARY HOSPITAL OF EASTERN INDIA

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Abstract

Background: The incidence of gallbladder diseases is common globally. Gallbladder diseases include cholelithiasis, gall bladder carcinoma, and gallbladder polyp and acalculous cholecystitis. Sex differences demonstrate a marked predominance of women over men worldwide. This study was done with the aim to study the prevalence of gallbladder disease and its risk factors influencing the pathogenesis of gallbladder disease among male and female population of Jharkhand. **Materials and Methods:** This Hospital based prospective, cross-sectional study was conducted on 150 patients of gallbladder disease in the Department of General Surgery, Rajendra Institute of Medical Sciences (RIMS), Ranchi Jharkhand. They were subjected to clinical history of right upper quadrant pain, nausea and vomiting, standard blood examinations of liver function test, lipid profile and undergone transabdominal ultrasound of the whole abdomen followed by CECT of the whole abdomen or MRCP when indicated. **Result:** Prevalence of gall bladder diseases in our study was 10.83/1000 population. In our study gallbladder diseases are more common among females (60%) than males (40%). Among females 31 to 40 age group has more prevalence (40%) of gallbladder diseases compared to other age groups. Among males also 31 to 40 age group has more prevalence (40%) of gallbladder diseases compared to other age groups. Mean alkaline phosphatase (ALP) and HDL level was more in males compared to females. In females mean waist circumference (82.11±15.46), thigh circumference (54.11±4.59), BMI (25.61±2.26), total cholesterol (190.12±2.50) and triglycerides (127.06±8.86) were more than in males and were statistically significant. **Conclusion:** Among female patients, greater BMI, waist circumference, thigh circumference, has strong influence in the pathogenesis of the gallbladder diseases, compared to male patients. High cholesterol and triglycerides had also been found to be associated with gallbladder diseases in females than males.

INTRODUCTION

Worldwide the diseases of the gallbladder are common and increasing, incidence being 3 to 21.9%.[1] The prevalence of gallstone diseases is about 10% among American adults whereas in Western Europe the prevalence varies from 5.9% to 21.9%. In Asia the incidence is 3.2 to 5.6%.[2] In India it is 2-29% with difference in different regions or states.[3] Gallbladder diseases considered here include cholelithiasis, gall bladder carcinoma, gallbladder polyp and acalculous cholecystitis. The prevalence was 20% of women had gallstones, and 14% of men had gallstones in an Italian study. In a Danish study, gallstone prevalence was 1.8% for men and 4.8% for women aged 30 years and

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gallstone prevalence was 12.9% for men and 22.4% for women aged 60 years.[4]

There is a marked predominance of gallbladder disease in women as compared to men globally, especially in North India, Pakistan, and in American Indian females.[5] The ratio of women and men is 2-6:1. The female sex hormones could be considered a causative factor as there is higher incidence of gallbladder cancer in females with a high parity and greater number of pregnancies.[6] Even though the estrogen receptor and progesterone receptor expression in gallbladder cancer between men and women is not significantly different, the co-expression of both receptors is increased in females with gallbladder cancer as compared with males, thereby identifying a potential target for treatment.[7]

The incidence of gallbladder polyps in adults is 5%. Most are pseudopolyps, without neoplastic potential.[8] For gallbladder polyps, there are no identified risk factors, like age, sex or the metabolic syndrome.[9]

Acalculous cholecystitis is an inflammatory disease of the gallbladder without evidence of gallstones or cystic duct obstruction.[10,11] It is most commonly observed in the setting of very ill patients who are on mechanical ventilation, with sepsis after severe trauma or severe burn injuries.[12] Acalculous cholecystitis has a slight male predominance, unlike other gallbladder diseases, which has a female predominance.[13]

The risk factors include female gender, age older than 40, obesity, pregnancy, diets high in cholesterol, refined carbohydrates like white bread, and saturated fats like cheese, butter, and red meat,sedentary lifestyle, slimming, underlying diseases like diabetes, metabolic syndrome, cirrhosis, Crohn's disease, sickle cell disease, cystic fibrosis or a spinal cord injury, medications containing oestrogen, like oral contraceptives or hormone replacement therapy.[14] Most gallbladder diseases have female predominance, but regarding gallbladder polyp, it's still indistinct.

Factors involved in the causation of gallbladder diseases among males are not clearly explained. Thus, gender predominance and risk factors involved in the pathogenesis of the gallbladder diseases should be further studied.

Aims and Objectives

Aim: - To study the prevalence of gallbladder diseases and its risk factors involved in the pathogenesis of gallbladder diseases in males and females.

Secondary Objective:- To perform histopathological examination of the gallbladder after the patient underwent surgery to support radiological findings and to confirm the diagnosis.

MATERIALS AND METHODS

After approval from the Institutional Ethics Committee, this hospital based prospective cross-sectional study was conducted on 150 patients of gallbladder diseases in the Department of General Surgery, Rajendra Institute of Medical Sciences (RIMS), Ranchi from November 2020 to October 2021. Convenience sampling was done from patients admitted through Outdoor patient and emergency. A written informed consent was taken. The sample size was calculated by using the following Kish Leslie formula (1965):

$n= z^2x\ p\ x\ q\ /\ d^2$

Where:

n= sample size, z= 1.96 (at 95% confidence interval), p= prevalence, q= 1-p, d= margin of error

Based on the prevalence of gall bladder diseases in Asia being 4-15% (9), we calculate a sample size as:

p= 9% = 0.09

q= 1- 0.09= 0.91

e= 6%= 0.06

$n=4\ x\ p\ x\ q/d^2$

n = 91

Applying design effect of 1.5

91 x 1.5= 136.5 =137

Considering 10% loss to follow up we take a sample of 137+13=150.

Inclusion Criteria

- Adult Patients above 14 years of age who had been admitted in surgical ward with right upper abdominal pain, nausea and vomiting, with clinical suspicion of gallbladder diseases.
- Patients with ultrasound diagnosed gall bladder diseases.

Exclusion Criteria

- Patients with mental illness or is unfit for radiological study due to other medical conditions.

A complete clinical history of all patients relevant to risk factors was taken followed by complete physical examination for height, weight, waist circumference, thigh circumference by calibrated mechanical patient scale. Blood pressure was measured by automatic blood pressure machine. They were subjected to standard blood examinations including complete blood count, liver function test, alkaline phosphatase, lipid profile including total cholesterol, HDL, triglyceride, fasting and post prandial blood sugar levels. They had undergone transabdominal ultrasound of the whole abdomen followed by CECT of the whole abdomen or MRCP as and when indicated. The patients were followed up and diagnosis was established histologically or intraoperatively supported by radiological evidence.

For statistical analysis data was entered into a Microsoft Excel spreadsheet and then analyzed by SPSS (version 24.0; SPSS Inc., Chicago, IL, USA) and MS Excel, 2010 (Microsoft Corporation, USA). Data was summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean were involved independent samples or unpaired samples.

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RESULTS

In this study, prevalence of gall bladder diseases was 10.83/1000 population. Among 13839 patients from OPD and emergency, 150 patients were enrolled in this study. Out of these 90 were females and 60 were males. Female patients' age ranges from 20 years to 80 years with mean age 38.08 years. In this study most patients (36 i.e. 40%) were in the age range of 31 to 40 years. Male patients' age ranges from 20 years to 80 years with mean age 36.6 years. Most patients (24 i.e. 40%) in this study were in the age range of 31 to 40 years.

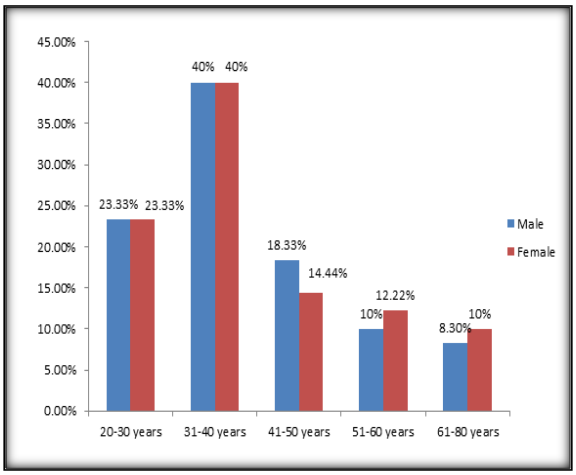

Figure 1: Age incidences of study population

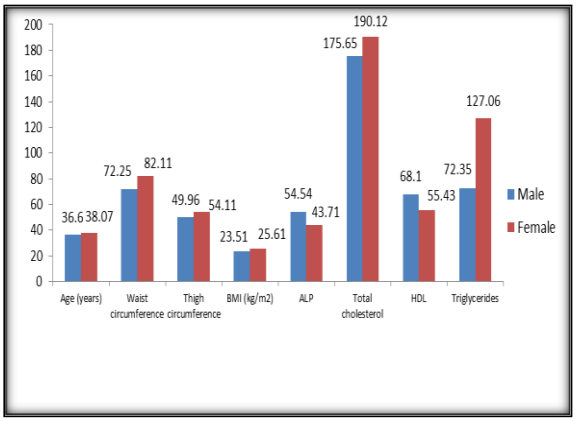

Figure 2: Comparison of variables affecting gall bladder diseases in gender

Diseases of gallbladder usually present as pain in the abdomen, nausea/ vomiting, dyspepsia, fever, jaundice. Out of 90 female patients, 42 patients presented with pain, 31 patients with vomiting, 11 patients with dyspepsia, 3 patients with fever, 3 patients with jaundice. Out of 60 male patients, 30 patients presented with pain, 13 patients with vomiting, 10 patients with dyspepsia, 2 patients with fever, and 5 patients with jaundice.

Out of 60 male patients, 6 patients (6.67%) had diabetes mellitus (DM), 8 (13.33 %) patients had hypertension (HTN). Out of 90 female patients, 9 patients had DM (10%) and 7 patients (7.77%) had HTN.

The mean waist circumference for male and female was 72.25 cm and 82.11 cm respectively. The mean thigh circumference for male and female was 49.96 cm and 54.11cm respectively. Out of 150 patients, 14 male patients and 44 female patients having body mass index (BMI) of more than 25 kg/m^2. 46 male patients and 46 female patients having BMI of less than 25 kg/m^2. The mean BMI for male and female patients were 23.51 and 25.61 respectively. Mean alkaline phosphatase (ALP) in male patients was 54.54 and in female patients was 43.71. Mean Total cholesterol in female patients was 190.12 mg/dl and 175.65 mg/dl in male patients. Mean HDL in female patients was 55.43 mg/dl and 68.10 mg/dl in male patients. Mean triglycerides in female patients was 127.06 mg/dl and 72.35 mg/dl in male patients.

Above table shows the relation between food habit and addiction in male and female patients in symptomatic gallbladder diseases. In both males and females, the incidence of gallstone diseases was higher in non-vegetarians than vegetarians. Alcoholic and smoking males have more incidences of gallbladder diseases than females but non-alcoholic and non-smoking females have higher incidence of gallbladder diseases. Thus alcohol and smoking has indistinct relation with the causation of gallbladder diseases.

Out of 60 male patients, cholelithiasis without the evidence of cholecystitis in 35 patients, gallbladder polyp in10, acute calculus cholecystitis in 7, acute acalculous cholecystitis in 2, gangrenous cholecystitis in 1, gallbladder perforation in 2, and gallbladder mass in 3 patients in their USG report.

Out of 90 female patients, cholelithiasis without the evidence of cholecystitis in 53 patients, gallbladder polyp in13, acute calculus cholecystitis in 13, acute acalculus cholecystitis in 3, gangrenous cholecystitis in 2, gallbladder perforation in 1 and gallbladder mass in 5 patients.

Out of 60 male patients, 14 treated with conservative approach, 46 underwent surgical procedure. Out of 46 patients, 26 had laparoscopic surgery and 20 had open surgical procedure. Out of 90 female patients, 26 treated with conservative approach, 64 underwent surgical procedure. Out of 64 patients, 49 had laparoscopic surgery and 15 had open surgical procedure.

Out of 46 male patients who underwent cholecystectomy, 5 (10.9%) had acute cholecystitis, 25 (54.3%) had chronic cholecystitis, 4 (8.7%) had cholesterolosis, 10 (21.7%) had gall bladder polyp, 2 (4.3%) had malignancy in their histopathological (HPE) report.

Out of 64 female patients who underwent cholecystectomy, 4 (6.3%) had acute cholecystitis, 42 (65.6%) had chronic cholecystitis, 4 (6.2%) had cholesterolosis, 13 (20.3%) had gallbladder polyp, and 1 (1.5%) had malignancy in their HPE report.

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Table 1: Presenting symptoms

Symptoms	Female	%	Male	%
Pain	42	46.67	30	50.00
Nausea / vomiting	31	34.44	13	21.67
Dyspepsia	11	12.22	10	16.67
Fever	3	3.33	2	3.33
Jaundice	3	3.33	5	8.33
Total	90	100.00	60.00	100.00

Table 2: Co-morbidities associated with Gallbladder Diseases

Co-morbidities	Male	%	Female	%
DM	6	6.67	9	10.00
HTN	8	13.33	7	7.77

Table 3: Comparison of variables affecting gall bladder diseases in gender

Variables	Male (mean±SD)	Female (mean±SD)	p value
Age (years)	36.60±11.80	38.07±12.49	0.47
Waist circumference	72.25±5.35	82.11±15.46	<0.001
Thigh circumference	49.96±5.32	54.11±4.59	<0.001
BMI (kg/m^2)	23.51±2.11	25.61±2.26	<0.001
ALP	54.54±14.46	43.71±18.84	<0.001
Total cholesterol	175.65±2.60	190.12±2.50	<0.0001
HDL	68.10±9.78	55.43±11.02	<0.0001
Triglycerides	72.35±14.70	127.06±8.86	<0.0001
Variables	**Male (n=60)**	**Female (n=90)**	**p value**
Vegetarian	07 (11.66%)	19 (21.11%)	0.0310
Non-vegetarian	53 (88.34%)	71 (78.89%)	0.1268
Alcoholic	27 (45%)	9 (10%)	0.0046
Non-alcoholic	33 (55%)	81 (90%)	<0.0001
Smoker	19 (31.67%)	5 (5.55%)	0.0080
Non-smoker	41 (68.33%)	85 (94.45%)	<0.0001

Table 4: Comparison of USG findings

Findings	Male (n=60)	Female (n=90)
Cholelithiasis	35 (58.33 %)	53 (58.89 %)
Gallbladder Polyp	10 (16.67 %)	13 (14.44%)
Acute Calculus cholecystitis	7 (11.67 %)	13 (14.44%)
Acute Acalculous cholecystitis	2 (3.33 %)	3 (3.33 %)
Gangrenous Cholecystitis	1 (1.67 %)	2 (2.22%)
Gallbladder perforation	2 (3.33 %)	1 (1.11%)
Gallbladder Mass	3 (5 %)	5 (5.57 %)

Table 5: Comparison of treatment modalities of patients of gallbladder diseases

Management	Male (n=60)	Female (n=90)
Conservative Approach	14 (23.33 %)	26 (28.89%)
Surgical Approach:		
• Laparoscopic cholecystectomy	26 (56.52 %)	49 (76.57 %)
• Open cholecystectomy	20 (43.48 %)	15 (23.43 %)

Table 6: Comparison of histopathological findings of gallbladder

HPE Findings	Male (n=46)	Female (n=64)
Acute Cholecystitis	5 (10.9%)	4 (6.3%)
Chronic Cholecystitis	25 (54.3 %)	42 (65.6%)
Cholesterolosis	4 (8.7%)	4 (6.2 %)
Gallbladder polyp	10 (21.7%)	13 (20.3%)
Malignancy	2 (4.3%)	1 (1.5%)

DISCUSSION

Worldwide prevalence of gall bladder diseases varies from region to region i.e. 3-21.9%.[1] In our study, prevalence of gall bladder diseases was found to be 10.83/1000 population. Total number of 150 patients was enrolled as participants. Out of these 150 patients, 90 (60 %) were females and 60 (40%) were males.

Female gender is the most important risk factor for gallstone diseases.[15,16] In 2005 Korean National Health Insurance Study stated that overall prevalence of gallbladder diseases was 4.2% with both sexes having similar prevalence. Females showed higher prevalence of the diseases compared to males younger than 40 years, whereas it was higher in males older than 50 years. In 2005 Korean National Health Insurance study, asymptomatic cholelithiasis the average increase in the prevalence in every decade of age was 1.46-fold in males and 1.32-fold in females. Consequently, the prevalence of asymptomatic cholelithiasis showed a greater

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increase in males than females older than 50 years, and at age above 50 years, higher prevalence of asymptomatic cholelithiasis was observed in males than females significantly.[17]

In our study female patients' age ranges from 20 years to 80 years with mean age 38.08 years. Most patients (36 i.e. 40%) in this study were in the age range of 31 to 40 years. Male patients' age ranges from 20 years to 80 years with mean age 36.6 years. Most patients (24 i.e. 40%) in this study were in the age range of 31 to 40 years. John Huang et al (2009) also reported that all gallstone-related complications and procedures increased significantly in the age group 20-39 years and hospital admission was required.[18] In the Western societies about 80% are primarily cholesterol gallstones. There are several risk factors responsible for gallstone formation. The ratio of gallstones formation is 2-3:1 higher among women than men. Primarily this phenomenon is attributed to childbearing age. A major risk factor for gallstone formation is pregnancy.

In our study mean BMI of female patients was more than that of male patients which was statistically significant ($p<0.0001$). Aune D (2015) reported that the risk of gallbladder diseases has positive association between both general and abdominal fatness. There is an almost twofold increase in the risk even within the "normal" BMI range, suggesting that even moderate increases in BMI may increase risk.[19] A Mendelian Randomization Study states that elevated BMI as measured at baseline, as well as genetically (lifelong and unconfounded) elevated BMI, is associated with increased risk of symptomatic gallstone diseases. This indicates that elevated BMI per se is likely a causal risk factor for symptomatic gallstone diseases, which is most dominant in women. Kharga B et al (2016) also stated that with every increase in BMI the risk of symptomatic cholelithiasis increases. As the age advances in women risk of symptomatic cholelithiasis also increases.[20]

Diseases of gallbladder usually present as abdominal pain, nausea and vomiting, dyspepsia, fever, jaundice. In our study both sexes had abdominal pain, nausea and vomiting and dyspepsia were the common symptoms of gallbladder diseases. Joshi HN et al (2020) in their series found that abdominal pain was one of the commonest symptoms (97.84%) followed by nausea (28.11%), dyspepsia (28.11%), vomiting (18.38%), fever (1.62) and jaundice (1.08%).[21]

In our study co-morbidities like hypertension, hyperlipidemia and diabetes mellitus were found to be associated with symptomatic gall stone disease. In male patients, diabetes mellitus and dyslipidemia was associated as risk factor, more than females. However, in females' hypertension as a risk factor were more than in males.

Chen CH et al (2018) reported that the relative risk of gallstone diseases in the T2DM cohort was higher than that in the non-diabetes cohort in each group of age, sex, and patients with or without co-morbidity.[22]

Yalan Zhang et al (2022) stated that hypertension was significantly associated with the risk of gallstone diseases and gallstones and the association between hypertension and gallstone diseases was stronger in women than in men.[23]

When mean waist circumference and mean thigh circumference were compared, we found that association with gallbladder diseases was significant ($p < 0.001$) in male and female gender. In Liu T et al (2018) study higher waist circumference and waist to hip ratio (WHR) were significantly associated with higher risks of gallstone diseases in both genders.[24]

In this study, mean levels of alkaline phosphatase were more in males than females and it was statistically significant ($p < 0.001$). Naseem A. Channa et al (2005) stated that risk of gallstone diseases in females is associated with high serum alkaline phosphatase level.[25]

In our study we found that there was a strong association of gall bladder stone diseases with hypercholesterolemia and hypertriglyceridemia in females. Mean levels of total cholesterol and triglycerides was more in females than males and their difference was highly significant ($p < 0.0001$) and mean HDL level was higher in males than females and it was significant statistically ($p < 0.0001$). Hui Sun et al (2009) in their study found that hypertriglyceridemia was significant in gallstone diseases ($p < 0.05$) in women.[26] However a cross-sectional study in Denmark could not found a significant association between gallstone diseases and plasma lipid levels.[27]

In our study, the relation between food habits in male and female patients in symptomatic gallbladder diseases was assessed and it was observed that in both males and females, the incidence of gallstone diseases was higher in non-vegetarians than vegetarians.

Mahsa Jessri and Bahram Rashidkhani (2015) reported that healthy dietary pattern, high in fruits, vegetables, whole grain, and vegetable oil was associated with decreased risk of gall bladder diseases.[28] It is reported that fruits and vegetables have a protective role against gallstone diseases through their high fibre, antioxidants, magnesium, and vitamin C content.[29-32]

We found that alcohol consumption was associated with an increased incidence of gallbladder diseases in male patients than females. However, in various other studies alcohol consumption was found to have a inverse relation in gall bladder stone diseases.[33,34]

In our study, smoking males have more incidences of gallbladder diseases than females but non-alcoholic and non-smoking females have higher incidence of gallbladder diseases. Masako Okamoto et al (2002) stated that cigarette smoking was inversely related to gallbladder polyps in males and

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was positively related to the post cholecystectomy state.[34]

CONCLUSION

In our study gallbladder diseases are more common among females than males. Females are more prone during fertile age and reasons are multifactorial. Greater BMI, waist circumference, thigh circumference, has strong influence in the pathogenesis of the gallbladder diseases, among female patients compared to male patients. High cholesterol and triglycerides had also been found to be associated with gallbladder diseases in females than males. Higher values of alkaline phosphatase and HDL, as a risk factor, were observed in males than females. It is recommended that other risk factors apart from this study should be evaluated in a larger study population.

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