



Original Article

## A cross sectional study on causes and risk factors of gallstone disease among patients with symptomatic Cholelithiasis.

### Abstract:

**Background:** Gallstones are one of the most prevalent and most expensive gastroenterological diseases, leading to a great economic burden so to identify the risk factors leading to cholelithiasis in Nepalese.

**Objectives:** The aim of this study was to determine the causes and risk factors of gallstone disease (GSD) in patients with symptomatic cholelithiasis admitted to surgical unit of Manipal Teaching Hospital Pokhara Nepal.

**Methodology:** A cross-sectional study was conducted in Manipal teaching hospital Pokhara Nepal. Total of 132 cholelithiasis clients admitted to surgery ward was interrogated. Data was collected by interviewing, physical assessment, from laboratory investigations, old records. Convenience sampling method was used and data was analyzed by using descriptive and inferential statistics by SPSS 16.

**Results:** The most commonly involved age group for cholelithiasis (22%) is found to be 55-64yrs with a female predominance (M: F= 1:4.7), cholelithiasis was found more commonly among non-vegetarians(93.93%),multiparous women (90.82%),and BMI mean average score in women was found to be overweight/pre-obese (26.16kg/m<sup>2</sup>) and also women had a history of oral contraceptives (birth controlling pills) about 21.10% (23) and a history of hypothyroidism was found only 3%(4), in habit of alcohol 39.13%(9) were found to be males and 22.93%(22.93%) females and only 10(7.6%) of the samples had a history of diabetes. There was an association between gender and alcohol (p=0.015), BMI (p=0.74), diet (p=0.009) and smoking (p=0.0001) at 0.05 level.

**Conclusion:** Gallstone disease is predominant in female population and it increases with age, parity, non vegetarian food , overweight/ pre-obese and in those who had a history of taking oral contraceptives.

**Key words:** Gall stone, Cholelithiasis, Risk factors

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### Introduction

Gallstones are a major public health problem in all developing countries. Many epidemiological studies have been performed with the aim of establishing gallstone prevalence and incidence rates, and of defining risk factors, amenable to prevention. The adage 'fair, fat, fertile, female and forty' is only part of the story. Gallstone formation is multifactorial, both constitutional (unmodifiable) and environmental (modifiable) risk factors competing to lithogenesis.<sup>1</sup>

The aim of this study was to determine the causes and risk factors of gallstone disease (GSD) in patients with symptomatic cholelithiasis admitted to surgical unit of Manipal Teaching Hospital Pokhara Nepal.

In all populations of the world, regardless of overall gallstone prevalence, women are almost twice as likely as men to experience cholelithiasis. Gender is one of the most powerful influences on gallstones, which are more common in females during their fertile years as in males. Majority of persons with gallstone disease had not had a cholecystectomy and were unaware of having gallstones.<sup>1</sup>

The influence of the female sex hormones has been studied in normal females, during pregnancy, and in women using oral contraceptives. The risk of gallstones is greater in younger females.<sup>2</sup>

This risk seems to apply to both the number and age of pregnancies. For example, a woman who has four pregnancies

before the age of 25 has a fourfold to 12-fold increased risk of cholesterol gallstones compared with an age matched, weight matched nulliparous woman.<sup>3</sup>

Pregnancy favours gallstone formation through the hormonal influences on bile composition (increased biliary cholesterol secretion, decreased and unbalanced bile acid pool). Oestrogens induce an increased input to the hepatic free cholesterol pool by up-regulating the low density lipoprotein receptor. Decreased gallbladder motility during the third trimester of pregnancy and an altered function of gallbladder mucosa may favour nucleation and growth of stones. The occurrence of sludge increases steadily during pregnancy (30%–35%), but gallstones develop at a lesser frequency (2%–3%). Biliary sludge and most gallstones will disappear spontaneously within a few weeks after delivery.<sup>4</sup>

All epidemiological studies showed that increasing age was associated with an increased prevalence of gallstones. Gallstones are four to 10 times more frequent in older than younger subjects. Biliary cholesterol saturation increases with age, due to a decline in the activity of cholesterol 7 $\alpha$  hydroxylase, the rate limiting enzyme for bile acid synthesis.<sup>5</sup> In the elderly, bile acid synthesis is reduced, biliary cholesterol output is increased and cholesterol saturation of bile increases, and that is true both in men and women. Deoxycholic acid proportion in bile increases with age through enhanced 7 $\alpha$  dehydroxylation of the primary bile acids by the intestinal bacteria. In addition, increasing age allows the cumulative lithogenic action of more risk factors.<sup>6</sup>

Obesity is an important risk factor for gallstone disease, more so for women than for men. It raises the risk of cholesterol gallstones by increasing biliary secretion of cholesterol, as a result of an increase in HMGCoA reductase activity. Epidemiological studies have found that the lithogenic risk of obesity is strongest in young women and that slimness protects against cholelithiasis.<sup>1</sup>

Although gallbladder function is impaired in the presence of diabetic neuropathy, and regulation of hyperglycaemia with insulin seems to raise the lithogenic index, association of gallstones with diabetes mellitus remains controversial. Relationships are more complex; only some diabetics are at risk<sup>1</sup>

One of the main environmental exposures contributing to gallstone formation is the nutritional exposure. The progressive increase in the prevalence rate of gallstones during this century supports the role of lifestyle and dietary factors in gallstone pathogenesis.<sup>1</sup>

Some experimental studies have suggested the protective effect of alcohol against gallstone formation. Alcohol intake has been shown to reduce bile lithogenicity in humans.<sup>7</sup> The protective effect of alcohol may occur via the liver, by increasing the conversion of cholesterol to bile acids or by altering the enterohepatic circulation of bile acids, including deoxycholic acid. Moderate alcohol consumption also raises plasma HDL cholesterol concentrations.<sup>8</sup>

Data related to smoking as a risk factor for gallstones are inconsistent. Some authors found a linear relationship between amount smoked and gallstone risk, while other studies found no relation between smoking and gallstones. Smoking is associated with low plasma HDL cholesterol concentrations, a risk factor for gallstones. It also depresses prostaglandin synthesis and mucus production in the gallbladder.<sup>9</sup>

In Manipal Teaching Hospital the patients with symptomatic cholelithiasis got admitted and the statistics was reviewed for the past 7 months of 2012-13 around 72 clients had cholecystectomy due to cholelithiasis. Hence to identify the causative and risk factors of gall stone disease which leading to increase hospital admissions .

## Hypothesis

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**H1**-There will be a significant association between selected demographic variables and risk factors of cholelithiasis

## Methods

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A cross-sectional study was conducted from 1st January 2013 – 30th March 2014 in Manipal teaching hospital Pokhara Nepal. During this period total of 132 clients admitted to surgery ward with diagnosis of cholelithiasis and the data was collected from each subject regarding demographic characteristics, habits of smoking and alcohol, dietary habits (vegetarian/non-vegetarian), history of diabetes, oral contraceptives, hypothyroidism parity (nulliparous/parous/multiparous), BMI was measured and, USG reports, laboratory values and type of surgery (open/lap cholecystectomy) was retrieved from case sheets. Data was analyzed by using descriptive statistics ( SPSS 16).

Results

Table 1. Relation between age and incidence of cholelithiasis

| No. | Age group (in Years) | Frequency (M:F)    | Percentage  |
|-----|----------------------|--------------------|-------------|
| 1   | 15-24                | 11(0:11)           | 8.3%        |
| 2   | 25-34                | 19(3:16)           | 14.4%       |
| 3   | 35-44                | 21(6:15)           | 15.9%       |
| 4   | 45-54                | 19(3:16)           | 14.4%       |
| 5   | 55-64                | 29(5:24)           | 22%         |
| 6   | 65-74                | 22(3:19)           | 16.7%       |
| 7   | >75                  | 11(3:8)            | 8.3%        |
|     | <b>Total</b>         | <b>132(23:109)</b> | <b>100%</b> |

Table 1 shows that about 22% of them are age group of 55-64 years and with female gender predominance of 109 patients and 23 male patients with ratio of (M: F= 1:4.7)

Fig 1. Smoking Habit by Gender

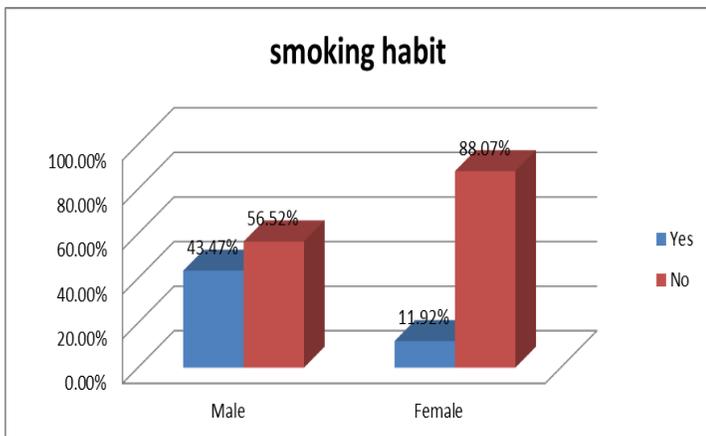


Fig 1 shows that 43.47% Male clients were smokers and 11.92% were females.

Fig 2 Alcohol Consumption by Gender

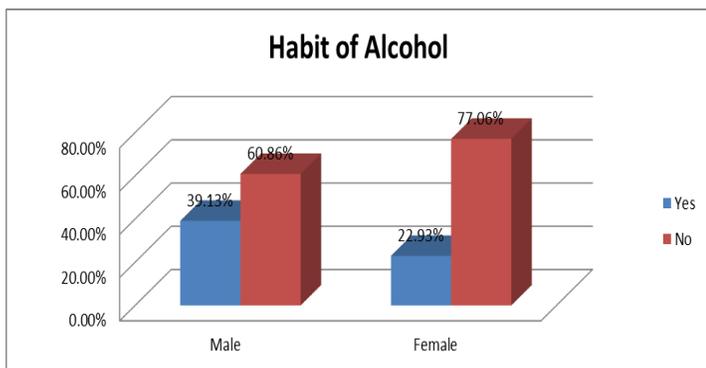


Fig 2 denoted that 39.13% males were alcoholics and 22.93% are female alcoholics.

Fig 3. Type of Diet

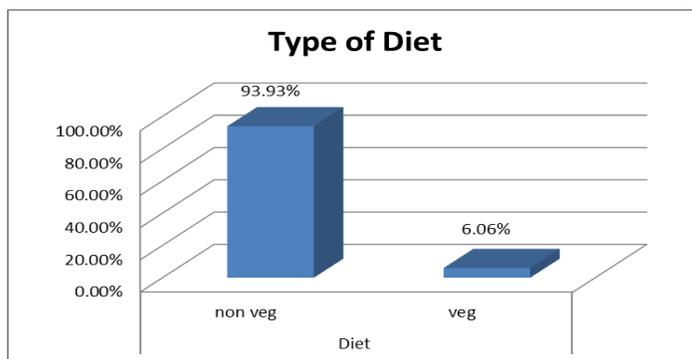


Fig 3 shows that 93.930% clients are no vegetarians and 6.06% are vegetarians.

Fig 4. Parity

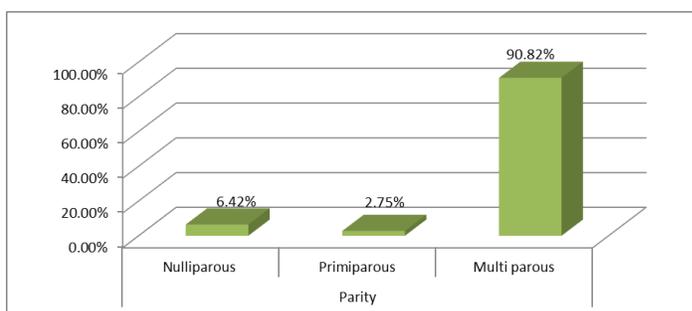


Fig .4 shows that .90.82% women were multiparous and 6.42% were nulliparous.

Fig 5. History of taking oral contraceptives

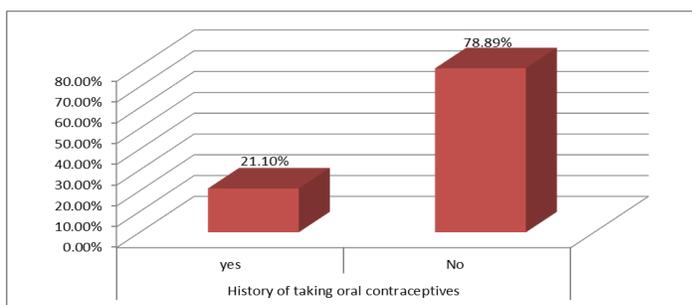


Fig 5 shows that 21.10% were had a history of taking oral contraceptives.

Fig 6. History of Diabetes

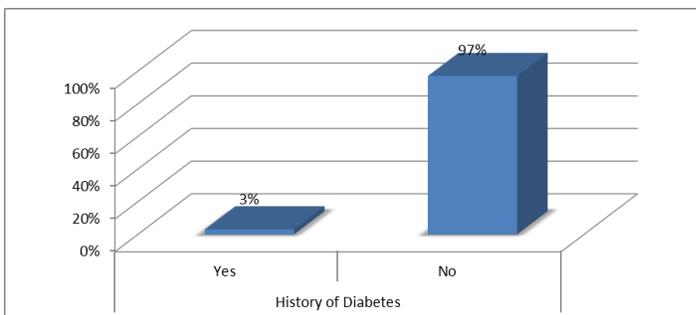


Fig. 6 shows only 3% patients had a history of diabetes mellitus.

Fig 7 History of Hypothyroid

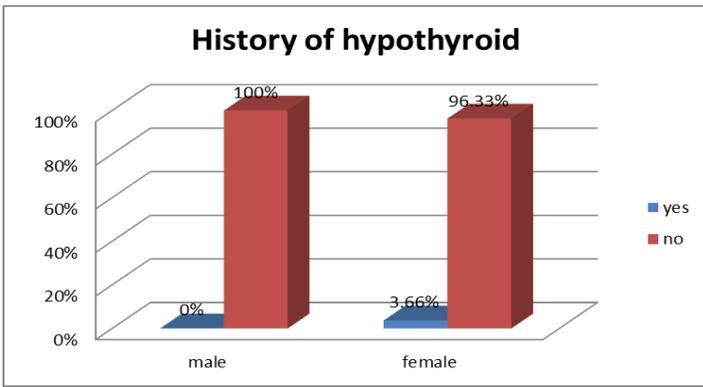


Fig 7 shows only 3.66% were known case of hypothyroid disorder and all were female patients.

Fig 8. Body mass index [BMI]

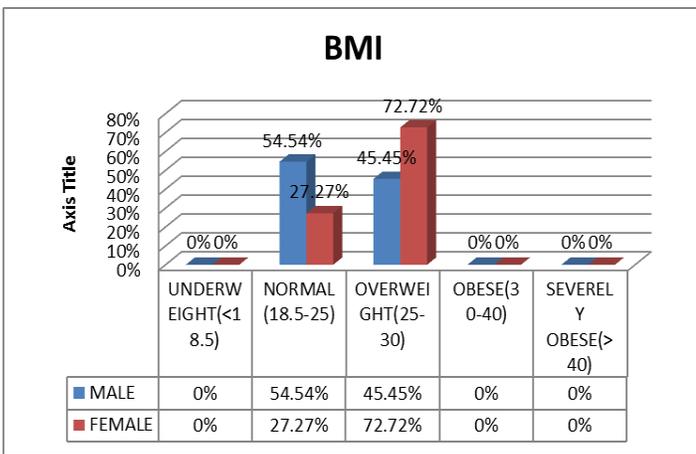


Fig 8 denotes that 72.72% females were pre obese/overweight and 45.45% were males.

Fig 9. Serum values

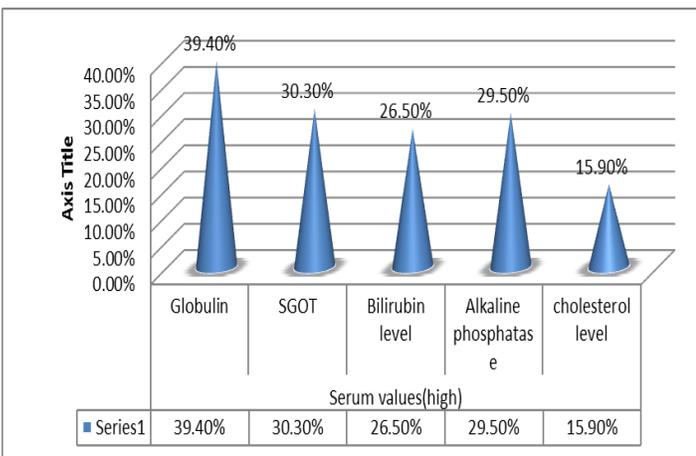


Fig 9 shows that 39.40% patients globulin level was high, 30.30% SGOT, 15.90% cholesterol level, 26.50% bilirubin level was high.

Fig 10. Ultrasonography Results

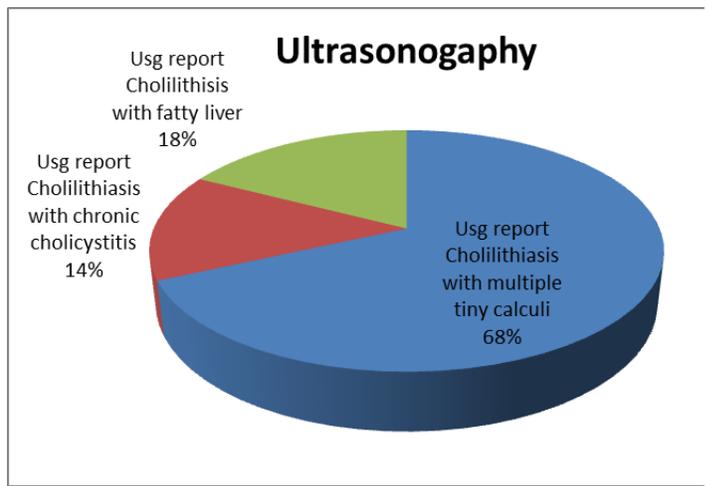


Fig 10. shows that all of them had calculi in gall bladder in that 68% with multiple calculi, 18%with fatty liver, 14%with chronic cholecystitis.

Fig 11. Cholecystectomy

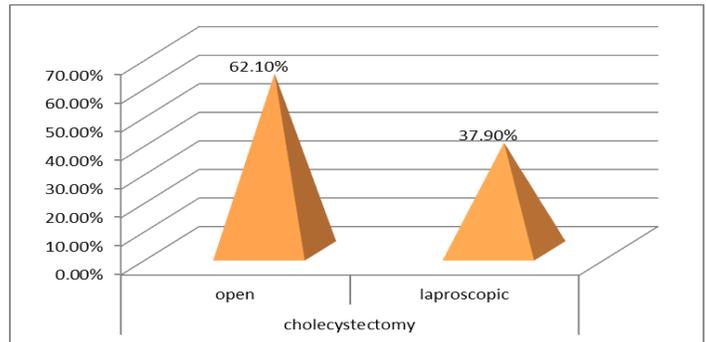


Fig. 11 shows 62.10% of patients undergone open cholecystectomy and 37.90% laproscopic cholecystectomy.

Table 2: Association between demographic characteristics and risk factors of cholilithiasis

| Sl no. | Demographic characteristics    | Chi square value | p value | Significance |
|--------|--------------------------------|------------------|---------|--------------|
| 1      | Gender*smoking                 | 14.416           | 0.00014 | S*           |
| 2      | Gender*hypothyroid             | 0.825            | 0.3637  | NS           |
| 3      | Gender*diet                    | 6.812            | 0.009   | S*           |
| 4      | Gender*diabetes                | 1.384            | 0.239   | NS           |
| 5      | Gender*serum cholesterol level | 1.090            | 0.296   | NS           |
| 6      | Gender*BMI                     | 0.109            | 0.741   | S*           |
| 7      | Gender*alcohol                 | 5.890            | 0.015   | S*           |

Table 2 shows that there was an association between gender and smoking, diet, BMI, alcohol at 0.05 level of significance. So, alternative hypothesis was accepted.

## Discussion

In the present study the females are predominant and age ranges from 55-60 yrs, the findings were similar with the study conducted by Liu CM, Hsu CT et al that the age and gender distributions of both groups were similar, with a mean age of 60 years and a predominance of females.<sup>10</sup>

Non-vegetarians were found to be more commonly involved with cholelithiasis than vegetarians. In my study 97.7% patients are non vegetarian, the findings were similar with the findings of a study done by Maskey et al in 1990 AD in Nepal where incidence of cholelithiasis was found more frequently among the people who consumed more fat and protein. In the similar study done by Katwal MR et al in Sikkim and North Bengal, India, 97% cases of cholelithiasis were found in non-vegetarian.<sup>11</sup>

In the present study the average BMI was 26.26kg/m<sup>2</sup> indicating pre obese and 26.50% patients bilirubin level was high and the findings were similar with the findings of the study conducted by Llatas Pérez J, Hurtado Roca et al that BMI 25.59 kg/m<sup>2</sup> and 55.6% were women. Total bilirubin in the group with choledocholithiasis was 5.8 mg / dl at baseline and 4.2 mg / dl in hospitalization<sup>12</sup>

In the present study the male and female ratio was (M: F= 1:4.7), multiparous women (90.82%) and also women had a history of taking oral contraceptives (birth controlling pills) about 21.10% (23) the findings are similar with the study conducted by Mohammed A. Taher that the ratio of females : males was (7.3:1), this high ratio may be due to multiple factors including high percentage of multiparity (63.64%), the use of contraceptives (46.97%).<sup>13</sup>

## Conclusion

Gallstone disease is predominant in female population and it increases with age, among multiparous women, non vegetarians, overweight/ pre-obese and in those who had a history of taking oral contraceptives and smoking habit. Preventive measures to be undertaken towards risk factors (modifiable) which are competing to lithogenesis.

## Recommendation

The above study can be replicated by conducting the study on prevalence and incidence of cholelithiasis in community settings of Nepal. Preventive strategies can be promoted by identifying the kinds of gallstones which is commonly affects.

## Acknowledgement

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## Ethical clearance

Prior permission was taken from the Research Committee of Manipal Teaching Hospital Pokhara Nepal. Verbal consent was obtained from the study samples.

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