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Association Of Type 2 Diabetes Mellitus in Patients with Cholelithiasis in A Tertiary Care Centre – Chengalpattu District

Dr. Vigneshwar[1], Dr. Susan Hilton, M.D[2]*, Dr. Kulothungan, M.D[3], Dr. Udhayanandhini, M.D[4], Catherin Rexy[5]

[1]Postgraduate, Department of General Medicine, Karpaga Vinayaga Institute of Medical Sciences and Research Institute, Madhurantagam,
Email ID : vigneshwarpandian16@gmail.com
[2]*Assistant Professor, Department of General Medicine, Karpaga Vinayaga Institute of Medical Sciences and Research Institute, Madhurantagam
Email ID: passoverlamb@gmail.com
[3]Professor, Department of General Medicine, Karpaga Vinayaga Institute of Medical Sciences and Research Institute, Madhurantagam,
Email ID: kthungan@hotmail.com
[4]Assistant Professor, Department of General Medicine, Karpaga Vinayaga Institute of Medical Sciences and Research Institute, Madhurantagam,
Email ID: udhayanandhini1994@gmail.com
[5]Statistician, Karpaga Vinayaga Institute of Medical Sciences and Research Institute, Madhurantagam,
Email ID: catherinerexy.stat@gmail.com

***Corresponding author:**

Dr. Susan Hilton, M.D
Assistant Professor, Department of General Medicine, Karpaga Vinayaga Institute of Medical Sciences and Research Institute, Madhurantagam
Email ID: passoverlamb@gmail.com

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ABSTRACT

Objectives: Cholelithiasis is becoming more prevalent in developing countries like India with huge financial burden and it has many risk factors, such as age, sex, dyslipidaemia, diabetes mellitus (DM), and obesity. It is characterized by the formation of gallstones in the hepatic bile duct, common bile duct, or gallbladder. The aim of this study is to assess the prevalence and to establish the association between diabetes and gallstone disease.

Materials & Methods: This retrospective study using descriptive cross-sectional design, enrolled patients with gallstones attending Karpaga Vinayaga Institute of Medical Sciences, a tertiary care hospital in Chengalpattu District. All patients with cholelithiasis from ultrasound abdomen were enrolled in this study

Results: 113 subjects were selected through consecutive sampling, wherein 65.5% were female and 34.5% were male with 77.9% aged more than 40 years. The majority had obesity grade II with mean BMI 26.5 kg/m2 for males and 27.4 kg/m2 for females. Dyslipidaemia was found in 85 subjects with proportion of high total cholesterol was 84.5%, high LDL 90.9%, high triglycerides 73.3%, and low HDL 56.2%. DM was found in 65(57.5%) subjects. Female and age > 40 years had more proportion in cholelithiasis patients namely 77.9 %.

Conclusion:

In this study, we concluded that there is a higher prevalence of T2DM in cholelithiasis patients, and hence there is an association between cholelithiasis and T2DM. This study also reiterated the association between obesity and gallstone disease(GD). Female sex and advancing age also contribute to the formation of cholelithiasis**.** Patients with obesity grade II, high LDL and high PPBS should be considered at risk for cholelithiasis

Keywords: cholelithiasis/gallstone disease (GD), diabetes mellitus, dyslipidaemia, obesity, risk factor

1. INTRODUCTION

Cholelithiasis, or gallstone disease (GD), refers to the presence of stones in the gallbladder or biliary tract, resulting from an imbalance in the composition of bile. It is a globally prevalent condition, with increasing incidence in developing countries.

like India due to rapid lifestyle transitions and dietary changes [4,5]. Gallstones are primarily composed of cholesterol, and their formation is strongly linked to metabolic derangements including obesity, insulin resistance, and dyslipidaemia [5]

Recent studies have emphasized the growing recognition of cholelithiasis as a metabolic disorder, rather than merely a gastrointestinal condition. The underlying pathophysiology involves cholesterol supersaturation of bile, impaired gallbladder motility, and mucin hypersecretion—all of which are strongly influenced by components of metabolic syndrome such as obesity, diabetes mellitus (DM), and abnormal lipid profiles [5,6].

Obesity, particularly visceral or central obesity, is a major contributor to cholesterol gallstone formation. It enhances cholesterol synthesis and hepatic secretion into bile, increasing its lithogenicity [1,5]. Hendarto et al. (2023) demonstrated a significant association between obesity and cholelithiasis, suggesting that nearly half of gallstone patients are either overweight or obese, with a predominance of Grade I obesity[1].

Type 2 diabetes mellitus (T2DM) is another critical risk factor. Insulin resistance in diabetic patients alters hepatic lipid metabolism, leading to excess cholesterol in bile. Additionally, autonomic neuropathy in long-standing diabetes impairs gallbladder contractility, promoting stasis and gallstone formation [1,3,7]. Malik et al. (2019), in a hospital-based Indian study, reported a statistically significant co-occurrence of diabetes and gallstone disease, reinforcing the pathophysiological link [7].

Dyslipidaemia, a hallmark of metabolic syndrome, is also implicated in gallstone pathogenesis. Elevated LDL cholesterol and triglycerides, combined with low HDL levels, increase hepatic cholesterol secretion and impaired bile salt function, promoting cholesterol crystallization [1, 3, 5].

Du et al. (2024) found that the atherogenic index of plasma is positively correlated with gallstone presence, and that this association is mediated through the presence of diabetes mellitus [3].

International data corroborate these findings. In a Sudanese cohort, Almobarak et al. (2020) reported high prevalence rates of both diabetes (22.7%) and metabolic syndrome (29.5%) among gallstone patients, emphasizing the shared risk profile of these disorders in different ethnic groups [2].

The current guidelines from the Japanese Society of Gastroenterology also acknowledge the impact of metabolic factors especially insulin resistance and dyslipidaemia in the aetiology and progression of cholelithiasis [4]. This paradigm shift highlights the need to consider gallstone disease not only as a surgical issue, but also as a metabolic manifestation requiring early screening and intervention.

In view of this, the present study was undertaken to explore the prevalence and association of diabetes mellitus and dyslipidaemia with cholelithiasis among patients attending a tertiary care hospital in southern India. By examining these relationships, we aim to contribute to the understanding of metabolic risk stratification in gallstone disease and support the formulation of preventive healthcare strategies in high-risk populations.

2. MATERIALS & METHODS

Study Design & Participants

This is a retrospective study using descriptive cross-sectional study design. The data of cholelithiasis patients were obtained from abdominal ultrasound examination through medical records in Karpaga Vinayaga Institute of Medical Sciences, Chengalpattu from January 2023 to May 2024.

Sample Size & Measurement Tools

A total of 113 subjects were selected using consecutive sampling method. The inclusion criteria encompassed inpatients and outpatient aged 18 to 80 years old, diagnosed with abdominal ultrasound proven gallstones and patients who are diagnosed to have dyslipidaemia, obesity, type 2 Diabetes mellitus, and prediabetes. The descriptive and statistically analysis was performed using Microsoft Excel 2016 and SPSS 22.0.

3. RESULTS

A total of 113 patients diagnosed with cholelithiasis by abdominal ultrasound at Karpaga Vinayaga Institute of Medical Sciences were enrolled in this retrospective, cross-sectional study. The demographic and clinical characteristics of the study population are summarized below.

Demographic Profile

Most of gallstone subjects were female and age more than 40 years old, accounted for 79.9%. subjects. The most prevalent was age was 46-55 years which shows 29.3% and similar results in 36-45 years which shows 28.3% as shown in Table 1.

Table 1. Age and Sex Distribution

Parameter	Classification	Frequency (n)	Proportion (%)
Sex	Male	39	34.5%
	Female	74	65.5%
Age	18–25 years	3	3.0%
	26–35 years	19	19.2%
	36–45 years	28	28.3%
	46–55 years	29	29.3%
	56–65 years	20	20.2%
	>65 years	14	12.3%

Table 1. Age and Sex Distribution among Cholelithiasis Patients (n = 113)

Sex Distribution: 65.5% Female, 34.5% Male

Age Distribution: 77.9% patients are over 40 years old

BMI Classification (Asian):

Underweight: <18.5

Normal: 18.5–22.9

Overweight: 23–24.9

Obese I: 25–29.9

Obese II: ≥30

Table 2: Nutritional Status (BMI Classification)

Classification	Frequency (n)	Proportion (%)
Normal Weight	19	16.8%
Overweight	24	21.2%
Obesity Grade 1	27	23.9%
Obesity Grade 2	43	38.1%

Figure 2. BMI Classification Distribution

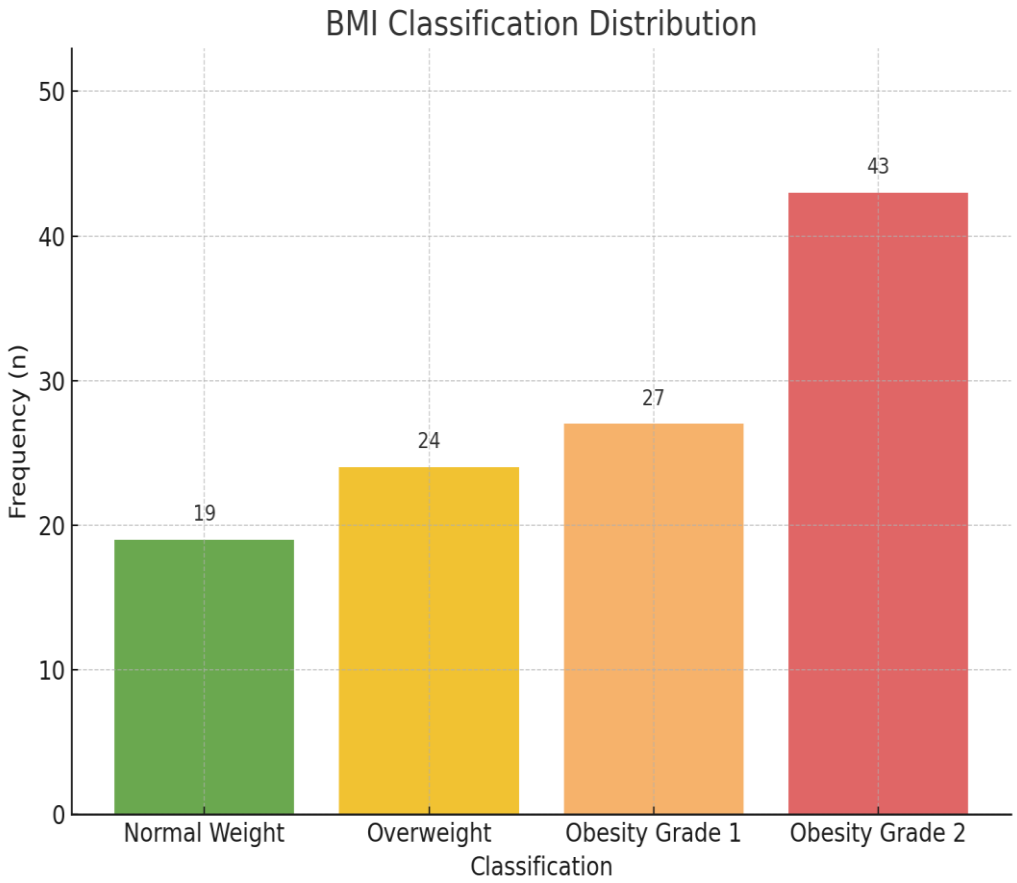


Table 3. Cross tabulation of BMI Classification by Gender

BMI Classification	Gender	
	Male (n=39)	Female (n=74)
Normal Weight	6 (15.4)	13 (17.6)
Overweight	9 (23.1)	15 (20.3)
Obesity Grade I	9 (23.1)	18 (24.3)
Obesity Grade II	15 (38.4)	28 (37.8)
Mean BMI (kg/m²)	~26.5	~27.4

Overweight also played a role as a risk factor for cholelithiasis, accounting 23.1% for males and 20.3% for females. Table 3 showed 15.4% of men were normal weight, while 23.1% were classified as obesity grades I and 38.4% were classified as obesity grade II. Proportion of normal weight in female was 17.6% and overweight was 20.3%, while obesity grade I was found at 24.3% and obesity grade II was 37.8%. The mean BMI for male and female are 26.5 kg/m² and 27.4 kg/m² respectively

Diabetes Mellitus (DM)

DM diagnosed in: 65 out of 113 patients (57.5%)

Table 4. The association between gender and elevated blood glucose types

Blood Glucose Type	Gender		P* Value
	Male	Female	
High Random Blood Glucose	5	8	0.000*
High Fasting Blood Glucose	6	10	
High Post-Prandial Glucose	12	20	

***Chi square at 5% level of significance, P < 0.05 is considered significant**

Among participants with high random blood glucose, 5 were male and 8 were female. In the case of high fasting blood glucose, 6 males and 10 females were affected. Similarly, 12 males and 20 females showed elevated post-prandial glucose levels. These findings indicate a higher prevalence of abnormal blood glucose levels among females compared to males in all categories, with the association being statistically significant ($P < 0.05$).

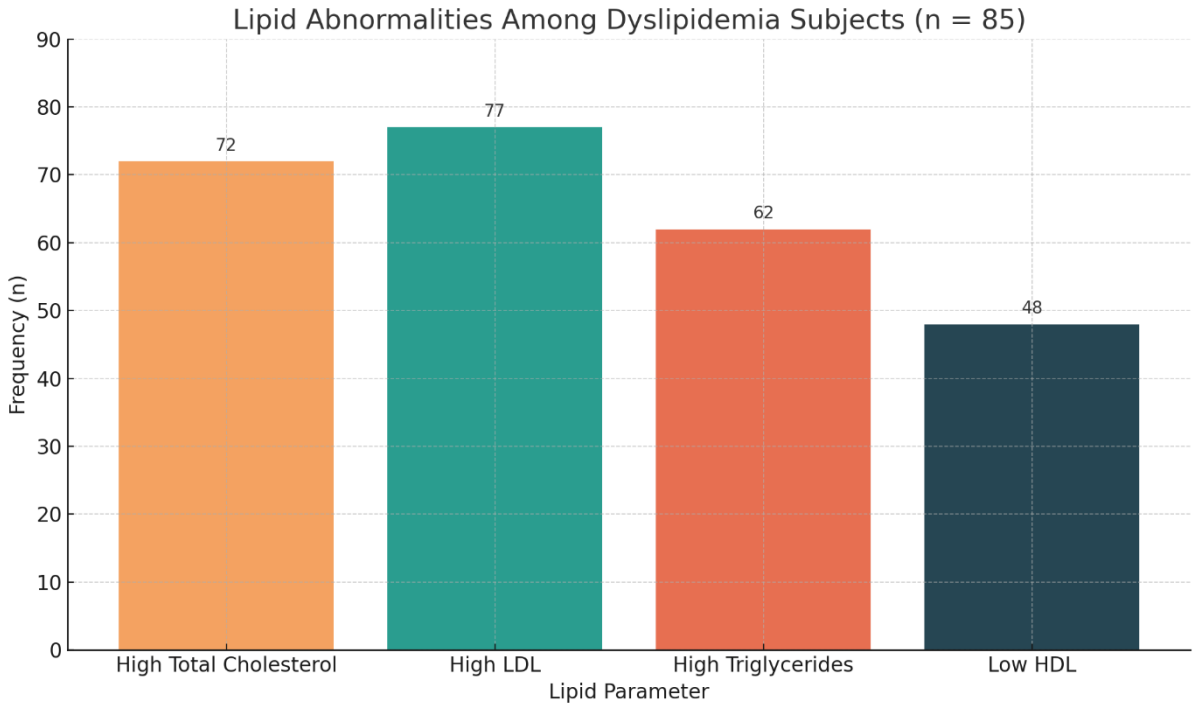
Table 5. Dyslipidemia Profile

Lipid Profile	Laboratory Values
Total Cholesterol	> 200 mg/dL
Low-Density Lipoprotein (LDL)	> 100 mg/dL
Triglycerides	> 150 mg/dL
High-Density Lipoprotein (HDL)	< 40 mg/dL

Table 6. Lipid Abnormalities Among Subjects with Dyslipidemia (n = 85)

Lipid Parameter	Frequency (n)	Proportion (%)
High Total Cholesterol	72	84.5%
High LDL	77	90.9%
High Triglycerides	62	73.3%
Low HDL	48	56.2%

Figure 3. Distribution of Subjects with respect to Lipid abnormalities and Dyslipidemia



Risk Factor of Dyslipidaemia in Cholelithiasis

Among the 113 subjects, 85(75.2%) subjects exhibited dyslipidaemia, a condition characterized by multiple abnormalities in lipid function tests. These abnormalities include high LDL cholesterol, total cholesterol, serum triglycerides, or low HDL cholesterol.

In this study high LDL cholesterol was the most prevalent lipid profile accounting 90.9% subjects. High total cholesterol also had high prevalence in 84.5% subjects with Mean: 76.2%, Standard Deviation: 13.2%

Table. 6 The association between various lipid profile parameters and diabetes status

Outcome Parameter	**Diabetes**		**P* Value**
	Yes (n = 44) %	**No (n = 69) %**	
Total Cholesterol			
Normal	28 (63.6)	61 (88.4)	**0.002***
High	16 (36.4)	8 (11.6)	
Triglycerides Level			
Normal	20 (45.0)	58 (84.1)	**0.000***
High	24 (54.5)	11 (15.9)	
High Density Lipoproteins			
Abnormal	16 (36.4)	2 (2.9)	**0.000***
Normal	28 (63.6)	67 (97.1)	
Low-Density Lipoprotein			
Abnormal	16 (36.4)	40 (58.0)	**0.025***

Normal	28 (63.6)	29 (42.0)	

***Chi square at 5% level of significance, P < 0.05 is considered significant**

Using the Chi-square test, as presented in Table 6. A significant association was observed between total cholesterol levels and diabetes ($p = 0.002$). Among participants with diabetes, 36.4% had elevated total cholesterol, compared to only 11.6% in the non-diabetic group. Triglyceride levels were also significantly associated with diabetes status ($p < 0.001$). Over half of the diabetic participants (54.5%) had elevated triglycerides, in contrast to only 15.9% among non-diabetics.

A highly significant association was found between High-Density Lipoproteins (HDL) and diabetes ($p < 0.001$). 36.4% of diabetics had abnormal (low) HDL levels, whereas this was observed in only 2.9% of non-diabetics. Similarly, Low-Density Lipoprotein (LDL) levels showed a significant association with diabetes ($p = 0.025$). Among diabetics, 36.4% had abnormal LDL, compared to 58% in the non-diabetic group, indicating a complex pattern of LDL distribution. These findings suggest that dyslipidemia—particularly elevated triglycerides and reduced HDL—is more prevalent among diabetic individuals, emphasizing the need for comprehensive lipid monitoring in this population

4. DISCUSSION:

The association between diabetes mellitus and cholelithiasis has been increasingly recognized in both clinical and epidemiological studies. In this study, a significant proportion of patients diagnosed with gallstone disease were also found to have diabetes mellitus, highlighting a possible interplay between metabolic dysfunction and gallbladder pathology. This relationship is biologically plausible and clinically relevant, considering the shared risk factors and overlapping mechanisms involved in both conditions.

Diabetes mellitus, particularly type 2, is associated with various metabolic derangements that contribute to gallstone formation. One of the key mechanisms is altered lipid metabolism, where insulin resistance leads to increased hepatic cholesterol output. This excess cholesterol is secreted into bile, resulting in supersaturation, a critical step in cholesterol stone formation.

Additionally, hyperinsulinemia, commonly seen in early type 2 diabetes, promotes hepatic lipogenesis and further increases biliary cholesterol concentration.

Another important factor in diabetic patients is gallbladder dysmotility. Diabetic autonomic neuropathy can impair the neuromuscular function of the gallbladder, leading to incomplete emptying and bile stasis. This stagnant bile creates a favourable environment for cholesterol crystals to nucleate and aggregate into stones. The reduced contractility of the gallbladder also contributes to the development of sludge and, eventually, gallstones.

In our patient cohort, many diabetic individuals presented with multiple gallstones, which is consistent with prior findings that diabetes is linked with more advanced gallstone disease. Additionally, most diabetic patients were either overweight or obese, both of which are independent risk factors for cholelithiasis. Obesity not only contributes to insulin resistance but also increases cholesterol turnover, resulting in cholesterol-rich bile. This overlap of metabolic risk factors suggests that the combination of diabetes and obesity significantly elevates the risk for gallstone formation.

Gender and age also appear to influence the association. In our study, middle-aged women represented a large proportion of diabetic cholelithiasis patients. Estrogen increases cholesterol secretion into bile, and when combined with diabetes-related bile stasis, the risk for gallstones rises further. Hormonal factors, therefore, may exacerbate the metabolic and motility-related changes seen in diabetic individuals.

Clinically, diabetic patients often present with atypical or silent gallbladder disease. Due to neuropathy, visceral pain perception may be reduced, delaying diagnosis and increasing the risk of complications such as acute cholecystitis or gallbladder empyema. This emphasizes the importance of proactive screening and management in diabetic patients, even in the absence of classical symptoms. Oestrogen plays a significant role in the development of cholesterol gallstones, particularly in women of reproductive age, those taking hormone replacement therapy, or during pregnancy. Its influence on gallstone formation involves multiple mechanisms that affect both bile composition and gallbladder function.

One of the primary actions of oestrogen is to increase cholesterol secretion by the liver into bile. Oestrogen stimulates the expression of hepatic enzymes involved in cholesterol biosynthesis, particularly HMG-CoA reductase, the rate-limiting enzyme in the cholesterol synthesis pathway. This results in an elevated cholesterol concentration in bile, often exceeding the solubilizing capacity of bile salts and phospholipids. When bile becomes supersaturated with cholesterol, the risk of crystal formation and gallstone development increases significantly.

In addition to altering bile composition, oestrogen reduces the hepatic secretion of bile acids. Bile acids are crucial for maintaining cholesterol in a dissolved state within bile. A reduction in bile acid concentration leads to decreased solubility of cholesterol, further contributing to bile supersaturation and stone formation. This imbalance between cholesterol and bile acids creates the perfect biochemical environment for cholesterol precipitation.

Estrogen also affects gallbladder motility. It has been observed to impair gallbladder emptying by reducing the sensitivity of gallbladder smooth muscle to cholecystokinin (CCK), the hormone responsible for stimulating gallbladder contraction after meals. As a result, bile remains in the gallbladder longer than normal, leading to bile stasis. Stagnant bile allows cholesterol crystals more time to grow and aggregate, ultimately forming gallstones.

The combination of cholesterol supersaturation, reduced bile acid concentration, and impaired gallbladder motility explains why oestrogen is a key factor in gallstone pathogenesis. These effects are particularly evident in physiological or pharmacological states of elevated oestrogen, such as pregnancy, oral contraceptive use, and hormone therapy during menopause.

In conclusion, oestrogen contributes to gallstone formation through its impact on hepatic cholesterol metabolism, bile acid secretion, and gallbladder motility. Understanding these mechanisms is essential for identifying high-risk populations and implementing preventive strategies in women exposed to elevated oestrogen levels.

This study showed most prevalent age who had cholelithiasis were above 40 years old, accounting 77.9%. The age distribution was similar with a study conducted in Sri Lanka that the mean of age 46.10±11.60 years [6]. This results also similar with a study in Korea, whereas the mean age cholelithiasis patients was 47.30±10.90 years [16]. Study in India stated prevalence of gallstone increased with increasing age with peak in the sixth decade (23.4% in cases and 4.4% in controls (p=0.001) [11].

Our study showed obesity grade I was found in 23.1% male subjects, obesity grade II found in 38.4% male subjects, while obesity grade I was found at 24.3% in female and obesity grade II was about 37.8% in female population. The mean BMI for male and female were similar, accounting 26.5kg/m² for men and 27.4kg/m² for female. This study was compared to a study conducted in China that participants with gallstones had a higher prevalence of metabolic syndromes (gallstones: 46.3% vs. no gallstones: 30.7%) and higher BMI (gallstones: 24.70 kg/m2 vs. no gallstones: 23.70 kg/m2) [17].

Obesity is known to increase the secretion of intra-hepatic cholesterol, which contributes to formation of gallstone. Also, body fat distribution was observed to play a role in gallstone formation [18]. Visceral fat release vasoactive substances directly into the portal venous system, triggering a pro-inflammatory response through macrophage activation and the release of inflammatory cytokines such as TNF-α and IL-6. These cytokines inhibit the expression of adiponectin, an adipocyte-derived hormone that enhances insulin sensitivity and fatty acid oxidation, thereby exerting anti-diabetic and anti-atherogenic effects. Consequently, this process leads to insulin resistance and manifestation of metabolic syndrome.

The proportion obesity or central obesity have become serious health problems in developing countries such as Indonesia. A study was conducted in Indonesia for ten years survey from the largest national health survey using total sampling method from 33 provinces showed the prevalence of obesity and central obesity in the Indonesian adult population are 23.1% and 28.0%, with BMI cutoff value of ≥25.00 kg/m2. Moreover, based on the World Health Organization data, the prevalence of obesity in Indonesia was the highest in Southeast Asia with more than 30.0% of adult population. Both rates are higher in females than in males. Obesity and central obesity also associated with the risk of diabetes and hypertension. Obesity rates in Indonesia are increasing rapidly in both rich and poor households as they shifted from traditional diets towards processed products, which is unhealthy food with high fat and sugar, and less expensive than wholesome foods.

The other factor was sedentary lifestyle due to modernization and advanced technology leading to reduced physical activity. Economic growth in Indonesia also influenced the rates of obesity [19, 20].

Understanding the risk factors for gallstone is useful in assisting physicians to provide resources and education for patients who are diagnosed with gallstones, and also develop novel preventive measures for the disease.

This study revealed that 19.3% of gallstone patients had dyslipidaemia, indicating a correlation between dyslipidaemia and risk factors for gallstone formation. Furthermore, a significant elevation in LDL cholesterol levels (90.9%) was observed in gallstone patients with dyslipidaemia. This finding aligns with study conducted by Atamanalp SS, et al., which identified high LDL cholesterol as a marker for an increased risk of cholesterol gallstone disease. An elevation in LDL levels in the blood serum leads to increased cholesterol accumulation in the liver, thereby increasing risk of cholesterol stone formation in the gallbladder or ducts. A study conducted in Iran, reported a higher prevalence of elevated LDL in cholelithiasis subject compared to other lipid functions [7]. This study showed 48 subjects (56.2) with low HDL. Another study by Kim showed that those with low HDL had a significantly high risk for cholelithiasis [23]. However, some studies found no significant association between HDL cholesterol and cholelithiasis [24].

This study also reported that 57.5% of cholelithiasis patients had DM. The elevated blood glucose levels in DM can inhibit gluconeogenesis including lipogenesis. Consequently, accumulation of fat would be converted into glucose for energy, will increase cholesterol synthesis, resulting in deposition of cholesterol in the gallbladder. Besides that, bile of diabetic patients is more lithogenic since the supersaturation of cholesterol in bile is higher and the concentration of bile acids is lower that leads to the formation of gallstones [16]. DM can impact gallbladder neuropathy, affecting both autonomic and peripheral functions. This can manifest through an imbalance in cholecystokinin (CCK) release and reduced responsiveness of gallbladder muscles to CCK stimulation. These mechanisms can impair gallstone contraction, ultimately contributing

increased risk of gallstone formation. Different result was found in the study in Pakistan that showed 36.6% gallstone subjects have DM [25]. The difference between this study can be caused by genetic variability.

5. CONCLUSION

As a conclusion, significant proportion of gallstone patients were female (65.5%), while the age range of 46-55 years old constituted the highest percentage (29.3%), and 77.9% of patients were above 40 years with cholelithiasis in this study. Proportion of gallstone with obesity are 62%, dyslipidemia 75.2% and diabetes 57.5%. Obesity grade II with mean BMI 26.5 kg/m2 for males and 27.4 kg/m2 for females was most prevalent in this study.

However, the proportion of obesity, dyslipidemia and diabetes was lower than other studies in Asia or developing countries. Patients with high LDL cholesterol, high total cholesterol, obesity grade II, and high PPBS have to be aware of the risk of developing cholelithiasis.

Further studies in India with larger sample size in multiple centres should be done to identify more risk factors of cholelithiasis. In this study, we concluded that there is a higher prevalence of T2DM in cholelithiasis patients and there is an association between cholelithiasis and T2DM.Female sex and advancing age also contribute to the formation of cholelithiasis.

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